SULFONAMIDES AS TRPM8 MODULATORS

FIELD OF THE INVENTION

The present invention relates to sulfonamides that act as modulators of the TRPM8 receptor. The present invention also relates to processes for the preparation of sulfonamides and to their use in treating various diseases, syndromes, and disorders, including, those that cause inflammatory or neuropathic pain, cold intolerance or cold allodynia, peripheral vascular pain, itch, urinary incontinence, chronic obstructive pulmonary disease (COPD), pulmonary hypertension and anxiety, including other stress-related disorders, and combinations thereof.

BACKGROUND OF THE INVENTION

Transient receptor potential (TRP) channels are non-selective cation channels that are activated by a variety of stimuli. Numerous members of the ion channel family have been identified to date, including the cold-menthol receptor, also called TRPM8 (McKemy D.D., et al., *Nature* 2002, 416(6876), 52-58). Collectively, the TRP channels and related TRP-like receptors connote sensory responsivity to the entire continuum of thermal exposure, selectively responding to threshold temperatures ranging from noxious hot through noxious cold as well as to certain chemicals that mimic these sensations. Specifically, TRPM8 is known to be stimulated by cool to cold temperatures as well as by chemical agents such as menthol and icilin, which may be responsible for the therapeutic cooling sensation that these agents provoke.

TRPM8 is located on primary nociceptive neurons (A-delta and C-fibers) and is also modulated by inflammation-mediated second messenger signals (Abe, J., *et al.*, *Neurosci Lett* 2006, 397(1-2), 140-144; Premkumar, L.S., *et al.*, *J. Neurosci*, 2005, 25(49), 11322-11329). The localization of TRPM8 on both A-delta and C-fibers may provide a basis for abnormal cold sensitivity in pathologic conditions wherein these neurons are altered, resulting in pain, often of a burning nature (Kobayashi, K., *et al.*, *J Comp Neurol*, 2005, 493(4), 596-606; Roza, C., *et al.*, *Pain*, 2006, 120(1-2), 24-35; and Xing, H., *et al.*, *J Neurophysiol*, 2006, 95(2), 1221-30). Cold intolerance and paradoxical burning sensations induced by chemical or thermal cooling closely parallel symptoms seen in a wide range of clinical disorders and thus provide a strong rationale

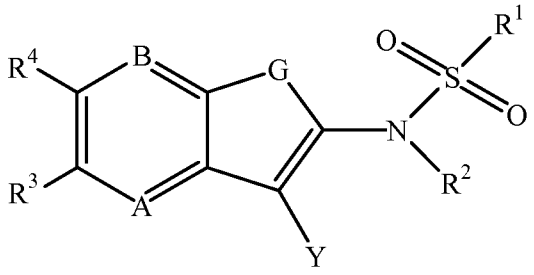
for the development of TRPM8 modulators as novel antihyperalgesic or antiallodynic agents. TRPM8 is also known to be expressed in the brain, lung, bladder, gastrointestinal tract, blood vessels, prostate and immune cells, thereby providing the possibility for therapeutic modulation in a wide range of maladies.

International patent application WO 2006/040136 A1from Bayer Healthcare AG purportedly describes substituted 4-benzyloxy-phenylmethylamide derivatives as cold menthol receptor-1 (CMR-1) antagonists for the treatment of urological disorders. International patent application WO 2006/040103 A1 from Bayer Healthcare AG purportedly describes methods and pharmaceutical compositions for treatment and/or prophylaxis of respiratory diseases or disorders. International patent applications WO 2007/017092A1, WO 2007/017093A1 and WO 2007/017094A1, from Bayer Healthcare AG, purportedly describe benzyloxyphenylmethyl carbamate, substituted 2-benzyloxybenzoic acid amide and substituted 4-benzyloxybenzoic acid amide derivatives for the treatment of diseases associated with the cold menthol receptor (CMR), a.k.a. TRPM8.

There is a need in the art for TRPM8 antagonists that can be used to treat a disease, syndrome, or condition in a mammal in which the disease, syndrome, or condition is affected by the modulation of TRPM8 receptors, such as pain, the diseases that lead to such pain, and pulmonary or vascular dysfunction.

SUMMARY OF THE INVENTION

The present invention provides, *inter alia*, compounds of Formula (I)



(I)

wherein

A is CR^5 or N;

B is CR^6 or N; with the proviso that A and B are $C(R^5)$ and $C(R^6)$, respectively, when G is $S(O)_2$;

G is S or $S(O_2)$;

Y is

(i) H;

(ii) isopropenyl;

(iii) C_{1-6} alkylcarbonyl optionally substituted with 1 chloro or 1 to 3 fluoro substituents;

(iv) C_{3-6} cycloalkylcarbonyl;

(v) phenylcarbonyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, fluoro, or chloro;

(vi) phenylcarbonyl substituted with trifluoromethyl and optionally one additional substituent selected from trifluoromethyl, chloro, fluoro, or C_{1-4} alkyl;

(vii) heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkyl, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

(viii) benzo-fused heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

(ix) bromo;

(x) chloro;

(xi) fluoro;

(xii) iodo;

(xiii) cyano;

(xiv) formyl;

(xv) C_{1-6} alkyl optionally substituted with 1 to 3 substituents independently selected from hydroxy, fluoro, or chloro;

(xvi) $C(OH)(C_{1-3}$ alkyl$)_2$;

(xvii) C_{3-6} cycloalkyl;

(xviii) C_{1-2} alkyl substituted with 1 substituent independently selected from C_{1-4} alkoxycarbonyl, cyano, C_{1-3} alkylthio, C_{1-4} alkoxy, or NR^7R^8 wherein R^7 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^8 is hydrogen or C_{1-4} alkyl; or R^7 and R^8 are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur;

(xix) C_{1-4} alkoxycarbonyl;

(xx) C_{1-3} alkoxy;

(xxi) hydroxy;

(xxii) C_{6-10} aryl optionally substituted with one to three substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkoxy, hydroxy, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, or C_{1-6} alkyl optionally substituted with one to three halogen substituents; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, and C_{1-6} alkyl substituted with one to three halogen substituents;

(xxiii) NR^9R^{10} wherein R^9 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^{10} is hydrogen or C_{1-4} alkyl, or R^9 and R^{10} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said 5 or 6 membered ring is optionally substituted with a C_{1-4} alkyl substituent; with the proviso that when G is S and R^{10} is hydrogen, R^9 is other than hydrogen and C_{1-4} alkyl;

(xxiv) aminocarbonyl;

(xxv) methylaminocarbonyl;

(xxvi) dimethylaminocarbonyl; or

(xxvii) arylhydroxy(C_{1-3})alkyl;

R^1 is

(i) CF_3;

(ii) C_{1-6} alkyl optionally substituted with 1 substituent selected from C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, formyl, hydroxy, carboxy, trifluoromethyl, C_{1-4} alkoxy, C_{1-3} alkylthio, bromo, cyano, R^{11}, or R^{12};

(iii) aryl(C_{1-2} alkyl) wherein the ring of the aryl group is optionally substituted with 1 to 3 substituents independently selected from C_{1-4} alkyl, fluoro, chloro, trifluoromethyl, hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, or carboxy; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxycarbonyl, and carboxy;

(iv) heteroaryl(C_{1-6} alkyl) wherein the heteroaryl group is bound through a nitrogen heteroatom and is selected from imidazolyl, triazolyl, or tetrazolyl; and wherein the imidazolyl group is optionally substituted with 1 substituent selected from C_{1-4} alkyl, fluoro, chloro, trifluoromethyl, hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, carboxy, aminomethyl, methylamino-methyl, or dimethylamino-methyl; and imidazolyl is optionally substituted with one additional substituent selected from C_{1-4} alkyl, fluoro, or chloro;

(v) C_{3-8} cycloalkyl or cyclohexyl substituted at the 4-position with one substitutent selected from the group consisting of cyano, C_{1-4} alkoxycarbonyl, carboxy, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3} alkyl)aminocarbonyl, amino-methyl, methylamino-methyl, dimethylamino-methyl, R^{11}, and R^{12};

(vi) benzo-fused C_{5-6}cycloalkyl attached at the benzo portion of the ring system, and wherein the C_{5-6}cycloalkyl portion of benzo-fused C_{5-6}cycloalkyl is optionally substituted with amino, (C_{1-3}alkyl)amino, or di(C_{1-3}alkyl)amino;

(vii) phenyl substituted with 3- or 4-imidazolyl, wherein the point of attachment of the imidazolyl is through a nitrogen heteroatom; and wherein the imidazolyl is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, 2-cyano, chloro, bromo, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl; wherein di(C_{1-3} alkyl) is optionally taken together with the nitrogen atom to which it is attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein the ring formed by di(C_{1-3} alkyl)amino is optionally substituted with C_{1-3}alkyl; with the proviso that not more than one of the substituents is amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, or di(C_{1-2} alkyl)amino-C_{1-2} alkyl;

(viii) phenyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl optionally substituted with one to three chloro or fluoro substituents or one hydroxy substituent, chloro, fluoro, bromo, C_{1-4} alkoxy, trifluoromethoxy, 3- or 4- phenyloxy, 3- or 4- heteroaryloxy wherein the heteroaryl ring is a 6 membered ring containing carbon ring members and 1 or 2 nitrogen heteroatom ring members, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, hydroxy, carboxy, cyano, nitro, 3- or 4- heteroaryl wherein said heteroaryl is other than imidazolyl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonylaminocarbonyl, di(C_{1-3})alkylaminosulfonyl, P(O)(OC_{1-3} alkyl)$_2$, P(O)$(OH)_2$, SO_3H, C(O)NHOH, C(=N)NH_2, C(=NOH)NH_2, C(=N(methylcarbonyloxy))NH_2, or SO_2NH_2; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethoxy, 3- or 4- substituted phenyloxy, 3- or 4- heteroaryloxy, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, carboxy, cyano, 3- or 4- heteroaryl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3}

alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonylaminocarbonyl, di(C_{1-3})alkylaminosulfonyl, and $P(O)(OC_{1-3}$ alkyl$)_2$ and not more than one of the substituents is selected from the group consisting of – $P(O)(OH)_2$, -SO_3H, carboxy, C(O)NHOH, $C(=N)NH_2$, $C(=NOH)NH_2$, $C(=N(C_{1-3}$alkylcarbonyloxy))NH_2, and -SO_2NH_2; wherein the phenyloxy is optionally substituted with one to two substituents independently selected from the group consisting of methyl and fluoro;

and wherein the heteroaryl substituent is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, trifluoromethyl, trifluoromethoxy, cyano, amino, methylamino, dimethylamino, chloro, bromo, carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl; with the proviso that not more than one of the substituents is selected from the group consisting of carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl;

(ix) naphthyl optionally substituted with one substituent selected from the group consisting of hydroxy, chloro, fluoro, bromo, C_{1-4} alkoxycarbonyl, and carboxy;

(x) C_{6-10} aryl substituted with phenyl optionally substituted with one to two substituents selected from chloro, fluoro, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, carboxy, hydroxy, or C_{1-3} alkyl; (xi)

phenyl substituted with R^{11} or R^{12} at the 3 or 4 position; and optionally one additional substituent selected from fluoro, chloro, or C_{1-3} alkyl;

(xii) pyridin-3-yl substituted at a carbon atom other than that adjacent to the carbon bearing $S(O)_2$ with a substituent selected from *N*-imidazolyl, oxadiazolyl, thiazolyl, R^{11}, or R^{12}; wherein pyridin-3-yl is optionally substituted with one additional substituent

selected from fluoro, chloro, or C_{1-3} alkyl; and further, wherein the *N*-imidazolyl group is optionally substituted with one to two substituents, and the oxadiazolyl and thiazolyl groups are optionally substituted one substituent, said substituent(s) independently selected from the group consisting of C_{1-4} alkyl, trifluoromethyl, cyano, amino, methylamino, dimethylamino, chloro, bromo, carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl; with the proviso that not more than one of the substituents is selected from the group consisting of carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, trifluoromethyl, cyano, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl;

(xiii) imidazolyl substituted with R^{11} or R^{12}; and imidazolyl is optionally substituted at a nitrogen heteroatom with C_{1-4} alkyl;

(xiv) a ring selected from phenyl or pyridin-3-yl, wherein said ring is substituted with $NR^{15}R^{16}$; wherein R^{15} is hydrogen, C_{1-4} alkyl, C_{1-4} alkylcarbonyl, trifluoromethylcarbonyl, trifluoromethylsulfonyl, C_{3-6} cycloalkylsulfonyl, or C_{1-3} alkylsulfonyl; and R^{16} is hydrogen or C_{1-4} alkyl; or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur optionally substituted with one or two oxo substituents; and wherein the ring formed by $NR^{15}R^{16}$ is optionally substituted with C_{1-3}alkyl, C_{1-2} alkoxycarbonyl, or carboxy; and wherein said phenyl is optionally substituted with one to two additional substituents independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, fluoro, chloro, and bromo;

(xv) phenyl substituted with $C(O)NR^{17}R^{18}$ wherein R^{17} is hydrogen, C_{1-4} alkyl, C_{1-4} alkylcarbonyl, pyrrolidin-3-yl, or C_{1-3} alkylsulfonyl; and R^{18} is hydrogen or C_{1-4} alkyl; or R^{17} and R^{18}

are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said ring is optionally substituted with C_{1-3}alkyl;

(xvi) phenyl substituted with 4 or 5 fluoro substituents;

(xvii) phenyl substituted at the 4-position with –Q-$C(R^xR^y)$-$(CH_2)_{0-1}CO_2H$ wherein Q is a bond or O; and wherein R^x and R^y are independently hydrogen or methyl; or R^x and R^y are taken together with the carbon atom to which they are both attached to form a cyclopropyl ring;

(xviii) heteroaryl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, morpholin-4-yl, or heteroaryl; wherein the heteroaryl group is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, trifluoromethyl, fluoro, and chloro; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, and di(C_{1-3})alkylamino;

(xix) benzo-fused heteroaryl optionally substituted at a carbon atom with one to three substituents independently selected from C_{1-4} alkyl, chloro, fluoro, bromo, difluoromethyl, trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, and di(C_{1-3})alkylamino; and

benzo-fused heteroaryl is optionally substituted at a nitrogen atom with C_{1-3} alkyl;

(xx) benzo-fused heterocycle optionally substituted with one to two substituents independently selected from trifluoromethyl, C_{1-3} alkylcarbonyl, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethylcarbonyl, fluoro, chloro, bromo, hydroxy, oxo, carboxy, or C_{1-4} alkoxycarbonyl; such that when the benzo-fused heterocycle is substituted on the heterocyclic ring, the substituents on the heterocyclic ring are selected from oxo, hydroxy, C_{1-4} alkyl, or trifluoromethylcarbonyl; with the proviso that not more than one substituent is trifluoromethylcarbonyl; and with the proviso that when the benzo-fused heterocycle is substituted with trifluoromethylcarbonyl, at least one of the ring members of the heterocycle is a nitrogen heteroatom and the point of attachment to the trifluoromethylcarbonyl substituent is through the nitrogen heteroatom;

(xxi) amino;

(xxii) C_{1-6} alkylamino; or

(xxiii) di(C_{1-6} alkyl)amino;

R^2 is

(i) C_{3-6} cycloalkyl;

(ii) C_{1-2} alkyl substituted with adamantyl or norbornanyl;

(iii) C_{1-6} alkyl substituted with two C_{6-10} aryl groups wherein one of said aryl groups is optionally substituted with 1 to 3 substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro

substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl; and the other of said aryl groups is optionally substituted with 1 substituent selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl;

(iv) C_{1-6} alkyl substituted with one C_{6-10} aryl group and optionally one additional substituent selected from hydroxy or oxo, wherein said C_{6-10} aryl group is optionally substituted with 1 to 3 substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, trifluoromethylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, trifluoromethylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl;

(v) C_{1-6} alkyl substituted with phenyl, wherein phenyl is substituted with 4 or 5 fluoro substituents; or phenyl is substituted with methoxy and 3 to 4 fluoro substituents;

(vi) C_{1-6} alkyl substituted with one heteroaryl group and optionally one additional substituent selected from oxo or hydroxy wherein said heteroaryl group is optionally substituted with one to three fluoro substituents or 1 substituent selected from chloro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, or C_{1-4} alkyl;

(vii) C_{1-6} alkyl substituted with one benzo-fused heteroaryl group and optionally one additional substituent selected from oxo or hydroxy, wherein said benzo-fused heteroaryl group is optionally substituted with 1 substituent selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, or C_{1-4} alkyl;

(viii) C_{1-6} alkyl substituted with one heterocycle group wherein said heterocycle group is optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, oxo, or hydroxy; with the proviso that not more than two of the substituents are selected from the group consisting of oxo and hydroxy;

(ix) C_{1-6} alkyl substituted with benzo[1,3]dioxol-5-yl, 2,2-difluoro-benzo[1,3]dioxol-5-yl, or 2,3-dihydro-benzo[1,4]dioxin-6-yl; or

(x) C_{2-6} alkyl optionally substituted with 1 to 2 substituents independently selected from cyano, trifluoromethyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, fluoro, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-4} alkoxycarbonylamino, hydroxy, $P(O)(OC_{1-3})_2$, C_{3-6} cycloalkyloxy, C_{3-4} cycloalkyl, or C_{5-8} cycloalkyl optionally substituted with one to three substituents independently selected from the group consisting of halogen, hydroxy, oxo and C_{1-4} alkyl optionally substituted with one to three substituents independently selected from halogen or

hydroxy; with the proviso that not more than one of the substituents on the C_{1-4} alkyl of the C_{1-4} alkyl substituted C_{5-8} cycloalkyl is hydroxy, and not more than two of the substituents on the C_{5-8} cycloalkyl are oxo;

R^3 is

(i) hydrogen,
(ii) C_{1-6} alkyl,
(iii) trifluoromethyl,
(iv) C_{1-4} alkoxy,
(v) bromo,
(vi) chloro,
(vii) fluoro, or
(viii) hydroxy;

R^4 is

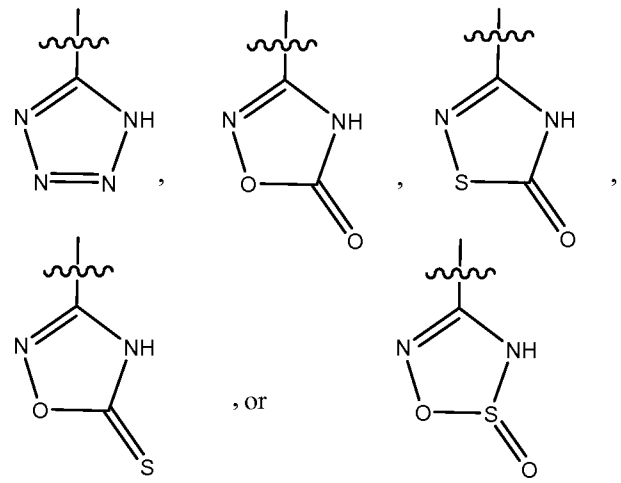
(i) hydrogen,
(ii) fluoro,
(iii) chloro, or
(iv) methyl;

R^5 is hydrogen;

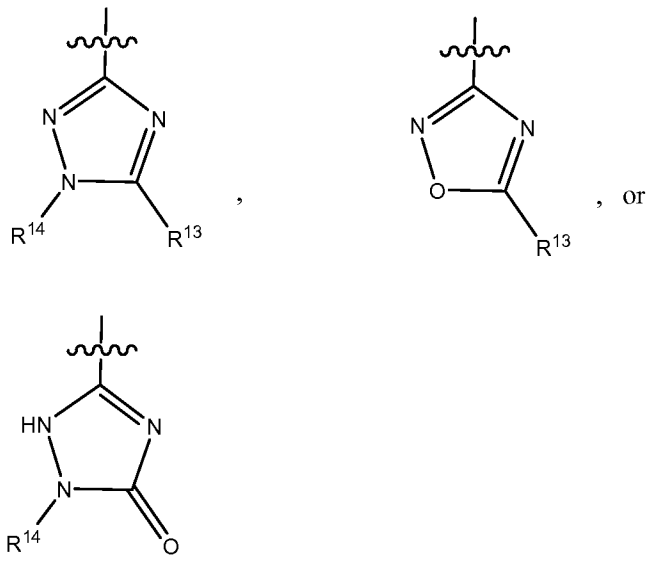
R^6 is

(i) hydrogen,
(ii) fluoro,
(iii) chloro,
(iv) methoxy, or
(v) methyl;

R^{11} is selected from



R^{12} is selected from



wherein R^{13} is H, -C_{1-4} alkyl, -$CH_2CO_2CH_3$, -$CH_2NH(C_{1-3}alkyl)$, -CH_2 $N(C_{1-3}alkyl)_2$, or -CH_2CO_2H; and R^{14} is -C_{6-10} aryl, -C_{1-6} alkyl, -C_{1-3} alkyl-OH, or -$C_{1-3}alkylCO_2H$;

with the proviso that when R^1 is C_{6-10} aryl, wherein C_{6-10} aryl is phenyl, substituted with carboxy at the 2 position, Y is not hydrogen;

with the proviso that when R^2 is C_{1-6} alkyl substituted with at least one $P(O)(OCH_3)_2$ substituent,R^1 is optionally substituted C_{6-10} aryl;

with the proviso that when R^2 is C_{1-6} alkyl substituted with at least one C_{1-6} alkoxycarbonyl substituent, R^1 is optionally substituted C_{6-10} aryl;

with the proviso that when Y is unsubstituted phenyl, and R^1 is ethyl, R^2 is not 4-fluoro-3-trifluoromethyphenylmethyl;

with the proviso that when R^2 is C_{1-6} alkyl substituted with an unsubstituted heterocycle comprising at least one nitrogen heteroatom, the point of attachment to the pendant group is through a nitrogen heteroatom;

with the proviso that when R^2 is substituted or unsubstituted C_{1-6} alkyl, R^1 is other than phenyl substituted at the 3-position with R^{11} or R^{12};

with the proviso that Formula (I) is other than

a compound wherein G is S, Y is H, R^1 is 4-cyanophenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is octahydro-quinolizin-1-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is 1-hydroxyethyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methyl, R^1 is 4-piperazin-1-ylcarbonylphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylcarbonylamino, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-aminocarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylaminocarbonyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is $S(O_2)$, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is 4-methyl-piperazin-1-ylcarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-(1-hydroxyethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is dimethylaminomethyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; and

a compound wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is $S(O_2)$, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

and enantiomers, diastereomers, solvates, and pharmaceutically acceptable salts thereof.

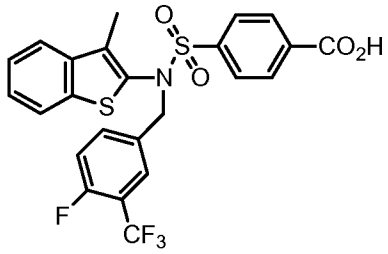
The present invention also provides, *inter alia,* a pharmaceutical composition comprising, consisting of and/or consisting essentially of a pharmaceutically acceptable carrier, a pharmaceutically acceptable excipient, and/or a pharmaceutically acceptable diluent and a compound of Formula (I) or a pharmaceutically acceptable salt form thereof.

Also provided are processes for making a pharmaceutical composition comprising, consisting of, and/or consisting essentially of admixing a compound of

Formula (I) and a pharmaceutically acceptable carrier, a pharmaceutically acceptable excipient, and/or a pharmaceutically acceptable diluent.

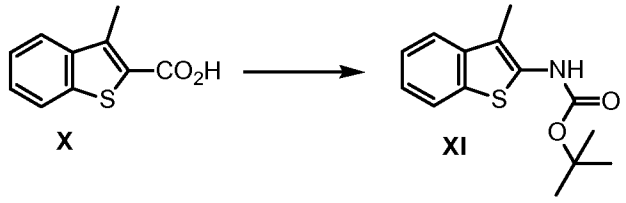
The present invention further provides, *inter alia,* methods for treating or ameliorating a TRPM8-modulated disorder in a subject, including a mammal and/or human in which the disease, syndrome, or condition is affected by the modulation of TRPM8 receptors, such as pain, the diseases that lead to such pain, and pulmonary or vascular dysfunction using a compound of Formula (I). In particular, the methods of the present invention are directed to treating or ameliorating a TRPM8 receptor-modulated disorder including inflammatory pain, cold-intolerance or cold allodynia, peripheral vascular pain, itch, urinary incontinence, chronic obstructive pulmonary disease, pulmonary hypertension and anxiety, including other stress-related disorders, using a compound of Formula (I).

The present invention also provides, *inter alia,* methods for producing the instant compounds and pharmaceutical compositions and medicaments thereof. A process included in the scope of this invention includes the following process for the preparation of Compound 306



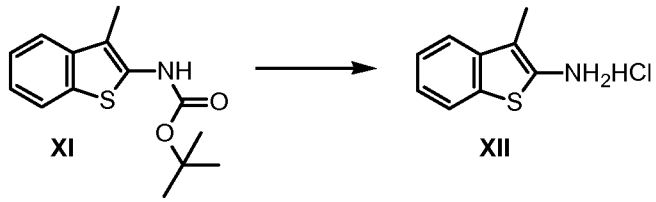
Compound 306

Comprising, consisting of and/or consisting essentially of



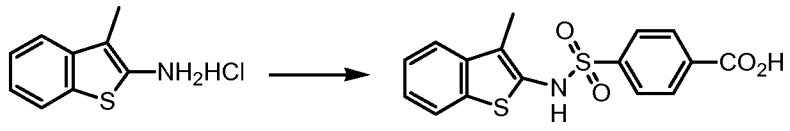
X XI

reacting a compound of formula X with *t*-butyl alcohol and a tertiary amine; in an organic solvent; followed by the addition of a mixture of diphenylphosphorylazide in an organic solvent; at temperature of about 110°C; to yield a compound of formula XI;



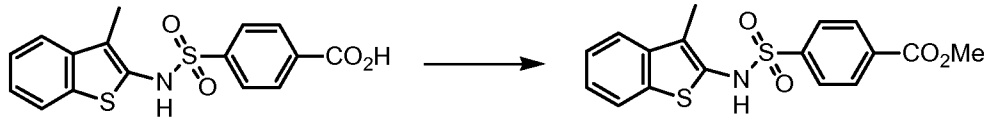
XI XII

reacting a compound of formula XI with a mineral acid or organic acid; neat or in an organic solvent; at temperature of from about 21°C to about 22°C; to yield a compound of formula XII;



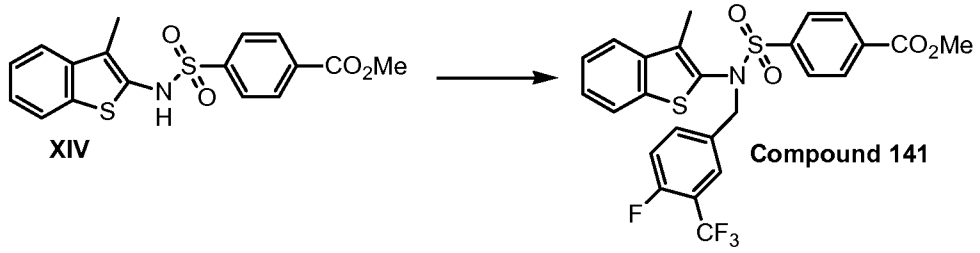
XII XIII

reacting a compound of formula XII with 4-(chlorosulfonyl)benzoic acid; in an organic solvent; at a temperature of about 21°C to about 22°C; to afford a compound of Formula XIII;



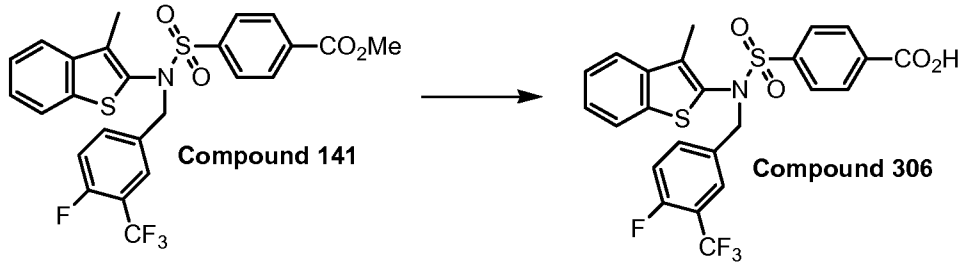
XIII XIV

reacting a compound of Formula XIII in the presence of methanol; followed by the addition of sulfuric acid; at a temperature of from about 64°C to about 65°C; to afford a compound of the Formula XIV;



XIV

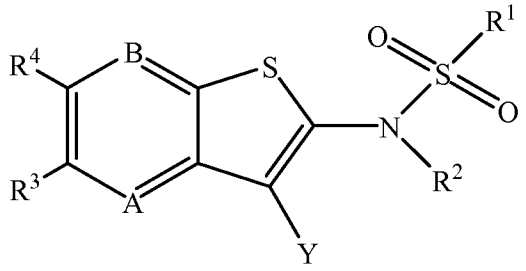
reacting a compound of Formula XIV in an organic solvent; in the presence of an inorganic base; followed by the addition of 4-fluoro-3-(trifluoromethyl)benzyl bromide; at a temperature of from about 21°C to about 22°C; to afford Compound 141;



treating Compound 141 with a metal hydroxide; neat or in an organic solvent; at a temperature of about 64°C to about 66°C; to afford Compound 306.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

The present invention provides, *inter alia*, compounds of Formula (I)



(I)

wherein

A is CR^5 or N;

B is CR^6 or N;

Y is

(i) H;

(ii) C_{1-6} alkylcarbonyl optionally substituted with 1 chloro substituent or 1 to 3 fluoro substituents;

(iii) C_{3-6} cycloalkylcarbonyl;

(iv) phenylcarbonyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, fluoro, or chloro;

(v) phenylcarbonyl substituted with trifluoromethyl and optionally one additional substituent selected from trifluoromethyl, chloro, fluoro, or C_{1-4} alkyl;

(vi) heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkyl, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

(vii) benzo-fused heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

(viii) bromo;

(ix) chloro;

(x) fluoro;

(xi) iodo;

(xii) cyano;

(xiii) formyl;

(xiv) C_{1-6} alkyl optionally substituted with 1 to 3 substituents independently selected from hydroxy, fluoro, or chloro;

(xv) C(OH)(C_{1-3} alkyl)$_2$;

(xvi) C_{3-6} cycloalkyl;

(xvii) C_{1-6} alkyl substituted with 1 substituent independently selected from C_{1-4} alkoxycarbonyl, cyano, C_{1-3} alkylthio, C_{1-4} alkoxy, or NR^7R^8 wherein R^7 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^8 is hydrogen or C_{1-4} alkyl; or R^7 and R^8 are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur;

(xviii) C_{1-4} alkoxycarbonyl;

(xix) C_{1-3} alkoxy;

(xx) hydroxy;

(xxi) C_{6-10} aryl optionally with one to three substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkoxy, hydroxy, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, or C_{1-6} alkyl optionally substituted with one to three halogen substituents; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, and C_{1-6} alkyl substituted with one to three halogen substituents;

(xxii) NR^9R^{10} wherein R^9 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^{10} is hydrogen or C_{1-4} alkyl, or R^9 and R^{10} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; or

(xxiii) arylhydroxy(C_{1-3})alkyl;

R^1 is

(i) C_{1-6} alkyl optionally substituted with 1 substituent selected from C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, hydroxy, carboxy, trifluoromethyl, C_{1-4} alkoxy, C_{1-3} alkylthio, or cyano;

(ii) aryl(C_{1-2} alkyl) wherein the ring of the aryl group is optionally substituted with 1 to 3 substituents independently selected from C_{1-4} alkyl, fluoro, chloro, trifluoromethyl, hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, or carboxy; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxycarbonyl, and carboxy;

(iii) heteroaryl(C_{1-2} alkyl) wherein the ring of the heteroaryl group is optionally substituted with 1 to 2 substituents independently selected from C_{1-4} alkyl, fluoro, chloro, trifluoromethyl, hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, or carboxy;

(iv) C_{3-8} cycloalkyl;

(v) C_{6-10} aryl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl optionally substituted with one to three chloro or fluoro substituents, chloro, fluoro, bromo, C_{1-4} alkoxy, phenyloxy, heteroaryloxy wherein the heteroaryl ring is a 6 membered ring containing carbon ring members and 1 or 2 nitrogen heteroatom ring members, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, hydroxy, carboxy, cyano, heteroaryl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, P(O)(OC_{1-3} alkyl)$_2$, P(O)$(OH)_2$, SO_3H, C(O)NHOH, or SO_2NH_2; with the proviso that not more than two of the substituents are selected from the group consisting of phenyloxy, heteroaryloxy, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, carboxy, cyano, heteroaryl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, and P(O)(OC_{1-3} alkyl)$_2$ and not more than one of the substituents is selected from the group consisting of – P(O)$(OH)_2$, -SO_3H, carboxy, C(O)NHOH, and -SO_2NH_2;

(vi) C_{6-10} aryl substituted with phenyl optionally substituted with one to two substituents selected from chloro, fluoro, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, carboxy, hydroxy, or C_{1-3} alkyl;

(vii) phenyl substituted with R^{11} or R^{12} at the 3 or 4 position; and optionally one additional substituent selected from fluoro, chloro, or C_{1-3} alkyl;

(viii) phenyl substituted with 4 or 5 fluoro substituents;

(ix) heteroaryl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl,

C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, and di(C_{1-3})alkylamino;

(x) benzo-fused heteroaryl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, and di(C_{1-3})alkylamino;

(xi) benzo-fused heterocycle optionally substituted with one to two substituents independently selected from trifluoromethyl, C_{1-3} alkylcarbonyl, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethylcarbonyl, fluoro, chloro, bromo, hydroxy, oxo, carboxy, or C_{1-4} alkoxycarbonyl; such that when the benzo-fused heterocycle is substituted on the heterocyclic ring, the substituents on the heterocyclic ring are selected from oxo, hydroxy, C_{1-4} alkyl, or trifluoromethylcarbonyl; with the proviso that not more than one substituent is trifluoromethylcarbonyl; and with the proviso that when the benzo-fused heterocycle is substituted with trifluoromethylcarbonyl, at least one of the ring members of the heterocycle is a nitrogen heteroatom and the point of attachment to the trifluoromethylcarbonyl substituent is through the nitrogen heteroatom;

(xii) amino;

(xiii) C_{1-6} alkylamino; or

(xiv) di(C_{1-6} alkyl)amino;

R^2 is

(i) C_{3-6} cycloalkyl;

(ii) C_{1-2} alkyl substituted with adamantyl;

(iii) C_{1-6} alkyl substituted with two C_{6-10} aryl groups wherein one of said aryl groups is optionally substituted with 1 to 3 substituents

independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl; and the other of said aryl groups is optionally substituted with 1 substituent selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl;

(iv) C_{1-6} alkyl substituted with one C_{6-10} aryl group and optionally one additional substituent selected from hydroxy or oxo, wherein said C_{6-10} aryl group is optionally substituted with 1 to 3 substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group

consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl;

(v) C_{1-6} alkyl substituted with one heteroaryl group and optionally one additional substituent selected from oxo or hydroxy wherein said heteroaryl group is optionally substituted with 1 substituent selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, or C_{1-4} alkyl;

(vi) C_{1-6} alkyl substituted with one benzo-fused heteroaryl group and optionally one additional substituent selected from oxo or hydroxy, wherein said benzo-fused heteroaryl group is optionally substituted with 1 substituent selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, or C_{1-4} alkyl;

(vii) C_{1-6} alkyl substituted with one heterocycle group wherein said heterocycle group is optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, oxo, or hydroxy; with the proviso that not more than two of the substituents are selected from the group consisting of oxo and hydroxy; or

(viii) C_{1-6} alkyl optionally substituted with 1 to 2 substituents independently selected from cyano, trifluoromethyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, fluoro, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-4} alkoxycarbonylamino, hydroxy, $P(O)(OC_{1-3})_2$, C_{3-4} cycloalkyl, or C_{5-8} cycloalkyl optionally substituted with one to three substituents independently selected from the group consisting of halogen, hydroxy, oxo and C_{1-4} alkyl optionally substituted with one to three substituents independently selected from halogen or

hydroxy; with the proviso that not more than one of the substituents on the C_{1-4} alkyl of the C_{1-4} alkyl substituted C_{5-8} cycloalkyl is hydroxy, and not more than two of the substituents on the C_{5-8} cycloalkyl are oxo;

R^3 is

(i) hydrogen,
(ii) C_{1-6} alkyl,
(iii) trifluoromethyl,
(ix) C_{1-4} alkoxy,
(x) bromo,
(xi) chloro,
(xii) fluoro, or
(xiii) hydroxy;

R^4 is

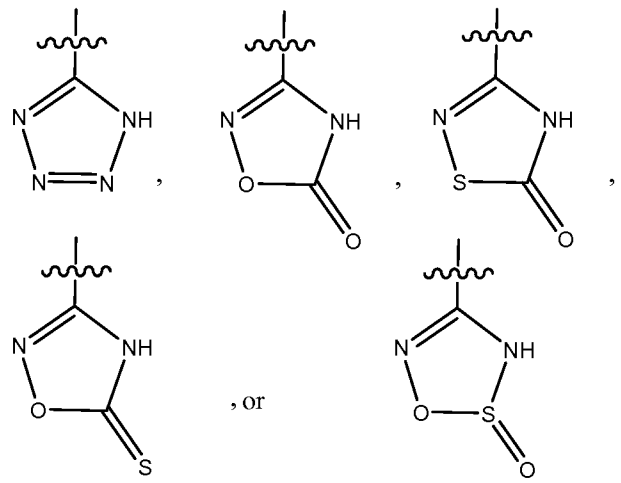
(i) hydrogen,
(ii) fluoro,
(iii) chloro, or
(iv) methyl;

R^5 is hydrogen;

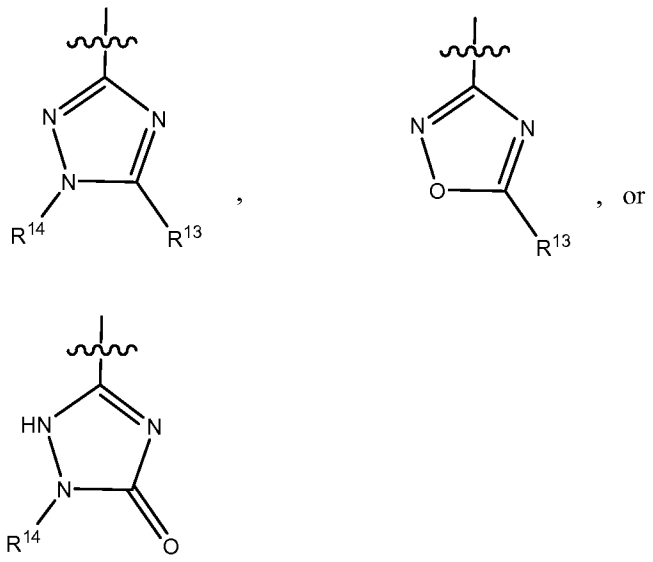
R^6 is

(i) hydrogen,
(ii) fluoro,
(iii) chloro,
(iv) methoxy, or
(v) methyl;

R^{11} is selected from



R^{12} is selected from



wherein R^{13} is H, -C_{1-4} alkyl, -$CH_2CO_2CH_3$, or -CH_2CO_2H; and R^{14} is -C_{6-10} aryl, -C_{1-6} alkyl, -C_{1-3} alkyl-OH, or -C_{1-3}alkylCO_2H;

with the proviso that when R^1 is C_{6-10} aryl, wherein C_{6-10} aryl is phenyl, substituted with carboxy at the 2 position, Y is not hydrogen;

with the proviso that when R^2 is C_{1-6} alkyl substituted with at least one $P(O)(OCH_3)_2$ substituent,R^1 is optionally substituted C_{6-10} aryl;

with the proviso that when R^2 is C_{1-6} alkyl substituted with at least one C_{1-6} alkoxycarbonyl substituent, R^1 is optionally substituted C_{6-10} aryl;

with the proviso that when Y is unsubstituted phenyl, and R^1 is ethyl, R^2 is not 4-fluoro-3-trifluoromethyphenylmethyl;

with the proviso that when R^2 is C_{1-6} alkyl substituted with an unsubstituted heterocycle comprising at least one nitrogen heteroatom, the point of attachment to the pendant group is through a nitrogen heteroatom;

and enantiomers, diastereomers, racemates, and pharmaceutically acceptable salts thereof.

As used herein, with reference to substituents, the term "independently" means that when more than substituent is possible, the substituents may be the same or different from each other.

As used herein, unless otherwise noted, the term "alkyl" whether used alone or as part of a substituent group, refers to straight and branched carbon chains having 1 to 8 carbon atoms. Therefore, designated numbers of carbon atoms (e.g. C_{1-8}) refer independently to the number of carbon atoms in an alkyl moiety or to the alkyl portion of a larger alkyl-containing substituent. In substituent groups with multiple alkyl groups such as $(C_{1-6}alkyl)_2amino$- the $C_{1-6}alkyl$ groups of the dialkylamino may be the same or different.

As used herein, unless otherwise noted, the term "alkoxy" refers to an -O-alkyl group, wherein the term "alkyl" is as defined above.

As used herein, unless otherwise noted, the terms "alkenyl" and "alkynyl" refer to straight and branched carbon chains having 2 or more carbon atoms, wherein an alkenyl chain contains at least one double bond and an alkynyl chain contains at least one triple bond.

As used herein, unless otherwise noted, the term "cycloalkyl" refers to saturated or partially saturated, monocyclic or polycyclic hydrocarbon rings of 3 to 14 carbon atoms. Examples of such rings include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and adamantyl.

As used herein, unless otherwise noted, the term "heterocycle" refers to a nonaromatic monocyclic or bicyclic ring system having 3 to 10 ring members and which contains carbon atoms and from 1 to 4 heteroatoms independently selected from the group consisting of N, O, and S. Included within the term heterocycle is a nonaromatic cyclic ring of 5 to 7 members in which 1 to 2 members are nitrogen, or a nonaromatic cyclic ring of 5 to 7 members in which zero, one or two members are

nitrogen and up to two members are oxygen or sulfur and at least one member must be either nitrogen, oxygen or sulfur; wherein, optionally, the ring contains zero to one unsaturated bonds, and, optionally, when the ring is of 6 or 7 members, it contains up to two unsaturated bonds. The carbon atom ring members that form a heterocycle ring may be fully saturated or partially saturated. The term "heterocycle" also includes two 5 membered monocyclic heterocycloalkyl groups bridged to form a bicyclic ring. Such groups are not considered to be fully aromatic and are not referred to as heteroaryl groups. When a heterocycle is bicyclic, both rings of the heterocycle are non-aromatic and at least one of the rings contains a heteroatom ring member. Examples of heterocycle groups include, and are not limited to, pyrrolinyl (including 2*H*-pyrrole, 2-pyrrolinyl or 3-pyrrolinyl), pyrrolidinyl, imidazolinyl, imidazolidinyl, pyrazolinyl, pyrazolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, and piperazinyl. Unless otherwise noted, the heterocycle is attached to its pendant group at any heteroatom or carbon atom that results in a stable structure.

As used herein, unless otherwise noted, the term "benzo-fused heterocycle" refers to a 5 to 7 membered monocyclic heterocycle ring fused to a benzene ring. The heterocycle ring contains carbon atoms and from 1 to 4 heteroatoms independently selected from the group consisting of N, O, and S. The carbon atom ring members that form the heterocycle ring may be fully saturated or partially saturated. The benzo-fused heterocycle ring is attached to its pendant group at a carbon atom of the benzene ring.

As used herein, unless otherwise noted, the term "aryl" refers to an unsaturated, aromatic monocyclic or bicyclic ring of 6 to 10 carbon members. Examples of aryl rings include phenyl and naphthalenyl.

As used herein, unless otherwise noted, the term "heteroaryl" refers to an aromatic monocyclic or bicyclic aromatic ring system having 5 to 10 ring members and which contains carbon atoms and from 1 to 4 heteroatoms independently selected from the group consisting of N, O, and S. Included within the term heteroaryl are aromatic rings of 5 or 6 members wherein the ring consists of carbon atoms and has at least one heteroatom member. Suitable heteroatoms include nitrogen, oxygen, and sulfur. In the case of 5 membered rings, the heteroaryl ring preferably contains one member of nitrogen, oxygen or sulfur and, in addition, up to three additional nitrogens. In the case of 6 membered rings, the heteroaryl ring preferably contains from one to three nitrogen

atoms. For the case wherein the 6 membered ring has three nitrogens, at most two nitrogen atoms are adjacent. When a heteroaryl is bicyclic, at least one heteroatom is present in each ring. Examples of heteroaryl groups include furyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl and pyrazinyl. Unless otherwise noted, the heteroaryl is attached to its pendant group at any heteroatom or carbon atom that results in a stable structure.

As used herein, unless otherwise noted, the term "benzo fused heteroaryl" refers to a 5 to 6 membered monocyclic heteroaryl ring fused to a benzene ring. The heteroaryl ring contains carbon atoms and from 1 to 4 heteroatoms independently selected from the group consisting of N, O, and S. Examples of heteroaryl groups with the optionally fused benzene rings include indolyl, isoindolyl, indolinyl, benzofuryl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, benzisoxazolyl, benzothiadiazolyl, benzotriazolyl, quinolinyl, isoquinolinyl and quinazolinyl. Unless otherwise noted, the benzo-fused heteroaryl is attached to its pendant group at any heteroatom or carbon atom that results in a stable structure.

The term "halogen" or "halo" refers to fluorine, chlorine, bromine and iodine.

The term "formyl" refers to the group –C(=O)H.

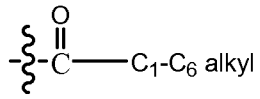
As used herein, unless otherwise noted, the term "alkylsulfonyl," refers to the group $-S(O)_2-R'$ where R' is an alkyl group as previously defined.

As used herein, unless otherwise noted, the term "alkylsulfanyl," refers to the group -SR' where R' is an alkyl group as previously defined.

The term "oxo" refers to the group (=O).

Whenever the term "alkyl" or "aryl" or either of their prefix roots appear in a name of a substituent (*e.g.*, arylalkyl, alkylamino) the name is to be interpreted as including those limitations given above for "alkyl" and "aryl." Designated numbers of carbon atoms (e.g., C_1-C_6) refer independently to the number of carbon atoms in an alkyl moiety, an aryl moiety, or in the alkyl portion of a larger substituent in which alkyl appears as its prefix root. For alkyl and alkoxy substituents, the designated number of carbon atoms includes all of the independent members included within a given range specified. For example C_{1-6} alkyl would include methyl, ethyl, propyl, butyl, pentyl and hexyl individually as well as sub-combinations thereof (e.g. C_{1-2}, C_{1-3}, C_{1-4}, C_{1-5}, C_{2-6}, C_{3-6}, C_{4-6}, C_{5-6}, C_{2-5}, etc.).

In general, under standard nomenclature rules used throughout this disclosure, the terminal portion of the designated side chain is described first followed by the adjacent functionality toward the point of attachment. Thus, for example, a "C_1-C_6 alkylcarbonyl" substituent refers to a group of the formula:



As used herein, the term "R" at a stereocenter designates that the stereocenter is purely of the *R*-configuration as defined in the art; likewise, the term "S" means that the stereocenter is purely of the *S*-configuration. As used herein, the terms "*R" or "*S" at a stereocenter are used to designate that the stereocenter is of pure but unknown configuration. As used herein, the term "RS" refers to a stereocenter that exists as a mixture of the *R*- and *S*-configurations. Similarly, the terms "*RS" or "*SR" refer to a stereocenter that exists as a mixture of the *R*- and *S*-configurations and is of unknown configuration relative to another stereocenter within the molecule.

Compounds containing one stereocenter drawn without a stereo bond designation are a mixture of two enantiomers. Compounds containing two stereocenters both drawn without stereo bond designations are a mixture of four diastereomers. Compounds with two stereocenters both labeled "RS" and drawn with stereo bond designations are a two-component mixture with relative stereochemistry as drawn. Compounds with two stereocenters both labeled "*RS" and drawn with stereo bond designations are a two-component mixture with relative stereochemistry unknown. Unlabeled stereocenters drawn without stereo bond designations are a mixture of the *R*- and *S*-configurations. For unlabeled stereocenters drawn with stereo bond designations, the absolute stereochemistry is as depicted.

Unless otherwise noted, it is intended that the definition of any substituent or variable at a particular location in a molecule be independent of its definitions elsewhere in that molecule. It is understood that substituents and substitution patterns on the compounds of formula (I) can be selected by one of ordinary skill in the art to provide compounds that are chemically stable and that can be readily synthesized by techniques known in the art as well as those methods set forth herein.

The term "subject" as used herein, refers to an animal, preferably a mammal, most preferably a human, who has been the object of treatment, observation or

experiment.

The term "therapeutically effective amount" as used herein, refers to an amount of an active compound or pharmaceutical agent that elicits the biological or medicinal response in a tissue system, animal or human that is being sought by a researcher, veterinarian, medical doctor or other clinician, which includes alleviation or partial alleviation of the symptoms of the disease, syndrome, condition, or disorder being treated.

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in therapeutically effective amounts, as well as any product that results, directly or indirectly, from combinations of the specified ingredients in the specified amounts.

For the purposes of the present invention, the term "antagonist" is used to refer to a compound capable of producing, depending on the circumstance, a functional antagonism of an ion channel, including but not limited to competitive antagonists, non-competitive antagonists, desensitizing agonists, and partial agonists.

For the purposes of the present invention, the term "inflammatory hypersensitivity" is used to refer to a condition that is characterized by one or more hallmarks of inflammation, including edema, erythema, hyperthermia and pain, and/or by an exaggerated physiologic or pathophysiologic response to one or more than one type of stimulation, including thermal, mechanical and/or chemical stimulation.

For purposes of the present invention, the term "TRPM8-modulated" is used to refer to the condition of being affected by the modulation of the TRPM8 receptor, including but not limited to, the state of being mediated by the TRPM8 receptor.

Compounds of the present invention include those wherein:

a) A is CR^5;

b) A is N; with the proviso that A is not N when G is $S(O_2)$;

c) B is CR^6;

d) B is N; with the proviso that B is not N when G is $S(O_2)$;

e) A is CR^5 and B is CR^6;

f) A is CR^5 and B is CH;

g) A is N and B is CR^6; with the proviso that A is not N when G is $S(O_2)$;

h) A is N and B is CH; with the proviso that A is not N when G is $S(O_2)$;

i) B is N and A is CR^5; with the proviso that B is not N when G is $S(O_2)$;

j) G is S;

k) G is $S(O_2)$; and A and B are $C(R^5)$ and $C(R^6)$, respectively;

l) Y is H;

m) Y is isopropenyl;

n) Y is C_{1-6} alkylcarbonyl optionally substituted with 1 chloro substituent or 1 to 3 fluoro substituents;

o) Y is C_{3-6} cycloalkylcarbonyl;

p) Y is phenylcarbonyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, fluoro, or chloro;

q) Y is phenylcarbonyl substituted with trifluoromethyl and optionally one additional substituent selected from trifluoromethyl, chloro, fluoro, or C_{1-4} alkyl;

r) Y is heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkyl, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

s) Y is benzo-fused heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

t) Y is bromo;

u) Y is chloro;

v) Y is fluoro;

w) Y is iodo;

x) Y is cyano;

y) Y is formyl;

z) Y is C_{1-6} alkyl optionally substituted with 1 to 3 substituents independently selected from hydroxy, fluoro, or chloro;

aa) Y is $C(OH)(C_{1-3}$ alkyl$)_2$;

bb) Y is C_{3-6} cycloalkyl;

cc) Y is C_{1-2} alkyl substituted with 1 substituent independently selected from C_{1-4} alkoxycarbonyl, cyano, C_{1-3} alkylthio, C_{1-4} alkoxy, or NR^7R^8 wherein R^7 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^8 is hydrogen or C_{1-4} alkyl; or R^7 and R^8 are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur;

dd) Y is C_{1-4} alkoxycarbonyl;

ee) Y is C_{1-3} alkoxy;

ff) Y is hydroxy;

gg) Y is C_{6-10} aryl optionally with one to three substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkoxy, hydroxy, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, or C_{1-6} alkyl optionally substituted with one to three halogen substituents; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, and C_{1-6} alkyl substituted with one to three halogen substituents;

hh) Y is NR^9R^{10} wherein R^9 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^{10} is hydrogen or C_{1-4} alkyl, or R^9 and R^{10} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said 5 or 6 membered ring is optionally substituted with a C_{1-4} alkyl substituent; with the proviso that when G is S and R^{10} is hydrogen, R^9 is other than hydrogen and C_{1-4} alkyl;

ii) Y is aminocarbonyl;

jj) Y is methylaminocarbonyl;

kk) Y is dimethylaminocarbonyl;

ll) Y is arylhydroxy(C_{1-3})alkyl;

mm) Y is hydrogen; isopropenyl; pyrimidinyl; thienyl; bromo; chloro; fluoro; iodo; cyano; formyl; aminocarbonyl; methylaminocarbonyl;

dimethylaminocarbonyl; C_{1-6} alkylcarbonyl; C_{3-6} cycloalkyl; C_{1-3} alkoxy; C_{1-2} alkyl optionally substituted with 1 to 3 groups independently selected from hydroxy, C_{1-4} alkoxy, fluoro, chloro, or NR^7R^8 wherein R^7 is hydrogen, C_{1-4} alkyl, C_{1-3} carbonyl, or C_{1-3} alkylsulfonyl and R^8 is hydrogen or C_{1-4} alkyl or R^7 and R^8 are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; NR^9R^{10} wherein R^9 is C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^{10} is hydrogen or C_{1-4} alkyl, or R^9 and R^{10} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said 5 or 6 membered ring is optionally substituted with a C_{1-4} alkyl substituent; with the proviso that when G is S and R^{10} is hydrogen, R^9 is other than hydrogen and C_{1-4} alkyl; or C_{6-10} aryl optionally substituted with 1 to three groups independently selected from chloro, fluoro, or bromo; or Y is methylamino or dimethylamino when G is $S(O)_2$;

nn) Y is hydrogen, isopropenyl, formyl, methyl, isopropyl, trifluoromethyl, methoxy, chloro, acetyl, hydroxymethyl, 1-hydroxyethyl, 1-methoxyethyl, 1-hydroxy-1-methyl-ethyl, methylamino-methyl, dimethylamino-methyl, *n*-propylamino-methyl, pyrrolidin-1-ylmethyl, 4-methyl-piperazin-1-yl, piperazin-1-yl; cyclopropyl, cyclobutyl, cyclopentyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, methylcarbonyl, methanesulfonylamino, bromo, cyano, pyrimidin-5-yl, thien-3-yl, 2-fluorophenyl, or 4-fluorophenyl; or Y is methylamino or dimethylamino when G is $S(O)_2$;

oo) Y is hydrogen, methyl, isopropyl, isopropenyl, trifluoromethyl, methoxy, chloro, acetyl, hydroxymethyl, 1-hydroxyethyl, 1-methoxyethyl, 1-hydroxy-1-methyl-ethyl, methylamino-methyl, dimethylamino-methyl, cyclopropyl, cyclobutyl, cyclopentyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, methylcarbonyl, or bromo; or Y is dimethylamino when G is SO_2;

pp) R^1 is C_{6-10} aryl, wherein when C_{6-10} aryl is phenyl, substituted with carboxy at the 2 position, Y is chloro;

qq) R^1 is CF_3;

rr) R^1 is C_{1-6} alkyl optionally substituted with 1 substituent selected from C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, formyl, hydroxy, carboxy, trifluoromethyl, C_{1-4} alkoxy, C_{1-3} alkylthio, bromo, cyano, R^{11}, or R^{12};

ss) R^1 is aryl(C_{1-2} alkyl) wherein the ring of the aryl group is optionally substituted with 1 to 3 substituents independently selected from C_{1-4} alkyl, fluoro, chloro, trifluoromethyl, hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, or carboxy; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxycarbonyl, and carboxy;

tt) R^1 is heteroaryl(C_{1-6} alkyl) wherein the heteroaryl group is bound through a nitrogen heteroatom and is selected from imidazolyl, triazolyl, or tetrazolyl; wherein the imidazolyl group is optionally substituted with 1 substituent selected from C_{1-4} alkyl, trifluoromethyl, hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, carboxy, aminomethyl, methylamino-methyl, or dimethylamino-methyl; and imidazolyl is optionally substituted with one additional substitutent selected from fluoro and chloro;

uu) R^1 is unsubstituted C_{3-8} cycloalkyl or cyclohexyl substituted at the 4-position with one substituent selected from the group consisting of cyano, C_{1-4} alkoxycarbonyl, carboxy, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3} alkyl)aminocarbonyl, aminomethyl, methylamino-methyl, dimethylamino-methyl, R^{11}, and R^{12};

vv) R^1 is benzo-fused C_{5-6}cycloalkyl attached at the benzo portion of the ring system, and wherein the C_{5-6}cycloalkyl portion of benzo-fused C_{5-6}cycloalkyl is optionally substituted with amino, methylamino, or dimethylamino;

ww) phenyl substituted with 3- or 4-imidazolyl, wherein the point of attachment of the imidazolyl is through a nitrogen heteroatom; and wherein the imidazolyl is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, 2-cyano, chloro, bromo, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl; wherein di(C_{1-3} alkyl) is optionally taken together

with the nitrogen atom to which it is attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein the ring formed by di(C_{1-3} alkyl)amino is optionally substituted with C_{1-3}alkyl; with the proviso that not more than one of the substituents is amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, or di(C_{1-2} alkyl)amino- C_{1-2} alkyl;

xx) R^1 is C_{6-10} aryl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl optionally substituted with one to three chloro or fluoro substituents, chloro, fluoro, bromo, C_{1-4} alkoxy, phenyloxy, heteroaryloxy wherein the heteroaryl ring is a 6 membered ring containing carbon ring members and 1 or 2 nitrogen heteroatom ring members, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, hydroxy, carboxy, cyano, heteroaryl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, $P(O)(OC_{1-3}$ alkyl$)_2$, $P(O)(OH)_2$, SO_3H, C(O)NHOH, or SO_2NH_2; with the proviso that not more than two of the substituents are selected from the group consisting of phenyloxy, heteroaryloxy, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, hydroxy, carboxy, cyano, heteroaryl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, and $P(O)(OC_{1-3}$ alkyl$)_2$ and not more than one of the substituents is selected from the group consisting of – $P(O)(OH)_2$, -SO_3H, -C(O)NHOH, and -SO_2NH_2;

yy) R^1 is phenyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl optionally substituted with one to three chloro or fluoro substituents or one hydroxy substituent, chloro, fluoro, bromo, C_{1-4} alkoxy, trifluoromethoxy, 3- or 4- phenyloxy, 3- or 4-heteroaryloxy wherein the heteroaryl ring is a 6 membered ring containing carbon ring members and 1 or 2 nitrogen heteroatom ring members, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, hydroxy, carboxy, cyano, nitro, 3- or 4-heteroaryl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonylaminocarbonyl, di(C_{1-3})alkylaminosulfonyl, $P(O)(OC_{1-3}$ alkyl$)_2$, $P(O)(OH)_2$, SO_3H, C(O)NHOH, $C(=N)NH_2$, $C(=NOH)NH_2$,

$C(=N(methylcarbonyloxy))NH_2$, or SO_2NH_2; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethoxy, 3- or 4-phenyloxy, 3- or 4-heteroaryloxy, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, carboxy, cyano, 3- or 4-heteroaryl wherein the heteroaryl is other than imidazolyl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonylaminocarbonyl, and $P(O)(OC_{1-3}$ alkyl$)_2$ and not more than one of the substituents is selected from the group consisting of – $P(O)(OH)_2$, $-SO_3H$, carboxy, C(O)NHOH, $C(=N)NH_2$, $C(=NOH)NH_2$, $C(=N(C_{1-3}$alkylcarbonyloxy$))NH_2$, and $-SO_2NH_2$; wherein the phenyloxy is optionally substituted with one to two substituents independently selected from the group consisting of methyl and fluoro;

and wherein the heteroaryl substituent is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-4} alkyl, trifluoromethyl, trifluoromethoxy, cyano, amino, methylamino, dimethylamino, chloro, bromo, carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl; with the proviso that not more than one of the substituents is selected from the group consisting of carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl;

zz) R^1 is naphthyl optionally substituted with one substituent selected from the group consisting of hydroxy, chloro, fluoro, bromo, C_{1-4} alkoxycarbonyl, and carboxy;

aaa) R^1 is C_{6-10} aryl substituted with phenyl optionally substituted with one to two substituents selected from chloro, fluoro, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, carboxy, hydroxy, amino, di(C_{1-3})alkylamino, C_{1-3} alkylamino, or C_{1-3} alkyl;

bbb) R^1 is a ring selected from indanyl or tetralinyl wherein said ring is attached via an unsaturated carbon atom and the saturated portion of the ring is substituted with amino, (C_{1-3} alkyl)amino, or di(C_{1-3} alkyl)amino;

ccc) R^1 is phenyl substituted with R^{11} or R^{12} at the 3 or 4 position; and phenyl is optionally substituted with one additional substituent selected from fluoro, chloro, or C_{1-3} alkyl;

ddd) R^1 is pyridin-3-yl substituted at a carbon atom other than that adjacent to the carbon bearing $S(O)_2$ with a substituent selected from *N*-imidazolyl, oxadiazolyl, thiazolyl, R^{11}, or R^{12}; wherein pyridin-3-yl is optionally substituted with one additional substituent selected from fluoro, chloro, or C_{1-3} alkyl; and further, wherein the *N*-imidazolyl group is optionally substituted with one to two substituents, and the oxadiazolyl and thiazolyl groups are optionally substituted one substituent, said substituent(s) independently selected from the group consisting of C_{1-4} alkyl, trifluoromethyl, cyano, amino, methylamino, dimethylamino, chloro, bromo, carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl; with the proviso that not more than one of the substituents is selected from the group consisting of carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, trifluoromethyl, cyano, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino- C_{1-2} alkyl;

eee) R^1 is imidazolyl substituted with R^{11} or R^{12}; and imidazolyl is optionally substituted at a nitrogen atom with C_{1-4} alkyl;

fff) R^1 is a ring selected from phenyl or pyridin-3-yl, wherein said ring is substituted with $NR^{15}R^{16}$; wherein R^{15} is hydrogen, C_{1-4} alkyl, C_{1-4} alkylcarbonyl, trifluoromethylcarbonyl, trifluoromethylsulfonyl, C_{3-6} cycloalkylsulfonyl, or C_{1-3} alkylsulfonyl; and R^{16} is hydrogen or C_{1-4} alkyl; or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur optionally substituted with one or two oxo substituents; and wherein the ring formed by $NR^{15}R^{16}$ is optionally substituted with C_{1-3}alkyl, C_{1-2} alkoxycarbonyl, or carboxy; and wherein said phenyl is optionally substituted with one to two additional substituents independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, fluoro, chloro, and bromo;

ggg) R^1 is phenyl substituted with $C(O)NR^{17}R^{18}$ wherein R^{17} is hydrogen, C_{1-4} alkyl, C_{1-4} alkylcarbonyl, pyrrolidin-3-yl, or C_{1-3} alkylsulfonyl; and R^{18} is hydrogen or C_{1-4} alkyl; or R^{17} and R^{18} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said ring is optionally substituted with C_{1-3}alkyl;

hhh) R^1 is phenyl substituted with 4 or 5 fluoro substituents;

iii) R^1 is phenyl substituted at the 4-position with $-Q-C(R^xR^y)-(CH_2)_{0-1}CO_2H$ wherein Q is a bond or O; and wherein R^x and R^y are independently hydrogen or methyl; or R^x and R^y are taken together with the carbon atom to which they are both attached to form a cyclopropyl ring;

jjj) R^1 is heteroaryl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, and di(C_{1-3})alkylamino;

kkk) R^1 is benzo-fused heteroaryl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy, oxo, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, carboxy, amino, C_{1-3} alkylamino, and di(C_{1-3})alkylamino;

lll) R^1 is benzo-fused heterocycle optionally substituted with one to two substituents independently selected from trifluoromethyl, C_{1-3} alkylcarbonyl, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethylcarbonyl, fluoro, chloro, bromo, hydroxy, oxo, carboxy, or C_{1-4} alkoxycarbonyl; such that when the benzo-fused heterocycle is substituted on the heterocyclic ring, the

substituents on the heterocyclic ring are selected from oxo, hydroxy, C_{1-4} alkyl, or trifluoromethylcarbonyl; with the proviso that not more than one substituent is trifluoromethylcarbonyl; and with the proviso that when the benzo-fused heterocycle is substituted with trifluoromethylcarbonyl, at least one of the ring members of the heterocycle is a nitrogen heteroatom and the point of attachment to the trifluoromethylcarbonyl substituent is through the nitrogen heteroatom;

mmm) R^1 is amino;

nnn) R^1 is C_{1-6} alkylamino;

ooo) R^1 is di(C_{1-6} alkyl)amino;

ppp) R^1 is C_{1-6} alkyl optionally substituted with 1 substituent selected from the group consisting of C_{1-3} alkylsulfonyl, C_{1-3} alkoxycarbonyl, hydroxy, carboxy, formyl, trifluoromethyl, bromo, and a 5 to 6 membered heteroaryl optionally substituted with C_{1-4} alkyl, aminomethyl, methylamino-methyl, or dimethylamino-methyl;

qqq) R^1 is methyl, ethyl, propyl, butyl, phenylmethyl, carboxymethyl, methoxycarbonylmethyl, 2-(methoxycarbonyl)ethyl, 2,2,2-trifluoroethyl, 2-bromoethyl, 2-hydroxyethyl, 2-formylethyl, 2-carboxyethyl, 3-bromopropyl, 3-hydroxypropyl, 3-(methoxycarbonyl)propyl, 3-(imidazol-1-yl)propyl , 4-(imidazol-1-yl)butyl, 3-hydroxy-3-methyl-butyl, 4-bromobutyl, 4-hydroxybutyl, 4-(4-methyl-piperazin-1-yl)butyl, 4-hydroxy-4-methylpentyl, or methanesulfonylmethyl;

rrr) R^1 is phenyl optionally substituted with one to three substituents independently selected from hydroxy, fluoro, chloro, bromo, cyano, nitro, 3- or 4-heteroaryl, 3- or 4-phenyloxy, 3- or 4-heteroaryloxy, C_{1-3} alkylsulfonylaminocarbonyl, di(C_{1-3})alkylaminosulfonyl, $C(=NOH)NH_2$, $C(O)NHOH$, $C(C=N(methylcarbonyloxy))NH_2$, aminocarbonyl, C_{1-4} alkyl subsitituted with one to three chloro or fluoro substitituents or one hydroxy substituent, C_{1-3} alkylcarbonyl, C_{1-3} alkoxycarbonyl, C_{1-3} alkoxy, or carboxy; wherein the phenyloxy is optionally substituted with one to two substituents independently selected from the group consisting of methyl and fluoro;

sss) R^1 is phenyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl optionally substituted with one

hydroxy substituent, hydroxy, fluoro, bromo, cyano, nitro, thiadazolyl, pyrazol-1-yl, 2-methyl-pyrimidin-4-yl, oxazol-5-yl, 1*H*-tetrazol-5-yl, 2*H*-tetrazol-5-yl, 1*H*-tetrazol-5-yl, 3- or 4-phenyloxy, 3- or 4-pyridinyloxy, methanesulfonylaminocarbonyl, di(methyl)aminosulfonyl, $C(=NOH)NH_2$, $C(O)NHOH$, $C(C=N(methylcarbonyloxy))NH_2$, trifluoromethyl, methoxycarbonyl, aminocarbonyl, methoxy, or carboxy; wherein the phenyloxy is optionally substituted with a fluoro substituent;

ttt) R^1 is phenyl substituted with R^{11} or R^{12} at the 3 or 4 position; and optionally one additional substituent selected from fluoro, chloro, or C_{1-3} alkyl;

uuu) R^1 is phenyl, 3-cyanophenyl, 4-cyanophenyl, 2,5-dibromophenyl, 4-bromophenyl, 4-nitrophenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 4-(1-hydroxy-1-methyl-ethyl)phenyl, phenyl, 4-hydroxy-3-fluorophenyl, 4-[1,2,3]thiadiazol-4-ylphenyl, 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, 4-(5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)phenyl, 4-(1-methyl-5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-phenyl, 3-(5-methyl-[1,3,4]oxadiazol-2-yl)phenyl, 3-phenoxyphenyl, 3-fluoro-4-(phenylmethoxy)phenyl, 3-fluoro-4-(4-fluorophenylmethoxy)phenyl, 4-pyridin-3-yloxyphenyl, 4-pyridin-4-yloxyphenyl, 3-fluorophenyl, 2-fluorophenyl, 4-perfluoromethylphenyl, 4-methoxycarbonylphenyl, 4-methylcarbonylphenyl, 3-methoxycarbonylphenyl, 2-methoxycarbonylphenyl, 3-dimethylaminosulfonylphenyl, 4-(methanesulfonylaminocarbonyl)phenyl, 4-fluorophenyl, 3,4-difluorophenyl, 4-methoxyphenyl, 4-aminocarbonyl, 4-carboxyphenyl, 3-carboxyphenyl, 2-carboxyphenyl, 4-(2-dimethylaminomethyl-imidazol-1-yl)phenyl, 4-(*N*-hydroxy-acetamidinyl)phenyl, 4-hydroxyaminocarbonylphenyl, 4-(N-(methylcarbonyloxy)acetamidinyl)phenyl, 4-(pyrazol-1-yl)phenyl, 3-(2-methyl-pyrimidin-4-yl)phenyl, 4-(oxazol-5-yl)phenyl, 3-(1*H*-tetrazol-5-yl)phenyl, 3-(2*H*-tetrazol-5-yl)phenyl, 4-(1*H*-tetrazol-5-yl)phenyl, or 3-methoxyphenyl;

vvv) R^1 is 2-aminoindan-5-yl;

www) R^1 is pyridin-3-yl substituted with 5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl or 1*H*-tetrazol-5-yl;

xxx) R^1 is a ring selected from phenyl or pyridin-3-yl wherein said ring is substituted with $NR^{15}R^{16}$; wherein R^{15} is hydrogen, C_{1-4} alkyl, methylcarbonyl, trifluoromethylcarbonyl, cyclopropylsulfonyl, or C_{1-3} alkylsulfonyl; and R^{16} is hydrogen or C_{1-4} alkyl; or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form morpholin-4-yl, piperazin-1-yl, piperadin-1-yl, thiomorpholin-4-yl, or pyrrolidin-1-yl; and wherein the ring formed by $NR^{15}R^{16}$ is optionally substituted with C_{1-3}alkyl; and wherein said phenyl is optionally substituted with one to two additional substituents independently selected from the group consisting of methoxy, hydroxy, chloro, and bromo;

yyy) R^1 is phenyl substituted with $C(O)NR^{17}R^{18}$ wherein R^{17} is hydrogen, C_{1-4} alkyl, pyrrolidin-3-yl, or C_{1-3} alkylsulfonyl; and R^{18} is hydrogen; or R^{17} and R^{18} are taken together with the nitrogen atom to which they are attached to form 4-methyl-piperazin-1-yl;

zzz) R^1 is pyridinyl, quinolinyl, quinoxalinyl, imidazo[2,1-*b*]thiazol-5-yl, thienyl, imidazolyl, benzothiophenyl, benzothiazolyl, benzooxazolyl, isoxazolyl, isoquinolinyl, benzooxazinyl, thiadiazolyl, furanyl, thiazolyl, pyrazolyl, imidazolyl, benzoxadiazolyl, benzothiadiazolyl, benzimidazolyl, pyrimidinyl, or furanyl, any of which can be optionally substituted with one to three substituents independently selected from C_{1-3} alkyl, C_{1-3} alkoxy, hydroxy, oxo, chloro, bromo, trifluoromethyl, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, di(C_{1-3})alkylamino, or heteroaryl selected from the group consisting of 1*H*-tetrazol-5-yl, isoxazolyl, and pyrazolyl; wherein the heteroaryl other than tetrazol-5-yl is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, chloro, and trifluoromethyl; with the proviso that not more than two of the substituents are selected from the group consisting of hydroxy, heteroaryl, and oxo;

aaaa) R^1 is pyridinyl, quinolinyl, quinoxalinyl, imidazo[2,1-*b*]thiazol-5-yl, thienyl, imidazolyl, benzothiophenyl, benzothiazolyl, benzimidazolyl,

furanyl, isoquinolinyl, thiazolyl, pyrazolyl, imidazolyl, or pyrimidinyl, any of which can be optionally substituted with one to three substituents independently selected from C_{1-3} alkyl, methoxy, hydroxy, oxo, chloro, bromo, trifluoromethyl, methoxycarbonyl, carboxy, methylthio, dimethylamino, or heteroaryl selected from the group consisting of 1*H*-tetrazol-5-yl, isoxazolyl, and pyrazolyl; wherein the heteroaryl other than tetrazol-5-yl is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, chloro, and trifluoromethyl; with the proviso that not more than two of the substituents are selected from the group consisting of hydroxy, heteroaryl, and oxo;

bbbb) R^1 is tetrahydroisoquinolinyl, dihydrobenzooxazinyl, tetrahydropyrimidinyl, or dihydrobenzooxazolyl, any of which can be optionally substituted with one to two substituents independently selected from C_{1-4} alkyl, trifluoromethylcarbonyl, or oxo; with the proviso that not more than one substituent is trifluoromethylcarbonyl and the point of attachment to the trifluoromethylcarbonyl substituent is through a nitrogen heteroatom;

cccc) R^1 is 1-methyl-1*H*-imidazol-4-yl, pyridin-3-yl, 6-(1*H*-tetrazol-5-yl)pyridin-3-yl, 2-chloropyridin-3-yl, 6-chloropyridin-3-yl, 6-dimethylaminopyridin-3-yl, 2-dimethylaminopyridin-3-yl, 6-methoxypyridin-3-yl, 2-methoxypyridin-3-yl, 5-bromo-6-chloropyridin-3-yl, 5,6-dichloropyridin-3-yl, 6-methylthiopyridin-3-yl, 2-methylthiopyridin-3-yl, quinoxalin-5-yl, thien-2-yl, thien-3-yl, 4-carboxythien-2-yl, 5-carboxy-3-methyl-thien-2-yl, 5-(5-trifluoromethyl-isoxazol-3-yl)-thien-2-yl, 5-(2-methyl-5-trifluoromethyl-2*H*-pyrazol-3-yl)-thien-2-yl, 6-chloro-imidazo[2,1-*b*]thiazol-5-yl, benzo[*b*]thiophen-2-yl, quinolin-8-yl, 8-methoxyquinolin-5-yl, isoquinolin-5-yl, benzothiazol-6-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, 5-chloro-1-methyl-benzimidazol-2-yl, 2-oxo-2,3-dihydro-benzooxazol-6-yl, 4-methyl-3,4-dihydro-2*H*-benzo[1,4]oxazin-7-yl, 2,4-dihydroxy-6-methylpyrimidin-5-yl, 2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinolin-8-yl, 2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl, 2-methyl-1,2,3,4-tetrahydro-isoquinolin-7-yl, 1,3,5-trimethyl-1*H*-pyrazol-4-yl, 1-methyl-3-

trifluoromethyl-1*H*-pyrazol-4-yl, 5-methoxycarbonylfuran-2-yl, 5-carboxyfuran-2-yl, 2,4-dimethyl-thiazol-5-yl, 1,2,3,4-tetrahydro-isoquinolin-8-yl, or 2-chloropyridin-5-yl;

dddd) R^1 is 1-methyl-1*H*-imidazol-4-yl, pyridin-3-yl, 6-(1*H*-tetrazol-5-yl)pyridin-3-yl, 2-chloropyridin-3-yl, 2-chloropyridin-5-yl, 6-chloropyridin-3-yl, 6-dimethylaminopyridin-3-yl, 2-dimethylaminopyridin-3-yl, 6-methoxypyridin-3-yl, 2-methoxypyridin-3-yl, 5-bromo-6-chloropyridin-3-yl, 5,6-dichloropyridin-3-yl, 6-methylthiopyridin-3-yl, quinoxalin-5-yl, thien-2-yl, thien-3-yl, 4-carboxythien-2-yl, 5-carboxy-3-methyl-thien-2-yl, 6-chloro-imidazo[2,1-*b*]thiazol-5-yl, benzo[*b*]thiophen-2-yl, quinolin-8-yl, 8-methoxyquinolin-5-yl, isoquinolin-5-yl, 2-methyl-1,2,3,4-tetrahydro-isoquinolin-7-yl, benzothiazol-6-yl, benzimidazol-2-yl, 2-oxo-2,3-dihydro-benzooxazol-6-yl, 4-methyl-3,4-dihydro-2*H*-benzo[1,4]oxazin-7-yl, 2,4-dihydroxy-6-methylpyrimidin-5-yl, 1,3,5-trimethyl-1*H*-pyrazol-4-yl, 1-methyl-3-trifluoromethyl-1*H*-pyrazol-4-yl, 5-methoxycarbonylfuran-2-yl, 2,4-dimethyl-thiazol-5-yl, 1,2,3,4-tetrahydro-isoquinolin-8-yl, or 2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinolin-8-yl;

eeee) R^1 is thienyl optionally independently substituted with one to two substituents selected from the group consisting of methyl or carboxy; imidazolyl optionally substituted with 1 methyl substituent; pyridinyl optionally substituted with 1*H*-tetrazol-5-yl, dimethylamino, chloro, methoxy, or methylthio, and optionally substituted with one additional bromo or chloro substituent; furanyl optionally substituted with 1 methoxycarbonyl substituent; quinolinyl optionally substituted with 1 methoxy substituent; isoquinolinyl; benzothiophenyl; imidazo[2,1-*b*]thiazol-5-yl optionally substituted with 1 chloro substituent; benzothiazolyl; benzimidazol-2-yl; dihydrobenzooxazolyl optionally substituted with one oxo substituent; dihydrobenzooxazinyl optionally substituted with one substituent selected from methyl or oxo; pyrimidinyl optionally substituted with from one to three substituents independently selected from oxo or hydroxy; tetrahydroisoquinolinyl optionally substituted on a nitrogen heteroatom with a trifluoromethylcarbonyl substituent; or pyrazolyl optionally substituted with from one to three substituents selected

from methyl or trifluoromethyl with the proviso that not more than 1 substituent is trifluoromethyl;

ffff) R^1 is amino, methylamino, or dimethylamino;

gggg) R^2 is C_{1-2} alkyl substituted with adamantyl;

hhhh) R^2 is C_{1-6} alkyl substituted with two C_{6-10} aryl groups wherein one of said aryl groups is optionally substituted with 1 to 3 substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl; and the other of said aryl groups is optionally substituted with 1 substituent selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl;

iiii) R^2 is C_{1-6} alkyl substituted with one C_{6-10} aryl group and optionally one additional substituent selected from hydroxy or oxo, wherein said C_{6-10} aryl group is optionally substituted with 1 to 3 substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, trifluoromethylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro,

amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, trifluoromethylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl;

jjjj) R^2 is C_{1-6} alkyl substituted with phenyl, wherein phenyl is substituted with 4 or 5 fluoro substituents; or phenyl is substituted with methoxy and 3 to 4 fluoro substituents;

kkkk) R^2 is C_{1-6} alkyl substituted with one heteroaryl group and optionally one additional substituent selected from oxo or hydroxy wherein said heteroaryl group is optionally substituted with one to three fluoro substituents or 1 substituent selected from chloro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, or C_{1-4} alkyl;

llll) R^2 is C_{1-6} alkyl substituted with one benzo-fused heteroaryl group and optionally one additional substituent selected from oxo or hydroxy, wherein said benzo-fused heteroaryl group is optionally substituted with 1 substituent selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, or C_{1-4} alkyl;

mmmm) R^2 is C_{1-6} alkyl substituted with one heterocycle group wherein said heterocycle group is optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, oxo, or hydroxy; with the proviso that not more than two of the substituents are selected from the group consisting of oxo and hydroxy;

nnnn) R^2 is C_{1-6} alkyl substituted with benzo[1,3]dioxol-5-yl, 2,2-difluoro-benzo[1,3]dioxol-5-yl, or 2,3-dihydro-benzo[1,4]dioxin-6-yl;

oooo) R^2 is C_{2-6} alkyl optionally substituted with 1 to 2 substituents independently selected from cyano, trifluoromethyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, C_{2-}

$_6$ alkenyl, C_{2-6} alkynyl, fluoro, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-4} alkoxycarbonylamino, hydroxy, $P(O)(OC_{1-3})_2$, C_{3-6} cycloalkyloxy, C_{3-4} cycloalkyl, or C_{5-8} cycloalkyl optionally substituted with one to three substituents independently selected from the group consisting of halogen, hydroxy, oxo and C_{1-4} alkyl optionally substituted with one to three substituents independently selected from halogen or hydroxy; with the proviso that not more than one of the substituents on the C_{1-4} alkyl of the C_{1-4} alkyl substituted C_{5-8} cycloalkyl is hydroxy, and not more than two of the substituents on the C_{5-8} cycloalkyl are oxo;

pppp) R^2 is C_{1-6} alkyl substituted with one substituent selected from cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl;

qqqq) R^2 is cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, 2-(cyclopropyl)ethyl, or cyclohexylmethyl;

rrrr) R^2 is C_{1-6} alkyl substituted with one substituent selected from pyrrolidinyl, imidazolidinyl, morpholinyl, tetrahydropyranyl, or piperidinyl; any of which is optionally substituted with from one to three substituents independently selected from C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, or oxo; with the proviso that not more than two of the substituents are oxo;

ssss) R^2 is 2-(2-oxo-pyrrolidin-1-yl)-ethyl, (N-tert-butoxycarbonylpyrrolidinyl)methyl, (2,5-dioxo-pyrrolidin-1-yl)-ethyl, morpholin-4-yl-ethyl, tetrahydropyran-4-ylmethyl, 2-(piperidin-1-yl)ethyl, 2-(morpholin-4-yl)ethyl, (N-tert-butoxycarbonylpyrrolidinyl)methyl, 5-oxo-pyrrolidin-2-ylmethyl, 2-(morpholin-4-yl)ethyl, (N-tert-butoxycarbonylpyrrolidinyl)methyl, 2-(2-oxo-imidazolidin-1-yl) ethyl, 2-(piperidin-1-yl)ethyl, 5-oxo-pyrrolidin-2-ylmethyl, pyrrolidin-2-ylmethyl, or piperidin-4-ylmethyl;

tttt) R^2 is C_{1-6} alkyl substituted with phenyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, trifluoromethyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, C_{1-3} alkylthio, trifluoromethylthio, C_{1-3} alkoxycarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3}) alkylaminocarbonyl, C_{1-4} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, chloro, fluoro, bromo, hydroxy, or nitro with the proviso that not more than two of

the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-3} alkylthio, trifluoromethylthio, C_{1-3} alkoxycarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3}) alkylaminocarbonyl; C_{1-4} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, and nitro;

uuuu) R^2 is C_{1-6} alkyl substituted with phenyl optionally substituted with one to two substituents independently selected from methoxy, fluoro, nitro, trifluoromethoxy, trifluoromethyl, methylthio, trifluoromethylthio, methoxycarbonyl, methylsulfonyl, trifluoromethylsulfonyl, methyl, chloro, bromo, or hydroxy;

vvvv) R^2 is 3-methoxyphenylmethyl, 4-methoxyphenylmethyl, 2-fluorophenylmethyl, 3-fluorophenylmethyl, 4-fluorophenylmethyl, 3,4,5-trifluorophenylmethyl, 3,4-difluorophenylmethyl, 2-nitrophenylmethyl, 2-trifluoromethoxyphenylmethyl, 3-trifluoromethoxyphenylmethyl, 4-trifluoromethoxyphenylmethyl, 4-difluoromethoxyphenylmethyl, 4-chloro-2-fluoro-5-methoxyphenylmethyl, phenylmethyl, 4-fluoro-3-trifluoromethylphenylmethyl, 4-fluoro-2-trifluoromethylphenylmethyl, 2-methylphenylmethyl, 3-methylphenylmethyl, 2,5-dichlorophenylmethyl, 3-chloro-4-fluorophenylmethyl, 4-chloro-3-fluorophenylmethyl, 2-(phenyl)ethyl, 4-chlorophenylmethyl, 2-methoxyphenylmethyl, 5-bromo-2-methoxyphenylmethyl, 3-methoxyphenylmethyl, 4-fluoro-3-methoxyphenylmethyl, 2-bromo-5-methoxyphenylmethyl, 4-methoxy-3-bromophenylmethyl, 3-nitrophenylmethyl, 3-methoxycarbonylphenylmethyl, 4-methoxycarbonylphenylmethyl, 4-trifluoromethylthiophenylmethyl, 4-trifluoromethylsulfonylphenylmethyl, or 3-hydroxyphenylmethyl;

wwww) R^2 is C_{1-6} alkyl substituted with one substituent selected from pyridinyl, benzo[1,3]dioxol-5-ylmethyl, 2,2-difluoro-benzo[1,3]dioxol-5-ylmethyl, or quinolinyl; wherein said pyridinyl is optionally substituted with one to three fluoro substitutents or 1 substituent selected from chloro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, or C_{1-4} alkyl;

xxxx) R^2 is quinolin-8-ylmethyl, benzo[1,3]dioxol-5-ylmethyl, 2,2-difluoro-benzo[1,3]dioxol-5-ylmethyl, pyridin-2-ylmethyl, pyridin-3-ylmethyl, pyridin-4-ylmethyl, 2,3,6-trifluoro-pyridin-4-ylmethyl, or 2-fluoro-pyridin-4-ylmethyl;

yyyy) R^2 is C_{1-2} alkyl substituted with adamantyl; or R^2 is C_{1-6} alkyl optionally substituted with 1 to 2 substituents independently selected from C_{1-6} alkoxy; C_{1-4} alkoxycarbonylamino; di(C_{1-3})alkylamino; C_{1-6} alkylsulfonyl; C_{1-6} alkylthio; fluoro; C_{2-6} alkenyl; C_{1-6} alkoxycarbonyl; hydroxy; trifluoromethyl; C_{2-6} alkynyl; C_{1-6} alkylcarbonyl; $P(O)(OC_{1-3})_2$; C_{3-6} cycloalkyloxy; or amino;

zzzz) R^2 is ethyl, 2-(tertbutoxy)ethyl, propyl, butyl, isobutyl, pentyl, hexyl, allyl, 2-(tert-butoxycarbonylamino)ethyl, 2-(dimethylamino)ethyl, 2-(methanesulfonyl)ethyl, 2-(methoxycarbonyl)-2(*R*)-methylethyl, 2-(methoxycarbonyl)-2(*S*)-methylethyl, 2-(methylsulfanyl)ethyl, methoxycarbonylmethyl, 2-methoxyethyl, 3-methoxy-3-methyl-butyl, 3,3,3,-trifluoropropyl, 4,4,4-trifluorobutyl, 5,5,5-trifluoropentyl, pent-3-ynyl, 2-fluoroethyl, 3-fluoropropyl, 2,2-difluoroethyl, 2-cyclohexyloxy-ethyl, 2-t-butoxyethyl, 3-t-butoxypropyl, 5- (ethoxycarbonyl)pentyl, 2(*R*),3-dihydroxypropyl, 2(*S*)-methoxycarbonyl-2-methylethyl, 2(*R*)-methoxycarbonyl-2-methylethyl, or 3-(methylcarbonyl)propyl;

a5) R^3 is hydrogen;

b5) R^3 is C_{1-6} alkyl;

c5) R^3 is trifluoromethyl;

d5) R^3 is C_{1-4} alkoxy;

e5) R^3 is bromo;

f5) R^3 is chloro;

g5) R^3 is fluoro;

h5) R^3 is hydroxy;

i5) R^4 is hydrogen;

j5) R^4 is fluoro;

k5) R^4 is chloro;

l5) R^4 is methyl;

m5) R^5 is hydrogen;

n5) R^6 is hydrogen,

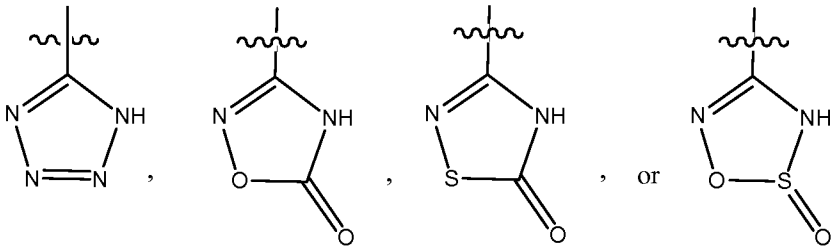
o5) R^6 is fluoro,

p5) R^6 is chloro,

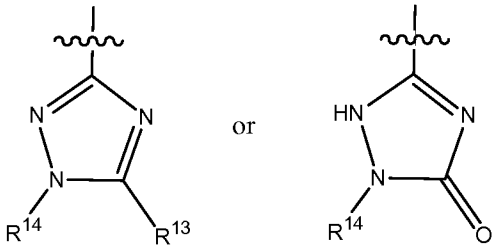
q5) R^6 is methoxy,

r5) R^6 is methyl;

s5) R^{11} is selected from



t5) R^{12} is selected from



wherein R^{13} is H, -C_{1-4}alkyl, -$CH_2NH(C_{1-3}alkyl)$, -$CH_2NH(C_{1-3}alkyl)_2$, or -CH_2CO_2H; and R^{14} is -C_{1-2} alkyl, -C_{1-3} alkyl-OH, or -C_{1-3}alkylCO_2H;

and any combination of embodiments a) through t5) above, provided that it is understood that combinations in which different embodiments of the same substituent would be combined are excluded; and with the proviso that when R^1 is C_{6-10} aryl, wherein C_{6-10} aryl is phenyl, substituted with carboxy at the 2 position, Y is not hydrogen; when R^2 is C_{1-6} alkyl substituted with at least one $P(O)(OCH_3)_2$ substituent, R^1 is optionally substituted C_{6-10} aryl; when R^2 is C_{1-6} alkyl substituted with at least one C_{1-6} alkoxycarbonyl substituent, R^1 is optionally substituted C_{6-10} aryl; when Y is unsubstituted phenyl, and R^1 is ethyl, R^2 is not 4-fluoro-3-trifluoromethyphenylmethyl; when R^2 is C_{1-6} alkyl substituted with an unsubstituted heterocycle comprising at least

one nitrogen heteroatom, the point of attachment to the pendant group is through a nitrogen heteroatom; when R^2 is substituted or unsubstituted C_{1-6} alkyl, R^1 is other than phenyl substituted at the 3-position with R^{11} or R^{12};

with the proviso that Formula (I) is other than a compound selected from the group consisting of

a compound wherein G is S, Y is H, R^1 is 4-cyanophenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is octahydro-quinolizin-1-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is 1-hydroxyethyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methyl, R^1 is 4-piperazin-1-ylcarbonylphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylcarbonylamino, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-aminocarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylaminocarbonyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is $S(O_2)$, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is 4-methyl-piperazin-1-ylcarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-(1-hydroxyethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is dimethylaminomethyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; and

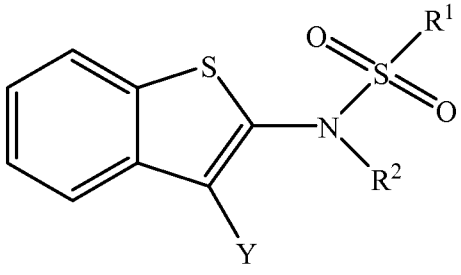
a compound wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is $S(O_2)$, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

and enantiomers, diastereomers, solvates, and pharmaceutically acceptable salts thereof.

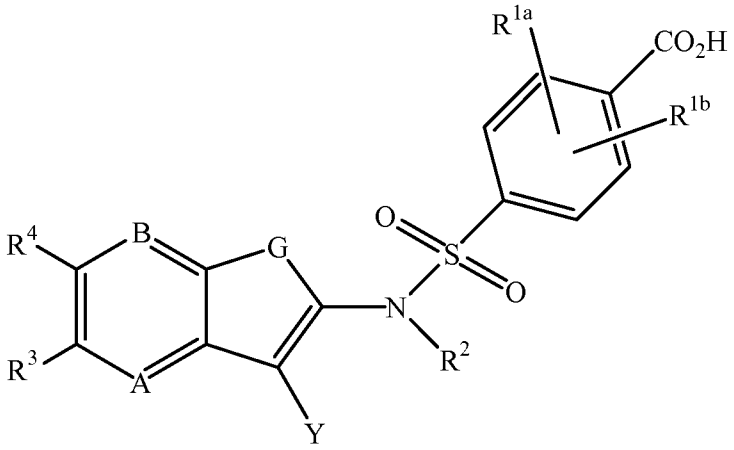
Compounds of Formula (I) include compounds of Formula (II)



(II)

wherein Y, R^1 and R^2 are as defined herein; and enantiomers, diastereomers, racemates, solvates, and pharmaceutically acceptable salts thereof.

Compounds of Formula (I) include compounds of Formula (III)



(III)

wherein A, B, G, Y, and R^2 are as defined herein;

R^{1a} and R^{1b} are selected from the group consisting of

a) 2-methyl and H;
b) 2-fluoro and hydrogen;
c) 3-fluoro and hydrogen;
d) 3-methyl and hydrogen;
e) 3-fluoro and 5-fluoro;
f) 2-fluoro and 5-fluoro;
g) 2-chloro and hydrogen;
h) 3-chloro and hydrogen;
i) 2-chloro and 6-chloro;
j) 2-trifluoromethyl and hydrogen;
k) 3-trifluoromethyl and hydrogen;
l) 3-trifluoromethoxy and hydrogen; and
m) 3-cyano and hydrogen;

and enantiomers, diastereomers, solvates, and pharmaceutically acceptable salts thereof.

A further embodiment of the present invention is directed to a compound of Formula (I) selected from:

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methylethyl, c is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is adamant-1-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-ethyl, R^1 is methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is adamant-1-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is cyclohexylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methyl-3,4-dihydro-2*H*-benzo[1,4]oxazine-7-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-hydroxyphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 4-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is thien-2-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is thien-2-yl, R^2 is 4-trifluoromethyl-3-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-[1,2,3]thiadiazol-4-yl-phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is pyridin-3-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3-methylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 4-methoxy-3-bromophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is thien-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is pyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is thien-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(piperidin-1-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 3-fluorophenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-oxo-2,3-dihydro-benzooxazol-6-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-ethyl, R^1 is methyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is thien-3-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-hydroxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 3-hydroxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinolin-8-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is thien-3-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 thien-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is thien-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(morpholin-4-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is pyridin-3-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 3-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-phenoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is dimethylamino, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 2-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxyphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is pyridin-3-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 2-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-fluorophenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is *n*-hexyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3-phenylpropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is phenyl, R^2 is 2-phenylethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-fluorophenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is dimethylamino, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 4-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyano, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3-nitrophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 4-chlorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(methoxycarbonyl)-2(*R*)-methylethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is pyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinolin-6-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2(*S*)-methoxycarbonyl-2-methylethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is pyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is ethyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 5-(ethoxycarbonyl)pentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is pyrimidin-5-yl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, $R^2$is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 4-chlorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is methyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3 and R^4 are hydrogen, R^6 is hydrogen, A is N, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3 and R^4 are hydrogen, R^6 is hydrogen, A is N, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is pyridin-2-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2(*R*)-methoxycarbonyl-2-methylethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 3-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(methylsulfanyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(*tert*-butoxy)ethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinolin-8-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 1-methyl-1*H*-imidazol-4-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is dimethylamino, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1-methyl-1*H*-imidazol-4-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is methyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is benzothiazol-6-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-methoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,4-dimethyl-thiazol-5-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(methoxycarbonyl)-2(*S*)-methylethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-methoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is *n*-propyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is pyridin-3-yl, R^2 is quinolin-8-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxy-3-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 ethyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-nitrophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxyphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is isoquinolin-5-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 3-hydroxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-methoxyphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is (N-*tert*-butoxycarbonylpiperidin-4-yl)methyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1,3,5-trimethyl-1*H*-pyrazol-4-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is methyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-chloropyridin-5-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is pyridin-3-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is dimethylamino, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is thien-3-yl, R^2 is quinolin-8-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinolin-6-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-phenylethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-chloropyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is thien-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(phenyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(morpholin-4-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,4-dihydroxy-6-methyl-pyrimidin-5-yl, $R^2$is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 3-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 4-hydroxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 3-(methylcarbonyl)propyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 4-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is cyclohexylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3-hydroxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(piperidin-1-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is methoxycarbonylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 4-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is isoquinolin-5-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinolin-8-yl, R^2 is quinolin-8-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is methyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is isoquinolin-5-yl, R^2 is quinolin-8-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1-methyl-1*H*-imidazol-4-yl, $R^2$is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is ethyl, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is ethyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, $R^2$is allyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R^2 is 2-methylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is 2-methoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is *n*-butyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinolin-6-yl, R^2 is quinolin-8-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is ethyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is methoxycarbonylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2,2-difluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is pent-3-ynyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is 2-(morpholin-4-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is dimethylamino, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R_2 is 2,2-difluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 3-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is pyridin-2-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 3-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-fluorophenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is cyclohexylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(methylsulfanyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is (*N*-*tert*-butoxycarbonylpyrrolidin-2-yl)methyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(*tert*-butoxycarbonylamino)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-oxo-3,4-dihydro-2*H*-benzo[1,4]oxazin-6-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 5-bromo-2-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is pyridin-3-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-methylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methanesulfonylmethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is ethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 2-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is quinolin-8-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, $R^1{}_1$ is phenyl, R^2 is 2-bromo-5-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-nitrophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is ethyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(morpholin-4-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is ethyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-carboxyphenyl, R^2 is 2,2-difluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, $R^1$is phenyl, R^2 is 3-methylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is cyclohexylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is *n*-propyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3-nitrophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, and R^5 are hydrogen, A is CR^5, and B is N;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R^2 is 3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-phenylethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is benzo[*b*]thiophen-2-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 4-chlorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 4-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is (N-*tert*-butoxycarbonylpyrrolidin-2-yl)methyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(methanesulfonyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2,2-difluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is ethyl, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(dimethylamino)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is *n*-butyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is allyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is $CR^6{}_6$;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 1-methyl-1*H*-imidazol-4-yl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is N-methylpyrrolidin-2(*S*)-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is pyridin-2-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(dimethylphospho)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is cyclohexyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-(methylsulfanyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R^2 is pyridin-3-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 4-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(dimethylamino)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, $R^1$is ethyl, R^2 is 2,2-difluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is (N-*tert*-butoxycarbonylpyrrolidin-2-yl)methyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1-methyl-1*H*-imidazol-4-yl, R^2 is quinolin-8-yl methyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(methanesulfonyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(2-oxo-pyrrolidin-1-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-aminoethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is pent-3-ynyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2-(methylsulfanyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1,2,3,4-tetrahydro-isoquinolin-8-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is dimethylamino, R^2 is 2,2-difluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is amino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is ethyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(2,5-dioxo-pyrrolidin-1-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is ethyl, R^2 is 2-(*tert*-butoxy)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is amino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 3-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is thien-3-yl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 2-fluorophenyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-oxo-pyrrolidin-5(*R*)-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, $R^2$is 2-oxo-pyrrolidin-5(*S*)-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinolin-8-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

compound of formula (I) wherein G is S, Y is acetyl, R^1 is ethyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is amino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is 2-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2-methoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2-(morpholin-4-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 2-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is pyridin-3-yl, R^2 is 3,4-difluorophenylmethyl, R^3 is hydrogen, R^4 is methoxy, R^5 and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is ethyl, R^2 is 2-(morpholin-4-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2-oxo-pyrrolidin-5(*S*)-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is acetyl, R^1 is ethyl, R^2 is 2-(morpholin-4-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 4-fluorophenyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(2-oxo-pyrrolidin-1-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is 4-trifluoromethylphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3 is hydrogen, R^4 is Cl, R^5 is hydrogen, R^6 is methoxy, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, and R^5 are hydrogen, R^6 is methoxy, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is benzo[*b*]thiophen-2-yl, R^2 is quinolin-8-yl methyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-trifluoromethylphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2(*R*),3-dihydroxypropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, and R^5 are hydrogen, R^6 is methoxy, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenylmethyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is Br, R^1 is phenyl, R^2 is 2-(2-oxo-imidazolidin-1-yl)-ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; or

a compound of formula (I) wherein G is S, Y is Cl, R^1 is phenyl, R^2 is 2-(2-oxo-imidazolidin-1-yl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is amino, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is amino, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is methylamino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 2-chloropyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 6-chloro-pyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is dimethylamino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is dimethylamino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 2-chloropyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 6-chloro-pyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 2-chloropyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is pyridin-3-yl, R^2 is 3-fluoro-4-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is pyridin-3-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is pyridin-3-yl, R^2 is 3-chloro-6-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is trifluoromethyl, R^1 is phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5-(2-methyl-5-trifluoromethyl-2*H*-pyrazol-3-yl)-thien-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5-methoxycarbonyl-furan-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1-methyl-3-trifluoromethyl-1*H*-pyrazol-4-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5-(5-trifluoromethyl-isoxazol-3-yl)-thien-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5-bromo-6-chloropyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5,6-dichloropyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(pyrazol-1-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(5-methyl-[1,3,4]oxadiazol-2-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(oxazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-ethyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-chloro-4-methylcarbonylamino-phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-chloro-imidazo[2,1-*b*]thiazol-5-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 6-chloro-pyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is pyridin-3-yl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methylcarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is pyridin-3-yl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylamino-methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylamino-methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is *n*-propylamino-methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is pyrrolidin-1-ylmethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is methanesulfonyl-methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methylcarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(2-methyl-pyrimidin-4-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(2-methyl-pyrimidin-4-yl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 8-methoxyquinolin-5-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 8-methoxyquinolin-5-yl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-methoxypyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-dimethylaminopyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-methoxypyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-dimethylaminopyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methanesulfonyl-methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 2-*t*-butoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 3,4-difluoro-phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-pyridin-4-yloxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-pyridin-3-yloxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-methylthio-pyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-methylthiopyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is pyridin-3-yl, R^2 is 3-methoxycarbonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is pyridin-3-yl, R^2 is 4-methoxycarbonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is pyrrolidin-1-ylmethyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is pyridin-3-yl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-oxo-2,3-dihydro-benzooxazol-6-yl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is propyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is pentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is hexyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 3-*t*-butoxypropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-*t*-butoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is propyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is pyridin-3-yl, R^2 is 3-methoxycarbonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is pyridin-3-yl, R^2 is 4-methoxycarbonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is pyridin-3-yl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is pyridin-3-yl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluoro-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-aminocarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-aminocarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 3-*t*-butoxypropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylamino-methyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylamino-methyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylamino-methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is H, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methoxy, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methoxy, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is H, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is bromo, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is H, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is bromo, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methoxy, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methoxy, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is cyclobutylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is cyclopentylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is bicyclo[2.2.1]hept-2-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is tetrahydropyran-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 2-dimethylamino-ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-dimethylaminophenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-pyrrolidin-1-ylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-morpholin-4-yl-phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1-methyl-piperazin-4-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-dimethylaminopyridin-3-yl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl , R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is isobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 2-cyclohexyloxy-ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 3-methoxy-3-methyl-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(2*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylaminocarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylaminocarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is aminocarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methylcarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-dimethylaminosulfonylphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-dimethylaminosulfonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is 1-hydroxy-1-methyl-ethyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is 1-hydroxy-ethyl, R^1 is phenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is aminocarbonyl, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylaminocarbonyl, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylaminocarbonyl, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is aminocarbonyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylaminocarbonyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(*N*-hydroxy-acetamidinyl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(*N*-(methylcarbonyloxy)acetamidinyl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(*N*-hydroxy-acetamidinyl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-bromophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is cyclopropylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(*N*-hydroxy-acetamidinyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3-chloro-4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-difluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-methanesulfonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is pentafluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethylsulfonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is pyridin-2-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3-fluoro-4-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-nitrophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-aminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonylamino, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopentyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopentyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methanesulfonylamino, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonylamino, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-phenyl, R^2 is 4,4,4-trifluoro-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methoxycarbonylphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,4,5-trifluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-fluoro-5-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2,5-dichlorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-chloro-3-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-2-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is benzo[1,3]dioxol-5-ylmethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;$_6$

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2,2-difluoro-benzo[1,3]dioxol-5-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,4-dimethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethylthiophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxythien-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5-carboxy-3-methylthien-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5-carboxyfuran-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-methoxycarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-methoxycarbonylphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methylamino, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methylamino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1*S**-hydroxy-ethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1*R**--hydroxy-ethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is dimethylamino, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(2-oxo-2,3-dihydro-2 λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is methylamino, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is methylamino, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(hydroxyaminocarbonyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^4 is trifluoromethyl, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is *n*-butyl, R^4 is trifluoromethyl, R^3, R^5, and R^6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(morpholin-4-yl)phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-dimethylaminophenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-dimethylaminophenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-morpholin-4-yl-phenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 3-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is bromo, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-aminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-amino-3-chloro-phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-aminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-amino-3-bromophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(methanesulfonylaminocarbonyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is dimethylamino, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methylamino, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is 4-methyl-piperazin-1-yl, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is amino, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is piperazin-1-yl, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is methylamino, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(O_2)$, Y is 4-methyl-piperazin-1-yl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-aminophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-amino-3-bromophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methanesulfonylaminophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-aminophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-bromophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-bromophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 3-bromo-4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is trifluoromethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is trifluoromethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is trifluoromethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is trifluoromethyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-aminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-amino-3-chloro-phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-aminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopropyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopropyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methanesulfonylaminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3,5-dichloro-4-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3,5-dichloro-4-(methanesulfonylamino)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 3-bromo-4-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-dimethylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-methylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3-chloro-4-methylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 3-bromo-4-methylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-methylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-trifluoromethylcarbonylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-trifluoromethylcarbonylaminophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclobutyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclobutyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxypropyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(2-dimethylaminomethyl-imidazol-1-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is methylamino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-methanesulfonylaminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;6

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 3-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(cyclopropylsulfonylamino)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(cyclopropylsulfonylamino)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1*H*-benzimidazol-2-yl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinoxalin-5-yl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1-methyl-benzimidazol-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is quinoxalin-5-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-formylethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxy-3-methyl-butyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S , Y is methyl, R^1 is 1*H*-benzimidazol-2-yl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 5-chloro-1-methyl-benzimidazol-2-yl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1*H*-benzimidazol-2-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1*H*-benzimidazol-2-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is 3-chloro-4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is 3-chloro-4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-dimethylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-diethylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(thiomorpholin-4-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(morpholin-4-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(piperazin-1-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methanesulfonylamino-2-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-methanesulfonylamino-2-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1-methyl-benzimidazol-2-yl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 1-methyl-benzimidazol-2-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-amino-indan-5-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-dimethylaminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(thiomorpholin-4-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(morpholin-4-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(piperidin-1-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(piperidin-1-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopropyl, R^1 is 4-(methoxycarbonyl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclobutyl, R^1 is 4-(methoxycarbonyl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopropyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclobutyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(methoxycarbonyl)propyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-hydroxybutyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-hydroxy-4-methylpentyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methoxycarbonylmethyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxy-3-methyl-butyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxypropyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-carboxypropyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 5-chloro-2-methoxy-4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-methyl-1,2,3,4-tetrahydro-isoquinolin-7-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropenyl, R^1 is ethyl, R^2 is 4-chloro-2-fluoro-5-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-bromopropyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is cyclopropyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-bromobutyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-cyanophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-cyanophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-3-fluorophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-3-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is ethyl, R^2 is 2-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(4-methyl-piperazin-1-ylcarbonyl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(imidazol-1-yl)propyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(imidazol-1-yl)butyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 2-hydroxy-4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(pyrrolidin-3*S*-ylaminocarbonyl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(pyrrolidin-3*R*-ylaminocarbonyl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1*H*-tetrazol-5-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-dimethylamino-pyridin-3-yl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-dimethylamino-pyridin-3-yl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;$_6$

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-morpholin-4-yl-pyridin-3-yl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-dimethylamino-pyridin-3-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-morpholin-4-yl-pyridin-3-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methoxycarbonylmethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is carboxymethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-hydroxyethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-methoxycarbonylethyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxy-3-methyl-butyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-bromoethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-morpholin-4-yl-pyridin-3-yl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-dimethylaminophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(morpholin-4-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is ethyl, R^2 is 2,4,5-trifluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropenyl, R^1 is ethyl, R^2 is 2,4,5-trifluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-(1*H*-tetrazol-5-yl)pyridin-3-yl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-(1*H* -tetrazol-5-yl)pyridin-3-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-(1*H* -tetrazol-5-yl)pyridin-3-yl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)pyridin-3-yl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-pyridin-3-yl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)pyridin-3-yl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-1*H* -[1,2,4]triazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1-methyl-5-oxo-4,5-dihydro-1*H* -[1,2,4]triazol-3-yl)-phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, and R^5 are hydrogen, A is CR^5, and B is N;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, and R^5 are hydrogen, A is CR^5, and B is N;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, and R^5 are hydrogen, A is CR^5, and B is N;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, and R^5 are hydrogen, A is CR^5, and B is N;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-ethyl, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-methoxy-ethyl, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3,4-difluorophenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3,4-difluorophenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-ethyl, R^1 is ethyl, R^2 is 4-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is ethyl, R^2 is 4-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2-fluoro-pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3,4-difluorophenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methoxymethyl, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is phenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is 2,5-dibromophenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-ethyl, R^1 is ethyl, R^2 is 2-fluoro-pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is ethyl, R^2 is 2-fluoro-pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is ethyl, R^2 is 4-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is ethyl, R^2 is 4-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-methoxy-ethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is ethyl, R^2 is 2,3,5-trifluoro-pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3,4-difluorophenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methoxycarbonylphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methoxycarbonylphenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is phenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-fluoro-4-(4-fluorophenylmethoxy)phenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-fluoro-4-(phenylmethoxy)phenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is ethyl, R^2 is 2-fluoro-pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

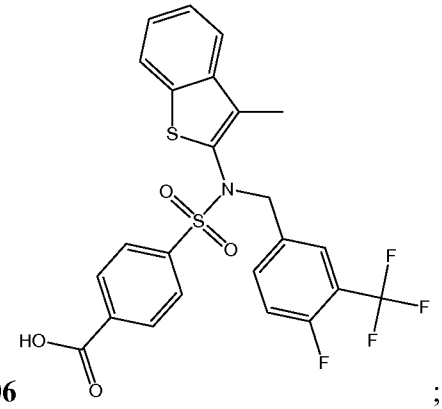
a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is ethyl, R^2 is 2-fluoro-pyridin-4-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

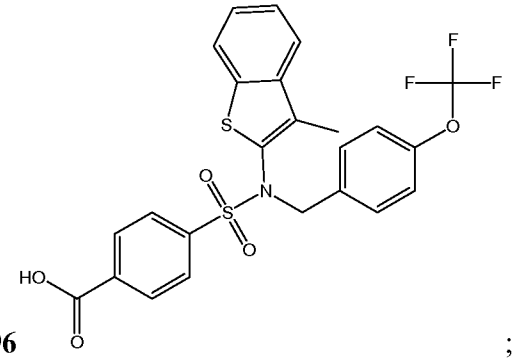
a compound of formula (I) wherein G is S, Y is bromo, R^1 is *n*-butylamino, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

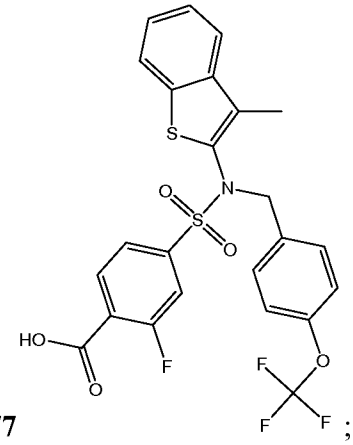
a compound of formula (I) wherein G is S, Y is H, R^1 is *n*-butylamino, R^2 is *n*-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

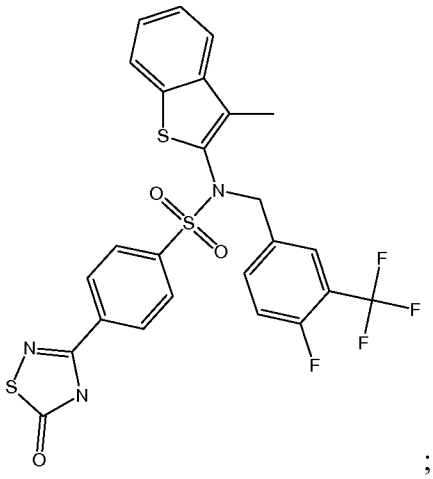
or a pharmaceutically acceptable salt form thereof.

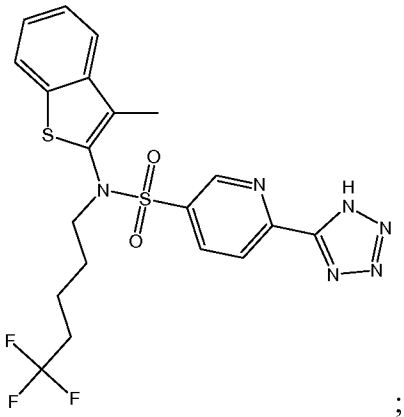
A further embodiment of the present invention is directed to compounds of formula (I) wherein the compounds have a formula selected from the group consisting of

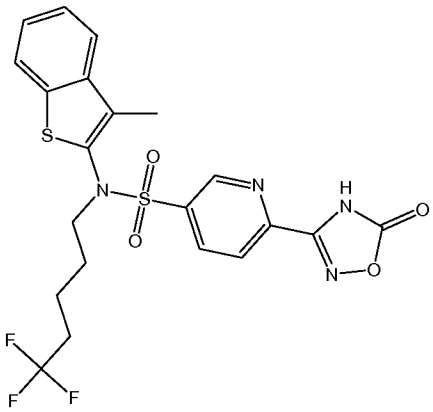
a) **Cpd 306**  ;

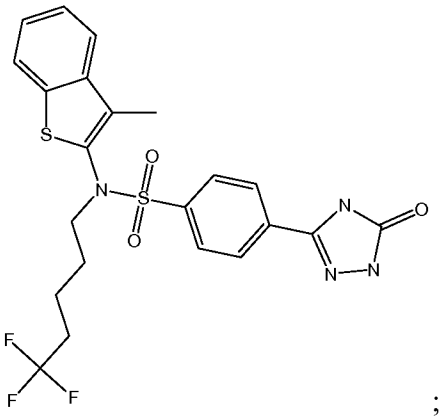
b) **Cpd 496**  ;

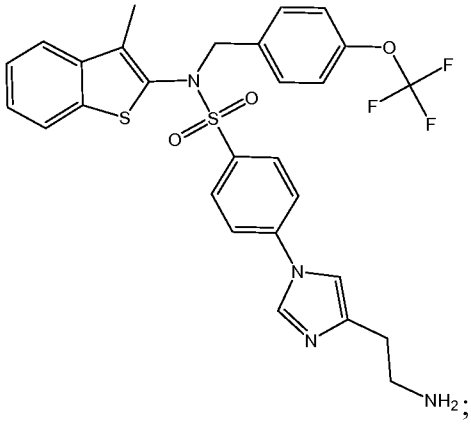
c) **Cpd 777**  ;

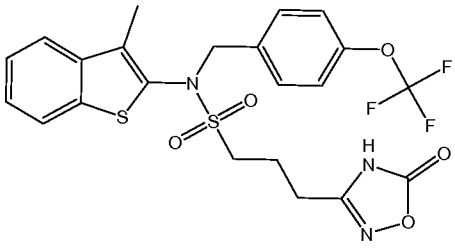
d)  **Cpd 788** ;

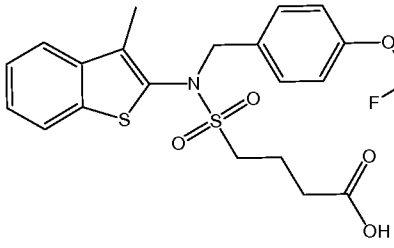
e)  **Cpd 810** ;

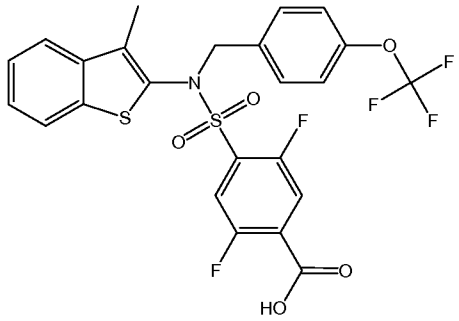
f)  **Cpd 813** ;

g) **Cpd 815**  ;

h)  ;

i)  ;

j)  ; and

k)  ;

or a pharmaceutically acceptable salt form thereof.

For use in medicine, salts of compounds of formula (I) refer to non-toxic "pharmaceutically acceptable salts." Other salts may, however, be useful in the preparation of compounds of formula (I) or of their pharmaceutically acceptable salts thereof. Suitable pharmaceutically acceptable salts of compounds of formula (I) include acid addition salts which can, for example, be formed by mixing a solution of the compound with a solution of a pharmaceutically acceptable acid such as hydrochloric acid, sulfuric acid, fumaric acid, maleic acid, succinic acid, acetic acid, benzoic acid, citric acid, tartaric acid, carbonic acid or phosphoric acid. Furthermore, where the compounds of formula (I) carry an acidic moiety, suitable pharmaceutically acceptable salts thereof may include alkali metal salts, such as sodium or potassium salts; alkaline earth metal salts, such as calcium or magnesium salts; and salts formed with suitable organic ligands, such as quaternary ammonium salts. Thus, representative pharmaceutically acceptable salts include acetate, benzenesulfonate, benzoate, bicarbonate, bisulfate, bitartrate, borate, bromide, calcium edetate, camsylate, carbonate, chloride, clavulanate, citrate, dihydrochloride, edetate, edisylate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, glycollylarsanilate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isothionate, lactate, lactobionate, laurate, malate, maleate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, N-methylglucamine ammonium salt, oleate, pamoate (embonate), palmitate, pantothenate, phosphate/diphosphate, polygalacturonate, salicylate, stearate, sulfate, subacetate, succinate, tannate, tartrate, teoclate, tosylate, triethiodide and valerate.

Representative acids and bases that may be used in the preparation of pharmaceutically acceptable salts include acids including acetic acid, 2,2-dichloroactic acid, acylated amino acids, adipic acid, alginic acid, ascorbic acid, L-aspartic acid,

benzenesulfonic acid, benzoic acid, 4-acetamidobenzoic acid, (+)-camphoric acid, camphorsulfonic acid, (+)-(1S)-camphor-10-sulfonic acid, capric acid, caproic acid, caprylic acid, cinnamic acid, citric acid, cyclamic acid, dodecylsulfuric acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, 2-hydroxy-ethanesulfonic acid, formic acid, fumaric acid, galactaric acid, gentisic acid, glucoheptonic acid, D-gluconic acid, D-glucoronic acid, L-glutamic acid, α-oxo-glutaric acid, glycolic acid, hippuric acid, hydrobromic acid, hydrochloric acid, (+)-L-lactic acid, (±)-DL-lactic acid, lactobionic acid, maleic acid, (-)-L-malic acid, malonic acid, (±)-DL-mandelic acid, methanesulfonic acid, naphthalene-2-sulfonic acid, naphthalene-1,5-disulfonic acid, 1-hydroxy-2-naphthoic acid, nicotinic acid, nitric acid, oleic acid, orotic acid, oxalic acid, palmitic acid, pamoic acid, phosphoric acid, L-pyroglutamic acid, salicylic acid, 4-amino-salicylic acid, sebaic acid, stearic acid, succinic acid, sulfuric acid, tannic acid, (+)-L-tartaric acid, thiocyanic acid, p-toluenesulfonic acid and undecylenic acid; and bases including ammonia, L-arginine, benethamine, benzathine, calcium hydroxide, choline, deanol, diethanolamine, diethylamine, 2-(diethylamino)-ethanol, ethanolamine, ethylenediamine, N-methyl-glucamine, hydrabamine, 1H-imidazole, L-lysine, magnesium hydroxide, 4-(2-hydroxyethyl)-morpholin, piperazine, potassium hydroxide, 1-(2-hydroxyethyl)-pyrrolidine, secondary amine, sodium hydroxide, triethanolamine, tromethamine and zinc hydroxide.

Embodiments of the present invention include prodrugs of compounds of formula (I). In general, such prodrugs will be functional derivatives of the compounds that are readily convertible *in vivo* into the required compound. Thus, in the methods of treating or preventing embodiments of the present invention, the term "administering" encompasses the treatment or prevention of the various diseases, conditions, syndromes and disorders described with the compound specifically disclosed or with a compound that may not be specifically disclosed, but which converts to the specified compound *in vivo* after administration to a patient. Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in "Design of Prodrugs", ed. H. Bundgaard, Elsevier, 1985.

Where the compounds according to embodiments of this invention have at least one chiral center, they may accordingly exist as enantiomers. Where the compounds possess two or more chiral centers, they may additionally exist as diastereomers. It is

to be understood that all such isomers and mixtures thereof are encompassed within the scope of the present invention. Furthermore, some of the crystalline forms for the compounds may exist as polymorphs and as such are intended to be included in the present invention. In addition, some of the compounds may form solvates with water (i.e., hydrates) or common organic solvents, and such solvates are also intended to be encompassed within the scope of this invention. The skilled artisan will understand that the term compound as used herein, is meant to include solvated compounds of Formula I.

Where the processes for the preparation of the compounds according to certain embodiments of the invention give rise to mixture of stereoisomers, these isomers may be separated by conventional techniques such as preparative chromatography. The compounds may be prepared in racemic form, or individual enantiomers may be prepared either by enantiospecific synthesis or by resolution. The compounds may, for example, be resolved into their component enantiomers by standard techniques, such as the formation of diastereomeric pairs by salt formation with an optically active acid, such as (-)-di-p-toluoyl-d-tartaric acid and/or (+)-di-p-toluoyl-l-tartaric acid followed by fractional crystallization and regeneration of the free base. The compounds may also be resolved by formation of diastereomeric esters or amides, followed by chromatographic separation and removal of the chiral auxiliary. Alternatively, the compounds may be resolved using a chiral HPLC column.

One embodiment of the present invention is directed to a composition, including a pharmaceutical composition, comprising, consisting of, and/or consisting essentially of the (+)-enantiomer of a compound of formula (I) wherein said composition is substantially free from the (-)-isomer of said compound. In the present context, substantially free means less than about 25 %, preferably less than about 10 %, more preferably less than about 5 %, even more preferably less than about 2 % and even more preferably less than about 1 % of the (-)-isomer calculated as.

$$\%(+)\text{-enantiomer} = \frac{(mass\,(+)\text{-enantiomer})}{(mass\,(+)\text{-enantiomer}) + (mass(-)\text{-enantiomer})} \times 100$$

Another embodiment of the present invention is a composition, including a pharmaceutical composition, comprising, consisting of, and consisting essentially of

the (-)-enantiomer of a compound of formula (I) wherein said composition is substantially free from the (+)-isomer of said compound. In the present context, substantially free from means less than about 25 %, preferably less than about 10 %, more preferably less than about 5 %, even more preferably less than about 2 % and even more preferably less than about 1 % of the (+)-isomer calculated as

$$\%(-)\text{-enantiomer} = \frac{(mass\,(-)\text{-enantiomer})}{(mass\,(+)\text{-enantiomer}) + (mass(-)\text{-enantiomer})} \times 100$$

.

During any of the processes for preparation of the compounds of the various embodiments of the present invention, it may be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This may be achieved by means of conventional protecting groups, such as those described in *Protective Groups in Organic Chemistry*, *Second Edition*, J.F.W. McOmie, Plenum Press, 1973; T.W. Greene & P.G.M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, 1991; and T.W. Greene & P.G.M. Wuts, *Protective Groups in Organic Synthesis*, *Third Edition,* John Wiley & Sons, 1999. The protecting groups may be removed at a convenient subsequent stage using methods known from the art.

Even though the compounds of embodiments of the present invention (including their pharmaceutically acceptable salts and pharmaceutically acceptable solvates) can be administered alone, they will generally be administered in admixture with a pharmaceutically acceptable carrier, a pharmaceutically acceptable excipient and/or a pharmaceutically acceptable diluent selected with regard to the intended route of administration and standard pharmaceutical or veterinary practice. Thus, particular embodiments of the present invention are directed to pharmaceutical and veterinary compositions comprising compounds of formula (I) and at least one pharmaceutically acceptable carrier, pharmaceutically acceptable excipient, and/or pharmaceutically acceptable diluent

By way of example, in the pharmaceutical compositions of embodiments of the present invention, the compounds of formula (I) may be admixed with any suitable binder(s), lubricant(s), suspending agent(s), coating agent(s), solubilizing agent(s), and combinations thereof.

Solid oral dosage forms, such as tablets or capsules, containing the compounds of the present invention may be administered in at least one dosage form at a time, as appropriate. It is also possible to administer the compounds in sustained release formulations.

Additional oral forms in which the present inventive compounds may be administered include exilirs, solutions, syrups, and suspensions; each optionally containing flavoring agents and coloring agents.

Alternatively, compounds of formula (I) can be administered by inhalation (intratracheal or intranasal) or in the form of a suppository or pessary, or they may be applied topically in the form of a lotion, solution, cream, ointment or dusting powder. For example, they can be incorporated into a cream comprising, consisting of, and/or consisting essentially of an aqueous emulsion of polyethylene glycols or liquid paraffin. They can also be incorporated, at a concentration of between about 1 % and about 10 % by weight of the cream, into an ointment comprising, consisting of, and/or consisting essentially of a white wax or white soft paraffin base together with any stabilizers and preservatives as may be required. An alternative means of administration includes transdermal administration by using a skin or transdermal patch.

The pharmaceutical compositions of the present invention (as well as the compounds of the present invention alone) can also be injected parenterally, for example intracavernosally, intravenously, intramuscularly, subcutaneously, intradermally or intrathecally. In this case, the compositions will also include at least one of a suitable carrier, a suitable excipient, and a suitable diluent.

For parenteral administration, the pharmaceutical compositions of the present invention are best used in the form of a sterile aqueous solution that may contain other substances, for example, enough salts and monosaccharides to make the solution isotonic with blood.

For buccal or sublingual administration, the pharmaceutical compositions of the present invention may be administered in the form of tablets or lozenges, which can be formulated in a conventional manner.

By way of further example, pharmaceutical compositions containing at least one of the compounds of formula (I) as the active ingredient can be prepared by mixing the compound(s) with a pharmaceutically acceptable carrier, a pharmaceutically acceptable diluent, and/or a pharmaceutically acceptable excipient according to conventional

pharmaceutical compounding techniques. The carrier, excipient, and diluent may take a wide variety of forms depending upon the desired route of administration (e.g., oral, parenteral, etc.). Thus for liquid oral preparations, such as suspensions, syrups, elixirs and solutions, suitable carriers, excipients and diluents include water, glycols, oils, alcohols, flavoring agents, preservatives, stabilizers, coloring agents and the like; for solid oral preparations, such as powders, capsules and tablets, suitable carriers, excipients and diluents include starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like. Solid oral preparations also may be optionally coated with substances, such as, sugars, or be enterically -coated so as to modulate the major site of absorption and disintegration. For parenteral administration, the carrier, excipient and diluent will usually include sterile water, and other ingredients may be added to increase solubility and preservation of the composition. Injectable suspensions or solutions may also be prepared utilizing aqueous carriers along with appropriate additives, such as solubilizers and preservatives.

A therapeutically effective amount of a compound of formula (I) or a pharmaceutical composition thereof includes a dose range from about 0.1 mg to about 3000 mg, in particular from about 1 mg to about 1000 mg or, more particularly, from about 10 mg to about 500 mg of active ingredient in a regimen of about 1 to 4 times per day for an average (70 kg) human; although, it is apparent to one skilled in the art that the therapeutically effective amount for active compounds of the invention will vary as will the diseases, syndromes, conditions, and disorders being treated.

For oral administration, a pharmaceutical composition is preferably provided in the form of tablets containing about 0.01, about 10, about 50, about 100, about 150, about 200, about 250, and about 500 milligrams of the inventive compound as the active ingredient.

Advantageously, a compound of formula (I) may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three and four times daily.

Optimal dosages of a compound of formula (I) to be administered may be readily determined and will vary with the particular compound used, the mode of administration, the strength of the preparation, and the advancement of the disease, syndrome, condition, or disorder. In addition, factors associated with the particular subject being treated, including subject age, weight, diet and time of administration,

will result in the need to adjust the dose to achieve an appropriate therapeutic level. The above dosages are thus exemplary of the average case. There can be, of course, individual instances wherein higher or lower dosage ranges are merited, and such are within the scope of this invention.

Compounds of formula (I) may be administered in any of the foregoing compositions and dosage regimens or by means of those compositions and dosage regimens established in the art whenever use of a compound of formula (I) is required for a subject in need thereof.

As antagonists of the TRPM8 ion channel, the compounds of formula (I) are useful in methods for treating and preventing a disease, a syndrome, a condition, or a disorder in a subject, including an animial, a mammal and a human in which the disease, the syndrome, the condition, or the disorder is affected by the modulation of TRPM8 receptors. Such methods comprise, consist of, and consist essentially of administering to a subject, including an animal, a mammal, and a human in need of such treatment or prevention a therapeutically effective amount of a compound, salt, or solvate of formula (I). In particular, the compounds of formula (I) are useful for preventing or treating pain, or diseases, syndromes, conditions, or disorders causing such pain, or pulmonary or vascular dysfunction. More particularly, the compounds of formula (I) are useful for preventing or treating inflammatory pain, inflammatory hypersensitivity conditions, neuropathic pain, anxiety, depression, and cardiovascular disease aggravated by cold, including peripheral vascular disease, vascular hypertension, pulmonary hypertension, Raynaud's disease, and coronary artery disease, by administering to a subject in need thereof a therapeutically effective amount of a compound of formula (I).

Examples of inflammatory pain include pain due to a disease, condition, syndrome, disorder, or a pain state including inflammatory bowel disease, visceral pain, migraine, post operative pain, osteoarthritis, rheumatoid arthritis, back pain, lower back pain, joint pain, abdominal pain, chest pain, labor, musculoskeletal diseases, skin diseases, toothache, pyresis, burn, sunburn, snake bite, venomous snake bite, spider bite, insect sting, neurogenic bladder, interstitial cystitis, urinary tract infection, rhinitis, contact dermatitis/hypersensitivity, itch, eczema, pharyngitis, mucositis, enteritis, irritable bowel syndrome, cholecystitis, pancreatitis, postmastectomy pain syndrome, menstrual pain, endometriosis, sinus headache, tension headache, or arachnoiditis.

One type of inflammatory pain is inflammatory hyperalgesia, which can be further distinguished as inflammatory somatic hyperalgesia or inflammatory visceral hyperalgesia. Inflammatory somatic hyperalgesia can be characterized by the presence of an inflammatory hyperalgesic state in which a hypersensitivity to thermal, mechanical and/or chemical stimuli exists. Inflammatory visceral hyperalgesia can also be characterized by the presence of an inflammatory hyperalgesic state, in which an enhanced visceral irritability exists.

Examples of inflammatory hyperalgesia include a disease, syndrome, condition, disorder, or pain state including inflammation, osteoarthritis, rheumatoid arthritis, back pain, joint pain, abdominal pain, musculoskeletal diseases, skin diseases, post operative pain, headaches, toothache, burn, sunburn, insect sting, neurogenic bladder, urinary incontinence, interstitial cystitis, urinary tract infection, cough, asthma, chronic obstructive pulmonary disease, rhinitis, contact dermatitis/hypersensitivity, itch, eczema, pharyngitis, enteritis, irritable bowel syndrome, inflammatory bowel diseases including Crohn's Disease or ulcerative colitis.

One embodiment of the present invention is directed to a method for treating inflammatory somatic hyperalgesia in which a hypersensitivity to thermal, mechanical and/or chemical stimuli exists, comprising the step of administering to a mammal in need of such treatment a therapeutically effective amount of a compound, salt or solvate of formula (I).

A further embodiment of the present invention is directed to a method for treating inflammatory visceral hyperalgesia in which a enhanced visceral irritability exists, comprising, consisting of, and/or consisting essentially of the step of administering to a subject in need of such treatment a therapeutically effective amount of a compound, salt or solvate of formula (I).

A further embodiment of the present invention is directed to a method for treating neuropathic cold allodynia in which a hypersensitivity to a cooling stimuli exists, comprising, consisting of, and/or consisting essentially of the step of administering to a subject in need of such treatment a therapeutically effective amount of a compound, salt or solvate of formula (I).

Examples of an inflammatory hypersensitivity condition include urinary incontinence, benign prostatic hypertrophy, cough, asthma, rhinitis and nasal

hypersensitivity, itch, contact dermatitis and/ or dermal allergy, and chronic obstructive pulmonary disease.

Examples of a neuropathic pain include pain due to a disease, syndrome, condition, disorder, or pain state including cancer, neurological disorders, spine and peripheral nerve surgery, brain tumor, traumatic brain injury (TBI), spinal cord trauma, chronic pain syndrome, fibromyalgia, chronic fatigue syndrome, neuralgias (trigeminal neuralgia, glossopharyngeal neuralgia, postherpetic neuralgia and causalgia), lupus, sarcoidosis, peripheral neuropathy, bilateral peripheral neuropathy, diabetic neuropathy, central pain, neuropathies associated with spinal cord injury, stroke, amyotrophic lateral sclerosis (ALS), Parkinson's disease, multiple sclerosis, sciatic neuritis, mandibular joint neuralgia, peripheral neuritis, polyneuritis, stump pain, phantom limb pain, bony fractures, oral neuropathic pain, Charcot's pain, complex regional pain syndrome I and II (CRPS I/II), radiculopathy, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, optic neuritis, postfebrile neuritis, migrating neuritis, segmental neuritis, Gombault's neuritis, neuronitis, cervicobrachial neuralgia, cranial neuralgia, geniculate neuralgia, glossopharyngial neuralgia, migrainous neuralgia, idiopathic neuralgia, intercostals neuralgia, mammary neuralgia, Morton's neuralgia, nasociliary neuralgia, occipital neuralgia, red neuralgia, Sluder's neuralgia, splenopalatine neuralgia, supraorbital neuralgia, vulvodynia, or vidian neuralgia.

One type of neuropathic pain is neuropathic cold allodynia, which can be characterized by the presence of a neuropathy-associated allodynic state in which a hypersensitivity to cooling stimuli exists. Examples of neuropathic cold allodynia include allodynia due to a disease, condition, syndrome, disorder or pain state including neuropathic pain (neuralgia), pain arising from spine and peripheral nerve surgery or trauma, traumatic brain injury (TBI), trigeminal neuralgia, postherpetic neuralgia, causalgia, peripheral neuropathy, diabetic neuropathy, central pain, stroke, peripheral neuritis, polyneuritis, complex regional pain syndrome I and II (CRPS I/II) and radiculopathy.

Examples of anxiety include social anxiety, post traumatic stress disorder, phobias, social phobia, special phobias, panic disorder, obsessive compulsive disorder, acute stress, disorder, separation anxiety disorder, and generalized anxiety disorder.

Examples of depression include major depression, bipolar disorder, seasonal affective disorder, post natal depression, manic depression, and bipolar depression.

GENERAL SYNTHETIC METHODS

Representative compounds of the present invention can be synthesized in accordance with the general synthetic methods described below and illustrated in the schemes that follow. Since the schemes are an illustration, the invention should not be construed as being limited by the specific chemical reactions and specific conditions described in the schemes and examples. The various starting materials used in the schemes are commercially available or may be prepared by methods well within the skill of persons versed in the art. The variables are as defined herein and within the skill of persons versed in the art.

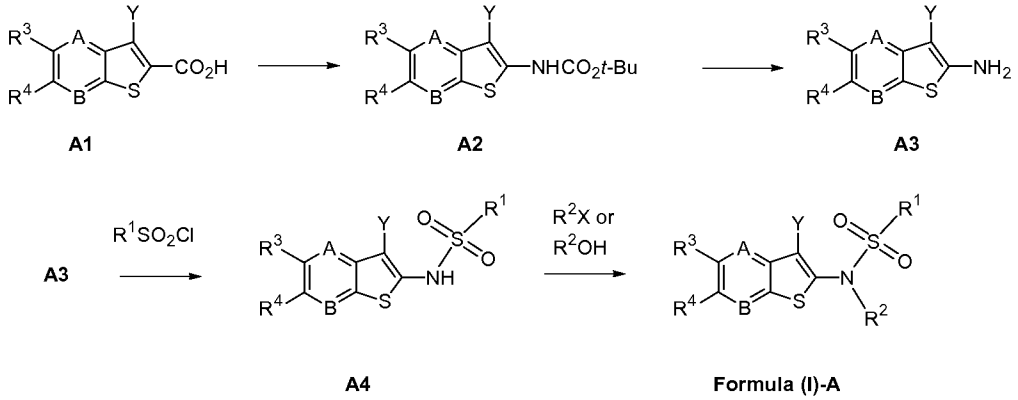
Abbreviations used in the instant specification, particularly the schemes and examples, are as follows:

AcCl	acetyl chloride
AcOH	glacial acetic acid
Bn or Bzl	benzyl
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
DEAD	diethyl azodicarboxylate
DIEA	diisopropyl-ethyl amine
DMAP	4-(dimethylamino)pyridine
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
DPPA	diphenylphosphoryl azide
EDC	1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride
ESI	electron-spray ionization
EtOAc	ethyl acetate
EtOH	ethanol
h	hour

HATU	2-(1*H*-7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uranium hexafluorophosphate methanaminium
HBTU	*O*-benzotriazole-*N,N,N',N'*-tetramethyl uronium hexafluorophosphate
HEK	human embryonic kidney
HPLC	high performance liquid chromatography
LHMDS	lithium bis(trimethylsilyl)amide
mCPBA	*meta*-chloroperbenzoic acid
Me	methyl
MeOH	methanol
MHz	megahertz
min	minutes
MS	mass spectroscopy
NaHMDS	sodium bis(trimethylsilyl)amide
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance
NT	not tested
PCC	pyridinium chlorochromate
Ph	phenyl
Pd/C	palladium on activated carbon
$Pd_2(dba)$	[tris(dibenzylideneacetone)dipalladium (0)]
Ph_3P	triphenylphosphine
PPA	polyphosphoric acid
rt	room temperature
TCDI	1,1'-thiocarbonyldiimidazole
TEA/ Et_3N	triethylamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMS	tetramethylsilane
TMSCN	trimethylsilyl cyanide

Scheme A illustrates a route for the synthesis of compounds of formula **(I)-A** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; Y is hydrogen, alkyl, chloro, trifluoromethyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl, aryl, heteroaryl, or benzo-fused heteroaryl; and R^1, R^2, R^3, R^4, R^5, and R^6 are as defined herein.

Scheme A

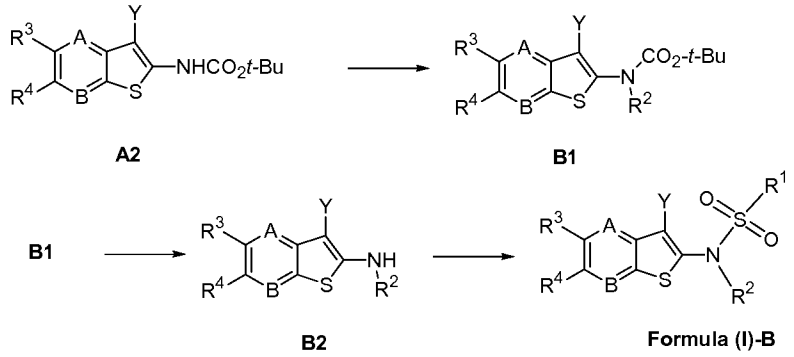


A compound of the formula **A1** is either commercially available or may be prepared by known methods described in the scientific literature. A compound of the formula **A1** may be converted to a compound of the formula **A2** using diphenylphosphoryl azide, *tert*-butanol and an organic base. A compound of the formula **A2** may be converted to the corresponding amine, a compound of the formula **A3**, by the action of HCl or another mineral acid, or by the action of an organic acid, such as trifluoroacetic acid. A compound of the formula **A3** may be treated with an appropriately substituted sulfonyl chloride in the presence of a base, and optionally in the presence of an aprotic organic solvent, to afford a compound of the formula **A4**. A compound of the formula **A4** may be treated with a base such as sodium hydride, lithium bis(trimethylsilyl)amide, *n*-butyllithium or potassium *tert*-butoxide followed by alkylation with a compound of the formula, $\mathbf{R^2X}$, where X is a leaving group such as bromo, chloro, iodo, tosylate, mesylate, and the like, to afford a compound of the formula **(I)-A**. Alternatively, a compound of the formula **A4** may be treated with a triarylphosphine such as triphenylphosphine, tri-*o*-tolylphosphine, tri-2-furylphosphine and the like; a C_{1-6} dialkyl azodicarboxylate such as diethyl-, diisopropyl-, or di-*t*-butyl-

azodicarboxylate, and the like; and an appropriately substituted alcohol, $\mathbf{R^2OH}$, to afford a compound of the formula **(I)-A**.

Scheme B illustrates a route for the synthesis of compounds of formula **(I)-B** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; Y is hydrogen, alkyl, or chloro; and R^1, R^2, R^3, R^4, R^5, and R^6 are as defined herein.

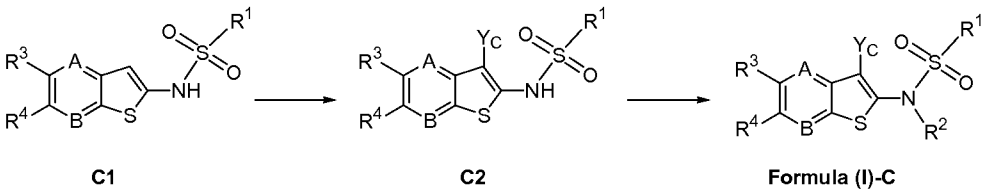
Scheme B



A compound of the formula **A2** may be treated with a base such as sodium hydride, lithium bis(trimethylsilyl)amide, *n*-butyllithium or potassium *tert*-butoxide followed by alkylation with a compound of the formula, $\mathbf{R^2X}$, where X is a leaving group such as bromo, chloro, iodo, tosylate or mesylate, to afford a compound of the formula **B1**. A compound of the formula **B1** may be converted to the corresponding amine, a compound of the formula **B2**, by the action of HCl or another mineral acid, or by the action of an organic acid, such as trifluoroacetic acid. A compound of the formula **B2** may be treated with an appropriately substituted sulfonyl chloride or trifluoromethylsulfonic anhydride in the presence of a base to afford a compound of the formula **(I)-B**.

Scheme C illustrates a route for the synthesis of compounds of formula **(I)-C** wherein Y_C is chloro, bromo, or iodo; A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; and R^1, R^2, R^3, R^4, R^5, and R^6 are as defined herein.

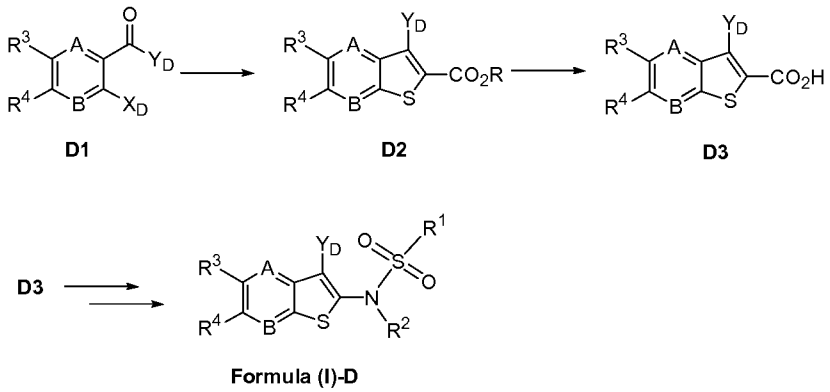
Scheme C



A compound of the formula **C1**, prepared using chemistry described in scheme A may be converted to a compound of the formula **C2**, wherein Y_C is chloro, bromo or iodo, by the action of appropriate reagents. For example, treatment of a compound of the formula **C1** with *N*-chlorosuccinimide, chlorine, or sulfuryl chloride affords a compound of the formula **C2** wherein Y_C is chloro; similarly, treatment of a compound of the formula **C1** with *N*-bromosuccinimide or bromine affords a compound of the formula **C2** wherein Y_C is bromo; and treatment with *N*-iodosuccinimide or iodine affords a compound of the formula **C2** wherein Y_C is iodo. A compound of the formula **C2** may be treated with a base such as sodium hydride, lithium bis(trimethylsilyl)amide, *n*-butyllithium or potassium *tert*-butoxide followed by alkylation with a compound of the formula, $\mathbf{R^2X}$, where X is a leaving group, such as bromo, chloro, iodo, tosylate, mesylate, and the like, to afford a compound of the formula **(I)-C**. Alternatively, a compound of formula **C2** may be treated with a triarylphosphine such as triphenylphosphine, tri-*o*-tolylphosphine, tri-2-furylphosphine and the like; a C_{1-6} dialkyl azodicarboxylate such as diethyl-, diisopropyl-, and di-*t*-butyl-azodicarboxylate, and the like; and an appropriately substituted alcohol, $\mathbf{R^2OH}$, to afford a compound of the formula **(I)-C**.

Scheme D illustrates a route for the synthesis of compounds of formula **(I)-D** wherein G is S; Y_D is hydrogen or alkyl; and A, B, R^1, R^2, R^3 and R^4 are as defined herein.

Scheme D

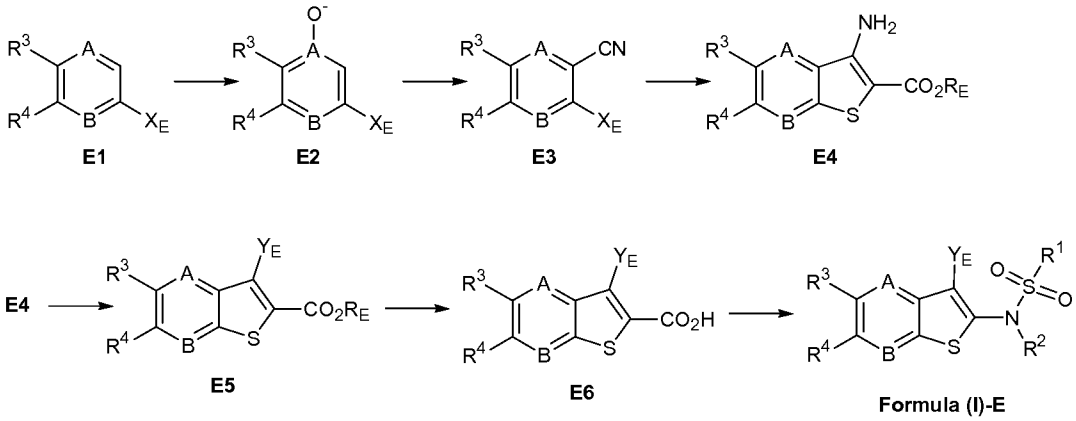


A compound of the formula **D1** is either commercially available or may be prepared by known methods described in the scientific literature. A compound of the formula **D1**, wherein X_D is chloro or fluoro and Y_D is hydrogen or alkyl, may be reacted with an R-substituted thioglycolate (wherein R is C_{1-6}alkyl) in the presence of

base to afford a compound of the formula **D2**, which may be saponified to afford a compound of the formula **D3** using conventional chemistry known to one skilled in the art. Using synthetic methods outlined in scheme A, a compound of the formula **D3** may be converted to compounds of the formula **(I)-D**.

Scheme E illustrates a route for the synthesis of compounds of the formula **(I)-E** wherein Y_E is chloro or bromo; A is nitrogen, B is C(R^6); G is S; and R^1, R^2, R^3, R^4 and R^6 are as defined herein.

Scheme E

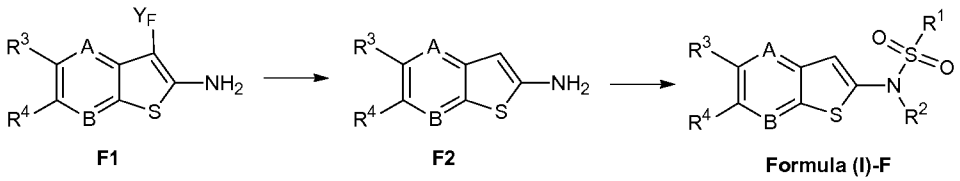


A compound of the formula **E1**, wherein X_E is a suitable leaving group such as bromo, chloro, iodo, tosylate, mesylate, or the like, is either commercially available or may be prepared by known methods described in the scientific literature. A compound of the formula **E1** may be treated with a suitable oxidizing agent, such as peroxide, peracetic acid or meta-chloroperbenzoic acid, using methods known to one skilled in the art, to afford a compound of the formula **E2**. A compound of the formula **E2** may be converted to a compound of the formula **E3** using trimethylsilyl cyanide in the presence of a base. A compound of the formula **E3** may be reacted with an (R_E)-substituted thioglycolate, wherein R_E is C_{1-6} alkyl, in the presence of a base to afford a compound of the formula **E4**. A compound of the formula **E4** may be treated with sodium nitrite or potassium nitrite in the presence of copper(I) chloride and hydrogen chloride to afford a compound of the formula **E5** wherein Y_E is chloro; or, in the presence of copper (I) bromide and hydrogen bromide to afford a compound of the formula **E5** wherein Y_E is bromo. A compound of the formula **E5** may be saponified to the corresponding carboxylic acid of a compound of the formula **E6** using conventional

chemistry known to one skilled in the art. Using the chemistry outlined in scheme A, a compound of the formula **E6** may be converted to a compound of the formula **(I)-E**.

Scheme F illustrates a route for the synthesis of compounds of the formula **(I)-F** wherein A is nitrogen, B is $C(R^6)$; G is S; Y is hydrogen; and R^1, R^2, R^3, R^4 and R^6 are as defined herein.

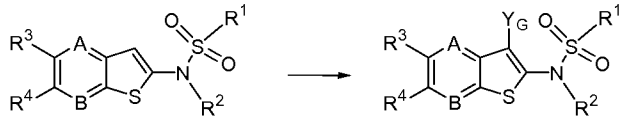
Scheme F



A compound of the formula **F1** (wherein Y_F is chloro or bromo) may be prepared from a compound of the formula **E6** using the synthetic methods described herein for the conversion of a compound of the formula **A1** to a compound of the formula **A3**. A compound of the formula **F1** may be converted to a compound of the formula **F2** by the action of a palladium catalyst, in the presence of hydrogen gas or a source of hydrogen such as 1,3-cyclohexadiene or ammonium formate. Using the chemistry outlined in scheme A, a compound of the formula **F2** may be converted to a compound of the formula **(I)-F**.

Scheme G illustrates a route for the synthesis of compounds of the formula **(I)-G** wherein Y_G is bromo, chloro or iodo; G is S; and A, B, R^1, R^2, R^3 and R^4 are as defined herein.

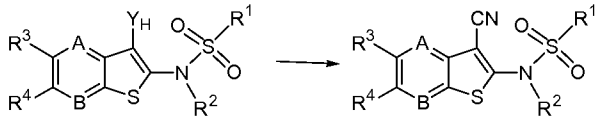
Scheme G



A compound of the formula **G1** may be converted to a compound of the formula **(I)-G** by the action of reagents such as *N*-chlorosuccinimide, chlorine, or sulfuryl chloride to afford a compound of the formula **(I)-G**, wherein Y_G is chloro. Likewise, a compound of the formula **(I)-G**, wherein Y_G is bromo, may be afforded by the action of *N*-bromosuccinimide or bromine; and a compound of the formula **(I)-G**, wherein Y_G is iodo, may be afforded by the action of *N*-iodosuccinimide or iodine.

Scheme H illustrates a route for the synthesis of compounds of the formula **(I)-H** wherein G is S; Y is cyano and A, B, R^1, R^2, R^3 and R^4 are as defined herein.

Scheme H

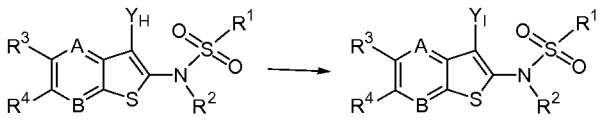


H1 **Formula (I)-H**

A compound of the formula **H1**, wherein Y_H is bromo or iodo, may be reacted with copper(I) cyanide to afford a compound of the formula **(I)-H**.

Scheme I illustrates a route for the synthesis of compounds of the formula **(I)-I** wherein G is S; Y_I is a substituted aryl, heteroaryl, or benzo-fused heteroaryl as defined herein; and A, B, R^1, R^2, R^3 and R^4 are as defined in formula (I).

Scheme I

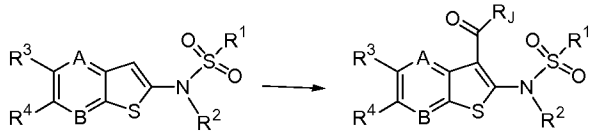


H1 **Formula (I)-I**

A compound of the formula **H1**, wherein Y_H is bromo or iodo, may be treated with an appropriately substituted aryl-, heteroaryl-, or benzo-fused heteroaryl-boronic acid or ester; in the presence of a palladium catalyst; and a base such as cesium carbonate, sodium bicarbonate, potassium fluoride, and the like; to afford a compound of the formula **(I)-I**.

Scheme J illustrates a route for the synthesis of compounds of formula **(I)-J** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R_J is C_{1-6} alkyl, C_{3-6} cycloalkyl, or aryl; R^1 and R^2 are other than a nitrogen-containing heteroaryl, and wherein R^3, R^4, R^5, and R^6 are as defined herein. One skilled in the art will recognize that conventional protection and deprotection steps may be required for certain chemical groups of R_1 and R_2 that are sensitive to the reaction conditions described in Scheme J.

Scheme J

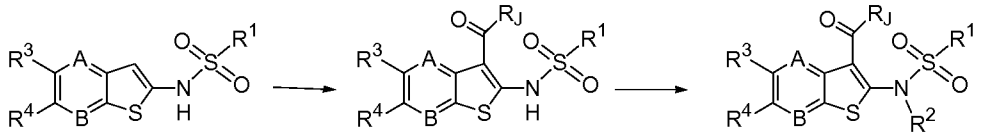


J1 Formula (I)-J

A compound of the formula **J1**, prepared using chemistry described in scheme C, may be converted to a compound of the formula **(I)-J** by the action of an R_J-substituted acid chloride and a Lewis acid, such as tin(IV) chloride or aluminum(III) chloride or other reagents and methods known to one skilled in the art.

Scheme K illustrates an alternate route to compounds of the formula **(I)-J**, wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R_J is C_{1-6} alkyl, C_{3-6} cycloalkyl, or aryl; R^1 and R^2 are other than a nitrogen-containing heteroaryl; and wherein R^3, R^4, R^5, and R^6 are as defined herein.

Scheme K



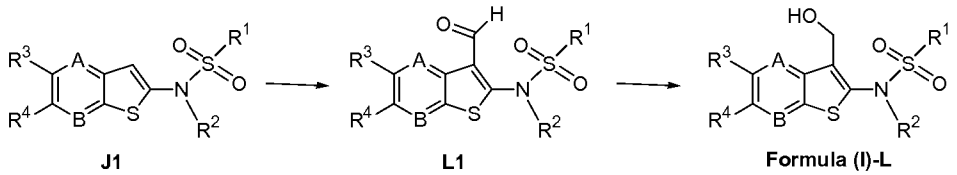
C1 K1 Formula (I)-J

A compound of the formula **C1** may be treated with an R_J-substituted acid chloride and a Lewis acid such as tin(IV) chloride or aluminum(III) chloride, to afford a product of the formula **K1**. A compound of the formula **K1** may be treated with a base, such as sodium hydride, lithium bis(trimethylsilyl)amide, *n*-butyllithium or potassium *tert*-butoxide, followed by alkylation with a compound of the formula $\mathbf{R^2X}$, defined herein, to afford a compound of the formula **(I)-J**. Alternatively, a compound of formula **K1** may be treated with a triarylphosphine such as triphenylphosphine, tri-*o*-tolylphosphine, tri-2-furylphosphine and the like; a C_{1-6} dialkyl azodicarboxylate such as diethyl-, diisopropyl-, or di-*t*-butyl-azodicarboxylate, and the like; and an appropriately substituted alcohol, $\mathbf{R^2OH}$, to afford a compound of the formula **(I)-J**.

Scheme L illustrates a route for the synthesis of compounds of the formula **(I)-L** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 and R^2 are other than a nitrogen-containing heteroaryl; and R^3, R^4, R^5, and R^6 are as defined herein. One skilled in the art will recognize that conventional protection and deprotection steps may be

required for certain chemical groups of R_1 and R_2 that are sensitive to the reaction conditions described in Scheme L.

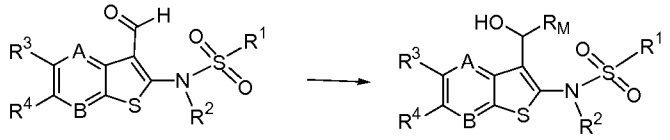
Scheme L



A compound of the formula **J1** may be treated with dichloromethyl methyl ether and a Lewis acid such as titanium(IV) chloride, to afford a compound of the formula **L1**. A compound of the formula **L1** may be converted to a compound of the formula **(I)-L** using a reducing agent such as borane, sodium borohydride, lithium borohydride, and the like, to effect reduction of an aldehyde to an alcohol.

Scheme M illustrates a route for the synthesis of compounds of the formula **(I)-M** wherein R_M is C_{1-5}alkyl or C_{6-10}aryl ; A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 and R^2 are other than a nitrogen-containing heteroaryl; and R^3, R^4, R^5, and R^6 are as defined herein. One skilled in the art will recognize that conventional protection and deprotection steps may be required for certain chemical groups of R^1 and R^2 that are sensitive to the reaction conditions described in Scheme M.

Scheme M

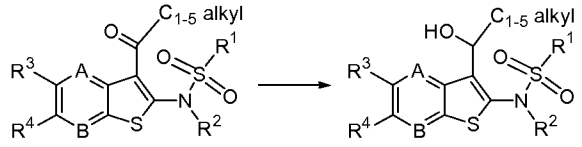


A compound of the formula **L1** may be treated with a metal-alkyl compound, such as C_{1-5}alkylmagnesium bromide, C_{1-5}alkylzinc chloride or C_{1-5}alkyllithium, to afford a compound of the formula **(I)-M** wherein R_M is C_{1-5}alkyl. Similarly, a compound of the formula **L1** may be treated with an metal-aryl compound, such as C_{6-10}arylmagnesium bromide, C_{6-10}arylzinc chloride or C_{6-10}aryllithium, to afford a compound of the formula **(I)-M** wherein R_M is C_{6-10}aryl.

Scheme N illustrates an alternate route to the compounds of the formula **(I)-M** wherein R_M is C_{1-5}alkyl. In formula **(I)-N**, A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 and R^2 are other than a nitrogen-containing heteroaryl; and R^3, R^4, R^5, and R^6

are as defined herein. One skilled in the art will recognize that conventional protection and deprotection steps may be required for certain chemical groups of R_1 and R_2 that are sensitive to the reaction conditions described in Scheme N.

Scheme N

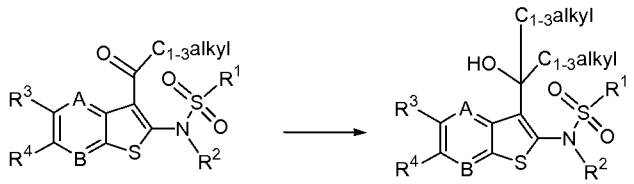


N1 Formula (I)-N

A compound of the formula **N1** may be converted to a compound of the formula **(I)-N** using reagents such as borane, sodium borohydride, lithium borohydride, and the like, to effect reduction of a ketone to an alcohol.

Scheme O illustrates a route for the synthesis of compounds of the formula **(I)-O** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 and R^2 are other than a nitrogen-containing heteroaryl; and R^3, R^4, R^5, and R^6 are as defined herein. One skilled in the art will recognize that added conventional protection and deprotection steps may be required for certain chemical groups of R^1 and R^2 that are sensitive to the reaction conditions described in Scheme O.

Scheme O

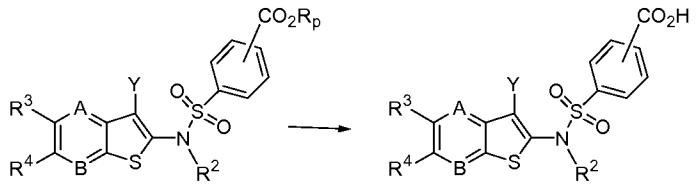


O1 Formula (I)-O

A compound of the formula **O1** may be treated with a metal-C_{1-3}alkyl compound, such as C_{1-3}alkylmagnesium bromide, C_{1-3}alkylzinc chloride or C_{1-3}alkyllithium, to afford a compound of the formula **(I)-O**.

Scheme P illustrates a route for the synthesis of compounds of formula **(I)-P** wherein G is S; and Y, A, B, R^2, R^3 and R^4 are as defined herein.

Scheme P

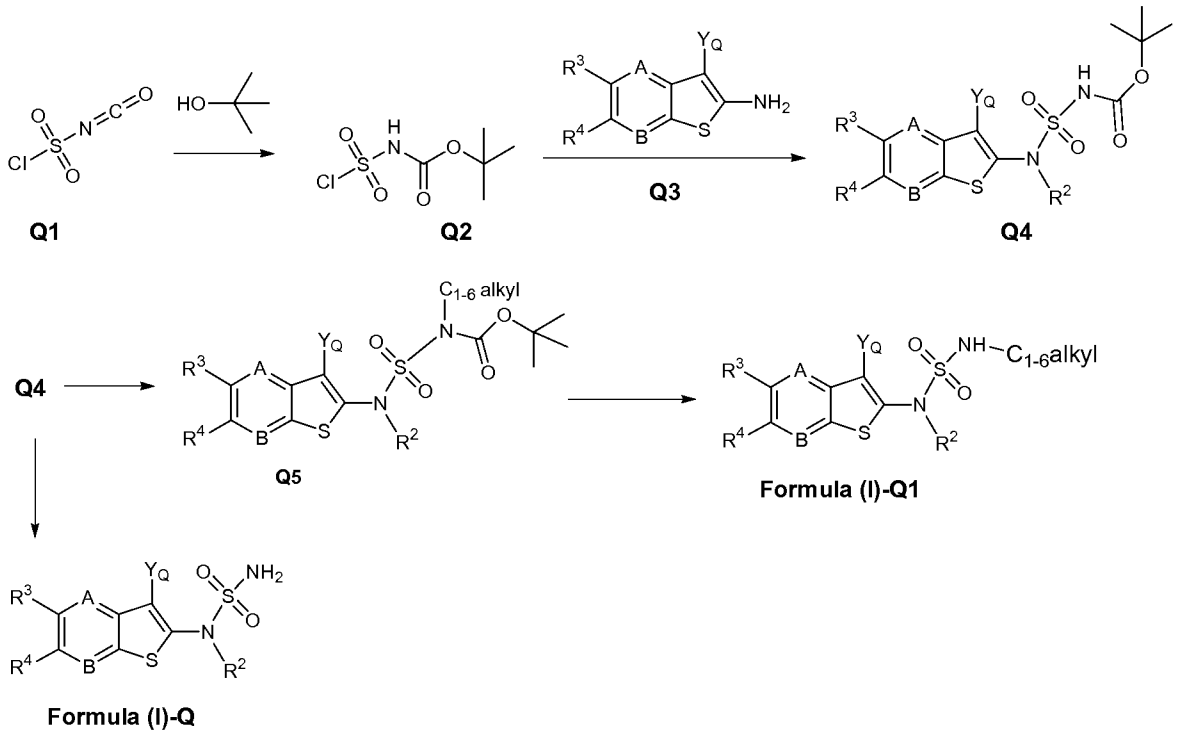


P1 **Formula (I)-P**

A compound of the formula **P1** (wherein R_p is C_{1-4} alkyl) may be prepared using chemistry described in scheme A. A compound of the formula **P1** may be converted to a compound of the formula **(I)-P** by the action of agents such as hydroxide, hydrochloric acid, trimethylsilyl iodide, or other reagents and conditions known to one skilled in the art, to effect the conversion of esters to carboxylic acids.

Scheme Q illustrates a route for the synthesis of compounds of the formula **(I)-Q** and formula **(I)-Q1** wherein Y_Q is hydrogen, C_{1-6} alkyl, or chloro; G is S; and A, B, R^2, R^3 and R^4 are as defined herein.

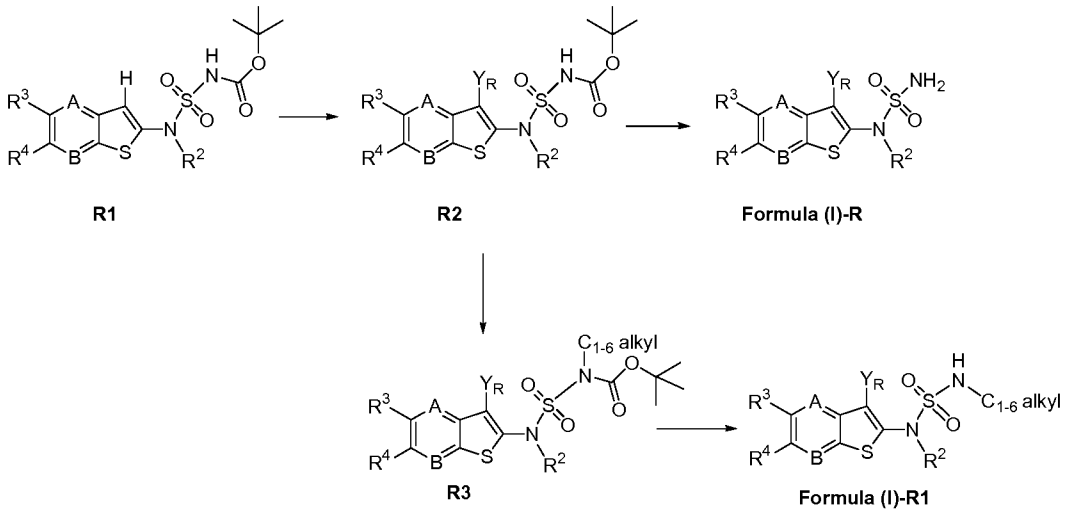
Scheme Q



Chlorosulfonyl isocyanate, compound **Q1**, may be treated with *tert*-butanol to afford compound **Q2**, which may be reacted with a compound of the formula **Q3** to afford a compound of the formula **Q4**. A compound of the formula **Q4** may be converted to the corresponding amine, a compound of the formula **(I)-Q**, by the action of HCl or another mineral acid, or by the action of an organic acid, such as trifluoroacetic acid. Alkylation of a compound of the formula **Q4** using a conventional alkylating agent such as C_{1-6}alkyl halide or C_{1-6}alkyl tosylate, in the presence of a base such as sodium hydride, affords a compound of the formula **Q5** which, upon amino deprotection, affords a compound of the formula **(I)-Q1**.

Scheme R illustrates a route for the synthesis of compounds of the formula **(I)-R** and formula **(I)-R1** wherein Y_R is chloro, bromo or iodo; G is S; R^1 is amino or C_{1-6} alkylamino, respectively; and A, B, R^2, R^3 and R^4 are as defined herein.

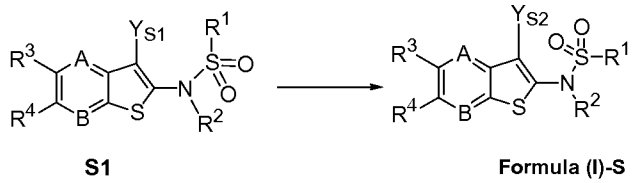
Scheme R



A compound of the formula **R1** may be converted to a compound of the formula **R2**, wherein Y_R is chloro, bromo or iodo, using chemistry described in scheme C for the conversion of a compound of the formula **C1** to a compound of the formula **C2**. A compound of the formula **R2** may be converted to a compound of the formula **(I)-R**, using chemistry described in scheme Q for the conversion of a compound of the formula **Q4** to a compound of the formula **(I)-Q**. A compound of the formula **R2** may be alkylated using conventional alkylating agents and condition such as a C_{1-6}alkyl halide in the presence of TEA or pyridine to afford a compound of the formula **R3**. Subsequent removal of the amino protecting group as described herein affords a compound of the formula **(I)-R1**.

Scheme S illustrates a route for the synthesis of compounds of formula **(I)-S** wherein Y_{S2} is C_{1-3}dialkylamino, or a 5 or 6 membered heterocycle with 1 to 2 nitrogens, wherein the point of attachment is via a nitrogen atom; G is S; and A, B, R^1, R^2, R^3 and R^4 are as defined herein.

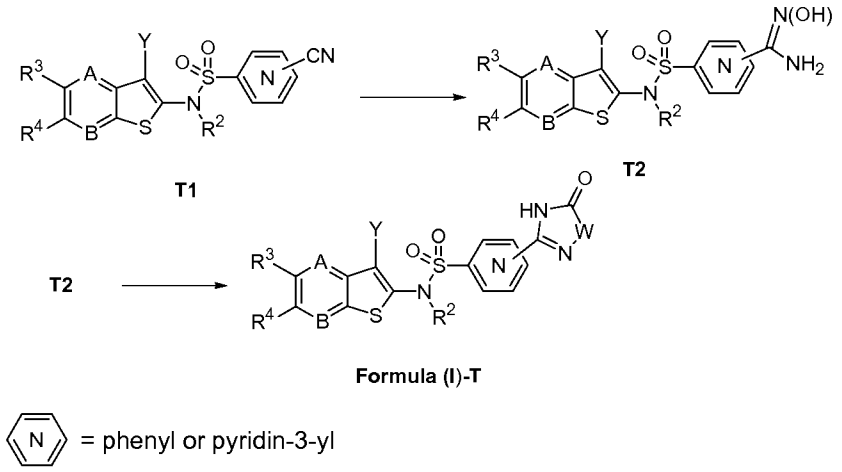
Scheme S



A compound of the formula **S1** wherein Y_{S1} is bromo or iodo, may be converted to a compound of the formula **(I)-S** by the action of an appropriately substituted amine, in the presence of a palladium catalyst and a base.

Scheme T illustrates a route for the synthesis of compounds of formula **(I)-T**, wherein W is O or S; G is S; and A, B, Y, R^2, R^3 and R^4 are as defined herein.

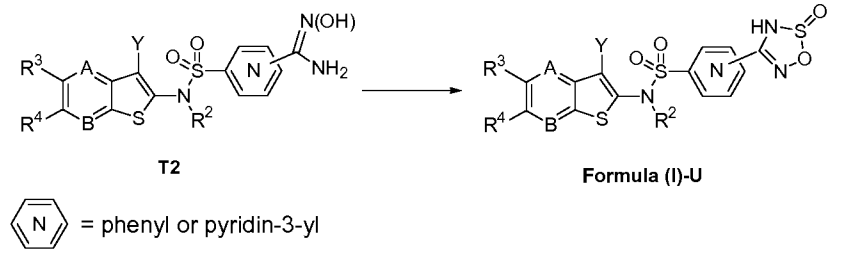
Scheme T



A compound of the formula **T1** may be treated with hydroxylamine hydrochloride, in the presence of a tertiary base such as triethylamine, to afford a compound of the formula **T2**. A compound of the formula **T2** may be converted to a compound of the formula **(I)-T** by the reaction of either 1,1'-thiocarbonyldiimidazole (W = S) or 1,1'-carbonyldiimidazole (W = O).

Scheme U illustrates a route for the synthesis of compounds of formula **(I)-U** wherein G is S; and A, B, Y, R^2, R^3, and R^4 are as defined herein..

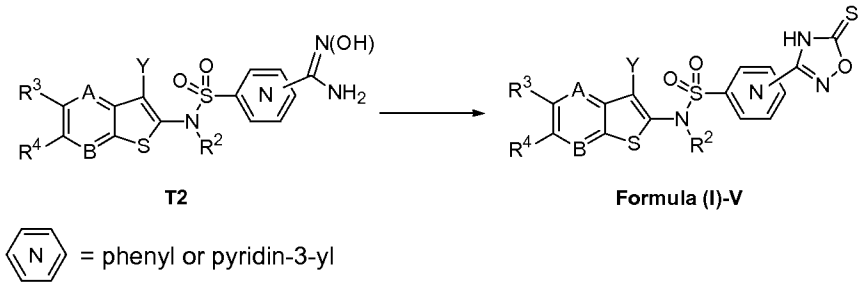
Scheme U



A compound of the formula **T2** may be treated with thionyl chloride, in the presence of a non-nucleophilic base, such as pyridine, to afford a compound of the formula **(I)-U**.

Scheme V illustrates a route for the synthesis of compounds of the formula **(I)-V** wherein G is S; and A, B, Y, R^2, R^3, and R^4 are as defined herein.

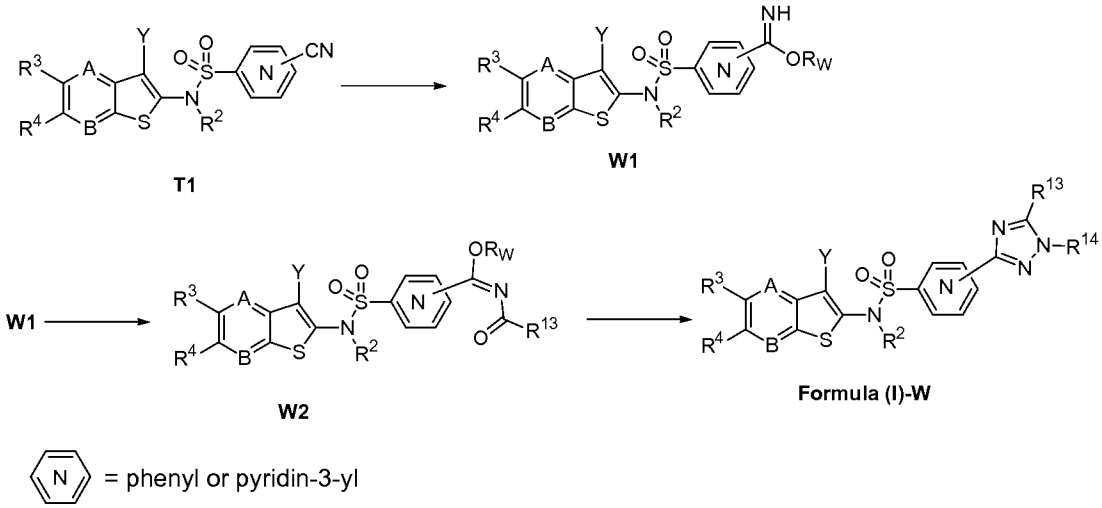
Scheme V



A compound of the formula **T2** may be treated with a base, such as sodium hydride, in the presence of carbon disulfide, to afford a compound of the formula **(I)-V**.

Scheme W illustrates a route for the synthesis of compounds of the formula **(I)-W** wherein G is S; and A, B, Y, R^2, R^3, R^4, R^{13}, and R^{14} are as defined herein.

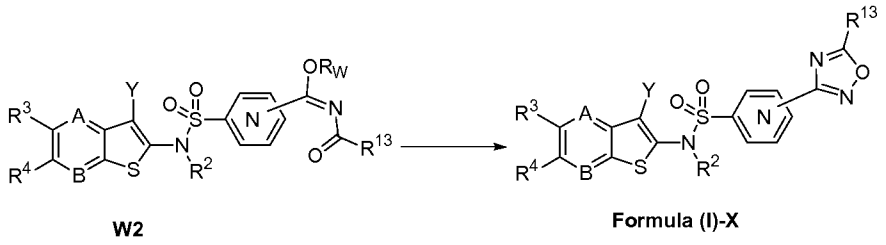
Scheme W



A compound of the formula **T1**, may be converted to a compound of the formula **W1** wherein R_W is methyl or ethyl, by treatment of a compound of the formula **T1** with an alcohol, such as methanol or ethanol, in the presence of hydrochloric acid,. A compound of the formula **W1** may be treated with a base, such as triethylamine, in the presence of a R^{13}-substituted acid chloride, to afford a compound of the formula **W2**. Treatment of a compound of the formula **W2** with a R^{14}-substituted hydrazine, may afford a compound of the formula **(I)-W**.

Scheme X illustrates a route for the synthesis of compounds of the formula **(I)-X** wherein G is S; and A, B, Y, R^2, R^3, R^4, and R^{13} are as defined herein.

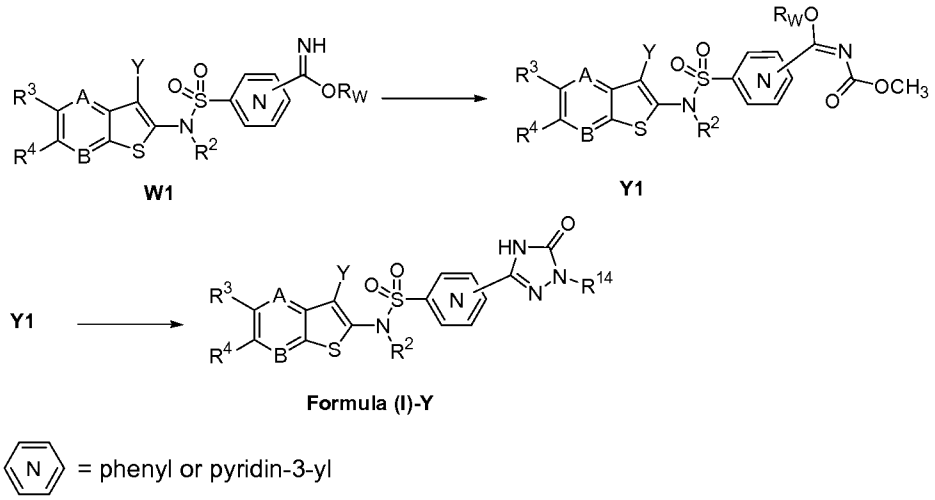
Scheme X



A compound of the formula **W2** may be treated with a base, such as sodium methoxide, and in the presence of hydroxylamine hydrochloride, to afford a compound of the formula **(I)-X**.

Scheme Y illustrates a route for the synthesis of compounds of the formula **(I)-Y** wherein G is S; and A, B, Y, R^2, R^3, R^4, and R^{14} are as defined herein.

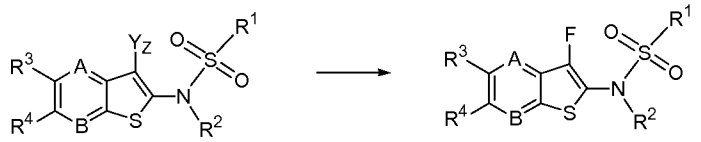
Scheme Y



A compound of the formula **W1** may be treated with 2,4,6-trimethylpyridine, in the presence of methyl chloroformate, to afford a compound of the formula **Y1**. Treatment of a compound of the formula **Y1** with a R^{14}-substituted hydrazine, may afford a compound of the formula **(I)-Y**.

Scheme Z illustrates a route for the synthesis of compounds of the formula **(I)-Z** wherein R^3 is a substituent as defined herein other than bromo; G is S; and A, B, R^1, R^2, and R^4 are as defined herein.

Scheme Z

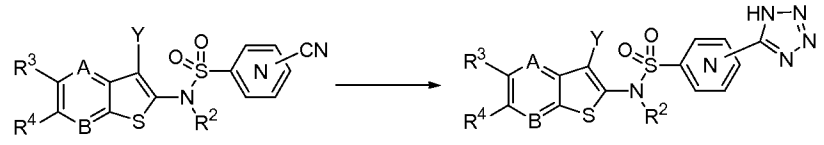


Z1 Formula (I)-Z

A compound of the formula **Z1** may be prepared according to the chemistry described in scheme A. A compound of the formula **Z1**, wherein Y_Z is bromo or iodo, may be reacted with an C_{1-4} alkyllithium, followed by treatment with an electrophilic fluorinating reagent such as $FClO_3$ or *N*-fluorobenzenesulfonamide, to afford a compound of the formula **(I)-Z**.

Scheme AA illustrates a route for the synthesis of compounds of the formula **(I)-AA** wherein G is S; and A, B, Y, R^2, R^3, and R^4 are as defined herein.

Scheme AA



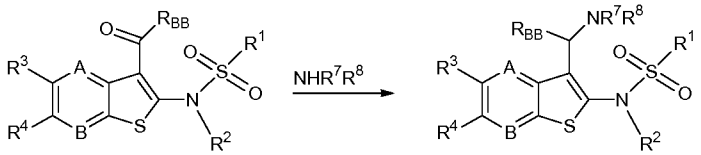
T1 Formula (I)-AA

= phenyl or pyridin-3-yl

A compound of the formula **T1** may be treated with sodium azide, in the presence of a ammonium chloride or triethylamine hydrochloride, to afford a compound of the formula **(I)-AA**.

Scheme BB illustrates a route for the synthesis of compounds of the formula **(I)-BB** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; Y is C_{1-2} alkyl substituted with NR^7R^8; and R^1, R^2, R^3 and R^4 are as defined herein.

Scheme BB



BB1 Formula (I)-BB

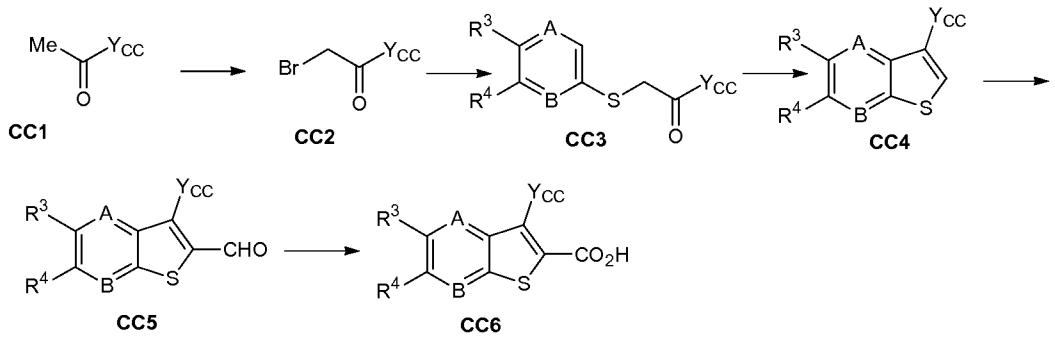
R_{BB} is H or Me

A compound of the formula **BB1** (R_{BB} is hydrogen or methyl) may be reacted with an amine of the formula **NHR^7R^8** (wherein R^7 is other than C_{1-3} alkylcarbonyl and

C_{1-3} alkylsulfonyl and R^8 is C_{1-4} alkyl) in the presence of a hydride source such as sodium borohydride, sodium triacetoxyborohydride, and the like, in an organic solvent to afford a compound of the formula **(I)-BB**. A compound of the formula **(I)-BB** wherein R^7 is hydrogen may be treated in the presence of a base, optionally in the presence of an organic solvent, with an appropriately substituted acylating agent such as a C_{1-3}alkyl acid chloride, or with an appropriately substituted sulfonylating agent, to afford a corresponding compound of the present invention wherein R^7 is C_{1-3} alkylcarbonyl or C_{1-3} alkylsulfonyl, respectively.

Scheme CC illustrates a route for the synthesis of intermediates of the formula **CC6** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; Y_{CC} is C_{1-6}alkyl; and R^1, R^2, R^3 and R^4 are as defined herein.

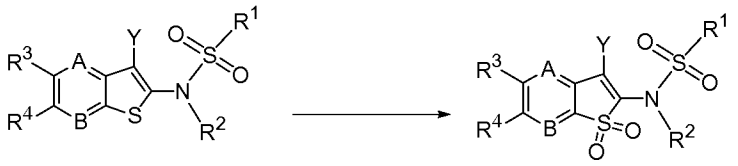
Scheme CC



A compound of the formula **CC1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. A compound of the formula **CC1** may be converted to a methyl bromide of the formula **CC2** by the action of bromine in methanol. The bromide of a compound of the formula **CC2** may undergo a nucleophilic displacement with an appropriately substituted thiol, in the presence of a base, to afford a compound of the formula **CC3**, which may subsequently be cyclized in the presence of PPA, optionally in an organic solvent such as chlorobenzene, to afford a compound of the formula **CC4**. Deprotonation with an organometallic base such as *n*-butyllithium followed by the addition of DMF affords an aldehyde of the formula **CC5**. The aldehyde group may be oxidized in the presence of a strong oxidizing agent such as potassium permanganate to afford a carboxylic acid of the formula **CC6**, which may be converted to a compound of the general formula **(I)** by the synthetic methods outlined in scheme A.

Scheme DD illustrates a route for the synthesis of compounds of the formula **(I)-DD** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is $S(O_2)$; R^1 is other than an C_{1-3} alkylthio-substituted substituent; and Y, R^2, R^3 and R^4 are as defined herein.

Scheme DD

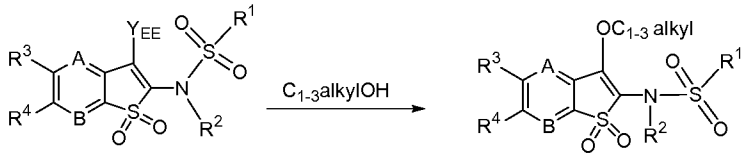


DD1 Formula (I)-DD

A compound of the formula **DD1** may be prepared by the synthetic methods described herein. A compound of the formula **DD1** may be treated with and oxidizing agent such as mCPBA, oxone, peracetic acid, and the like, in an organic solvent such as chloroform to afford a compound of the formula **(I)-DD**.

Scheme EE illustrates a route for the synthesis of compounds of the formula **(I)-EE** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is $S(O_2)$; Y is C_{1-3} alkoxy; and R^1, R^2, R^3 and R^4 are as defined herein.

Scheme EE

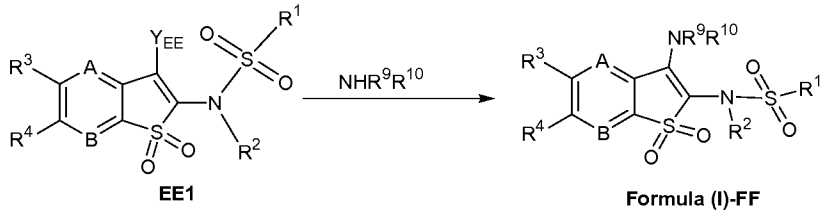


EE1 Formula (I)-EE

A compound of the formula **EE1** wherein Y_{EE} is chloro, bromo, or iodo, may be treated with a strong non-nucleophilic base such as sodium hydride, a lower alkoxide, sodium hydroxide or potassium hydroxide, DBU, and the like; in the presence of a C_{1-3}alcoholic solvent; to afford the corresponding compound of the formula **(I)-EE** wherein Y is a C_{1-3}alkoxy group.

Scheme FF illustrates a route for the synthesis of compounds of the formula **(I)-FF** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is $S(O_2)$; Y is NR^9R^{10}; R^1 is other than C_{1-6} alkyl substituted with bromo; and R^2, R^3 and R^4 are as defined herein.

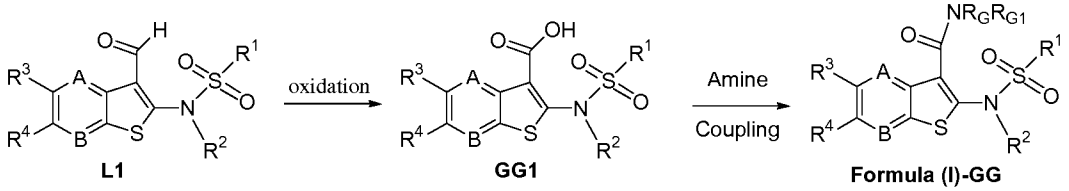
Scheme FF



A compound of the formula **EE1** may be treated with an appropriately substituted amine of the formula **NHR^9R^{10}** (wherein R^9 is other than C_{1-3} alkylcarbonyl and C_{1-3} alkylsulfonyl and R^{10} is C_{1-4} alkyl) in an aprotic organic solvent to afford a compound of the formula **(I)-FF**. A compound of the formula **(I)-FF** wherein R^9 is hydrogen may be treated in the presence of a base, optionally in the presence of an organic solvent, with an appropriately substituted acylating agent such as a C_{1-3}alkyl acid chloride, or with an appropriately substituted sulfonylating agent, to afford a corresponding compound of the present invention wherein R^9 is C_{1-3} alkylcarbonyl or C_{1-3} alkylsulfonyl, respectively.

Scheme GG illustrates a route for the synthesis of compounds of the formula **(I)-GG** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 and R^2 are other than a nitrogen containing heteroaryl; R_G and R_{G1} are independently hydrogen or methyl such that Y is aminocarbonyl, methylaminocarbonyl, or dimethylaminocarbonyl; and R^3 and R^4 are as defined herein.

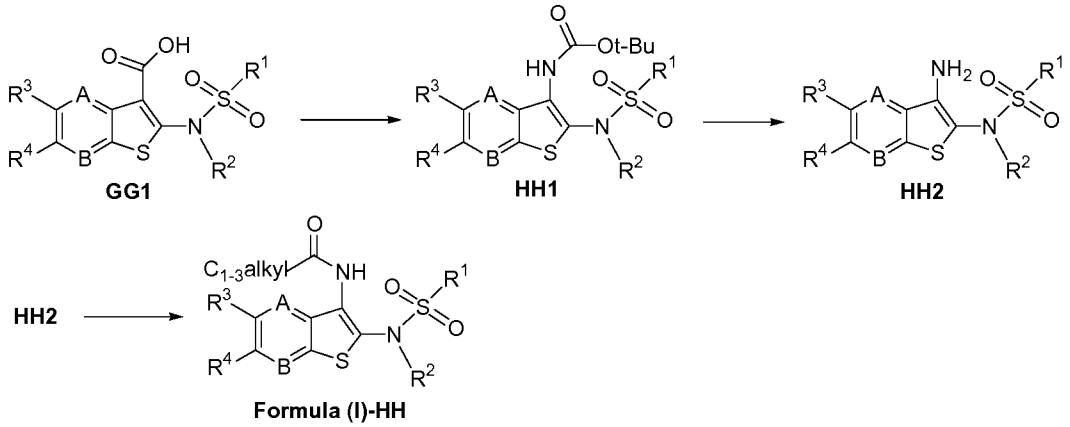
Scheme GG



A compound of the formula **L1** wherein Y is formyl may be converted to a carboxylic acid of the formula **GG1** by the action of an oxidizing agent such as potassium permanganate. Treatment of a compound of the formula **GG1** with an amine of the formula **NHR_GR_{G1}** in the presence of a coupling agent such as HBTU, DCC, HATU, and the like; and a tertiary amine such as diisopropylethylamine; in an aprotic solvent, affords an amide of the formula **(I)-GG**.

Scheme HH illustrates a route for the synthesis of compounds of the formula **(I)-HH** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; Y is NR^9R^{10}, R^9 is C_{1-3} alkylcarbonyl or C_{1-3} alkylsulfonyl, and R^{10} is hydrogen.

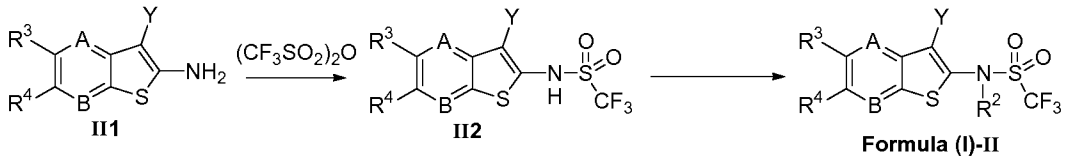
Scheme HH



A compound of the formula **GG1** may be treated with DPPA and *t*BuOH in the presence of a tertiary amine such as DIEA to afford a *t*-butyl carbamate of the formula **HH1**. Upon treatment with a mineral acid such as HCl in dioxane, the corresponding amine of the formula **HH2** may be prepared. The amino group of a compound of the formula **HH2** may be acylated with a C_{1-3}alkyl-substituted acid chloride or anhydride to afford a compound of the formula **(I)-HH**. Further treatment with a conventional C_{1-3} alkylating agent may provide compounds of the present invention wherein R^{10} is C_{1-3}alkyl. Likewise, a compound of the formula **HH2** may be treated with an appropriately substituted sulfonylating agent to afford a corresponding compound of the present invention wherein R^9 is C_{1-3} alkylsulfonyl, respectively.

Scheme II illustrates a route for the synthesis of compounds of the formula **(I)-II** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 is CF_3; and Y, R^2, R^3 and R^4 are as defined herein.

Scheme II

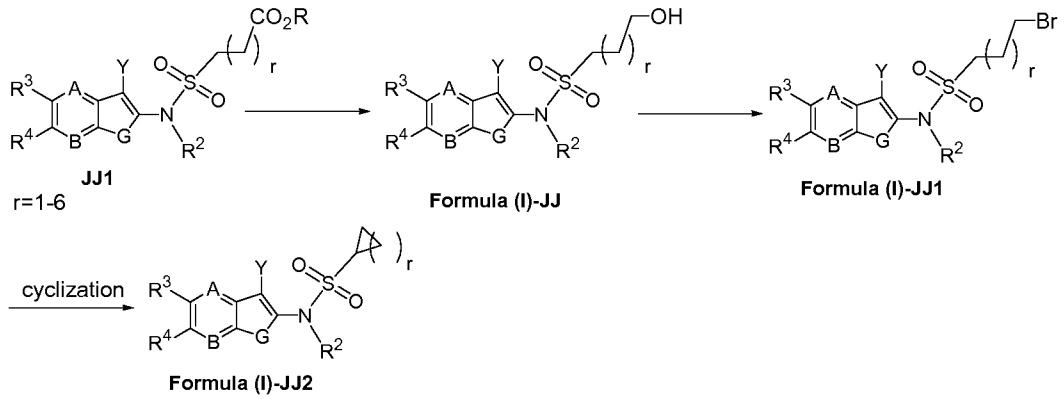


A compound of the formula **II1** may be converted to a compound of the formula **II2** by the action of trifluoromethanesulfonic anhydride and a tertiary amine followed

by treatment with hydroxide. A compound of the formula **II2** may be treated with a base such as sodium hydride, lithium bis(trimethylsilyl)amide, *n*-butyllithium or potassium *tert*-butoxide followed by alkylation with a compound of the formula, $\mathbf{R^2X}$, where X is a leaving group such as bromo, chloro, iodo, tosylate, mesylate, and the like, to afford a compound of the formula **(I)-II**. Alternatively, a compound of the formula **II2** may be treated with a triarylphosphine such as triphenylphosphine, tri-*o*-tolylphosphine, tri-2-furylphosphine and the like; a C_{1-6} dialkyl azodicarboxylate such as diethyl-, diisopropyl-, or di-*t*-butyl-azodicarboxylate, and the like; and an appropriately substituted alcohol, $\mathbf{R^2OH}$, to afford a compound of the formula **(I)-II**.

Scheme JJ illustrates a route for the synthesis of compounds of the formula **(I)-JJ** wherein R^1 is C_{1-6} alkyl substituted with hydroxy; formula **(I)-JJ1** wherein R^1 is C_{1-6} alkyl substituted with bromo; and formula **(I)-JJ2** wherein R^1 is unsubstituted C_{3-8} cycloalkyl; A and B are $C(R^5)$ and $C(R^6)$, respectively; and G, Y, R^2, R^3 and R^4 are as defined herein.

Scheme JJ

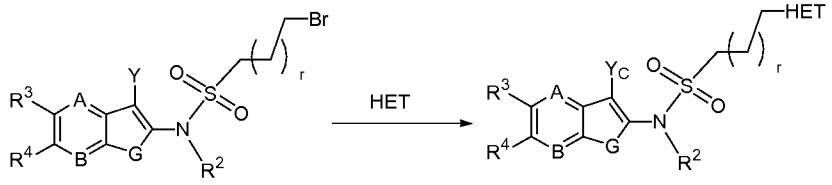


A compound of the formula **JJ1** (wherein R is C_{1-4} alkyl) may be prepared according to the synthetic methods outlined in scheme A using an appropriately substituted alkylating agent of the formula $\mathbf{R^2X}$ or $\mathbf{R^2OH}$. A compound of the formula **JJ1** may be converted to its corresponding alcohol of the formula **(I)-JJ** by the action of a reducing agent such as lithium aluminum hydride, lithium borohydride, and the like. The alcohol of the formula **(I)-JJ** may be treated with a brominating agent such as thionyl bromide; phosphorus tribromide; carbon tetrabromide in the presence of a triarylphosphine such as triphenylphosphine, tri-*o*-tolylphosphine, tri-2-furylphosphine; and the like, to afford a bromide of the formula **(I)-JJ1** wherein R^1 is C_{1-6} alkyl substituted with bromo. Treatment with a base such as sodium imidazolide, DBU,

potassium tert-butoxide, and LDA, affords a cyclized product of the formula **(I)-JJ2** wherein R^1 is unsubstituted C_{3-8} cycloalkyl.

Scheme KK illustrates a route for the synthesis of compounds of the formula **(I)-JJ** wherein R^1 is C_{1-6} alkyl substituted with a heteroaryl as defined herein, wherein the point of attachement is a nitrogen atom; A and B are $C(R^5)$ and $C(R^6)$, respectively; and G, Y, R^2, R^3 and R^4 are as defined herein.

Scheme KK

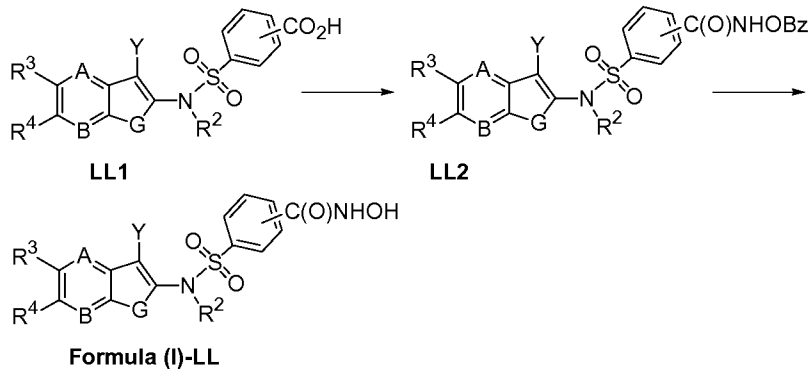


Formula (I)-JJ1 **Formula (I)-KK**

A bromide of the formula **(I)-JJ1** may be displaced by a 5 to 6 membered NH-containing heteroaryl (HET) in an organic solvent to afford a compound of the formula **(I)-KK**.

Scheme LL illustrates a route for the synthesis of compounds of the formula **(I)-LL** wherein R^1 is phenyl substituted with C(O)NHOH; and G, A, B, Y, R^2, R^3 and R^4 are as defined herein. One skilled in the art will recognize that added protection and deprotection steps may be required for certain chemical groups of Y that are sensitive to the reaction conditions described in Scheme LL.

Scheme LL



LL1 **LL2**

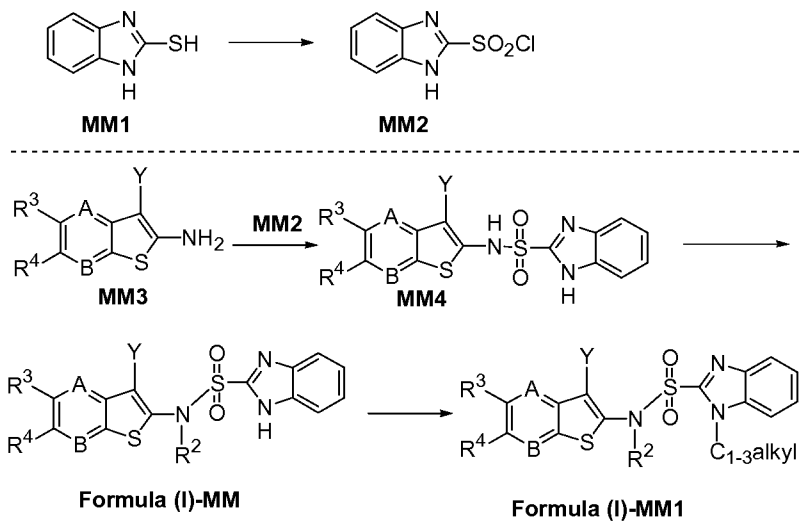
Formula (I)-LL

A compound of the formula **LL1** may be treated with *O*-benzyl-hydroxylamine in the presence of a coupling agent such as EDC, HATU, HBTU, and the like to afford a compound of the formula **LL2**. Removal of the benzyl group by the action of boron

tribromide or TFA in an organic solvent such as DCM; or with a palladium catalyst in the presence of a hydrogen source such as hydrogen gas; affords a compound of the formula **(I)-LL**.

Scheme MM illustrates a route for the synthesis of compounds of the formula **(I)-MM** wherein R^1 is heteroaryl; and formula **(I)-MM1** wherein R^1 is a benzo-fused heteroaryl substituted at a nitrogen atom within the ring with C_{1-3} alkyl; G is S; and Y, A, B, R^2, R^3 and R^4 are as defined herein.

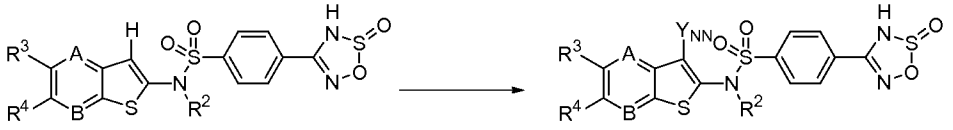
Scheme MM



A compound of the formula **MM1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. A compound of the formula **MM1** may be converted to a useful intermediate of the formula **MM2** by the action of aqueous acetic acid and chlorine gas. A compound of the formula **MM3** may be sulfonylated with a sulfonyl chloride of the formula **MM2** to afford a compound of the formula **MM4**. The R^2 group of the present invention may be installed as previously described herein to afford a compound of the formula **(I)-MM**. Treatment of a compound of the formula **(I)-MM** with a base such as DBU in the presence of an alkylating agent such as a C_{1-3} alkyl halide or dimethylsulfate in DMF affords a methylated compound of the formula **(I)-MM1** of the present invention.

Scheme NN illustrates a route for the synthesis of compounds of the formula **(I)-NN** wherein G is S; Y_{NN} is bromo, chloro, iodo; and A, B, R^2, R^3, and R^4 are as defined herein.

Scheme NN

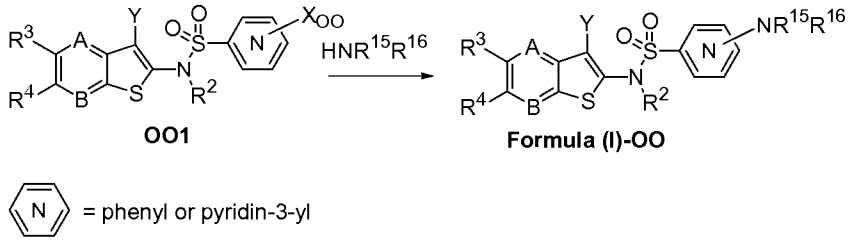


Formula (I)-U **Formula (I)-NN**

A compound of the formula **(I)-U** may be treated with *N*-chlorosuccinimide or chlorine to afford a compound of the formula **(I)-NN**, wherein Y_{NN} is chloro. Likewise, a compound of the formula **(I)-NN** wherein Y_{NN} is bromo may be afforded by the action of *N*-bromosuccinimide or bromine; and a compound of the formula **(I)-NN** wherein Y_{NN} is iodo may be afforded by the action of *N*-iodosuccinimide or iodine.

Scheme OO illustrates a route for the synthesis of compounds of the formula **(I)-OO** wherein G is S; R^1 is a ring selected from phenyl or pyridin-3-yl, wherein said ring is substituted with $NR^{15}R^{16}$ wherein $NR^{15}R^{16}$ is other than NH_2; and A, B, Y, R^2, R^3, and R^4 are as defined herein.

Scheme OO



OO1 **Formula (I)-OO**

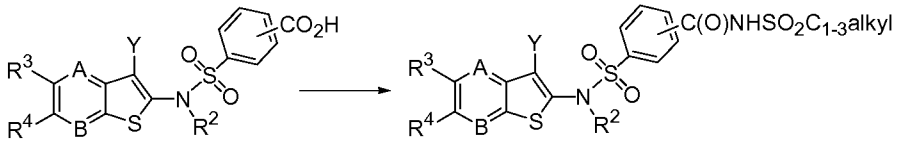
 = phenyl or pyridin-3-yl

A compound of the formula **OO1** (wherein X_{oo} is a reactive leaving group such as fluoro, chloro, or bromo) may be prepared according to the synthetic methods described herein. A compound of the formula **OO1** may be treated with a cyclic or acyclic amine of the formula $\mathbf{HNR^{15}R^{16}}$ under basic conditions, in the presence of a palladium catalyst such as $Pd_2(dba)$ and an appropriate ligand such as 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, to afford a compound of the formula **(I)-OO**.

Scheme PP illustrates a route for the synthesis of compounds of the formula **(I)-PP** wherein G is S; R^1 is phenyl substituted with $C(O)NR^{17}R^{18}$ wherein R^{17} is C_{1-3} alkylsulfonyl and R^{18} is hydrogen; and A, B, Y, R^2, R^3, and R^4 are as defined herein.

One skilled in the art will recognize that added protection and deprotection steps may be required for certain chemical groups of Y that are sensitive to the reaction conditions described in Scheme PP.

Scheme PP

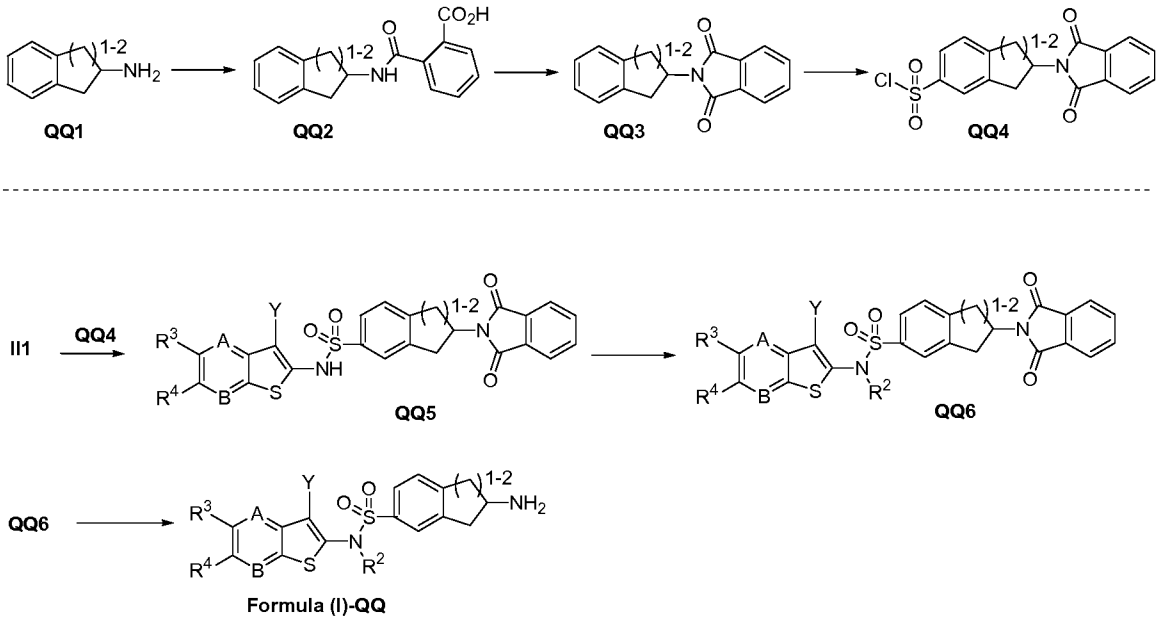


Formula (I)-P Formula (I)-PP

A compound of the formula **(I)-P** may be treated with the coupling agent CDI, followed by the addition of a C_{1-3}alkylsulfonamide in the presence of DBU and dimethylaminopyridine to afford a compound of the formula **(I)-PP**.

Scheme QQ illustrates a route for the synthesis of compounds of the formula **(I)-QQ** wherein G is S; R^1 is a ring selected from indanyl or tetralinyl, wherein said ring is attached via an unsaturated carbon atom and the unsaturated portion of the ring is substituted with an amino, alkylamino, or dialkylamino group; and A, B, Y, R^2, R^3, and R^4 are as defined herein.

Scheme QQ



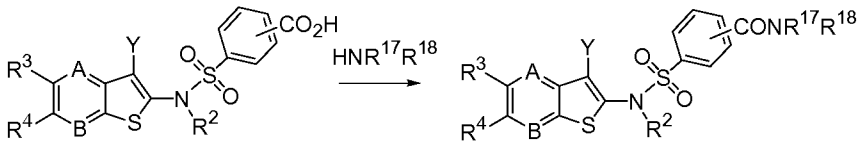
A compound of the formula **QQ1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. A

compound of the formula **QQ1** may be treated with phthalic anhydride to afford a compound of the formula **QQ2**, which may be converted to a compound of the formula **QQ3** by the action of DMF and DMAP. A compound of the formula **QQ3** may be treated with chlorosulfonic acid to afford a compound of the formula **QQ4**. A compound of the formula **II1** may be sulfonylated with a compound of the formula **QQ4** in the presence of an aprotic organic base, such as pyridine, to afford a compound of the formula **QQ5**. A compound of the formula **QQ5** may be alkylated as described herein to install the R^2 group and form a compound of the formula **QQ6**. Treatment of the phthalimido group of a compound of the formula **QQ6** with hydrazine in methanol affords a compound of the formula **(I)-QQ**.

Scheme RR illustrates a route for the synthesis of compounds of the formula **(I)-RR** wherein G is S; R^1 is phenyl substituted with $C(O)NR^{17}R^{18}$; and A, B, Y, R^2, R^3, and R^4 are as defined herein.

One skilled in the art will recognize that added protection and deprotection steps may be required for certain chemical groups of Y that are sensitive to the reaction conditions described in Scheme RR.

Scheme RR

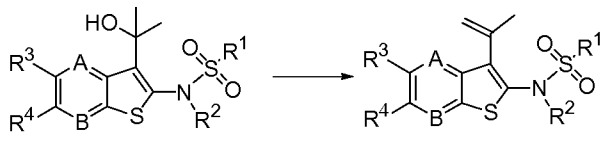


Formula (I)-P **Formula (I)-RR**

A compound of the formula **(I)-P** may be coupled with an amine of the formula **$HNR^{17}R^{18}$**, wherein R^{17} and R^{18} are as defined herein, in the presence of a coupling agent such as HATU, DCC, and the like, and a tertiary amine such as DIEA, to afford a compound of the formula **(I)-RR**.

Scheme SS illustrates a route for the synthesis of compounds of the formula **(I)-SS** wherein G is S; Y is isopropenyl; and A, B, R^1, R^2, R^3, and R^4 are as defined herein.

Scheme SS

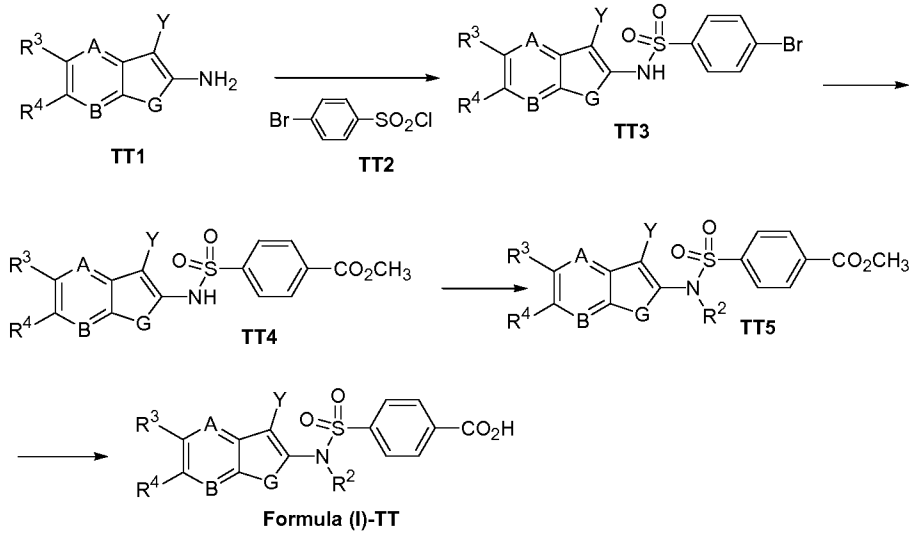


SS1 **Formula (I)-SS**

A compound of the formula **SS1** may be treated with an solution of a mineral acid such as HCl, or an organic acid such as trifluoroacetic acid, to afford a dehydrated compound of the formula **(I)-SS**.

Scheme TT illustrates a route for the synthesis of compounds of the formula **(I)-TT** wherein Y is other than bromo or iodo; R^1 is phenyl substituted with carboxy; R^2 is other than an aromatic bromide; and A, B, G, R^3, and R^4 are as defined herein.

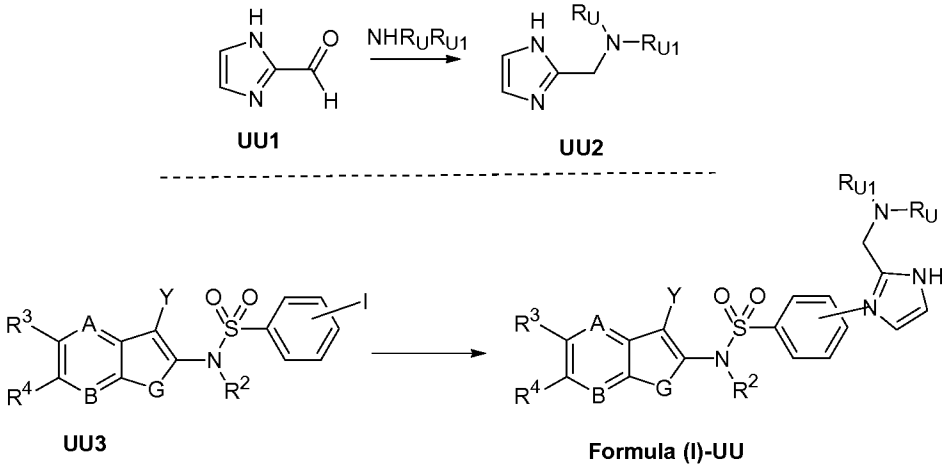
Scheme TT



A compound of the formula **TT1** may be prepared using the synthetic methods outlined herein. A compound of the formula **TT1** may be sulfonylated with a bromo-substituted phenylsulfonyl chloride of the formula **TT2** in the presence of a base such as pyridine or DIEA to afford a compound of the formula **TT3**. A compound of the formula **TT3** may be converted to its corresponding ester of the formula **TT4** by the action of carbon monoxide in the presence of a palladium catalyst and an alcoholic solvent, such as methanol. A compound of the formula **TT4** may be alkylated with an appropriate R^2-substituted alkylating agent as described herein to afford a compound of the formula **TT5** which, upon saponification with hydroxide, affords a carboxylic acid of the formula **(I)-TT**.

Scheme UU illustrates a route for the synthesis of compounds of the formula **(I)-UU** wherein R^1 is phenyl substituted at the 3- or 4-position with imidazolyl substituted with an aminomethyl, methylamino-methyl, or dimethylamino-methyl substitutent; R_U and R_{U1} are independently hydrogen or methyl; and A, B, G, Y, R^2, R^3, and R^4 are as defined herein.

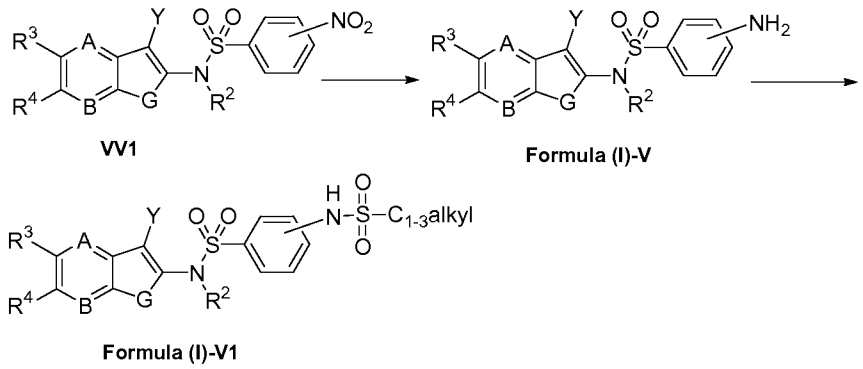
Scheme UU



A compound of the formula **UU1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. A compound of the formula **UU1** may be treated with an amine of the formula $\mathbf{NHR_UR_{U1}}$ in the presence of a hydride source such as sodium borohydride, sodiumtriacetoxyborohydride, and the like, in an alcoholic solvent such as methanol to afford a compound of the formula **UU2**. A 3- or 4-iodo substituted compound of the formula **UU3** may be prepared by the synthetic methods outlined herein. A compound of the formula **UU3** may be coupled with a compound of the formula **UU2** in the presence of a catalyst such as copper iodide in an organic solvent such as DMSO and a base such as K_2CO_3 to afford a compound of the formula **(I)-UU**.

Scheme VV illustrates a route for the synthesis of compounds of the formula **(I)-VV** wherein R^1 is phenyl substituted with $NR^{15}R^{16}$ wherein R^{15} is hydrogen or C_{1-3}alkylsulfonyl; and R^{16} is as defined; and A, B, G, R^2, R^3, and R^4 are as defined herein.

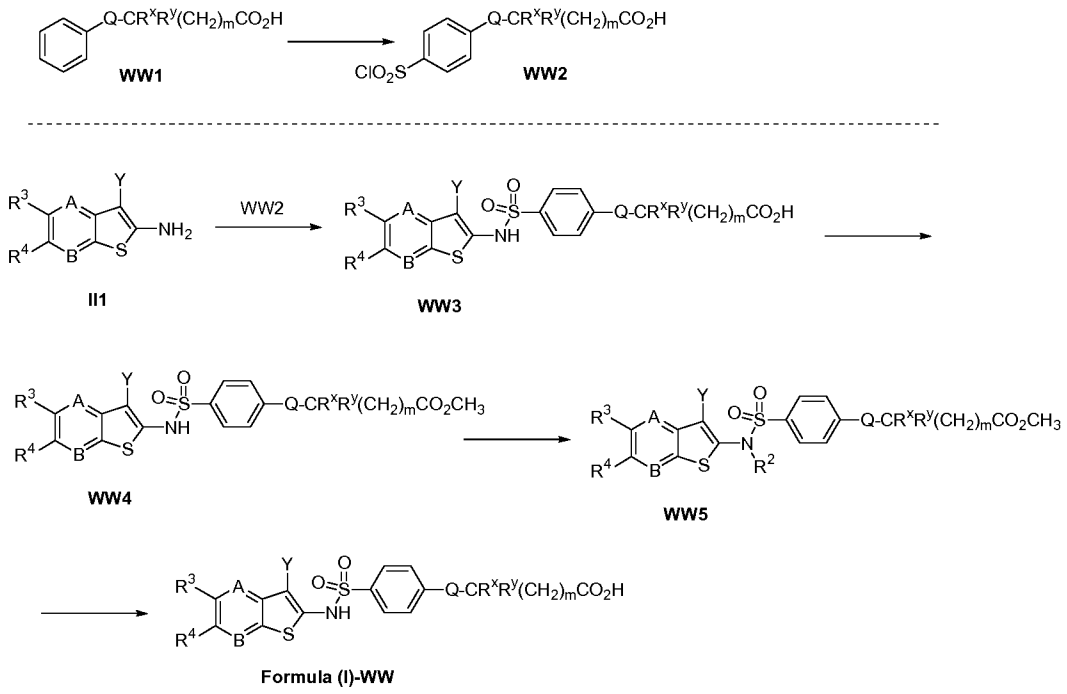
Scheme VV



A compound of the formula **VV1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. The reduction of the nitro group of a compound of the formula **VV1** may be achieved by a number of conventional methods, such as in the presence of a palladium catalyst under a hydrogen gas atmosphere in an alcoholic solvent such as methanol; or, by the action of iron metal in the presence of a suitable acidic reagent or solvent such as hydrochloric acid or acetic acid; or by using zinc and ammonium chloride in methanol and water; to afford the corresponding aniline of the formula **(I)-V**. A compound of the formula **(I)-V** may be sulfonylated using an appropriately substituted sulfonyl chloride in the presence of a base such as pyridine, DIEA, and the like to afford a compound of the formula **(I)-V1**. Compounds of the formulae **(I)-V** and **(I)-V1** may be alkylated using conventional C_{1-3}alkylating agents to afford compounds of the invention wherein R^{16} is an alkyl group.

Scheme WW illustrates a route for the synthesis of compounds of the formula **(I)-WW** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^x and R^y are both hydrogen or taken together with the carbon atom to which they are both attached to form a cyclopropyl ring; Q is a bond; m is 0 or 1; and Y, R^2, R^3 and R^4 are as defined herein.

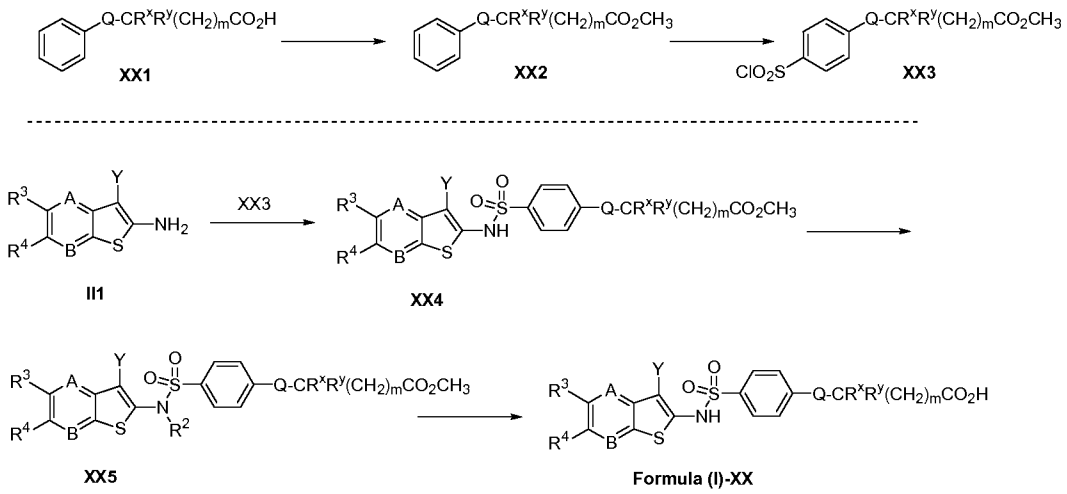
Scheme WW



A compound of the formula **WW1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. A compound of the formula **WW1** may be converted to a compound of the formula **WW2** using chlorosulfonic acid, with or without organic solvent. A compound of the formula **II1** may be sulfonylated with a sulfonyl chloride of the formula **WW2** to afford a compound of the formula **WW3**. A compound of formula **WW3** may be converted to a methyl ester by treatment with a reagent such as diazomethane, concentrated sulfuric acid in methanol, and the like, to afford a compound of the formula **WW4**. The R^2 group of the present invention may be installed as previously described herein to afford a compound of the formula **WW5**. A compound of the formula **WW5** may be converted to the corresponding carboxylic acid, a compound of the formula **(I)-WW**, by the action of agents such as hydroxide, hydrochloric acid, trimethylsilyl iodide, or other reagents and conditions known to one skilled in the art, to effect the conversion of esters to carboxylic acids.

Scheme XX illustrates a route for the synthesis of compounds of the formula **(I)-XX** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^xR^y are each methyl; Q is a bond; m is 0 or 1; and Y, R^2, R^3 and R^4 are as defined herein.

Scheme XX

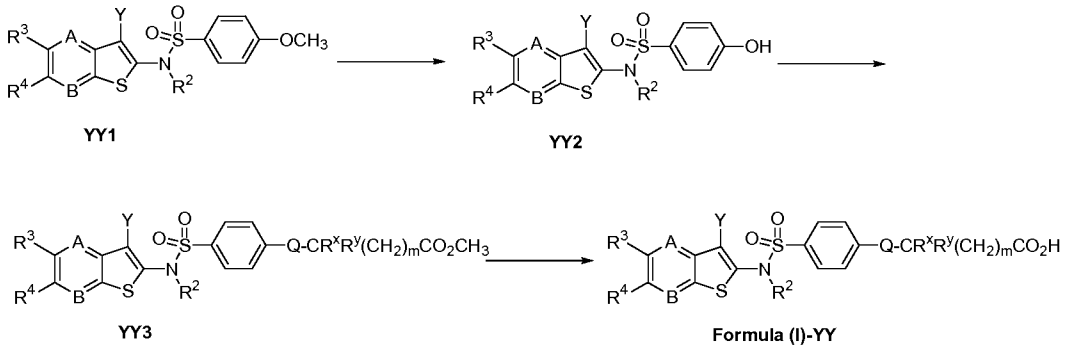


A compound of the formula **XX1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. A compound of the formula **XX1** may be converted to a compound of the formula **XX2** by treatment with a reagent such as diazomethane, concentrated sulfuric acid in

methanol, and the like, to afford a compound of the formula **XX2**. A compound of the formula **XX2** may be converted to a compound of the formula **XX3** using chlorosulfonic acid, with or without organic solvent. A compound of the formula **II1** may be sulfonylated with a sulfonyl chloride of the formula **XX3** to afford a compound of the formula **XX4**. The R^2 group of the present invention may be installed as previously described herein to afford a compound of the formula **XX5**. A compound of the formula **XX5** may be converted to the corresponding carboxylic acid, a compound of the formula **(I)- XX**, by the action of agents such as hydroxide, hydrochloric acid, trimethylsilyl iodide, or other reagents and conditions known to one skilled in the art, to effect the conversion of esters to carboxylic acids.

Scheme YY illustrates a route for the synthesis of compounds of the formula **(I)-YY** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^x and R^y are independently selected from hydrogen or methyl; or R^x and R^y are taken together with the carbon atom to which they are both attached to form a cyclopropyl ring; Q is oxygen; m is 0 or 1; and Y, R^2, R^3 and R^4 are as defined herein.

Scheme YY

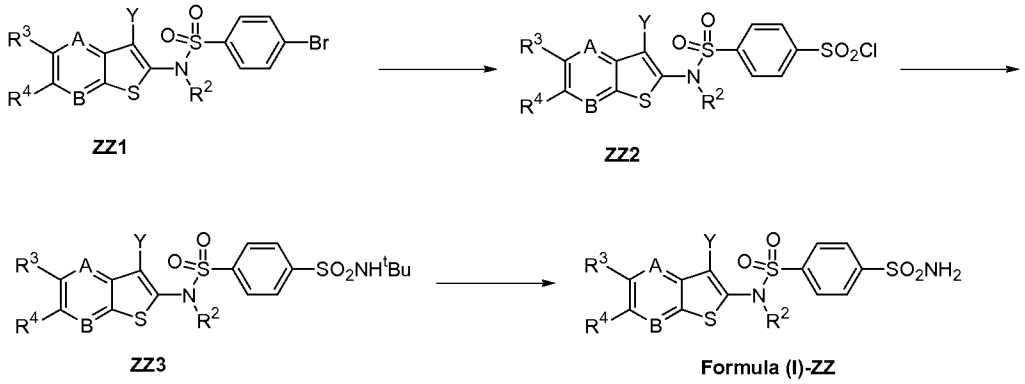


A compound of the formula **YY1** of the present invention may be prepared as previously described herein. A compound of the formula **YY1** may be converted to a compound of the formula **YY2** by treatment with boron tribromide in dichloromethane. A compound of the formula **YY2** may be alkylated with an alkylating agent such as methyl bromoacetate, methyl 2-bromoisobutyrate, and the like, in the presence of a base, such as cesium carbonate or potassium carbonate, in a solvent such as DMF, THF, or DMSO to afford a compound of the formula **YY3**. A compound of the formula **YY3** may be converted to the corresponding carboxylic acid, a compound of the formula **(I)-YY**, by the action of reagents such as hydroxide, hydrochloric acid,

trimethylsilyl iodide, or other reagents and conditions known to one skilled in the art, to effect the conversion of esters to carboxylic acids.

Scheme ZZ illustrates a route for the synthesis of compounds of the formula **(I)-ZZ** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; and Y, R^2, R^3 and R^4 are as defined herein.

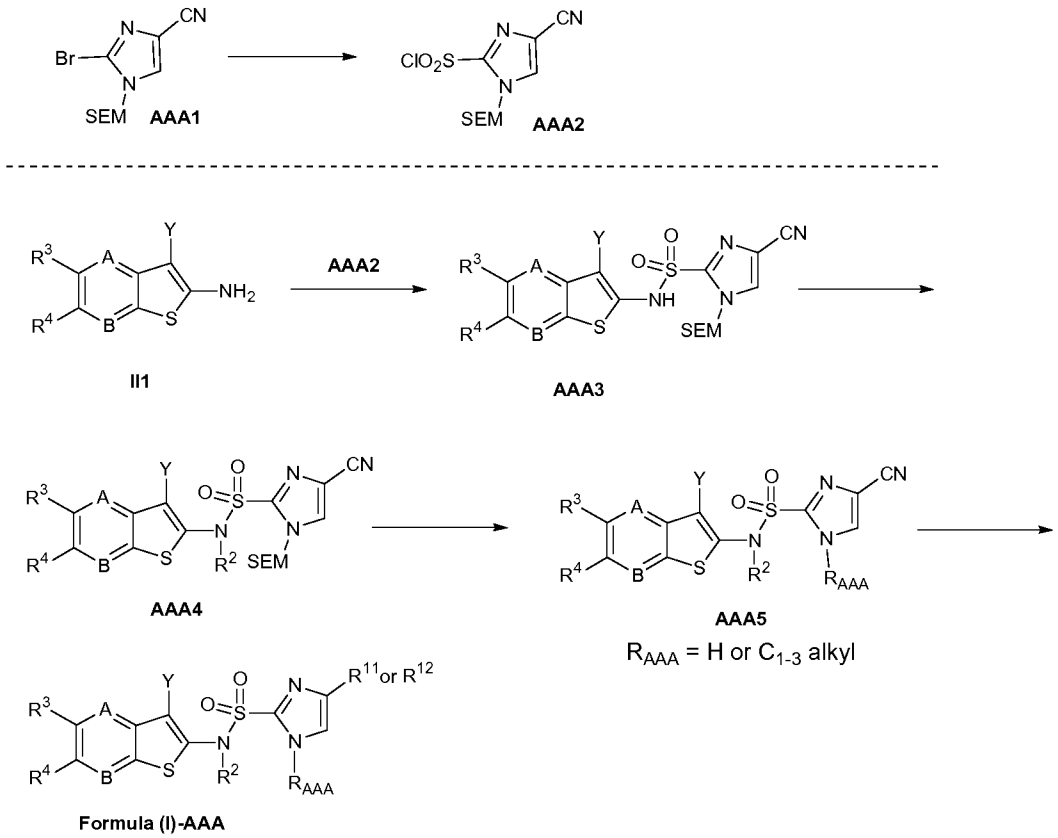
Scheme ZZ



A compound of the formula **ZZ1** of the present invention may be prepared as previously described herein. A compound of the formula **ZZ1** may be treated with a base, such as *n*-butyllithium, and sulfur dioxide, followed by treatment with *n*-chlorosuccinimide, in a solvent such as THF, to afford a compound of formula **ZZ2**. A compound of formula **ZZ2** may be converted to a protected sulfonamide of the formula **ZZ3** by treatment with *tert*-butyl amine. Amino deprotection of a compound of the formula **ZZ3** using conventional chemistry known to one skilled in the art provides a compound of formula **(I)-ZZ**.

Scheme AAA illustrates a route for the synthesis of compounds of the formula **(I)-AAA** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 is imidazolyl substituted with R^{11} or R^{12}; and Y, R^2, R^3 and R^4 are as defined herein.

Scheme AAA



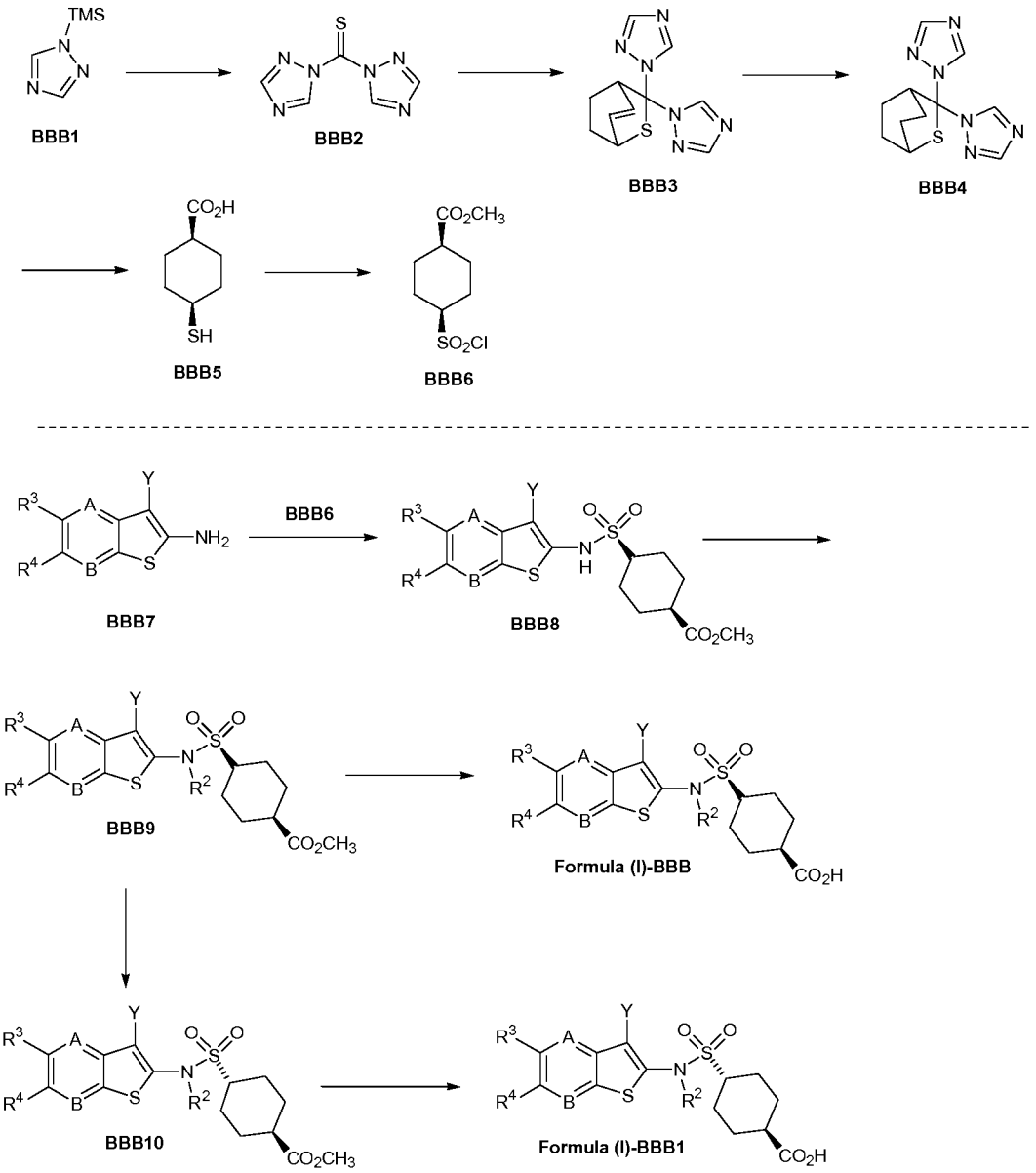
R_{AAA} = H or C_{1-3} alkyl

A compound of the formula **AAA1** may be prepared by known methods such as those described in the scientific literature (WO2007/124369). A compound of the formula **AAA1** may be treated with an alkylmagnesium halide such as ethylmagnesium chloride and a sulfonating agent such as sulfur dioxide, followed by treatment with a chlorinating agent such as *N*-chlorosuccinimide, in a solvent such as THF, to afford a compound of the formula **AAA2**. A compound of the formula **II1** may be sulfonylated with a sulfonyl chloride of the formula **AAA2** to afford a compound of the formula **AAA3**. The R^2 group of the present invention may be installed as previously described herein to afford a compound of the formula **AAA4**. Amino deprotection of a compound of the formula **AAA4** using conventional chemistry known to one skilled in the art provides a compound of the formula **AAA5**, wherein R_{AAA} is hydrogen. A compound of the formula **AAA5** may be converted to a compound of the formula **(I)-AAA** using chemistry previously described herein. Alternatively, a compound of **AAA5** wherein R_{AAA} is hydrogen may be alkylated to form a compound of the formula

AAA5 wherein R_{AAA} is C_{1-3} alkyl, via treatment with a base such as DBU or potassium carbonate; and an electrophile such as iodo(C_{1-3})alkane or dimethyl sulfate; in a solvent such as DMF. A compound of the formula **AAA5** wherein R_{AAA} is C_{1-3} alkyl may be converted to a compound of the formula **(I)-AAA** using chemistry previously described herein.

Scheme BBB illustrates a route for the synthesis of compounds of the formula **(I)-BBB** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 is cyclohexyl substituted at the 4-position with one substitutent selected from C_{1-4} alkoxycarbonyl or carboxy; and Y, R^2, R^3 and R^4 are as defined herein.

Scheme BBB

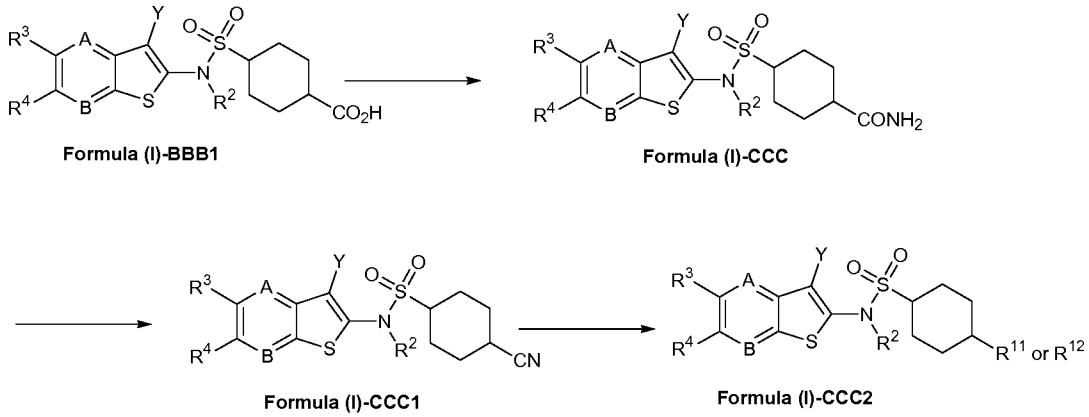


A compound of the formula **BBB6** may be prepared by known methods such as those described in the scientific literature (Can. J. Chem., 64(16), 1986, 2184). A compound of the formula **BBB1**, may be treated with thiophosgene in an aprotic non-polar solvent, such as carbon tetrachloride (J. Org. Chem. 43 (2), 1978, 337-339), to afford a compound of the formula **BBB2**. A compound of the formula **BBB2** may be treated with cyclohexa-1,3-diene in a solvent, such as benzene (J. Org. Chem. 45, 1980, 3713-3716), to afford a compound of the formula **BBB3**. Reduction of the alkenyl

group of formula **BBB3** may be achieved using a catalyst, such as palladium, and a hydrogen source in a solvent such as ethyl acetate, to afford a compound of the formula **BBB4**. A compound of the formula **BBB4** may be treated with an acid catalyst, such as sulfuric acid, in methanol to afford a compound of the formula **BBB5**. A compound of the formula **BBB5** may be treated with chorine gas in appropriate solvents such as acetic acid-water or dichloromethane-water to afford a compound of the formula **BBB6**. A compound of the formula **BBB7** may be sulfonylated with a sulfonyl chloride of the formula **BBB6** to afford a compound of the formula **BBB8**. A compound of formula **BBB8** can be converted to a compound of formula **(I)-BBB** using chemistry previously described herein. A compound of the formula **BBB9** may be treated with hydroxide to effectively epimerize a stereocenter of the cyclohexyl ring, affording a mixture of stereoisomers of the formula **BBB10**. Saponification of the esters using chemistry described herein affords the compounds of the formula **(I)-BBB1**. Pure stereoisomers of the formula **BBB10** or **(I)-BBB1** may be isolated using convention chromatographic techniques.

Scheme CCC illustrates a route for the synthesis of compounds of the formula **(I)-CCC** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 is cyclohexyl substituted at the 4-position with one substitutent selected from cyano, aminocarbonyl, R^{11}, or R^{12}; and Y, R^2, R^3 and R^4 are as defined herein.

Scheme CCC

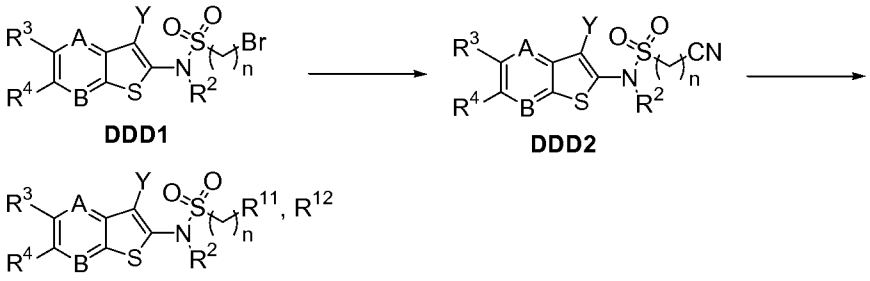


A compound of the formula **(I)-BBB1** may be converted to a compound of the formula **(I)-CCC** by the action of a reagent such as HBTU, CDI or HATU, followed by the addition of gaseous ammonia. A compound of the formula **(I)-CCC** may be converted to a compound of the formula **(I)-CCC1** by the action of reagents such as

trifluoroacetic anhydride in pyridine; in a solvent such as dichloromethane. The cyano group of a compound of the formula **(I)-CCC1** may be converted to R^{11} and R^{12} groups of the present invention using synthetic methods described in the previous schemes to afford a compound of the formula **(I)-CCC2**.

Scheme DDD illustrates a route for the synthesis of compounds of the formula **(I)-DDD** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; R^1 is R^{11} or R^{12}; and Y, R^2, R^3 and R^4 are as defined herein.

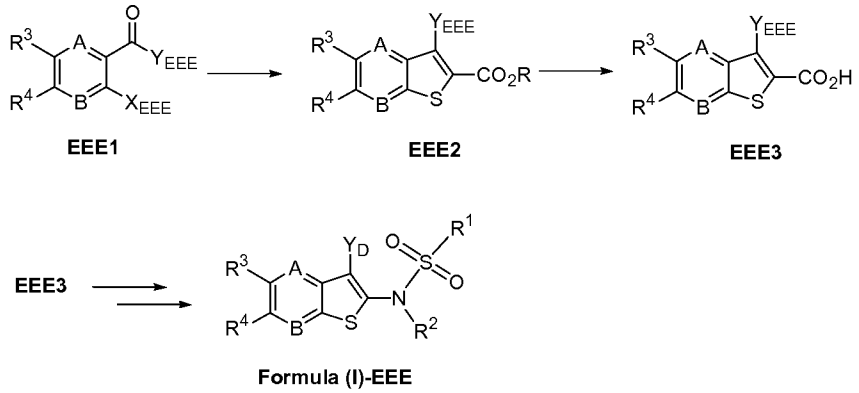
Scheme DDD



A compound of the formula **DDD1** may be prepared using chemistry previously described herein. A compound of the formula **DDD1** may be converted to a compound of the formula **DDD2** using sodium cyanide and a polar aprotic solvent such as DMF or DMSO. The cyano group of a compound of the formula **DDD2** may be converted to R^{11} and R^{12} groups of the present invention using synthetic methods described in the previous schemes to afford a compound of the formula **(I)-DDD**.

Scheme EEE illustrates a route for the synthesis of compounds of formula **(I)-EEE** wherein A and B are $C(R^5)$ and $C(R^6)$, respectively; G is S; Y_{EEE} is hydrogen, alkyl, C_{3-8} cycloalkyl, or trifluoromethyl; and R^1, R^2, R^3 and R^4 are as defined herein.

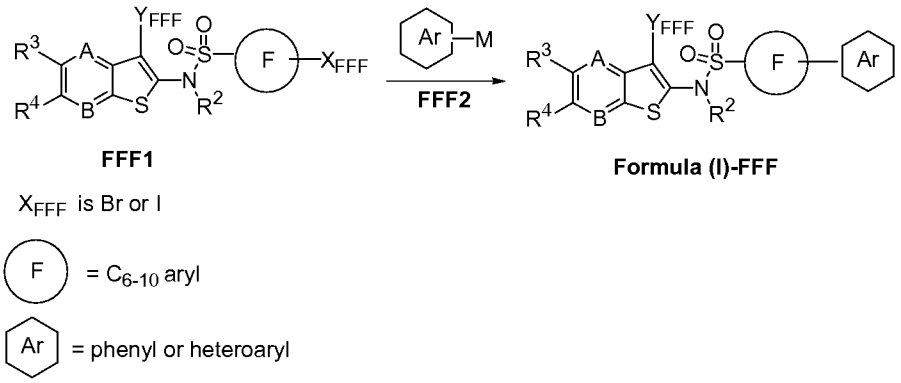
Scheme EEE



A compound of the formula **EEE1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. A compound of the formula **EEE1** wherein X_{EEE} is chloro or fluoro may be reacted with an R-substituted thioglycolate (wherein R is C_{1-6}alkyl) in the presence of base to afford a compound of the formula **EEE2**, which may be saponified to afford a compound of the formula **EEE3** using conventional chemistry known to one skilled in the art. Using synthetic methods outlined in scheme A, a compound of the formula **EEE3** may be converted to compounds of the formula **(I)-EEE**.

Scheme FFF illustrates a route for the synthesis of compounds of the formula **(I)-FFF** wherein Y_{FFF} is other than bromo or iodo; G is S; and R^1 is C_{6-10}aryl substituted with an optionally substituted phenyl; or R^1 is phenyl substituted with a heteroaryl; R^2 is a substituent that does not include bromo or iodo; R^3 is other than bromo; and R^4 and R^6 are as defined herein.

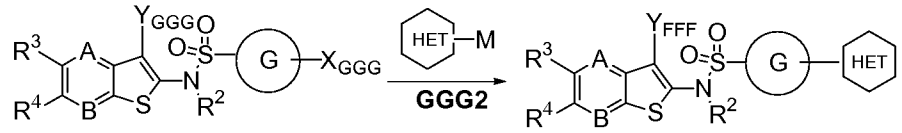
Scheme FFF



A compound of the formula **FFF1** wherein X_{FFF} is bromo or iodo can then prepared according to the chemistry described herein. A compound of the formula **FFF1** may be coupled with a suitably substituted aryl boronic acid, aryl trialkylsilane, aryl tin reagent, and the like of the formula **FFF2** (wherein M is the reactive coupling functionality) by a variety of coupling reactions that are well known to those versed in the art, such as a palladium-catalyzed Suzuki cross-coupling reaction. The reaction may be carried out in the presence or absence of added ligands for palladium; in the presence of a suitable base such as cesium carbonate, potassium carbonate, or sodium carbonate; in an organic solvent such as ethanol, THF, DMF, toluene, and the like. One skilled in the art will recognize that in some instances it may be favorable to reverse the coupling partners such that ring F bears the reactive coupling functionality M, and the Ar ring of the formula **FFF2** bears halide X_{FFF}.

Scheme GGG illustrates a route for the synthesis of compounds of the formula **(I)-GGG** wherein Y_{GGG} is other than bromo or iodo; G is S; and R^1 is heteroaryl substituted with an optionally substituted phenyl or heteroaryl; R^2 is a substituent that does not include bromo or iodo; R^3 is other than bromo; and R^4 and R^6 are as defined herein.

Scheme GGG



GGG1 **Formula (I)-GGG**

X_{GGG} is Br or I

G = heteroaryl

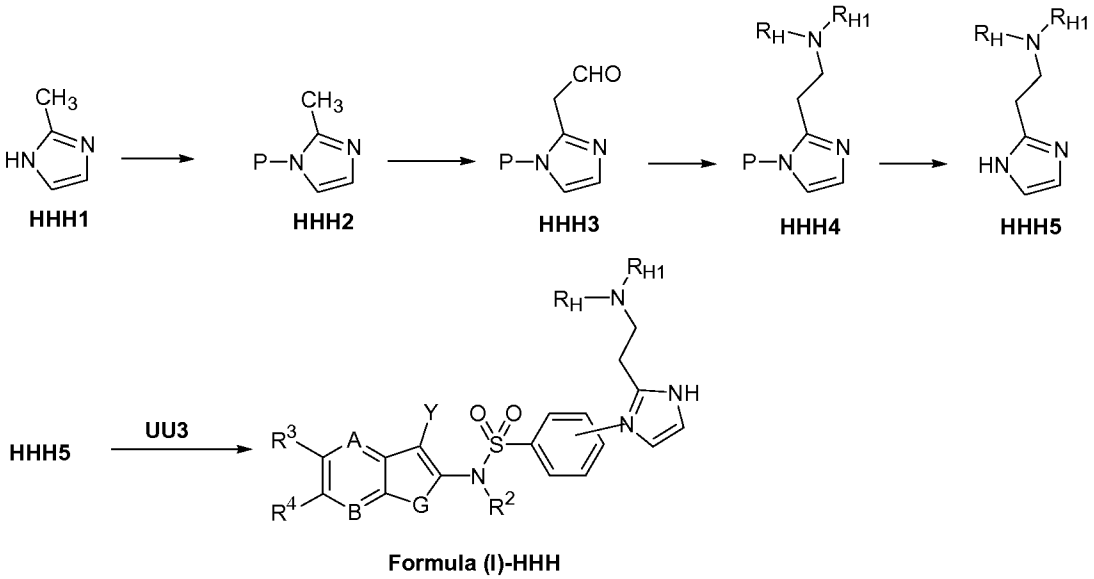
HET = heteroaryl

A compound of the formula **GGG1** wherein X_{GGG} is bromo or iodo can then prepared according to the chemistry described herein. A compound of the formula **GGG1** may be coupled with a suitably substituted heteroaryl boronic acid, heteroaryl trialkylsilane, heteroaryl tin reagent, and the like of the formula **GGG2** (wherein M is the reactive coupling functionality) by a variety of coupling reactions that are well known to those versed in the art, such as a palladium-catalyzed Suzuki cross-coupling reaction. The reaction may be carried out in the presence or absence of added ligands

for palladium; in the presence of a suitable base such as cesium carbonate, potassium carbonate, or sodium carbonate; in an organic solvent such as ethanol, THF, DMF, toluene, and the like. One skilled in the art will recognize that in some instances it may be favorable to reverse the coupling partners such that ring G bears the reactive coupling functionality M, and the HET ring of the formula **GGG2** bears halide X_{GGG}.

Scheme HHH illustrates a route for the synthesis of compounds of the formula **(I)-HHH** wherein R^1 is phenyl substituted at the 3- or 4-position with imidazolyl substituted with an 2-aminoethyl, 2-(C_{1-2} alkylamino)ethyl, or 2-(di(C_{1-2} alkyl)amino)ethyl substitutent; R_H and R_{H1} are independently hydrogen or C_{1-2} alkyl; or R_H and R_{H1} are taken together with the nitrogen atom to which it is attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein the ring formed by di(C_{1-2} alkyl)amino is optionally substituted with C_{1-3}alkyl; and A, B, G, Y, R^2, R^3, and R^4 are as defined herein.

Scheme HHH



A compound of the formula **HHH1** is either commercially available or may be prepared by known methods such as those described in the scientific literature. The nitrogen heteroatom of a compound of the formula **HHH1** may be protected with an appropriate protecting group (P) such as a trityl group, to afford a compound of the formula **HHH2**. A compound of the formula **HHH2** may be treated with a strong base such as *n*-butyllithium followed by the addition of ethylchloroformate in an organic

aprotic solvent afford an aldehyde of the formula **HHH3** (*Synlett* **1999**, No 12, 1875-1878). A compound of the formula **HHH3** may undergo a reductive alkylation with an amine of the formula $\mathbf{NHR_HR_{H1}}$ in the presence of a hydride source such as sodium borohydride, sodiumtriacetoxyborohydride, and the like, in an alcoholic solvent such as methanol to afford a compound of the formula **HHH4**. Conventional removal of the nitrogen protecting group affords a compound of the formula **HHH5**. A compound of the formula **UU3** may be coupled with a compound of the formula **HHH5** in an organic solvent such as DMSO and a base such as K_2CO_3 to afford a compound of the formula **(I)-HHH**.

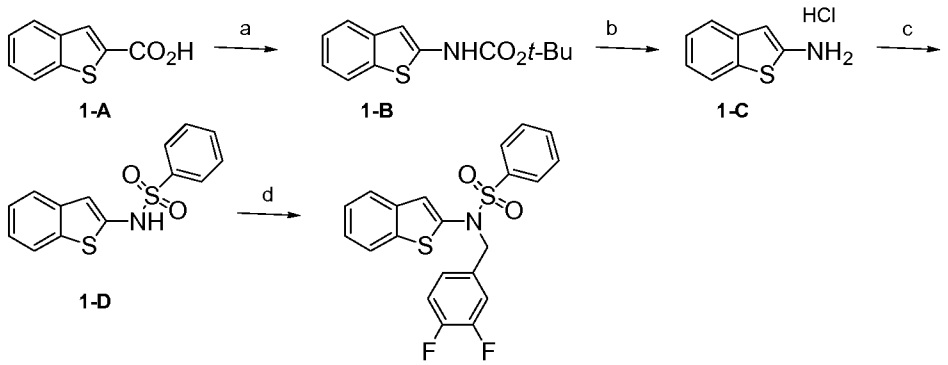
Compounds of Formula (I) that are chiral may be separated into their enantiomers by chromatography on a chiral stationary phase. Alternatively, basic or acidic compounds and intermediates to compounds of the present invention may be converted to diastereomeric salts by mixture with a chiral acid or base, respectively, and resolved into their enantiomers by fractional crystallization.

It is generally preferred that the respective product of each process step be separated from other components of the reaction mixture and subjected to purification before its use as a starting material in a subsequent step. Separation techniques typically include evaporation, extraction, precipitation and filtration. Purification techniques typically include column chromatography (Still, W. C. et. al., *J. Org. Chem.* 1978, *43*, 2921), thin-layer chromatography, crystallization and distillation. The structures of the final products, intermediates and starting materials are confirmed by spectroscopic, spectrometric and analytical methods including nuclear magnetic resonance (NMR), mass spectrometry (MS) and liquid chromatography (HPLC). In the descriptions for the preparation of compounds of this invention, ethyl ether, tetrahydrofuran and dioxane are common examples of an ethereal solvent; benzene, toluene, hexanes and heptanes are typical hydrocarbon solvents and dichloromethane and dichloroethane are representative halogenated hydrocarbon solvents. In those cases where the product is isolated as the acid addition salt the free base may be obtained by techniques known to those skilled in the art. In those cases in which the product is isolated as an acid addition salt, the salt may contain one or more equivalents of the acid. Enantiomers of the compounds of the present invention may be separated using chiral HPLC.

Specific Examples

Reagents were purchased from commercial sources. Microanalyses were performed at Quantitative Technologies, Inc., Whitehouse, New Jersey and are expressed in percentage by weight of each element per total molecular weight. Nuclear magnetic resonance (NMR) spectra for hydrogen atoms were measured in the indicated solvent with (TMS) as the internal standard on a Bruker Avance (300, 400, or 500 MHz) spectrometer. The values are expressed in parts per million downfield from TMS. The mass spectra (MS) were determined on a Micromass Platform LC spectrometer or an Agilent 1100 series LC/MSD spectrometer using an electrospray technique. Unless otherwise noted, the materials used in the examples were obtained from readily available commercial suppliers or synthesized by standard methods known to one skilled in the art of chemical synthesis. The substituent groups, which vary between examples, are hydrogen unless otherwise noted. Where reactions were carried out in a microwave reactor, a Personal Chemistry Smith Synthesizer™ was used.

Example 1



a) DPPA, DIEA, *t*-BuOH; b) HCl, dioxane; c) benzenesulfonyl chloride, pyridine; d) NaH, 3,4-difluorobenzy bromide, DMF.

Benzo[*b*]thiophen-2-yl-carbamic acid *tert*-butyl ester (1-B). A solution of compound **1-A** (14.4 g, 80.6 mmol), *N,N*-diisopropylethylamine (15.5 mL, 88.6 mmol) and diphenylphosphoryl azide (20.8 mL, 96.7 mmol) in *t*-butanol (150 mL) was heated at reflux for 8 h. The solvent was evaporated *in vacuo*, and the residue purified by flash column chromatography on silica gel, eluting with dichloromethane, to afford compound **1-B** as a colorless solid (18.9 g, 94%). ^{1}H-NMR (DMSO-d_6): δ 1.50 (s, 9H),

6.78 (s, 1H), 7.16 (d of d, 1H), 7.27 (d of d, 1H), 7.58 (d, 1H), 7.77 (d, 1H), 10.70 (br s, 1H); MS: *m/z* 250.2 (MH^+).

Benzo[*b*]thiophen-2-ylamine hydrochloride (1-C). Compound **1-B** (1.45 g, 5.81 mmol) was added to a solution of HCl in dioxane (4 N, 20 mL), and the mixture was stirred at rt until all the starting material was consumed. The mixture was diluted with diethyl ether, the product collected by filtration, and washed with diethyl ether, to afford compound **1-C** as an off-white solid (0.89 g, 83%). ^{1}H-NMR (DMSO-d_6): δ 6.43 (s, 1H), 6.8-7.2 (br s, 3H) superimposed on 7.05 (m, 1H) and 7.20 (m, 1H), 7.45 (d, 1H), 7.66 (d, 1H); MS: *m/z* 150.1 (MH^+).

***N*-Benzo[*b*]thiophen-2-yl-benzenesulfonamide (1-D).** Benzenesulfonyl chloride (0.661 mL, 5.15 mmol) was added to a solution of compound **1-C** (0.87 g, 4.69 mmol) in pyridine (10 mL) at 0 °C. The ice bath was removed and the solution was stirred at ambient temperature for 2 h. The solvent was evaporated *in vacuo*, and the residue was partitioned between 2 N HCl and dichloromethane. The organic layer was dried over magnesium sulfate and the solvent evaporated *in vacuo*. The residue was pre-absorbed on silica gel and purified by flash column chromatography, eluting with a gradient of ethyl acetate (10-50%) in heptane, to afford compound **1-D** as a colorless solid (1.19 g, 88%). ^{1}H-NMR ($CDCl_3$): δ 6.96 (s, 1H), 7.25-7.34 (m, 2H), 7.44-7.49 (m, 2H), 7.55-7.66 (m, 3H), 7.84-7.88 (m, 2H); MS: *m/z* 290.1 (MH^+).

Compound 1

***N*-Benzo[*b*]thiophen-2-yl-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide.** Sodium hydride (60% in oil, 100 mg, 2.48 mmol) was added to a solution of compound **1-D** (655 mg, 2.26 mmol) in DMF (8 mL) at 0 °C and the resultant mixture was stirred at 0 °C for 15 min. 3,4-Difluorobenzylbromide (0.318 mL, 2.48 mmol) was added to the reaction mixture, and the resultant solution was stirred at ambient temperature overnight. Water was added to the solution, and the product was extracted into ethyl acetate. The organic layer was washed with water (3X), brine, dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The residue was purified on silica gel by flash column chromatography eluting with a gradient of ethyl acetate (0-40%) in heptane, to afford compound **1** as a colorless solid (570 mg, 61%). ^{1}H-NMR (DMSO-d_6): δ 4.74 (s, 2H), 7.00-7.10 (s superimposed on m, 3H), 7.15-7.21 (m, 1H), 7.26-7.36 (m, 2H), 7.49-7.54 (m, 2H), 7.62-7.67 (m, 3H), 7.73-7.78 (m, 2H); MS: *m/z* 416.1 (MH^+).

Following the procedure described above for Example 1 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 2

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-1-methyl-1*H*-imidazole-4-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.02 (s, 3H), 3.72 (s, 3H), 4.82 (s, 2H), 7.10-7.17 (m, 1H), 7.32-7.41 (m, 4H), 7.63-7.68 (m, 1H), 7.79-7.84 (m, 1H), 7.88 (s, 1H), 8.00 (s, 1H); MS: *m/z* 434.26 (MH^+).

Compound 3

***N*-Benzo[*b*]thiophen-2-yl-*N*-(3-fluoro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.76 (s, 2H), 6.94-6.98 (m, 3H), 7.27-7.32 (m, 4H), 7.48-7.53 (d of d, 2H), 7.60-7.64 (m, 3H), 7.66-7.78 (m, 2H); MS: *m/z* 398.1 (MH^+).

Compound 4

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-benzyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.81 (s, 2H), 7.10 (t, 2H), 7.28-7.32 (m, 2H), 7.46-7.52 (m, 2H), 7.67-7.72 (m, 3H), 7.82 (t, 1H), 7.90-7.97 (m, 3H); MS: *m/z* 432.1 (MH^+).

Compound 5

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-quinolin-8-ylmethyl-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 5.56 (s, 2H), 7.43 (m, 3H), 7.57 (t, 1H), 7.63-7.74 (m, 3H), 7.78-7.96 (m, 6H), 8.31 (d of d, 1H), 8.75 (d of d, 1H); MS: *m/z* 465.1 (MH^+).

Compound 6

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.86 (s, 2H), 7.29 (d, 2H), 7.40-7.51 (m, 4H), 7.67-7.72 (m, 3H), 7.80 (t, 1H), 7.90-7.97 (m, 3H); MS: *m/z* 498.1 (MH^+).

Compound 7

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.93 (s, 2H), 7.41-7.54 (m, 3H), 7.65-7.73 (m, 5H), 7.83 (t, 1H), 7.92-8.00 (m, 3H); MS: *m/z* 500.1 (MH^+).

Compound 8

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethyl-benzyl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.94 (s, 2H), 7.46-7.60 (m, 4H), 7.66-7.72 (m, 5H), 7.83 (t, 1H), 7.91-7.99 (m, 3H); MS: *m/z* 482.1 (MH^+).

Compound 9

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-pyridine-2-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 5.10 (s, 2H), 7.17 (s, 1H), 7.25-7.32 (m, 3H), 7.37-7.46 (m, 2H), 7.69-7.73 (m, 1H), 7.76-7.82 (m, 2H), 7.95 (d, 1H), 8.09-8.14 (m, 1H), 8.89 (d, 1H); MS: *m/z* 417.1 (MH^+).

Compound 10

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-ylmethyl)-1-methyl-1*H*-imidazole-4-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 2.10 (s, 3H), 3.78 (s, 3H), 5.63 (s, 2H), 7.27-7.35 (m, 2H), 7.48-7.62 (m, 3H), 7.70-7.78 (m, 1H), 7.83-7.97 (m, 3H), 8.04 (s, 1H), 8.35 (d, 1H), 8.87 (d, 1H); MS: *m/z* 449.1 (MH^+).

Compound 11

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-1-methyl-1*H*-imidazole-4-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.96 (s, 3H), 3.73 (s, 3H), 4.85 (s, 2H), 7.28 (d, 2H), 7.32-7.48 (m, 4H), 7.61-7.65 (m, 1H), 7.79-7.83 (m, 1H) 7.86 (s, 1H), 7.99 (s, 1H); MS: *m/z* 482.1 (MH^+).

Compound 12

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-pyridine-3-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.98 (s, 3H), 4.81 (br s, 2H), 7.13-7.17 (m, 1H), 7.33-7.42 (m, 4H), 7.68-7.76 (m, 2H), 7.82-7.88 (m, 1H), 8.27-8.31 (m, 1H) , 8.97 (d of d, 1H), 9.02 (d, 1H); MS: *m/z* 431.1 (MH^+).

Compound 13

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-pyridine-3-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.92 (s, 3H), 4.83 (br s, 2H), 7.30 (d, 2H), 7.36-7.46 (m, 4H), 7.67-7.76 (m, 2H), 7.83-7.87 (m, 1H), 8.28 (d, 1H), 8.97 (d, 1H), 9.01 (d, 1H); MS: *m/z* 479.1 (MH^+).

Compound 14

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-ylmethyl)-pyridine-3-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.83 (s, 3H), 5.51 (s, 2H), 7.29-7.38 (m, 2H),

7.47-7.53 (m, 2H), 7.55-7.60 (m, 1H), 7.70-7.80 (m, 3H), 7.90 (d, 1H), 8.34 (d, 2H), 8.80 (d, 1H), 8.97 (d, 1H), 9.02 (d, 1H); MS: *m/z* 446.1 (MH^+).

Compound 15

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-thiophene-3-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.99 (s, 3H), 4.76 (br s, 2H), 7.10-7.16 (m, 1H), 7.28-7.45 (m, 4H), 7.49-7.51 (m, 1H), 7.63-7.70 (m, 1H), 7.81-7.85 (m, 1H), 7.89-7.92 (m, 1H), 8.37-8.38 (m, 1H); MS: *m/z* 451.0 (MH^+).

Compound 16

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-thiophene-3-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.94 (s, 3H), 4.78 (br s, 2H), 7.12 (d, 1H), 7.21-7.41 (m, 4H), 7.49-7.51 (m, 1H), 7.64-7.68 (m, 1H), 7.82-7.85 (m, 1H), 7.89-7.92 (m, 1H), 8.37-8.38 (m, 1H); MS: *m/z* 484.0 (MH^+).

Compound 17

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-ylmethyl)-thiophene-3-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.94 (s, 3H), 5.50 (s, 2H), 7.30-7.33 (m, 2H), 7.49-7.60 (m, 3H), 7.69-7.77 (m, 1H), 7.82-7.91 (m, 4H), 8.32-8.39 (m, 2H), 8.83-8.85 (m, 1H); MS: *m/z* 451.0 (MH^+).

Compound 18

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzo[*b*]thiophene-2-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 2.03 (s, 3H), 4.86 (br s, 2H), 7.14-7.20 (m, 1H), 7.30-7.47 (m, 3H), 7.54-7.75 (m, 3H), 7.82-7.87 (m, 1H), 8.10 (d, 1H), 8.20 (d, 1H), 8.26 (s, 1H); MS: *m/z* 486.1 (MH^+).

Compound 19

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-ylmethyl)-benzo[*b*]thiophene-2-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.97 (s, 3H), 5.60 (s, 2H), 7.30-7.35 (m, 2H), 7.47-7.65 (m, 6H), 7.73-7.78 (m, 1H), 7.83 (d, 1H), 7.89 (d, 1H), 8.12 (d, 1H), 8.21 (d, 1H), 8.27 (s, 1H), 8.32 (d of d, 1H), 8.76-8.79 (m, 1H); MS: *m/z* 501.1 (MH^+).

Compound 20

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-quinoline-8-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.74 (s, 3H), 5.29 (br s, 2H), 5.55 (br s, 1H), 7.16-7.22 (m, 1H), 7.27-7.44 (m, 4H), 7.56-7.61 (m, 1H), 7.64-7.70 (m, 2H), 7.82-7.87

(m, 1H), 8.23 (d of d, 1H), 8.36-8.40 (m, 1H), 8.65-8.67 (m, 1H), 9.28-9.30 (m, 1H); MS: *m/z* 481.2 (MH^+).

Compound 21

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-quinoline-8-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.70 (s, 3H), 5.32 (br s, 2H), 5.77 (br s, 1H), 7.26-7.35 (m, 4H), 7.44 (d, 2H), 7.54-7.59 (m, 1H), 7.62-7.69 (m, 2H), 7.83-7.87 (m, 1H), 8.22 (d of d, 1H), 8.38 (d of d, 1H), 8.66 (d of d, 1H), 9.28-9.33 (m, 1H); MS: *m/z* 529.2 (MH^+).

Compound 22

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-ylmethyl)-quinoline-8-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.64 (s, 3H), 6.06 (s, 2H), 7.21-7.25 (m, 2H), 7.43-7.48 (m, 2H), 7.58-7.69 (m, 3H), 7.83-7.87 (m, 1H), 7.91-7.98 (m, 2H), 8.24-8.39 (m, 3H), 8.65-8.72 (m, 2H), 9.29-9.30 (m, 1H); MS: *m/z* 496.2 (MH^+).

Compound 23

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(3-fluoro-benzyl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.85 (s, 2H), 7.04-7.15 (m, 2H), 7.27-7.37 (m, 1H), 7.46-7.52 (m, 2H), 7.66-7.97 (m, 8H); MS: *m/z* 432.1 (MH^+).

Compound 24

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.83 (s, 2H), 7.10-7.18 (m, 1H), 7.27-7.38 (m, 2H), 7.47-7.54 (m, 2H), 7.66-7.75 (m, 3H), 7.80-7.85 (m, 1H), 7.89-7.99 (m, 3H); MS: *m/z* 450.1 (MH^+).

Compound 25

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-methoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.97 (s, 3H), 3.82 (s, 3H), 4.75 (br s, 2H), 7.08-7.15 (m, 1H), 7.26-7.45 (m, 7H), 7.60 (t, 1H), 7.66-7.70 (m, 1H), 7.82-7.88 (m, 1H) ; MS: *m/z* 460.1 (MH^+).

Compound 26

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-methoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.98 (s, 3H), 3.88 (s, 3H), 4.70 (br s, 2H), 7.08-7.21 (m, 3H), 7.26-7.41 (m, 4H), 7.65-7.70 (m, 1H), 7.77-7.85 (m, 3H); MS: *m/z* 460.2 (MH^+).

Compound 27

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-isoquinoline-5-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.74 (s, 3H), 4.89 (br s, 2H), 7.06-7.13 (m, 1H), 7.24-7.42 (m, 4H), 7.58-7.64 (m, 1H), 7.75-7.80 (m, 1H), 7.88 (t, 1H), 8.33 (d, 1H), 8.45 (d, 1H), 8.56-8.61 (m, 2H), 9.59 (s, 1H); MS: *m/z* 481.2 (MH^+).

Compound 28

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-isoquinoline-5-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.76 (s, 3H), 6.03 (s, 2H), 7.25-7.72 (m), 8.25 (t, 1H), 8.76-8.92 (m, 4H), 10.47 (s, 1H); MS: *m/z* 529.1 (MH^+).

Compound 29

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-ylmethyl)-isoquinoline-5-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.47 (s, 3H), 5.54 (s, 2H), 7.27-7.52 (m, 5H), 7.60 (d, 1H), 7.72-7.76 (m, 1H), 7.87 (d, 1H), 8.01 (t, 1H), 8.30-8.35 (m, 1H), 8.61-8.68 (m, 3H), 8.71-8.76 (m, 2H), 9.87 (s, 1H); MS: *m/z* 496.2 (MH^+).

Compound 30

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-quinoline-6-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.97 (s, 3H), 4.85 (br s, 2H), 7.12-7.20 (m, 1H), 7.29-7.42 (m, 4H), 7.64-7.71 (m, 1H), 7.76-7.85 (m, 2H), 8.21 (d of d, 1H), 8.35 (d, 1H), 8.74-8.80 (m, 2H), 9.19-9.21 (m, 1H); MS: *m/z* 481.2 (MH^+).

Compound 31

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-quinoline-6-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.92 (s, 3H), 4.87 (s, 2H), 7.27-7.46 (m, 6H), 7.64-7.69 (m, 1H), 7.77-7.87 (m, 2H), 8.22 (d of d, 1H), 8.37 (d, 1H), 8.75-8.83 (m, 2H), 9.22 (d of d, 1H); MS: *m/z* 529.2 (MH^+).

Compound 32

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-ylmethyl)-quinoline-6-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.84 (s, 3H), 5.57 (s, 2H), 7.27-7.34 (m, 2H), 7.45-7.59 (m, 3H), 7.70-7.90 (m, 4H), 8.21 (d of d, 1H), 8.29 (d, 2H), 8.68-8.73 (m, 2H), 8.76 (d of d, 1H), 9.15 (d of d, 1H); MS: *m/z* 496.2 (MH^+).

Compound 33

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-pyridine-3-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.94 (s, 2H), 7.17-7.25 (m, 2H), 7.30-7.44 (m, 4H), 7.68-7.77

(m, 2H), 7.80-7.87 (m, 1H), 8.21-8.26 (m, 1H), 8.94 (d of d, 1H), 8.98 (d, 1H); MS: *m/z* 417.0 (MH^+).

Compound 34

***N*-Benzo[*b*]thiophen-2-yl-*N*-(3,4-difluoro-benzyl)-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.28 (s, 3H), 4.19 (s, 2H), 7.18-7.24 (m, 1H), 7.31-7.45 (m, 5H), 7.73-7.78 (m, 1H), 7.82-7.89 (m, 1H); MS: *m/z* 354.1 (MH^+).

Compound 35

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-ethanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.32 (t, 3H), 3.44 (q, 2H), 4.97 (s, 2H), 7.17-7.24 (m, 1H), 7.30-7.46 (m, 5H), 7.71-7.78 (m, 1H), 7.82-7.87 (m, 1H); MS: *m/z* 368.1 (MH^+).

Compound 36

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-propane-1-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.01 (t, 3H), 1.72-1.87 (m, 2H), 3.37-3.44 (m, 2H), 4.95 (s, 2H), 7.16-7.23 (m, 1H), 7.30-7.46 (m, 5H), 7.70-7.76 (m, 1H), 7.81-7.88 (m, 1H); MS: *m/z* 382.2 (MH^+).

Compound 37

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-butane-1-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.892 (t, 3H), 1.35-1.48 (m, 2H), 1.67-1.79 (m, 2H), 3.40-3.45 (m, 2H), 4.96 (s, 2H), 7.16-7.23 (m, 1H), 7.30-7.45 (m, 5H), 7.71-7.77 (m, 1H), 7.82-7.88 (m, 1H); MS: *m/z* 396.1 (MH^+).

Compound 38

***N*-(3-Fluoro-4-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-thiophene-2-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.01 (s, 3H), 4.87 (br s, 2H), 7.32-7.50 (m, 4H), 7.63-7.73 (m, 3H), 7.83-7.88 (m, 2H), 8.17 (d of d, 1H); MS: *m/z* 486.1 (MH^+).

Compound 39

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-pyridine-3-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.97 (s, 3H), 4.92 (br s, 2H), 7.37-7.53 (m, 3H), 7.63-7.79 (m, 4H), 7.84-7.88 (m, 1H), 8.27-8.32 (m, 1H), 8.97-9.04 (m, 2H); MS: *m/z* 481.2 (MH^+).

Compound 40

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.35 (t, 3H), 2.04 (s, 3H), 3.46 (q, 2H),

4.89 (s, 2H), 7.37-7.49 (m, 3H), 7.62-7.71 (m, 3H), 7.85-7.92 (m, 1H); MS: *m/z* 432.1 (MH^+).

Compound 41

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.35 (t, 3H), 2.06 (s, 3H), 3.44 (q, 2H), 4.79 (s, 2H), 7.10-7.17 (m, 1H), 7.29-7.44 (m, 4H), 7.67-7.72 (m, 1H), 7.87-7.90 (m, 1H); MS: *m/z* 382.2 (MH^+).

Compound 42

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.35 (t, 3H), 1.99 (s, 3H), 3.44 (q, 2H), 4.82 (s, 2H), 7.30 (d, 2H), 7.36-7.43 (m, 4H), 7.65-7.70 (m, 1H), 7.86-7.90 (m, 1H); MS: *m/z* 430.2 (MH^+).

Compound 43

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.33 (t, 3H), 3.46 (q, 2H), 5.07 (s, 2H), 7.30-7.40 (m, 3H), 7.50 (t, 1H), 7.70-7.77 (m, 3H) and 7.83-7.88 (m, 1H); MS: *m/z* 418.0 (MH^+).

Compound 44

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-N',N'-dimethylsulfamide**. ^{1}H-NMR (DMSO-d_6): δ 2.09 (s, 3H), 2.87 (s, 6H), 4.72 (s, 2H), 7.07-7.14 (m, 1H), 7.27-7.42 (m, 4H), 7.66-7.72 (m, 1H), 7.84-7.91 (m, 1H); MS: *m/z* 397.0 (MH^+).

Compound 45

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.30 (s, 3H), 5.01 (s, 2H), 7.31-7.38 (m, 2H), 7.40 (s, 1H), 7.49 (t, 1H), 7.70-7.78 (m, 3H), 7.83-7.89 (m, 1H); MS: *m/z* 404.1 (MH^+).

Compound 46

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-chloro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.76 (s, 2H), 7.00 (s, 1H), 7.21-7.32 (m, 6H), 7.48-7.53 (m, 2H), 7.61-7.66 (m, 3H), 7.76-7.80 (m, 2H); MS: *m/z* 414.0 (MH^+).

Compound 47

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.71 (s, 3H), 4.90 (s, 2H), 6.76-6.78 (d, 1H), 6.86-6.90 (t, 1H), 7.01 (s, 1H), 7.17-7.22 (m, 1H), 7.22-7.32 (m, 3H), 7.42-7.51 (m, 3H), 7.58-7.64 (m, 2H), 7.77-7.82 (d, 2H); MS: *m/z* 410.1 (MH^+).

Compound 48

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-methoxy-benzyl)-benzenesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 3.74 (s, 3H), 4.78 (s, 2H), 6.75-6.78 (m, 1H), 6.88-6.91 (m, 2H), 7.01 (s, 1H), 7.15-7.19 (m, 1H), 7.25-7.31 (m, 2H), 7.48-7.52 (m, 2H), 7.59-7.64 (m, 3H), 7.76-7.78 (d, 2H); MS: *m/z* 410.1 (MH^+).

Compound 49

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-methoxy-benzyl)-benzenesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 3.74 (s, 3H), 4.74 (s, 2H), 6.76-6.81 (d, 2H), 6.97 (s, 1H), 7.21-7.31 (m, 4H), 7.47-7.51 (m, 2H), 7.59-7.65 (m, 3H), 7.76-7.80 (d, 2H); MS: *m/z* 410.1 (MH^+), 432.0 (MNa^+).

Compound 50

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-benzyl)-benzenesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 4.92 (s, 2H), 6.92-6.97 (m, 1H), 7.01 (s, 1H), 7.06-7.11 (m, 1H), 7.19-7.31 (m, 3H), 7.48-7.53 (m, 3H), 7.60-7.65 (m, 3H), 7.77-7.81 (d, 2H); MS: *m/z* 398.1 (MH^+).

Compound 51

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-nitro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.89 (s, 2H), 7.05 (s, 1H), 7.26-7.31 (m, 2H), 7.46-7.54 (m, 3H), 7.62-7.68 (m, 3H), 7.74-7.79 (m, 3H), 8.05-8.19 (m, 2H); MS: *m/z* 425.1 (MH^+).

Compound 52

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(pyridin-2-ylmethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 5.17 (s, 2H), 7.07 (s, 1H), 7.26-7.32 (m, 3H), 7.38-7.43 (m, 1H), 7.48-7.55 (m, 2H), 7.60-7.67 (m, 2H), 7.77-7.79 (m, 2H), 7.87-7.89 (m, 1H), 7.94-7.98 (m, 1H), 8.59-8.61 (m, 1H); MS: *m/z* 381.0 (MH^+).

Compound 53

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(pyridin-3-ylmethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.97 (s, 2H), 7.07 (s, 1H), 7.32-7.34 (m, 2H), 7.52-7.57 (m, 3H),

7.63-7.71 (m, 3H), 7.76-7.83 (m, 3H), 8.48-8.49 (m, 1H), 8.75-8.76 (m, 1H), 8.83 (s, 1H); MS: *m/z* 381.0 (MH^+).

Compound 54

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(pyridin-4-ylmethyl)-benzenesulfonamide**

^{1}H-NMR ($CDCl_3$): δ 5.02 (s, 2H), 7.13 (s, 1H), 7.33-7.37 (m, 2H), 7.53-7.57 (m, 2H), 7.63-7.71 (m, 3H), 7.76-7.78 (m, 2H), 7.84-7.88 (m, 2H), 8.81-8.84 (m, 2H); MS: *m/z* 381.0 (MH^+).

Compound 55

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-nitro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 5.29 (s, 2H), 7.11 (s, 1H), 7.27-7.31 (m, 2H), 7.40-7.44 (m, 1H), 7.50-7.54 (m, 2H), 7.61-7.69 (m, 4H), 7.78-7.80 (m, 2H), 7.97-8.03 (m, 2H); MS: *m/z* 425.1 (MH^+).

Compound 56

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-trifluoromethoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.93 (s, 2H), 7.01 (s, 1H), 7.15-7.18 (m, 1H), 7.23-7.30 (m, 4H), 7.49-7.53 (m, 2H), 7.59-7.66 (m, 4H), 7.78-7.79 (m, 2H); MS: *m/z* 464.1 (MH^+).

Compound 57

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.81 (s, 2H), 7.01 (s, 1H), 7.07-7.09 (m, 1H), 7.19 (s, 1H), 7.25-7.31 (m, 4H), 7.48-7.53 (m, 2H), 7.61-7.66 (m, 3H), 7.76-7.78 (m, 2H); MS: *m/z* 464.1 (MH^+).

Compound 58

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.80 (s, 2H), 7.01 (s, 1H), 7.10-7.12 (d, 2H), 7.28-32 (m, 2H), 7.35-7.37 (m, 2H), 7.48-7.52 (m, 2H), 7.61-7.65 (m, 3H), 7.75-7.77 (m, 2H); MS: *m/z* 464.0 (MH^+).

Compound 59

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.80 (s, 2H), 6.99 (s, 1H), 7.22-7.28 (m, 5H), 7.31-7.33 (m, 2H), 7.48-7.51 (m, 2H), 7.59-7.64 (m, 3H), 7.77-7.79 (m, 2H); MS: *m/z* 380.1 (MH^+).

Compound 60

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.82 (s, 3H), 4.75 (s, 2H), 6.72-6.78 (m, 1H), 6.89-6.94 (m, 1H), 6.98-6.99 (m, 2H), 7.28-7.31 (m, 2H), 7.48-7.53 (m, 2H), 7.61-7.64 (m, 3H), 7.76-7.78 (m, 2H); MS: *m/z* 428.1 (MH^+).

Compound 61

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.80 (s, 2H), 7.03 (s, 1H), 7.08-7.14 (m, 1H), 7.28-7.34 (m, 2H), 7.49-7.55 (m, 5H), 7.63-7.68 (m, 3H), 7.75-7.77 (m, 2H); MS: *m/z* 466.0 (MH^+).

Compound 62

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-methyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.39 (s, 3H), 4.81 (s, 2H), 6.97 (s, 1H), 7.01-7.05 (m, 1H), 7.09-7.12 (m, 2H), 7.20-7.29 (m, 3H), 7.49-7.53 (m, 2H), 7.58-7.66 (m, 3H), 7.77-7.81 (d, 2H); MS: *m/z* 394.0 (MH^+).

Compound 63

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-methyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.25 (s, 3H), 4.76 (s, 2H), 7.00 (s, 1H), 7.02-7.04 (m, 1H), 7.09-7.16 (m, 3H), 7.47-7.53 (m, 2H), 7.59-7.64 (m, 3H), 7.76-7.78 (m, 2H); MS: *m/z* 394.0 (MH^+).

Compound 64

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-fluoro-4-methoxybenzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.98 (s, 3H), 3.97 (s, 3H), 4.87 (s, 2H), 7.35-7.48 (m, 4H), 7.62-7.71 (m, 4H), 7.76-7.88 (m, 2H); MS: *m/z* 528.0 (MH^+), 550.0 (MNa^+).

Compound 65

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzothiazole-6-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.96 (s, 3H), 4.90 (s, 2H), 7.33-7.52 (m, 3H), 7.63-7.70 (m, 3H), 7.78-7.83 (m, 1H), 7.97-8.01 (m, 1H), 8.31-8.42 (d, 1H), 8.91 (s, 1H), 9.77 (s, 1H); MS: *m/z* 537.0 (MH^+).

Compound 66

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-oxo-2,3-dihydro-benzooxazole-6-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.98 (s,

3H), 4.84 (s, 2H), 7.28-7.48 (m, 4H), 7.60-7.70 (m, 4H), 7.81-7.86 (m, 2H), 12.35 (s, 1H); MS: *m/z* 537.0 (MH^+).

Compound 67

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl))-3-oxo-3,4-dihydro-2*H*-benzo[1,4]oxazine-6-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.97 (s, 3H), 4.79 (m, 4H), 7.20-7.23 (d, 1H), 7.29-7.51 (m, 4H), 7.61-7.72 (m, 3H), 7.81-7.90 (m, 1H), 10.91 (s, 1H); MS: *m/z* 551.1 (MH^+).

Compound 68

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-methyl-3,4-dihydro-2*H*-benzo[1,4]oxazine-7-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.99 (s, 3H), 2.82 (s, 3H), 4.33-4.36 (m, 2H), 4.78 (s, 2H), 6.97-6.91 (d, 1H), 6.98-7.00 (m, 1H), 7.04-7.09 (m, 2H), 7.32-7.46 (m, 3H), 7.59-7.69 (m, 3H), 7.83-7.87 (m, 1H); MS: *m/z* 551.1 (MH^+).

Compound 69

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-[1,2,3]thiadiazol-4-yl-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.98 (s, 3H), 4.92 (s, 2H), 7.34-7.51 (m, 3H), 7.65-7.71 (m, 3H), 7.82-7.85 (m, 1H), 8.04-8.06 (d, 2H), 8.44-8.47 (d, 2H), 9.92 (s, 1H); MS: *m/z* 564.0 (MH^+), 586.0 (MNa^+).

Compound 70

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-phenoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.87 (s, 3H), 5.06 (s, 2H), 7.05-7.08 (d, 1H), 7.21-7.39 (m, 6H), 7.43-7.54 (m, 3H), 7.62-7.86 (m, 6H); MS: *m/z* 572.1 (MH^+).

Compound 71

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethylbenzyl)-2-carbomethoxypropanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.01 (s, 3H), 2.82-2.89 (t, 2H), 3.65 (s, 3H), 3.71-3.75 (t, 2H), 4.89 (s, 2H), 7.39-7.48 (m, 3H), 7.59-7.71 (m, 3H), 7.84-7.92 (m, 1H); MS: *m/z* 490.0 (MH^+), 512.0 (MNa^+).

Compound 72

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethylbenzyl)-(2,4-dihydroxy-6-methyl-pyrimidine-5-yl)sulfonamide** ^{1}H-NMR (DMSO-d_6): δ 1.94 (s, 3H), 2.08 (s, 3H), 4.98 (s, 3H), 7.34-7.50 (m, 3H), 7.60-7.69 (m, 3H), 7.84-7.92 (m, 1H), 11.66 (s, 1H), 11.85 (s, 1H); MS: *m/z* 528.0 (MH^+).

Compound 73

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinoline-8-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.94-1.98 (m, 3H), 3.02-3.09 (m, 2H), 3.80-3.90 (m, 2H), 4.76-4.90 (m, 4H), 7.34-7.53 (m, 4H), 7.60-7.69 (m, 5H), 7.82-7.85 (m, 1H), 7.96 (s, 1H); MS: *m/z* 631.0 (MH^+).

Compound 74

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-1,3,5-trimethyl-1*H*-pyrazole-4-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.04 (s, 6H), 2.18 (s, 3H), 3.72 (s, 3H), 4.76 (s, 2H), 7.34-7.46 (m, 3H), 7.60-7.69 (m, 3H), 7.82-7.89 (m, 1H); MS: *m/z* 512.0 (MH^+).

Compound 75

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2,4-dimethyl-thiazole-5-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.04 (s, 3H), 2.29 (s, 3H), 2.71 (s, 3H), 4.83 (s, 2H), 7.35-7.51 (m, 3H), 7.63-7.75 (m, 3H), 7.88-7.92 (m, 1H); MS: *m/z* 515.0 (MH^+).

Compound 76

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-6-chloro-pyridine-3-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.01 (s, 3H), 4.83 (s, 2H), 7.35-7.51 (m, 3H), 7.63-7.75 (m, 3H), 7.88-7.92 (m, 2H), 8.31-8.34 (m, 1H), 8.90 (d, 1H); MS: *m/z* 515.0 (MH^+).

Compound 77

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-chloro-pyridine-3-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.02 (s, 3H), 5.15 (s, 2H), 7.35-7.40 (m, 2H), 7.45-7.75 (m, 5H), 7.82-7.85 (m, 1H), 8.26-8.32 (m, 1H), 8.72-8.77 (m, 1H); MS: *m/z* 515.0 (MH^+).

Compound 78

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-thiophene-3-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.98 (s, 2H), 7.19 (s, 1H), 7.31-7.34 (m, 2H), 7.42-7.43 (m, 1H), 7.46-7.51 (m, 1H), 7.68-7.75 (m, 3H), 7.82-7.90 (m, 2H), 8.38-8.39 (m, 1H); MS: *m/z* 472.0 (MH^+).

Compound 462

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-*N'*, *N'*-dimethylsulfamoyl-benzenesulfonamide.** MS: *m/z* 573.2 (MH^+).

Compound 825

***N*-(Benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3,4-difluoro-benzenesulfonamide** ^{1}H-NMR ($CDCl_3$): δ 2.02 (s, 3H), 4.78 (br s, 2H), 7.28 (s, 5H), 7.41 (m, 3H), 7.62 (m, 2H), 7.72 (m, 2H); MS: *m/z* 452.0 (MNa^+).

Compound 826

***N*-(4-Fluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3,4-difluoro-benzenesulfonamide.** ^{1}H NMR ($CDCl_3$) δ 2.02 (s, 3H), 4.72 (br s, 2H), 6.95 (m, 2H), 7.22 (m, 2H), 7.42 (m, 3H), 7.61 (m, 2H), 7.72 (m, 2H); MS: *m/z* 447.9 (MH^+), 470.0 (MNa^+).

Compound 828

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-methoxy-benzyl)-ethanesulfonamide.** MS: *m/z* 380.0 (MH^+), 402 (MNa^+).

Compound 829

***N*-(2-Fluoro-pyridin-4-ylmethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.42 (t, 3H), 2.12 (s, 3H), 3.23 (q, 2H), 4.79 (s, 2H), 6.81 (s, 1H), 7.13 (m, 1H), 7.33 (m, 2H), 7.52 (m, 1H), 7.67 (m, 1H), 8.12 (m, 1H); MS: *m/z* 365.0 (MH^+).

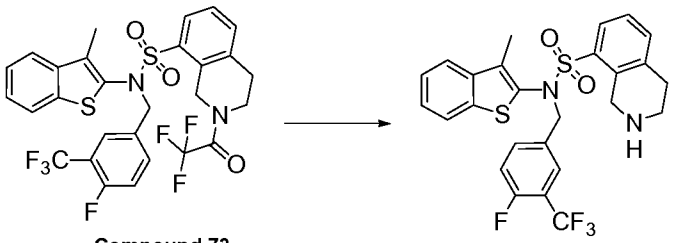
Compound 845

3-Fluoro-*N*-(4-fluoro-benzyl)-4-(4-fluoro-benzyloxy)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide. MS: *m/z* 554.0 (MH^+), 576.0 (MNa^+).

Compound 846

***N*-(Benzyl)-4-benzyloxy-3-fluoro-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** MS: *m/z* 540.0 (MNa^+).

Example 2

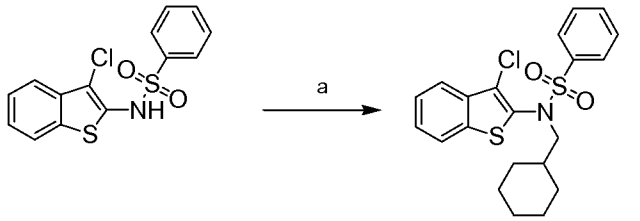


a) K_2CO_3, MeOH, H_2O.

Compound 79

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-1,2,3,4-tetrahydro-isoquinoline-8-sulfonamide.** To a solution of potassium carbonate (0.066 g; 0.48 mmol) in methanol and water (2 mL / 2 mL) was added compound **73** (0.06 g; 0.095 mmol) and the reaction was stirred for 18 h at room temperature. The reaction was partitioned between ethyl acetate and water, the layers separated, organics washed with brine, dried over sodium sulfate, flute filtered and the solvent evaporated under reduced pressure. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) eluting with a 40% to 60% MeCN-H_2O gradient to afford compound **79** as a yellow oil (0.035 g, 57%). ^{1}H-NMR (DMSO-d_6): δ 1.95 (s, 3H), 3.15 (m, 2H), 3.46 (m, 2H), 4.38 (m, 2H), 4.83 (m, 2H), 7.37-7.88 (m, 10H), 9.11 (s, 1H); MS: *m/z* 535.0 (MH^+).

Example 3



a)Ph_3P, DEAD, cyclohexylmethanol, THF.

Compound 80

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(cyclohexylmethyl)-benzenesulfonamide.** To triphenylphosphine (0.157 g, 0.60 mmol) dissolved in dry tetrahydrofuran (5 mL) was added a solution of DEAD (0.260 g of 40% solution by weight in toluene, 0.60 mmol). The reaction mixture was stirred at room temperature

for 2 minutes, to which was added compound **80-A** (0.130 g, 0.40 mmol). Cyclohexyl methanol (0.048 mL, 0.48 mmol) was added and the reaction mixture was stirred at room temperature for 16 h . The reaction mixture was evaporated *in vacuo*, the residue dissolved in 10 mL of dichloromethane, washed with 10 mL of brine, dried over Na_2SO_4, filtered and the solvent was evaporated *in vacuo*. The product was purified by flash column chromatography on silica gel eluting with an ethyl acetate-heptane (10-20%) gradient afford compound **80** as a light yellow solid, (0.121 g, 72%). ^{1}H-NMR ($CDCl_3$): δ 0.88-1.0 (m, 2H), 1.14-1.27 (m, 3H), 1.30-1.37 (m, 1H), 1.38-1.44 (m, 2H), 1.45-1.48 (m, 1H), 1.62-1.87 (m, 2H), 3.47 (d, 2H), 7.41-7.52 (m, 4H), 7.59-7.64 (m, 1H), 7.70-7.73 (m, 1H), 7.74-7.82 (m, 3H); MS: *m/z* 420.1 (MH^+).

Following the procedure described above for Example 3 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 81

***N*-(2-*tert*-Butoxy-ethyl)-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.10 (s, 9H), 3.56 (t, 2H), 3.83 (t, 2H), 7.42-7.52 (m, 4H), 7.56-7.68 (m, 1H), 7.70-7.78 (m, 2H), 7.85-7.87 (d, 2H); MS: *m/z* 446.1 (MNa^+).

Compound 82

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-[2-(2-oxo-pyrrolidin-1-yl)-ethyl]-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.06-2.16 (m, 2H), 2.48-2.53 (m, 2H), 3.49-3.73 (m, 2H), 3.87-3.91 (m, 2H), 7.44-7.81(m, 9H); MS: *m/z* 435.1 (MH^+).

Compound 83

***N*-(Butyl)-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.85-0.90 (m, 3H), 1.34-1.55 (m, 4H), 3.62-3.67 (t, 2H), 7.43-7.53 (m, 4H), 7.60-7.68 (m, 1H), 7.69-7.73 (m, 1H), 7.74-7.85 (m, 3H); MS: *m/z* 380.1 (MH^+).

Compound 84

***N*-(Allyl)-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.28-4.31 (m, 2H), 5.08-5.18 (m, 2H), 5.80-5.91 (m, 1H), 7.40-7.50 (m, 2H), 7.52-7.63 (m, 2H), 7.64-7.87 (m, 5H); MS: *m/z* 364.0 (MH^+).

Compound 85

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(phenethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.89-2.94 (m, 2H), 3.85-3.90 (m, 2H), 7.13-7.28 (m, 6H), 7.43-7.51 (m, 4H), 7.58-7.82 (m, 4H); MS: *m/z* 364.0 (MH^+).

Compound 86

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-[2-(carbo-*tert*-butoxyamino)ethyl]-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.38 (s, 9H), 3.28-3.32 (t, 2H), 3.75-3.79 (t, 2H), 5.03 (s, 1H, NH), 7.43-7.55 (m, 4H), 7.62-7.85 (m, 5H); MS: *m/z* 489.1 (MNa^+).

Compound 87

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-dimethylamino-ethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.98 (s, 6H), 3.38-3.42 (t, 2H), 4.06-4.11 (t, 2H), 7.48-7.57 (m, 4H), 7.67-7.82 (m, 5H); MS: *m/z* 395.1 (MH^+).

Compound 88

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-methanesulfonyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.03 (s, 3H), 3.40-3.45 (t, 2H), 4.11-4.16 (m, 2H), 7.47-7.57 (m, 4H), 7.66-7.85 (m, 5H); MS: *m/z* 430.0 (MH^+).

Compound 89

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-{[1-(carbo-*tert*-butoxy)pyrrolidin-2-yl]-methyl}-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.29 (s, 9H), 1.94-2.01 (m, 3H), 2.35 (bs, 1H), 3.35-3.36 (m, 2H), 3.61-3.82 (m, 3H), 7.39-7.54 (m, 4H), 7.59-7.71 (m, 2H), 7.75-7.81 (m, 3H); MS: *m/z* 407.1 (MH^+-BOC).

Compound 90

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-{[1-(carbo-*tert*-butoxy)piperidin-4-yl]-methyl}-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.58-1.65 (m, 5H), 1.73 (s, 9H), 3.52-3.54 (bd, 2H), 4.06-4.10 (bd, 2H), 7.44-7.53 (m, 4H), 7.61-7.66 (m, 1H), 7.70-7.77 (m, 1H), 7.78-7.81 (m, 3H); MS: *m/z* 543.2 (MNa^+).

Compound 91

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-[2-(2-oxo-imidazolidin-1-yl)-ethyl]-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.37-3.44 (m, 4H), 3.61-3.66 (m, 2H), 3.85-3.89 (m, 2H), 7.43-7.53 (m, 4H), 7.61-7.66 (m, 1H), 7.70-7.83 (m, 4H); MS: *m/z* 436.4 (MH^+).

Compound 92

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-morpholin-4-yl-ethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.39-2.42(m, 4H), 2.53-2.57 (m, 2H), 3.57-3.60 (m, 4H), 3.79-3.83 (m, 2H), 7.43-7.53 (m, 3H), 7.71-7.84(m, 3H), 7.85-7.86 (m, 2H); MS: *m/z* 437.1 (MH^+).

Compound 93

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-[2(*R*)-methyl-2-carbomethoxy-ethyl]-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.27(s, 3H), 2.34 (s, 3H), 2.61-2.68 (m, 1H), 3.42-4.17 (m, 5H), 7.33-7.40 (m, 2H), 7.42-7.62 (m, 2H), 7.64-7.78 (m, 5H); MS: *m/z* 404.1 (MH^+).

Compound 94

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-[2(*S*)-methyl-2-carbomethoxy-ethyl]-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.26 (s, 3H), 2.33 (s, 3H), 2.61-2.68 (m, 1H), 3.49 (s,3H), 3.58 (s, 2H), 7.33-7.42 (m, 2H), 7.42-7.61 (m, 2H), 7.62-7.78 (m, 5H); MS: *m/z* 404.1 (MH^+).

Compound 95

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-morpholin-4-yl-ethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.36 (s, 3H), 2.41-2.51 (m, 6H), 3.57-3.74 (m, 6H), 7.33-7.40 (m, 2H), 7.48-7.61 (m, 2H), 7.62-7.66 (m, 3H), 7.69-7.81(m, 2H); MS: *m/z* 417.3 (MH^+).

Compound 96

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-piperidin-1-yl-ethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.26-1.53 (m, 2H), 2.35 (m, 7H), 2.44-2.49 (t, 2H), 3.52-3.66 (m, 2H), 7.33-7.40 (m, 2H), 7.47-7.52 (m, 2H), 7.59-7.71 (m, 3H), 7.71-7.82 (m, 2H); MS: *m/z* 415.2 (MH^+).

Compound 97

***N*-(Cyclopropylmethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.18-0.20 (m, 2H), 0.43-0.46 (m, 2H), 0.92-1.00 (m, 1H), 2.39 (s, 3H), 7.35-7.39 (m, 2H), 7.48-7.53 (m, 2H), 7.59-7.71 (m, 3H), 7.72-7.81(m, 2H); MS: *m/z* 358.2 (MH^+).

Compound 98

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-methylsulfanyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.09 (s, 3H), 2.35 (s, 3H), 2.62-2.67 (m,

2H), 3.74 (bs, 2H), 7.35-7.41 (m, 2H), 7.48-7.55 (m, 2H), 7.60-7.72 (m, 3H), 7.78-7.82 (m, 2H); MS: *m/z* 378.1 (MH^+).

Compound 99

***N*-(2-Methoxy-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.32 (s, 3H), 3.29 (s, 3H), 3.45-3.50 (m, 2H), 3.72 (bs, 2H), 7.35-7.41 (m, 2H), 7.46-7.54 (m, 2H), 7.59-7.73 (m, 3H), 7.79-7.83 (m, 2H); MS: *m/z* 362.1 (MH^+).

Compound 100

***N*-(2-*tert*-Butoxy-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.10 (s, 9H), 2.30 (s, 3H), 3.46-3.50 (t, 2H), 3.71 (bs, 2H), 7.35-7.39 (m, 2H), 7.47-7.52 (m, 2H), 7.59-7.70 (m, 3H), 7.80-7.83 (m, 2H); MS: *m/z* 404.2 (MH^+).

Compound 101

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(carbomethoxy-methyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.10 (s, 9H), 2.33 (s, 3H), 3.70 (s, 3H), 4.42 (s, 2H), 7.35-7.40 (m, 2H), 7.47-7.53 (m, 2H), 7.60-7.70 (m, 3H), 7.79-7.84 (m, 2H); MS: *m/z* 376.2 (MH^+).

Compound 102

***N*-(2,2-Difluoro-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.30 (s, 3H), 3.88 (bs, 2H), 5.83-6.12 (m, 1H), 7.37-7.41 (m, 2H), 7.51-7.56 (m, 2H), 7.65-7.72 (m, 3H), 7.78-7.81 (m, 2H); MS: *m/z* 368.1 (MH^+).

Compound 103

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-{[1-(carbo-*tert*-butoxy)pyrrolidin-2-yl]-methyl}-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.17-1.36 (m, 11H), 1.82-1.97 (m, 2H), 2.32-2.52 (m, 2H), 3.21-3.46 (m, 2H), 3.59-3.74 (m, 1H), 7.31-7.41 (m, 2H), 7.46-7.51 (m, 2H), 7.58-7.79 (m, 5H); MS: *m/z* 487.2 (MH^+).

Compound 104

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(phenethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.31 (s, 3H), 2.82-2.89 (t, 2H), 3.66-3.93 (bs, 2H), 7.10-7.17 (m, 2H), 7.22-7.30 (m, 3H), 7.37-7.42 (m, 2H), 7.46-7.53 (m, 2H), 7.57-7.65 (m, 1H), 7.69-7.78 (m, 4H); MS: *m/z* 408.1 (MH^+).

Compound 105

***N*-(2-Methoxy-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.43-1.47 (t, 3H), 2.42 (s, 3H), 3.23-3.31 (q, 2H), 3.84-3.88 (t, 2H), 7.38-7.41 (m, 2H), 7.69-7.75 (m, 2H); MS: *m/z* 314.1 (MH^+).

Compound 106

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.43-1.48 (t, 3H), 2.42 (s, 3H), 2.45-2.52 (m, 2H), 3.18-3.25 (q, 2H), 3.91-3.97 (m, 2H), 7.41-7.44 (m, 2H), 7.70-7.78 (m, 2H); MS: *m/z* 352.2 (MH^+).

Compound 107

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(pent-3-ynyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.43-1.48 (t, 3H), 1.73-1.74 (t, 3H), 2.43 (s, 3H), 3.19-3.27 (q, 2H), 3.78-3.83 (t, 2H), 7.37-7.41 (m, 2H), 7.69-7.75 (m, 2H); MS: *m/z* 322.2 (MH^+).

Compound 108

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-methylsulfanyl-ethyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.43-1.48 (t, 3H), 2.11 (s, 3H), 2.44 (s, 3H), 2.66-2.71 (t, 2H), 3.20-3.27 (m, 2H), 3.85-3.90 (t, 2H), 7.38-7.42 (m, 2H), 7.70-7.76 (m, 2H); MS: *m/z* 330.1 (MH^+).

Compound 109

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5-oxo-(*S*)-pyrrolidin-2-ylmethyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.42-1.47 (t, 3H), 2.31-2.37 (m, 4H), 2.44 (s, 3H), 3.17-3.24 (q, 2H), 3.76-3.85 (m, 3H), 5.73 (bs, 1H), 7.41-7.44 (m, 2H), 7.70-7.76 (m, 2H); MS: *m/z* 353.1 (MH^+).

Compound 110

***N*-(2-*tert*-Butoxy-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.18 (s, 9H), 1.43-1.54 (q, 3H), 2.42 (s, 3H), 3.28-3.35 (q, 2H), 3.48-3.52 (t, 2H), 3.80-3.84 (t, 2H), 5.73 (bs, 1H), 7.37-7.40 (m, 2H), 7.68-7.75 (m, 2H); MS: *m/z* 356.3 (MH^+).

Compound 111

***N*-(2,2-Difluoro-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.44-1.49 (t, 3H), 2.43 (s, 3H), 3.22-3.35 (q, 2H), 3.95-4.06 (t, 2H), 5.78-6.18 (tt, 1H), 7.40-7.43 (m, 2H), 7.71-7.76 (m, 2H); MS: *m/z* 320.1 (MH^+).

Compound 112

***N*-(Cyclopropylmethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.00-0.35 (m, 2H), 0.24-0.30 (m, 2H), 0.78-0.88 (m, 1H), 1.19-1.24 (t, 3H), 2.24 (s, 3H), 2.95-3.02 (q, 2H), 3.32-3.34 (td 2H), 7.15-7.19 (m, 2H), 7.48-7.54 (m, 2H); MS: *m/z* 310.2 (MH^+).

Compound 113

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-morpholin-4-yl-ethyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.43-1.47 (t, 3H), 2.44 (s, 3H), 2.46-2.54 (m, 4H), 3.24-3.33 (q, 2H), 3.65-3.69 (m, 4H), 3.78-3.84 (m, 2H), 7.37-7.43 (m, 2H), 7.69-7.76 (m, 2H); MS: *m/z* 369.1 (MH^+).

Compound 114

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-{[1-(carbo-*tert*-butoxy)pyrrolidin-2-yl]-methyl}-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.20-1.47 (m, 12H), 2.06-2.25 (m, 4H), 2.43 (s, 3H), 3.11-3.41 (m, 4H), 3.60-3.95 (m, 3H), 7.31-7.47 (m, 2H), 7.64-7.78 (m, 2H); MS: *m/z* 439.2 (MH^+).

Compound 115

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(phenethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.83 (t, 2H), 3.89 (t, 2H), 7.19-7.25 (m, 4H), 7.26-7.33 (m, 2H), 7.34-7.41 (m, 2H), 7.58 (t, 2H), 7.66-7.74 (m, 3H), 7.77-7.81 (m, 1H), 7.85-7.90 (m, 1H); MS: *m/z* 394.2 (MH^+).

Compound 116

***N*-(Allyl)-*N*-(benzo[*b*]thiophen-2-yl)-benzenesulfonamide**. ^{1}H NMR-(DMSO-d_6): δ 4.32 (d, 2H), 5.15 (dd, 1H), 5.26 (dd, 1H), 5.75-5.86 (m, 1H), 7.16 (s, 1H), 7.31-7.38 (m, 2H), 7.62 (t, 2H), 7.71-7.79 (m, 4H), 7.82-7.87 (m, 1H); MS: *m/z* 330.1 (MH^+).

Compound 117

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.85 (t, 3H), 1.34 (m, 2H), 1.48 (m, 2H), 3.64 (t, 2H), 7.21 (s, 1H), 7.32-7.39 (m, 2H), 7.61 (t, 2H), 7.70-7.75 (m, 3H), 7.76-7.80 (m, 1H), 7.83-7.88 (m, 1H); MS: *m/z* 346.1 (MH^+).

Compound 118

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(cyclohexylmethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.90-1.02 (m, 2H), 1.03-1.17 (m, 3H), 1.38-1.49 (m, 1H), 1.54-

1.60 (m, 1H), 1.61-1.68 (m, 2H), 1.69-1.77 (m, 2H), 3.47 (d, 2H), 7.22 (s, 1H), 7.32-7.39 (m, 2H), 7.60 (t, 2H), 7.68-7.74 (m, 3H), 7.75-7.80 (m, 1H), 7.83-7.87 (m, 1H); MS: *m/z* 386.2 (MH^+).

Compound 119

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(cyclohexyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.79-0.93 (m, 1H), 1.17-1.41 (m, 4H), 1.49 (br d, 1H), 1.64-1.77 (m, 4H), 4.06-4.16 (m, 1H), 7.15 (s, 1H), 7.36-7.43 (m, 2H), 7.64 (t, 2H), 7.69-7.76 (m, 1H), 7.81-7.91 (m, 4H); MS: *m/z* 372.1 (MH^+).

Compound 120

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-methylsulfanyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.08 (s, 3H), 2.65 (t, 2H), 3.85 (t, 2H), 7.23 (s, 1H), 7.33-7.39 (m, 2H), 7.62 (t, 2H), 7.71-7.81 (m, 4H), 7.84-7.89 (m, 1H); MS: *m/z* 364.2 (MH^+).

Compound 121

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.88 (t, 3H), 1.24 (t, 3H), 1.36 (m, 2H), 1.65 (m, 2H), 2.59 (s, 3H), 3.34 (q, 2H), 3.79 (t, 2H), 7.44-7.50 (m, 2H), 7.97-8.02 (m, 1H), 8.06-8.11 (m, 1H); MS: *m/z* 340.1 (MH^+).

Compound 122

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.25-0.31 (m, 2H), 0.50-0.56 (m, 2H), 1.05-1.17 (m, 1H), 1.25 (t, 3H), 2.67 (s, 3H), 3.34 (q, 2H), 3.71 (d, 2H), 7.45-7.51 (m, 2H), 7.97-8.03 (m, 1H), 8.09-8.15 (m, 1H); MS: *m/z* 338.1 (MH^+).

Compound 123

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(2-*tert*-butoxy-ethyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.09 (s, 9H), 1.27 (t, 3H), 2.65 (s, 3H), 3.40 (q, 2H), 3.56 (t, 2H), 3.93 (t, 2H), 7.44-7.50 (m, 2H), 7.97-8.03 (m, 1H), 8.13-8.18 (m, 1H); MS: *m/z* 384.1 (MH^+).

Compound 124

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(2-morpholin-4-yl-ethyl)-ethanesulfonamide.** MS: *m/z* 397.2 (MH^+).

Compound 340

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-pyridin-3-yl-sulfonamide.** MS: *m/z* 347.2 (MH^+).

Compound 362

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*C*-methanesulfonyl-methanesulfonamide.** MS: *m/z* 482.1 (MH^+).

Compound 363

***N*-(Butyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** MS: *m/z* 298.0 (MH^+).

Compound 364

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-methanesulfonamide.** MS: *m/z* 338.0 (MH^+).

Compound 365

***N*-(Cyclopropylmethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** MS: *m/z* 296.0 (MH^+).

Compound 366

***N*-(2-*tert*-Butoxy-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** MS: *m/z* 364.0 (MNa^+).

Compound 382

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-methanesulfonamide.** MS: *m/z* 284.0 (MH^+).

Compound 422

***N*-(Butyl)-*N*-(3-methoxy-benzo[*b*]thiophen-2-yl)-4-carbomethoxybenzenesulfonamide.** Compound **422** was prepared as a solid from Example 1, steps A and B, substituting benzo[*b*]thiophene-2-carboxylic acid with 3-methoxy-benzo[*b*]thiophene-2-carboxylic acid and from Example 32, steps E and F. ^{1}H-NMR ($CDCl_3$): δ 0.88 (t, 3H), 1.29-1.41 (m, 2H), 1.51-1.61 (m, 2H), 3.54 (t, 2H), 3.98 (s, 3H), 4.09 (s, 3H), 7.33-7.39 (m, 2H), 7.55-7.60 (m, 1H), 7.75-7.78 (m, 1H), 7.92 (d, 2H), 8.17 (d, 2H); MS: *m/z* 434.1 (MH^+).

Compound 461

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-3-dimethylsulfamoyl-benzenesulfonamide.** MS: *m/z* 493.0 (MH^+).

Compound 476

***N*-(Benzo[*b*]thiophen-2-yl)-4-(bromo)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide.** MS: *m/z* 464, 466(MH^+).

Compound 498

***N*-(Benzo[*b*]thiophen-2-yl)-4-nitro-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.43-2.62 (m, 2H), 3.87-3.96 (m, 2H), 7.23 (s, 1H), 7.35-7.46 (m, 2H), 7.67-7.80 (m, 2H), 7.91 (d, 2H), 8.34 (d, 2H).

Compound 564

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-isopropyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 458.1 (MH^+).

Compound 565

***N*-(3-Isopropyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 514.0 (MH^+).

Compound 628

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ -0.04-0.02 (m, 2H), 0.31-0.51 (m, 2H), 0.55-0.77 (m, 1H), 1.33-1.52 (m, 2H), 2.37 (s, 3H), 3.37-3.82 (m, 2H), 3.94 (s, 3H), 7.30-7.46 (m, 2H), 7.53-7.76 (m, 3H), 7.93 (d, 1H), 8.30 (d, 1H), 8.48 (s, 1H); MS: *m/z* 430.0 (MH^+).

Compound 629

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.36 (s, 3H), 2.35-2.55 (m, 2H), 3.67-3.92 (m, 2H), 3.95 (s, 3H), 7.35-7.48 (m, 2H), 7.57-7.76 (m, 3H), 7.90-7.95 (m, 1H), 8.31-8.35 (m, 1H), 8.45-8.47 (m, 1H); MS: *m/z* 458.0 (MH^+).

Compound 630

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 472.0 (MH^+).

Compound 631

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.40-1.57 (m, 2H), 1.58-1.76 (m, 2H), 2.13-2.34 (m, 2H), 2.29 (s, 3H), 2.49-2.52 (m, 2H), 3.42-3.82 (m, 2H), 7.68-7.89 (m, 5H), 8.21-8.34 (m, 2H), 8.44-8.45 (m, 1H); MS: *m/z* 486.0 (MH^+).

Compound 817

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-fluoro-propyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.02 (m, 2H), 3.78 (t, 2H), 4.55 (dt, 2H), 7.12 (s, 1H), 7.32 (m, 2H), 7.48 (m, 2H), 7.59 (m, 1H), 7.69 (m, 4H); MS: *m/z* 350.0 (MH^+).

Compound 818

***N*-(2-Fluoro-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.25 (s, 3H), 3.81 (br s, 2H), 4.38 (t, 1H), 4.48 (t, 1H), 7.31 (m, 2H), 7.46 (m, 2H), 7.61 (m, 3H), 7.75 (m, 2H); MS: *m/z* 350.0 (MH^+).

Compound 819

***N*-(3-Fluoro-propyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.88 (m, 2H), 2.29 (s, 3H), 1.81-1.98 (m, 2H), 4.45 (dt, 2H), 7.31 (m, 2H), 7.45 (t, 2H), 7.62 (m, 3H), 7.70 (m, 2H); MS: *m/z* 364.0 (MH^+), 386 (MNa^+).

Compound 823

***N*-(3-Fluoro-propyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.85 (m, 2H), 2.38 (s, 3H), 3.78 (br s, 2H), 3.98 (s, 3H), 4.52 (dt, 2H), 7.39 (m, 2H), 7.69 (m, 2H), 7.84 (d, 2H), 8.17 (d, 2H); MS: *m/z* 422.0 (MH^+), 444 (MNa^+).

Compound 831

***N*-(3-Fluoro-propyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3,4-difluoro-benzenesulfonamide.** MS: *m/z* 400.0 (MH^+), 422 (MNa^+).

Compound 840

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2,3,5-trifluoro-pyridin-4-ylmethyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.45 (t, 3H), 2.23 (s, 3H), 3.32 (q, 2H), 5.08 (s, 2H), 7.41 (m, 2H), 7.65 (m, 1H), 7.72 (m, 1H), 7.81 (s, 1H); MS: *m/z* 401.0 (MH^+), 423 (MNa^+).

Compound 841

***N*-(2-Fluoro-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3,4-difluoro-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.38 (s, 3H), 3.98 (br s, 2H), 4.53 (dt, 2H), 7.34 (m, 1H), 7.53 (m, 2H), 7.62 (m, 1H), 7.72 (m, 3H); MS: *m/z* 386.0 (MH^+), 408 (MNa^+).

Compound 842

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-fluoro-propyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 408.0 (MH^+).

Compound 843

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-ethyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 394.0 (MH^+), 416 (MNa^+).

Compound 844

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-ethyl)-benzenesulfonamide.** MS: *m/z* 336.0 (MH^+).

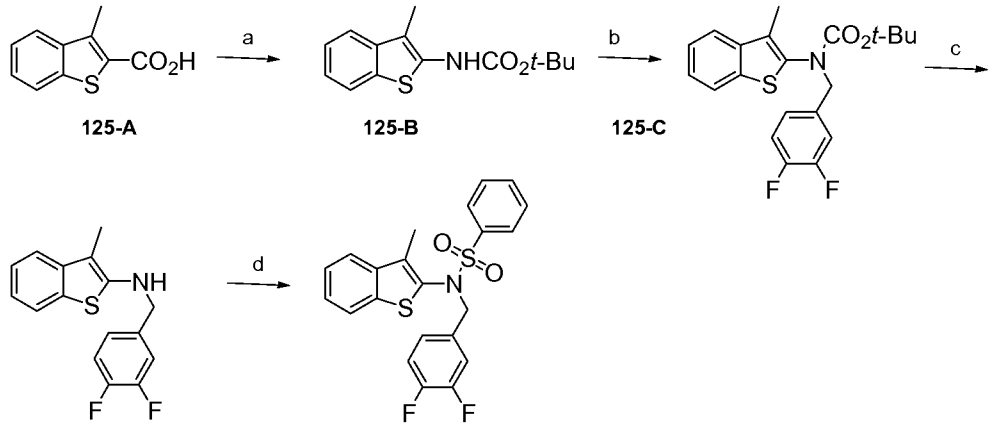
Compound 847

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-pyridin-4-ylmethyl)-ethane-sulfonamide.** MS: *m/z* 351.0 (MH^+).

Compound 848

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-pyridin-4-ylmethyl)-ethansulfonamide.** MS: *m/z* 393.0 (MH^+), 415 (MNa^+).

Example 4



125-A 125-B 125-C 125-D Compound 125

a)DPPA, DIEA, *t*-BuOH; b) NaH, 3,4-difluorobenzyl bromide, DMF; c) TFA, DCM; d) benzenesulfonyl chloride, DMAP, pyridine.

(3-Methyl-benzo[*b*]thiophen-2-yl)-carbamic acid *tert*-butyl ester (125-B) A solution of compound **125-A** (3.15 g, 16.4 mmol), *N,N*-diisopropylethylamine (3.15 mL, 18.0 mmol) and diphenyl phosphoryl azide (4.23 mL, 19.7 mmol) in *t*-butanol (40 mL) was heated at reflux for 8 h. The solvent was evaporated *in vacuo*, and the residue partitioned between dichloromethane and 1N aqueous sodium hydroxide. The organic layer was applied to a silica gel column, and the product isolated by flash column chromatography eluting with an ethyl acetate-heptane gradient, to afford compound

125-B as a colorless solid (2.3 g, 53%). ^{1}H-NMR ($CDCl_3$): δ 1.48 (s, 9H), 2.26 (s, 3H), 6.74 (br s, 1H), 7.21-7.26 (m, 1H), 7.31-7.36 (m, 1H), 7.54 (d, 1H), 7.71 (d, 1H); MS: *m/z* 264.1 (MH^+).

(3,4-Difluoro-benzyl)-(3-methyl-benzo[*b*]thiophen-2-yl)-carbamic acid *tert*-butyl ester (125-C) Sodium hydride (60%, 0.37 g, 9.19 mmol) was added to a solution of compound **125-B** (2.2 g, 8.35 mmol) in DMF (30 mL), at 0 °C and the resultant mixture was stirred for 15 minutes. 3,4-Difluorobenzylbromide (1.18 mL, 9.2 mmol) was added, and the solution was stirred at ambient temperature for 2 h. The reaction mixture was diluted with water, extracted with ethyl acetate, the organic extract washed with water (3X), brine, dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by flash column chromatography, eluting with an ethyl acetate-heptane gradient, to afford compound **125-C** as an oil (2.73 g, 84%). ^{1}H-NMR ($CDCl_3$): δ 1.40 (s, 9H), 1.97 (s, 3H), 4.72 (s, 2H), 6.93-7.19 (m, 3H), 7.28-7.39 (m, 2H), 7.61 (d, 1H), 7.70 (d, 1H).

(3,4-Difluoro-benzyl)-(3-methyl-benzo[*b*]thiophen-2-yl)-amine (125-D). A solution of compound **125-C** (2.7 g, 6.9 mmol) in dichloromethane (40 mL) and trifluoroacetic acid (40 mL) was stirred at rt for 4 h. The solvent was evaporated *in vacuo*, and the residue partitioned between dichloromethane and saturated aqueous sodium bicarbonate. The organic layer was dried over sodium sulfate, and the solvent evaporated *in vacuo* to afford compound **125-D** as a colorless solid (1.86 g, 93%). ^{1}H-NMR ($CDCl_3$): δ 2.16 (s, 3H), 4.37 (s, 2H), 7.09-7.32 (m, 5H), 7.40 (d, 1H), 7.60 (d, 1H); MS: *m/z* 290.1 (MH^+).

Compound 125

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** Benzenesulfonyl chloride (0.121 mL, 0.94 mmol) was added to a solution of compound **125-D** (237 mg, 0.473 mmol) and *N,N*-dimethylaminopyridine (catalytic amount) in pyridine (4 mL), at 0 °C. The resultant solution was stirred for 30 min, allowed to warm to room temperature and stirred at ambient temperature overnight. The solvent was evaporated *in vacuo*, the residue partitioned between 2N HCl and dichloromethane, the layers separated, and the organic layer dried over magnesium sulfate, filtered, and the solvent evaporated *in vacuo*. The residue was purified by HPLC (C_{18}) eluting with an acetonitrile (0.1% TFA)-water (0.1% TFA) (40-90%) gradient to afford compound **125** as a solid (0.11g, 54%). ^{1}H-NMR ($CDCl_3$): δ

2.04 (s, 3H), 4.64 (br s, 2H), 6.93-7.04 (m, 2H), 7.12-7.17 (m, 1H), 7.31-7.38 (m, 2H), 7.52-7.70 (m, 5H), 7.81-7.84 (m, 2H); MS: *m/z* 430.1 (MH^+).

Following the procedure described above for Example 4 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 126

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-phenyl-methanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.07 (s, 3H), 4.38 (d of d, 2H), 4.64 (d of d, 2H), 7.15-7.44 (m, 12H), 7.65 (d, 1H); MS: *m/z* 444.0 (MH^+).

Compound 127

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-fluoro-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ: 2.05 (s, 3H), 4.63 (br s, 2H), 6.94-7.07 (m, 2H), 7.10-7.18 (m, 1H), 7.33-7.40 (m, 3H), 7.50-7.69 (m, 5H); MS: *m/z* 448.0 (MH^+).

Compound 128

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-fluoro-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.50 (s, 3H), 4.88 (br s, 2H), 7.10-7.95 (m, 11H); MS: *m/z* 448.0 (MH^+).

Compound 129

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-thiene-2-ylsulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.02 (s, 3H), 4.76 (br s, 2H), 7.14-7.16 (m, 1H), 7.29-7.43 (m, 5H), 7.70 (d of d, 1H), 7.83-7.86 (m, 2H), 8.16 (d of d, 1H); MS: *m/z* 436.0 (MH^+).

Compound 130

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-1-methyl-1*H*-imidazole-4-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.71 (s, 3H), 4.98 (s, 2H), 7.17 (s, 1H), 7.23-7.45 (m, 5H), 7.69-7.73 (m, 1H), 7.78-7.81 (m, 1H), 7.92 (s, 1H), 7.95 (s, 1H); MS: *m/z* 420.1 (MH^+).

Compound 131

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-3-fluoro-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.93 (s, 2H), 7.17-7.24 (m, 2H), 7.30-7.86 (m, 10H); MS: *m/z* 434.1 (MH^+).

Compound 132

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-4-trifluoromethyl-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.93 (s, 2H), 7.17-7.25 (m, 2H), 7.30-7.44 (m, 4H), 7.71-7.75 (m, 1H), 7.82-7.89 (m, 1H), 8.05-8.07 (m, 4H); MS: *m/z* 484.2 (MH^+).

Compound 133

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-*C*-methanesulfonyl-methanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.26 (m, 3H), 4.97 (s, 2H), 5.62 (s, 2H), 7.17-7.23 (m, 1H), 7.33-7.47 (m, 5H), 7.76-7.82 (m, 1H), 7.85-7.90 (m, 1H); MS: *m/z* 432.0 (MH^+).

Compound 134

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methoxy-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 4.99 (s, 2H), 7.17 (s, 1H), 7.29-7.38 (m, 5H), 7.45-7.53 (m, 1H), 7.55-7.60 (t, 1H), 7.70-7.76 (m, 3H), 7.82-7.87 (m, 1H); MS: *m/z* 496.0 (MH^+).

Compound 135

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.91 (s, 3H), 5.01 (s, 2H), 7.19 (s, 1H), 7.30-7.36 (m, 2H), 7.45-7.51 (t, 1H), 7.69-7.73 (m, 3H), 7.82-7.85 (m, 1H), 7.97-7.99 (d, 2H), 8.17-8.20 (d, 2H); MS: *m/z* 524.1 (MH^+).

Compound 136

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.87 (s, 3H), 5.02 (s, 2H), 7.21 (s, 1H), 7.32-7.34 (m, 2H), 7.45-7.50 (t, 1H), 7.71-7.73 (m, 3H), 7.81-7.85 (m, 2H), 8.08-8.11 (m, 1H), 8.25-8.26 (m, 1H), 8.30-8.33 (s, 1H); MS: *m/z* 524.1 (MH^+).

Compound 137

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carbomethoxy-benzenesulfonamide** ^{1}H-NMR (DMSO-d_6): δ 1.96 (s, 3H), 3.89 (s, 3H), 4.88 (s, 2H), 7.38-7.47 (m, 3H), 7.62-7.68 (m, 2H), 7.69-7.72 (m, 1H), 7.84-7.88 (m, 2H), 8.15-8.18 (m, 1H), 8.27-8.28 (m, 1H), 8.33-8.35 (m, 1H); MS: *m/z* 538.0 (MH^+).

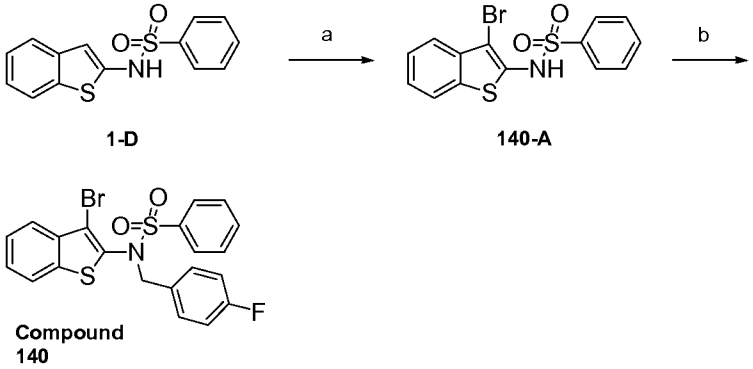
Compound 138

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.94 (s, 3H), 3.93 (s, 3H), 4.89 (s, 2H), 7.36-7.48 (m, 3H), 7.63-7.71 (m, 3H), 7.81-7.86 (m, 1H), 8.02-8.04 (m, 2H), 8.19-8.22 (m, 1H); MS: *m/z* 538.0 (MH^+).

Compound 139

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-carbomethoxy-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 5.08 (s, 2H), 7.24 (s, 1H), 7.31-7.34 (m, 2H), 7.47-7.52 (m, 1H), 7.66-7.85 (m, 8H); MS: *m/z* 524.1 (MH^+).

Example 5



a) Br_2, DCM; b) LHMDS, 4-fluorobenzyl bromide, THF.

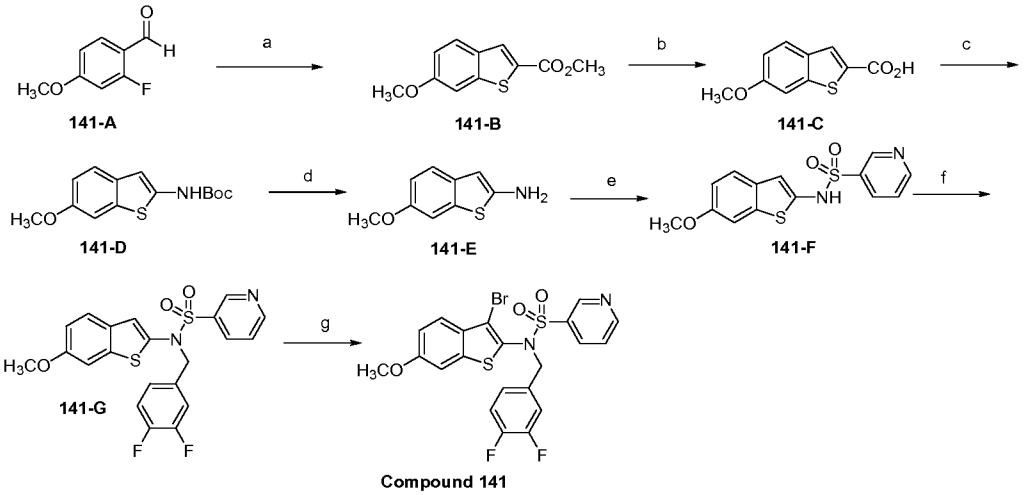
***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-benzenesulfonamide (140-A)**. Bromine (36 μL, 0.69 mmol) was added to a solution of compound **1-D** (0.20 g, 0.69 mmol) in dichloromethane (10 mL) at 0 °C, and stirred for 15 minutes. The resultant solution was washed with water then aqueous $NaHSO_3$, and dried over magnesium sulfate to afford compound **140-A** as a blue solid (0.295 g). ^{1}H-NMR ($CDCl_3$): δ 6.98 (s, 1H, exchanges with D_2O), 7.25-7.44 (m, 4H), 7.49-7.54 (m, 2H), 7.64 (d of d, 1H), 7.78-7.83 (m, 2H); MS: *m/z* 368 (MH^+).

Compound 140

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-benzyl)-benzenesulfonamide**. Lithium bis(trimethylsilyl)amide (1.0 M in hexanes, 0.67 mL, 0.67 mmol) was added dropwise to a solution of compound **140-A** (0.225 g, 0.61 mmol) in THF (3 mL) at -78 °C. The solution was stirred at -78 °C for 15 minutes, to

which was added a solution of 4-fluorobenzyl bromide (83 µL, 0.67 mmol) in THF (0.5 mL). The reaction mixture was allowed to warm to rt and stirred at ambient temperature for 6 days. The solution was washed with aqueous ammonium chloride, and the solvent was evaporated *in vacuo*. The crude residue was purified by reverse phase HPLC (C_{18}), eluting with an acetonitrile-water (0.1%) (10-90%) gradient to afford compound **140** as a colorless solid (0.130 g, 45%). ^{1}H-NMR ($CDCl_3$): δ 4.81 (s, 2H), 6.87-6.97 (m, 2H), 7.20-7.25 (m, 3H), 7.36-7.43 (m, 2H), 7.51-7.56 (m, 2H), 7.63-7.71 (m, 2H), 7.86-7.89 (m, 2H); MS: *m/z* 476.1 (MH^+).

Example 6



a) $HSCH_2CO_2Me$, TEA, DMF; b) NaOH, H_2O, MeOH; c) DPPA, DIEA, *t*-BuOH; d) HCl, EtOAc; e) 3-pyridinesulfonyl chloride, pyridine; f) KO-*t*-Bu, 3,4-difluorobenzyl bromide, THF; g) NBS, DCE, AcOH.

6-Methoxy-benzo[*b*]thiophene-2-carboxylic acid methyl ester (141-B). To a solution of compound **141-A** (21.4 g; 139 mmol) in anhydrous DMF (165 mL) was added triethylamine (25.2 mL; 181 mmol) followed methyl thioglycolate (5.3 mL; 278 mmol) and the reaction was heated at 100 °C for 72 h. The reaction was cooled, partitioned between EtOAc and H_2O, the layers separated, the aqueous phase extracted with EtOAc, the organic extracts combined, washed with 3N NaOH, H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure. The crude residue was triturated with CH_2Cl_2-heptanes, filtered, and the solid washed with heptanes and dried overnight to afford compound **141-B**. The filtrate was evaporated and purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc

gradient to afford a second crop of compound **141-B**. The combined yield of the two crops afforded a white solid (6.55 g, 21%). ^{1}H-NMR (DMSO-d_6): δ 3.85 (s, 3H), 3.86 (s, 3H), 7.07-7.10 (m, 1H), 7.63 (s, 1H), 7.89-7.91 (d, 1H), 8.11 (s, 1H); MS: *m/z* 223.0 (MH^+).

6-Methoxy-benzo[*b*]thiophene-2-carboxylic acid (141-C). To a solution of compound **141-B** (6.55 g; 29.4 mmol) in methanol (100 mL) was added 1N NaOH (44.2 mL; 44.2 mmol) and the reaction was heated at 65 °C for 18 h. The reaction was cooled, the solvent evaporated under reduced pressure, the residue dissolved in H_2O, cooled to 0 °C, acidified with 2N HCl, and the solid filtered, washed with H_2O, and dried *in vacuo* to afford compound **141-C** as a white solid (6.01 g, 98%). ^{1}H-NMR (DMSO-d_6): δ 3.84 (s, 3H), 7.05-7.08 (m, 1H), 7.60-7.61 (d, 1H), 7.87-7.89 (d, 1H), 8.01 (s, 1H), 13.24 (s, 1H); MS: *m/z* 208.9 (MH^+).

6-Methoxy-benzo[*b*]thiophen-2-yl)-carbamic acid *tert*-butyl ester (141-D). To a solution of compound **141-C** (6.01 g; 28.8 mmol) in *tert*-butanol (80 mL) was added DPPA (9.30 mL; 43.2 mmol) followed by DIEA (5.51 mL; 31.6 mmol) and the reaction was refluxed for 18 h. The reaction was cooled, the solvent evaporated under reduced pressure, and the crude residue purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford compound **141-D** as a beige solid (5.47 g, 68%). ^{1}H-NMR (DMSO-d_6): δ 1.49 (s, 9H), 3.77 (s, 3H), 6.68 (s, 1H), 6.89-6.90 (m, 1H), 7.37-7.38 (m, 1H), 7.47-7.52 (m, 1H), 10.52 (s, 1H); MS: *m/z* 280.0 (MH^+).

6-(Methoxy-benzo[*b*]thiophen-2-yl)-amine (141-E). To a solution of compound **141-D** (4.94 g; 17.7 mmol) in EtOAc (20 mL), cooled to 0 °C, was bubbled $HCl_{(g)}$, until the solution was saturated and the reaction was stirred at ambient temperature for 18 h. The solvent was evaporated under reduced pressure and the resulting residue was triturated with ether, filtered, washed with ether, and dried *in vacuo* to afford compound **141-E** as a beige solid (3.29 g, 86%). MS: *m/z* 180.0 (MH^+).

***N*-(6-Methoxy-benzo[*b*]thiophen-2-yl)-pyridin-3-yl-sulfonamide (141-F).** To a solution of compound **141-E** (1.0 g; 4.63 mmol) in pyridine (15 mL), cooled to 0 °C, was added 3-pyridyl sulfonyl chloride (1.49 g; 6.95 mmol) and the reaction was allowed to stir at ambient temperature for 2 h. The reaction was diluted with EtOAc, washed with 2N HCl, water, brine, dried over Na_2SO_4, filtered, the solvent evaporated

under reduced pressure. The crude residue was purified by trituration of the solid with CH_2Cl_2. The solid was filtered, washed with CH_2Cl_2, and dried *in vacuo* to afford compound **141-F** as a beige solid (1.01 g, 68%). ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 6.86 (s, 1H), 6.91-6.93 (m, 1H), 7.39-7.40 (d, 1H), 7.57-7.59 (d, 1H), 7.62-7.65 (m, 1H), 8.13-8.16 (m, 1H), 8.81-8.82 (m, 1H), 8.90-8.91 (d, 1H), 11.15 (s, 1H); MS: *m/z* 321.0 (MH^+).

***N*-(3.4-Difluoro-benzyl)-*N*-(6-methoxy-benzo[*b*]thiophen-2-yl)-pyridin-3-yl-sulfonamide (141-G)**. To a solution of compound **141-F** (0.488 g; 1.52 mmol) in THF (15 mL) was added 1M potassium *tert*-butoxide (2.28 mL; 2.28 mmol) and the reaction mixture was stirred at ambient temperature for 30 min. 3,4-Difluorobenzyl bromide (0.409 g; 1.97 mmol), dissolved in THF (1.0 mL), was added drop-wise, and the reaction was stirred at ambient temperature for 18 h. The reaction was diluted with EtOAc, washed with 2N HCl, water, brine, dried over Na_2SO_4, filtered, the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford an oily semi-solid, which was further purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 55% to 75% MeCN-H_2O gradient to afford compound **141-G** as a white solid (0.447 g, 66%). ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 4.89 (s, 2H), 6.93-6.96 (m, 1H), 7.11 (s, 1H), 7.19-7.20 (m, 1H), 7.34-7.43 (m, 3H), 7.60-7.62 (d, 1H), 7.70-7.73 (m, 1H), 8.21-8.24 (m, 1H), 8.93-8.96 (m, 2H); MS: *m/z* 447.0 (MH^+).

Compound 141

***N*-(3-Bromo-6-methoxy-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-pyridin-3-yl-sulfonamide**. To a solution of compound **141-G** (0.044 g; 0.097 mmol) in DCE (0.5 mL) and acetic acid (0.5 mL) was added *N*-bromosuccinimide (0.021 g; 0.117 mmol) and the reaction was stirred at ambient temperature for 6 h. The reaction was diluted with EtOAc, washed with 10% $NaHCO_3$, water, brine, dried over Na_2SO_4, filtered, the solvent evaporated under reduced pressure. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) eluting with a 65% to 85% MeCN-H_2O gradient to afford compound **141** as a beige solid (0.014 g, 28%). ^{1}H-NMR (DMSO-d_6): δ 3.80 (s, 3H), 4.86 (s, 2H), 7.08-7.16 (m, 2H), 7.32-7.40 (m, 2H), 7.54-7.57 (m, 2H), 7.72-7.75 (m, 1H), 8.29-8.32 (m, 1H), 8.91-8.97 (d, 1H), 9.00-9.05 (m, 1H); MS: *m/z* 525 (MH^+).

Following the procedure described above for Example 6 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 142

***N*-(3,4-Difluoro-benzyl)-*N*-(7-methoxy-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.88 (s, 3H), 4.88 (s, 2H), 6.87-6.91 (m, 1H), 7.14-7.41 (m, 6H), 7.63-7.79 (m, 2H), 7.80-7.91 (m, 3H); MS: *m/z* 446.1 (MH^+).

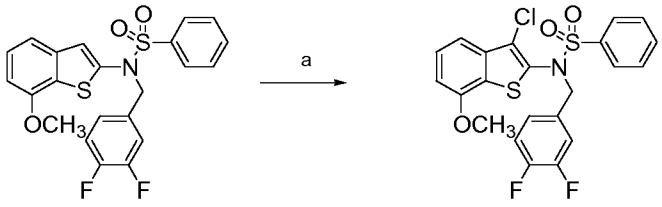
Compound 375

***N*-(6-Fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carbomethoxy-benzenesulfonamide.** MS: m/z 555.9 (MH^+).

Compound 412

***N*-(6-Fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carbomethoxybenzenesulfonamide.** MS: *m/z* 489.9 (MH^+).

Example 7



Compound 142 Compound 143

a) NCS, DCE, AcOH.

Compound 143

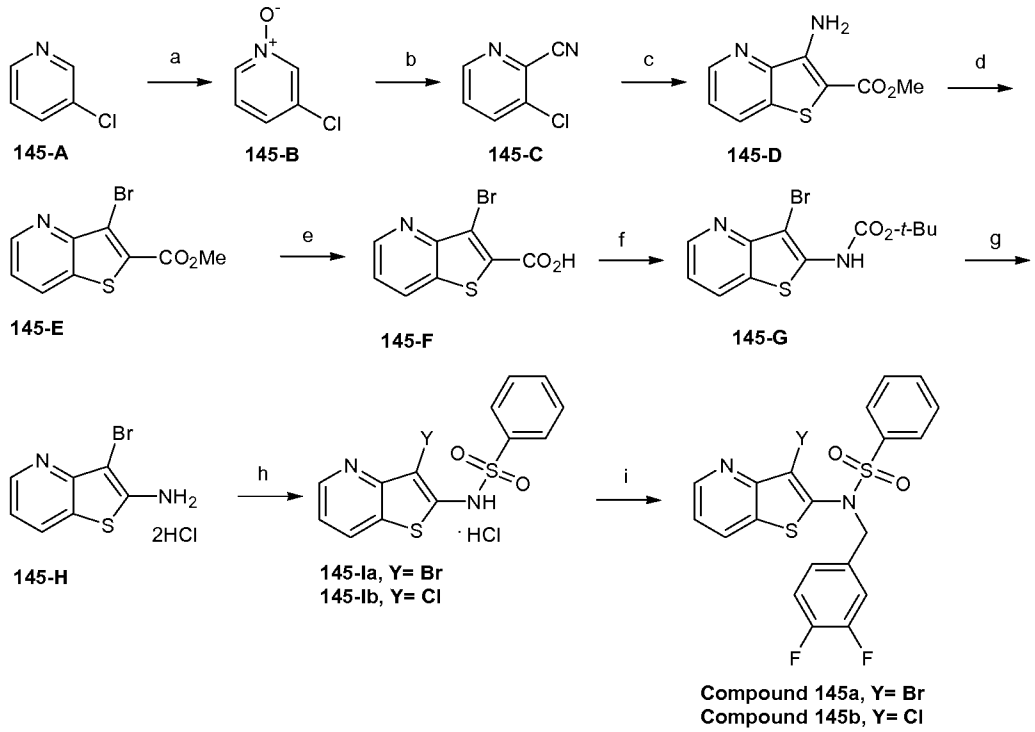
***N*-(3-Chloro-7-methoxy-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide.** To a solution of compound **142** (0.061 g; 0.137 mmol) in DCE (0.5 mL) and acetic acid (0.5 mL) was added *N*-chlorosuccinimide (0.027 g; 0.206 mmol) and the reaction was stirred at ambient temperature for 2 h. The reaction was diluted with EtOAc, washed with 10% $NaHCO_3$, water, brine, dried over Na_2SO_4, filtered, the solvent evaporated under reduced pressure. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) eluting with a 60% to 80% MeCN-H_2O gradient to afford compound **143** as a beige solid (0.011 g, 17%). ^{1}H-NMR (CD_3OD): δ 3.94 (s, 3H), 4.80 (s, 2H), 6.96-7.23 (m,

5H), 7.27-7.41 (m, 1H), 7.60-7.65 (m, 2H), 7.72-7.76 (m, 1H), 7.87-7.90 (m, 2H); MS: *m/z* 480.0 (MH^+).

Compound 144

***N*-(3,6-Dichloro-7-methoxy-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide.** ^{1}H-NMR (CD_3OD): δ 3.94 (s, 3H), 4.83 (s, 2H), 6.90-6.92 (m, 1H), 7.03-7.18 (m, 2H), 7.21-7.23 (m, 1H), 7.34-7.36 (m, 1H), 7.61-7.65 (m, 2H), 7.73-7.77 (m, 1H), 7.82-7.90 (m, 2H); MS: *m/z* 513.9 (MH^+).

Example 8



a) H_2O_2 (30%), acetic acid; b) TMSCN, acetonitrile, TEA; c) methyl thioglycolate, K_2CO_3, acetonitrile; d) CuBr, $NaNO_2$, HBr, H_2O; e) LiOH, H_2O, THF; f) DPPA, DIEA, *t*-BuOH; g) HCl, dioxane; h) $PhSO_2Cl$, pyridine; i) 1.0M NaHMDS, THF, 3,4-difluorobenzyl bromide, DMF.

3-Chloro-pyridine 1-oxide (145-B). To a solution of 3-chloropyridine, (22.71 g, 200 mmol) in acetic acid (80 mL) was added hydrogen peroxide solution (30% aqueous, 40 mL), and the mixture was heated at 80 °C for 15 h. Additional hydrogen peroxide solution (30% aqueous, 5 mL) was added to the reaction mixture and the heating continued an additional 5 h. After cooling, the reaction mixture was quenched into a solution of $NaHSO_3$ in water (400 mL), using starch-iodine paper to confirm the

destruction of excess hydrogen peroxide. The mixture was evaporated *in vacuo* and partitioned between water (100 mL)and dichloromethane (250 mL). The organics were washed with saturated $NaHCO_3$ solution (2X100 mL), and brine (100 mL). The combined aqueous layers were extracted with dichloromethane (8X100 mL),the organic extracts were combined, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The organic residue was partitioned between dichloromethane/water, treated with solid $NaHCO_3$, and filtered. The aqueous washes from the first extraction were treated with $NaHCO_3$, extracted with dichloromethane (3X100 mL), and the combined organics dried with Na_2SO_4, filtered, and evaporated *in vacuo* to afford compound **145-B** as an orange oil (22.37 g, 86%). ^{1}H-NMR (DMSO-d_6): δ 7.40-7.53 (m, 2H), 8.22 (d, 1H), 8.52 (s, 1H); MS: *m/z* 130.1 (MH^+).

3-Chloro-pyridine-2-carbonitrile (145-C). To a solution of compound **145-B**, (22.37 g, 172.7 mmol) in acetonitrile (175 mL) was added triethylamine (48 mL, 346 mmol) and TMS-CN (56 mL, 420 mmol). The solution was heated at reflux for 20 h then evaporated *in vacuo*. The residue was partitioned between EtOAc (250 mL), 10% aqueous Na_2CO_3 (50 mL), and filtered over celite. The organic portion of the filtrate was washed with 10% aqueous Na_2CO_3 (2X50 mL), brine (50 mL), and the organics dried over Na_2SO_4, filtered, and evaporated *in vacuo* to afford a dark crystalline residue, which was dissolved in warm diethyl ether (200 mL), filtered, and evaporated *in vacuo* to afford compound **145-C** as a tan-orange powder (23.41 g, 98%). ^{1}H-NMR (DMSO-d_6): δ 7.78-7.84 (m, 1H), 8.30 (d, 1H), 8.73 (d, 1H); MS: *m/z* 139.1 (MH^+).

3-Amino-thieno[3,2-*b*]pyridine-2-carboxylic acid methyl ester (145-D). To a solution of compound **145-C** (23.41 g, 169.0 mmol) in acetonitrile (170 mL) was added methyl thioglycolate (16.2 mL, 178 mmol) and K_2CO_3 (46.72 g, 338 mmol). The mixture was heated under reflux for 3 h then filtered hot and the filter cake rinsed with acetonitrile. The filter cake was suspended in refluxing acetonitrile, filtered hot, and rinsed with additional acetonitrile. The combined filtrates were evaporated *in vacuo*, the residue triturated with warm water (250 mL), filtered, and rinsed with water. The solid was dissolved in warm methanol (500 mL), treated with charcoal, filtered, and evaporated *in vacuo*. The residue was triturated with ethanol (25 mL), filtered, washed with ethanol (25 mL), and dried *in vacuo* to afford compound **145-D** as a brown powder (21.65 g, 62%). ^{1}H-NMR (DMSO-d_6): δ 3.83 (s, 3H), 6.91 (s, 2H), 7.52-7.59 (m, 1H), 8.40 (dd, 1H), 8.69 (dd, 1H); MS: *m/z* 209.1 (MH^+).

3-Bromo-thieno[3,2-*b*]pyridine-2-carboxylic acid methyl ester (145-E). To a solution of CuBr (15.09 g, 105.2 mmol) in 48 % aqueous HBr (250 mL), cooled in an ice bath, was added compound **145-D** (20.82 g, 100 mmol). To the reaction mixture was added a solution of $NaNO_2$ (8.29 g, 120 mmol) in water (200 mL) drop-wise over 1 h. After 30 min, solid $NaNO_2$ (0.83 g, 12.0 mmol) was added, and after another 30 min an additional portion of solid $NaNO_2$ (0.83 g, 12.0 mmol) was added. After 10 min the reaction mixture was carefully poured into a mixture of ice (1L) and $NaHCO_3$ (200 g). The mixture was extracted with dichloromethane (5X200 mL), and the combined organic extracts dried over $MgSO_4$, filtered, and evaporated *in vacuo* to afford compound **145-E** as a brown powder (25.16 g). ^{1}H-NMR (DMSO-d_6): δ 3.94 (s, 3H), 7.65 (m, 1H), 8.65 (dd, 1H), 8.88 (dd, 1H); MS: *m/z* 272.0 (MH^+).

3-Bromo-thieno[3,2-*b*]pyridine-2-carboxylic acid (145-F). To a solution of compound **145-E** (4.94 g, 18.2 mmol) in 5:1 THF/H_2O (200 mL) was added LiOH•H_2O (0.797 g, 19.0 mmol). The reaction was stirred for 3 days then concentrated *in vacuo*, to which was added water (100 mL) and 1N HCl (19.0 mL), and the resultant precipitate was isolated by filtration. The solid was rinsed with water and dried under vacuum to afford compound **145-F** as a tan-yellow solid (4.51 g, 96%). ^{1}H-NMR (DMSO-d_6): δ 7.62 (dd, 1H), 8.62 (dd, 1H), 8.86 (dd, 1H), 14.18 (br s, 1H); MS: *m/z* 257.9 (MH^+).

3-Bromo-thieno[3,2-*b*]pyridin-2-yl)-carbamic acid *tert*-butyl ester (145-G). A solution of compound **145-F** (2.0 g, 7.75 mmol), *N,N*-diisopropylethylamine (1.49 mL, 8.52 mmol) and diphenyl phosphoryl azide (2.07 mL, 9.30 mmol) in *t*-butanol (20 mL) was heated at reflux for 16 h. The solvent was evaporated *in vacuo*, the residue dissolved in dichloromethane, washed with 1N NaOH, brine, dried with Na_2SO_4, and evaporated to afford a crude residue which was purified by flash column chromatography (SiO_2), eluting with dichloromethane to afford compound **145-G** as a yellow solid (1.51 g, 56%). ^{1}H-NMR($CDCl_3$): δ 1.6 (s, 9H), 7.2 (d of d, 1H), 7.5 (br s, 1H), 8.0 (d, 1H), 8.7 (d, 1H); MS: *m/z* 251(MH^+).

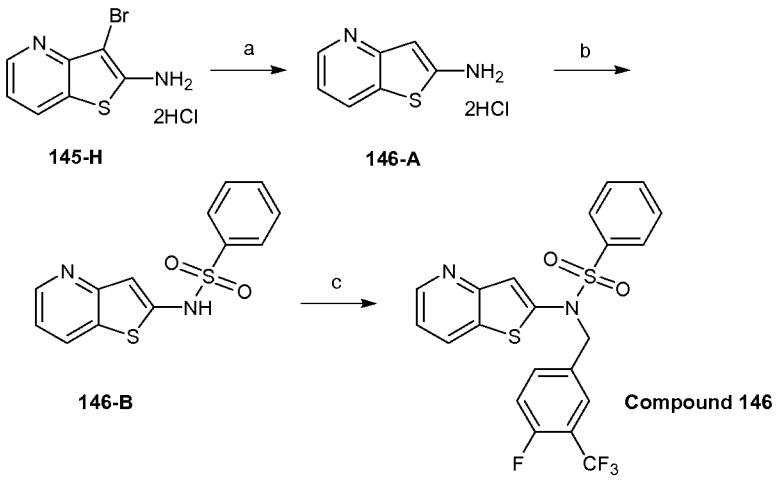
3-Bromo-thieno[3,2-*b*]pyridin-2-ylamine hydrochloride (145-H). Compound **145-G** (0.75 g, 2.28 mmol) was added to a solution of HCl in dioxane (4 N, 7.5 mL) and the reaction mixture was stirred at rt for 2 h. The solvent was evaporated under reduced pressure to afford compound **145-H** as a yellow solid (0.74 g). ^{1}H-NMR (DMSO-d_6): δ 7.3 (d, 1H), 8.3 (d, 1H), 8.5 (br s, 2H) superimposed on 8.55 (d, 1H).

***N*-(3-Bromo-thieno[3,2-*b*]pyridin-2-yl)-benzenesulfonamide hydrochloride (145-I).** To a solution of compound **145-H** (0.46 g, 1.52 mmol) in pyridine (4.6 mL), cooled to 0 °C, was added benzenesulfonyl chloride (0.206 mL, 1.60 mmol), and the reaction was heated to 50 °C for 72 h. Additional benzenesulfonyl chloride (0.412 mL, 3.20 mmol) was added and the reaction mixture was heated at 50 °C for an additional 16 h. The solvent was evaporated *in vacuo*, the residue dissolved in dichloromethane and washed with aqueous sodium bicarbonate. The aqueous layer was acidified with 1N HCl, extracted with dichloromethane, and the organic layer was evaporated *in vacuo* to afford a yellow solid (0.22 g, 36%) as a 1 / 3.5 mixture of the 3- bromo - and 3-chloro-substituted compounds, **145-Ia** and **145-Ib**, respectively. ^{1}H-NMR (DMSO-d_6): δ 7.1-7.2 (m, 1H), 7.4-7.6 (m, 3H), 7.8 (m, 2H), 8.1-8.2 (m, 1H), 8.25-8.35 (m, 1H); MS: *m/z* 465 and 509 (MH^+).

Compound 145

***N*-(3-Bromo-thieno[3,2-*b*]pyridin-2-yl)-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide and *N*-(3-chloro-thieno[3,2-*b*]pyridin-2-yl)-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide.** To a mixture of compounds **145-Ia** and **145-Ib** (90 mg, 0.222 mmol) in DMF (1 mL), at rt, was added 1.0M sodium bis(trimethylsilyl)amide in THF (0.44 mL, 0.444 mmol). The solution was stirred 30 min at rt to which was added 3,4-difluorobenzyl bromide (0.029 mL, 0.222 mmol). The resultant solution was stirred at ambient temperature for 16 h, to which was added additional DMF (1 mL) followed by 3,4-difluorobenzyl bromide (0.029 mL, 0.222 mmol), and the reaction mixture stirred at rt for 3 days. The solvent was evaporated and the residue purified by reverse-phase HPLC eluting with an acetonitrile-water gradient. Further purification by flash column chromatography (SiO_2), eluting with dichloromethane, afforded compound **145** as a clear, hard gum (19.7 mg, 18%). ^{1}H-NMR (DMSO-d_6): δ 4.74 (s, 2H), 7.00-7.10 (s superimposed on m, 3H), 7.15-7.21 (m, 1H), 7.26-7.36 (m, 2H), 7.49-7.54 (m, 2H), 7.62-7.67 (m, 3H), 7.73-7.78 (m, 2H); MS: *m/z* 416.1 (MH^+).

Example 9



a) 10%Pd/C, H_2, MeOH; b) benzenesulfonyl chloride, pyridine; c) 1.0M *t*-BuOK/THF, 4-fluoro-3-trifluoromethylbenzyl bromide, DMF.

Thieno[3,2-*b*]pyridin-2-ylamine hydrochloride (146-A). A mixture of compound **145-H**, (1.86 g, 6.16 mmol) and 10% Pd/C (0.49 g, 26.3% w/w)in methanol (75 mL) was catalytically hydrogenated on a Parr shaker at 25 psi. After 3 h, the catalyst was filtered, the reaction mixture recharged with 10% Pd/C (0.49 g, 26.3% w/w) and shaken an additional 16 h at 22 psi H_2. The reaction was filtered, recharged with 10% Pd/C (0.20 g, 10.8% w/w), and shaken at 20 psi H_2 for an additional 24 h. The reaction mixture was filtered, evaporated, and the free base isolated by washing with aqueous sodium bicarbonate. The resultant residue was purified by flash column chromatography (SiO_2), eluting with 3% MeOH / CH_2Cl_2 to afford compound **146-A** as a yellow solid (0.65 g, 57%). ^{1}H-NMR (DMSO-d_6): δ 6.4 (s, 1H), 7.1 (dd, 1H), 8.3 (2, 1H), 8.4 (s, 2H), 8.5 (d, 1H), 15.2 (br s, 1H); MS: *m/z* 151.1 (MH^+).

***N*-Thieno[3,2-*b*]pyridin-2-yl-benzenesulfonamide hydrochloride (146-B)**. To a suspension of compound **146-A** (0.65 g, 2.91 mmol) in pyridine (30 mL), at rt, was added benzenesulfonyl chloride (0.751 mL, 5.83 mmol), and the reaction was stirred for 16 h. Additional benzenesulfonyl chloride (0.225 mL, 1.76 mmol) was added and the reaction mixture was stirred at rt for an additional 16 h. The solvent was evaporated *in vacuo*, the residue treated with 1N HCl and extracted several times with dichloromethane and ethyl acetate. The aqueous layer was filtered, dissolved in methanol, and the combined organic extracts were evaporated *in vacuo*. The resultant residue was purified by reverse phase HPLC, eluting with an MeCN-H_2O gradient to afford compound **146-B** as an orange solid (0.24 g, 20%). ^{1}H-NMR (CD_3CN): δ 6.92

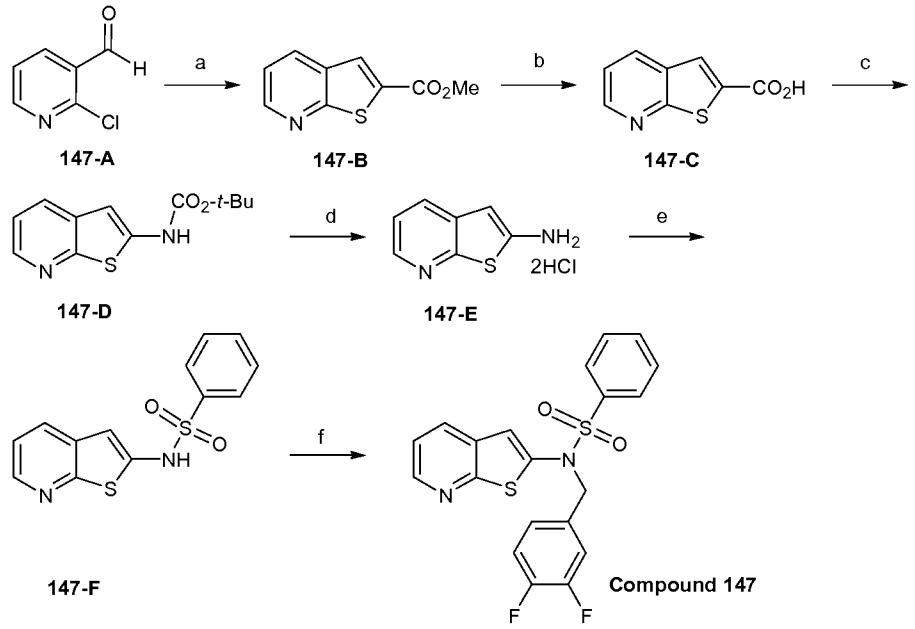
(s, 1H), 7.2 8.0 (d of d, 1H), 7.46 (m, 2H), 7.56 (m, 1H), 7.85 (m, 2H), 8.27 (d, 1H), 8.35 (d, 1H); MS: *m/z* 291.09 (MH^+).

Compound 146

***N*-(3,4-Difluoro-benzyl)-*N*-thieno[3,2-*b*]pyridin-2-yl-benzenesulfonamide.**

To compound **146-B**, (0.237 g, 0.725 mmol) in DMF (1 mL), cooled to 0 °C, was added 1.0M potassium *t*-butoxide in THF (1.71 mL, 1.71 mmol), drop-wise over 5 min. The solution was stirred for 30 min at 0 °C, to which was added 4-fluoro-3-trifluoromethylbenzyl bromide (0.132 mL, 0.898 mmol). The resultant solution was stirred 5 min at 0 °C and allowed to warm to rt and stirred overnight. Saturated sodium bicarbonate solution was added, and the mixture evaporated *in vacuo*. The residue was partitioned between water and diethyl ether, the organic phase separated, and the aqueous phase extracted with diethyl ether. The combined organic phases were evaporated *in vacuo* and the crude residue purified by reverse-phase HPLC to afford compound **146** as a dark solid (28 mg, 8%). ^{1}H-NMR ($CDCl_3$): δ 5.00 (s, 2H), 7.16 (t, 1H), 7.44 (d of d, 1H), 7.56 (m, 3H), 7.69 (m, 3H), 7.85 (m, 1H), 8.33 (d, 2H), 8.57 (d, 1H); MS: *m/z* 467.09 (MH^+).

Example 10



a) Ethyl thioglycolate, TEA, CH_3CN; b) NaOH, MeOH; c) DPPA, DIEA, *t*-BuOH; d) HCl, dioxane; e) benzenesulfonyl chloride, pyridine; f) 1.0M LiHMDS/THF, 3,4-difluorobenzyl bromide, DMF.

Thieno[2,3-*b*]pyridine-2-carboxylic acid methyl ester (147-B). To 2-chloro-3-pyridine carboxaldehyde, compound **147-A**, (5.07 g, 35.8 mmol), dissolved in MeCN (30 mL) was added triethylamine (6.5 mL, 46.5 mmol) followed by methyl thioglycolate (3.49 mL, 38.3 mmol) and the reaction was refluxed for 18 h. The reaction mixture was cooled and the solvent evaporated under reduced pressure. The crude residue was partitioned between H_2O and EtOAc, the layers separated and the aqueous phase extracted with EtOAc. The organic layers were combined, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford compound **147-B** as a white solid (2.01 g, 29%). ^{1}H-NMR (DMSO-d_6): δ 3.91 (s, 3H), 7.54-7.57 (m, 1H), 8.23 (s, 1H), 8.43-8.46 (m, 1H), 8.72-8.74 (m, 1H); MS: *m/z* 194.1 (MH^+).

Thieno[2,3-*b*]pyridine-2-carboxylic acid (147-C). To a solution of compound **147-B** (0.508 g, 2.63 mmol) in a mixture of MeOH (15 mL) and H_2O (3 mL) was added 3N NaOH (1.9 mL, 5.66 mmol) and the reaction mixture was stirred at ambient temperature for 5 h. The solvent was evaporated under reduced pressure, the residue dissolved in H_2O, and acidified with 1N HCl. The precipitate was filtered, washed with H_2O, and dried under vacuum to afford compound **147-C** as a white solid (0.366 g, 78%). MS: *m/z* 180.0 (MH^+).

Thieno[2,3-*b*]pyridin-2-yl-carbamic acid *tert*-butyl ester (147-D) A solution of compound **147-C** (0.36 g, 2.00 mmol), *N,N*-diisopropylethylamine (0.385 mL, 2.21 mmol) and diphenyl phosphoryl azide (0.536 mL, 2.41 mmol) in *t*-butanol (3.6 mL) was heated at reflux for 16 h. The solvent was evaporated *in vacuo*, the residue dissolved in dichloromethane, washed with 1 N NaOH, brine, dried with Na_2SO_4, filtered, and evaporated to afford a residue. Flash column chromatography (SiO_2) eluting with dichloromethane afforded compound **147-D** as a white solid (0.25 g, 50%). ^{1}H-NMR ($CDCl_3$): δ 1.55 (s, 9H), 6.60 (s, 1H), 7.20 (dd, 1H), 7.80 (d, 1H), 8.40 (d, 1H); MS: *m/z* 251.2 (MH^+).

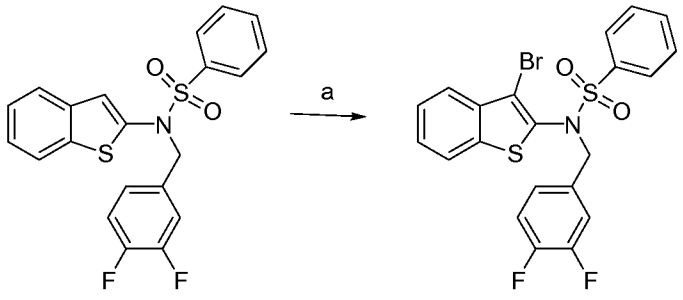
Thieno[2,3-*b*]pyridin-2-ylamine dihydrochloride (147-E). Compound **147-D** (3.76 g, 15.0 mmol) was added to a solution of HCl in dioxane (4 N, 40 mL). The mixture was stirred at rt for 3 days and the solid filtered to afford compound **147-E** as a yellow solid (3.24 g, 97%). ^{1}H-NMR (DMSO-d_6): δ 6.12 (s, 1H), 7.50 (dd, 1H), 8.02 (d, 1H), 8.28 (d, 1H), 9.60 (br s, 3H).

***N*-Thieno[2,3-*b*]pyridin-2-yl-benzenesulfonamide (147-F).** Compound **147-E** (0.22 g, 1.00 mmol) in pyridine (5.0 mL) was stirred at rt for 30 min, to which was added benzenesulfonyl chloride (0.135 mL, 1.05 mmol) and the reaction mixture was stirred at rt for 4 h. Another portion of benzenesulfonyl chloride (0.030 mL, 0.235 mmol) was added and the reaction mixture stirred at rt for 72 h. Water and saturated sodium bicarbonate solution were added and the mixture was extracted with dichloromethane, dried over sodium sulfate and evaporated *in vacuo* to afford a residue. Flash column chromatography (SiO_2) eluting with dichloromethane afforded compound **147-F** as a yellow solid (0.24 g, 83%).

Compound 147

***N*-(3,4-Difluoro-benzyl)-*N*-thieno[2,3-*b*]pyridin-2-yl-benzenesulfonamide.** To compound **147-F** (0.24 g, 0.827 mmol) in DMF (2.5 mL) at rt was added 1.0 M lithium bis(trimethylsilyl)amide in THF (0.87 mL, 0.87 mmol), drop-wise, and the solution was stirred 5 min. 3,4-Difluorobenzyl bromide (0.114 mL, 0.868 mmol) was added to the reaction mixture andthe resultant solution was stirred at ambient temperature overnight. Additional amounts of 1.0 M lithium bis(trimethylsilyl)amide in THF (0.44 mL, 0.44 mmol) and 3,4-difluorobenzyl bromide (0.052 mL, 0.406 mmol) were added and stirred for 18 h. Saturated sodium bicarbonate solution was added, the mixture evaporated *in vacuo,* andthe residue partitioned between water and diethyl ether and evaporated *in vacuo* to afford a residue Purification by reverse-phase HPLC eluting with an acetonitrile-water (0.1% TFA) gradient afforded a brownish gum that was dissolved in acetonitrile, and converted to its hydrochloride salt by the addition of ethereal hydrogen chloride. The solid was filtered, washed with diethyl ether, and dried under vacuum to afford compound **147** as a tan solid (32.3 mg, 9%). ^{1}H-NMR (DMSO-d_6): δ 4.95 (s, 2H), 7.20 (s, 1H), 7.25 (m, 1H), 7.40 (m, 3H), 7.70 (t, 2H), 7.80 (t, 1H), 7.90 (d, 2H), 8.20 (d, 2H), 8.30 (d, 2H), 12.4 (br s, 1H); MS: *m/z* 417.16 (MH^+).

Example 11



Compound 1 Compound 148

a) NBS, DCE, AcOH.

Compound 148

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide.** To a solution of compound **1** (440 mg, 1.06 mmol) in 1,2-dichloroethane (3 mL) and acetic acid (3 mL), at 0 °C, was added *N*-bromosuccinimide (207 mg, 1.16 mmol), and the reaction mixture was stirred at rt for 1 h. The solvent was evaporated *in vacuo*, and the residue partitioned between dichloromethane and a saturated solution of aqueous sodium bicarbonate. The organic layer was separated, the product pre-absorbed onto silica gel, and purified by flash column chromatography eluting with an ethyl acetate-heptane gradient (5-50%) to afford compound **148** as a colorless solid (190 mg, 36%). ^{1}H-NMR (DMSO-d_6): δ 4.82 (s, 2H), 7.11-7.14 (m, 1H), 7.28-7.39 (m, 2H), 7.46-7.58 (m, 2H), 7.67-7.72 (m, 3H), 7.80-7.85 (m, 1H), 7.91-7.97 (m, 3H); MS: *m/z* 494.1 (MH^+).

Following the procedure described above for example 11 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 149

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-pyridin-3-yl-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.89 (s, 2H), 7.12-7.19 (m, 1H), 7.32-7.42 (m, 2H), 7.48-7.55 (m, 2H), 7.66-7.77 (m, 2H), 7.94-8.00 (m, 1H), 8.30-8.35 (m, 1H), 8.98 (dd, 1H), 9.06 (d, 1H); MS: *m/z* 495 (MH^+).

Compound 150

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-1-methyl-1*H*-imidazole-4-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 4.87 (s, 2H), 7.11-

7.19 (m, 1H), 7.28-7.52 (m, 4H), 7.66-7.72 (m, 1H), 7.90-7.96 (m, 2H), 8.01 (s, 1H); MS: *m/z* 498 (MH^+).

Compound 151

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.39 (s, 3H), 4.87 (s, 2H), 7.15-7.21 (m, 1H), 7.32-7.54 (m, 4H), 7.70-7.76 (m, 1H), 7.95-8.01 (m, 1H); MS: *m/z* 432.0 (MH^+).

Compound 152

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.39 (t, 3H), 3.51 (q, 2H), 4.88 (s, 2H), 7.12-7.18 (m, 1H), 7.32-7.42 (m, 2H), 7.49-7.54 (m, 2H), 7.71-7.76 (m, 1H), 7.94-7.99 (m, 1H); MS: *m/z* 446 (MH^+).

Compound 153

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-propane-1-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.04 (t, 3H), 1.79-1.93 (m, 2H), 3.45-3.51 (m, 2H), 4.87 (s, 2H), 7.12-7.18 (m, 1H), 7.31-7.43 (m, 2H), 7.48-7.55 (m, 2H), 7.70-7.76 (m, 1H), 7.94-7.99 (m, 1H); MS: *m/z* 460 (MH^+).

Compound 154

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-butane-1-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.92 (t, 3H), 1.38-1.53 (m, 2H), 1.74-1.86 (m, 2H), 3.45-3.53 (m, 2H), 4.88 (s, 2H), 7.12-7.18 (m, 1H), 7.32-7.43 (m, 2H), 7.48-7.54 (m, 2H), 7.70-7.76 (m, 1H), 7.94-8.00 (m, 1H); MS: *m/z* 474.1 (MH^+).

Compound 155

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-3-fluoro-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.87 (br s, 2H), 7.10-7.17 (m, 1H), 7.30-7.41(m, 2H), 7.47-7.54 (m, 2H), 7.67-7.83 (m, 5H), 7.94-8.01 (m, 1H); MS: *m/z* 512 (MH^+).

Compound 156

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-4-trifluoromethyl-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.88 (s, 2H), 7.12-7.18 (m, 1H), 7.30-7.41 (m, 2H), 7.48-7.54 (m, 2H), 7.67-7.73 (m, 1H), 7.96-8.01 (m, 1H), 8.08 (d, 2H), 8.15 (d, 2H); MS: *m/z* 562 (MH^+).

Compound 157

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.40 (s, 3H), 4.96 (s, 2H), 7.43-7.55 (m, 3H), 7.68-7.80 (m, 3H), 7.97-8.02 (m, 1H); MS: *m/z* 482.1 (MH^+).

Compound 158

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-chloro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.79 (s, 2H), 7.21 (s, 4H), 7.38-7.41 (m, 2H) 7.51-7.56 (m, 2H), 7.61-7.72 (m, 3H), 7.85-7.87 (m, 2H); MS: *m/z* 447.9 (MH^+).

Compound 159

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-chloro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.81 (s, 2H), 7.21 (s, 4H), 7.38-7.41 (m, 2H) 7.51-7.56 (m, 2H), 7.63-7.71 (m, 3H), 7.85-7.87 (m, 2H); MS: *m/z* 492.0 (MH^+).

Compound 160

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.55 (s, 3H), 4.93 (s, 2H), 6.68-6.70 (d, 1H), 6.79-6.83 (t, 1H), 7.16-7.20 (m, 1H), 7.30-7.32 (m, 1H), 7.35-7.38 (m, 2H), 7.48-7.52 (m, 2H), 7.59-7.63 (m, 2H), 7.68-7.71 (m, 1H), 7.86-7.89 (m, 2H); MS: *m/z* 487.9 (MH^+).

Compound 161

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5-bromo-2-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.52 (s, 3H), 4.88 (s, 2H), 6.55-6.59 (d, 1H), 7.26-7.29 (m, 1H), 7.38-7.40 (m, 2H), 7.49-7.53 (m, 3H), 7.61-7.66 (m, 2H), 7.70-7.73 (m, 1H), 7.86-7.88 (m, 2H); MS: *m/z* 567.9 (MH^+).

Compound 162

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.72 (s, 3H), 4.82 (s, 2H), 6.74-6.87 (m, 3H), 7.09-7.14 (t, 1H), 7.36-7.40 (m, 2H), 7.51-7.56 (m, 2H), 7.62-7.71 (m, 3H), 7.86-7.89 (m, 2H); MS: *m/z* 488.0 (MH^+).

Compound 163

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-bromo-5-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.75 (s, 3H), 5.02 (s, 2H), 6.63-6.68 (m, 1H), 7.21-7.22 (m, 1H), 7.26-7.29 (m, 1H), 7.38-7.41 (m, 2H), 7.51-7.55 (m, 2H), 7.63-7.72 (m, 3H), 7.87-7.90 (m, 2H); MS: *m/z* 567.9, (MH^+), 589.8 (MNa^+).

Compound 164

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.73 (s, 3H), 4.79 (s, 2H), 6.70-6.74 (m, 2H), 7.15-7.18 (m, 2H), 7.34-7.39 (m, 2H), 7.51-7.55 (m, 2H), 7.61-7.72 (m, 3H), 7.86-7.88 (m, 2H); MS: *m/z* 488.0 (MH^+), 510.0 (MNa^+).

Compound 165

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-bromo-4-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.82 (s, 3H), 4.75 (s, 2H), 6.71-6.73 (d, 1H), 7.15-7.18 (m, 1H), 7.38-7.46 (m, 3H), 7.52-7.57 (m, 2H), 7.64-7.72 (m, 3H), 7.86-7.78 (m, 2H); MS: *m/z* 567.9 (MH^+), 589.8 (MNa^+).

Compound 166

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.93 (s, 2H), 6.88-6.93 (t, 1H), 7.02-7.07 (t, 1H), 7.18-7.22 (m, 1H), 7.36-7.47 (m, 3H), 7.49-7.55 (m, 2H), 7.62-7.73 (m, 3H), 7.87-7.90 (d, 2H); MS: *m/z* 475.9 (MH^+).

Compound 167

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-nitro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.94 (s, 2H), 7.39-7.49 (m, 3H), 7.51-7.58 (m, 2H), 7.64-7.76 (m, 4H), 7.88-7.89 (d, 2H), 8.10-8.12 (m, 2H); MS: *m/z* 524.8 (MH^+).

Compound 168

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(pyridin-2-ylmethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 5.08 (s, 2H), 7.27-7.31 (m, 1H), 7.37-7.41 (m, 2H), 7.51-7.55 (m, 2H), 7.64-7.74 (m, 3H), 7.80-7.88 (m, 4H), 8.47-8.49 (d, 1H); MS: *m/z* 459.0 (MH^+).

Compound 169

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(pyridin-3-ylmethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.86 (s, 2H), 7.27-7.30 (m, 1H), 7.38-7.42 (m, 2H), 7.51-7.57 (m, 2H), 7.62-7.71 (m, 3H), 7.83-7.91 (m, 3H), 8.41-8.42 (m, 1H), 8.51-8.42 (m, 1H); MS: *m/z* 459.0 (MH^+).

Compound 170

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(pyridin-4-ylmethyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 5.07 (s, 2H), 7.44-7.47 (m, 2H), 7.53-7.59

(m, 2H), 7.68-7.73 (m, 3H), 7.83-7.91 (m, 4H), 8.81-8.83 (m, 2H); MS: *m/z* 459.0, 461.0 (MH^+).

Compound 171

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-nitro-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 5.33 (s, 2H), 7.38-7.46 (m, 3H), 7.52-7.57 (m, 2H), 7.65-7.70 (m, 4H), 7.82-7.86 (m, 2H), 7.92-7.96 (d, 1H), 8.06-8.08 (d, 1H); MS: *m/z* 502.9,504.9 (MH^+).

Compound 172

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-trifluoromethoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 5.00 (s, 2H), 7.10-7.14 (m, 1H), 7.23-7.28 (m, 2H), 7.35-7.42 (m, 2H), 7.50-7.56 (m, 2H), 7.62-7.71 (m, 4H), 7.76-7.78 (m, 2H); MS: *m/z* 541.9, 543.9 (MH^+).

Compound 173

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.85 (s, 2H), 7.07-7.09 (m, 1H), 7.14 (s, 1H), 7.21-7.27 (m, 2H), 7.37-7.42 (m, 2H), 7.51-7.55 (m, 2H), 7.62-7.72 (m, 3H), 7.86-7.89 (m, 2H); MS: *m/z* 542.0, 543.9 (MH^+).

Compound 174

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.85 (s, 2H), 7.07-7.08 (d, 2H), 7.30-7.32 (m, 2H), 7.37-7.42 (m, 2H), 7.51-7.55 (d, 2H), 7.62-7.72 (m, 3H), 7.85-7.87 (m, 2H); MS: *m/z* 542.0 (MH^+).

Compound 175

***N*-(Benzyl)-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.85 (s, 2H), 7.20-7.29 (m, 5H), 7.35-7.40 (m, 2H), 7.51-7.55 (m, 2H), 7.61-7.70 (m, 3H), 7.87-7.89 (d, 2H); MS: *m/z* 458.0, 460.0 (MH^+).

Compound 176

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-methoxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 3.79 (s, 3H), 4.79 (s, 2H), 6.65-6.70 (m, 1H), 6.84-6.89 (m, 1H), 6.98-6.99 (m, 1H), 7.36-7.42 (m, 2H), 7.52-7.55 (m, 2H), 7.63-7.72 (m, 3H), 7.86-7.89 (d, 2H); MS: *m/z* 506.0 (MH^+).

Compound 177

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.84 (s, 2H), 7.04-7.09 (m, 1H), 7.39-7.44 (m, 2H), 7.47-7.57 (m, 4H), 7.65-7.73 (m, 3H), 7.85-7.88 (m, 2H); MS: *m/z* 544.0 (MH^+).

Compound 178

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-methyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.40 (s, 3H), 4.89 (s, 2H), 6.92-6.95 (m, 1H), 7.07-7.09 (m, 3H), 7.35-7.39 (m, 2H), 7.51-7.55 (m, 2H), 7.59-7.68 (m, 3H), 7.87-7.90 (d, 2H); MS: *m/z* 472.0 (MH^+).

Compound 179

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-methyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.23 (s, 3H), 4.82 (s, 2H), 6.99-7.11 (m, 4H), 7.35-7.39 (m, 2H), 7.49-7.57 (m, 2H), 7.61-7.72 (m, 3H), 7.86-7.88 (d, 2H); MS: *m/z* 472.0 (MH^+).

Compound 180

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-methoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.89 (s, 3H), 4.87 (s, 2H), 7.17-7.21 (d, 2H), 7.40-7.47 (m, 1H), 7.49-7.53 (m, 2H), 7.62-7.73 (m, 3H), 7.83-7.87 (d, 2H), 7.94-8.00 (m, 1H); MS: *m/z* 530.0 (MH^+).

Compound 181

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methoxy-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.84 (s, 3H), 4.90 (s, 2H), 7.38-7.54 (m, 6H), 7.58-7.75 (m, 4H), 7.97-8.01 (m, 1H); MS: *m/z* 530.0 (MH^+).

Compound 182

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.89 (s, 3H), 4.86 (s, 2H), 7.18-7.22 (d, 2H), 7.39-7.52 (m, 3H), 7.61-7.71 (m, 3H), 7.83-7.87 (d, 2H), 7.95-7.99 (m, 1H); MS: *m/z* 574.0 (MH^+).

Compound 183

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.36-1.41 (t, 3H), 3.50-3.57 (q, 2H), 4.96

(s, 2H), 7.43-7.54 (m, 3H), 7.66-7.76 (m, 3H), 7.96-7.99 (m, 1H); MS: *m/z* 495.9 (MH^+).

Compound 184

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-thiophene-2-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.93 (s, 2H), 7.34-7.38 (m, 1H), 7.41-7.47 (m, 1H), 7.48-7.53 (m, 2H), 7.65-7.72 (m, 3H), 7.90-7.91 (m, 1H), 7.98-8.02 (m, 1H), 8.19-8.21 (m, 1H); MS: *m/z* 549.9 (MH^+).

Compound 185

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-methoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.64 (s, 3H), 4.91 (s, 2H), 7.37-7.53 (m, 6H), 7.59-7.72 (m, 4H), 7.97-7.99 (m, 1H); MS: *m/z* 574.0 (MH^+).

Compound 186

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-thien-3-yl-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.92 (s, 2H), 7.41-7.54 (m, 4H), 7.64-7.71 (m, 3H), 7.91-7.99 (m, 2H), 8.46-8.47 (m, 1H); MS: *m/z* 549.9 (MH^+).

Compound 187

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-thien-3-yl-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.93 (s, 2H), 7.42-7.56 (m, 4H), 7.64-7.76 (m, 3H), 7.91-8.00 (m, 2H), 8.46-8.47 (m, 1H); MS: *m/z* 506.0 (MH^+).

Compound 188

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-pyridin-3-yl-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.99 (s, 2H), 7.43-7.53 (m, 3H), 7.67-7.76 (m, 4H), 7.96-8.02 (m, 1H), 8.32-8.36 (m, 1H), 8.98-9.01 (m, 1H), 9.08-9.09 (m, 1H); MS: *m/z* 545.0 (MH^+).

Compound 189

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-pyridin-3-yl-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 5.01 (s, 2H), 7.43-7.53 (m, 3H), 7.67-7.76 (m, 4H), 7.98-8.03 (m, 1H), 8.32-8.36 (m, 1H), 8.97-9.02 (m, 1H), 9.06-9.09 (m, 1H); MS: *m/z* 501.0 (MH^+).

Compound 190

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.22-1.44 (t, 3H), 3.49-3.57 (q, 2H), 4.97

(s, 2H), 7.44-7.54 (m, 3H), 7.67-7.79 (m, 3H), 7.96-8.03 (m, 1H); MS: *m/z* 452.0 (MH^+).

Compound 191

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-thiophene-2-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.93 (s, 2H), 7.34-7.36 (m, 2H), 7.43-7.57 (m, 3H), 7.66-7.76 (m, 2H), 7.89-7.92 (m, 1H), 7.97-8.03 (m, 1H), 8.19-8.23 (m, 1H); MS: *m/z* 528.0 (MH^+).

Compound 192

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.93 (s, 3H), 4.96 (s, 2H), 7.42-7.52 (m, 3H), 7.63-7.71 (m, 3H), 7.95-7.99 (m, 1H), 8.06-8.08 (dd, 2H), 8.20-8.23 (dd, 2H); MS: *m/z* 601.8 (MH^+).

Compound 193

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.89 (s, 3H), 4.96 (s, 2H), 7.41-7.49 (m, 1H), 7.50-7.54 (m, 2H), 7.63-7.72 (m, 3H), 7.84-7.88 (t, 1H), 7.98-8.01 (m, 1H), 8.19-8.22 (m, 1H), 8.32-8.36 (m, 2H); MS: *m/z* 603.9 (MH^+).

Compound 194

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.93 (s, 3H), 4.96 (s, 2H), 7.43-7.54 (m, 3H), 7.65-7.74 (m, 3H), 7.96-7.99 (m, 1H), 8.06-8.08 (dd, 2H), 8.20-8.23 (dd, 2H); MS: *m/z* 558.0 (MH^+).

Compound 195

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.89 (s, 3H), 4.96 (s, 2H), 7.42-7.47 (t, 1H), 7.49-7.54 (m, 2H), 7.64-7.68 (m, 2H), 7.72-7.74 (m, 1H), 7.85-7.89 (m, 1H), 7.98-8.02 (m, 1H), 8.19-8.22 (m, 1H), 8.31-8.36 (m, 2H); MS: *m/z* 558.0 (MH^+).

Compound 196

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-carbomethoxy-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.64 (s, 3H), 5.04 (s, 2H), 7.44-7.54 (m, 3H), 7.69-7.78 (m, 5H), 7.83-7.91 (m, 2H), 7.95-7.99 (m, 1H); MS: *m/z* 558.0 (MH^+).

Compound 197

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-N-(4-fluoro-3-trifluoromethyl-benzyl)-2-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.65 (s, 3H), 5.05 (s, 2H), 7.43-7.51 (m, 3H), 7.64-7.77 (m, 5H), 7.84-7.90 (m, 2H), 7.97-7.99 (m, 1H); MS: *m/z* 603.9 (MH^+).

Compound 312

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-acetyl-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.67 (s, 3H), 4.95 (s, 2H), 7.44-7.51 (m, 3H), 7.67-7.72 (m, 3H), 7.80-8.07 (m, 3H), 8.19-8.21 (m, 2H); MS: m/z 585.9 (MH^+).

Compound 317

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N',N'*-dimethlysulfamide.** ^{1}H-NMR (DMSO-d_6): δ 2.94 (s, 6H), 4.87 (s, 2H), 7.41-7.52 (m, 3H), 7.64-7.73 (m, 3H), 7.96-7.99 (m, 1H); MS: *m/z* 511, 513.1 (MH^+).

Compound 345

***N*-(3-Bromobenzo[*b*]thiophen-2-yl)-*N*-(butyl)-pyridin-3-yl-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.83 (t, 3H), 1.49-1.29 (m, 4H), 3.70 (t, 2H), 7.60-7.50 (m, 2H), 7.74-7.68 (m, 1H), 7.81-7.75 (m, 1H), 8.06-7.98 (m, 1H), 8.29-8.23 (m, 1H), 9.00-8.92 (m, 2H); MS: *m/z* 425.0 (MH^+).

Compound 350

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*C*-methanesulfonyl-methanesulfonamide.** MS: *m/z* 560, 562.0 (MH^+), 582, 584.0 (MNa^+).

Compound 576

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.98 (s, 2H), 7.38-7.55 (m, 3H), 7.61-7.74 (m, 3H), 7.90-8.01 (m, 2H), 8.14 (d, 1H), 8.48 (d, 1H), 8.55 (s, 1H); MS: *m/z* 612, 614.0 (MH^+).

Compound 578

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.98 (s, 2H), 7.35-7.58 (m, 3H), 7.63-7.78 (m, 3H), 7.90-8.03 (m, 2H), 8.14 (d, 1H), 8.49 (d, 1H), 8.55 (s, 1H); MS: *m/z* 567.6 (MH^+).

Compound 594

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.014-0.065 (m, 3H), 0.343-0.388 (m, 2H), 0.713-0.813 (m, 1H), 1.35-1.40 (m, 2H), 3.72-3.76 (t, 2H), 7.51-7.57 (m, 2H), 7.73-7.79 (m, 1H), 7.96-8.03 (m, 1H), 8.06-8.08 (d, 2H), 8.30-8.32 (d, 2H); MS: *m/z* 505.6 (MH^+).

Compound 595

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.57-2.67 (m, 2H), 3.96-4.02 (t, 2H), 7.53-7.57 (m, 2H), 7.74-7.77 (m, 1H), 8.00-8.04 (m, 1H), 8.07-8.09 (d, 2H), 8.29-8.31 (m, 2H); MS: *m/z* 533.5 (MH^+).

Compound 635

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.008-0.034 (m, 3H), 0.346-0.392 (m, 2H), 0.719-0.794 (m, 1H), 1.35-1.40 (m, 2H), 3.72-3.75 (t, 2H), 7.52-7.57 (m, 2H), 7.77-7.82 (m, 1H), 7.98-8.01 (m, 1H), 8.02-8.09 (m, 2H), 8.29-8.32 (m, 2H); MS: *m/z* 459.7 (MH^+).

Compound 636

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.55-2.67 (m, 2H), 3.97-4.01 (t, 2H), 7.52-7.58 (m, 2H), 7.76-7.82 (m, 1H), 8.00-8.05 (m, 1H), 8.07-8.09 (m, 2H), 8.29-8.31 (d, 2H); MS: *m/z* 487.6 (MH^+).

Compound 702

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2,2,2-trifluoro-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.07 (q, 2H), 4.96 (s, 2H), 7.12 (t, 1H), 7.42-7.55 (m, 4H), 7.65-7.76 (m, 1H), 7.76-7.86 (m, 1H); MS: *m/z* 573.9 (MNa^+).

Compound 703

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2,2,2-trifluoro-ethanesulfonamide.** MS: *m/z* 528.0 (MNa^+).

Compound 706

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ

0.013-0.050 (m, 2H), 0.314-0.376 (m, 2H), 0.695-0.794 (m, 1H), 1.33-1.38 (m, 2H), 3.70-3.74 (m, 2H), 7.50--7.56 (m, 2H), 7.73-7.78 (m, 1H), 7.96-7.98 (m, 1H), 8.00-8.01 (d, 2H), 8.18-8.20 (d, 2H), 13.69 (s, 1H); MS: *m/z* 538.0 (MH^+).

Compound 707

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.58-1.75 (m, 4H), 2.18-2.28 (m, 2H), 3.85-3.87 (m, 2H), 7.51-7.55 (m, 2H), 7.72-7.76 (m, 1H), 7.85-7.90 (m, 2H), 7.94-8.04 (m, 2H), 13.88 (s, 1H); MS: *m/z* 555.9 (MH^+).

Compound 708

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.55-2.66 (m, 2H), 3.98-4.01 (t, 2H), 7.53-7.57 (m, 2H), 7.74-7.78 (m, 1H), 8.00-8.04 (m, 3H), 8.18-8.20 (d, 2H), 13.70 (s, 1H); MS: *m/z* 566.0 (MH^+).

Compound 709

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.000-0.005 (m, 2H), 0.292-0.373 (m, 2H), 0.670-0.769 (m, 1H), 1.36-1.41 (m, 2H), 3.84-3.87 (t, 2H), 7.47-7.52 (m, 2H), 7.68-7.74 (m, 1H), 7.81-7.86 (m, 2H), 7.91-7.99 (m, 2H), 13.84 (s, 1H); MS: *m/z* 500.0 (MH^+).

Compound 710

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.58-2.68 (m, 2H), 4.12-4.16 (t, 2H), 7.51-7.57 (m, 2H), 7.71-7.77 (m, 1H), 7.83-7.89 (m, 2H), 7.96-8.06 (m, 2H), 13.89 (s, 1H); MS: *m/z* 528.0 (MH^+).

Compound 711

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 5.08 (s, 2H), 7.45-7.52 (m, 3H), 7.65-7.69 (m, 3H), 7.89-8.01 (m, 4H), 13.92 (s, 1H); MS: *m/z* 608.0 (MH^+).

Compound 712

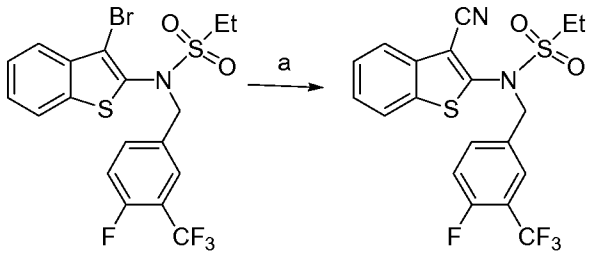
***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.52-

1.63 (m, 4H), 2.21-2.28 (m, 2H), 3.70 (m, 2H), 7.51-7.58 (m, 2H), 7.77-7.80 (m, 1H), 7.98-8.02 (m, 3H), 8.19-8.21 (m, 2H), 13.70 (s, 1H); MS: *m/z* 594.0 (MH^+).

Compound 785

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.93 (s, 3H), 4.68-4.96 (s, 2H), 7.23-7.35 (m, 2H), 7.36-7.42 (m, 4H), 7.65-7.68 (m, 1H), 7.80-7.84 (m, 1H), 8.10-8.12 (d, 2H), 8.31-8.33 (d, 2H); MS: *m/z* 546.0 (MH^+).

Example 12



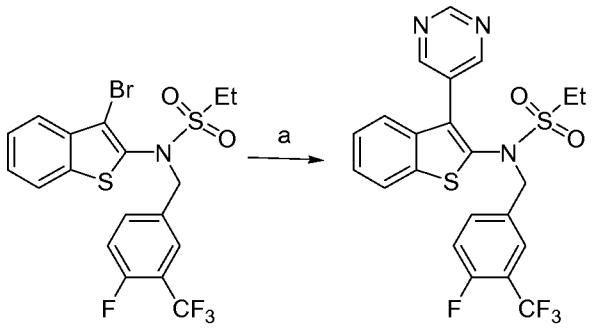
Compound 183 Compound 198

a) CuCN, DMF.

Compound 198

***N*-(3-Cyano-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide.** A mixture of compound **183** (97mg, 0.195 mmol) and CuCN (44 mg, 0.496 mmol) in DMF (3 mL) was heated at reflux for 6 h. The mixture was cooled, an additional portion of CuCN (55 mg, 0.614 mmol) was added, and the reaction heated overnight. The mixture was cooled, and the inorganics were removed by filtration. The resultant solution was partitioned between ethyl acetate and water. The organic layer was separated, washed with water (3X), brine, dried over sodium sulfate, filtered, and the solvent was evaporated *in vacuo*. The crude residue was purified by HPLC (C_{18}) eluting with a acetonitrile-water (0.1 % TFA) (10-40 %) gradient, to afford compound **198** as an oil (40 mg, 46%). ^{1}H-NMR (DMSO-d_6): δ 1.39 (t, 3H), 3.62 (q, 2H), 5.09 (s, 2H), 7.49 (t, 1H), 7.54-7.61 (m, 2H), 7.68-7.72 (m, 1H), 7.78-7.83 (m, 2H), 8.09-8.13 (m, 1H); MS: *m/z* 443.1 (MH^+).

Example 13



Compound 183 Compound 199

a) 5-Pyrimidineboronic acid, Na_2CO_3(aq), Pd(118), dioxane.

Compound 199

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-pyrimidin-5-yl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** A solution of compound **183** (140 mg, 0.28 mmol) and 5-pyrimidineboronic acid (42 mg, 0.34 mmol) in dioxane (2 mL) was treated with 2 M sodium carbonate (352 µL, 0.705 mmol) and palladium catalyst (Johnson Matthey Pd(118), 10 mg, 0.015 mmol). Dioxane was added, the tube was purged with argon, sealed and heated to 80 °C for 2 h. The solvent was evaporated *in vacuo*, and the residue partitioned between dichloromethane and water. The organic layer was separated, dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The residue was purified by HPLC (C_{18}) eluting with an acetonitrile-water (0.1% TFA) (30-90%) to afford compound **199** as a brown oil (19 mg, 14%). ^{1}H-NMR (DMSO-d_6): δ 1.35 (t, 3H), 3.58 (q, 2H), 4.77 (s, 2H), 7.24-7.42 (m, 5H), 7.49-7.56 (m, 1H), 8.09 (d, 1H), 8.50 (s, 2H), 9.15 (s, 1H); MS: *m/z* 496.2 (MH^+).

Following the procedure described above for example 13 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 200

***N*-[3-(2-Fluoro-phenyl)-benzo[*b*]thiophen-2-yl]-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.26 (t, 3H), 3.44 (q, 2H), 4.61 (d, 1H), 4.86 (d, 1H), 7.09-7.19 (m, 2H), 7.23-7.30 (m, 2H), 7.33-7.51 (m, 6H), 8.00 (d, 1H); MS: *m/z* 512.3 (MH^+).

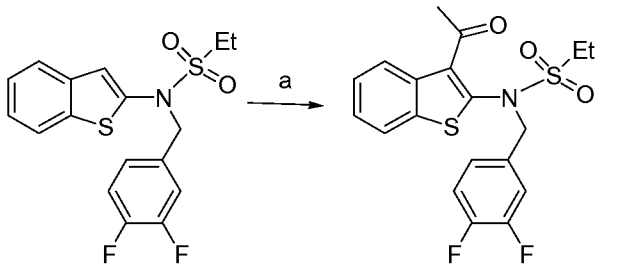
Compound 201

***N*-[3-(4-Fluoro-phenyl)-benzo[*b*]thiophen-2-yl]-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.30 (t, 3H), 3.47 (q, 2H), 4.71 (s, 2H), 7.15-7.40 (m, 9H), 7.44-7.50 (m, 1H), 8.00 (d, 1H); MS: *m/z* 512.2 (MH^+).

Compound 202

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-thiophen-3-yl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.27 (t, 3H), 3.39 (q, 2H), 4.76 (s, 2H), 7.06 (d, 1H), 7.28 (t, 1H), 7.36-7.52 (m, 5H), 7.55-7.58 (m, 1H), 7.62-7.65 (m, 1H), 7.97 (d, 1H); MS: *m/z* 500.1 (MH^+).

Example 14



Compound 35 **Compound 203**

a) $SnCl_4$, acetyl chloride, DCM.

Compound 203

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-formyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxybenzenesulfonamide.** A solution of acetylchloride (16 µL, 0.224 mmol) in dichloromethane (3 mL), at 0 °C, was treated with tin(IV)chloride (26 µL, 0.224 mmol) and the resultant solution was stirred at 0 °C for 15 min. Compound **35** (75 mg, 0.204 mmol) was added to the solution and the mixture stirred at ambient temperature overnight. The reaction mixture was washed with 2 N HCl, dried over sodium sulfate, filtered, and the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with an ethyl acetate-heptane (10-80%) gradient. The product was further purified by HPLC (C_{18}) eluting with an acetonitrile-water (0.1% TFA) (40-90%) gradient to afford compound **203** as a colorless solid (25 mg, 30%). ^{1}H-NMR (DMSO-d_6): δ 1.31 (t, 3H), 2.30 (s,

3H), 3.47 (q, 2H), 4.98 (s, 2H), 7.17 (m, 1H), 7.35 (m, 4H), 7.94-8.03 (m, 2H); MS: *m/z* 410.1 (MH^+).

Following the procedure described above for example 14 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 204

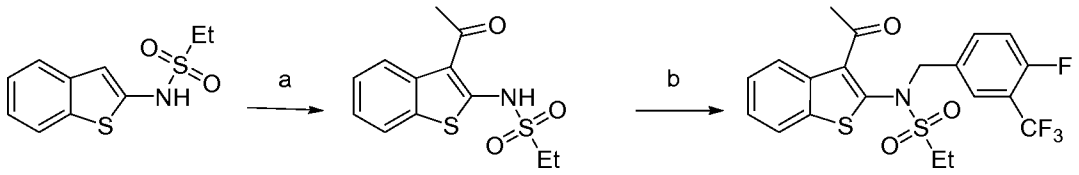
***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.37 (s, 3H), 4.86 (br s, 2H), 7.16-7.24 (m, 1H), 7.33-7.49 (m, 4H), 7.65-7.73 (m, 2H), 7.82-7.86 (m, 3H), 7.90-7.96 (m, 1H), 7.99-8.04 (m, 1H); MS: *m/z* 458.3 (MH^+).

Compound 833

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(3-fluoro-propyl)-benzenesulfonamide.**

^{1}H-NMR ($CDCl_3$): δ 2.08-2.21 (m, 2H), 2.79 (s, 3H), 3.81 (s, 2H), 4.48 (t, 1H), 4.61 (t, 1H), 7.41-7.78 (m, 8H), 8.25 (m, 1H).

Example 15



205-A **205-B** **Compound 205**

a) Acetyl chloride, $SnCl_4$, DCM; b) NaH, 15-Crown-5, 4-fluoro-3-trifluoromethylbenzyl bromide.

Compound **205-A** was prepared from compound **1-C** and 4-ethanesulfonyl chloride, following the procedure used to prepare compound **1-D**.

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide (205-B).** Tin(IV)chloride (173 µL, 1.48 mmol) was added to a solution of acetyl chloride (124 µL, 1.75 mmol) in dichloromethane (10 mL), at 0 °C, and the solution was stirred for 5 min. To the reaction mixture was added a solution of compound **205-A** (325 mg, 1.35 mmol) in dichloromethane (2 mL) at 0 °C. The resultant solution was allowed to warm to ambient temperature and stirred overnight. The solution was treated with water (10 mL), the organic layer separated, dried over sodium sulfate, filtered, and the solvent

evaporated *in vacuo* to afford compound **205-B** as a colorless solid (355 mg, 93%). ^{1}H-NMR (DMSO-d_6): δ 1.25 (t, 3H), 2.71 (s, 3H), 3.39 (q, 2H), 7.34-7.48 (m, 2H), 7.94 (d, 1H), 8.10 (d, 1H); MS: *m/z* 284.1 (MH^+).

Compound 205

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide.** Sodium hydride (60 % in oil, 46 mg, 1.15 mmol) was added to a solution of compound **205-B** (310 mg, 1.09 mmol) in DMF (4 mL), at 0 °C. The resultant mixture was stirred at 0 °C for 15 min, to which was added 4-fluoro-3-trifluoromethylbenzyl bromide (253 µL, 1.33 mmol) and the resultant mixture was stirred at ambient temperature for 2 h. 15-Crown-5 (220 µL, 1.33 mmol) and an additional equivalent of 4-fluoro-3-trifluoromethylbenzyl bromide was added to the reaction mixture. The resultant solution was stirred at ambient temperature overnight, water added, and the product extracted into ethyl acetate. The organic phase was washed with water (3X), brine, dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate-heptane gradient to afford compound **205** as an off-white solid (285 mg, 57%). ^{1}H-NMR (DMSO-d_6): δ 1.32 (t, 3H), 2.29 (s, 3H), 3.49 (q, 2H), 5.08 (s, 2H), 7.41-7.52 9m, 3H), 7.70-7.77 (m, 2H), 7.93-8.03 (m, 2H); MS: *m/z* 460.2 (MH^+).

Following the procedure described above for example 15 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 313

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.36 (s, 3H), 3.92 (s, 3H), 4.99 (s, 2H), 7.41-7.48 (m, 3H), 7.67-7.73 (m, 2H), 7.91-8.00 (m, 4H), 8.21 (d, 2H); MS: *m/z* 566.2 (MH^+).

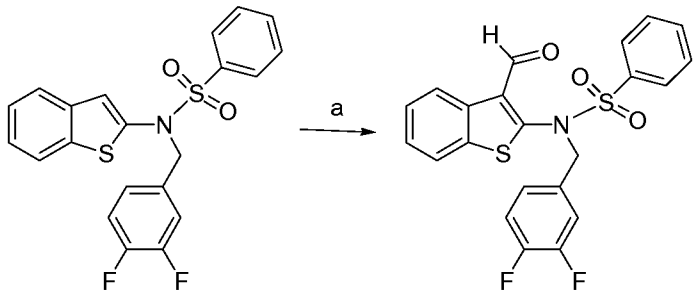
Compound 314

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.38 (s, 3H), 4.95 (s, 2H), 7.41-7.48 (m, 3H), 7.68-7.75 (m, 4H), 7.80-7.87 (m, 3H), 7.91-7.96 (m, 1H), 8.00-8.04 (m, 1H); MS: *m/z* 508.2 (MH^+).

Compound 837

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-methoxy-benzyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.46 (t, 3H), 2.36 (s, 3H), 3.19 (q, 2H), 3.81 (s, 3H), 4.91 (s, 2H), 6.82-6.86 (m, 1H), 6.97 (dd, 1H), 7.03 (dd, 1H), 7.40-7.44 (m, 2H), 7.72-7.75 (m, 1H), 8.07-8.11 (m, 1H); MS: *m/z* 444.1 (MNa^+).

Example 16



Compound 1 **Compound 206**

a) $TiCl_4$, α,α-dichloromethylmethyl ether, DCM.

Compound 206

***N*-(3,4-Difluoro-benzyl)-*N*-(3-formyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** A solution of titanium(IV) chloride (1.0 M in dichloromethane, 0.94 mL, 0.94 mmol) was added to a solution of compound **1** (270 mg, 0.65 mmol) in dichloromethane (6 mL), at -5 °C. The resultant solution was stirred at -5 °C for 15 min to which was added α,α-dichloromethylmethyl ether (75 mL, 0.845 mmol) and the reaction mixture was stirred at ambient temperature overnight. The solution was treated with 2N HCl (10 mL), the organic layer separated, dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate-heptane gradient (10-40%) to afford compound **206** as a colorless solid (180 mg, 62%). ^{1}H-NMR (DMSO-d_6): δ 4.94 (s, 2H), 7.15-7.25 (m, 1H), 7.33-7.55 (m, 4H), 7.68-7.72 (m, 2H), 7.83-7.87 (m, 3H), 7.98-8.01 (m, 1H), 8.43-8.46 (m, 1H), 9.87 (s, 1H); MS: *m/z* 444.1 (MH^+).

Following the procedure described above for example 16 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 207

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-formyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 5.06 (br s, 2H), 7.43-7.55 (m, 3H), 7.68-7.79 (m, 4H), 7.83-7.89 (m, 3H), 7.98-8.03 (m, 1H), 8.42-8.47 (m, 1H), 9.84 (s, 1H); MS: *m/z* 494.1 (MH^+).

Compound 208

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-formyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.45 (s, 3H), 5.11 (s, 2H), 7.44-7.55 (m, 3H), 7.73-7.79 (m, 2H), 8.04-8.09 (m, 1H), 8.42-8.46 (m, 1H), 9.91 (s, 1H); MS: *m/z* 432.0 (MH^+).

Compound 209

***N*-(3,4-Difluoro-benzyl)-*N*-(3-formyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.43 (s, 3H), 5.00 (s, 2H), 7.19-7.26 (m, 1H), 7.33-7.55 (m, 4H), 8.03-8.09 (m, 1H), 8.42-8.47 (m, 1H), 9.91 (s, 1H); MS: *m/z* 382.2 (MH^+).

Compound 210

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-formyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.36 (t, 3H), 3.61 (q, 2H), 5.15 (s, 2H), 7.45-7.55 (m, 3H), 7.71-7.78 (m, 2H), 8.03-8.10 (m, 1H), 8.40-8.47 (m, 1H), 9.83 (s, 1H); MS: *m/z* 446.1 (MH^+).

Compound 211

***N*-(3-Formyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.93 (s, 3H), 5.08 (s, 2H), 7.44-7.55 (m, 3H), 7.70-7.81 (m, 2H), 7.99-8.05 (m, 3H), 8.22 (d, 2H), 8.42-8.46 (m, 1H), 9.85 (s, 1H); MS: *m/z* 552.2 (MH^+).

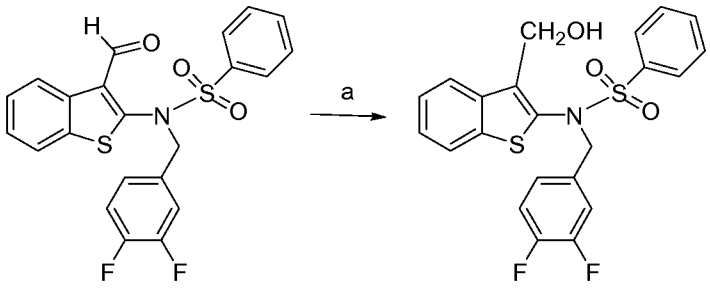
Compound 212

***N*-(3,4-Difluoro-benzyl)-*N*-(3-formyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.36 (t, 3H), 3.61 (q, 2H), 5.04 (s, 2H), 7.17-7.24 (m, 1H), 7.34-7.46 (m, 2H), 7.48-7.54 (m, 2H), 8.03-8.08 (m, 1H), 8.40-8.46 (m, 1H), 9.83 (s, 1H); MS: *m/z* 396.1 (MH^+).

Compound 419

***N*-(Butyl)-*N*-(3-formyl-benzo[*b*]thiophene-2-yl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 432.1 (MH^+).

Example 17



Compound 206 Compound 213

a) $NaBH_4$, EtOH.

Compound 213

***N*-(3,4-Difluoro-benzyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide**. Sodium borohydride (25 mg, 0.66 mmol) was added to a solution of compound **206** (50 mg, 0.112 mmol) in ethanol (2 mL), and the mixture was stirred at rt for 3 h. The solvent was evaporated, the residue partitioned between dichloromethane and water, the organic layer separated, dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate-heptane (10-40%) gradient to afford compound **213** as a colorless solid (42 mg, 84%). ^{1}H-NMR (DMSO-d_6): δ 4.26 (d, 2H, collapses to singlet with D_2O), 4.80 (s, 2H), 5.01 (t, 1H, exchanges with D_2O), 7.10-7.14 (m, 1H), 7.25-7.40 (m, 4H), 7.67 (t, 2H), 7.78-7.86 (m, 4H), 7.90-7.96 (m, 1H); MS: *m/z* 428.0 $(M - OH)^+$, 468.0 (MNa^+).

Following the procedure described above for example 17 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 214

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.29 (d, 2H), 4.90 (s, 2H), 5.02 (t, 1H), 7.35-7.45 (m, 3H), 7.61-7.71 (m, 4H), 7.78-7.87 (m, 4H), 7.90-7.95 (m, 1H); MS: *m/z* 478.0 $[(M - OH)^+]$, 518 (MNa^+).

Compound 215

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 3.32 (s, 3H),

4.55 (d, 2H), 4.92 (s, 2H), 5.10 (t, 1H), 7.36-7.50 (m, 3H), 7.65-7.72 (m, 2H), 7.84-7.90 (m, 1H), 7.93-7.98 (m, 1H); MS: *m/z* 416.1 $(M - OH)^+$, 456.1 (MNa^+).

Compound 216

***N*-(3,4-Difluoro-benzyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.49 (t, 1H), 3.11 (s, 3H), 4.44 (d, 2H), 4.77 (br s, 2H), 7.02-7.20 (m, 3H), 7.40-7.46 (m, 2H), 7.74-7.80 (m, 1H), 7.88-7.94 (m, 1H); MS: *m/z* 366.1 $(M - OH)^+$, 406.0 (MNa^+).

Compound 217

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.33 (t, 3H), 3.47 (q, 2H), 4.53 (d, 2H), 4.93 (s, 2H), 5.09 (t, 1H), 7.36-7.50 (m, 3H), 7.62-7.71 (m, 2H), 7.83-7.90 (m, 1H), 7.92-7.98 (m, 1H); MS: *m/z* 430.2 $(M - OH)^+$, 470.1 (MNa^+).

Compound 218

***N*-(3-Hydroxymethyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.98 (br s, 1H), 4.29 (s, 2H), 4.93 (s, 2H), 7.34-7.48 (m, 3H), 7.59-7.68 (m, 2H), 7.82-7.87 (m, 1H), 7.91-8.00 (m, 1H) superimposed on 7.98 (d, 2H), 8.18 (d, 2H), 13.63 (br s, 1H); MS: *m/z* 522.2 $(M - OH)^+$, 562.2 (MNa^+).

Compound 219

***N*-(3,4-Difluoro-benzyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.33 (t, 3H), 3.46 (q, 2H), 4.54 (d, 2H), 4.84 (s, 2H), 5.09 (t, 1H), 7.10-7.17 (m, 1H), 7.29-7.42 (m, 4H), 7.83-7.89 (m, 1H), 7.93-7.98 (m, 1H); MS: *m/z* 380.1 $(M - OH)^+$, 420.1 (MNa^+).

Compound 220

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 1.08 (br s, 3H), 1.50 (t, 3H), 3.27 (q, 2H), 4.42 (d, 1H), 4.94 (q, 1H), 5.29 (d, 1H), 7.13 (t, 1H), 7.35-7.40 (m, 2H), 7.49-7.54 (m, 2H), 7.58 (d, 1H), 7.74-7.77 (m, 1H), 8.12 (br d, 1H); MS: *m/z* 444.1 $(M - OH)^+$, 484.2 (MNa^+). Compound **220** (143 mg) was separated by chiral HPLC (Chiralpak IA) eluting with 100% MeOH to afford 54.4 mg of compound **534** and 48.0 mg of compound **535** as clear oils.

Compound 534

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*(S)*-*N*-[3-(1-hydroxy-ethyl)-(benzo[*b*]thiophen-2-yl)-ethyl-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.32-1.36 (t, 3H), 3.16-3.17 (d, 1H), 3.44-3.50 (m, 2H), 4.05-4.09 (m, 1H), 4.85-4.98 (m, 4H), 5.11 (s, 1H), 7.32-7.39 (m, 2H), 7.43-7.48 (m, 1H), 7.64-7.70 (m, 2H), 7.85-7.87 (m, 1H), 8.14-8.16 (m, 1H); MS: *m/z* 444.0 $(M - OH)^+$.

Compound 535

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*(R)*-*N*-[3-(1-hydroxy-ethyl)-(benzo[*b*]thiophen-2-yl)-ethyl-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.32-1.36 (t, 3H), 3.16-3.17 (d, 1H), 3.45-3.50 (m, 2H), 4.08 (m, 1H), 4.85-5.02 (m, 4H), 5.11 (s, 1H), 7.33-7.39 (m, 2H), 7.43-7.48 (m, 1H), 7.64-7.71 (m, 2H), 7.85-7.87 (m, 1H), 8.14-8.17 (m, 1H); MS: *m/z* 444.0 $(M - OH)^+$.

Compound 221

***N*-(3,4-Difluoro-benzyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ: 1.02-1.55 (br s, 3H) superimposed on 1.34 (t, 3H), 3.46 (q, 2H), 4.78 (br s, 2H), 4.94-5.04 (m, 1H), 5.12 (s, 1H), 7.11-7.19 (m, 1H), 7.30-7.42 (m, 4H), 7.84-7.89 (m, 1H), 8.13-8.20 (m, 1H); MS: *m/z* 394.2 $(M - OH)^+$, 434.1 (MNa^+).

Compound 335

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-4-carboxybenzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.15 (d, 3H), 5.03-5.47 (m, 3H), 7.18 (t, 1H), 7.32-7.70 (m, 5H), 7.87-8.00 (m, 2H), 8.12-8.20 (m, 1H), 8.27 (d, 2H); MS: *m/z* 536 $(M - OH)^+$, 576 (MNa^+).

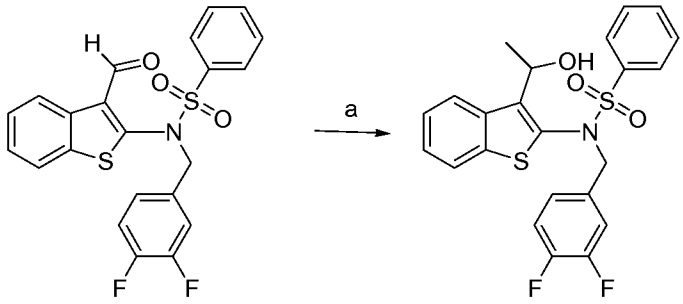
Compound 821

***N*-(3-Fluoropropyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.95 (dtt, 2H), 2.96 (t, 1H), 3.51-3.91 (br, 2H), 4.52 (dt, 2H), 4.89 (br d, 2H), 7.41 (dt, 1H), 7.48 (dt, 1H), 7.55 (t, 2H), 7.68-7.72 (m, 2H), 7.75-7.77 (m, 2H), 8.02-8.04 (m, 1H); MS: *m/z* 402.0 (MNa^+).

Compound 834

2,5-Dibromo-*N*-(3,4-difluoro-benzyl)-*N*-(3-hydroxymethyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide. MS: *m/z* 624.2, 626.2, 628.2 (MNa^+).

Example 18



Compound 206 Compound 222

a) MeMgBr, THF.

Compound 222

***N*-(3,4-Difluoro-benzyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** A solution of methylmagnesium bromide in THF/toluene (1.4 M, 0.31 mL, 0.41 mmol) was added to a solution of compound **206** (120 mg, 0.270 mmol) in THF (3 mL) at 0 °C. The resultant solution was stirred at ambient temperature for 3 h, then treated with a saturated aqueous solution of ammonium chloride. The product was extracted into ethyl acetate, washed with brine,dried over sodium sulfate, filtered, and the solvent evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate-heptane (10-40%) gradient to afford compound **222** as a colorless solid (103 mg, 83%). ^{1}H-NMR (DMSO-d_6): δ 0.65-1.50 (br m, 3H), 4.53-4.73 (br s, 1h), 4.75-4.97 (br s, 2H), 5.08 (d, 1H, exchanges with D_2O), 7.01-7.12 (m, 1H), 7.19-7.40 (m, 4H), 7.68 (t, 2H), 7.78-7.82 (d of d, 2H), 7.90 (d, 2H), 8.12-8.16 (m, 1h); MS: *m/z* 442 $(M - OH)^+$, 482.1 (MNa^+).

Following the procedure described above for example 18 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared.

Compound 223

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-benzenesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 1.10-1.28 (m, 3H), 2.64 (br s, 1H, exchanges with D_2O), 4.06-4.21 (m, 1H), 5.05-5.34 (m, 2H), 7.09 (t, 1H), 7.31-7.39 (m, 2H), 7.43-7.50 (m, 1H), 7.52-7.85 (m, 7H), 8.11-8.19 (m, 1H); MS: *m/z* 492.0 $[(M - OH)^+]$, 532.0 (MNa^+).

Compound 224

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-methanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.06-1.29 (br m, 3H), 2.53 (br s, 1H), 3.10 (s, 3H), 4.38 (br d, 1H), 4.98-5.30 (br m, 2H), 7.14 (t, 1H), 7.34-7.42 (m, 2H), 7.49-7.56 (m, 1H), 7.56-7.62 (m, 1H), 7.73-7.79 (m, 1H), 8.09-8.16 (m, 1H); MS: *m/z* 430 [(M -OH)$^+$], 470.2 (MNa^+).

Compound 225

***N*-(3,4-Difluoro-benzyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-methanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.06-1.63 (br m, 3H), 2.52 (br s, 1H), 4.32 (br d, 1H), 3.08 (s, 3H), 4.95-5.24 (br m, 2H), 7.01-7.24 (m, 3H), 7.34-7.41 (m, 2H), 7.73-7.79 (m, 1H), 8.09-8.17 (m, 1H); MS: *m/z* 380.1 [(M - OH)$^+$], 420.1 (MNa^+).

Compound 316

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.35 (s, 3H), 1.62 (s, 3H), 4.53-4.61 (m, 1H), 5.04-5.61 (m, 2H), 7.30-7.50 (m, 5H), 7.65-7.90 (m, 6H), 8.40 (s, 1H); MS: *m/z* 506.2 (M – OH)$^+$.

Compound 821

***N*-(3-Fluoropropyl)-*N*-[3-(1-hydroxyethyl)-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.60-2.10 (m, 5H), 2.71 (br s, 1H), 3.12-3.20 (m, 1H), 4.02-4.15 (m, 1H), 4.34-4.56 (m, 2H), 5.38-5.46 (m, 1H), 7.26-7.36 m, 2H), 7.43-7.47 (m, 2H), 7.57-7.61 (m, 2H), 7.65-7.72 (m, 2H), 8.16-8.21 (m, 1H); MS: *m/z* 416.0 (MNa^+).

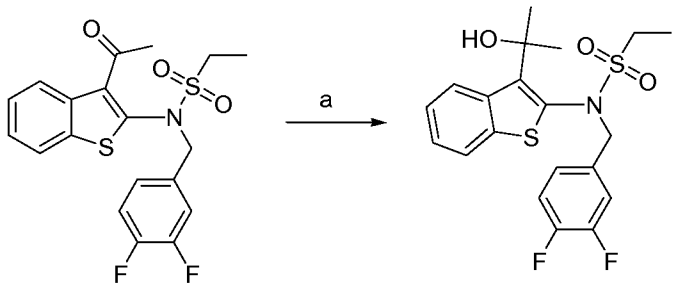
Compound 827

***N*-(4-Fluoro-3-methoxybenzyl)-*N*-[3-(1-hydroxyethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.10 (br s, 3H), 1.52 (t, 3H), 2.65 (br s, 1H), 3.27 (br q, 2H), 3.86 (br s, 3H), 4.35-4.39 (br m, 1H), 4.95-5.00 (m, 1H), 5.21-5.25 (m, 1H), 6.73-6.77 (m, 1H), 6.95 (dd, 1H), 7.02 (dd, 1H), 7.35-7.42 (m, 2H), 7.75-7.78 (m, 1H), 8.12-8.14 (m, 1H); MS: *m/z* 446.4 (MNa^+).

Compound 835

***N*-(2-Fluoropyridin-4-ylmethyl)-*N*-[3-(1-hydroxyethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide.** MS: *m/z* 395.2 (MH^+).

Example 19



Compound 203 Compound 226

a) MeMgBr, THF.

Compound 226

***N*-(3,4-Difluoro-benzyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide**. A solution of methylmagnesium bromide in THF/toluene (1.4 M, 0.21 mL, 0.29 mmol) was added to a solution of compound **203** (0.10 g, 0.24 mmol) in THF (2 mL), at 0 °C and the resultant solution was stirred at ambient temperature for 2 h. An additional portion of methylmagnesium bromide in THF/toluene (1.4 M, 0.21 mL, 0.29 mmol) was added, and the resultant solution stirred at rt for an additional 18 h, and the solution was quenched with a saturated aqueous solution of ammonium chloride. The product was extracted into ethyl acetate, washed with brine and dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate-heptane (10-30%) gradient to afford compound **226** as a colorless solid (66 mg, 65%). ^{1}H-NMR (DMSO-d_6): δ 1.30 (t, 3H), 1.41 (s, 3H), 1.60 (s, 3H), 3.31-3.45 (m, 2H), 4.74 (d, 1H), 4.86 (d, 1H), 5.14 (s, 1H), 7.11-7.17 (m, 1H), 7.31-7.45 (m, 4H) 7.79-7.85 (m, 1H), 8.31-8.36 (m, 1H); MS: *m/z* 408.1 [(M - OH)$^+$], 448.2 (MNa^+).

Following the procedure described above for example 19 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared.

Compound 227

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 1.41 (t, 3H), 1.49 (s, 3H), 1.75 (s, 3H), 3.16-3.36 (m, 2H), 3.65 (s, 1H), 4.87 (d, 1H), 4.98 (d, 1H), 7.12 (t,

1H), 7.34-7.40 (m, 2H), 7.55-7.72 (m, 3H), 7.87-7.92 (m, 1H); MS: *m/z* 458.1 [(M-OH)$^+$], 498.1 (MNa$^+$).

Compound 776

***N*-(2-Fluoro-3-methoxy-benzyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.45 (t, 3H), 1.61 (s, 3H), 1.76 (s, 3H), 3.25-3.40 (m, 2H), 3.54 (s, 1H), 3.82-3.89 (m, 3H), 4.90-5.14 (m, 2H), 6.82-6.99 (m, H), 7.28-7.38 (m, 2H), 7.60-7.68 (m, 1H), 7.88-7.97 (m, 1H); MS: *m/z* 420.1 (M – OH)$^+$.

Compound 802

***N*-[3-(1-Hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-*N*-(2,4,5-trifluoro-3-methoxy-benzyl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.45 (t, 3H), 1.59 (s, 3H), 1.79 (s, 3H), 3.31 (qd, 2H), 3.73 (s, 1H), 3.97 (s, 3H), 4.96 (s, 2H), 6.95 (ddd, 1H), 7.31-7.43 (m, 2H), 7.63-7.73 (m, 1H), 7.85-7.94 (m, 1H); MS: *m/z* 456.03 (M – OH)$^+$.

Compound 830

***N*-(3-Fluoropropyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.79 (s, 3H), 1.92 (s, 3H), 1.94-2.21 (m, 2H), 3.44-3.52 (m, 1H), 3.59 (s, 1H), 4.14-4.22 (m, 1H), 4.45-4.75 (m, 2H), 7.33-7.42 (m, 2H), 7.54 (t, 2H), 7.61-7.63 (m, 1H), 7.69 (t, 1H), 7.79-7.81 (m, 2H), 8.03 (d, 1H); MS: *m/z* 430.0 (MNa$^+$).

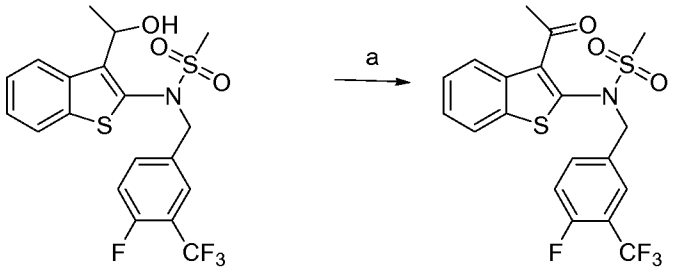
Compound 836

***N*-(2-Fluoro-pyridin-4-ylmethyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 1.43 (t, 3H), 1.57 (s, 3H), 1.80 (s, 3H), 3.22-3.38 (m, 2H), 3.77 (s, 1H), 4.90-4.95 (m, 2H), 7.05 (s, 1H), 7.26-7.28 (m, 1H), 7.35-7.40 (m, 2H), 7.67-7.71 (m, 1H), 7.87-7.90 (m, 1H), 8.16 (d, 1H). MS: *m/z* 409.4 (MH$^+$).

Compound 838

***N*-(4-Fluoro-3-methoxybenzyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.41 (t, 3H), 1.52 (s, 3H), 1.72 (s, 3H), 3.16-3.32 (m, 2H), 3.48 (s, 1H), 3.82 (s, 3H), 4.78 (d, 1H), 4.92 (d, 1H), 6.77-6.81 (m, 1H), 6.93 (dd, 1H), 7.09 (dd, 1H), 7.33-7.38 (m, 2H), 7.68-7.71 (m, 1H), 7.92-7.96 (m, 1H); MS: *m/z* 897.2 (M_2Na^+).

Example 20



Compound 224 Compound 228

a) PCC, DCM.

Compound 228

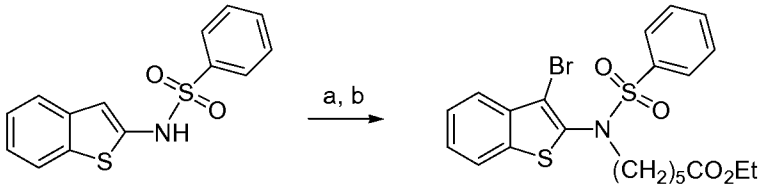
***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-methanesulfonamide**. Pyridinium chlorochromate (0.205 g, 0.955 mmol) was added to a solution of compound **224** (0.285 g, 0.637 mmol) in dichloromethane (10 mL) and stirred at rt for 18 h. The mixture was washed with water, absorbed onto silica gel, and the product isolated by flash column chromatography (SiO_2), eluting with an ethyl acetate-heptane (10-70%) gradient to afford compound **228** as a colorless solid (0.228 g, 80%). ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 3H), 3.34 (s, 3H), 5.03 (s, 2H), 7.43-7.52 (m, 3H), 7.70-7.78 (m, 2H), 7.97-8.03 (m, 2H); MS: *m/z* 446.1 (MH^+).

Following the procedure described above for example 20 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared**.**

Compound 229

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-methanesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 3H), 3.32 (s, 3H), 4.94 (s, 2H), 7.18-7.24 (m, 1H), 7.36-7.50 (m, 4H), 7.87-8.04 (m, 2H); MS: *m/z* 396.1 (MH^+).

Example 21



1-D Compound 230

a) PPh_3, DEAD, 6-hydroxy-hexanoic acid ethyl ester, THF, toluene; b) NBS, DCE, AcOH.

Compound 230

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5-carboethoxy-pentyl)benzenesulfonamide.** To a stock solution of Ph_3P in THF (1.0 mL, 0.375 M, 0.375 mmol) was added THF (2 mL) and a solution of DEAD (0.17 mL, 40% in toluene, 0.38 mmol). After stirring for a few minutes, compound **1-D** (0.072 g, 0.25 mmol) was added followed by 6-hydroxy-hexanoic acid ethyl ester (0.049 mL, 0.30 mmol), and the reaction mixture was stirred overnight. The reaction mixture was evaporated *in vacuo* and the crude residue was dissolved in 1:1 dichloroethane/acetic acid (2 mL), to which was added NBS (0.053 g, 0.30 mmol). After stirring for 6 h the reaction mixture was evaporated *in vacuo* and purified by reverse-phase chromatography (25-95% acetonitrile/water +0.1% TFA) to afford compound **230** as a waxy tan solid (0.090 g, 0.18 mmol). ^{1}H-NMR (DMSO-d_6): δ 1.14 (t, 3H), 1.28-1.52 (m, 6H), 2.21 (t, 2H), 3.59 (br t, 2H), 4.01 (q, 2H), 7.50-7.59 (m, 2H), 7.66 (t, 2H), 7.75-7.82 (m, 2H), 7.85 (d, 2H), 7.96-8.03 (m, 1H); MS: *m/z* 510.1 (MH^+).

Following the procedure described above for example 21 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared.

Compound 231

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.81 (t, 3H), 1.28-1.45 (m, 4H), 3.60 (br t, 2H), 7.49-7.58 (m, 2H), 7.67 (t, 2H), 7.75-7.82 (m, 2H), 7.85 (dd, 2H), 7.97-8.02 (m, 1H); MS: *m/z* 424.1 (MH^+).

Compound 232

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclohexylmethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.87-1.00 (m, 2H), 1.01-1.16 (m, 3H), 1.23-1.35 (m, 1H), 1.52-1.67 (m, 3H), 1.77 (br s, 2H), 3.44 (br s, 2H), 7.49-7.58 (m, 2H), 7.65 (t, 2H), 7.73-7.85 (m, 4H), 7.96-8.02 (m, 1H); MS: *m/z* 464.0 (MH^+).

Compound 233

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(phenethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.81 (t, 2H), 3.86 (t, 2H), 7.13-7.29 (m, 5H), 7.50-7.58 (m, 2H), 7.64 (t, 2H), 7.73-7.86 (m, 4H), 7.79-8.04 (m, 1H); MS: *m/z* 472.1 (MH^+).

Compound 234

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-*tert*-butoxy-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.98 (s, 9H), 3.41 (t, 2H), 3.79 (t, 2H), 7.48-7.56 (m, 2H), 7.64 (t, 2H), 7.71-7.79 (m, 2H), 7.83-7.89 (m, 2H), 7.97-8.02 (m, 1H); MS: *m/z* 490.0 (MNa^+).

Compound 235

(*R*)-*N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2,3-dihydroxy-propyl)-benzenesulfonamide. MS: *m/z* 464.0 (MNa^+).

Compound 236

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-[2-(2-oxo-pyrrolidin-1-yl)-ethyl]-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.84 (p, 2H), 2.14 (t, 2H), 3.29-3.38 (m, 4H), 3.78 (br t, 2H), 7.49-7.58 (m, 2H), 7.66 (t, 2H), 7.72-7.87 (m, 4H), 7.98-8.04 (m, 1H); MS: *m/z* 479.0 (MH^+).

Compound 237

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-morpholin-4-yl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.07-3.20 (m, 2H), 3.32-3.42 (m, 2H), 3.44-3.56 (m, 2H), 3.61-3.78 (m, 2H), 3.88-3.99 (m, 2H), 4.03-4.18 (m, 2H), 7.53-7.60 (m, 2H), 7.69 (t, 2H), 7.76-7.86 (m, 2H), 7.90 (d, 2H), 8.01-8.06 (m, 1H), 10.75 (br s, 1H); MS: *m/z* 481.0 (MH^+).

Compound 238

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-dimethylamino-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.85 (s, 6H), 3.33 (br t, 2H), 4.02 (br t, 2H), 7.53-7.60 (m, 2H), 7.69 (t, 2H), 7.75-7.80 (m, 1H), 7.83 (t, 1H), 7.89 (d, 2H), 8.01-8.07 (m, 1H), 9.59 (br s, 1H); MS: *m/z* 439.1 (MH^+).

Compound 239

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-methanesulfonyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.06 (s, 3H), 3.43 (br t, 2H), 4.05 (br t, 2H), 7.51-7.60 (m, 2H), 7.69 (t, 2H), 7.75-7.85 (m, 2H), 7.88 (dd, 2H), 8.00-8.06 (m, 1H); MS: *m/z* 495.9 (MNa^+).

Compound 240

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-[2-(2-oxo-imidazolidin-1-yl)-ethyl]-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.13 (t, 2H), 3.19 (t, 2H), 3.31 (t, 2H),

3.76 (t, 2H), 6.36 (br s, 1H), 7.50-7.58 (m, 2H), 7.66 (t, 2H), 7.72-7.81 (m, 2H), 7.85 (dd, 2H), 7.97-8.04 (m, 1H); MS: *m/z* 480.0 (MH^+).

Compound 241

(*S*)-*N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(1-methyl-pyrrolidin-2-ylmethyl)-benzenesulfonamide. MS: *m/z* 465.0 (MH^+).

Compound 242

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2,2-difluoro-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.16 (dt, 2H), 6.23 (tt, 1H), 7.50-7.57 (m, 2H), 7.65 (t, 2H), 7.71-7.76 (m, 1H), 7.79 (t, 1H), 7.86 (d, 2H), 7.98-8.04 (m, 1H); MS: *m/z* 432.1 (MH^+).

Compound 243

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(carbomethoxymethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.62 (s, 3H), 4.63 (s, 2H), 7.48-7.56 (m, 2H), 7.62 (t, 2H), 7.68-7.72 (m, 1H), 7.75 (t, 1H), 7.84 (dd, 2H), 7.97-8.03 (m, 1H); MS: *m/z* 440.1 (MH^+).

Compound 244

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-[2(*S*)-methyl-2-carbomethoxy-ethyl]-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.17 (d, 3H), 2.60 (q, 1H), 3.46 (s, 3H), 3.75 (br s, 1H), 3.86 (br s, 1H), 7.50-7.58 (m, 2H), 7.66 (t, 2H), 7.72-7.86 (m, 4H), 7.97-8.03 (m, 1H); MS: *m/z* 468.1 (MH^+).

Compound 245

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-[2(*R*)-methyl-2-carbomethoxy-ethyl]-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.17 (d, 3H), 2.60 (q, 1H), 3.46 (s, 3H), 3.74 (br s, 1H), 3.86 (br s, 1H), 7.50-7.57 (m, 2H), 7.66 (t, 2H), 7.73-7.86 (m, 4H), 7.97-8.03 (m, 1H); MS: *m/z* 468.1 (MH^+).

Compound 246

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-phenyl-propyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.71 (p, 2H), 2.65 (br t, 2H), 3.64 (br t, 2H), 7.09-7.19 (m, 3H), 7.23 (t, 2H), 7.50-7.59 (m, 2H), 7.67 (t, 2H), 7.75-7.86 (m, 4H), 7.97-8.03 (m, 1H); MS: *m/z* 486.1 (MH^+).

Compound 247

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.08 (t, 3H), 3.66 (q, 2H), 7.50-7.59 (m, 2H), 7.67 (t, 2H), 7.75-7.82 (m, 2H), 7.86 (dd, 2H), 7.98-8.03 (m, 1H); MS: *m/z* 396.0 (MH^+).

Compound 248

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(hexyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.81 (t, 3H), 1.11-1.25 (m, 4H), 1.26-1.36 (m, 2H), 1.36-1.46 (m, 2H), 3.59 (br t, 2H), 7.50-7.58 (m, 2H), 7.67 (t, 2H), 7.75-7.82 (m, 2H), 7.85 (d, 2H), 7.97-8.03 (m, 1H); MS: *m/z* 452.1 (MH^+).

Compound 249

***N*-(Adamant-1-ylmethyl)-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.42 (d, 3H), 1.53 (d, 6H), 1.62 (d, 3H), 1.87 (s, 3H), 3.06 (d, 1H), 3.62 (d, 1H), 7.48-7.56 (m, 2H), 7.62 (t, 2H), 7.73-7.80 (m, 4H), 7.94-8.00 (m, 1H); MS: *m/z* 516.2 (MH^+).

Compound 250

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.51-2.66 (m, 2H), 3.93 (t, 2H), 7.52-7.58 (m, 2H), 7.66 (t, 2H), 7.74-7.83 (m, 2H), 7.85 (dd, 2H), 8.00-8.04 (m, 1H); MS: *m/z* 464.0 (MH^+).

Compound 251

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(pent-3-ynyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.59 (t, 3H), 2.33-2.40 (m, 2H), 3.74 (t, 2H), 7.50-7.57 (m, 2H), 7.66 (t, 2H), 7.74-7.81 (m, 2H), 7.86 (dd, 2H), 7.98-8.03 (m, 1H); MS: *m/z* 434.0 (MH^+).

Compound 252

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-methoxy-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.13 (s, 3H), 3.40 (t, 2H), 3.82 (t, 2H), 7.49-7.56 (m, 2H), 7.65 (t, 2H), 7.73-7.80 (m, 2H), 7.85 (d, 2H), 7.97-8.02 (m, 1H); MS: *m/z* 426.1 (MH^+).

Compound 253

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-oxo-pentyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.59 (p, 2H), 2.04 (s, 3H), 2.58 (t, 2H), 3.57 (br t, 2H), 7.50-

7.58 (m, 2H), 7.67 (t, 2H), 7.75-7.86 (m, 4H), 7.97-8.03 (m, 1H); MS: *m/z* 452.0 (MH^+).

Compound 254

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(dimethoxyphosphinoyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.02-2.13 (m, 2H), 3.58 (s, 3H), 3.61 (s, 3H), 3.76-3.86 (m, 2H), 7.51-7.58 (m, 2H), 7.68 (t, 2H), 7.74-7.87 (m, 4H), 7.98-8.04 (m, 1H); MS: *m/z* 504.1 (MH^+).

Compound 255

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.06-0.11 (m, 2H), 0.35-0.41 (m, 2H), 0.83-0.95 (m, 1H), 3.52 (dd, 2H), 7.50-7.57 (m, 2H), 7.66 (t, 2H), 7.74-7.80 (m, 2H), 7.83-7.88 (m, 2H), 7.97-8.02 (m, 1H); MS: *m/z* 422.0 (MH^+).

Compound 256

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-piperidin-1-yl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.27-1.38 (m, 1H), 1.50-1.71 (m, 3H), 1.75-1.84 (m, 2H), 2.88-3.01 (m, 2H), 3.26-3.34 (m, 2H), 3.46-3.55 (m, 2H), 3.99-4.08 (m, 2H), 7.53-7.59 (m, 2H), 7.69 (t, 2H), 7.76-7.80 (m, 1H), 7.83 (t, 1H), 7.88 (dd, 2H), 8.01-8.06 (m, 1H), 9.16 (br s, 1H); MS: *m/z* 479.0 (MH^+).

Compound 257

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-[2-(2,5-dioxo-pyrrolidin-1-yl)-ethyl]-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.54 (s, 4H), 3.56 (t, 2H), 3.82 (t, 2H), 7.52-7.57 (m, 2H), 7.66 (t, 2H), 7.72-7.81 (m, 4H), 8.01-8.06 (m, 1H); MS: *m/z* 492.9 (MH^+).

Compound 258

(*R*)-*N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5-oxo-pyrrolidin-2-ylmethyl)-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ 1.87-2.00 (m, 1H), 2.02-2.25 (m, 3H), 3.45-3.75 (m, 3H), 7.46 (br s, 1H), 7.51-7.57 (m, 2H), 7.67 (t, 2H), 7.74-7.83 (m, 2H), 7.86 (d, 2H), 7.98-8.03 (m, 1H); MS: *m/z* 464.9 (MH^+).

Compound 259

(*S*)-*N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5-oxo-pyrrolidin-2-ylmethyl)-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ 1.85-1.99 (m, 1H), 2.02-2.25 (m, 3H), 3.44-3.76 (m, 3H), 4.76 (br s, 1H), 7.51-7.57 (m, 2H), 7.67 (t, 2H), 7.74-7.83 (m, 2H), 7.86 (d, 2H), 7.98-8.03 (m, 1H); MS: *m/z* 465.0 (MH^+).

Compound 260

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-methylsulfanyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.02 (s, 3H), 2.62 (t, 2H), 3.83 (t, 2H), 7.51-7.57 (m, 2H), 7.66 (t, 2H), 7.73-7.82 (m, 2H), 7.87 (d, 2H), 7.98-8.04 (m, 1H); MS: *m/z* 441.9 (MH^+).

Compound 261

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.84 (t, 3H), 1.30-1.41 (m, 5H), 1.47 (p, 2H), 3.38 (q, 2H), 3.69 (t, 2H), 7.51-7.60 (m, 2H), 7.77-7.83 (m, 1H), 7.99-8.05 (m, 1H); MS: *m/z* 376.0 (MH^+).

Compound 262

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.11-0.17 (m, 2H), 0.40-0.46 (m, 2H), 0.92-1.03 (m, 1H), 1.34 (t, 3H), 3.38 (q, 2H), 3.57 (d, 2H), 7.51-7.59 (m, 2H), 7.77-7.83 (m, 1H), 8.00-8.05 (m, 1H); MS: *m/z* 374.0 (MH^+).

Compound 263

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2,2-difluoro-ethyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.35 (t, 3H), 3.47 (q, 2H), 4.17 (dt, 2H), 6.22 (tt, 1H), 7.52-7.59 (m, 2H), 7.77-7.83 (m, 1H), 8.01-8.06 (m, 1H); MS: *m/z* 384.1 (MH^+).

Compound 264

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-*tert*-butoxy-ethyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.10 (s, 9H), 1.35 (t, 3H), 3.38-3.47 (m, 4H), 3.81 (t, 2H), 7.50-7.58 (m, 2H), 7.76-7.81 (m, 1H), 7.99-8.06 (m, 1H); MS: *m/z* 442.0 (MNa^+).

Compound 265

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-*N'*,*N'*-dimethylsulfamide..** ^{1}H-NMR (DMSO-d_6): δ 0.84 (t, 3H), 1.34 (h, 2H), 1.45 (p, 2H), 2.89 (s, 6H), 3.58 (t, 2H), 7.50-7.58 (m, 2H), 7.76-7.81 (m, 1H), 7.98-8.04 (m, 1H); MS: *m/z* 391.0 (MH^+).

Compound 266

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)- *N'*,*N'*-dimethylsulfamide.** ^{1}H-NMR (DMSO-d_6): δ 0.08-0.14 (m, 2H), 0.37-0.44 (m, 2H), 0.89-1.01 (m, 1H), 2.87 (s, 6H), 3.48 (d, 2H), 7.50-7.57 (m, 2H), 7.76-7.82 (m, 1H), 7.98-8.04 (m, 1H); MS: *m/z* 389.0 (MH^+).

Compound 267

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-*tert*-butoxy-ethyl)- *N'*,*N'*-dimethylsulfamide.** ^{1}H-NMR (DMSO-d_6): δ 1.08 (s, 9H), 2.91 (s, 6H), 3.42 (t, 2H), 3.72 (t, 2H), 7.49-7.56 (m, 2H), 7.75-7.80 (m, 1H), 7.98-8.03 (m, 1H); MS: *m/z* 435.1 (MH^+).

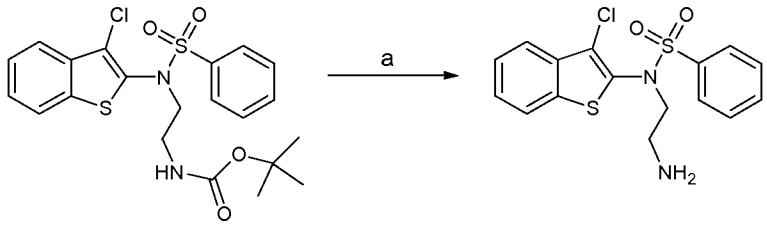
Compound 268

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2,2-difluoro-ethyl)- *N'*,*N'*-dimethylsulfamide.** ^{1}H-NMR (DMSO-d_6): δ 2.89 (s, 6H), 4.07 (dt, 2H), 6.21 (tt, 1H), 7.51-7.58 (m, 2H), 7.76-7.82 (m, 1H), 8.00-8.06 (m, 1H); MS: *m/z* 399.0 (MH^+).

Compound 269

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoropropyl)- *N'*,*N'*-dimethylsulfamide.** ^{1}H-NMR (DMSO-d_6): δ 2.54-2.68 (m, 2H), 2.89 (s, 6H), 3.87 (t, 2H), 7.52-7.59 (m, 2H), 7.77-7.84 (m, 1H), 8.01-8.07 (m, 1H); MS: *m/z* 431.0 (MH^+).

Example 22



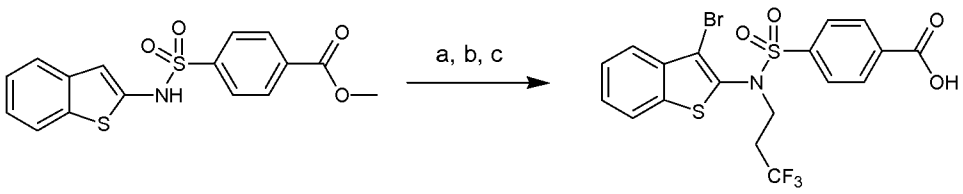
Compound 86 **Compound 270**

a) TFA, CH_2Cl_2.

Compound 270

***N*-(2-Amino-ethyl)-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** To compound **86** (0.035 g, 0.075 mmol), dissolved in CH_2Cl_2 (1 mL), was added trifluoroacetic acid (1 mL) and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was evaporated *in vacuo*, and the residue triturated with hexanes (2 mL) to afford compound **270** as a brown solid (0.031 g, 86%). ^{1}H-NMR ($CDCl_3$): δ 3.17-3.28 (t, 2H), 3.58-3.62 (t, 2H), 7.34-7.55 (m, 4H), 7.58-7.70 (m, 5H); MS: *m/z* 367.1 (MH^+).

Example 23



271-A Compound 271

a) Ph_3P, DEAD, 3,3,3-trifluoropropan-1-ol, THF; b). aq NaOH; c) NBS, DCE, HOAc.

Compound 271

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carboxy-benzenesulfonamide.** To a solution of Ph_3P (0.888 g, 3.39 mmol) in THF (27 mL) was added a solution of DEAD (1.50 mL, 3.38 mmol). After stirring for 2 min, compound **271-A** (0.782 g, 2.25 mmol) was added. To a portion (0.25 mmol of **271-A**) of the aforementioned reaction mixture was added 3,3,3-trifluoropropan-1-ol (0.025 mL, 0.30 mmol). The reaction was stirred for 2 days, 1N NaOH (0.5 mL, 0.5 mmol) was added, and the reaction was evaporated *in vacuo*. The crude residue was re-dissolved in 1:1 dichloroethane/acetic acid (2 mL), and NBS (0.053 g, 0.30 mmol) was added. After stirring overnight an additional portion of NBS (0.041 g, 0.23 mmol) was added, and the reaction stirred for an additional 4 h. The reaction mixture was evaporated *in vacuo* and purified by reverse-phase chromatography (25-95% acetonitrile/water + 0.1% TFA) to afford compound **271** as a tan powder (0.069 g, 0.14 mmol). ^{1}H-NMR (DMSO-d_6): δ 2.54-2.68 (m, 2H), 3.98 (t, 2H), 7.52-7.59 (m, 2H), 7.73-7.79 (m, 1H), 7.97 (d, 2H), 8.00-8.06 (m, 1H), 8.16 (d, 2H), 13.60 (br s, 1H); MS: *m/z* 507.9 (MH^+).

Following the procedure described above for example 23 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared.

Compound 272

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.83 (t, 3H), 1.30-1.47 (m, 4H), 3.65 (br t, 2H), 7.50-7.58 (m, 2H), 7.75-7.80 (m, 1H), 7.96 (d, 2H), 7.99-8.03 (m, 1H), 8.17 (d, 2H), 13.58 (s, 1H); MS: *m/z* 468.0 (MH^+).

Compound 273

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.06-0.15 (m, 2H), 0.36-0.43 (m, 2H), 0.85-0.97 (m, 1H), 3.56 (d, 2H), 7.50-7.58 (m, 2H), 7.74-7.80 (m, 1H), 7.97 (d, 2H), 7.99-8.03 (m, 1H), 8.16 (d, 2H), 13.58 (br s, 1H); MS: *m/z* 465.9 (MH^+).

Compound 274

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-methoxyethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 3.14 (s, 3H), 3.41 (t, 2H), 3.87 (t, 2H), 7.50-7.57 (m, 2H), 7.72-7.78 (m, 1H), 7.96 (d, 2H), 7.99-8.03 (m, 1H), 8.15 (d, 2H), 13.57 (s, 1H); MS: *m/z* 470.0 (MH^+).

Compound 275

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-*tert*-butoxy-ethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.98 (s, 9H), 3.42 (t, 2H), 3.84 (t, 2H), 7.49-7.56 (m, 2H), 7.71-7.78 (m, 1H), 7.95-8.03 (m, 3H), 8.15 (d, 2H), 13.56 (br s, 1H); MS: *m/z* 512.0 (MH^+).

Compound 276

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2,2-difluoro-ethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ: 4.19 (dt, 2H), 6.24 (tt, 1H), 7.51-7.58 (m, 2H), 7.71-7.77 (m, 1H), 7.98 (d, 2H), 8.01-8.05 (m, 1H), 8.15 (d, 2H), 13.61 (s, 1H); MS: *m/z* 475.9 (MH^+).

Compound 277

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-morpholin-4-yl-ethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (CD_3OD): δ 3.38 (br s, 4H), 3.46 (t, 2H), 3.91 (br s, 4H), 4.20 (t, 2H), 7.49-7.56 (m, 2H), 7.76-7.82 (m, 1H), 7.84-7.90 (m, 1H), 7.97 (d, 2H), 8.23 (d, 2H); MS: *m/z* 525.0 (MH^+).

Compound 278

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(adamant-1-yl-methyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.40-1.48 (m, 3H), 1.50-1.58 (m, 6H), 1.58-1.66 (m, 3H), 1.88 (br s, 3H), 3.12 (d, 1H), 3.65 (d, 1H), 7.48-7.56 (m, 2H), 7.74-7.79 (m, 1H), 7.88 (d, 2H), 7.96-8.01 (m, 1H), 8.13 (d, 2H), 13.57 (s, 1H); MS: *m/z* 560.0 (MH^+).

Compound 279

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclohexylmethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.89-1.02 (m, 2H), 1.02-1.19 (m, 3H), 1.25-1.38 (m, 1H), 1.52-1.60 (m, 1H), 1.60-1.94 (m, 4H), 3.49 (br s, 2H), 7.50-7.58 (m, 2H), 7.73-7.80 (m, 1H), 7.94 (d, 2H), 7.97-8.03 (m, 1H), 8.15 (d, 2H), 13.58 (br s, 1H); MS: *m/z* 508.0 (MH^+).

Compound 390

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(ethyl)-4-carboxy-benzenesulfonamide.**

MS: *m/z* 438.1 $(M - H)^-$.

Compound 391

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(propyl)-4-carboxy-benzenesulfonamide.**

MS: *m/z* 452.1 $(M - H)^-$.

Compound 392

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(pentyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.80 (t, 3H), 1.37-1.15 (m, 4H), 1.50-1.38 (m, 2H), 3.64 (t, 2H), 7.59-7.50 (m, 2H), 7.81-7.74 (m, 1H), 8.03-7.93 (m, 3H), 8.17 (d, 2H), 13.59 (s, 1H); MS: *m/z* 480.1$(M - H)^-$.

Compound 393

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(hexyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.81 (t, 3H), 1.25-1.12 (m, 4H), 1.49-1.26 (m, 4H), 3.64 (t, 2H), 7.59-7.50 (m, 2H), 7.81-7.74 (m, 1H), 8.04-7.94 (m, 3H), 8.17 (d, 2H), 13.59 (s, 1H); MS: *m/z* 494 $(M - H)^-$.

Compound 394

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carboxy-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.76-1.64 (m, 2H), 2.48-2.34 (m, 2H), 3.74 (t, 2H), 7.60-7.51 (m, 2H), 7.82-7.76 (m, 1H), 7.97 (d, 2H), 8.06-8.00 (m, 1H), 8.18 (d, 2H), 13.62 (s, 1H); MS: *m/z* 520 $(M - H)^-$.

Compound 395

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.65-1.46 (m, 4H), 2.34-2.14 (m, 2H),

3.68 (br t, 2H), 7.59-7.50 (m, 2H), 7.82-7.74 (m, 1H), 8.04-7.95 (m, 3H), 8.17 (d, 2H), 13.59 (s, 1H); MS: *m/z* 534.1 (M - H)$^-$.

Compound 396

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropylethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.03-0.04 (m, 2H), 0.39-0.31 (m, 2H), 0.81-0.68 (m, 1H), 1.39 (q, 2H), 3.72 (t, 2H), 7.58-7.49 (m, 2H), 7.79-7.74 (m, 1H), 8.03-7.94 (m, 3H), 8.17 (d, 2H), 13.59 (s, 1H); MS: *m/z* 478.1 (M - H)$^-$.

Compound 397

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-*tert*-butoxypropyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.06 (s, 9H), 1.60 (p, 2H), 3.32 (t, 2H), 3.71 (br t, 2H), 7.59-7.49 (m, 2H), 7.81-7.75 (m, 1H), 7.96 (d, 2H), 8.04-7.98 (m, 1H), 8.17 (d, 2H), 13.59 (br s, 1H); MS: *m/z* 524 (M - H)$^-$.

Compound 437

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclobutylmethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.71-1.60 (m, 2H), 1.83-1.72 (m, 2H), 1.95-1.85 (m, 2H), 2.40-2.31 (m, 1H), 3.68 (br s, 2H), 7.57-7.50 (m, 2H), 7.79-7.73 (m, 1H), 8.02-7.94 (m, 3H), 8.17 (d, 2H), 13.59 (s, 1H); MS: *m/z* 478 (M - H)$^-$.

Compound 438

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopentylmethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.29 (br s, 2H), 1.49-1.39 (m, 2H), 1.60-1.50 (m, 2H), 1.73-1.60 (br m, 2H), 1.89 (p, 1H), 3.73-334 (br m, 2H), 7.58-7.50 (m, 2H), 7.79-7.74 (m, 1H), 7.95 (d, 2H), 8.02-7.97 (m, 1H), 8.16 (d, 2H), 13.59 (s, 1H); MS: *m/z* 492.2 (M - H)$^-$.

Compound 439

***RS, RS*-*N*-(Bicyclo[2.2.1]heptan-2-ylmethyl)-*N*-(3-bromobenzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.21-0.62 (m, 11H), 3.63 (br s, 2H), 7.58-7.49 (m, 2H), 7.80-7.74 (m, 1H), 8.02-7.93 (m, 3H), 8.18-8.13 (m, 2H), 13.59 (br s, 1H); MS: *m/z* 518.2 (M - H)$^-$.

Compound 440

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.23 (m, 2H), 1.84-1.52 (m, 3H), 3.23-3.13 (m, 2H), 3.55 (br s, 2H), 3.85-3.76 (m, 2H), 7.58-7.50 (m,

2H), 7.80-7.74 (m, 1H), 7.95 (d, 2H), 8.03-7.98 (m, 1H), 8.16 (d, 2H), 13.59 (s, 1H); MS: *m/z* 508.1 $(M - H)^-$.

Compound 441

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 481 $(M - H)^-$.

Compound 452

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(isobutyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.93 (d, 6H), 1.66-1.54 (m, 1H), 3.38 (br s, 2H), 7.57-7.50 (m, 2H), 7.79-7.74 (m, 1H), 7.94 (d, 2H), 8.02-7.97 (m, 1H), 8.15 (d, 2H), 13.58 (s, 1H); MS: *m/z* 466.1 $(M - H)^-$.

Compound 453

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-(cyclohexyloxy)ethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.16-0.97 (m, 5H), 1.42-1.33 (m, 1H), 1.56-1.47 (m, 2H), 1.66-1.57 (m, 2H), 3.14-3.07 (m, 1H), 3.46 (t, 2H), 3.86 (t, 2H), 7.56-7.49 (m, 2H), 7.78-7.73 (m, 1H), 8.03-7.96 (m, 3H), 8.15 (d, 2H), 13.55 (s, 1H); MS: *m/z* 536.2 $(M - H)^-$.

Compound 454

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-methoxy-3-methylbutyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.05 (s, 6H), 1.72-1.65 (m, 2H), 2.98 (s, 3H), 3.73-3.64 (m, 2H), 7.58-7.51 (m, 2H), 7.80-7.75 (m, 1H), 7.97 (d, 2H), 8.03-7.99 (m, 1H), 8.18 (d, 2H), 13.59 (s, 1H); MS: *m/z* 510.2 $(M - H)^-$.

Compound 523

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(*C*-benzo[1,3]dioxol-5-yl-methy)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.82-2.03 (m, 3H), 4.67 (br s, 2H), 5.97 (s, 2H), 6.67 (dd, 1H), 6.78 (d, 2H), 7.25-7.44 (m, 2H), 7.61-7.73 (m, 1H), 7.73-7.88 (m, 1H), 7.98 (m, 2H), 8.17 (m, 2H), 13.60 (br s, 1H); MS: *m/z* 504.0 (MH^+).

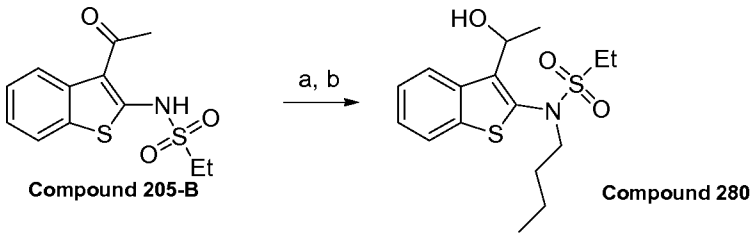
Compound 524

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(*C*-(2,2-difluoro-benzo[1,3]dioxol-5-yl)-methyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.95 (s, 3H), 4.81 (br s, 2H), 7.11 (dd, 1H), 7.22-7.48 (m, 4H), 7.57-7.73 (m, 1H), 7.76-7.92 (m, 1H), 7.99 (m, 2H), 8.18 (m, 2H), 13.61 (br s, 1H); MS: *m/z* 540.0 (MH^+).

Compound 525

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,4-dimethoxy-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.97 (s, 3H), 3.31 (s, 4H), 3.62-3.75 (m, 3H), 4.66 (br s, 1H), 6.61-6.74 (m, 1H), 6.74-6.89 (m, 2H), 7.25-7.44 (m, 2H), 7.61-7.72 (m, 1H), 7.72-7.85 (m, 1H), 7.99 (m, 2H), 8.18 (m, 2H), 13.59 (s, 1H); MS: *m/z* 520.0 (MH^+).

Example 24



Compound 205-B Compound 280

a) PPh_3, DEAD, *n*-BuOH, THF, toluene; b) $NaBH_4$, MeOH.

Compound 280

***N*-(Butyl)-*N*-[3-(1-hydroxy-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide.** To a solution of Ph_3P (0.494 g, 1.88 mmol) in THF (15 mL) was added a solution of DEAD (0.84 mL, 1.89 mmol). After stirring for a few minutes, compound **205-B** (0.354 g, 1.25 mmol) was added. To a portion of the aforementioned reaction mixture (0.25 mmol of **205-B**) was added *n*-butan-1-ol (0.027 mL, 0.30 mmol) and the reaction stirred for 2 days. Methanol (0.50 mL) was added followed by $NaBH_4$ (0.019 g, 0.50 mmol) and the reaction was stirred for 3 h. The reaction mixture was evaporated *in vacuo* and purified by reverse-phase chromatography (25-95% acetonitrile/water + 0.1% TFA) to afford compound **280** as a tan semi-solid (0.053 g, 0.16 mmol). ^{1}H-NMR (DMSO-d_6): δ 0.86 (t, 3H), 1.22-1.37 (m, 5H), 1.44-1.57 (m, 5H), 3.26-3.41 (m, 2H), 3.46 (br s, 1H), 3.70 (br s, 1H), 5.09-5.18 (br d, 1H), 5.26 (br s, 1H), 7.37-7.43 (m, 2H), 7.87-7.93 (m, 1H), 8.22-8.27 (m, 1H); MS: *m/z* 364.0 (MH^+).

Following the procedure described above for example 24 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared.

Compound 281

***N*-(Cyclopropylmethyl)-*N*-(3-(1-hydroxyethyl)benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.15-0.26 (m, 2H), 0.48 (d, 2H), 1.01 (br s, 1H), 1.30 (t, 3H), 1.54 (d, 3H), 3.26-3.39 (m, 2H), 3.39-3.57 (m, 2H), 5.17-5.27 (m, 2H), 7.37-7.43 (m, 2H), 7.39-7.88 (m, 1H), 8.22-8.28 (m, 1H); MS: *m/z* 362.1 (MNa^+).

Compound 282

***N*-(3-(1-Hydroxyethyl)benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.30 (t, 3H), 1.54 (d, 3H), 2.57-2.73 (m, 2H), 3.32-3.53 (m, 2H), 3.67 (br s, 1H), 4.07 (br s, 1H), 5.10 (br s, 1H), 5.34 (br s, 1H), 7.40-7.46 (m, 2H), 7.91-7.96 (m, 1H), 8.23-8.29 (m, 1H); MS: *m/z* 404.1 (MNa^+).

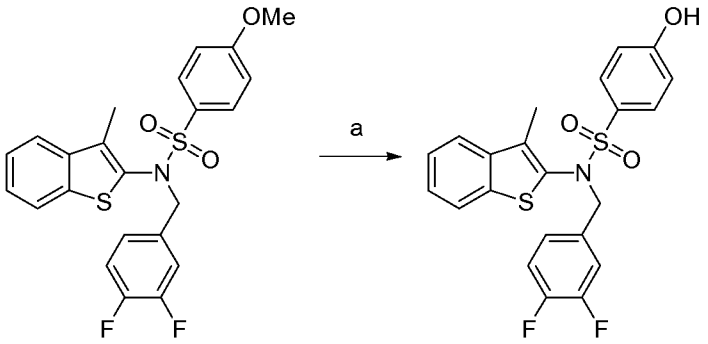
Compound 283

***N*-(2-*tert*-Butoxyethyl)-*N*-(3-(1-hydroxyethyl)benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.16 (s, 9H), 1.31 (t, 3H), 1.53 (d, 3H), 3.36-3.52 (m, 4H), 3.73 (m, 2H), 5.11 (br s, 1H), 5.30 (br s, 1H), 7.37-7.44 (m, 2H), 7.88-7.93 (m, 1H), 8.21-8.26 (m, 1H); MS: *m/z* 408.1 (MNa^+).

Compound 284

***N*-(3-(1-Hydroxyethyl)benzo[*b*]thiophen-2-yl)-*N*-(2-morpholinoethyl)-ethanesulfonamide.** MS: *m/z* 399.1 (MH^+).

Example 25



Compound 26 **Compound 285**

a) BBr_3, DCM.

Compound 285

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-hydroxy-benzenesulfonamide.** A solution of boron tribromide (1.0 M in dichlorormethane, 1.57 mL, 1.57 mmol) was added to a solution of compound **26** (180 mg, 0.392 mmol)

in dichloromethane (10 mL), at 0 °C. The resultant solution was stirred at 0 °C for 1 h, then treated with 2 N hydrochloric acid. The organic layer was separated, dried over sodium sulfate, filtered, and the solvent evaporated *in vacuo*. The residue was purified by HPLC (C_{18}) eluting with an acetonitrile-water (0.1% TFA) gradient (40-90%). The resulting residue was further purified by flash column chromatography (SiO_2), eluting with an ethyl acetate-heptane gradient to afford compound **285** as a colorless solid (33 mg, 19%). ^{1}H-NMR (DMSO-d_6): δ 1.98 (s, 3H), 4.67 (br s, 2H), 6.96 (d, 2H), 7.11-7.14 (m, 1H), 7.25-7.40 (m, 4H), 7.64-7.68 (m, 3H), 7.80-7.85 (m, 1H), 10.73 (br s, 1H); MS: *m/z* 446.1 (MH^+).

Following the procedure described above for example 25 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared.

Compound 286

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-hydroxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.97 (s, 3H), 4.71 (s, 2H), 7.09-7.17 (m, 3H), 7.26-7.40 (m, 5H), 7.49 (t, 1H), 7.65-7.70 (m, 1H), 7.81-7.86 (m, 1H), 10.24 (br s, 1H); MS: *m/z* 446.1 (MH^+).

Compound 287

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-hydroxy-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.75 (s, 2H), 6.69-6.71 (m, 1H), 6.85-6.87 (m, 2H) 7.01 (s, 1H), 7.10-7.14 (t, 1H), 7.26-7.29 (m, 2H), 7.48-7.52 (m, 2H), 7.60-7.63 (m, 3H), 7.76-7.78 (d, 2H); MS: *m/z* 396.0 (MH^+).

Compound 288

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-hydroxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.83 (s, 2H), 6.97-6.99 (d, 2H), 7.40-7.51 (m, 3H), 7.63-7.73 (m, 5H), 7.96-7.98 (m, 1H), 10.76 (s, 1H); MS: *m/z* 516.0 (MH^+).

Compound 289

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-hydroxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.88 (s, 2H), 7.15-7.22 (m, 2H), 7.35-7.52 (m, 4H), 7.63-7.73 (m, 3H), 7.97-8.01 (m, 1H), 10.27 (s, 1H); MS: *m/z* 516.0 (MH^+).

Compound 290

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-hydroxy-benzenesulfonamide**. ^{1}H NMR (DMSO-d_6): δ 4.83 (s, 2H), 6.96-6.99 (d, 2H), 7.37-7.52 (m, 3H), 7.60-7.74 (m, 5H), 7.95-7.98 (m, 1H), 10.75 (s, 1H); MS: *m/z* 561.9 (MH^+), 584.0 (MNa^+).

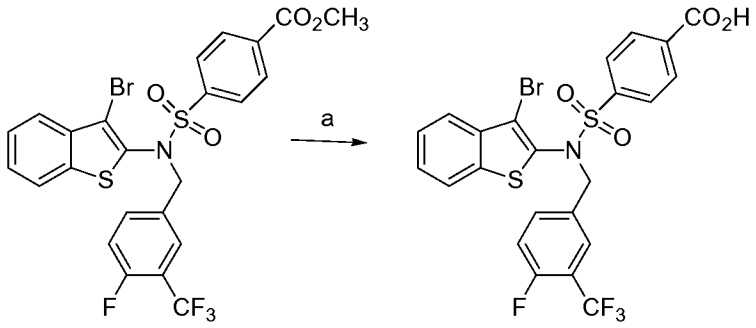
Compound 291

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-hydroxy-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.87 (s, 2H), 7.14-7.23 (m, 2H), 7.35-7.52 (m, 5H), 7.59-7.71 (m, 3H), 7.96-7.99 (m, 1H), 10.26 (s, 1H); MS: *m/z* 561.9 (MH^+).

Compound 780

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-hydroxy-4-methanesulfonylamino-benzenesulfonamide**. MS: *m/z* 608.89 (MH^+).

Example 26



Compound 192 Compound 292

a) MeOH, 3N NaOH.

Compound 292

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide**. To a solution of compound **192** (87.1 mg, 0.145 mmol) in MeOH (2 mL) was added 3N NaOH (73 μL, 0.218 mmol) and the reaction was refluxed for 18 h. The reaction was cooled to ambient temperature and the solvent evaporated under reduced pressure. The residue was dissolved in H_2O, cooled to 0 °C, and acidified with 1N HCl. The precipitate was filtered, washed extensively with H_2O, and dried under vacuo to afford compound **292** as a white solid (0.063 g, 74%). ^{1}H-NMR (CD_3OD): δ 4.94 (s, 2H), 7.16-7.21 (t, 1H), 7.42-7.46 (m, 2H), 7.52-7.56 (m,

1H), 7.61-7.63 (m, 1H), 7.68-7.70 (m, 1H), 7.75-7.77 (m, 1H), 7.99-8.01 (d, 2H), 8.22-8.25 (d, 2H); MS: *m/z* 588.0 (MH^+).

Following the procedure described above for example 26 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 293

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carboxy-benzenesulfonamide.** ^{1}H-NMR (CD_3OD): δ 4.93 (s, 2H), 7.16-7.21 (t, 1H), 7.42-7.45 (m, 2H), 7.45-7.52 (m, 1H), 7.53-7.56 (m, 1H), 7.60-7.79 (m, 3H), 8.08-8.10 (d, 1H), 8.34-8.36 (d, 1H), 8.48 (s, 1H); MS: *m/z* 588.0 (MH^+).

Compound 294

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.95 (s, 2H), 7.42-7.53 (m, 3H), 7.65-7.74 (m, 3H), 7.97-7.99 (m, 2H), 8.03-8.05 (m, 2H), 8.18-8.20 (m, 1H), 13.64 (s, 1H); MS: *m/z* 544.0 (MH^+).

Compound 295

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 5.01 (s, 2H), 7.20 (s, 1H), 7.31-7.35 (m, 2H), 7.45-7.50 (t, 1H), 7.69-7.73 (m, 3H), 7.78-7.85 (m, 2H), 8.05-8.08 (m, 1H), 8.25-8.30 (m, 2H), 13.59 (s, 1H); MS: *m/z* 510.0 (MH^+).

Compound 296

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 5.01 (s, 2H), 7.19 (s, 1H), 7.30-7.35 (m, 2H), 7.45-7.50 (t, 1H), 7.69-7.73 (m, 3H), 7.82-7.84 (m, 2H), 7.94-7.96 (m, 2H), 8.15-8.17 (m, 2H), 13.60 (s, 1H); MS: *m/z* 510.0 (MH^+).

Compound 297

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 5.06 (s, 2H), 7.42-7.53 (m, 3H), 7.61-7.82 (m, 7H), 7.95-7.99 (m, 1H), 13.81 (s, 1H); MS: *m/z* 543.9 (MH^+).

Compound 298

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 5.08 (s, 2H), 7.40-7.51 (m, 3H), 7.59-7.81 (m, 7H), 7.95-7.98 (m, 1H), 13.86 (s, 1H); MS: *m/z* 590.0 (MH^+).

Compound 299

***N*-(3-Formyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 5.08 (br s, 2H), 7.42-7.54 (m, 3H), 7.69-7.80 (m, 2H), 7.97-8.04 (m, 3H), 8.20 (d, 2H), 8.42-8.47 (m, 1H), 9.85 (s, 1H), 13.70 (br s, 1H); MS: *m/z* 538.2 (MH^+).

Compound 305

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.96 (s, 3H), 3.89 (s, 3H), 4.88 (br s, 2H), 7.38-7.42 (m, 3H), 7.69-7.72 (m, 1H), 7.84-7.88 (m, 2H), 8.16-8.18 (m, 1H), 8.27-8.28 (t, 1H), 8.33-8.35 (m, 1H).

Compound 306

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.00 (s, 3H), 4.89 (s, 2H), 7.40-7.45 (m, 2H), 7.47-7.52 (m, 1H), 7.68-7.74 (m, 3H), 7.80-7.82 (d, 2H), 7.87-7.90 (m, 1H), 8.09-8.11 (d, 2H); MS: *m/z* 524.0 (MH^+).

Compound 307

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.95 (s, 2H), 7.41-7.55 (m, 3H), 7.64-7.76 (m, 3H), 7.82-7.86 (m, 1H), 7.97-8.00 (m, 1H), 8.16-8.19 (m, 1H), 8.31-8.34 (m, 2H), 13.61 (s, 1H); MS: *m/z* 543.9 (MH^+).

Compound 318

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesufonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.38 (s, 3H), 5.00 (s, 2H), 7.42-7.50 (m, 3H), 7.68-7.75 (m, 2H), 7.93-7.97 (m, 3H), 8.01-8.05 (m, 1H), 8.18 (d, 2H); MS: *m/z* 552.2 (MH^+).

Compound 376

***N*-(6-Fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.94 (s, 3H), 4.87 (s, 2H), 7.23-7.35 (m, 1H), 7.42-7.49 (m, 1H), 7.61-7.86 (m, 5H), 8.12-8.15 (d, 1H), 8.27-8.33 (m, 2H), 13.61 (s, 1H); MS: *m/z* 542.0 (MH^+).

Compound 423

***N*-(Butyl)-*N*-(3-methoxy-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesufonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.83 (t, 3H), 1.26-1.38 (m, 2H), 1.42-

1.52 (m, 2H), 3.56 (t, 2H), 3.97 (s, 3H), 7.39-7.46 (m, 2H), 7.75-7.84 (m, 2H), 7.96 (d, 2H), 8.15 (d, 2H), 13.58 (br s, 1H); MS: *m/z* 420.1 (MH^+).

Compound 426

***N*-(6-Fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.65-1.69 (m, 2H), 2.21 (s, 3H), 2.30-2.40 (m, 2H), 3.66 (m, 2H), 7.30-7.35 (m, 1H), 7.81-7.84 (m, 2H), 7.85-7.91 (m, 2H), 8.15-8.17 (d, 1H), 13.62 (s, 1H); MS: m/z 476.0 (MH^+).

Compound 427

***N*-(6-Fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.91 (s, 3H), 4.89 (s, 2H), 7.22-7.27 (m, 1H), 7.42-7.47 (t, 1H), 7.63-7.80 (m, 6H), 8.03-8.05 (d, 1H), 13.62 (s, 1H); MS: *m/z* 542.0 (MH^+).

Compound 432

***N*-(Butyl)-*N*-(1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesufonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.87 (t, 3H), 1.16-1.41 (m, 2H), 1.49-1.67 (m, 2H), 3.72 (t, 2H), 7.56-7.76 (m, 4H), 7.80 (d, 1H), 8.01 (d, 2H), 8.12 (d, 2 H); MS: *m/z* 422.1 (MH^+).

Compound 450

***N*-(6-Fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.828-0.864 (t, 3H), 1.28-1.44 (m, 4H), 2.22 (s, 3H), 3.51-3.56 (m, 2H), 7.28-7.33 (m, 1H), 7.79-7.82 (m, 2H), 7.83-7.90 (m, 2H), 8.13-8.15 (m, 2H), 13.62 (s, 1H); MS: *m/z* 422.1 (MH^+).

Compound 451

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carboxy-benzenesulfonamide**. MS: m/z 444.0 (MH^+).

Compound 456

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carboxy-benzenesulfonamide**. MS: m/z 430.0 (MH^+).

Compound 468

***N*-(Butyl)-*N*-(3-carbamoyl-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesufonamide.** MS: *m/z* 433.0 (MH^+).

Compound 469

***N*-(Butyl)-*N*-(3-dimethylcarbamoyl-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesufonamide.** MS: *m/z* 461.1 (MH^+).

Compound 486

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 1.98 (s, 3H), 3.50 (br s, 2H), 7.24 (d, 5H), 7.29-7.40 (m, 2 H), 7.52-7.61 (m, 1H), 7.61-7.70 (m, 1H), 7.95 (m, 2H), 8.26 (m, 2H); MS: *m/z* 452.5 (MH^+).

Compound 487

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 1.98 (s, 3H), 3.50 (br s, 2H), 6.83-7.00 (m, 2H), 7.20-7.25 (m, 2H), 7.30-7.40 (m, 2H), 7.55-7.69 (m, 2H), 7.94 (m, 2H), 8.26 (m, 2H); MS: *m/z* 456.0 (MH^+).

Compound 488

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluoro-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.00-2.09 (m, 3H), 4.67 (br s, 1H), 6.91-7.08 (m, 2H), 7.08-7.21 (m, 1H), 7.31-7.43 (m, 2H), 7.53-7.71 (m, 2H), 7.94 (m, 2H), 8.27 (m, 2H); MS: *m/z* 474.0 (MH^+).

Compound 489

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-chloro-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.06 (s, 3H), 4.67 (br s, 1H), 7.00 (t, 1H), 7.12 (m, 1H), 7.30-7.44 (m, 3H), 7.54-7.71 (m, 2H), 7.94 (m, 2H), 8.27 (m, 2H); MS: *m/z* 490.0 (MH^+).

Compound 490

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-difluoromethoxy-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.00 (s, 3H), 4.71 (br s, 2H), 6.2-6.7 (m, 1H), 6.99 (d, 2H), 7.24-7.26 (m, 2H), 7.30-7.44 (m, 2H), 7.52-7.74 (m, 2H), 7.95 (m, 2H), 8.27 (m, 2H); MS: *m/z* 504.0 (MH^+).

Compound 491

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.04 (s, 3H), 4.77 (br s, 2H), 7.31-7.40 (m, 3H), 7.44 (d, 1H), 7.51 (d, 1H), 7.54-7.62 (m, 2H), 7.62-7.68 (m, 1H), 7.95 (m, 2H), 8.28 (m, 2H); MS: *m/z* 506.1 (MH^+).

Compound 492

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-methylsulfone-benzyl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 538.0 (MH^+).

Compound 493

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2,3,4,5,6-pentafluoro-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.03-2.20 (m, 3H), 3.50 (br s, 2H), 7.31-7.45 (m, 2H), 7.58-7.73 (m, 2H), 7.95 (m, 2H), 8.26 (m, 2H); MS: *m/z* 528.0 (MH^+).

Compound 494

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethylsulfone-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.00 (s, 3H), 3.50 (br s,2H), 7.30-7.46 (m, 2H), 7.51-7.72 (m, 4H), 7.94 (dd, 4H), 8.15-8.33 (m, 2H); MS: *m/z* 570.0 (MH^+).

Compound 495

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(pyridin-3-ylmethyl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 439.0 (MH^+).

Compound 496

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 1.98 (s, 3H), 4.70 (br s, 2H), 7.27-7.33 (m, 2H), 7.33-7.40 (m, 2H), 7.53-7.64 (m, 1H), 7.64-7.72 (m, 1H), 7.95 (m, 2H), 8.27 (m, 2H); MS: *m/z* 522.0 (MH^+). Anal. ($C_{24}H_{17}F_3NO_5S_2 \cdot Na \cdot H_2O$) C, H, N, F, S, Na, KF.

Compound 497

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-fluoro-4-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.10 (s, 3H), 4.74 (br s, 2H), 7.12-7.23 (m, 2H), 7.32-7.44 (m, 2H), 7.50 (t, 1H), 7.57-7.72 (m, 2H), 7.94 (m, 2H), 8.28 (m, 2H); MS: *m/z* 524.0 (MH^+).

Compound 502

***N*-(3-Cyclopentyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.69 (s, 1H), 1.25-1.63 (m, 3H), 1.63-1.91 (m, 4H), 3.05 (d, 1H), 4.35 (d, 1H), 5.24 (d, 1H), 7.13-7.48 (m,

3H), 7.49-7.70 (m, 3H), 7.75-7.87 (m, 1H), 7.97 (d, 2H), 8.13 (d, 2H); MS: *m/z* 578.1 (MH^+).

Compound 517

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,4,5-trifluoro-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 2.00 (s, 3H), 4.80 (br s, 2H), 7.25 (dd, 2H), 7.34-7.49 (m, 2H), 7.70 (dd, 1H), 7.78-7.91 (m, 1H), 7.99 (m, 2H), 8.18 (m, 2H), 13.62 (s, 1H); MS: *m/z* 492.5 (MH^+).

Compound 518

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.94 (s, 3H), 4.89 (br s, 2H), 7.24-7.46 (m, 2H), 7.52 (d, 2H), 7.61-7.78 (m, 3H), 7.83 (dd, 1H), 8.00 (m, 2H), 8.18 (m, 2H), 13.61 (s, 1H); MS: *m/z* 506.1 (MH^+).

Compound 519

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-5-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.92 (s, 3H), 4.96 (br s, 2H), 7.33-7.44 (m, 3H), 7.58-7.64 (m, 1H), 7.64-7.70 (m, 1H), 7.76 (br. s., 1H), 7.80-7.92 (m, 1H), 8.00 (m, 2H), 8.19 (m, 2H), 13.62 (s, 1H); MS: *m/z* 524.0 (MH^+).

Compound 520

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2,5-dichloro-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.94 (s, 3H), 4.93 (br s, 2H), 7.22-7.51 (m, 5H), 7.62-7.75 (m, 1H), 7.75-7.91 (m, 1H), 7.99 (m, 2H), 8.18 (m, 2H), 13.62 (br s, 1H); MS: *m/z* 528.0 (MH^+).

Compound 521

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-chloro-3-fluoro-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.97 (s, 3H), 4.80 (br s, 2H), 7.18 (dd, 1H), 7.30 (dd, 1H), 7.38 (dd, 2H), 7.54 (t, 1H), 7.62-7.76 (m, 1H), 7.76-7.91 (m, 1H), 7.99 (d, 2H), 8.18 (d, 2H), 13.62 (br s, 1H); MS: *m/z* 490.0 (MH^+).

Compound 522

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-2-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.87 (s, 3H), 4.99 (br s, 2H), 7.23-7.45 (m, 2H), 7.45-7.75 (m, 4H), 7.75-7.93 (m, 1H), 7.99 (m, 2H), 8.18 (m, 2H), 13.63 (br s, 1H); MS: *m/z* 524.0 (MH^+).

Compound 526

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethylsulfanyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.90 (s, 3H), 4.85 (br s, 2H), 7.32-7.46 (m, 4H), 7.65 (d, 3H), 7.73-7.89 (m, 1H), 7.99 (m, 2H), 8.18 (m, 2H), 13.60 (s, 1H); MS: *m/z* 538.0 (MH^+).

Compound 527

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-thien-2-ylsulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 2.02 (s, 4H), 4.93 (br s, 2H), 7.35-7.51 (m, 4H), 7.58-7.79 (m, 4H), 7.79-7.95 (m, 1H), 8.04 (d, 1H), 8.74 (d, 1H), 13.36 (s, 1H); MS: *m/z* 530.0 (MH^+).

Compound 528

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-(5-carboxy-3-methyl-thien-2-yl)-sulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 2.01 (s, 3H), 2.19 (s, 3H), 4.94 (br s, 2H), 7.28-7.54 (m, 3H), 7.54-7.80 (m, 4H), 7.80-8.03 (m, 1H), 13.91 (br s, 1H); MS: *m/z* 544.0 (MH^+).

Compound 529

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-5-carboxy-furan-2-yl-sulfonamide.** MS: *m/z* 514.0 (MH^+).

Compound 556

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carboxy-benzenesulfonamide**. MS: m/z 390.0 (MH^+).

Compound 557

***N*-(3-Methyl-6-trifluoromethyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide**. ^{1}H-NMR (CD_3OD): δ 2.03 (s, 3H), 7.19-7.24 (t, 1H), 7.53-7.55 (m, 3H), 7.80-7.82 (d, 1H), 7.95-7.98 (d, 2H), 8.09 (s, 1H), 8.23-8.25 (d, 2H).

Compound 558

***N*-(3-Methyl-6-trifluoromethyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carboxy-benzenesulfonamide**. MS: m/z 472.0 (MH^+).

Compound 566

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-isopropyl-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.78 (d, 3H), 1.43 (d, 3H),

3.28 (q, 1H), 4.17 (d, 1H), 5.24 (d, 1H), 7.07 (t, 1H), 7.27-7.38 (m, 2H), 7.38-7.46 (m, 1H), 7.59 (dd, 1H), 7.62-7.71 (m, 1H), 7.85-7.93 (m, 1H), 7.98 (d, 2H), 8.30 (d, 2H).

Compound 567

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-isopropyl-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ -0.08-0.07 (m, 2H), 0.37-0.49 (m, 2H), 0.57-0.74 (m, 1H), 1.19 (m, 1H), 1.42 (d, 3H), 1.52 (d, 3H), 1.57-1.72 (m, 1H), 3.18-3.32 (m, 1H), 3.55-3.69 (m, 1H), 3.87-4.08 (m, 1H), 7.29-7.40 (m, 2H), 7.63-7.71 (m, 1H), 7.95 (d, 2H), 7.98-8.06 (m, 1H), 8.26 (d, 2H); MS: *m/z* 444.1 (MH^+).

Compound 568

***N*-(5,5,5-Trifluoro-pentyl)-*N*-(3-isopropyl-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.43 (d, 3H), 1.53 (d, 3H), 1.53 - 1.78 (m, 4H), 1.94-2.19 (m, 2H), 3.14-3.30 (m, 1H), 3.62 (q, 1H), 3.80-4.00 (m, 1H), 7.31-7.42 (m, 2H), 7.64-7.73 (m, 1H), 7.92 (d, 2H), 7.98-8.08 (m, 1H), 8.26 (d, 2H); MS: *m/z* 500.1 (MH^+).

Compound 675

***N*-(3-Cyclopropyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.59 (m, 4H), 1.38-1.63 (m, 1H), 4.24-5.37 (m, 2H), 7.36 (d, 3H), 7.54-7.67 (m, 2H), 7.70-7.90 (m, 4H), 8.04 (d, 2H); MS: *m/z* 550.0 (MH^+).

Compound 698

***N*-(3-Cyclobutyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.59-2.44 (m, 6H), 3.67 (q, 1H), 4.44 (d, 1H), 5.26 (d, 1H), 7.26-7.54 (m, 3H), 7.54-7.67 (m, 2H), 7.80-7.93 (m, 1H), 7.95-8.11 (m, 3H), 8.19 (d, 2H), 13.64 (s, 1H); MS: *m/z* 562 $(M - H)^-$.

Compound 755

***N*-(3-Cyclopropyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxyl-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.30-0.80 (m, 4H), 1.42-1.66 (m, 1H), 4.26-5.32 (m., 2H), 7.22-7.44 (m, 6H), 7.69-7.79 (m, 1H), 7.80-7.89 (m, 1H), 8.02 (d, 2H), 8.12-8.27 (m, 2H), 13.62 (s, 1H), MS: *m/z* 546.2 $(M - H)^-$.

Compound 756

***N*-(3-Cyclobutyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.57-2.38 (m, 6H), 3.66 (t,

1H), 4.29 (d, 1H), 5.26 (d, 1H), 7.29-7.42 (m, 6H), 7.82-7.90 (m, 1H), 7.95-8.06 (m, 3H), 8.18 (d, 2H), 13.63 (s., 1H); MS: *m/z* 560.1 $(M - H)^-$.

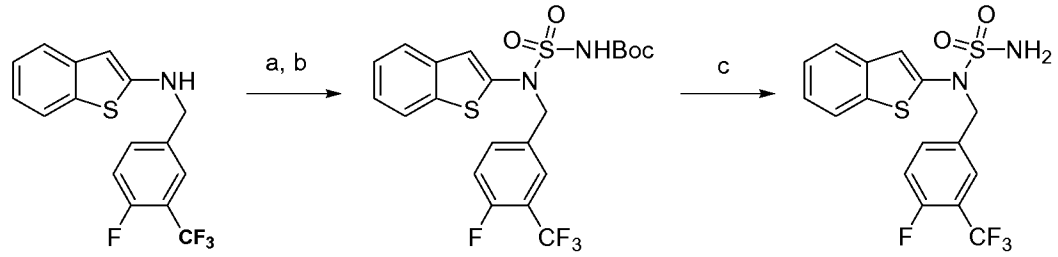
Compound 765

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-carboxy-propanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.05 (s, 3H), 2.24 (q, 2H), 2.63 (t, 2H), 3.26-3.40 (m, 2H), 4.82 (s, 2H), 7.09 (t, 1H), 7.34-7.42 (m, 2H), 7.44-7.51 (m, 1H), 7.53-7.64 (m, 2H), 7.69-7.77 (m, 1H); MS: *m/z* 490.0 (MH^+).

Compound 792

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-carboxy-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.00 (s, 3H), 4.54 (s, 2H), 4.90 (s, 2H), 7.32-7.52 (m, 3H), 7.57-7.75 (m, 3H), 7.86-7.96 (m, 1H), 13.64 (s, 1H); MS: *m/z* 462.0 (MH^+).

Example 27



300-A **300-B** **Compound 300**

a) Chlorosulfonyl isocyanate, CH_2Cl_2, *t*-BuOH; b) CH_2Cl_2, pyridine; c) 4N HCl. Compound **300-A** was prepared from compound **1-C**, following the procedure used to prepare compound **127-D**.

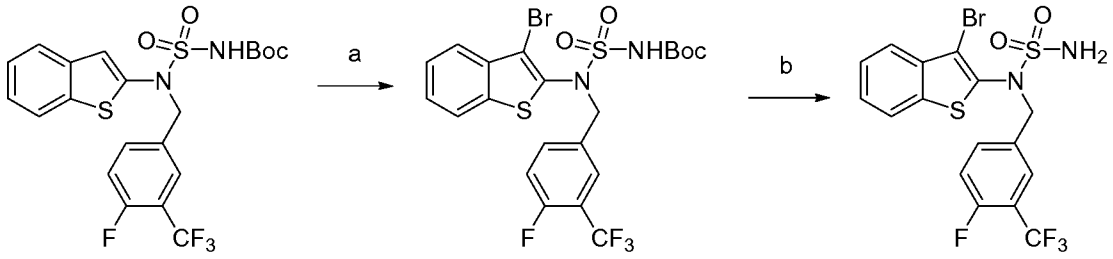
***N*-(4-Fluoro-3-trifluorobenzyl)-*N*-(benzo[*b*]thiophen-2-yl)-[N'-*tert*-butyloxycarbonyl]-sulfonamide (300-B).** To a solution of chlorosulfonyl isocyanate (200 mg, 1.41 mmol) in CH_2Cl_2 (2 mL) was added *tert*-butanol (0.135 mL, 1.41 mmol) and the reaction was stirred at ambient temperature for 2 h. This solution was added drop-wise to a cooled (0 °C) solution of compound **300-A** (485 mg; 1.34 mmol) in CH_2Cl_2 (2.5 mL) and pyridine (2.5 mL). The reaction mixture was stirred at ambient temperature for 18 h, diluted with EtOAc, washed with 1N HCl (2X), H_2O, brine, dried over Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with a

heptane-EtOAc gradient to afford compound **300-B** as a yellow solid (0.389 g, 58%). ^{1}H-NMR (DMSO-d_6): δ 1.48 (s, 9H), 5.13 (s, 2H), 7.30 (s, 1H), 7.34-7.37 (m, 2H), 7.47-7.52 (m, 1H), 7.70-7.79 (m, 3H), 7.88-7.91 (m, 1H), 11.77 (s, 1H).

Compound 300

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-sulfamide.** To compound **300-B** (167 mg, 0.331 mmol) was added solution of 1N HCl in dioxane (6 mL) and the reaction was stirred at ambient temperature for 18 h. The reaction mixture was evaporated under reduced pressure, the residue dried under vacuo, and purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford compound **300** as a pink oil (0.097 g, 73%). ^{1}H-NMR (DMSO-d_6): δ 4.88 (s, 2H), 7.22 (s, 1H), 7.28-7.33 (m, 2H), 7.44-7.49 (m, 1H), 7.69-7.83 (m, 6H); MS: *m/z* 405.0 (MH^+).

Example 28



300-B **301-A** **Compound 301**

a) DCE, NBS; b) 4N HCl.

***N*-(4-Fluoro-3-trifluorobenzyl)-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-[N'-*tert*-butyloxycarbonyl]-sulfonamide (301-A).** To a solution compound **300-B** (306 mg; 0.606 mmol) in DCE (3 mL) was added *N*-bromosuccinimide (119 mg, 0.666 mmol) and the reaction was allowed to stir at ambient temperature for 2 h. The resultant solution was evaporated under reduced pressure and the crude residue purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford compound **301-A** as a beige solid (0.254 mg, 72%). ^{1}H-NMR (DMSO-d_6): δ 1.51 (s, 9H), 5.06 (s, 1H), 7.41-7.46 (t, 1H), 7.49-7.54 (m, 2H), 7.62-7.66 (m, 1H), 7.70-7.77 (m, 2H), 8.00-8.03 (m, 1H), 11.81 (s, 1H).

Compound 301

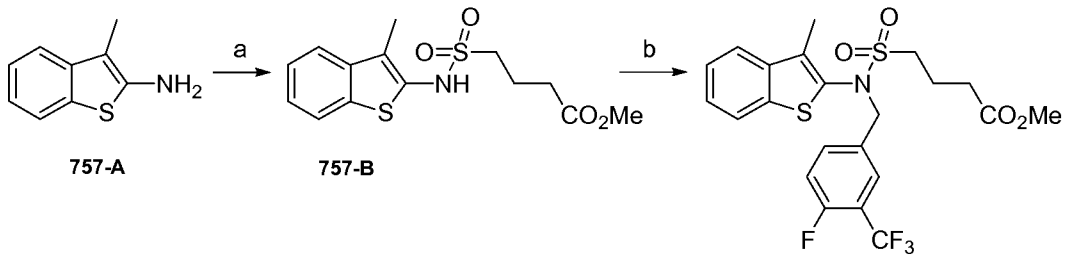
***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N* (4-fluoro-3-trifluoromethyl-benzyl)-sulfamide.** To compound **301-B** (200 mg, 0.342 mmol) was added solution of 1N HCl in dioxane (6 mL) and the reaction was stirred at ambient temperature for 18 h. The reaction mixture was evaporated under reduced pressure, the residue dried under vacuo, and purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford compound **301** as a light purple oil (0.117 g, 71%).. ^{1}H-NMR (DMSO-d_6): δ 3.16-3.17 (d, 2H), 4.80 (s, 2H), 7.39-7.49 (m, 3H), 7.67-7.82 (m, 3H), 7.96-7.98 (m, 1H); MS: *m/z* 483 (MH^+).

Following the procedure described above for example 28 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 302

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-sulfamide.** ^{1}H-NMR (DMSO-d_6): δ 3.33 (s, 2H), 4.81 (s, 2H), 7.44-7.47 (t, 1H), 7.40-7.49 (m, 3H), 7.69-7.72 (m, 2H), 7.78-7.82 (m, 3H), 7.96-7.98 (m, 1H); MS: *m/z* 439.0 (MH^+).

Example 29



757-A 757-B Compound 757

a) $ClSO_2(CH_2)_3CO_2Me$, pyridine, DCM; b) KO-*t*-Bu, 4-fluoro-3-trifluoromethybenzyl bromide, DMF.

Compound **757-A,** was prepared by the method used to synthesize compound **1-C** in Example 1, steps A and B. MS: *m/z* 164.1 (MH^+).

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-3-carbomethoxy-propanesulfonamide (757-B).** To a solution of compound **757-A** (1.45 g, 7.25 mmol) and pyridine (1.42 mL, 17.6 mmol) in dichloromethane (20 mL), cooled to -10 °C, was added 4-

chlorosulfonyl-butyric acid methyl ester (1.6 g, 7.97 mmol) and the reaction mixture was stirred at ambient temperature for 2 days. The solvent was evaporated in vacuo, and the product was purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (10-50%) in heptane gradient, to afford 1.75 g of compound **757-B** as a pale orange solid. ^{1}H-NMR (DMSO-d_6): δ 1.87-2.10 (m, 2H), 2.32 (s, 3H), 2.42-2.58 (m, 2H), 3.11-3.29 (m, 2H), 3.59 (s, 3H), 7.25-7.48 (m, 2H), 7.71 (d, 1H), 7.77-7.94 (m, 1H), 10.07 (s, 1H); MS: *m/z* 328.0 (MH^+).

Compound 757

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-carbomethoxy-propanesulfonamide.** To a solution of compound **757-B** (0.85 g, 2.59 mmol) in DMF (15 mL), cooled to 0 °C, was added a solution of potassium t-butoxide (1.0 M in THF, 2.59 mL, 2.59 mmol) and the reaction mixture was stirred for 15 min. 4-Fluoro-3-trifluorobenzyl bromide (0.75 mL, 3.89 mL) was added in one-portion and the resultant solution was stirred at ambient temperature for 2 days. The reaction was partitioned between H_2O and EtOAc, the organic layer washed with water (3X), brine, dried over sodium sulfate, filtered, and the solvent was evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate (5-40%) in heptane gradient, to afford 1.11 g of compound **757** as an oil. ^{1}H-NMR ($CDCl_3$): δ 2.04 (s, 3H), 2.24 (q, 2H), 2.45-2.62 (m, 2H), 3.23-3.43 (m, 2H), 3.71 (s, 3H), 4.82 (s, 2H), 7.09 (t, 1H), 7.32-7.43 (m, 2H), 7.43-7.52 (m, 1H), 7.52-7.65 (m, 2H), 7.73 (dd, 1H); MS: *m/z* 504.1 (MH^+).

Following the procedure described above for example 29 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 310

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-chloro-pyridin-3-ylsulfonamide.** MS: *m/z* 501.0 (MH^+).

Compound 311

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-chloro-pyridin-5-ylsulfonamide.** MS: *m/z* 501.0 (MH^+).

Compound 315

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)- *N'*,*N'*-dimethlysulfamide.** MS: *m/z* 433.1 (MH^+).

Compound 319

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-chloro-pyridin-3-ylsulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 5.27 (s, 2H), 7.14 (t, 1H), 7.30 (dd, 1H), 7.38-7.46 (m, 2H), 7.57 (dd, 2H), 7.62-7.69 (m, 2H), 8.16 (dd, 1H), 8.59 (dd, 1H); MS: *m/z* 578.8 (MH^+).

Compound 320

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-chloro-pyridin-5-ylsulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 4.89 (s, 2H), 7.11 (t, 1H), 7.40-7.47 (m, 2H), 7.47-7.59 (m, 3H), 7.64-7.75 (m, 2H), 8.01 (dd, 1H), 8.83 (d, 1H); MS: *m/z* 580.9 (MH^+).

Compound 321

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-chloro-pyridin-3-ylsulfonamide.** MS: *m/z* 537.0 (MH^+).

Compound 322

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-fluoro-4-trifluoromethyl-benzyl)-pyridin-3-ylsulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 4.95 (s, 2H), 7.18-7.25 (m, 2H), 7.39-7.49 (m, 2H), 7.49-7.61 (m, 2H), 7.63-7.75 (m, 2H), 8.11-8.19 (m, 1H), 8.91 (dd, 1H), 9.10 (d, 1H); MS: *m/z* 545.0 (MH^+).

Compound 323

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-pyridin-3-ylsulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 4.86 (s, 2H), 6.97-7.11 (m, 2H), 7.19 (dd, 1H), 7.39-7.48 (m, 2H), 7.58 (dd, 1H), 7.64-7.76 (m, 2H), 8.17 (dt, 1H), 8.90 (dd, 1H), 9.10 (d, 1H); MS: *m/z* 543.0 (MH^+).

Compound 324

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-fluoro-5-chloro-benzyl)-pyridin-3-ylsulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 4.96 (s, 2H), 6.88 (t, 1H), 7.20 (m, 1H), 7.39-7.48 (m, 3H), 7.51 (dd, 1H), 7.66-7.77 (m, 2H), 8.14 (dt, 1H), 8.88 (dd, 1H), 9.09 (d, 1H); MS: *m/z* 512.8 (MH^+).

Compound 326

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-5-(2-methyl-5-trifluoromethyl-2*H*-pyrazol-3-yl)-thien-2-ylsulfonamide.** MS: *m/z* 633.9 (MH^+).

Compound 327

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-5-carbomethoxy-furan-2-yl-sulfonamide.** MS: *m/z* 527.8 (MH^+).

Compound 328

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-1-methyl-3-trifluoromethyl-1*H*-pyrazol-4-ylsulfonamide.** MS: *m/z* 551.8 (MH^+).

Compound 329

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-5-(5-trifluoromethyl-isoxazol-3-yl)-thien-2-ylsulfonamide.** MS: *m/z* 620.8 (MH^+).

Compound 330

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-5-bromo-6-chloro-pyridin-3-ylsulfonamide.** MS: *m/z* 594.8 (MH^+).

Compound 331

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-5,6-dichloro-pyridin-3-ylsulfonamide.** MS: *m/z* 550.8 (MH^+).

Compound 332

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-pyrazol-1-yl-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.04-2.12 (m, 4H), 3.51 (br s, 1H), 6.53- 6.63 (m, 1H), 7.06 (t, 1H), 7.30-7.40 (m, 2H), 7.40-7.49 (m, 1H), 7.55 (dd, 1H), 7.58-7.70 (m, 2H), 7.83 (d, 1H), 7.86-7.94 (m, 4H), 8.04 (d, 1H); MS: *m/z* 633.9 (MH^+).

Compound 333

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.07 (s, 3H), 2.63 (s, 3H), 3.50 (s, 2H), 7.07 (t, 1H), 7.32-7.40 (m, 2H), 7.40-7.49 (m, 1H), 7.50-7.57 (m, 1H), 7.58-7.67 (m, 2H), 7.70 (t, 1H), 7.90-7.99 (m, 2H), 8.38 (dt, 1H), 8.41-8.44 (m, 1H); MS: *m/z* 561.9 (MH^+).

Compound 334

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-oxazol-5-yl-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.07 (s, 3H), 2.74 (br s, 2H), 7.06 (t, 1H), 7.29-7.41 (m, 2H), 7.41-7.48 (m, 1H), 7.48-7.70 (m, 4H), 7.77-7.86 (m, 2H), 7.86-7.93 (m, 2H), 8.08 (s, 1H); MS: *m/z* 546.9 (MH^+).

Compound 336

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-(3-chloro-4-acetamide)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.07 (s, 3H), 2.32 (s, 3H), 3.52 (br s, 2H), 7.06 (t, 1H), 7.32-7.39 (m, 2H), 7.42 (d, 1H), 7.53 (dd, 1H), 7.58-7.63 (m, 1H), 7.64-7.69 (m, 1H), 7.72 (dd, 1H), 7.79-7.88 (m, 2H), 8.68 (d, 1H); MS: *m/z* 570.9 (MH^+).

Compound 337

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-(6-chloro-imidazo[2,1-*b*]thiazol-5-yl-sulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.06 (s, 3H), 3.53 (br s, 2H), 6.76 (d, 1H), 7.08 (t, 1H), 7.23 (d, 1H), 7.31-7.39 (m, 2H), 7.43-7.50 (m, 1H), 7.55-7.62 (m, 3H); MS: *m/z* 559.8 (MH^+).

Compound 338

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-chloro-pyridin-3-ylsulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 4.87 (s, 2H), 7.07-7.19 (m, 1H), 7.26 (s, 1H), 7.38-7.63 (m, 4H), 7.63-7.83 (m, 2H), 8.01 (dd, 1H), 8.83 (d, 1H); MS: *m/z* 536.8 (MH^+).

Compound 367

***N*-(3,4-Difluoro-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.10 (s, 3H), 3.29 (s, 3H), 4.77 (s, 2H), 7.12-7.17 (m, 1H), 7.31-7.44 (m, 4H), 7.67-7.73 (m,1H), 7.87-7.92 (m, 1H); MS: *m/z* 368.0 (MH^+).

Compound 368

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.08 (s, 3H), 3.31 (s, 3H), 4.88 (s, 2H), 7.37-7.49 (m, 3H), 7.65-7.73 (m, 3H), 7.87-7.91 (m, 1H); MS: *m/z* 417.9 (MH^+).

Compound 369

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-methanesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.04 (s, 3H), 3.29 (s, 3H), 4.81 (s, 2H), 7.29 (d, 2H), 7.35-7.42 (m, 4H), 7.65-7.71 (m, 1H), 7.87-7.92 (m, 1H); MS: *m/z* 416.0 (MH^+).

Compound 379

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3-carbomethoxy-benzyl)-pyridin-3-ylsulfonamide.** MS: *m/z* 438.9 (MH^+).

Compound 380

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-carbomethoxy-benzyl)-pyridin-3-ylsulfonamide.** MS: *m/z* 438.9 (MH^+).

Compound 383

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-pyridin-3-ylsulfonamide.** MS: *m/z* 401.1 (MH^+).

Compound 384

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-2-oxo-2,3-dihydro-benzooxazol-6-yl-sulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.64 (d, 3H), 2.21-2.31 (m, 3H), 2.38 (m, 3H), 7.30 (d, 1H), 7.39-7.51 (m, 2H), 7.55 (dd, 1H), 7.71 (d, 1H), 7.80 (dd, 1H), 7.84-7.93 (m, 1H), 7.95 (s, 1H), 12.3 (s, 1H); MS: *m/z* 470.9 (MH^+).

Compound 405

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3-carbomethoxy-benzyl)-pyridin-3-ylsulfonamide.** MS: *m/z* 518.8 (MH^+).

Compound 406

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-carbomethoxy-benzyl)-pyridin-3-ylsulfonamide.** MS: *m/z* 518.8 (MH^+).

Compound 407

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-pyridin-3-yl-sulfonamide.** MS: *m/z* 480.8 (MH^+).

Compound 408

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-3-pyridin-3-yl-sulfonamide.** MS: *m/z* 434.9 (MH^+).

Compound 546

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-cyano-benzenesulfonamide.** MS: *m/z* 505.0 (MH^+).

Compound 547

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-isopropyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.78 (d, 3H), 1.41 (d, 3H), 3.30 (q, 1H), 4.14 (d, 1H), 5.20 (d, 1H), 7.04 (t, 1H), 7.27-7.34 (m, 2H), 7.37-7.45 (m, 1H), 7.52-7.60 (m, 3H), 7.62-7.72 (m, 2H), 7.84-7.91 (m, 3H); MS: *m/z* 508.0 (MH^+).

Compound 669

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2,2,2-trifluoro-ethanesulfonamide.** MS: *m/z* 486.0 (MH^+).

Compound 697

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2,2,2-trifluoro-ethanesulfonamide.** MS: *m/z* 472.0 (MH^+).

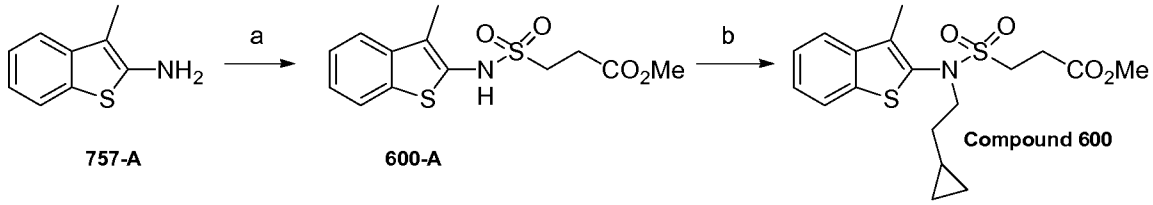
Compound 700

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinoline sulfonamide.** MS: *m/z* 631.1 (MH^+).

Compound 760

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-2-carbomethoxy-ethanesulfonamide.** MS: *m/z* 488.1 (MH^+).

Example 30



757-A 600-A

a) DCM, pyridine, $ClSO_2CH_2CH_2CO_2Me$; b) PPh_3, DEAD, $HOCH_2CH_2$-*c*-Pr, THF.

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-2-carbomethoxy-ethanesulfonamide (600-A).** A solution of compound **757-A** (1.0 g, 5.01 mmol) and pyridine (851 µL, 10.5 mmol) in dichloromethane (20 mL), cooled to 10 °C was treated with 3-chlorosulfonyl-propionic acid methyl ester (716 µL, 5.25 mmol) and stirred at ambient temperature for 18 h. The solvent was evaporated in vacuo, and the crude residue purified by flash column chromatography (SiO_2), eluting with an ethyl acetate (10-50%) in heptane gradient to afford 1.1 g of compound **600-A** as an off white solid. ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 3H), 2.82 (t, 2H), 3.43 (t, 2H), 3.62 (s, 3H), 7.24-7.50 (m, 2H), 7.58-7.77 (m, 1H), 7.80-7.95 (m, 1H), 10.17 (s, 1H); MS: *m/z* 314.1 (MH^+).

Compound 600

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-carbomethoxy-ethanesulfonamide.** A solution of triphenylphosphine (0.251 g, 0.957 mmol) in THF (3 mL) was treated with DEAD (40% in toluene, 425 µL, 0.957 mmol) and stirred at ambient temperature for 5 min. Compound **600-A** (0.20 g, 0.638 mmol) was added to the solution and stirred for 5 min. 2-Cyclopropyethanol (77 mL, 0.830 mmol) was added to the solution and the reaction mixture was stirred at ambient temperature for 18 h. The solvent was evaporated in vacuo, and the crude residue purified by flash column chromatography (SiO_2), eluting with an ethyl acetate (10-40%) in heptane gradient to afford 223 mg of compound **600** as a colorless oil. ^{1}H-NMR ($CDCl_3$): δ -0.02-0.06 (m, 2H), 0.35-0.52 (m, 2H), 0.56-0.80 (m, 1H), 1.49 (q, 2H), 2.40 (s, 3H), 2.81-2.97 (m, 2H), 3.41-3.57 (m, 2H), 3.64 - 3.84 (s superimposed on m, 5H), 7.33-7.49 (m, 2H), 7.59-7.80 (m, 2H); MS: *m/z* 382.4 (MH^+).

Following the procedure described above for example 30 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 308

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-acetyl-benzenesulfonamide.** MS: *m/z* 508.0 (MH^+).

Compound 351

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-acetyl-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.52-1.73 (m, 2H), 2.24 (s, 3H), 2.29-2.46 (m, 2H), 2.67 (s, 3H), 3.49-3.67 (m, 2H), 7.36-7.48 (m, 2H), 7.76-7.94 (m, 5H), 8.16-8.19 (m, 2H); MS: *m/z* 456.0 (MH^+).

Compound 352

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-acetyl-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.95 (s, 3H), 3.33 (s, 3H), 4.88 (s, 2H), 7.25-7.49 (m, 3H), 7.62-7.71 (m, 3H), 7.81-7.87 (m, 1H), 8.01-8.04 (d, 2H), 8.19-8.22 (d, 2H); MS: *m/z* 522.0 (MH^+).

Compound 353

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-(2-methyl-pyrimidin-4-yl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.97 (s,

3H), 2.66 (s, 3H), 4.91 (s, 2H), 7.36-7.48 (m, 3H), 7.66-7.76 (m, 3H), 7.80-7.89 (m, 2H), 8.02-8.04 (d, 2H), 8.57-8.62 (m, 2H), 8.82-8.84 (d, 1H); MS: *m/z* 572.0 (MH^+).

Compound 354

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-3-(2-methyl-pyrimidin-4-yl)-benzenesulfonamide**. MS: *m/z* 506.0 (MH^+).

Compound 355

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-8-methoxy-quinolin-5-ylsulfamide**. ^{1}H-NMR (DMSO-d_6): δ 1.76 (s, 3H), 4.07 (s, 3H), 4.91 (s, 2H), 7.19-7.45 (m, 4H), 7.52-7.63 (m, 4H), 7.59-7.81 (m, 1H), 8.23-8.26 (d, 2H), 8.81-8.84 (dd, 1H), 8.96-8.98 (m, 1H); MS: m/z 561.0 (MH^+).

Compound 356

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-8-methoxyquinolin-5-ylsulfonamide**. MS: m/z 495.0 (MH^+).

Compound 370

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-cyano-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 5.05 (s, 2H), 7.22 (s, 1H), 7.31-7.37 (m, 2H), 7.46-7.52 (m, 4H), 7.69-7.74 (m, 3H), 7.82-7.92 (m, 2H), 8.04-8.07 (m, 1H), 8.26-8.29 (m, 1H), 8.43-8.44 (m, 1H).

Compound 372

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-(pyridin-4-yloxy)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.53-1.73 (m, 2H), 2.26 (s, 3H), 2.33-2.46 (m, 2H), 4.08 (m, 2H), 7.35-7.37 (m, 2H), 7.40-7.48 (m, 2H), 7.50-7.54 (m, 2H), 7.79-7.82 (m, 1H), 7.84-7.94 (m, 3H), 8.73-8.75 (d, 2H); MS: *m/z* 507.0 (MH^+).

Compound 373

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-(pyridin-3-yloxy)-benzenesulfonamide**. MS: *m/z* 507.0 (MH^+).

Compound 411

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-cyano-benzenesulfonamide**. MS: m/z 490.9 (MH^+).

Compound 548

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-isopropyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ -0.11-0.07 (m, 2H), 0.38-0.44 (m, 2H), 0.65 (m, 1H), 1.06-1.26 (m, 1H), 1.41 (d, 3H), 1.50 (d, 3H), 1.55-1.68 (m, 1H), 3.12-

3.32 (m, 1H), 3.54-3.74 (m, 1H), 3.85-4.07 (m, 1H), 7.28-7.38 (m, 2H), 7.48-7.56 (m, 2H), 7.60-7.69 (m, 2H), 7.83 (d, 2H), 8.00 (dd, 1H); MS: *m/z* 400.0 (MH^+).

Compound 549

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-cyano-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ -0.07-0.08 (m, 2H), 0.44 (d, 2H), 0.54-0.77 (m, 1H), 1.32-1.52 (m, 2H), 2.38 (s, 3H), 3.37-3.87 (m, 2H), 7.40 (ddd, 2H), 7.59-7.78 (m, 3H), 7.91 (d, 1H), 7.99 (d, 1H), 8.10 (s, 1H); MS: *m/z* 397.0 (MH^+).

Compound 550

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-3-cyano-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.27 - 2.65 (m, 2H) superimposed on 2.38 (s, 3H), 3.61-4.03 (m, 2H), 7.36-7.51 (m, 2H), 7.62-7.80 (m, 3H), 7.94 (d, 1H), 8.00 (d, 1H), 8.08 (s, 1H); MS: *m/z* 425.1 (MH^+).

Compound 551

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-3-cyano-benzenesulfonamide**. MS: *m/z* 439.0 (MH^+).

Compound 552

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-3-cyano-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.52-1.74 (m, 4H), 1.93-2.20 (m, 2H), 2.39 (s, 3H), 3.23-3.91 (m, 2H), 7.33-7.50 (m, 2H), 7.60-7.79 (m, 3H), 7.91 (d, 1H), 7.97 (d, 1H), 8.07 (s, 1H); MS: *m/z* 453.0 (MH^+).

Compound 573

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-3-cyano-benzenesulfonamide.** MS: *m/z* 410.7 (MH^+).

Compound 574

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-3-cyano-benzenesulfonamide.** MS: *m/z* 424.6 (MH^+).

Compound 575

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-3-cyano-benzenesulfonamide.** MS: *m/z* 382.8 (MH^+).

Compound 601

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-2-carbomethoxy-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.36-2.57 ((m, 2H)

superimposed on 2.42 (s, 3H), 2.81-2.96 (m, 2H), 3.42-3.59 (m, 2H), 3.75 (s, 3H), 3.81-4.00 (m, 2H), 7.43 (q, 2H), 7.68-7.82 (m, 2H); MS: *m/z* 382.4 (MH^+).

Compound 602

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-2-carbomethoxy-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.73-1.90 (m, 2H), 2.10-2.33 (m, 2H), 2.42 (s, 3H), 2.77-2.94 (m, 2H), 3.37-3.57 (m, 2H), 3.65-3.84 (s superimposed on m, 5H), 7.32-7.50 (m, 2H), 7.62-7.84 (m, 2H); MS: *m/z* 424.2 (MH^+).

Compound 603

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-2-carbomethoxy-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.65 (m, 4H), 1.94-2.20 (m, 2H), 2.41 (s, 3H), 2.76-2.99 (m, 2H), 3.36-3.56 (m, 2H), 3.69 (br s, 2H), 3.74 (s, 3H), 7.32-7.50 (m, 2H), 7.63-7.82 (m, 2H); MS: *m/z* 438.3 (MH^+).

Compound 614

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ -0.12-0.06 (m, 2H), 0.31-0.47 (m, 2H), 0.53-0.73 (m, 1H), 1.30-1.51 (m, 2H), 2.36 (s, 3H), 3.35-3.86 (m, 2H), 7.30-7.43 (m, 2H), 7.47-7.55 (m, 2H), 7.59-7.72 (m, 3H), 7.79 (d, 2H); MS: *m/z* 372.1 (MH^+).

Compound 615

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.34 (s, 3H), 2.35-2.50 (m, 2H), 3.53-4.03 (m, 2H), 7.35-7.46 (m, 2H), 7.49-7.57 (m, 2H), 7.62-7.75 (m, 3H), 7.77 (d, 1H), 7.80 (s, 1H); MS: *m/z* 400.0 (MH^+).

Compound 616

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.70-1.84 (m, 2H), 2.14-2.35 (m, 2H), 2.36 (s, 3H), 3.40-3.78 (m, 2H), 7.32-7.45 (m, 2H), 7.47-7.56 (m, 2H), 7.60-7.74 (m, 3H), 7.77 (d, 2H); MS: *m/z* 414.0 (MH^+).

Compound 617

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.51-1.74 (m, 4H), 1.93-2.18 (m, 2H), 2.36 (s, 3H), 3.41-3.69 (m., 2H), 7.32-7.44 (m, 2H), 7.47-7.55 (m, 2H), 7.60-7.73 (m, 3H), 7.74-7.80 (m, 2H); MS: *m/z* 428.1 (MH^+).

Compound 670

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2,2,2-trifluoro-ethanesulfonamide.** MS: *m/z* 378.0 (MH^+).

Compound 671

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-2,2,2-trifluoro-ethanesulfonamide.** MS: *m/z* 406.0 (MH^+).

Compound 672

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-2,2,2-trifluoro-ethanesulfonamide.** MS: *m/z* 420.0 (MH^+).

Compound 673

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-2,2,2-trifluoro-ethanesulfonamide.** MS: *m/z* 434.1 (MH^+).

Compound 721

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-quinoxalin-5-yl-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.60-1.65 (m, 2H), 2.17 (s, 3H), 2.22-2.33 (m, 2H), 3.96-4.07 (m, 2H), 7.31-7.39 (m, 2H), 7.69-7.72 (m, 2H), 7.88-7.92 (m, 1H), 8.26-8.28 (m, 1H), 8.42-8.44 (m, 1H), 9.20-9.25 (m, 2H); MS: *m/z* 480.0 (MH^+).

Compound 723

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-quinoxalin-5-yl-sulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.75 (s, 3H), 5.31 (s, 2H), 7.28-7.34 (m, 2H), 7.46-7.51 (m, 1H), 7.58-7.61 (m, 1H), 7.66-7.71 (m, 3H), 7.91-7.95 (m, 1H), 8.31-8.33 (m, 1H), 8.47-8.49 (m, 1H), 9.26-9.32 (m, 2H); MS: *m/z* 532.0 (MH^+).

Compound 761

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-carbomethoxy-methanesulfonamide.** MS: *m/z* 474.0 (MH^+).

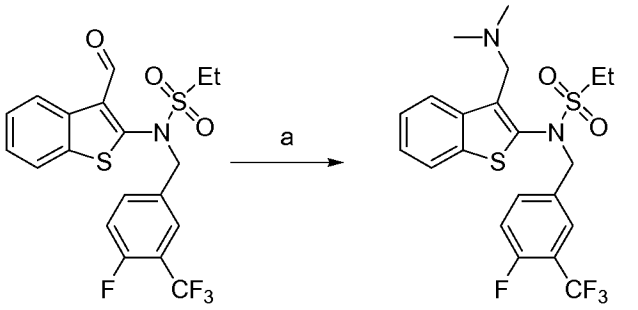
Compound 791

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-carbomethoxy-methanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.96 (s, 3H), 3.91 (s, 3H), 4.25 (s, 2H), 4.95 (br s, 2H), 7.08 (t, 1H), 7.33-7.49 (m, 3H), 7.49-7.66 (m, 2H), 7.71-7.85 (m, 1H); MS: *m/z* 476.1 (MH^+).

Compound 794

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-2-carbomethoxy-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.96 (s, 3H), 2.85-2.97 (m, 2H), 3.48-3.61 (m, 2H), 3.75 (s, 3H), 4.78 (br s, 2H), 7.11 (d, 2H), 7.28-7.42 (m, 4H), 7.55-7.62 (m, 1H), 7.70-7.77 (m, 1H); MS: *m/z* 488.1 (MH^+).

Example 31



Compound 210 **Compound 346**

a) $(Me)_2NH$, $Na(OAc)_3BH$, DCM.

Compound 346

***N*-(3-Dimethylaminomethyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-ethanesulfonamide.** To a solution of compound **210** (0.116 g, 0.26 mmol) in dichloromethane (4 mL) was added dimethylamine (2 M in THF, 195 µL, 0.39 mmol) and the reaction mixture stirred at ambient temperature for 15 min. Sodium triacetoxyborohydride (0.11g, 0.52 mmol) was added to the reaction mixture and stirred at ambient temperature for 6 h. The solution was treated with saturated aqueous sodium bicarbonate, the organic layer separated, dried over Na_2SO_4, filtered, and the solvent evaporated in vacuo. The crude residue was purified by reverse phase prep HPLC (eluting with an 20-90% acetonitrile in water with 0.1% TFA gradient) to afford the 90 mg of compound **346** as the TFA salt (90 mg, 59%). MS: *m/z* 475.2 (MH^+).

Following the procedure described above for example 31 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 347

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methylaminomethyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** MS: *m/z* 461.2 (MH^+).

Compound 348

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-propylaminomethyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** MS: *m/z* 489.3 (MH^+).

Compound 349

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-pyrrolidin-1-yl-methyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** MS: *m/z* 501.2 (MH^+).

Compound 381

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-pyrrolidin-1-yl-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** MS: *m/z* 549.3 (MH^+).

Compound 417

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methylaminomethyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** MS: *m/z* 509.1 (MH^+).

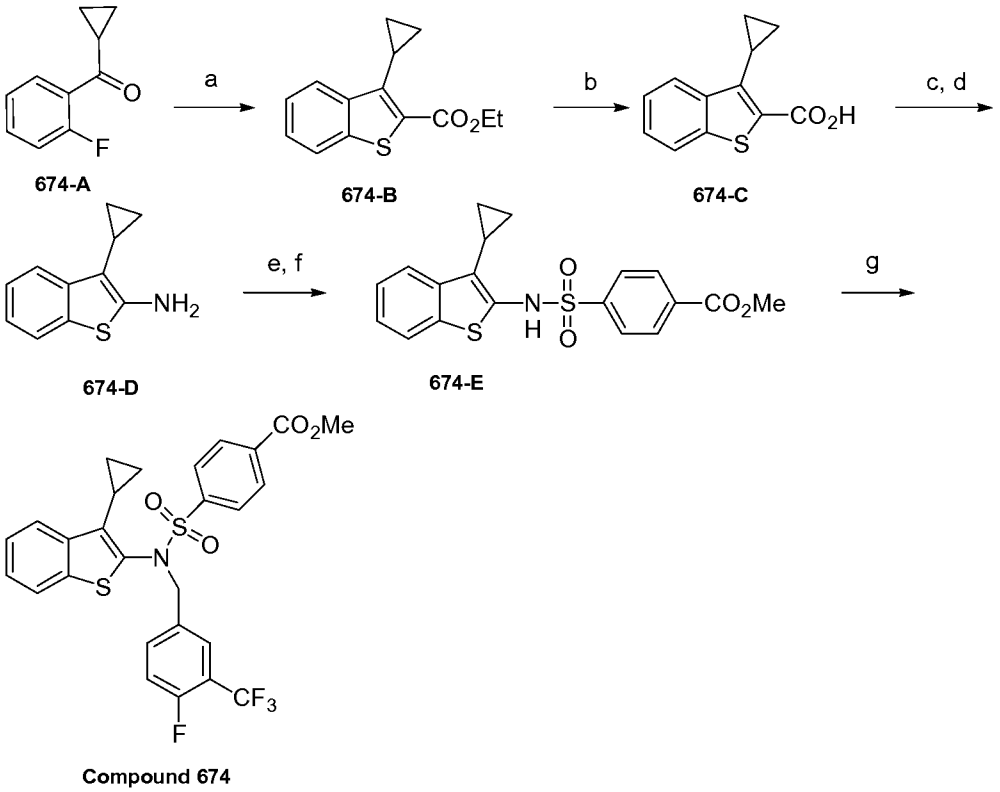
Compound 418

***N*-(3-Dimethylaminomethyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** MS: *m/z* 523.2 (MH^+).

Compound 420

***N*-(3-Dimethylaminomethyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 461.27 (MH^+).

Example 32



a) NaH, ethylthioglycolate, THF; b) 3N NaOH, MeOH; c) DPPA, DiEA, t-BuOH; d) HCl/dioxane; e) 4-chlorosulfonylbenzoic acid, pyridine, DCM; f) MeOH, H_2SO_4; g) *t*-BuOK, 4-fluoro-3-trifluoromethylbenzyl bromide, DMF.

3-Cyclopropyl-benzo[*b*]thiophene-2-carboxylic acid ethyl ester (674-B). To a suspension of 60% NaH (0.26 g; 7.74 mmol) in THF (10 mL), at ambient temperature, was added ethyl thioglycolate (0.86 g; 7.14 mmol) drop-wise, and the reaction was stirred at ambient temperature for 30 min. Compound **674-A** (0.98 g; 5.96 mmol) was added in one-portion. The reaction was allowed to reflux for 18 h, cooled, diluted with EtOAc, washed sequentially with 1N NaOH, H_2O, and brine, dried over Na_2SO_4, filtered, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2), eluting with a heptane-EtOAc gradient to afford 0.484 g of compound **674-B** as an oil. ^{1}H-NMR (DMSO-d_6): δ 1.08-1.16 (m, 4H), 1.32-1.36 (t, 3H), 2.36-2.51 (m, 1H), 4.31-4.37 (q, 2H), 7.32-7.54 (m, 2H), 7.64-7.75 (m, 1H), 7.99-8.05 (m, 1H); MS: m/z 247.1 (MH^+).

3-Cyclopropyl-benzo[*b*]thiophene-2-carboxylic acid (674-C). A solution of compound **674-B** (2.68 g, 10.9 mmol) in ethanol (30 mL) was treated with 3N aqueous

sodium hydroxide (5.4 mL, 16.2 mmol) and refluxed for 2 h. The solution was cooled, and the solvent was evaporated in vacuo. The residue was dissolved in water and washed with dichloromethane. The aqueous phase was acidified with concentrated hydrochloric acid, and the product was extracted into ethyl acetate, washed with brine, dried over Na_2SO_4, filtered and the solvent was evaporated in vacuo, to afford 1.9 g of compound **674-C** as a colorless solid. ^{1}H-NMR (DMSO-d_6): δ 0.58-1.37 (m, 4H), 2.44-2.47 (m, 1H), 7.13-7.61 (m, 2H), 7.98 (dd, 2H), 13.33 (br s, 1H).

2-Amino-3-cyclopropyl-benzo[*b*]thiophene (674-D). A solution of compound **647-C** (6.9 g, 31.6 mmol) and diisopropylethylamine (6.63 mL, 37.9 mmol) in t-butanol (100 mL) was treated with DPPA (8.2 mL, 37.9 mmol) and refluxed for 4 h. The solvent was evaporated in vacuo, and the crude residue was purified by flash column chromatography (SiO_2) eluting an ethyl acetate (0-15%) in heptane gradient, to afford 7.1 g of the BOC-protected amine (MS: *m/z* 290.1 (MH^+)). The BOC-protected amine was dissolved in a solution of 4N HCl in dioxane (100 mL) and stirred at ambient temperature for 4 h. The solid precipitate was collected by filtration, washed with diethyl ether and dried under vacuo to afford 2.36 g of the hydrochloride salt of compound **674-D** as a colorless solid. The combined solvents were evaporated in vacuo to afford 3.1 g of additional **674-D** as a yellow solid. MS: *m/z* 190.1 (MH^+).

***N*-(3-Cyclopropyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide (674-E).** A solution of compound **674-D** (0.60 g, 2.07 mmol) and pyridine (343 μL, 4.25 mmol) in dichloromethane, cooled to -10 °C was treated with 4-chlorosulfonylbenzoic acid (0.480 g, 2.17 mmol) and stirred at ambient temperature for 2 days. The solution was cooled to -10 °C and treated with additional portions of pyridine (120 μL) and 4-chlorosulfonylbenzoic acid (0.16 g) and stirred at ambient temperature for 18 h. The reaction mixture was partitioned between 2N HCl and ethyl acetate, the organic layer washed with brine, dried over sodium sulfate, filtered, and the solvent evaporated under reduced pressure to afford 0.95 g of the crude acid. The crude acid was suspended in methanol (25 mL), treated with sulfuric acid (0.1 mL) and refluxed for 6 h. The yellow solid was filtered, the solution concentrated in vacuo, diluted with water, extracted with ethyl acetate, the organic layer washed with brine, dried over sodium sulfate, filtered and the solvent evaporated under reduced pressure. The crude material was purified by flash column chromatography (SiO_2),

eluting with an ethyl acetate (10-50%) gradient to afford 0.483 g of compound **674-E** as a yellow oil. MS: *m/z* 388.0 (MH^+).

Compound 674

***N*-(3-Cyclopropyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** To a solution of compound **674-E** (0.176 g, 0.454 mmol) in DMF (3 mL), cooled to 0 °C was added a solution of potassium t-butoxide (1.0 M in THF, 454 μL, 0.454 mmol) and the reaction mixture was stirred for 15 min. 4-Fluoro-3-trifluorobenzyl bromide (131 μL, 0.681 mmol) was added and the solution was stirred at ambient temperature for 18 h. The solution was diluted with water (20 mL), extracted with ethyl acetate, and the organic layer was washed with brine, dried over sodium sulfate, filtered, and the solvent evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an ethyl acetate-heptane (10-50%) gradient to afford 0.187 g of compound **674** as an oil. ^{1}H-NMR ($CDCl_3$): δ 0.65-0.99 (m, 4H), 1.42-1.67 (m, 1H), 3.99 (s, 3H), 4.16-5.33 (m, 2H), 7.05 (t, 1H), 7.30-7.46 (m, 3H), 7.55 (dd, 1H), 7.59-7.70 (m, 1H), 7.70-7.84 (m, 1H), 7.92 (d, 2H), 8.20 (d, 2H); MS: *m/z* 564.2 (MH^+).

Following the procedure described above for example 32 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 325

***N*-(3-Trifluoromethyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-benzenesulfonamide.** Compound **325** was prepared substituting 2-fluoro-2,2,2,-trifluoroacetopheneone for cyclopropyl-(2-fluoro-phenyl)-methanone, triethylamine for NaH and acetonitrile for THF in Step A of Example 32. ^{1}H-NMR ($CDCl_3$): δ 4.57 (br s, 1H), 4.89 (br s, 1H), 7.08 (d, 2H), 7.18-7.35 (m, 2H), 7.37-7.49 (m, 2H), 7.49-7.62 (m, 2H), 7.62-7.75 (m, 2H), 7.83 (d, 3H); MS: *m/z* 531.9 (MH^+).

Compound 501

***N*-(3-Cyclopentyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 564.2 (MH^+).

Compound 696

***N*-(3-Cyclobutyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.91 (m, 3H), 2.17-2.60 (m, 3H), 3.66-3.89 (m, 1H), 3.99 (s, 3H), 4.11-4.34 (m, 1H), 5.07-5.27 (m,

1H), 6.99-7.15 (m, 1H), 7.37 (dd, 3H), 7.49-7.59 (m, 1H), 7.61-7.71 (m, 1H), 7.88 (d, 2H), 7.99-8.10 (m, 1H), 8.19 (d, 2H); MS: *m/z* 578.1 (MH^+).

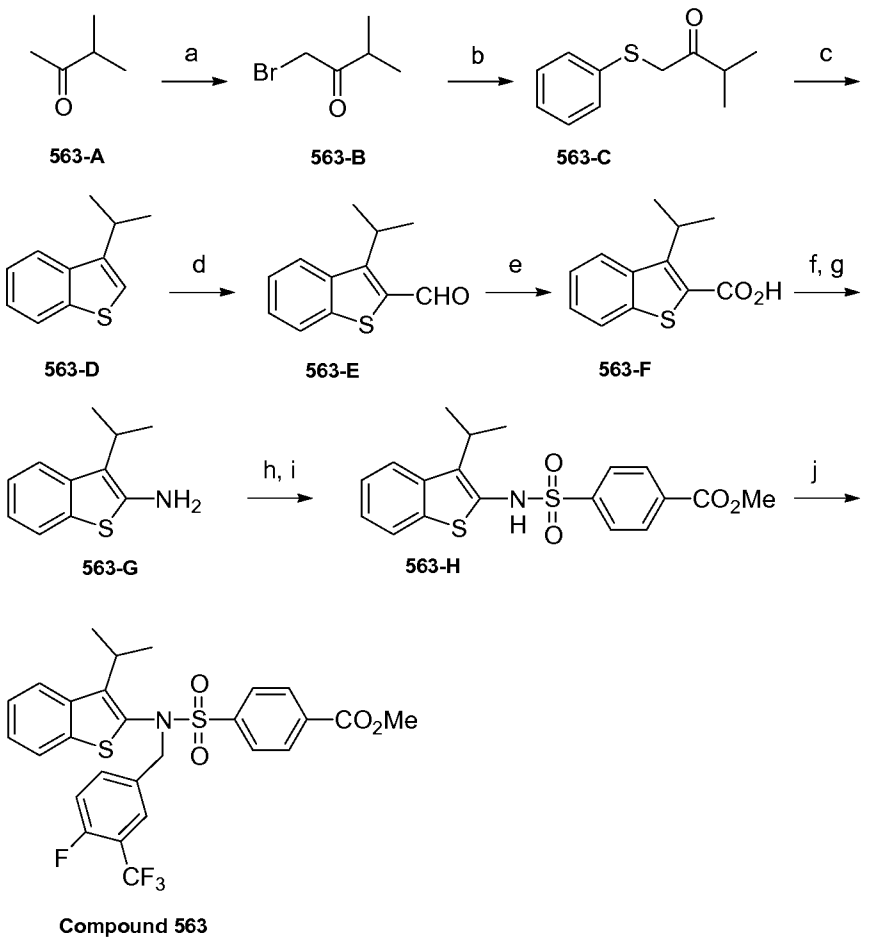
Compound 753

***N*-(3-Cyclopropyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.44-0.79 (m, 4H), 1.22-1.63 (m, 1H), 3.99 (s, 3H), 4.30-5.15 (m, 2H), 7.08 (d, 2H), 7.25-7.37 (m, 4H), 7.60-7.68 (m, 1H), 7.74-7.83 (m, 1H), 7.91 (d, 2H), 8.15-8.25 (m, 2H); MS: *m/z* 562.0 (MH^+).

Compound 754

***N*-(3-Cyclobutyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.59-2.11 (m, 4H), 2.13-2.49 (m, 3H), 3.99 (s, 3H), 4.16 (d, 1H), 5.17 (d, 1H), 7.09 (d, 2H), 7.23-7.43 (m, 4H), 7.60-7.71 (m, 1H), 7.89 (d, 2H), 7.97-8.07 (m, 1H), 8.14 - 8.26 (m, 2H); MS: *m/z* 576.2 (MH^+).

Example 33



Compound 563

a) Br_2, MeOH; b) thiophenol, pyridine, Et_2O; c) PPA, PhCl; d) *n*-BuLi, THF, DMF; e) $KMnO_4$, acetone, H_2O; f) DPPA, DiEA, *t*-BuOH; g) 4 N HCl in dioxane; h) 4-chlorosulfonyl-benzoic acid, pyridine, DCM; i) MeOH, H_2SO_4; j) *t*-BuOK, 4-fluoro-3-trifluorobenzyl bromide, DMF.

1-Bromo-3-methyl-butan-2-one (563-B). To a solution of compound **563-A** (6.0 g; 69.7 mmol) dissolved in MeOH (40 mL) and cooled to 0 °C, was added bromine (3.56 mL; 69.7 mmol), at a rate such that the internal temperature did not exceed 10 °C. The reaction was allowed to stir for 45 min at 5-10 °C, to which was then added H_2O (20 mL) and the reaction was stirred for an additional 18 h at ambient temperature. Water was added to the reaction mixture, which was then extracted with diethyl ether. The combined ether extracts were washed sequentially with 10% aq. $NaHCO_3$, H_2O, and brine, dried over Na_2SO_4, filtered, and the filtrate was evaporated under reduced

pressure to afford compound **563-B** as an oil. ^{1}H-NMR ($CDCl_3$): δ 1.10-1.17 (d, 6H), 2.95-3.02 (m, 1H), 3.98 (s, 2H).

3-Methyl-1-phenylsulfanyl-butan-2-one (563-C). To a solution of thiophenol (4.44 mL; 43.4 mmol) in diethyl ether (29 mL) was added pyridine (17.2 mL; 0.21 mol), followed by the drop-wise addition of a solution of compound **563-B** (7.18 g; 43.5 mmol) in diethyl ether (15 mL), at ambient temperature, and the reaction was stirred for 72 h. The reaction was diluted with EtOAc, washed with 2N HCl, H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford compound **563-C** as an oil. ^{1}H-NMR ($CDCl_3$): δ 1.09-1.10 (d, 6H), 2.90-2.97 (m, 1H), 3.75 (s, 2H), 7.18-7.35 (m, 5H).

3-Isopropyl-benzo[*b*]thiophene (563-D). To a hot solution (136 °C) of PPA (8.2 g) in chlorobenzene (50 mL) is added a solution of compound **563-C** (4.34 g; 22.4 mmol) in chlorobenzene (35 mL). The reaction was stirred at 136 °C for 18 h, cooled to ambient temperature, diluted with EtOAc, quenched with H_2O, and the EtOAc layer was washed with H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2), eluting with a heptane-EtOAc gradient to afford compound **563-D** as an oil. ^{1}H-NMR (DMSO-d_6): δ 1.31-1.33 (d, 6H), 3.26-3.31 (m, 1H), 7.33-7.43 (m, 2H), 7.83-7.85 (m, 1H), 7.95-7.97 (m, 1H); MS: *m/z* 328.0 (MH^+).

3-Isopropyl-benzo[*b*]thiophene-2-carboxaldehyde (563-E). To a solution of compound **563-D** (3.8 g, 21.5 mmol) in THF (70 mL), cooled to -70 to -78 °C was added a solution of *n*-butyl lithium (2.5 M in hexanes, 8.6 mL, 21.5 mmol), drop-wise. The reaction mixture was allowed to warm slowly to -20 °C , then re-cooled to -73 °C. DMF (2.5 mL) was added drop-wise to the solution at -70 to -78 °C. The reaction mixture was allowed to warm ambient temperature and stirred for 18 h. The reaction mixture was cooled on an ice bath, and quenched with several ice chips. The reaction mixture was treated with saturated aqueous NH_4Cl, extracted with ethyl acetate, and the organic phase washed with brine, dried over Na_2SO_4, filtered, and the solvent was evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate (0-10%) in heptane gradient, to afford 2.06 g of

compound **563-E** as a yellow oil. ^{1}H-NMR ($CDCl_3$): δ 1.60 (d, 6H), 3.99 (q, 1H), 7.33-7.61 (m, 2H), 7.87 (d, 1H), 8.05 (d, 1H), 10.44 (s, 1H); MS: *m/z* 205.1 (MH^+).

3-Isopropyl-benzo[*b*]thiophene-2-carboxylic acid (563-F). A solution of compound **563-E** (1.95 g, 9.5 mmol) in acetone (30 mL) was refluxed for 30 min. A mixture of potassium permanganate (3.02 g, 19.1 mmol) in water (10 mL) was added in portions, and the resultant mixture was refluxed for an additional 30 min. The mixture was cooled to ambient temperature and concentrated in vacuo. A solution of aqueous Na_2SO_3 (1M, 50 mL) was added followed by sulfuric acid (1 M, 50 mL). Two additional portions of Na_2SO_3 (1M, 20 mL) were added followed by sulfuric acid (1 M, 20 mL), which resulted in the disappearance of the dark brown color. The resultant suspension was diluted with H_2O, filtered, washed with H_2O and dried under vacuo to afford 1.52 g of compound **563-F** as a yellow solid. MS: *m/z* 221.1 (MH^+).

2-Amino-3-isopropyl-benzo[*b*]thiophene, hydrochloride (563-G). A solution of compound **563-F** (1.52 g, 6.90mmol) and DIEA (1.45 mL, 8.27 mmol) in t-butanol (30 mL) was treated with DPPA (1.8 mL, 8.27 mmol) and refluxed for 6 h. The reaction mixture was cooled and the solvent evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (0-20%) in heptane gradient, to afford 1.41 g of the BOC-protected amine (not shown). ^{1}H-NMR ($CDCl_3$): δ 1.41 (d, 6H), 1.55 (s, 9H), 3.26 (dt, 1H), 6.74 (br s, 1H), 7.12-7.39 (m, 2H), 7.57-7.86 (m, 2H); MS: *m/z* 292.2 (MH^+). The BOC-protected amine (1.41 g, 4.84 mmol) was dissolved in 4N HCl in dioxane (20 mL) and stirred at ambient temperature for 6 h. The suspension was diluted with diethyl ether, the solid filtered, washed with diethyl ether, and dried under vacuo to afford 1.09 g of the hydrochloride salt of compound **563-G** as a pale yellow solid. ^{1}H-NMR (DMSO-d_6): δ 1.35 (d, 6H), 3.33 (q, 1H), 7.03-7.20 (m, 1H), 7.27 (t, 1H), 7.73 (dd, 2H), 8.73 (br s, 1H); MS: *m/z* 192.0 (MH^+).

***N*-(3-Isopropyl-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** A solution of compound **563-G** (0.774 g, 3.40 mmol) and pyridine (577 μL, 7.14 mmol) in dichloromethane, cooled to -10 °C, was treated with chlorosulfonyl-benzoic acid (0.787 g, 3.56 mmol) and the reaction mixture was stirred at ambient temperature for 4 h. The solvent was evaporated in vacuo, the residue treated with 2N HCl, the aqueous phase extracted with ethyl acetate, the organic phase washed with brine, dried over Na_2SO_4, filtered, and the solvent evaporated in vacuo to afford 1.16 g of the crude

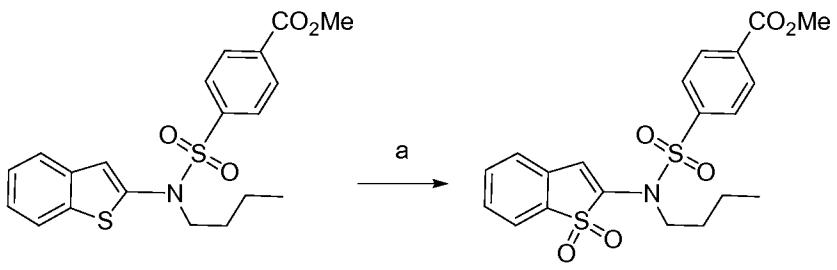
benzoic acid (not shown). ^{1}H-NMR (DMSO-d_6): δ 1.15 (d, 6H), 3.25 (dt, 1H), 7.25-7.37 (m, 2H), 7.67-7.99 (m, 4H), 8.13 (d, 2H), 10.66 (s, 1H); MS: *m/z* 192.0 (MH^+).

***N*-(3-Isopropyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide (563-H).** A solution of the crude benzoic acid (1.1 g, 2.93 mmol) and sulfuric acid (0.15 mL) in methanol (30 mL) was refluxed for 13 h. The solution cooled, concentrated in vacuo, and partitioned between dichloromethane and water. The organic layer was separated, and by flash column chromatography (SiO_2) eluting with an ethyl acetate (5-40%) in heptane gradient to afford 0.9 g of compound **563-H** as a pale pink solid. ^{1}H-NMR (DMSO-d_6): δ 1.16 (d, 6H), 3.26 (dt, 1H), 3.89 (s, 3H), 7.28-7.34 (m, 2H), 7.73-7.83 (m, 1H), 7.83-7.95 (m, 3H), 8.15 (d, 2H), 10.67 (s, 1H); MS: *m/z* 390.1 (MH^+).

Compound 563

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-isopropyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** A solution of compound **563-H** (0.30 g, 0.77 mmol) in DMF (6 mL), at 0 °C, was treated with a solution of potassium *t*-butoxide (1.0 M in THF, 0.81 mL, 0.81 mmol) and stirred for 10 min. 4-Fluoro-3-trifluoromethylbenzyl bromide (293 μL, 1.54 mmol) was added and the resultant solution was stirred at ambient temperature for 18 h. Water was added, the reaction mixture extracted with ethyl acetate, and the organic layer was washed with water (3X), brine, dried over Na_2SO_4, filtered, and the solvent was evaporated in vacuo. The product was purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (1-35%) in heptane gradient to afford 0.29 g of compound **563** as a colorless solid. ^{1}H-NMR ($CDCl_3$): δ 0.77 (d, 3H), 1.42 (d, 3H), 3.17-3.35 (m, 1H), 4.00 (s, 3H), 4.14 (d, 1H), 5.23 (d, 1H), 7.06 (t, 1H), 7.28-7.36 (m, 2H), 7.38-7.45 (m, 1H), 7.58 (dd, 1H), 7.65 (dd, 1H), 7.85-7.95 (m, 3H), 8.22 (d, 2H); MS: *m/z* 566.0 (MH^+).

Example 34



430-A Compound 430

a) *m*CPBA, $CHCl_3$.

***N*-(Butyl)-*N*-(benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** Compound **430-A** was prepared utilizing Compound **1-C**, Example 32, steps E and F, and Example 3, step A. MS: *m/z* 404.2 (MH^+).

Compound 430

***N*-(Butyl)-*N*-(1,1-dioxo-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** A solution of compound **430-A** (0.199 g, 0.493 mmol) in chloroform (10 mL) was treated with *meta*-chloroperbenzoic acid (77%, 0.243 g, 1.08 mmol), and the reaction mixture was stirred at ambient temperature for 18 h. The mixture was washed with saturated aqueous sodium bicarbonate, dried over sodium sulfate, filtered and the solvent evaporated in vacuo. The crude residue was purified flash column chromatography (SiO_2), eluting with an ethyl acetate (10-50%) in heptane gradient to afford 0.120 g of compound **430** as a colorless solid. ^{1}H-NMR $CDCl_3$): δ 0.94 (t, 3H), 1.35-1.48 (m, 2H), 1.71-1.82 (m, 2H), 3.81 (t, 2H), 3.93 (s, 3H), 7.24 (s, 1H), 7.36 (d, 1H), 7.44-7.50 (m, 1H), 7.54-7.90 (m, 2H), 7.94 (d, 2H), 8.14 (d, 2H); MS: *m/z* 436.2 (MH^+).

Following the procedure described above for example 34 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 421

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(1,1-dioxo-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** MS: m/z 498.1 (MH^+).

Compound 431

***N*-(3-Bromo-1,1-dioxo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl) -benzenesulfonamide.** The precursor, *N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide, was synthesized from *N*-(benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide as per Example 5, step A. ^{1}H-NMR ($CDCl_3$): δ 4.76 (br s, 2 H), 7.08 (t, 1H), 7.51-7.72 (m, 8 H), 7.76 (dd, 1 H), 8.10 (d, 2H); MS: *m/z* 576 & 578.1 (MH^+).

Compound 433

***N*-(3-Bromo-1,1-dioxo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carbomethoxy-benzenesulfonamide.** The precursor, *N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-

carbomethoxy-benzenesulfonamide, was synthesized from *N*-(benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carbomethoxy-benzenesulfonamide as per Example 5, step A. ^{1}H-NMR ($CDCl_3$): δ 0.89 (t, 3 H), 1.36 (m, 2H), 1.69 (q, 2H), 3.53-3.65 (m, 2H), 3.97 (s, 3H), 7.60-7.76 (m, 4H), 8.12-8.18 (m, 2H), 8.19-8.25 (m, 2H); MS: *m/z* 514 & 516.0 (MH^+).

Compound 460

***N*-(3-Acetyl-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** The precursor, *N*-(3-acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide, was synthesized from *N*-(benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carbomethoxy-benzenesulfonamide as per Example 14, step A. ^{1}H-NMR ($CDCl_3$): δ 2.27 (s, 3 H), 4.96 (s, 2 H), 7.19 (t, 1H), 7.48-7.74 (m, 7H), 7.79-7.89 (m, 1H), 7.89-8.00 (m, 3H); MS: *m/z* 540.2 (MH^+), 562.0 (MNa^+).

Compound 463

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-1,1-dioxo-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** The precursor, *N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl]-benzenesulfonamide, was synthesized from N-(3-acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide as per Example 19, step A. ^{1}H-NMR ($CDCl_3$): δ 1.46 (s, 3H), 1.78 (s, 3H), 3.52 (br s, 1H), 4.88 (d, 1H), 4.95 (d, 1H), 7.05 (t, 1H), 7.45-7.49 (m, 2H), 7.52-7.68 (m, 3H), 7.69-7.73 (m, 3H), 7.79 (dd, 1H), 7.92 (d, 2H); MS: m/z 538.0 $(M - OH)^+$, 578.1 (MNa^+).

Compound 464

***N*-(3,4-Difluoro-benzyl)-*N*-[3-(1-hydroxy-ethyl)-1,1-dioxo-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** The precursor, *N*-(3,4-difluorobenzyl)-*N*-[3-(1-hydroxy-1-ethyl)-benzo[*b*]thiophen-2-yl]benzenesulfonamide, was synthesized from *N*-(3-acetyl-benzo[*b*]thiophen-2-yl)-*N*-(3,4-difluorobenzyl)-benzenesulfonamide as per Example 18, step A. ^{1}H-NMR ($CDCl_3$): δ 1.04 (d, 3H), 4.58 (d, 1H), 4.87-4.93 (m, 2H), 7.08-7.18 (m, 1H), 7.41-7.45 (m, 1H), 7.53-7.72 (m, 7H), 7.95 (d, 1H), 8.04 (d, 2H); MS: m/z 474.1 $(M - OH)^+$, 514.0 (MNa^+).

Compound 577

***N*-(3-Bromo-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropylethyl) – benzenesulfonamide.** The precursor, *N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropylethyl)-benzenesulfonamide, was synthesized from *N*-(benzo[*b*]thiophen-2-

yl)-*N*-(2-cyclopropylethyl)-benzenesulfonamide as per Example 5, step A. ^{1}H-NMR ($CDCl_3$): δ -0.02-0.06 (m, 2H), 0.24-0.47 (m, 2H), 0.52-0.75 (m, 1H), 1.47-1.73 (m, 2H), 3.48-3.80 (m, 2H), 7.49-7.79 (m, 7H), 8.03-8.19 (m, 2H); MS: *m/z* 468 & 470.1 (MH^+).

Compound 618

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.02-0.09 (m, 2H), 0.27-0.49 (m, 2H), 0.51-0.74 (m, 1H), 1.45-1.75 (m, 2H), 2.38 (s, 3H), 3.66 (t, 2H), 7.42-7.71 (m, 7H), 7.97-8.30 (m, 2H); MS: *m/z* 404.1 (MH^+).

Comound 619

***N*-(3-Methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.39 (s, 3H), 2.44-2.70 (m, 2H), 3.86 (t, 2H), 7.47-7.62 (m, 4H), 7.62-7.72 (m, 3H), 8.05 (d, 2H); MS: *m/z* 432.0 (MH^+).

Compound 620

***N*-(3-Methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.77-2.03 (m, 2H), 2.04-2.31 (m, 2H), 2.40 (s, 3H), 3.67 (t, 2H), 7.49-7.61 (m, 4H), 7.61-7.69 (m, 3H), 8.01-8.05 (m, 2H); MS: *m/z* 446.1 (MH^+).

Compound 621

***N*-(3-Methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.36-1.68 (m, 2H), 1.70-1.84 (m, 2H), 1.91-2.20 (m, 2H), 2.39 (s, 3H), 3.60 (t, 2H), 7.47-7.60 (m, 4H), 7.60-7.69 (m, 3H), 8.01 - 8.07 (m, 2H); MS: *m/z* 460.0 (MH^+).

Compound 622

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** MS: *m/z* 512.0 (MH^+).

Compound 632

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 447.7 (MH^+).

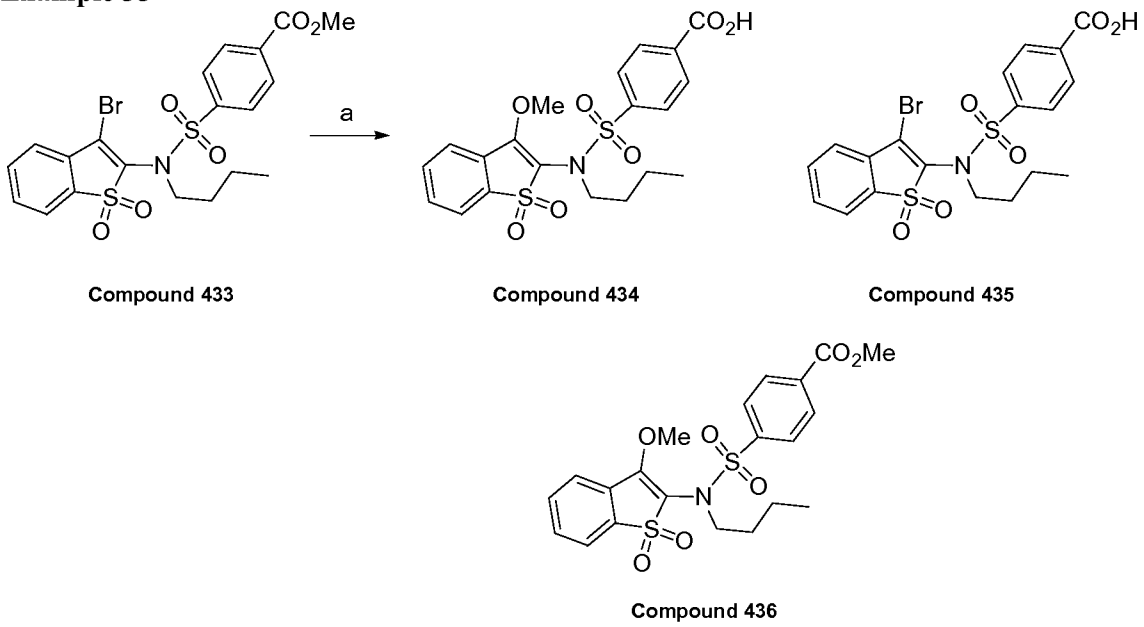
Compound 633

***N*-(3-Methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 503.7 (MH^+).

Compound 634

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-1,1-dioxo-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 555.6 (MH^+).

Example 35



Compound 433 Compound 434 Compound 435

Compound 436

a) 1N NaOH, MeOH.

Compounds 434, 435, 436

***N*-(Butyl)-*N*-(3-methoxy-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide, *N*-(butyl)-*N*-(3-bromo-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide, and *N*-(butyl)-*N*-(3-methoxy-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** A solution of compound **433** (0.525 g, 1.02 mmol) in methanol (10 mL) was treated with 1N sodium hydroxide (1.3 mL, 1.3 mmol) and refluxed for 30 minutes. The solution was cooled, neutralized with 1N hydrochloric acid the solvent evaporated in vacuo, and the crude residue purified by reverse phase pHPLC (C_{18}) using a gradient of acetonitrile (30-90%) in water (0.1% TFA), to afford 0.015 g of compound **434**, 0.050 g of compound **435**, and 0.15 g of compound **436**.

Compound 434

***N*-(Butyl)-*N*-(3-methoxy-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.94 (t, 3H), 1.33-1.43 (m, 2H), 1.78-1.86

(m, 2H), 3.70 (t, 2H), 4.47 (s, 3H), 7.58-7.70 (m, 4H), 8.17 (d, 2H), 8.30 (d, 2H); MS: m/z 452.1 (MH^+).

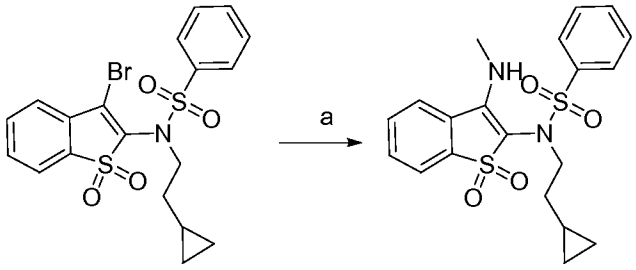
Compound 435

***N*-(Butyl)-*N*-(3-bromo-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.90 (t, 3H), 1.33-1.42 (m, 2H), 1.67-1.74 (m, 2H), 3.61 (t, 2H), 7.60-7.74 (m, 4H), 8.19 (d, 2H), 8.28 (d, 2H); MS: m/z 500 & 502.0 (MH^+).

Compound 436

***N*-(Butyl)-*N*-(3-methoxy-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.93 (t, 3H), 1.32-1.41 (m, 2H), 1.74-1.82 (m, 2H), 3.65 (t, 2H), 3.96 (s, 3H), 4.44 (s, 3H), 7.55-7.70 (m, 4H), 8.10 (d, 2H), 8.18 (d, 2H); MS: m/z 466.2 (MH^+).

Example 36



Compound 577 Compound 644

a) THF, $MeNH_2$.

Compound 644

***N*-(2-Cyclopropylethyl)-*N*-(3-methylamino-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** A solution of compound **577** (56 mg, 0.120 mmol) in THF (1 mL) was treated with a solution of methylamine in THF (2.0 M, 1 mL, 2.0 mmol) and stirred at ambient temperature for 1 h. The solvent was evaporated in vacuo and the crude residue purified by reverse phase pHPLC, eluting with an acetonitrile (20-90%) in water (0.1% TFA) gradient to afford 30 mg of compound **644** as a colorless solid. ^{1}H-NMR (DMSO-d_6): δ -0.01-0.03 (m, 2H), 0.19-0.47 (m, 2H), 0.47-0.77 (m, 1H), 1.20-1.47 (m, 1H), 1.66 (tt, 1H), 3.19 (d, 3H), 3.47 (td, 1H), 3.65 (td, 1H), 7.32-7.89 (m, 7H), 7.84-8.14 (m, 3H); MS: *m/z* 419.1 (MH^+).

Following the procedure described above for example 36 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 536

***N*-(Butyl)-*N*-(3-dimethylamino-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 465.1 (MH^+).

Compound 643

***N*-(2-Cyclopropylethyl)-*N*-(3-dimethylamino-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ -0.02-0.06 (m, 2H), 0.25-0.46 (m, 2H), 0.51-0.74 (m, 1H), 1.47-1.86 (m, 2H), 3.03-3.27 (s, 6H), 3.62 (td, 1H), 3.70-3.90 (m, 1H), 7.42-7.71 (m, 7H), 8.02 (d, 2H); MS: *m/z* 433.0 (MH^+).

Compound 645

***N*-(2-Cyclopropyl-ethyl)-*N*-[3-(4-methyl-piperazin-1-yl)-1,1-dioxo-1*H*-1λ^6-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** MS: *m/z* 488.1 (MH^+).

Compound 646

***N*-(3-Amino-1,1-dioxo-1*H*-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropylethyl) – benzenesulfonamide.** MS: *m/z* 405.1 (MH^+).

Compound 647

***N*-(2-Cyclopropyl-ethyl)-*N*-(1,1-dioxo-3-piperazin-1-yl-1*H*-1λ^6-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** MS: *m/z* 474.1 (MH^+).

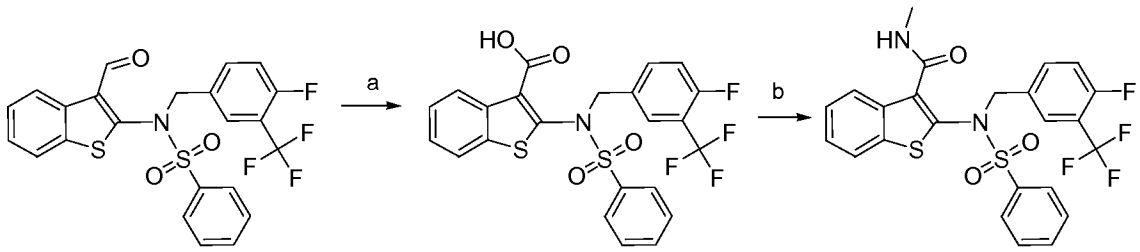
Compound 648

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methylamino-1,1-dioxo-1*H*-1λ^6-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** MS: *m/z* 527.1 (MH^+).

Compound 649

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(4-methyl-piperazin-1-yl)-1,1-dioxo-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** MS: *m/z* 596.1 (MH^+).

Example 37



Compound 207 458-A Compound 458

a) $KMnO_4$, acetone, water; b) HBTU, DIEA, $MeNH_2$, THF, CH_3CN.

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-carboxy-benzo[*b*]thiophen-2-yl)-benzenesulfonamide (458-A).** A solution of compound **207** (0.4 g, 0.81 mmol) in acetone 1(15 mL) was heated to reflux and treated with a solution of potassium permanganate (0.192 g, 1.21 mmol) in water (~3 mL). The resultant mixture was refluxed for an additional 2 h. The mixture was concentrated in vacuo, diluted with water, treated with 1M Na_2SO_3 (4 mL) and 1M sulfuric acid (4 mL). The clear colorless solution was extracted with dichloromethane, washed with 1N hydrochloric acid, dried over sodium sulfate, filtered and the solvent was evaporated in vacuo to afford 0.41 g of compound **458-A** as a colorless solid. ^{1}H-NMR ($CDCl_3$): δ 4.88 (s, 2 H), 7.04 (t, 1H), 7.30-7.79 (m, 10H), 8.32 (d, 1H); MS: m/z 510.0 (MH^+).

Compound 458

***N*-(3-Methyl-carbamoyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** A solution of compound **458-A** (0.41 g, 0.804 mmol) in acetonitrile (12 mL) was treated with diisopropylethylamine (350 μL, 2.01 mmol) and HBTU (0.336 g, 0.885 mmol) and stirred at ambient temperature for 5 min. The resultant solution was split into 3 equal portions. One portion was treated with methylamine (2.0 M in THF, 402 μL, 402 mmol) and stirred for 18 h. The reaction mixture was partitioned between dichloromethane and water, the organic layer dried over sodium sulfate, filtered and the solvent evaporated in vacuo. The crude residue was purified by reverse phase pHPLC (C_{18}), eluting with an acetonitrile (30-90%) in water (0.1% TFA) gradient to afford 73 mg of compound **458** as a colorless solid. ^{1}H-NMR ($CDCl_3$): δ 2.96 (d, 2H), 4.47 (br s, 1H), 4.74 (br s, 2H), 7.04 (t, 1H),

7.19-7.32 (m, 1H), 7.32-7.46 (m, 2H), 7.49-7.71 (m, 4H), 7.72-7.84 (m, 1H), 7.85 - 8.01 (m, 3H); MS: *m/z* 523.2 (MH^+).

Following the procedure described above for example 37 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 457

***N*-(3-Dimethyl-carbamoyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** MS: *m/z* 537.2 (MH^+).

Compound 459

***N*-(3-Carbamoyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 4.77 (br s, 2H), 6.86 (br s, 1H), 7.04 (t, 1H), 7.32-7.48 (m, 3H), 7.52 (dd,1H), 7.60-7.68 (m, 2H), 7.70-7.80 (m, 3H), 7.90 (d, 2H), 8.02 (d, 1H); MS: *m/z* 509.1 (MH^+).

Compound 465

***N*-(Butyl)-*N*-(3-carbamoyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 447.1 (MH^+).

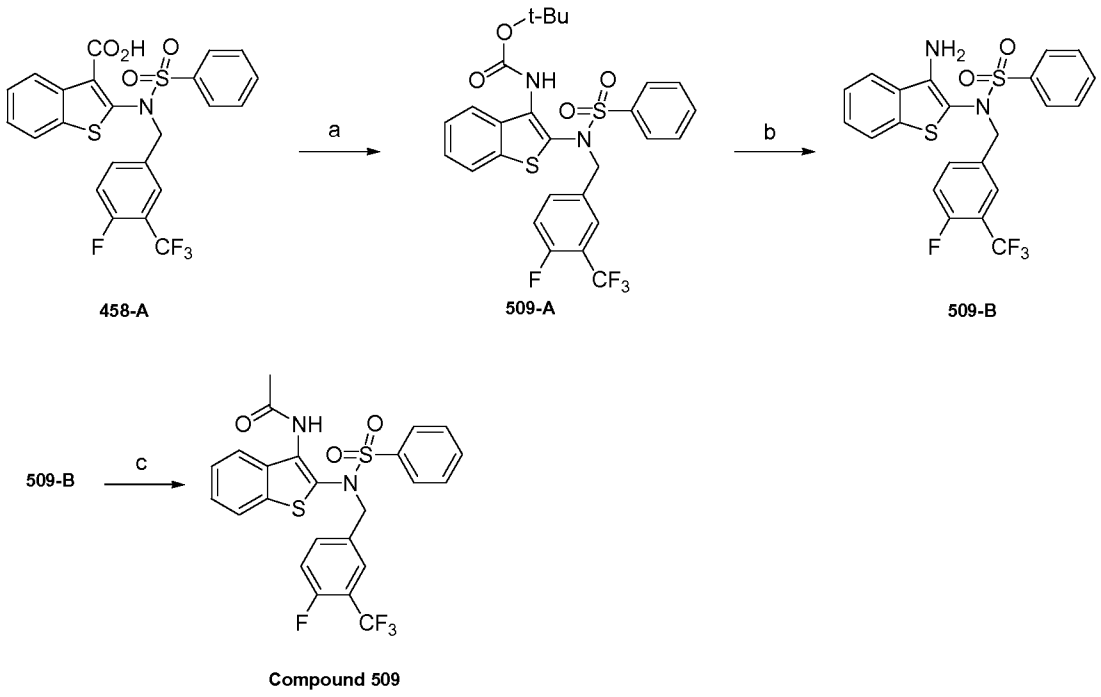
Compound 466

***N*-(Butyl)-*N*-(3-methyl-carbamoyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 461.1 (MH^+).

Compound 467

***N*-(Butyl)-*N*-(3-dimethyl-carbamoyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 0.85 (t, 3H), 1.19-1.37 (m, 2H), 1.43-1.58 (m, 1H), 1.61-1.81 (m, 1H), 2.90 (s, 3H), 3.16 (s, 3H), 3.45 (ddd, 1H), 3.86 (ddd, 1H), 3.98 (s, 3H), 7.34-7.44 (m, 2H), 7.51-7.60 (m, 1H), 7.66-7.75 (m, 1H), 7.90 (d, 2H), 8.19 (d, *J*=8.67 Hz, 2H); MS: *m/z* 475.2 (MH^+).

Example 38



a) DPPA, DIEA, *t*BuOH; b) HCl, dioxane; c) DIEA, CH_3COCl, DCM.

{2-[Benzenesulfonyl-(4-fluoro-3-trifluoromethyl-benzyl)-amino]-benzo[*b*]thiophen-3-yl}-carbamic acid *t*-butyl ester (509-A). A solution of compound **458-A** (1.96 g, 3.85 mmol) and diisopropylethylamine (806 µL, 4.61 mmol) in *t*-butanol (30 mL) was treated with DPPA (1.0 mL, 4.61 mmol) and refluxed for 6 h. The solvent was evaporated in vacuo, and the crude residue purified by flash column chromatography (SiO_2), eluting with an ethyl acetate (10-35%) in heptane gradient, to afford compound **509-A** (1.0 g, 45%) as a yellow amorphous solid. ^{1}H-NMR ($CDCl_3$): δ 1.48 (br s, 9H), 4.74 (s, 2H), 6.92-7.14 (m, 2H), 7.29-7.39 (m, 2H), 7.43-7.58 (m, 5H), 7.62-7.77 (m, 4 H); MS: *m/z* 603.0 (MNa^+).

***N*-(3-Amino-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide (509-B).** Compound **509-A** (1.0 g, 1.72 mmol) was dissolved in 4N HCl in dioxane (20 mL) and stirred at ambient temperature for 18 h. The resultant suspension was diluted with diethyl ether, filtered, washed with diethyl ether and dried under vacuo to afford 0.65 g of compound **509-B**. MS: *m/z* 481.0 (MH^+).

Compound 509

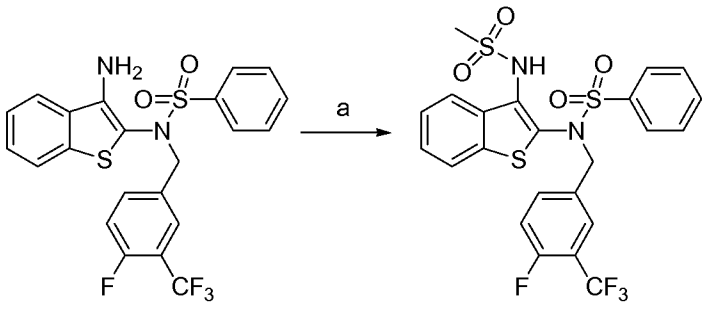
***N*-{2-[Benzenesulfonyl-(4-fluoro-3-trifluoromethyl-benzyl)-amino]-benzo[*b*]thiophen-3-yl}-acetamide.** A solution of compound **509-B** (80 mg, 0.155

mmol) and diisopropylethylamine (68 μL, 0.387 mmol) in dichloromethane, cooled to 0 °C, was treated with acety chloride (15 μL, 0.201 mmol) and the resultant solution was stirred at ambient temperature for 18 h. An additional portion of acetyl chloride (15 μL, 0.201 mmol) was added, and the solution was stirred an additional hour. The solution was washed with 2N HCl, saturated aqueous sodium bicarbonate, dried over sodium sulfate, filtered and the solvent evaporated in vacuo. The crude residue was purified by reverse phase pHPLC (C_{18}), eluting with a gradient of acetonitrile (40-90%) in water (0.1%TFA) to afford crude compound **509**. Crude compound **509** was further purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (20-70%) in heptane gradient to afford 51 mg of compound **509** an off-white solid. ^{1}H-NMR ($CDCl_3$): δ 2.11 (s, 3H), 4.68 (br s, 2H), 6.75-7.08 (m, 1H), 7.11-7.71 (m, 11H), 7.88 (br s, 1H); MS: *m/z* 523.0 (MH^+).

Compound 500

***N*-(3-Acetylamino-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 461.1 (MH^+).

Example 39



509-B Comopund 508

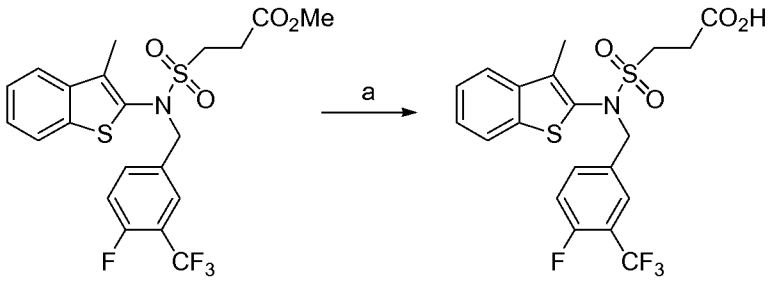
a) pyridine, CH_3SO_2Cl, DCE, DIEA.

Compound 508

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methanesulfonylamino-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** To a solution of compound **509-B** (75 mg, 0.145 mmol) and pyridine (25 μL, 0.304 mmol) in dichloroethane (2 mL), cooled to 0 °C, was added a solution of methanesulfonyl chloride 1M in dichloromethane (0.145 mL, 0.145 mmol). After stirring the reaction at ambient temperature for 1 h, pyridine (2 mL) was added and the solution cooled on an ice bath. An additional

portion of methanesulfonyl chloride (30 μL) was added, and the solution stirred 4 h at ambient temperature. Diisopropylethylamine (60 mL) was added followed by another portion of methanesulfonyl chloride (30 μL), and the reaction mixture stirred for 2 days. The solution was partitioned between dichloromethane and 2N HCl, dried over sodium sulfate filtered, and the solvent was evaporated in vacuo. The crude residue was purified by reverse phase pHPLC, using a gradient of acetonitrile (40-90%) in water (0.1%TFA) to afford 11 mg of compound **508** as a colorless solid. ^{1}H-NMR ($CDCl_3$): δ 2.69 (s, 3H), 4.77 (br s, 2H), 7.11 (t, 1H), 7.35-7.47 (m, 3H), 7.50-7.62 (m, 5H), 7.64-7.73 (m, 3H), 8.02 (d, 1H); MS: m/z 559.0 (MH^+).

Example 40



Compound 71 Compound 510

a) conc. HCl, AcOH.

Compound 510

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-carboxy-ethanesulfonamide.** A solution of compound **71** (110 mg, 0.225 mmol) in acetic acid (5 mL) and 6N HCl (5 mL) was refluxed for 2 h. The reaction mixture was cooled and the solvent evaporated in vacuo. The crude residue was purified by pHPLC (C_{18}), eluting with an acetonitrile (30-90%) in water (0.1% TFA) gradient, to afford 60 mg of compound **510** as a colorless solid. ^{1}H-NMR ($CDCl_3$): δ 2.04 (s, 3H), 2.91-3.04 (m, 2H), 3.48-3.63 (m, 2H), 4.82 (br s, 2H), 7.10 (t, 1H), 7.32-7.42 (m, 2H), 7.42-7.51 (m, 1H), 7.51-7.64 (m, 2H), 7.68-7.82 (m, 1H); MS: *m/z* 476.1 (MH^+).

Following the procedure described above for example 40 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 604

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-2-carboxy-ethanesulfonamide.** MS: *m/z* 396.0 (MH^+).

Compound 605

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-2-carboxy-ethanesulfonamide.** MS: *m/z* 410.1 (MH^+).

Compound 606

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-2-carboxy-ethanesulfonamide.** MS: *m/z* 424.0 (MH^+).

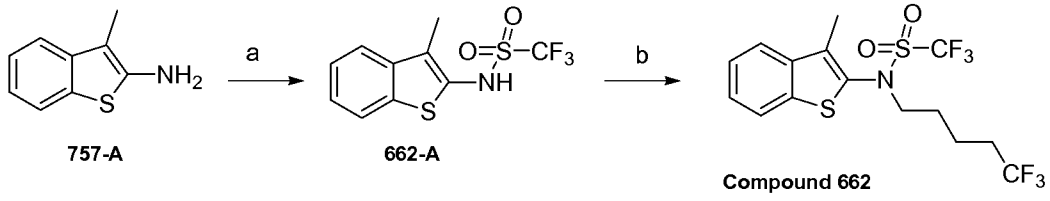
Compound 762

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-2-carboxy-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.00 (s, 3H), 2.88-3.06 (m, 2H), 3.55 (t, 2H), 4.81 (br s, 2H), 7.11-7.41 (m, 6H), 7.55-7.62 (m, 1H), 7.70-7.78 (m, 1H); MS: *m/z* 474.0 (MH^+).

Compound 795

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-2-carboxy-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.98 (s, 3H), 2.77 (t, 2H), 2.67 (t, 2H), 4.83 (br s, 2H), 7.23-7.35 (m, 2H), 7.35-7.46 (m, 4H), 7.62-7.73 (m, 1H), 7.84-7.96 (m, 1H), 12.57 (br s, 1H); MS: *m/z* 474.0 (MH^+).

Example 41



a) 1. $(CF_3SO_2)_2O$, TEA, DCM; 2. 3N NaOH, MeOH; b) PPh_3, DEAD, $HO(CH_2)_4CF_3$.

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*C,C,C*-trifluoromethanesulfonamide (662-A).** A solution of compound **757-A** (0.25 g, 1.25 mmol) and triethylamine (540 µL, 3.88 mmol) in dichloromethane (10 mL,) cooled to -10 °C , was treated with trifluoromethanesulfonic anhydride (442 µL, 2.62 mmol). The reaction mixture was stirred at -10 °C for 1 h, washed with 1N HCl, dried over Na_2SO_4, filtered, and the

solvent was evaporated in vacuo to afford crude a bis-sulfonylated by-product. The bis-sulfonylated by-product was dissolved in methanol (4 mL), treated with 4 N NaOH (625 mL, 1.88 mmol) and stirred at ambient temperature for 1 h. The solution was concentrated in vacuo, diluted with H_2O, acidified with 2N HCl, extracted with EtOAc, and the organic phase washed with brine, dried over Na_2SO_4, filtered, and the solvent was evaporated in vacuo to afford 0.35 g of crude compound **662-A**. MS: *m/z* 294.0 $(M - H)^-$.

Compound 662

***C,C,C*-Trifluoro-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-methanesulfonamide.** A solution of triphenylphosphine (0.404 g, 1.54 mmol) in THF (10 mL) was treated with DEAD (40% in toluene, 684 μL, 1.54 mmol) and stirred at ambient temperature for 5 min. Compound **662-A** (0.35 g) was added and the reaction mixture stirred for 15 min, to which was added 5,5,5-trifluoropentanol (164 μL, 1.42 mmol), and the resultant solution was stirred at ambient temperature for 4 h. The solvent was evaporated in vacuo, and the crude residue purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (1-30%) in heptane gradient to afford crude compound **662**. Further purification by pHPLC (C_{18}), eluting with an acetonitrile (40-90%) in water (0.1% TFA) gradient, to afford 0.126 g of compound **662** as an oil. ^{1}H-NMR ($CDCl_3$): δ 1.58-1.78 (m, 4H), 1.96-2.18 (m, 2H), 2.42 (s, 3H), 3.73-3.90 (m., 2H), 7.35-7.50 (m, 2H), 7.62-7.83 (m, 2H); MS: *m/z* 420.0 (MH^+).

Following the procedure described above for example 41 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

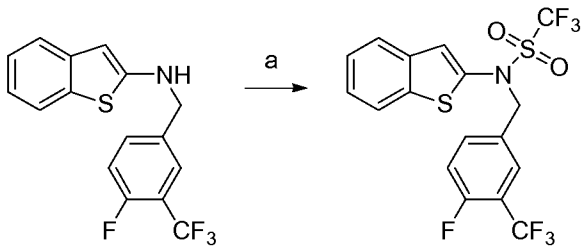
Compound 664

***C,C,C*-Trifluoro-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** MS: *m/z* 472.0 (MH^+).

Compound 665

***N*-(2-Cyclopropyl-ethyl)-*C,C,C*-trifluoro-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-methanesulfonamide.** MS: *m/z* 364.0 (MH^+).

Example 42



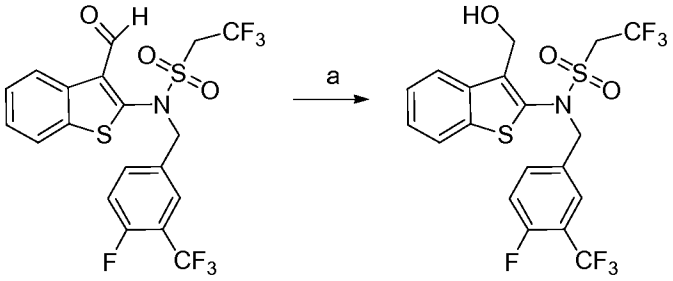
300-A **Compound 663**

a) TEA, $(CF_3SO_2)_2O$, DCM.

Compound 663

***N*-Benzo[*b*]thiophen-2-yl- *N*-(4-fluoro-3-trifluoromethyl-benzyl)- *C,C,C*-trifluoro-methanesulfonamide.** A solution of compound **300-A** (0.101 g, 0.279 mmol) and triethylamine (86 µL, 0.614 mmol) in dichloromethane (4 mL), cooled to -10 °C, was treated with trifluoromethanesulfonic anhydride (52 µL, 0.307 mmol) and stirred at -10 °C for 1 h. The reaction mixture was washed with 2N HCl, dried over Na_2SO_4, filtered, and the solvent evaporated in vacuo. The crude residue was purified by pHPLC (C_{18}), eluting with an acetonitrile (30-90%)-water gradient, to afford 40 mg of compound **663** as a brown oil. ^{1}H-NMR ($CDCl_3$): δ 4.49 (s, 2H), 7.11-7.26 (m, 3H), 7.36 (t, 1H), 7.47-7.68 (m, 4H).

Example 43



704-A **Compound 704**

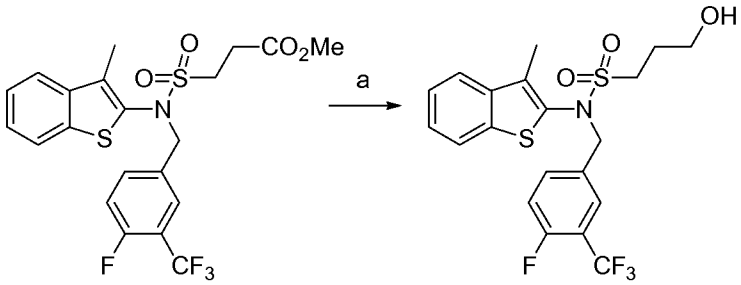
a) $LiBH_4$, THF.

(4-Fluoro-3-trifluoromethyl-benzyl)-(3-formyl-benzo[*b*]thiophen-2-yl)-2,2,2-trifluoro-ethanesulfonamide (704-A). Compound **704-A** was prepared using the procedure in Example 16, step A, substituting compound **1** with compound **697**.

Compound 704

***N*-(3-Hydroxymethyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2,2,2-trifluoro-ethanesulfonamide.** A solution of compound **704-A** (0.16 g, 0.32 mmol) in THF (5 mL) was treated with lithium borohydride (10 mg, 0.46 mmol) and stirred at ambient temperature for 2 h. The reaction mixture was quenched with H_2O, stirred for 2 h and extracted ethyl acetate. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and the solvent was evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2), eluting with an ethyl acetate (10-50%) in heptane gradient to afford 70 mg of compound **704** as a colorless solid. ^{1}H-NMR ($CDCl_3$): δ 2.21 (t, 1H), 4.03 (q, 2H), 4.22 (d, 2H), 4.87 (s, 2H), 7.13 (t, 1H), 7.39-7.54 (m, 4H), 7.76-7.85 (m, 1H), 7.85-8.01 (m, 1H); MS: *m/z* 484.0 $[M-(OH^-)]^+$, 524.1 (MNa^+).

Example 44



Compound 71 Compound 699

a) $LiBH_4$, THF.

Compound 699

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-hydroxy-propanesulfonamide.** A solution of compound **71** (0.47 g, 0.96 mmol) in THF (5 mL) was treated with lithium borohydride (21 mg, 0.96 mmol) and stirred at ambient temperature for 1 h. An additional portion of lithium borohydride (30 mg, 1.38 mmol) was added and the resultant mixture was stirred at ambient temperature for 2 h. Water (2 mL) was added, the reaction mixture stirred for 5 min and then partitioned between ethyl acetate and water. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and the solvent evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (30-100%) in heptane gradient to afford 0.334 g of compound **699** as a colorless oil. ^{1}H-

NMR ($CDCl_3$): δ 1.61 (t, 1H), 2.06 (s, 3H), 2.11-2.23 (m, 2H), 3.34-3.44 (m, 2H), 3.83 (q, 2H), 4.82 (br s, 2H), 7.09 (t, 1H), 7.34-7.43 (m, 2H), 7.43-7.53 (m, 1H), 7.52-7.65 (m, 2H), 7.69-7.78 (m, 1H); MS: *m/z* 462.1 (MH^+).

Following the procedure described above for example 44 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 758

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-hydroxy-butanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.38 (t, 1H), 1.68-1.82 (m, 2H), 1.97 - 2.15 (m, 2H) superimposed on 2.09 (s, 3H), 3.20-3.36 (m, 2H), 3.72 (q, 2H), 4.82 (br s, 2H), 7.09 (t, 1H), 7.34-7.42 (m, 2H), 7.44-7.51 (m, 1H), 7.53-7.63 (m, 2H), 7.70-7.77 (m, 1H); MS: *m/z* 476.1 (MH^+).

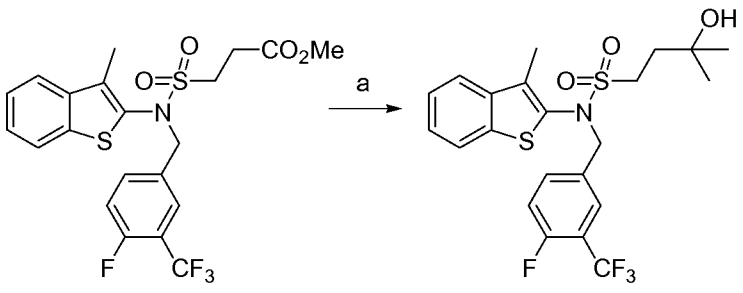
Compound 764

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluormethoxy-benzyl)-3-hydroxy-propanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.64 (t, 1H), 2.02 (s, 3H), 2.10-2.25 (m, 2H), 3.29-3.43 (m, 2H), 3.82 (q, 2H), 4.81 (br s, 2H), 7.10-7.41 (m, 6H), 7.59 (dd, 1H), 7.68 - 7.76 (m, 1H); MS: *m/z* 460.0 (MH^+).

Compound 793

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-hydroxy-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 2.04 (s, 3H), 2.45 (t, 1H), 3.41-3.56 (m, 2H), 4.08-4.25 (m, 2H), 4.83 (br s, 2H), 7.10 (t, 1H), 7.34-7.43 (m, 2H), 7.43-7.51 (m, 1H), 7.53-7.64 (m, 2H), 7.69-7.77 (m, 1H); MS: *m/z* 448.0 (MH^+).

Example 45



Compound 71 Compound 725

a) MeMgBr, THF.

Compound 725

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-hydroxy-3-methyl-butane-1-sulfonamide.** A solution of compound **71** (0.11 g, 0.225 mmol) in THF (4 mL) cooled to -10 °C, was treated with methylmagnesium bromide (3 M in Et_2O, 2 mL, 6 mmol) and stirred at -10 °C for 1 h. Saturated aqueous ammonium chloride (0.5 mL) was added, the mixture partitioned between H_2O and EtOAc, the organic layer washed with brine, and dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (10-60%) in heptane gradient to afford 73 mg of compound **725** as a colorless oil. ^{1}H-NMR ($CDCl_3$): δ 1.18-1.33 (br s, 1H) superimposed on 1.30 (s, 6H), 1.98-2.11 (m, 2H) superimposed on 2.06 (s, 3H), 3.33-3.44 (m, 2H), 4.82 (br s, 2H), 7.09 (t, 1H), 7.35-7.42 (m, 2H), 7.44-7.51 (m, 1H), 7.54-7.63 (m, 2H), 7.70-7.77 (m, 1H); MS: *m/z* 490.0 (MH^+).

Following the procedure described above for example 45 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 371

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-(1-hydroxy-1-methyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.46 (s, 6H), 1.60-1.67 (m, 2H), 2.22 (s, 3H), 2.30-2.39 (m, 2H), 3.16-3.18 (d, 1H), 3.60 (m, 1H), 7.39-7.47 (m, 2H), 7.72 (s, 4H), 7.75-7.80 (m, 1H), 7.82-7.89 (m, 1H); MS: *m/z* 472.0 (MH^+).

Compound 374

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(1-hydroxy-1-methyl-ethyl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.48 (s, 6H), 1.94 (s, 3H), 4.82 (s, 2H), 5.33 (s, 1H), 7.35-7.47 (m, 3H), 7.61-7.87 (m, 8H); MS: *m/z* 537.9 (MH^+).

Compound 759

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-hydroxy-4-methyl-pentane-1-sulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.23 (s, 1H), 1.26 (s, 6H), 1.57-1.67 (m, 2H), 1.97-2.09 (m, 2H) superimposed on 2.09 (s, 3H), 3.21-3.32 (m, 2H), 4.82 (br s, 2H), 7.09 (t, 1H), 7.35-7.42 (m, 2H), 7.45-7.51 (m, 1H), 7.53-7.63 (m, 2H), 7.67-7.83 (m, 1H); MS: *m/z* 526.0 (MNa^+).

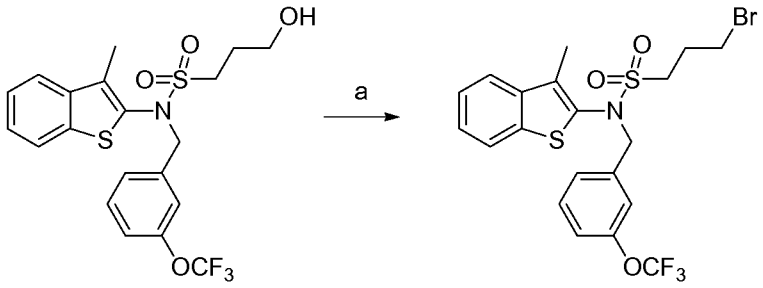
Compound 763

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-3-hydroxy-3-methyl-butane-1-sulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.29 (s, 6H), 1.30 (s, 1H), 1.98-2.10 (m, 2H) superimposed on 2.02 (s, 3H), 3.32-3.45 (m, 2H), 4.81 (br s, 2H), 7.10-7.41 (m, 6H), 7.55-7.62 (m, 1H), 7.73 (dd, 1H); MS: *m/z* 488.1 (MH^+).

Compound 796

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-3-hydroxy-3-methyl-butane-1-sulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.29 (s, 6H) superimposed on 1.33 (br s, 1H), 1.99 (s, 3H), 2.01-2.09 (m, 2H), 3.26-3.49 (m, 2H), 4.80 (br s, 2H), 7.10 (d, 2H), 7.28-7.41 (m, 4H), 7.53-7.63 (m, 1H), 7.68-7.79 (m, 1H); MS: *m/z* 488.1 (MH^+).

Example 46



Compound 764 **Compound 769**

a) DCM, PPh_3, CBr_4.

Compound 769

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-3-bromo-propane-1-sulfonamide.** A solution of compound **764** (0.80 g, 1.7 mmol) and CBr_4 (0.635 g, 1.92 mmol) in dichloromethane (25 mL) was treated with triphenylphosphine (0.503 g, 1.92 mmol) and stirred at ambient temperature for several hours. Additional portions of CBr_4 (0.20 g, 0.6 mmol) and triphenylphosphine (0.15 g, 0.57 mmol) were added and stirred an additional 18 h. The solvent was evaporated and the crude residue purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (1-25%) in heptane gradient to afford 0.90 g of compound **769** as an oil. ^{1}H-NMR ($CDCl_3$): δ 2.02 (s, 3H), 2.39-2.51 (m, 2H), 3.34-3.43 (m, 2H), 3.55 (t, 2H), 4.81 (br s, 2H), 7.10-7.41 (m, 6H), 7.55-7.62 (m, 1H), 7.70 - 7.77 (m, 1H); MS: *m/z* 522, 524 (MH^+).

Following the procedure described above for example 46 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

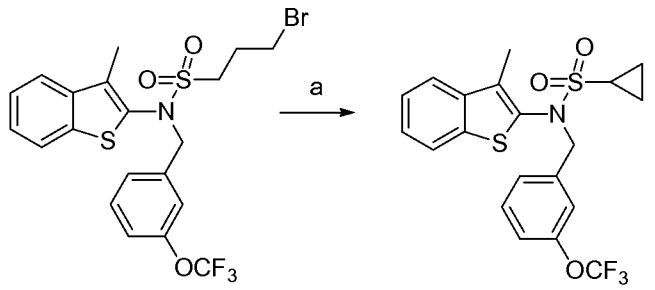
Compound 771

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-bromo-butane-1-sulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.98-2.20 (m, 4H) superimposed on 2.04 (s, 3H), 3.17-3.31 (m, 2H), 3.45 (t, 2H), 4.83 (br s, 2H), 7.10 (t, 1H), 7.34-7.43 (m, 2H), 7.44-7.51 (m, 1H), 7.53-7.64 (m, 2H), 7.70-7.78 (m, 1H); MS: *m/z* 538.0, 540.0 (MH^+).

Compound 797

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-2-bromo-ethane-1-sulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.97-2.11 (m, 3H), 3.62-3.79 (m, 4H), 4.82 (br s, 2H), 7.10 (t, 1H), 7.36-7.51 (m, 3H), 7.54 (dd, 1H), 7.58-7.64 (m, 1H), 7.72-7.79 (m, 1H); MS: *m/z* 510, 512.0 (MH^+).

Example 47



Compound 769 Compound 770

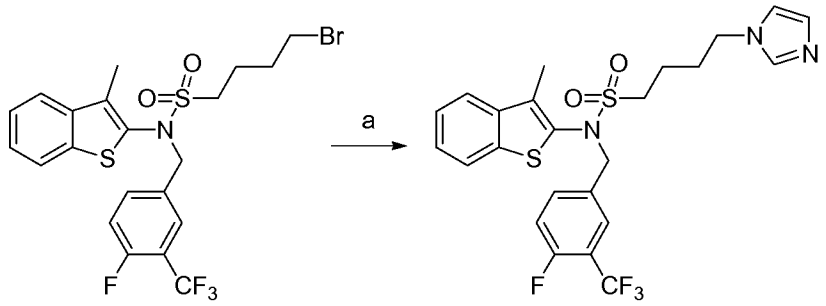
a) sodium imidazolide, DMF.

Compound 770

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-cyclopropanesulfonamide.** A solution of compound **769** (90 mg, 0.172 mmol) in DMF (2 mL) was treated with sodium imidazolide (0.10 g, 1.1 mmol), and the resultant mixture was stirred at ambient temperature for 18 h. The solvent was evaporated, and the crude residue pre-absorbed onto silica gel. The product was isolated by flash column chromatography (SiO_2) eluting with an ethyl acetate (5-40%)-heptane gradient to afford 51 mg of compound **770** as an oil. ^{1}H-NMR ($CDCl_3$): δ 1.03-1.14 (m, 2H),

1.20-1.32 (m, 2H), 2.05 (s, 3H), 2.61 (tt, 1H), 4.81 (br s, 2H), 7.11 (d, 1H), 7.18-7.31 (m, 3H), 7.31-7.41 (m, 2H), 7.54-7.62 (m, 1H), 7.69-7.76 (m, 1H); MS: *m/z* 442.0.

Example 48



Compound 771 Compound 779

a) imidazole, CH_3CN.

Compound 779

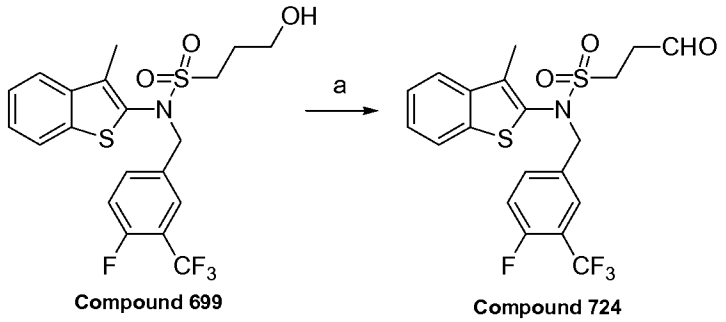
***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-(imidazol-1-yl)-butane-1-sulfonamide.** A solution of compound **771** (96 mg, 0.18 mmol) in acetonitrile (1 mL) was treated with imidazole (0.25 g, 3.7 mmol) and heated at 80 °C for 18 h. The solvent was evaporated in vacuo, and the crude residue was purified by pHPLC (C_{18}) eluting with an acetonitrile (20-90%) in water (0.1% TFA) gradient to afford 58 mg of compound **779** as the product as the TFA salt. ^{1}H-NMR (DMSO-d_6): δ 1.67-1.82 (m, 2H), 1.90-2.06 (m, 2H) superimposed on 2.02 (s, 3H), 3.40-3.61 (m, 2H), 4.27 (t, 2H), 4.86 (br s, 2H), 7.34-7.52 (m, 3H), 7.58-7.76 (m, 4H), 7.81 (t, 1H), 7.84-7.97 (m, 1H), 9.15 (s, 1H); MS: *m/z* 526.2 (MH^+).

Following the procedure described above for example 48 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 778

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-trifluoromethoxy-benzyl)-3-imidazol-1-yl-propane-1-sulfonamide.** MS: *m/z* 510.1 (MH^+).

Example 49



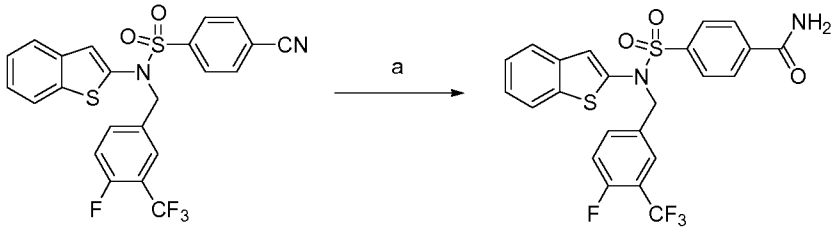
Compound 699 Compound 724

a) Dess-Martin periodinane, DCM.

Compound 724

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-3-oxo-propane-1-sulfonamide.** A solution of compound **699** (0.415 g, 0.899 mmol) in dichloromethane (20 mL) was treated with Dess-Martin periodinane (0.57 g, 1.35 mmol) and stirred at ambient temperature for 3 days. The crude residue was preabsorbed onto silica gel and purified by flash column chromatography (SiO_2) eluting with an ethyl acetate (10-60%) in heptane gradient to afford 0.255 g of compound **724** as an oil. ^{1}H-NMR ($CDCl_3$): δ 2.04 (s, 3H), 3.11 (t, 2H), 3.55 (t, 2H), 4.81 (br s, 2H), 7.10 (t, 1H), 7.34-7.43 (m, 2H), 7.44-7.51 (m, 1H), 7.53-7.63 (m, 2H), 7.70-7.77 (m, 1H), 9.84 (s, 1H); MS: *m/z* 460.0.

Example 50



Compound 411 Compound 413

a) MeOH, HCl.

Compound 413

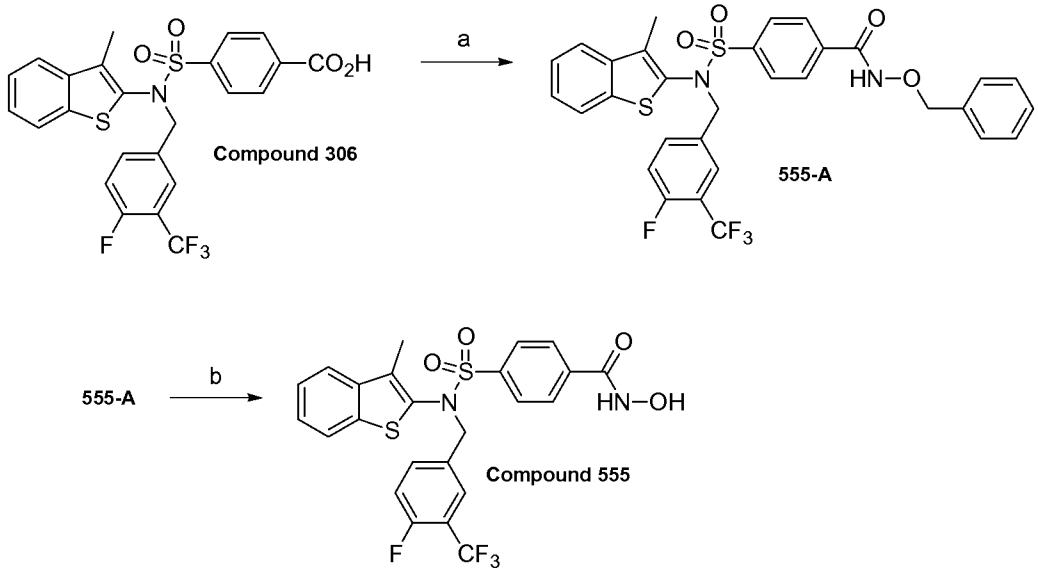
***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-carboxamide-benzenesulfonamide**. To a pressure vessel containing compound **411** (266 mg; 0.542 mmol) was added methanol (5 mL). The suspension was cooled to 0 °C, hydrogen chloride$_g$ was bubbled into the suspension for 10 min, the reaction was sealed and allowed to stir at ambient temperature for 2 h. The reaction was cooled, the

pressure released, and the solvent evaporated under reduced pressure. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 55 to 75% gradient to afford 61 mg of compound **413** as a white solid. MS: *m/z* 509.0 (MH^+).

Following the procedure described above for example 50 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 414
***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carboxamide-benzene-sulfonamide**. MS: *m/z* 443.0 (MH^+)

Example 51



a) DCM, EDC-HCl, H_2NOBz; b) DCM, BBr_3.

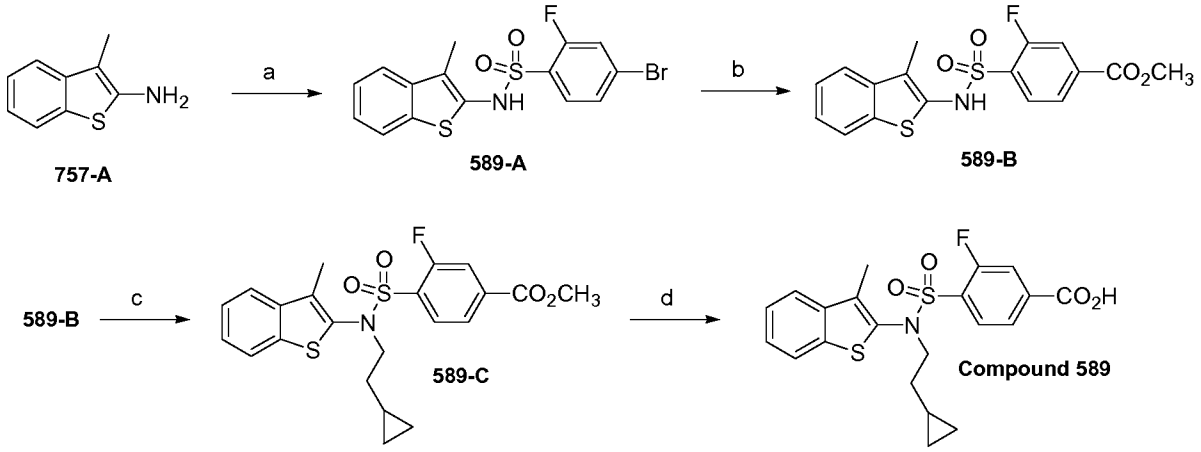
4-Benzyloxy-4-[4-fluoro-3-trifluoromethyl-benyzl)-(3-methyl-benzo[*b*]thiophen-2-yl)-sulfamoyl]-benzamide (555-A). To a suspension of compound **306** (127.6 mg; 0.244 mmol) in CH_2Cl_2 (1 mL) was added H_2NOBz (60 mg; 0.488 mmol) followed by EDC-HCl (94 mg; 0.488 mmol) and the reaction was allowed to stir at ambient temperature for 5h. The reaction mixture was diluted with EtOAc, washed with H_2O (2X), brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude residue was purified by flash chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford 118.4 mg of compound **555-A** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 1.94 (s, 3H), 4.97 (s, 4H), 7.37-7.49 (m, 8H),

7.64-7.70 (m, 3H), 7.82-7.85 (m, 1H), 7.99 (s, 5H), 12.10 (s, 1H); MS: *m/z* 629.1 (MH^+).

Compound 555

4-([4-Fluoro-3-trifluoromethyl-benyzl)-(3-methyl-benzo[*b*]thiophen-2-yl)-sulfamoyl]-*N*-hydroxy-benzamide. To a solution of compound **555-A** (91.6 mg; 0.175 mmol) in CH_2Cl_2 (2 mL), cooled to 0 °C, was added a 1.0M soln of BBr_3-CH_2Cl_2 (0.263 mL) and the reaction was stirred at ambient temperature for 8h. The solvent was evaporated under reduced pressure and the crude residue purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 50% to 70% MeCN-H_2O gradient to afford 46.0 mg of compound **555** as a red oil. ^{1}H-NMR (DMSO-d_6): δ 1.94 (s, 3H), 4.88(s, 2H), 7.36-7.40 (m, 2H), 7.43-7.48 (m, 1H), 7.64-7.69 (m, 3H), 7.81-7.86 (m, 1H), 7.95-8.02 (m, 4H), 9.28 (s, 1H), 11.53 (s, 1H); MS: *m/z* 539.1 (MH^+).

Example 52



a) DCM, pyridine, 4-bromo-2-fluorobenzene sulfonyl chloride; b) DMF, MeOH, $(PPh_3)_2PdCl_2$, CO; c) THF, DEAD, PPh_3, cyclopropylethanol; d) MeOH, NaOH.

4-Bromo-2-fluoro-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide (589-A). T o a suspension of compound **757-A** (1.64 g; 8.23 mmol) in CH_2Cl_2 (10 mL), was added pyridine (1.33 mL; 16.5 mmol) and the reaction was cooled to 5 °C. 4-Bromo-2-fluorobenzene sulfonyl chloride(2.5 g; 9.14 mmoL), dissolved in CH_2Cl_2 (5 mL) was added drop-wise, and the reaction was allowed to stir at ambient temperature

for 18 h. The reaction was diluted with EtOAc, washed with 1N HCl, water, brine, dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure. The crude solid was triturated with CH_2Cl_2-MeOH, filtered, and the solid washed with ether and dried under vacuo to afford 450 mg of compound **589-A** as a white solid. The solvent was evaporated and the crude residue dried under vacuo to afford an additional 2.4 g of compound **589-A** as a pink solid. MS: m/z 423.9 (MH^+ + MeCN).

2-Fluoro-4-(3-methyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzene-sulfonamide (589-B). To a solution of compound **589-A** (2.46 g; 6.14 mmol), in DMF (30 mL) and MeOH (70 mL), was added TEA (2.57 mL; 18.4 mmol), and $(PPh_3)_2PdCl_2$ (194 mg). The reaction mixture was added to a high pressure vessel, purged with vacuo and CO (3x). Carbon monoxide was added to the vessel to 50 psi, and the reaction was heated at 80 °C for 18h. An additional 239 mg of palladium catalyst was added, CO added and the reaction heated at 80 °C for an additional 96h (convenient – over weekend). The reaction was cooled, the pressure carefully released, and the solvent concentrated under reduced pressure. The crude residue was diluted with EtOAc, washed with H_2O (2X), brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude residue was purified by flash chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford 1.12 g of compound **589-B** as a yellow foam. ^{1}H-NMR (DMSO-d_6): δ 2.13 (s, 3H), 3.89 (s, 2H), 7.31-7.38 (m, 2H), 7.64-7.66 (m, 1H), 7.78-7.80 (m, 1H), 7.84-7.89 (m, 2H), 7.95-7.98 (m, 1H), 11.05 (s, 1H); MS: *m/z* 380.1 (MH^+).

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-2-fluoro-4-carbomethoxy-benzenesulfonamide (589-C)**. To PPh_3 (155 mg; 0.593 mmol) was added THF (3.5 mL) followed by DEAD (0.275 mL; 0.604 mmol) and the reaction mixture was stirred at RT for 3 min, to which was then added compound **589-B** (42 mg; 0.482 mmol). The reaction mixture was stirred for 5 min, to which was added cyclopropyl-ethanol and the reaction was stirred for 72 h. The reaction was diluted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure to afford compound **589-C**, which was used as is in the next step.

Compound 589

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-2-fluoro-4-carboxy-benzenesulfonamide**. To a solution of compound **589-C** (~ 0.395 mmol) in

MeOH (2mL) was added 3N NaOH (0.198 mL; 0.593 mmol) and the reaction was stirred at 63 °C for 18h. The reaction was cooled, the solvent evaporated under reduced pressure, and the crude residue partitioned between 1N HCl and EtOAc. The organic layer was washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 53 to 73% gradient to afford 109.8 mg of compound **589** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 0.005-0.03 (t, 3H), 0.366-0.410 (m, 2H), 0.668-0.754 (m, 1H), 1.39-1.40 (m, 2H), 2.23 (s, 3H), 3.77-3.96 (m, 2H), 7.38-7.44 (m, 2H), 7.76-7.88 (m, 4H), 7.96-7.97 (m, 1H), 13.84 (s, 1H); MS: *m/z* 433.8 (MH^+).

Following the procedure described above for example 52 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 590

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.25 (s, 3H), 2.51-2.67 (m, 2H), 3.91-4.00 (m, 2H), 7.40-7.46 (m, 2H), 7.76-7.88 (m, 4H), 7.96-7.99 (m, 1H), 13.92 (s, 1H); MS: *m/z* 461.7 (MH^+).

Compound 591

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.57 (m, 4H), 2.24 (s, 3H), 3.75 (m, 2H), 7.38-7.45 (m, 2H), 7.76-7.88 (m, 4H), 7.94-7.97 (m, 1H), 13.90 (s, 1H); MS: *m/z* 489.6 (MH^+).

Compound 592

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.90 (s, 3H), 5.00 (m, 2H), 7.35-7.40 (m, 2H), 7.45-7.50 (t, 1H), 7.63-7.69 (m, 3H), 7.82-7.89 (m, 3H), 7.99-8.02 (d, 1H), 13.93 (s, 1H); MS: *m/z* 541.7 (MH^+).

Compound 593

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.838-0.875 (t, 3H), 1.30-1.39 (m, 2H), 1.42-1.49 (m, 2H), 2.24 (s, 3H), 3.71 (m, 2H), 7.38-7.45 (m, 2H), 7.47-7.87 (m, 4H), 7.94-7.97 (m, 1H), 13.91 (s, 1H); MS: *m/z* 421.7 (MH^+).

Compound 638

***N*-(3-Benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-2-fluoro-4-carboxy-benzenesulfonamide.** MS: *m/z* 419.7 (MH^+).

Compound 639

***N*-(3-Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-2-fluoro-4-carboxy-benzenesulfonamide.** MS: *m/z* 447.7 (MH^+).

Compound 685

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.56-1.60 (m, 4H), 2.22-2.35 (m, 2H), 3.83-3.87 (m, 2H), 7.33-7.39 (m, 3H), 7.77-7.80 (m, 1H), 7.84-7.94 (m, 4H), 13.80 (s, 1H); MS: *m/z* 476.1 (MH^+).

Compound 686

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 5.14 (s, 2H), 7.25 (s, 1H), 7.30-7.35 (m, 2H), 7.47-7.54 (t, 1H), 7.69-7.75 (m, 3H), 7.81-7.88 (m, 1H), 7.91-8.00 (m, 4H), 13.97 (s, 1H); MS: *m/z* 528.0 (MH^+).

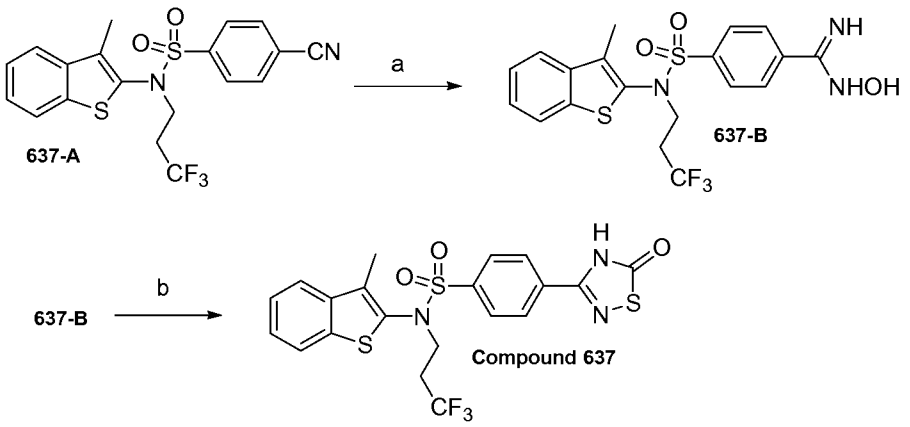
Compound 774

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-3-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.93 (s, 3H), 4.62-4.93 (s, 2H), 7.14-7.16 (m, 2H), 7.23-7.44 (m, 4H), 7.48-7.54 (m, 2H), 7.57-7.67 (m, 2H), 7.85-7.88 (m, 1H), 13.92 (s, 1H); MS: *m/z* 540.0 (MH^+).

Compound 775

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-fluoro-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 4.71-4.86 (m, 2H), 7.36-7.51 (m, 6H), 7.59-7.69 (m, 3H), 7.85-7.88 (m, 1H), 12.84 (s, 1H); MS: *m/z* 542.1 (MH^+).

Example 53



a) DMSO, $H_2NOH{\cdot}HCl$, TEA; b) 1. TCDI; 2. $BF_3{\cdot}OEt$.

Compound **637-A** was prepared as per Example 1, step A, substituting 3-methyl-benzo[*b*]thiophen-2-carboxylic acid for benzo[*b*]thiophen-2-carboxylic acid, step C, substituting 4-cyanobenzenesulfonyl chloride for benzenesulfonyl chloride, and Example 3, step A, substituting trifluoropropan-1-ol for cyclohexylmethanol.

***N*-Hydroxy-4-[(3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide (637-B).** To a solution of compound **637-A** (354 mg; 0.834 mmol) in DMSO (4 mL), purged with N_2, was added hydroxylamine hydrochloride (290 mg; 4.17 mmol) followed by TEA (581 µL; 4.17 mmol) and the reaction was heated under microwave irradiation at 100 °C for 10 min. The reaction was partitioned between H_2O and EtOAc, the layers separated, the organic phase washed with H_2O, brine, dried over $MgSO_4$, filtered and the solvent evaporated under reduced pressure to afford 410.2 mg of compound **637-B** as a white foam. ^{1}H-NMR (DMSO-d_6): δ 2.23 (s, 3H), 2.52-2.59 (m, 2H), 3.85 (s, 2H), 6.03 (s, 2H), 7.39-7.46 (m, 2H), 7.77-7.80 (m, 3H), 7.86-7.93 (m, 3H), 10.04 (s, 1H); MS: *m/z* 457.6 (MH^+).

Compound 637

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** A mixture of compound **637-B** (403 mg; 0.882 mmol) and TCDI (90%; 259 mg; 1.32 mmol) in THF (3.5 mL) was stirred at rt for 30 min. The reaction was diluted with water and extracted with EtOAc. The extract was washed with H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure to afford an off-white foam. The solid was dissolved in THF (3.5 mL) to which was added boron trifluoride diethyl etherate (332

μL; 2.64 mmol) and the reaction stirred at room temperature for 1h. The reaction mixture was partitioned between H_2O and EtOAc, the layers separated, the organic phase washed with H_2O, brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The solid was triturated with MeOH, filtered, washed to MeOH and dried under vacuo to afford 274 mg of compound **637** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 2.23 (s, 3H), 2.52-2.59 (m, 2H), 3.89 (s, 2H), 7.40-7.47 (m, 2H), 7.78-7.79 (m, 1H), 7.80-7.82 (m, 1H), 7.85-7.87 (m, 2H), 7.95-8.19 (m, 2H), 13.68 (s, 1H); MS: *m/z* 499.6 (MH^+).

Following the procedure described above for example 53 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 640

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.54-1.56 (m, 4H), 2.22-2.31 (m, 5H), 3.63-3.74 (m, 2H), 7.38-7.47 (m, 2H), 7.78-7.80 (m, 1H), 7.81-7.87 (m, 1H), 7.93-7.96 (m, 2H), 8.16-8.19 (m, 2H), 13.70 (s, 1H); MS: *m/z* 527.7 (MH^+).

Compound 641

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.000-0.074 (m, 3H), 0.353-0.412 (m, 2H), 0.685-0.751 (m, 1H), 1.35-1.36 (m, 2H), 2.25 (s, 3H), 3.63 (m, 2H), 7.38-7.46 (m, 2H), 7.76-7.82 (m, 1H), 7.83-7.86 (m, 1H), 7.93-7.95 (m, 2H), 8.17-8.19 (m, 1H), 13.69 (s, 1H); MS: *m/z* 471.7 (MH^+).

Compound 642

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** MS: *m/z* 457.7 (MH^+).

Compound 684

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** MS: *m/z* 486.0 (MH^+).

Compound 687

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** MS: *m/z* 514.0 (MH^+).

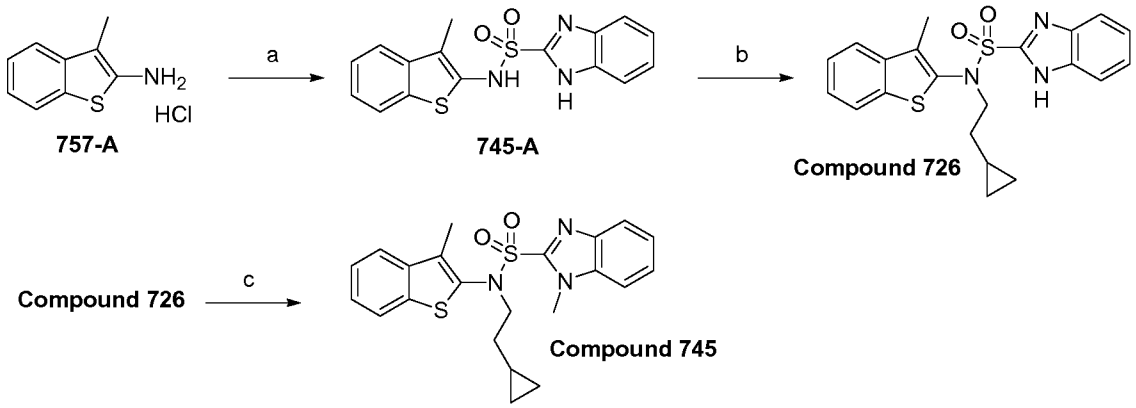
Compound 784

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.95 (s, 3H), 4.87-4.88 (m, 2H), 7.25-7.54 (m, 3H), 7.59-7.68 (m, 4H), 7.83-7.85 (m, 3H), 8.20-8.22 (d, 2H); MS: *m/z* 580.0 (MH^+).

Compound 810

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 1.91 (s, 3H), 4.80-4.85 (m, 2H), 7.28-7.34 (m, 2H), 7.35-7.41 (m, 4H), 7.63-7.66 (m, 1H), 7.81-7.84 (m, 3H), 8.20-8.22 (d, 2H); MS: *m/z* 578.0 (MH^+).

Example 54



a) DCM, pyridine, compound **Int-5**; b) THF, DEAD, PPh_3, cyclopropyl-ethanol; c) DMF, DBU, $(MeO_2)SO_2$.

(3-Methyl-benzo[*b*]thiophen-2-yl)-1*H*-benzoimidazole-2-sulfonamide. To a suspension of compound **757A** (1.89 g; 9.45 mmol) in DCM (20 mL), cooled to 0 °C, was added pyridine (1.68 mL; 20.8 mmol), followed by the addition of compound **Int-5** (2.2 g; 10.1 mmol) in one-portion. The reaction mixture was allowed to stir at ambient temperature for 4 h, diluted with CH_2Cl_2, washed with H_2O (2X), dried over Na_2SO_4, filtered, the solvent evaporated under reduced pressure and the crude residue purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford 1.72 g of compound **745A** as an off-white solid. ^{1}H-NMR (DMSO-d_6): δ 2.13 (s, 3H), 7.31-7.38 (m, 4H), 7.66-7.68 (m, 2H), 7.77-7.79 (m, 2H), 11.18 (s, 1H), 13.63 (s, 1H); MS: m/z 344.0 (MH^+).

Compound 726

***N*-(Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-1*H*-benzimidazole-2-sulfonamide.** To PPh_3 (0.462 g; 1.76 mmol) was added THF (10 mL) followed by DEAD (40%; 815 μL; 1.79 mmol) and the reaction mixture was stirred at ambient temperature for 3 min, to which was added compound **745-A** (0.403 g; 1.17 mmol). The reaction mixture was stirred for 5 min, to which was added cyclopropyl ethanol (0.123 g; 1.43 mmol) and the reaction was stirred for an additional 18 h. The reaction was diluted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude oil was purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 55% to 75% gradient to afford 189 mg of compound **726** as an off-white solid. ^{1}H-NMR (DMSO-d_6): δ 0.008-0.056 (m, 2H), 0.394-0.438 (m, 2H), 0.727-0.802 (m, 1H), 1.45 (m, 2H), 2.28 (s, 3H), 3.83-3.91 (m, 2H), 7.36-7.57 (m, 4H), 7.77-7.82 (m, 4H), 13.78 (s, 1H); MS: m/z 412.0 (MH^+).

Compound 745

***N*-(Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-1-methyl-1*H*-benzimidazole-2-sulfonamide.** To a solution of compound **726** (0.125 g; 0.132 mmol) in DMF (2 mL) was added DBU (99 μL; 0.666 mmol) followed by dimethyl sulfate (32 μL; 0.332 mmol) and the reaction was stirred at 67 °C for 18h. An additional portion of DBU (226 μL; 1.51 mmol) and dimethyl sulfate (144 μL; 1.51 mmol) was added and the reaction mixture was stirred at 67 °C for an additional 18 h. The reaction mixture was cooled, diluted with H_2O, extracted with EtOAc, the layers separated, and the organic phase washed with H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude oil was purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 55% to 75% gradient to afford 107 mg of compound **745** as an oil. ^{1}H-NMR (DMSO-d_6): δ 0.008-0.013 (m, 2H), 0.346-0.391 (m, 2H), 0.685-0.759 (m, 1H), 1.43 (m, 2H), 2.31 (s, 3H), 3.79 (s, 3H), 3.84-3.97 (m, 2H), 7.33-7.38 (m, 3H), 7.39-7.49 (m, 1H), 7.69-7.72 (d, 1H), 7.75-7.81 (m, 2H), 7.88-7.90 (d, 1H); MS: m/z 426.1 (MH^+).

Following the procedure described above for example 54 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 720

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-1*H*-benzimidazole-2-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.48-1.75 (m, 4H), 2.13-2.27 (m, 5H), 3.40-387 (m, 2H), 7.37-7.47 (m, 4H), 7.60-7.83 (m, 4H), 13.83 (s, 1H); MS: m/z 468.1 (MH^+).

Compound 722

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-1-methyl-1*H*-benzimidazole-2-sulfonamide.** MS: m/z 534.2 (MH^+).

Compound 728

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-1*H*-benzimidazole-2-sulfonamide.** MS: m/z 520.0 (MH^+).

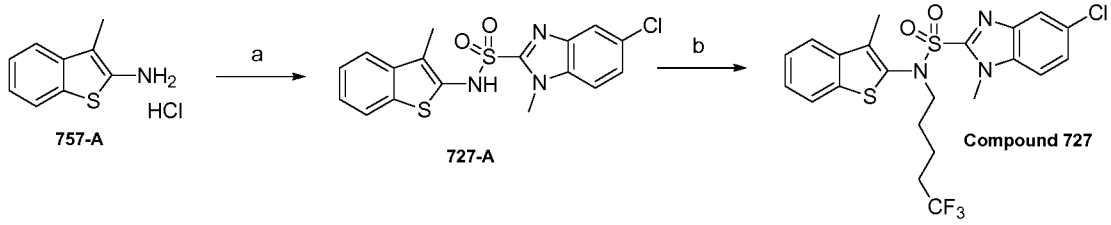
Compound 729

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-1*H*-benzimidazole-2-sulfonamide.** MS: m/z 518.1 (MH^+).

Compound 746

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-1-methyl-1*H*-benzimidazole-2-sulfonamide.** MS: m/z 532.0 (MH^+).

Example 55



a) DCM, pyridine, compound **Int-7**; b) THF, PPh_3, DEAD, 5,5,5-trifluoro-pentan-1-ol.

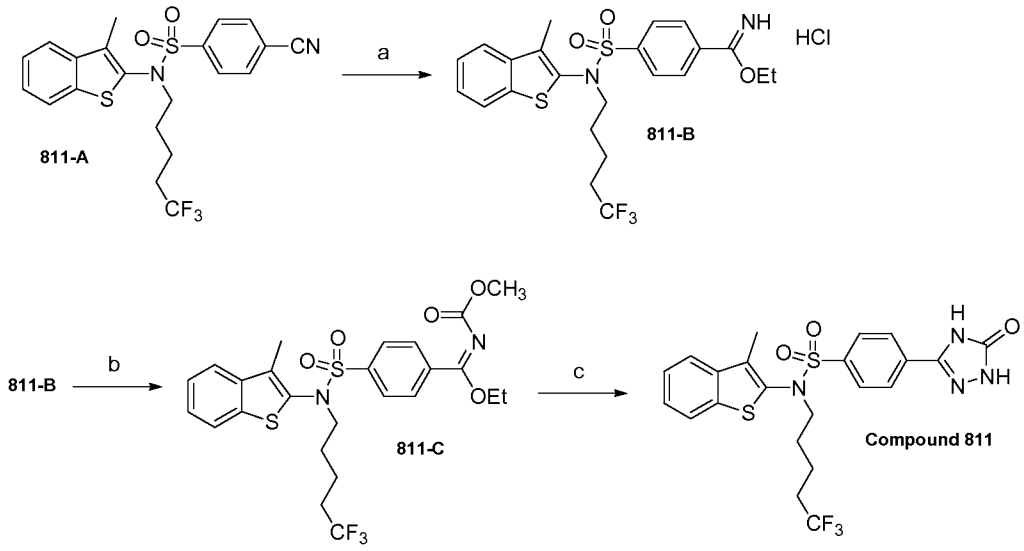
(3-Methyl-benzo[*b*]thiophen-2-yl)-1*H*-benzimidazole-2-sulfonamide (727-A). To a suspension of compound **757-A** (0.589 g; 2.95 mmol) in DCM (20 mL), cooled to 0 °C, was added pyridine (525 μL; 6.49 mmol), followed by the addition of compound **Int-7** (0.5 g; 1.88 mmol) in one-portion. The reaction was allowed to stir at ambient temperature for 4 h, diluted with CH_2Cl_2, washed with H_2O (2X), dried over Na_2SO_4, filtered, the solvent evaporated under reduced pressure and the crude residue purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient

to afford crude compound **727-A**. Compound **727-A** was further purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 60% to 80% gradient to afford 131 mg of compound **727-A** as a white solid. MS: *m/z* 392.0 (MH^+).

Compound 727

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5,-trifluoro-pentyl)-1*H*-benzimidazole-2-sulfonamide.** To PPh_3 (0.068 g; 0.258 mmol) was added THF (1.5 mL) followed by DEAD (40%; 120 μL; 0.263 mmol) and the reaction mixture was stirred at ambient temperature for 3 min, to which was then added compound **727-A** (0.067 g; 0.172 mmol). The reaction mixture was stirred for 5 min, to which was added 5,5,5-trifluoro-pentan-1-ol (0.03 g; 0.210 mmol) and the reaction was stirred for an additional 18 h. The reaction mixture was diluted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude oil was purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 65% to 85% gradient to afford 34 mg of compound **727** as a white solid. MS: *m/z* 516.2 (MH^+).

Example 56



a) EtOH, HCl; b) methyl chloroformate, $CHCl_3$, 2,4,6-collidine; c) CCl_4, H_2NNH_2.

Compound **811-A,** was prepared by the method used to synthesize compound **600** in Example 30, steps A and B.

4-[(3-Methyl-benzo[*b*]thiophen-2-yl)-(5,5,5-trifluoro-pentyl)-sulfamoyl)]-benzimidic acid ethyl ester (811-B). To a solution of compound **811-A** (706 mg; 1.56 mmol), cooled to 0 °C was bubbled HCl(g) for 15 min. The reaction was sealed and allowed to stir 18 h at ambient temperature. The solvent was evaporated under reduced pressure and the solid dried to afford 777 mg of compound **811-B** as a white solid.

(Ethoxy-{4-[(3-methyl-benzo[*b*]thiophen-2-yl)-(5,5,5-trifluoro-pentyl)-sulfamoyl]-phenyl}-methylene)-carbamic acid methyl ester (811-C). To a suspension of compound **811-B** (777 mg; 1.45 mmol), in $CHCl_3$ (1 mL), was added 2,4,6-collidine (275 μL; 1.93 mmol), followed by methyl chloroformate (115 μL; 2.18 mmol) and the reaction was stirred at ambient temperature for 72 h. TEA (200 μL) was added to the reaction, followed by another 1.5 equiv of methyl chloroformate and the reaction was stirred at ambient temperature for 18 h. The reaction was diluted with CH_2Cl_2, washed with H_2O, dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure to afford crude compound **811-C**.

Compound 811

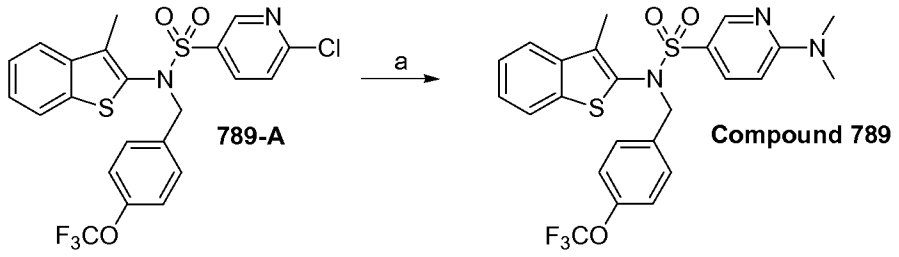
***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-benzenesulfonamide.** To a solution of compound **811-C** (403 mg; 0.775 mmol), in carbontetrachloride (3.5 mL), was added hydrazine (25 μL; 797 mmol) and the reaction was refluxed in a sealed tube for 18 h. The reaction was cooled and the solvent evaporated. The crude reaction was purified by reverse-phase semi-prep HPLC (Gemini, C-18 column; 100 x 30 mm I.D.; 5 μ) eluting with a 50 to 70% gradient to afford 75 mg of compound **811** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 1.52-1.55 (m, 4H), 2.19-2.22 (m, 5H), 3.50-3.69 (m, 2H), 7.39-7.46 (m, 2H), 7.78-7.79 (m, 1H), 7.80-7.90 (m, 3H), 8.00-8.02 (d, 2H), 11.97 (s, 1H), 12.29 (s, 1H); MS: *m/z* 511.0 (MH^+).

Compound 812

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(1-methyl-5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.36-1.40 (m, 4H), 1.92-2.06 (m, 5H), 3.23 (s, 3H), 3.28-3.42 (m, 2H), 7.22-7.29

(m, 2H), 7.61-7.62 (m, 1H), 7.63-7.70 (m, 1H), 7.72-7.74 (d, 2H), 7.83-7.85 (d, 2H), 12.32 (s, 1H); MS: *m/z* 525.0 (MH^+).

Example 57



a) DMSO, dimethylamine.

Compound **789-A,** was prepared by the method used to synthesize compound **757** in Example 29.

Compound 789

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-dimethylamino-3-pyridylsulfonamide**. To a solution of compound **789-A** (0.07 g, 0.14 mmol) in DMSO (1 mL) was added a solution of 2.0 M dimethylamine-tetrahydrofuran (0.205 mL, 0.41 mmol) and the reaction mixture was stirred at ambient temperature for 18 h. The crude reaction was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.06 g of comound **789** as a white solid. ^{1}H NMR (DMSO-d_6) δ 1.98 (s, 3H), 3.16 (s, 6H), 4.72 (br s, 2H), 6.79 (d, 1H), 7.28 (d, 2H), 7.33-7.47 (m, 4H), 7.60-7.71 (m, 1H), 7.76-7.94 (m, 2H), 8.42 (d, 1H); MS: *m/z* 522.2 (MH^+).

Following the procedure described above for example 57 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 786

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-dimethylamino-3-pyridyl-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ -0.10 - 0.07 (m, 2H), 0.27-0.47 (m, 2H), 0.61-0.82 (m, 1H), 1.34 (br s, 2H), 2.31 (s, 3H), 3.16 (s, 6H), 3.40-3.67 (m, 2H), 6.78 (d, 1H), 7.34-7.55 (m, 2H), 7.67-7.85 (m, 2H), 7.85-7.96 (m, 1H), 8.34 (d, 1H); MS: *m/z* 416.1 (MH^+).

Compound 787

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-dimethylamino-3-pyridyl-sulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.51 (br s, 4H), 2.30 (s, 6H), 2.4-2.5 (m, 2H), 3.14 (s, 6H), 6.76 (d, 1H), 7.32-7.52 (m, 2H), 7.72 (dd, 1H), 7.79 (dd, 1H), 7.88 (dd, 1H), 8.34 (d, 1H); MS: *m/z* 472.0 (MH^+).

Compound 788

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-morpholino-3-pyridyl-sulfonamide.** ^{1}H NMR (DMSO-d_6): δ 1.51 (br s, 5H), 2.31 (s, 6H), 3.57 (s, 2H), 3.61-3.82 (m, 9H), 6.97 (d, 1H), 7.35-7.56 (m, 2H), 7.69-7.84 (m, 2H), 7.84-7.94 (m, 1H), 8.39 (d, 1H); MS: *m/z* 514.0 (MH^+).

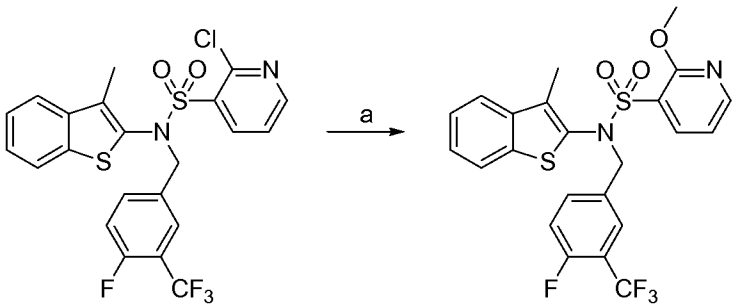
Compound 790

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-morpholino-3-pyridyl-sulfonamide.** ^{1}H NMR (DMSO-d_6): δ 1.99 (s, 3H), 3.65-3.87 (m, 8H), 4.72 (br s, 2H), 7.00 (d, 1H), 7.29 (d, 2H), 7.33-7.50 (m, 4H), 7.60-7.74 (m, 1H), 7.79-7.94 (m, 2H), 8.46 (d, 1H); MS: *m/z* 564.0 (MH^+).

Compound 798

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-morpholino-3-pyridyl-sulfonamide.** MS: *m/z* 451.8 (MH^+).

Example 58



Compound 77 **Compound 357**

a) Toluene, sodium methoxide 0.5 M in MeOH.

Compound 357

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-methoxy-pyridin-3-ylsulfonamide.** To a solution of compound **77** (0.07 g, 0.14 mmol) in toluene (1 mL) was added a solution of 0.5M solution of sodium methoxide in MeOH (0.82 mL, 0.41 mmol) and the reaction mixture was refluxed for 2 h. The

reaction mixture was cooled, diluted with H_2O, extracted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.06 g of compound **357** as a white solid. ^{1}H-NMR ($CDCl_3$) δ 1.78-1.97 (s, 3H), 4.23 (s, 3H), 5.02 (br s, 2H), 6.93 (dd, 1H), 7.10 (t, 1H), 7.30-7.36 (m, 2H), 7.42-7.67 (m, 4H), 8.00 (dd, 1H), 8.38 (dd, 1H); MS: *m/z* 510.9 (MH^+).

Following the procedure described above for example 58 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 358

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-dimethylamino-pyridin-3-yl-sulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 1.88 (s, 3H), 3.07 (s, 6H), 4.95 (br s, 2H), 6.93 (dd, 1H), 7.07 (t, 1H), 7.28-7.36 (m, 2H), 7.37-7.47 (m, 1H), 7.47-7.55 (m, 2H), 7.55-7.62 (m, 1H), 8.02 (dd, 1H), 8.47 (dd, 1H); MS: *m/z* 524.0 (MH^+).

Compound 359

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methoxy-pyridin-3-yl-sulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.04-2.15 (m, 3H), 4.05 (s, 3H), 4.68 (br s, 2H), 6.85 (d, 1H), 7.07 (t, 1H), 7.30-7.50 (m, 3H), 7.50-7.75 (m, 3H), 7.88 (dd, 1H), 8.62 (d, 1H); MS: *m/z* 510.9 (MH^+).

Compound 360

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-dimethylamino-pyridin-3-yl-sulfonamide.** MS: *m/z* 524.0 (MH^+).

Compound 377

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-2-thiomethyl-pyridin-3-yl-sulfonamide.** MS: *m/z* 527.0 (MH^+).

Compound 378

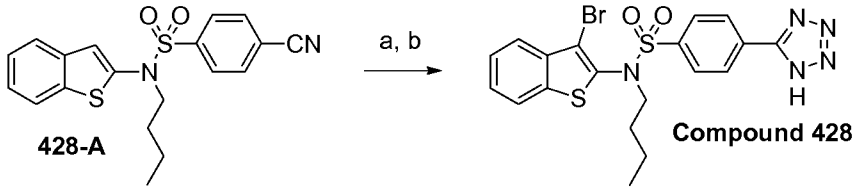
***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-thiomethyl-pyridin-3-yl-sulfonamide.** MS: *m/z* 527.0 (MH^+).

Compound 448

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-2-dimethylamino-pyridin-3-yl-sulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, 3H), 1.37 (m, 2H), 1.45-1.62 (m, 2H),

2.38 (s, 3H), 3.17 (s, 6H), 3.72 (m., 2H), 6.99 (dd, 1H), 7.37 (m, 2H), 7.59-7.80 (m, 2H), 8.14-8.29 (m, 1H), 8.37-8.50 (m, 1H); MS: *m/z* 404.1 (MH^+).

Example 59



a) NaN_3, NH_4Cl, DMF; b) NBS, DMF.

Compound **428-A,** was prepared by the method used to synthesize compound **600** in Example 30, steps A and B.

Compound 428

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** Dimethylformamide (2 mL), sodium azide (0.098 g, 1.5 mmol), ammonium chloride (0.08 g, 1.5 mmol) and compound **428-A** (0.185g, 0.5 mmol) were added to a microwave vessel with stir bar, sealed, and heated in a 300 watt microwave reactor to 160 °C for 10 min. The solution was decanted, *N*-bromosuccinimide (0.356 g, 2.0 mmol) was added to the solution and stirred for 3 h at ambient temperature. The solution was diluted with H_2O, extracted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent was evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.124 g of compound **428** as a white solid. ^{1}H-NMR (CD_3OD) δ 0.91 (t, 3H), 1.48 (tt, 4H), 3.74 (t, 2H), 7.35-7.59 (m, 2H), 7.73-7.88 (m, 2H), 7.93 (m, 2H), 8.26 (m, 2H); MS: *m/z* 492.0 (MH^+).

Following the procedure described above for example 59 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 424

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 4.98 (s, 2H), 7.16 (s, 1H), 7.25-7.29 (m, 2H), 7.41-7.46 (t, 1H), 7.65-7.69 (m, 3H), 7.76-7.79 (m, 1H), 8.00-8.02 (d, 2H), 8.24-8.26 (d, 2H); MS: m/z 534.0 (MH^+).

Compound 425

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. MS: m/z 468.0 (MH^+).

Compound 429

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-butyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (CD_3OD) δ 1.82 (br s, 2H), 2.41 (br s, 2H), 3.83 (s, 2H), 7.44-7.60 (m, 2H), 7.77-7.89 (m, 2H), 7.93 (m, 2H), 8.27 (m, 2H); MS: *m/z* 546.0 (MH^+).

Compound 449

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. MS: m/z 414.0 (MH^+).

Compound 455

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. MS: m/z 548.0 (MH^+).

Compound 474

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-methyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 0.05-0.17 (m, 2H), 0.38 (d, 2H), 0.90 (br s, 1H), 3.55 (br s, 2H), 7.40-7.63 (m, 2H), 7.72-7.81 (m, 1H), 7.85 (m, 2H), 7.94-8.08 (m, 1H), 8.20 (m, 2H); MS: *m/z* 490.0 (MH^+).

Compound 475

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 4.92 (br s, 2H), 7.35-7.54 (m, 3H), 7.60-7.80 (m, 3H), 7.85-8.03 (m, 3H), 8.24 (d, 2H); MS: *m/z* 612.0 (MH^+).

Compound 539

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)- 4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, 3H), 1.28-1.45 (m, 2H), 1.45-1.59 (m, 2H), 2.39 (s, 3H), 3.54 (s, 2H), 7.30-7.48 (m, 2H), 7.58-7.77 (m, 2H), 7.93 (m, 2H), 8.27 (m, 2H); MS: *m/z* 428.1 (MH^+).

Compound 542

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.07 (s, 3H), 3.53 (br

s, 2H), 7.01-7.14 (m, 1H), 7.30-7.41 (m, 2H), 7.45 (dd, 1H), 7.55 (dd, 1H), 7.57-7.68 (m, 2H), 7.98 (m, 2H), 8.34 (m, 2H); MS: *m/z* 548.1 (MH^+).

Compound 569

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. MS: m/z 425.7 (MH^+).

Compound 570

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ -0.12-0.09 (m, 2H), 0.25-0.47 (m, 2H), 0.59-0.84 (m, 1H), 1.34 (br s, 2H), 2.26 (s, 3H), 3.62 (br s, 2H), 7.31-7.51 (m, 2H), 7.69-7.83 (m, 3H), 7.83-7.92 (m, 1H), 8.20 (d, 2H); MS: *m/z* 440.1 (MH^+).

Compound 571

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. MS: m/z 453.7 (MH^+).

Compound 572

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide**. ^{1}H-NMR (DMSO-d_6): δ 2.25 (s, 3H), 2.51-2.67 (m, 2H), 3.90 (m, 2H), 7.40-7.47 (m, 2H), 7.78-7.82 (dd, 1H), 7.84-7.88 (m, 1H), 8.02-8.04 (d, 2H), 8.28-8.30 (d, 2H); MS: *m/z* 467.7 (MH^+).

Compound 579

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.56 (d, 4H), 2.10-2.33 (m, 2H), 3.71 (br s, 2H), 7.43-7.60 (m, 2H), 7.72-7.85 (m, 1H), 7.94-8.06 (m, 1H), 8.09 (m, 2H), 8.31 (m, 2H); MS: *m/z* 561.6 (MH^+).

Compound 580

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(1*H*-tetrazol-5-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.41-1.69 (m, 4H), 2.15-2.36 (m, 2H), 3.66 (t, 2H), 7.42-7.64 (m, 2H), 7.74-7.92 (m, 3H), 7.94-8.09 (m, 1H), 8.21 (d, 2H); MS: *m/z* 516.0 (MH^+).

Compound 804

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(1*H*-tetrazol-5-yl)-pyridin-3-ylsulfonamide.** Compound **804** was prepared using the procedure in Example 59, step A, substituting compound **428-A** with compound **Int-9**. ^{1}H-NMR (DMSO-d_6) δ -0.01 (q, 2H), 0.22-0.45 (m, 2H), 0.57-0.80 (m, 1H), 1.37 (br s, 2H), 2.27

(s, 3H), 3.67 (br s, 2H), 7.31-7.53 (m, 2H), 7.79 (dd, 1H), 7.81-7.93 (m, 1H), 8.33-8.57 (m, 2H), 9.04 (d, 1H); MS: *m/z* 441.0 (MH^+).

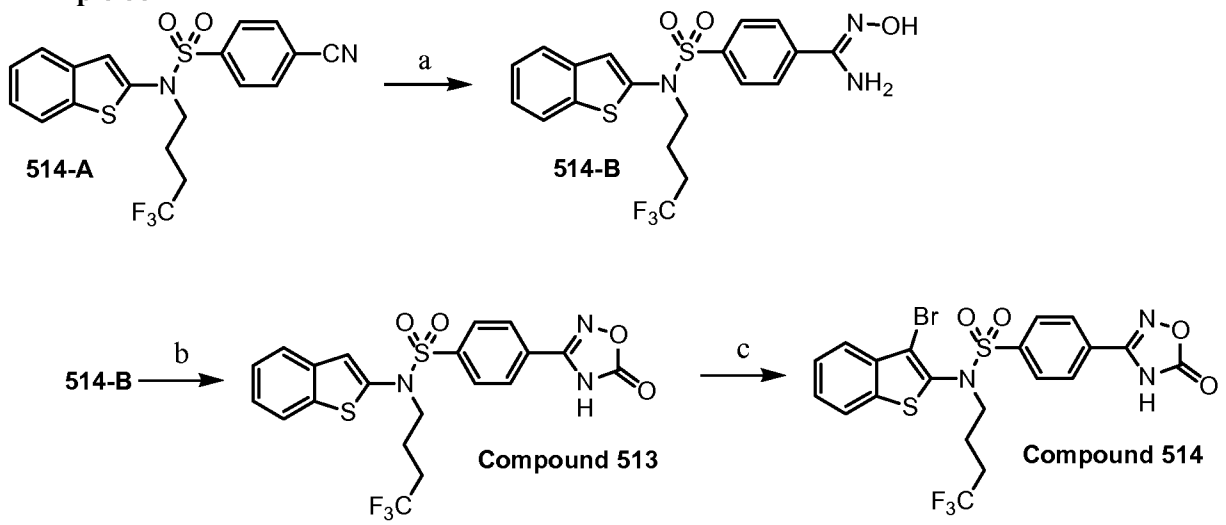
Compound 805

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-(1*H*-tetrazol-5-yl)-pyridin-3-ylsulfonamide.** Compound **805** was prepared using the procedure in Example 59, step A, substituting compound **428-A** with compound **Int-9**. ^{1}H-NMR (DMSO-d_6) δ 1.83-2.01 (m, 3H), 4.88 (br s, 2H), 7.32 (d, 2H), 7.34-7.52 (m, 4H), 7.61-7.74 (m, 1H), 7.80-7.96 (m, 1H), 8.50 (d, 1H), 8.57 (dd, 1H), 9.18 (d, 1H); MS: *m/z* 547.0 (MH^+).

Compound 806

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(1*H*-tetrazol-5-yl)-pyridin-3-ylsulfonamide.** Compound **806** was prepared using the procedure in Example 59, step A, substituting compound **428-A** with compound **LMR-2-B**. ^{1}H-NMR (DMSO-d_6) δ 1.45 (d, 5H), 2.10 (br s, 3H), 2.13-2.22 (m, 3H), 7.16-7.42 (m, 2H), 7.71 (dd, 1H), 7.77 (dd, 1H), 8.24-8.44 (m, 2H), 8.97 (d, 1H); MS: *m/z* 497.1 (MH^+).

Example 60



a) DMSO, $NH_2OH{\cdot}HCl$, TEA; b) DMF, 2-ethylhexylchloroformate, pyridine; c) DCE, NBS.

Compound **514-A,** was prepared by the method used to synthesize compound **600** in Example 30, steps A and B.

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-*N*-hydroxy-benzamidine sulfonamide (514-B).** Compound **514-A** (1.0 g, 2.7 mmol), triethylamine (1.88 mL, 13.5 mmol), hydroxylamine hydrochloride (0.938 g, 13.5 mmol), and dimethylsulfoxide (4 mL) were added to a microwave vessel with stir bar, sealed and heated in a 300 watt microwave reactor to 160 °C for 10 min. The solids were rinsed with DMSO, filtered, the organic washes diluted with H_2O, extracted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. Crude compound **514-B** crystallized to afford 1.0 g of an off white solid. MS: *m/z* 458.0 (MH^+).

Compound 513

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** To an ice-cooled solution of pyridine (0.10 mL, 1.24 mmol) and compound **514-B** (0.50 g, 1.24 mmol), sealed in a microwave vessel, under N_2, was added 2-ethylhexylchloroformate (0.239 g, 1.24 mmol), drop-wise. The reaction mixture was stirred at 0 °C for 30 mins and heated at 140 °C for 30 min in a 300 watt microwave. The solution was diluted with H_2O, extracted with EtOAc, washed with H_2O, brine, Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.175 g of compound **513** as a white solid. ^{1}H-NMR (DMSO-d_6) δ 1.66-1.82 (m, 2H), 2.26-2.45 (m, 2H), 3.78 (t, 2H), 7.25-7.37 (m, 1H), 7.37-7.46 (m, 2 H), 7.77-7.84 (m, 1H), 7.86-7.93 (m, 1H), 7.96 (m, 2H), 8.04 (m, 2H), 13.21 (br s, 1H); MS: *m/z* 484.1 (MH^+).

Compound 514

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** *N*-Bromosuccinimide (0.037 g, 0.21 mmol) was added to a solution of dichloroethane (2 mL), and compound **513** (0.10 g, 0.21mmol) and the reaction mixture was stirred at ambient temperature for 18 h. The solution was diluted with H_2O, extracted with EtOAc, washed with H_2O, brine, Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.024 g of compound **514** as a white solid. ^{1}H-NMR (DMSO-d_6): δ1.60-1.79 (m,

2H), 2.24-2.45 (m, 2H), 3.68-3.83 (m, 2 H), 7.45-7.66 (m, 2H), 7.69-7.92 (m, 1H), 7.92-8.17 (m, 5H), 13.25 (br s, 1H); MS: *m/z* 562.8 (MH^+).

Following the procedure described above for example 60 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 442

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide**. MS: *m/z* 430.0 (MH^+).

Compound 443

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (CD_3OD) δ 0.91 (t, 3H), 1.32-1.60 (m, 4H), 3.63-3.83 (m, 2H), 7.46-7.62 (m, 2H), 7.74-7.88 (m, 2H), 7.90 (m, 2H), 8.00 (s, 2H), 8.06 (m, 2H); MS: *m/z* 507.9 (MH^+).

Compound 471

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-*N*-hydroxy-benzamidinesulfonamide.** MS: *m/z* 404.1 (MH^+).

Compound 473

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-*N*-hydroxy-benzamidinesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 0.73-0.89 (m, 3H), 1.30-1.46 (m, 4H), 3.64 (br s, 2H), 7.46-7.61 (m, 3H), 7.74-7.84 (m, 1H), 7.92 (d, 2H), 7.97-8.03 (m, 1H), 8.09 (d, 2H), 8.24 (s, 1H); MS: *m/z* 484.4 (MH^+).

Compound 482

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-*N*-hydroxy-benzamidinesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 5.03 (s, 2H), 7.19 (s, 1H), 7.29-7.38 (m, 2H), 7.50 (t, 1H), 7.66-7.78 (m, 3H), 7.78-7.88 (m, 1H), 7.95 (s, 4H); MS: *m/z* 524.5 (MH^+).

Compound 483

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 5.03 (s, 2H), 7.21 (s, 1H), 7.26-7.39 (m, 2H), 7.41-7.59 (m, 1H), 7.62-7.78 (m, 3H), 7.78-7.93 (m, 1H), 7.98-8.16 (m, 4H), 13.24 (br s, 1H); MS: *m/z* 550.1 (MH^+).

Compound 511

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 4.91 (s, 2H), 7.05-7.17 (m, 1H), 7.35-7.48 (m, 2H), 7.48-7.57 (m, 2H), 7.71 (dd, 2H), 7.95 (m, 2H), 8.03 (m, 2H); MS: *m/z* 628.0 (MH^+).

Compound 512

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** Compound **512** was synthesized as per compound **514** of Example 60, substituting NBS with NCS. ^{1}H-NMR ($CDCl_3$) δ 4.89 (s, 2H), 7.12 (d, 1H), 7.39-7.48 (m, 2H), 7.53 (d, 2H), 7.63-7.76 (m, 2H), 7.94 (m, 2H), 8.03 (m, 2H); MS: *m/z* 584.0 (MH^+).

Compound 515

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** Compound **515** was synthesized as per compound **514** of Example 60, substituting NBS with NCS. MS: *m/z* 515.8 (MH^+).

Compound 541

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, 3H), 1.31-1.44 (m, 2H), 1.5-1.6 (m, 2H), 2.40 (s, 3H), 3.55 (br s, 2H), 7.31-7.49 (m, 2H), 7.58-7.79 (m, 2H), 7.84-8.04 (m, 4H), 10.72 (s, 1H); MS: *m/z* 444.1 (MH^+).

Compound 544

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.02-2.19 (m, 3H), 4.76 (br s, 2H), 7.08 (t, 1H), 7.34-7.41 (m, 2H), 7.42-7.48 (m, 1H), 7.54 (dd, 1H), 7.58-7.68 (m, 2H), 7.99 (m, 4H), 11.25 (br s, 1H); MS: *m/z* 564.0 (MH^+).

Compound 583

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.40-1.68 (m, 4H), 2.12-2.34 (m, 2H), 3.70 (br s, 2H), 7.39-7.64 (m, 2H), 7.64-7.86 (m, 1H), 7.98-8.04 (m, 1H), 8.07 (s, 4H), 13.24 (br s, 1H); MS: *m/z* 577.6 (MH^+).

Compound 584

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** Compound **584** was synthesized as per compound **514** of Example 60, substituting NBS with NCS. ^{1}H-NMR (DMSO-d_6) δ 1.57-1.62 (m 4H) 2.18-2.39 (m, 2H) 3.57-3.86 (m, 2H) 7.46-7.65 (m, 2H) 7.68-7.87 (m, 1H) 7.98-8.04 (m, 1H) 8.07 (s, 4H) 13.24 (br s, 1H); MS: *m/z* 531.6 (MH^+).

Compound 597

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** MS: *m/z* 496.6 (MH^+).

Compound 599

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 2.24 (s, 3H), 2.54-2.63 (m, 2H), 3.88 (br s, 2H), 7.35-7.56 (m, 2H), 7.78-7.83 (m, 1H), 7.84-7.90 (m, 1H), 7.99-8.08 (m, 4H), 13.23 (br s, 1H); MS: *m/z* 483.6 (MH^+).

Compound 608

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 2.54-2.77 (m, 2H), 4.00 (t, 2H), 7.44-7.64 (m, 2H), 7.68-7.85 (m, 1H), 7.94-8.21 (m, 5H), 13.25 (br s, 1H); MS: *m/z* 549.6 (MH^+).

Compound 609

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide**. Compound **609** was synthesized as per compound **514** of Example 60, substituting NBS with NCS. MS: *m/z* 503.7 (MH^+).

Compound 612

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide**. MS: *m/z* 441.7 (MH^+).

Compound 613

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 0.1-0.2 (m, 2H), 0.4-0.48 (m, 2H), 0.52-0.77 (m, 1H), 1.36 (br s, 2H), 2.26 (s, 3H), 3.65 (br s,

2H), 7.26-7.55 (m, 2H), 7.74-7.82 (m, 1H), 7.82-7.89 (m, 1H), 8.00 (m, 2H), 8.06 (m, 2H), 13.24 (br s, 1H); MS: *m/z* 455.7 (MH^+).

Compound 626

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 0.1-0.2 (m, 2H), 0.30-0.54 (m, 2H), 0.69-0.91 (m, 1H), 1.39 (br s, 2H), 3.64-3.89 (m, 2H), 7.55 (dd, 2H), 7.70-7.93 (m, 1H), 7.94-8.24 (m, 5H), 13.25 (br s, 1H); MS: *m/z* 520.1 (MH^+).

Compound 627

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** Compound **627** was synthesized as per compound **514** of Example 60, substituting NBS with NCS. ^{1}H-NMR (DMSO-d_6) δ 0.1-0.2 (m, 2H), 0.26-0.43 (m, 2H,) 0.69-0.80 (m, 1H), 1.38 (q, 2H), 3.73 (t, 2H), 7.47-7.61 (m, 2H,) 7.68-7.85 (m, 1H), 7.89-8.18 (m, 5H), 13.25 (br s, 1H); MS: *m/z* 476.6 (MH^+).

Compound 801

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.92 (s, 3H), 4.83 (br s, 2H), 7.26-7.35 (m, 2H), 7.35-7.45 (m, 4H), 7.63-7.72 (m, 1H), 7.83 (dd, 1H), 8.09 (s, 4H), 13.27 (br s, 1H); MS: *m/z* 562.0 (MH^+).

Compound 807

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-pyrid-3-ylsulfonamide.** Compound **807** was prepared using the procedure in Example 60, step A, substituting compound **514-A** with compound **Int-9**. ^{1}H-NMR (DMSO-d_6) δ -0.16-0.13 (m, 2H), 0.23-0.46 (m, 2H), 0.72 (br s, 1H), 1.3–1.4 (m, 2H), 3.61 (br s, 2H), 7.29-7.54 (m, 2H), 7.81 (dd, 1H), 7.88 (dd, 1H), 8.24 (d, 1H), 8.46 (dd, 1H), 9.02 (d, 1H), 13.49 (s, 1H); MS: *m/z* 457.0 (MH^+).

Compound 808

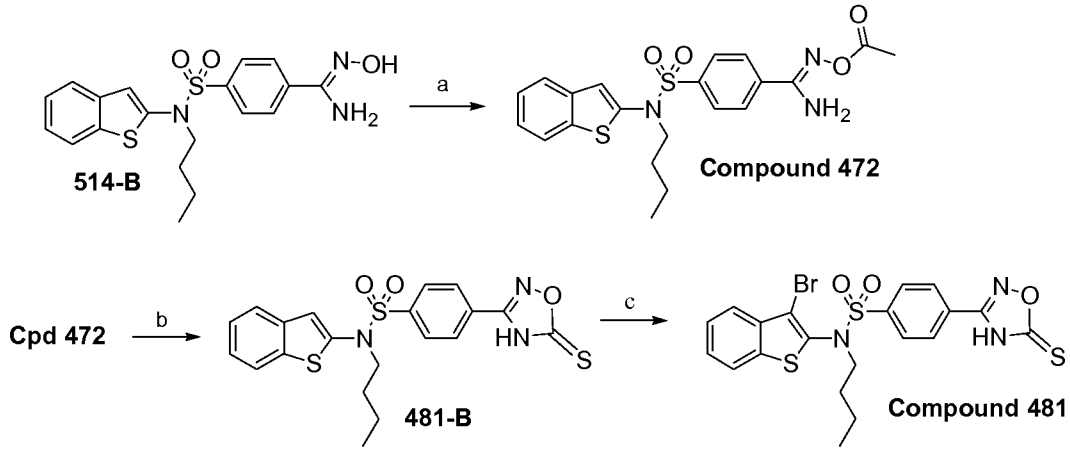
***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-pyrid-3-ylsulfonamide.** Compound **808** was prepared using the procedure in Example 60, step A, substituting compound **514-A** with compound **Int-9**. ^{1}H-NMR (DMSO-d_6) δ 1.79-2.08 (m, 3H,) 4.90 sa(br s, 2H),

7.32 (d, 2H), 7.35-7.48 (m, 4H), 7.59-7.78 (m, 1H), 7.78-7.91 (m, 1H), 8.27 (d, 1H), 8.53 (dd, 1H), 9.14 (d, 1H), 13.46-13.57 (m, 1H); MS: *m/z* 563.0 (MH^+).

Compound 809

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-pyrid-3-ylsulfonamide.** Compound **809** was prepared using the procedure in Example 60, step A, substituting compound **514-A** with compound **Int-9**. ^{1}H-NMR (DMSO-d_6) δ 1.43-1.63 (m, 5H), 2.24 (br s, 3H), 2.27-2.37 (m, 3H), 7.30-7.57 (m, 2H), 7.82 (dd, 1H), 7.87-8.00 (m, 1H), 8.24 (d, 1H), 8.46 (dd, 1H), 9.04 (d, 1H), 13.49 (br s, 1H); MS: *m/z* 513.0 (MH^+).

Example 61



a) DCM, acetic anhydride, TEA; b) DMF, CS_2, NaH; c) DMF, DCE, NBS.

Compound 472

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-*N*-hydroxyacetyl-benzamidine sulfonamide**. A solution of compound **514-B** (0.5 g 1.24 mmol), DCM (5 mL), acetic anhydride (0.126 g 1.24 mmol), and triethylamine (0.125 g 1.24 mmol) was stirred at ambient temperature for 18 h. The solution was diluted with H_2O, extracted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.340 g of compound **472** as a white solid. MS: *m/z* 446.1 (MH^+).

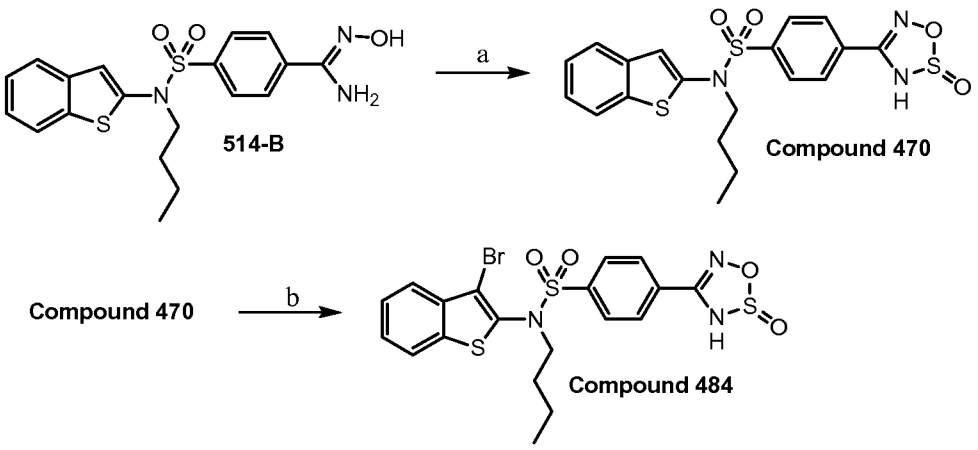
***N*-Benzo[*b*]thiophen-2-yl-*N*-(butyl)-4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide (481-B)**. To an ice-cooled mixture of

compound **472** (0.220 g, 0.494 mmol) and carbon disulfide (0.113 mL, 1.88 mmol) in DMF was added sodium hydride (0.036 g, 1.48 mmol) and the reaction mixture was stirred at 0 °C and allowed to warm to ambient temperature over 18 h. The reaction mixture was diluted with 1N hydrochloric acid, the aqueous phase extracted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.110 g of compound **481-B** as a pale, yellow solid. ^{1}H-NMR (DMSO-d_6) δ 0.86 (t, 3H), 1.25-1.42 (m, 2H), 1.42-1.58 (m, 2H), 3.68 (t, 4H), 7.25 (s, 1H), 7.29-7.45 (m, 2H), 7.72-7.83 (m, 1H), 7.83-7.94 (m, 3H), 8.08 (d, 2H); MS: *m/z* 446.1 (MH^+).

Compound 481

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-benzenesulfonamide**. *N*-Bromosuccinimide (0.048 , 0.27 mmol) was added to a solution of dichloroethane (2 mL), dimethylformamide (2 mL) and compound **481-B** (0.120 g, 0.27 mmol) and stirred at ambient temperature for 18h. The reaction mixture was diluted with H_2O, the aqueous phase extracted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.019 g of compound **481** pale, pink solid. ^{1}H-NMR (DMSO-d_6) δ 0.83 (t, 3H), 1.24-1.51 (m, 4H), 3.66 (br s, 3H), 7.44-7.60 (m, 2H), 7.69-7.83 (m, 1H), 7.94-8.07 (m, 3H), 8.07-8.21 (m, 2H); MS: *m/z* 525.1 (MH^+).

Example 62



a) THF, pyridine, $SOCl_2$; b) DCE, DMF, NBS.

Compound 470

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** To an ice-cooled solution of compound **514-B** (0.250 g, 0.62 mmol), pyridine (0.098 g, 1.24 mmol) and THF (4 mL) was added, drop-wise, a solution of thionyl chloride (0.073 g, 0.62 mmol) in DCM (1 mL), and the resulting mixture was stirred for 30 min at 0 °C. The solvent was evaporated *in vacuo*, the residue dissolved in water and extracted with $CHCl_3$. The solvent was evaporated *in vacuo* and the crude residue purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.224 g of compound **470** as a white solid. MS: *m/z* 450.0 (MH^+).

Compound 484

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** To a solution of compound **470** (0.130 g, 0.289 mmol), DCE (2 mL), and DMF(2 mL) was added *N*-bromosuccinimide (0.051 g, 0.289 mmol) and the reaction mixture was stirred at ambient temperature for 18 h. The reaction mixture was washed with H_2O, the organics separated, and the solvent was evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.084 g of compound **484** as a white solid. ^{1}H-NMR (DMSO-d_6) δ 0.73-0.93 (m, 3H), 1.27-1.53 (m, 4H), 3.59-3.81 (m, 2H), 7.44-7.62 (m, 2H), 7.73-7.85 (m, 1H), 7.93-8.07 (m, 3H), 8.07-8.21 (m, 2H); MS: *m/z* 529.4 (MH^+).

Following the procedure described above for example 62 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 485

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** Compound **485** was synthesized as per compound **484** of Example 62, substituting NBS with NCS. ^{1}H-NMR (DMSO-d_6) δ 0.75-0.91 (m, 3H), 1.26-1.52 (m, 4H), 3.67 (t, 2H), 7.45-7.61 (m, 2H), 7.75-7.89 (m, 1H), 7.95-8.07 (m, 3H), 8.07-8.20 (m, 2H); MS: *m/z* 485.4 (MH^+).

Compound 540

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, 3H), 1.28-1.44 (m, 2H), 1.44-1.59 (m, 2H), 2.38 (s, 3H), 3.51 (s, 2H), 7.30-7.46 (m, 2H), 7.60-7.76 (m, 2H), 7.78-7.91 (m, 3H), 7.99 (s, 1H); MS: *m/z* 464.1 (MH^+).

Compound 543

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** ^{1}H-NMR ($CDCl_3$) δ 2.02-2.12 (s, 3H), 4.67 (br s, 2H), 7.08 (t, 1H), 7.31-7.38 (m, 2H), 7.44 (dt, 1H), 7.49-7.57 (m, 1H), 7.57-7.73 (m, 2H), 7.82-7.99 (m, 4H); MS: *m/z* 548.1 (MH^+).

Compound 581

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.57 (m, 4H), 2.10-2.36 (m, 2H), 3.71 (br s, 2H), 7.43-7.66 (m, 2H), 7.74-7.85 (m, 1H), 7.94-8.09 (m, 3H), 8.09-8.21 (m, 2 H); MS: *m/z* 597.1 (MH^+).

Compound 582

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** Compound **582** was synthesized as per compound **484** of Example 62, substituting NBS with NCS. MS: *m/z* 551.5 (MH^+).

Compound 596

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** MS: *m/z* 489.6 (MH^+).

Compound 598

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 2.15-2.30 (s, 3H), 2.54-2.64 (m, 2H), 3.41 (br s, 2H), 7.36-7.53 (m, 2H), 7.75-7.83 (m, 1H), 7.83-7.94 (m, 1H), 8.00 (m, 2H), 8.10 (m, 2H); MS: *m/z* 503.7 (MH^+).

Compound 607

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** MS: *m/z* 569.9 (MH^+).

Compound 610

***N*-(Benzo[b]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** MS: *m/z* 461.7 (MH^+).

Compound 611

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 0.1-0.2 (m, 2H) 0.28-0.43 (m, 2H) 0.70 (d, 1H) 1.36 (br s, 2H) 2.26 (s, 3H) 3.64 (br s, 2H) 7.28-7.51 (m, 2H) 7.70-7.83 (m, 1H) 7.83-7.93 (m, 1H) 7.99 (d, 2H) 8.04-8.19 (m, 2H); MS: *m/z* 475.6 (MH^+).

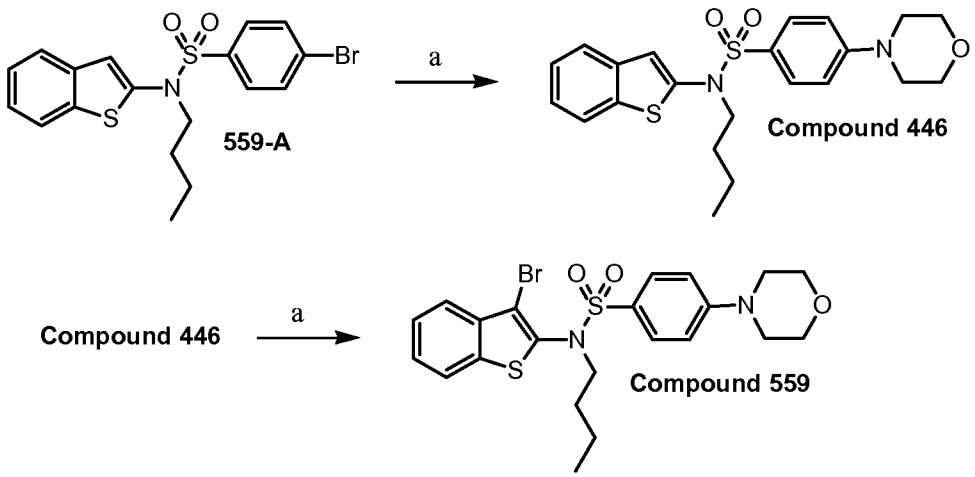
Compound 624

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 0.1-0.2 (m, 2H), 0.29-0.46 (m, 2H), 0.63-0.86 (m, 1H), 1.38 (q, 2H), 3.74 (t, 2H), 7.44-7.62 (m, 2H), 7.71-7.84 (m, 1H), 7.93-8.07 (m, 3H), 8.07-8.20 (m, 2H); MS: *m/z* 539.4 (MH^+).

Compound 625

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-(3*H*-[1,2,3,5]oxathiadiazole-2-oxide)-benzenesulfonamide.** CompoundCompound **625** was synthesized as per compound **484** of Example 62, substituting NBS with NCS. ^{1}H-NMR (DMSO-d_6) δ 0.1-0.2 (m, 2H) 0.29-0.43 (m, 2H) 0.68-0.83 (m, 1H) 1.38 (q, 2H) 3.74 (t, 2H) 7.47-7.60 (m, 2H) 7.72-7.87 (m, 1H) 7.96-8.07 (m, 3H) 8.07-8.18 (m, 2H); MS: *m/z* 495.5 (MH^+).

Example 63



a) KO-*t*Bu, $Pd_2(dba)$, 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthine, morpholine, dioxane.

Compound **559-A,** was prepared by the method used to synthesize compound **600** in Example 30, steps A and B.

Compound 446

***N*-Benzo[*b*]thiophen-2-yl-*N*-(butyl)-4-morpholin-4-yl-benzenesulfonamide.** Compound **559-A** (0.10 g, 0.236 mmol), 1.0 M potassium t-butoxide-THF (1.41 mL, 1.41mmol), Pd(dba) (0.01 g, 0.011 mmol), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthine, (0.006 g, 0.011 mmol), morpholine (0.04 mL, 0.47 mmol) and dioxane (4 mL) were added to a microwave vessel with stir bar and heated at 100 °C for 30 min in a 300 watt microwave reactor. The reaction mixture was diluted with H_2O, extracted with EtOAc, and the solvent evaporated under reduced pressure. The crude residue was dissolved in acetonitrile, the solution filtered and purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.021 g of compound **446** as a dark, viscous oil. ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, 3H), 1.29-1.46 (m, 2H), 1.50-1.63 (m, 2H), 3.23-3.34 (m, 4H), 3.57 (t, 2H), 3.81-3.93 (m, 4H), 6.84 (m, 2H), 7.13 (s, 1H), 7.29-7.40 (m, 2H), 7.57 (m, 2H), 7.63-7.73 (m, 2H); MS: *m/z* 431.1 (MH^+).

Compound 559

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-morpholine-benzenesulfonamide.** N-Bromosuccinimide (0.030 g, 0.167 mmol) was added to a solution of dichloroethane (2 mL), and compound **446** (0.072 g, 0.167 mmol) and

stirred at ambient temperature for 2 h. The reaction mixture was diluted with H_2O, extracted with EtOAc, and the solvent evaporated under reduced pressure. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.050 g of compound **559** as a dark, green gum. ^{1}H-NMR ($CDCl_3$): δ 0.86 (t, 3H), 1.29-1.45 (m, 2H), 1.45-1.59 (m, 2H), 3.23-3.38 (m, 4H), 3.60 (t, 2H), 3.82-3.98 (m, 4H), 6.78-6.95 (m, 2H), 7.34-7.49 (m, 2H), 7.63-7.75 (m, 3H), 7.75-7.84 (m, 1H); MS: *m/z* 511.0 (MH^+).

Following the procedure described above for example 63 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 444

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-dimethylamino-benzenesulfonamide.** MS: *m/z* 389.1 (MH^+).

Compound 445

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-pyrrolidin-1-yl-benzenesulfonamide.** MS: *m/z* 415.0 (MH^+).

Compound 447

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-(4-methyl-piperazin-1-yl)-benzenesulfonamide.** MS: *m/z* 444.1 (MH^+).

Compound 560

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-dimethylamino-benzenesulfonamide.** MS: *m/z* 467.0 (MH^+).

Compound 561

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-dimethylamino-benzenesulfonamide.** Compound **561** was synthesized as per compound **559** of Example 63, substituting NBS with NCS. ^{1}H-NMR ($CDCl_3$) δ 0.86 (t, 3H) 1.28-1.44 (m, 2H) 1.44-1.55 (m, 2H) 3.06 (s, 6H) 3.57 (t, 2H) 6.65 (m, 2H) 7.35-7.50 (m, 2H) 7.65 (m, 2H) 7.67-7.74 (m, 1H) 7.75-7.86 (m, 1H); MS: *m/z* 423.0 (MH^+).

Compound 562

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-morpholin-4-yl-benzenesulfonamide.** Compound **562** was synthesized as per compound **559** of Example 63, substituting NBS with NCS. MS: *m/z* 465.0 (MH^+).

Compound 738

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-dimethylamino-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ -0.11-0.05 (m, 2H), 0.31-0.46 (m, 2H), 0.59-0.81 (m, 1H), 1.34 (br s, 2H), 2.31 (s, 3H), 3.08 (s, 6H), 3.52 (br s, 2H), 6.76-6.93 (m, 2H), 7.35-7.51 (m, 2 H), 7.51-7.63 (m, 2H), 7.73-7.84 (m, 1H), 7.84-7.97 (m, 1H); MS: *m/z* 415.2 (MH^+).

Compound 739

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-diethylamino-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ -0.11-0.06 (m, 2H), 0.31-0.50 (m, 2H), 0.62-0.80 (m, 1H), 1.36 (br s, 2H), 2.27 (s, 3H), 3.01 (br s, 4H), 3.62 (br s, 3H), 3.80 (br s, 3H), 3.98 (s, 1H), 7.36-7.58 (m, 2H), 7.65-7.76 (m, 2H), 7.76-7.84 (m, 1H), 7.84-7.98 (m, 3H); MS: *m/z* 443.3 (MH^+).

Compound 740

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-thiomorpholin-4-yl-benzenesulfonamide**. MS: *m/z* 473.2 (MH^+).

Compound 741

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-morpholino-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ -0.09-0.11 (m, 2H), 0.26-0.47 (m, 2H), 0.72 (d, 1H), 1.34 (br s, 2H), 2.19-2.35 (m, 3H), 3.24-3.44 (m, 4H), 3.53 (br s, 2H), 3.69-3.89 (m, 4H), 7.12 (d, 2H), 7.36-7.50 (m, 2H), 7.52-7.66 (m, 2H), 7.75-7.86 (m, 1H), 7.86-7.97 (m, 1H); MS: *m/z* 457.2 (MH^+).

Compound 742

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)- 4-(piperazin-1-yl)-benzenesulfonamide**. MS: *m/z* 456.2 (MH^+).

Compound 748

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-dimethylamino-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.49 (br s, 4H), 2.27 (s, 6H), 3.03 (s, 6H), 6.79 (d, 2H), 7.32-7.46 (m, 2H), 7.46-7.55 (m, 2H), 7.73-7.82 (m, 1H), 7.84-7.93 (m, 1H); MS: *m/z* 471.2 (MH^+).

Compound 749

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-thiomorpholin-4-yl-benzenesulfonamide.** MS: *m/z* 526.2 (MH^+).

Compound 750

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-morpholino-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.35-1.64 (m, 4H), 2.13-2.35 (m, 5H), 2.99 (br s, 2H), 3.21-3.39 (m, 4H), 3.48 (br s, 2H), 3.53 (br s, 2H), 3.67-3.91 (m, 4H), 7.07 (d, 2H), 7.33-7.52 (m, 2H), 7.56 (d, 2H), 7.78 (dd, 1H), 7.83-8.00 (m, 1H); MS: *m/z* 513.2 (MH^+).

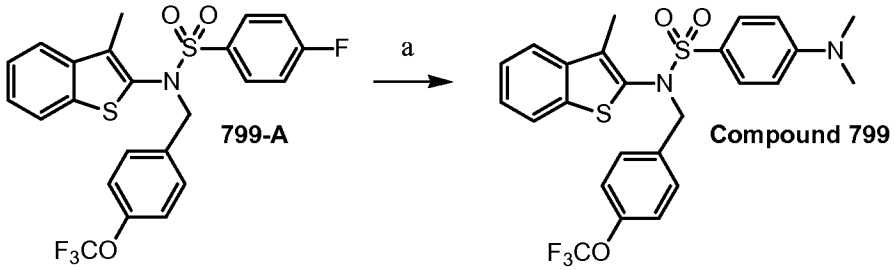
Compound 751

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropyl-ethyl)-4-piperidin-1-yl-benzenesulfonamide.** MS: *m/z* 455.2 (MH^+).

Compound 752

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-piperdine-benzenesulfonamide.** MS: *m/z* 511.16 (MH^+).

Example 64



a) DMSO, dimethylamine.

Compound **799-A,** was prepared by the method used to synthesize compound **757** in Example 29, steps A and B.

Compound 799

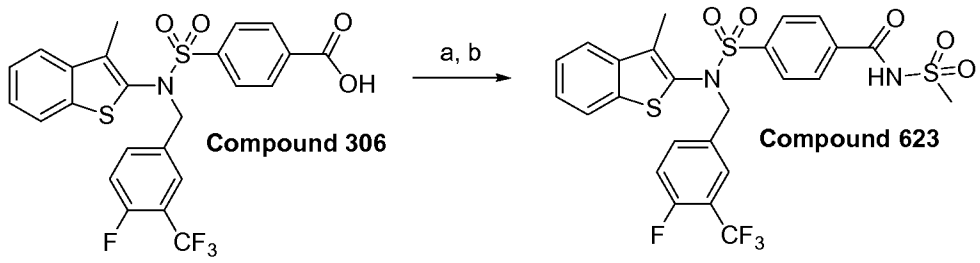
***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-dimethylamino-benzenesulfonamide.** To a solution of compound **799-A** (0.07 g, 0.14 mmol) in dimethylsulfoxide (2 mL) was added a 2.0 M solution of dimethylamine-THF (0.42 mmol), the reaction mixture was sealed and heated at 100 °C in a 300W microwave. The crude solution was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.053 g of compound **799** as an off-white solid. ^{1}H-NMR (DMSO-d_6) δ 1.96 (s, 3H), 3.05 (s, 6H), 4.65 (br s, 2H), 6.76-6.87 (m, 2H), 7.27 (d, 2H), 7.31-7.45 (m, 4H), 7.52-7.62 (m, 2H), 7.62-7.70 (m, 1H), 7.76-7.91 (m, 1H); MS: *m/z* 521.1 (MH^+).

Following the procedure described above for example 64 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 800

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-morpholino-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.96 (s, 3H),, 3.24-3.39 (m, 4H) 3.65-3.85 (m, 4H), 4.68 (br s, 2H), 7.11 (d, 2H), 7.28 (d, 2H), 7.32-7.46 (m, 4H), 7.58-7.73 (m, 3H), 7.76-7.89 (m, 1H); MS: *m/z* 563.1 (MH^+).

Example 65

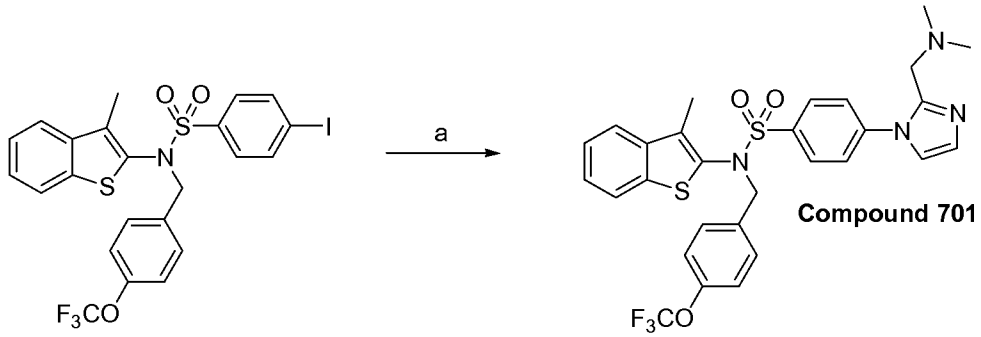


a) THF, CDI; b) $MeSO_2NH_2$, DBU, DMAP.

Compound 623

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylaminocarbonyl-benzenesulfonamide.** To a solution of compound **306** (0.50 g, 0.96 mmol) in THF (30 mL) was added CDI (0.232 g, 1.43 mmol) and the reaction mixture was refluxed for 5 h. Methyl sulfonamide (0.136 g, 1.43 mmol), DBU (0.218 g, 1.43 mmol) and DMAP (0.012 g, 0.096 mmol) were added to the reaction mixture and the reaction was refluxed for 1 h. The solution was diluted with H_2O, extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.2 g of compound **623** as a white solid. ^{1}H-NMR (DMSO-d_6) δ 1.93 (s, 3H), 3.40 (s, 3H), 4.91 (br s, 2H), 7.34-7.43 (m, 2H), 7.47 (t, 1H), 7.57-7.75 (m, 3H), 7.75-7.89 (m, 1H), 8.02 (m, 2H), 8.18 (m, 2H); MS: *m/z* 601.0 (MH^+).

Example 66



Compound 701-A

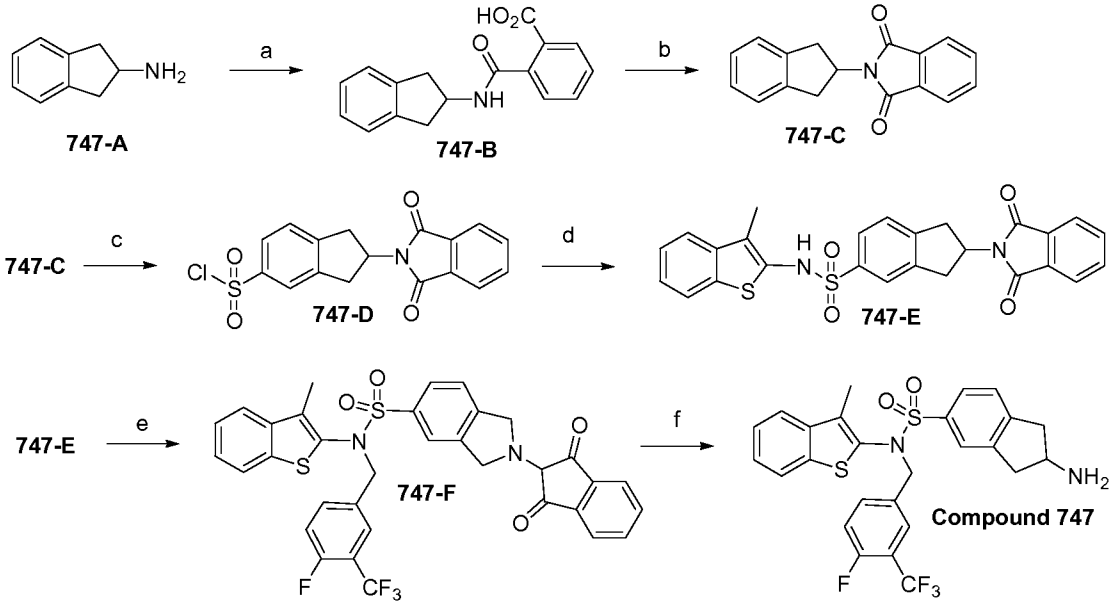
a) DMSO, CuI, K_2CO_3, compound **Int-16**.

Compound **701-A,** was prepared by the method used to synthesize compound **757** in Example 29, steps A and B.

Compound 701

4-(2-Dimethylaminomethyl-imidazol-1-yl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-benzenesulfonamide. A solution of compound **701-A** (0.250 g, 0.414 mmol), DMSO (3 mL), CuI (0.016 g, 0.083 mmol), and K_2CO_3 (0.115 g, 0.828 mmol) was stirred at ambient temperature for 15 min. Compound **Int-16** (0.078 g, 0.628 mmol) was added, the reaction mixture refluxed for 18 h, cooled to ambient temperature, and partitioned between H_2O and EtOAc. The aqueous phase was extracted with chloroform, the organics combined, dried over $MgSO_4$, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.10 g of compound **701** as a yellow oil. ^{1}H-NMR (DMSO-d_6) δ 1.89-2.01 (m, 3H), 2.80 (s, 5H), 3.17 (s, 3H), 4.49 (s, 2H), 4.85 (br s, 2H), 7.32 (d, 3H), 7.36-7.50 (m, 4H), 7.69 (dd, 1H), 7.75 (s, 1H), 7.80-7.91 (m, 3H), 8.01-8.15 (m, 2H); MS: *m/z* 601.2 (MH^+).

Example 67



a) $CHCl_3$, phthalic anhydride; b) DMF, DMAP; c) MeCN, $ClSO_3H$; d) DCM, pyridine, compound **757-A**; e) DMF, K_2CO_3, 4-fluoro-3-trifluoromethylbenzyl bromide; f) MeOH, H_2NNH_2.

***N*-Indan-2-yl-phthalamic acid (747-B).** To a solution of compound **747-A** (1.5 g, 11.3 mmol) in $CHCl_3$ (100 mL) was added phthalic anhydride (2.25 g, 15.2 mmol) and the reaction mixture was heated at 70 °C for 18 h. The reaction mixture was cooled, the solvent evaporated under reduced pressure, H_2O added to the residue, and the residue was extracted with EtOAc, the organic extracts combined, and concentrated *in vacuo*. The crude residue was triturated with MeOH, the solid filtered and dried under vacuo to afford 2.0 g of compound **747-B** as an amber, crystalline solid. MS: *m/z* 282.1 (MH^+).

2-Indan-2-yl-isoindole-1,3-dione (747-C). To a solution of compound **747-B** (1.8 g, 0.74 mmol) in DMF (20 mL) was added DMAP (0.782 g; 0.74 mmol) and the reaction mixture was heated at 120 °C for 18 h. The reaction mixture was cooled, diluted with H_2O, and the precipitate filtered and dried under vacuo to afford 1.2 g of compound **747-C** as a light brown solid. ^{1}H-NMR ($CDCl_3$) δ 3.18 (dd, 2H), 3.63 (dd, 2H), 5.16 (q, 1H), 7.14-7.24 (m, 4H), 7.68-7.77 (m, 2H), 7.79-7.90 (m, 2H); MS: *m/z* 264.1 (MH^+).

2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-indan-5-sulfonyl chloride (747-D). To a solution of compound **747-C** (0.72 g, 2.7 mmol) in MeCN (50 mL) was added chlorosulfonic acid (3.72 g, 32.4 mmol), drop-wise, and the reaction mixture was stirred at ambient temperature for 48 h. The reaction mixture was diluted with H_2O, extracted with CH_2Cl_2, dried over Na_2SO_4, filtered, and dried to afford 0.976 g of compound **747-D** as a brown solid. ^{1}H-NMR ($CDCl_3$) δ 3.26-3.43 (m, 2H,) 3.60-3.78 (m, 2H), 5.26 (t, 1H), 7.46 (d, 1H), 7.68-7.79 (m, 2H), 7.79-7.93 (m, 4H); MS: *m/z* 384.1 (MNa^+).

2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-indan-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-*N*-sulfonamide (747-E). To a solution of compound **757-A** (0.449 g, 2.25 mmol) in DCM (5 mL) and pyridine (0.355 g, 4.5 mmol), cooled to 0 °C, was added compound **747-D** (0.976 g; 2.7 mmol) in DCM (2 mL) and the reaction mixture was stirred at ambient temperature for 48 h. The reaction mixture was diluted with H_2O, extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.73 g of compound **747-E** as a brown solid. MS: *m/z* 489.1 (MH^+).

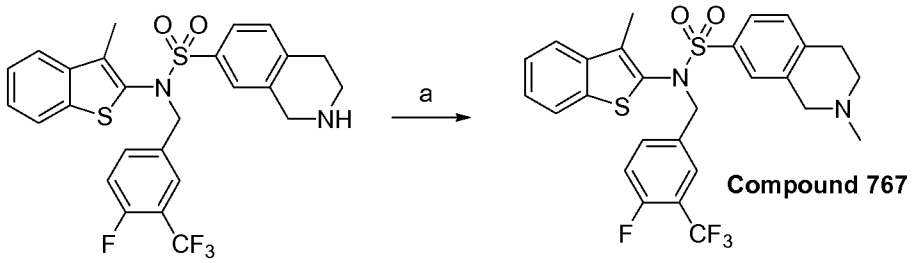
2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-indan-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N*-sulfonamide (747-F). To a solution of compound **747-E** (0.73 g, 1.49 mmol) in DMF (10 mL) was added K_2CO_3 (0.248 g;1.79 mmol) and the reaction mixture was stirred for 30 min. A solution of 4-fluoro-3-trifluoromethylbenzyl bromide (0.460 g, 1.79 mmol) in DMF (2 mL) was added drop-wise and the reaction mixture stirred at ambient temperature for 18 h. The reaction mixture was diluted with H_2O, extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered and the solvent was evaporated *in vacuo* to afford 0.94 g of crude compound **747-F** as a white solid. ^{1}H-NMR (DMSO-d_6) δ 1.99 (s, 3H), 3.47 (m, 4H), 4.86 (br s, 2H), 5.14 (s, 1H), 7.31-7.56 (m, 4H), 7.58-7.75 (m, 4H), 7.79 (s, 1H), 7.82-7.99 (m, 5H); MS: *m/z* 665.1 (MH^+). MS: *m/z* 663.1 (MH^+).

Compound 747

2-Amino-indan-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N*-sulfonamide. Compound **747-F** (0.91 g, 1.37 mmol) was added a 0.2M hydrazine-methanol solution (20 mL) and the reaction mixture was stirred for 2 h at ambient temperature. The solvent was evaporated *in vacuo* and the

crude residue purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.4 g of compound **747** as an orange gum. ^{1}H-NMR (DMSO-d_6) δ 1.78-1.92 (m, 3H), 2.85-3.03 (m, 2H), 3.22-3.43 (m, 2H), 4.00 (br s, 1H), 4.71 (br s, 2H), 7.20-7.42 (m, 3H), 7.42-7.65 (m, 5H), 7.65-7.81 (m, 2H), 7.97 (br s, 2H); MS: *m/z* 535.1 (MH^+).

Example 68



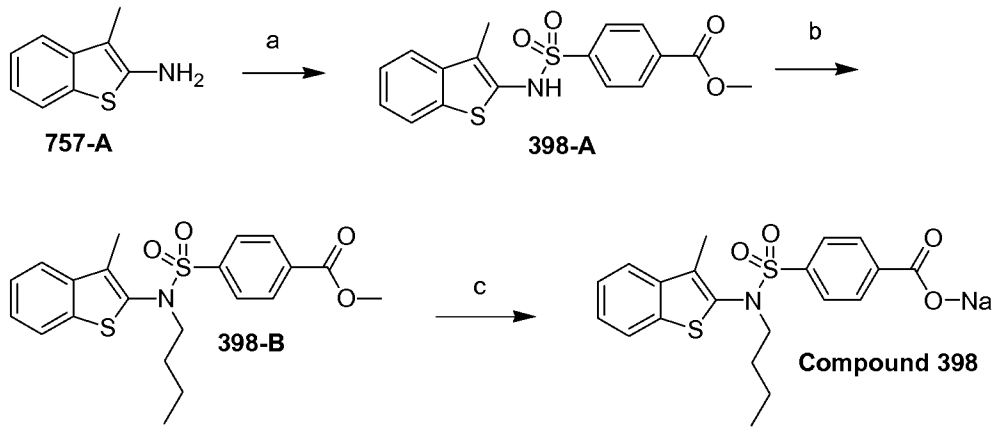
Compound 79

a) HCO_2H, 37% HCHO.

Compound 767

2-Methyl-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-1,2,3,4-tetrahydroisoquinolin-7-yl-sulfonamide. To compound **79** (0.10 g, 0.19 mmol) was added 37% aqueous formaldehyde (0.3 mL) and concentrated formic acid (0.4 mL) and the reaction mixture was heated at 50 °C for 7 days. The reaction mixture was cooled, diluted with H_2O, extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. The crude residue was purified by reverse-phase semi-prep HPLC (Gemini, C_{18} column; 100 x 30 mm I.D.; 5 μ) to afford 0.02 g of compound **767** as a clear, viscous oil. ^{1}H-NMR (DMSO-d_6) δ 1.83-2.02 (m, 3H), 2.96 (s, 3H), 3.13-3.29 (m, 2H), 3.41 (br s, 1H), 3.73 (br s, 1H), 4.40 (br s, 1H), 4.62 (br s, 1H), 4.84 (br s, 2H), 7.33-7.44 (m, 2H), 7.48 (t, 1H), 7.59 (d, 1H), 7.61-7.74 (m, 3H), 7.74-7.92 (m, 3H); MS: *m/z* 549.2 (MH^+).

Example 69



a) 1. 4-(Chlorosulfonyl)benzoic acid, pyridine, DCM; 2. MeOH, H_2SO_4; b) Ph_3P, DEAD, butan-1-ol, THF; c) 1. $LiOH•H_2O$, THF, H_2O; 2. aq HCl; 3. aq NaOH.

***N*-(3-Methylbenzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide (398-A).** To a stirred solution of compound **757-A** (4.99 g, 25.0 mmol) in pyridine (50 mL) and methylene chloride (25 mL), cooled on an ice bath, was added 4-(chlorosulfonyl)benzoic acid (5.52 g, 25.0 mmol), portion-wise, for 4 min, and the reaction was allowed to stir at ambient temperature for 4 days. The reaction mixture was concentrated under reduced pressure, the residue stirred with 1N HCl (100 mL), the resulting solid filtered, washed with 1N HCl and air dried. The crude product was triturated with MeOH (15 mL), filtered, rinsed with MeOH (2 x 5 mL) and air-dried to afford crude benzoic acid (not shown). The benzoic acid was suspended in MeOH (100 mL), treated with concentrated H_2SO_4 (0.1 mL) and the reaction mixture refluxed for 5 days. The reaction mixture was cooled, the solvent evaporated under reduced pressure, and the residue was triturated with MeOH (15 mL), filtered, washed with methanol (2 x 5mL) and once with another portion of methanol (10 mL). The solid was dried to afford 6.31 g of compound **398-A** as a tan-yellow powder. ^{1}H-NMR (DMSO-d_6) δ: 2.02 (s, 3H), 3.89 (s, 3H), 7.40-7.29 (m, 2H), 7.67-7.61 (m, 1H), 7.83-7.77 (m, 1H), 7.89 (d, 2H), 8.14 (d, 2H), 10.66 (s, 1H); MS: *m/z* 360.2 ($M-H^+$).

***N*-(Butyl)-*N*-(3-methylbenzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide (398-B).** To a solution of triphenyl phosphine (0.396 g, 1.51 mmol) in THF (10 mL) was added 40% DEAD in toluene solution (0.67 mL, 1.51 mmol) and the reaction mixture was stirred at ambient temperature for 2 min. Compound **398-A** (0.361 g, 1.00 mmol) was added in one-portion and the reaction

stirred for an additional 5 min. *n*-Butanol (0.11 mL, 1.20 mmol) was added and the reaction mixture was stirred for 18 h at ambient temperature. The reaction mixture was concentrated under reduced pressure and the crude material purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.372 g of compound **398-B** as a viscous, colorless oil. ^{1}H-NMR (DMSO-d_6) δ: 0.84 (t, 3H), 1.48-1.27 (m, 4H), 2.24 (s, 3H), 3.57 (s, 2H), 3.92 (s, 3H), 7.48-7.37 (m, 2H), 7.82-7.76 (m, 1H), 7.88-7.83 (m, 1H), 7.93 (d, 2H), 8.17 (d, 2H); MS: *m/z* 418.3 (MH^+).

Compound 398

Sodium, *N*-(Butyl)-*N*-(3-methylbenzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide. To a solution of compound **398-B** (0.371 g, 0.89 mmol) in a 5:1 THF/water mixture (10 mL) was added LiOH•H_2O (0.042 g, 1.00 mmol), the reaction mixture was stirred for 18 h, and the organics were evaporated in vacuo. The crude residue was diluted with H_2O (10 mL), acidified with 1N HCl (1.00 mL), the solid filtered, washed with H_2O and dried under vacuum. The benzoic acid (0.337 g, 0.84 mmol) was dissolved in a mixture of H_2O (10 mL) and 1N NaOH (0.84 mL, 0.84 mmol), with gentle heating. The turbid solution was filtered, frozen and lyophilized to afford 0.359 g of the sodium salt of compound **398** as an off-white solid. ^{1}H-NMR (DMSO-d_6) δ: 0.83 (t, 3H), 1.43-1.27 (m, 4H), 2.24 (s, 3H), 3.51 (br s, 2H), 7.45-7.37 (m, 2H), 7.64 (d, 2H), 7.79-7.75 (m, 1H), 7.87-7.83 (m, 1H), 7.99 (d, 2H); MS: *m/z* 402.3 $(M - H)^-$.

Following the procedure described above for example 69 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 399

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 401.9 (MH^+).

Compound 400

Sodium, *N*-(2-Cyclopropylethyl)-*N*-(3-methylbenzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ 0.01-0.06 (m, 2H), 0.40-0.32 (m, 2H), 0.74-0.63 (m, 1H), 1.38-1.26 (br m, 2H), 2.23 (s, 3H), 3.58 (br s, 2H), 7.45-7.36 (m, 2H), 7.63 (d, 2H), 7.79-7.74 (m, 1H), 7.87-7.83 (m, 1H), 7.98 (d, 2H); MS: *m/z* 414.2 $(M - H)^-$.

Compound 401

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(2-*tert*-butoxy-ethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 0.91-1.14 (m, 9H), 2.22 (s, 3H), 3.22-3.49 (m, 4H), 7.34-7.51 (m, 2H), 7.71-7.83 (m, 1H), 7.83-7.89 (m, 1H), 7.92 (m, 2H), 8.14 (m, 2H); MS: *m/z* 447.9 (MH^+).

Compound 402

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(ethyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 389.9 (MH^+).

Compound 403

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(ethyl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 375.9 (MH^+).

Compound 404

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(propyl)-4-carboxy-benzenesulfonamide.** MS: *m/z* 398.9 (MH^+).

Compound 409

Sodium, *N*-(3-Methylbenzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carboxy-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ 2.22 (s, 3H), 2.58-2.45 (m, 2H), 3.81 (br s, 2H), 7.46-7.37 (m, 2H), 7.66 (d, 2H), 7.81-7.75 (m, 1H), 7.89-7.83 (m, 1H), 8.00 (d, 2H); MS: *m/z* 442.2 $(M - H)^-$.

Compound 410

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.68 (q, 2H), 2.23 (s, 3H), 2.29-2.45 (m, 2H), 3.67 (br s, 2H), 7.28-7.57 (m, 2H), 7.71-8.02 (m, 4H), 8.16 (d, 2H), 13.62 (br s, 1H); MS: *m/z* 458.0 (MH^+).

Compound 416

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(3-*tert*-butoxy-propyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.08 (s, 9H), 1.59 (t, 2H), 2.26 (s, 3H), 3.21-3.43 (m, 2H), 3.67 (br s, 2H), 3.92 (s, 3H), 7.31-7.54 (m, 2H), 7.79 (dd, 1H), 7.82-7.89 (m, 1H), 7.92 (m, 2H), 8.18 (m, 2H); MS: *m/z* 476.0 (MH^+).

Compound 477

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carboxy-benzenesulfonamide.** ^{1}H NMR (DMSO-d_6) δ 0.71-0.93 (m, 3H), 1.23-1.50 (m, 4H),

3.58 (t, 2H), 7.43-7.64 (m, 2H), 7.72 (d, 2H), 7.77-7.88 (m, 1H), 7.94-8.13 (m, 3H); MS: *m/z* 423.9 (MH^+).

Compound 478

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ -0.14-0.07 (m, 2H), 0.19-0.39 (m, 2H), 0.67-0.94 (m, 1H), 3.40 (d, 2H), 7.33-7.55 (m, 2H), 7.64 (d, 2H), 7.68-7.82 (m, 1H), 7.82-8.07 (m, 3 H); MS: *m/z* 421.8 (MH^+).

Compound 479

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-2-(cyclopropyl)ethyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ -0.01 (q, 2H), 0.22-0.45 (m, 2H), 0.64-0.84 (m, 1H), 1.34 (q, 2H), 3.66 (t, 2H), 7.46-7.64 (m, 2H), 7.67-7.90 (m, 3H), 7.91-8.17 (m, 3H); MS: *m/z* 435.9 (MH^+).

Compound 480

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 2.54-2.70 (m, 2H), 3.90 (t, 2H), 7.45-7.61 (m, 2H), 7.74 (d, 2H), 7.79 (dd, 1H), 7.96-8.17 (m, 3H); MS: *m/z* 464.0 (MH^+).

Compound 530

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 491.9 (MH^+).

Compound 531

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carbomethoxy-benzenesulfonamide.** MS: *m/z* 506.0 (MH^+).

Compound 537

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4,4,4-trifluoro-butyl)-4-carboxy-benzenesulfonamide.** ^{1}H NMR (DMSO-d_6) δ 1.67 (q, 2H), 2.26-2.45 (m, 2H), 3.68 (t, 2H), 7.48-7.61 (m, 2H), 7.73 (d, 2H), 7.78-7.92 (m, 1H), 7.94-8.13 (m, 3H); MS: *m/z* 477.9 (MH^+).

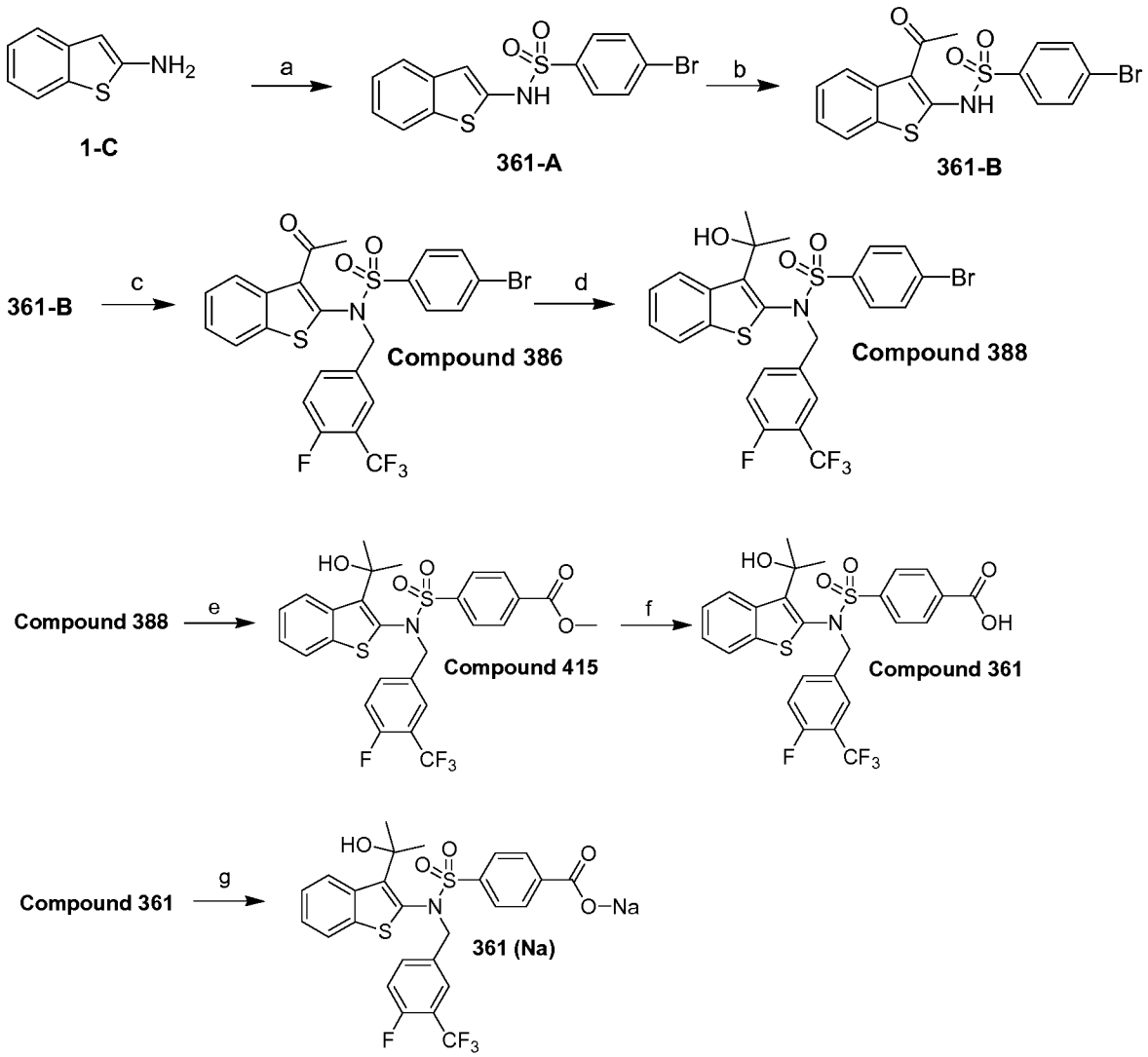
Compound 538

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6) δ 1.35-1.70 (m, 4H), 2.07-2.36 (m, 2H), 3.62 (t, 2H), 7.45-7.63 (m, 2H), 7.73 (d, 2H), 7.76-7.86 (m, 1H), 7.92-8.14 (m, 3H); MS: *m/z* 492.0 (MH^+).

Compound 545

Sodium, *N*-(3-Methylbenzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carboxy-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ 1.62-1.45 (m, 4H), 2.32-2.17 (m, 5H), 3.56 (br s, 2H), 7.45-7.37 (m, 2H), 7.66 (d, 2H), 7.80-7.75 (m, 1H), 7.88-7.83 (m, 1H), 8.00 (m, 2H); MS: *m/z* 470.2 (M - H)$^-$.

Example 70



a) 4-Bromobenzene-1-sulfonyl chloride, pyridine, DCM; b) AcCl, $SnCl_4$, DCM; c) 4-(bromomethyl)-1-fluoro-2-(trifluoromethyl)benzene, KOtBu, 18-C-6, DMF; d) MeMgCl, THF; e) CO, Pd catalyst, iPr_2NEt, MeOH, DMF; f) 1. $LiOH•H_2O$, THF, H_2O; 2. aq. HCl; g) aq. NaOH.

***N*-(Benzo[*b*]thiophen-2-yl)-4-bromobenzenesulfonamide (361-A).** To a stirred solution of compound **1-C** (9.28 g, 49.9 mmol) in pyridine (100 mL) and methylene chloride (50 mL), cooled on an ice bath, was added 4-bromobenzene-1-sulfonyl chloride (12.8 g, 49.9 mmol), portion-wise over a period of 4 minutes. The reaction mixture was allowed to warm to ambient temperature and stirred for 18 h. The reaction mixture was concentrated under reduced pressure, the crude residue partitioned between EtOAc (500 mL) and 1N HCl (250 mL), the layers separated, the organic phase washed with 1N HCl (125 mL), brine, dried over $MgSO_4$, filtered and evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-Heptane gradient to afford 13.5 g of compound **361-A** as a tan powder. ^{1}H-NMR (DMSO-d_6) δ: 6.89 (s, 1H), 7.33-7.20 (m, 2H), 7.75-7.64 (m, 3H), 7.84-7.76 (m, 3H), 11.30 (s, 1H); MS: *m/z* 366.1 $(M - H)^-$.

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-bromobenzenesulfonamide (361-B).** To a suspension of compound **361-A** (9.21 g, 25.0 mmol) in DCM (50 mL), cooled in an ice-bath, was added an ice-cold solution of acetyl chloride (2.30 mL, 32.3 mmol), followed by $SnCl_4$ (27.9 mmol) in DCM (200 mL). The reaction mixture was allowed to warm to ambient temperature and stirred for 18 h. The reaction mixture was quenched with saturated NH_4Cl solution (125 mL), filtered over a pad of celite, dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was dissolved in refluxing EtOAc (75 mL), filtered hot and the filtrate allowed to cool. The solid was filtered and washed EtOAc (10 mL). Another batch of product was obtained by evaporation of the mother liquor, dissolving the residue in refluxing EtOAc (25 mL), filtering hot and allowing the filtrate to cool. The solid was filtered and washed with EtOAc (2 mL). The combined batches of solid were air-dried to afford 8.54 g of compound **361-B** as a tan-orange powder. ^{1}H-NMR (DMSO-d_6) δ: 2.57 (s, 3H), 7.40-7.24 (m, 2H), 7.83-7.70 (m, 5H), 8.14 (d, 1H); MS: *m/z* 408.1 $(M - H)^-$.

Compound 386

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-bromo-*N*-(4-fluoro-3-trifluoromethyl-benzyl)benzenesulfonamide.** To a solution compound **361-B** (8.54 g, 20.8 mmol) in DMF (125 mL) was added KOtBu solution (23.0 mL, 1M in THF) and the reaction was stirred for 5 minutes. 18-Crown-6 (5.51 g, 20.8 mmol) and 4-(bromomethyl)-1-fluoro-2-(trifluoromethyl)-benzene (9.60 mL, 62.0 mmol) were added and the reaction was stirred for 18 h. An additional portion of KOtBu solution (10.0

mL, 1M in THF) and 18-crown-6 (2.42 g, 9.14 mmol) were added to the reaction mixture and the reaction was stirred for an additional 3 days. The reaction mixture was concentrated in vacuo and the crude material purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford compound **386** as a semi-pure material. The solid was triturated with EtOAc (10 mL), filtered, washed with an additional EtOAc (10 mL) and air-dried to afford 6.92 g of compound **386** as a white crystalline powder. ^{1}H-NMR (DMSO-d_6) δ: 2.38 (s, 3H), 4.97 (s, 2H), 7.41-7.50 (m, 3H), 7.66-7.70 (m, 4H), 7.92 (d, 2H), 7.94-7.98 (m, 1H), 7.98-8.03 (m, 1H); MS: *m/z* 586.1 $(M - H)^-$.

Compound 388

4-Bromo-*N*-(4-fluoro-3-trifluoromethylbenzyl)-*N*-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)benzenesulfonamide. To a solution of compound **386** (6.89 g, 11.76 mmol) in THF (120 mL) was added MeMgCl (15.6 mL, 3M in THF) and the reaction was stirred for 18 h at ambient temperature. The crude reaction was quenched with saturated NH_4Cl solution (40 mL), the layers separated, and the organic phase washed with brine (40 mL), dried over $MgSO_4$, filtered and evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 6.29 g of compound **388** as a glassy yellow-orange solid. ^{1}H-NMR (DMSO-d_6): δ 1.34 (s, 3H), 1.62 (s, 3H), 4.61 (d, 1H), 5.11-5.04 (m, 2H), 7.37-7.30 (m, 2H), 7.45-7.38 (m, 1H), 7.54-7.45 (m, 2H), 7.83-7.78 (m, 3H), 7.91-7.86 (m, 2H), 8.41-8.35 (m, 1H); MS: *m/z* 584 $(M - OH)^+$.

Compound 415

***N*-(4-Fluoro-3-trifluoromethylbenzyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** A solution of compound **388** (5.67 g, 9.41 mmol) in a 1:1 mixture of DMF and MeOH (100 mL) was treated with iPr_2NEt (3.3 mL, 18.9 mmol) and (1,1'-bis(di-tert-butylphosphino)ferrocene)palladium(II) chloride (0.311 g, 0.48 mmol) and the reaction mixture was heated at 80 °C under a pressure of 50-60 psi carbon monoxide for 18 h, cooled and the reaction mixture was concentrated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 4.33 g of compound **415** as an orange-tan glassy solid. ^{1}H-NMR (DMSO-d_6): δ 1.35 (s 3H), 1.63 (s, 3H), 3.94 (s, 3H), 4.66 (d, 1H), 5.14-5.06 (m, 2H),

7.55-7.29 (m, 5H), 7.83-7.76 (m, 1H), 8.02 (d, 2H), 8.19 (d, 2H), 8.41-8.33 (m, 1H); MS: *m/z* 564.2 $(M - OH)^+$.

Compound 361

***N*-(4-Fluoro-3-trifluoromethylbenzyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** To a solution of compound **415** (5.33 g, 7.44 mmol) in a 5:1 THF/water mixture (100 mL) was added $LiOH•H_2O$ (0.420 g, 10.0 mmol) and the reaction was stirred for 18 h at ambient temperature. An additional portion of $LiOH•H_2O$ (0.084 g, 2.0 mmol) was added, the reaction was stirred for an additional 18 h, and the organics were evaporated in vacuo. The crude residue was diluted with water (100 mL), acidified with 1N HCl (12.0 mL), the precipitate filtered, washed with water and dried under vacuum to afford 4.10 g of compound **361** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 1.36 (s, 3H), 1.63 (s, 3H), 4.66 (d, 1H), 5.15-5.04 (m, 2H), 7.55-7.29 (m, 5H), 7.84-7.76 (m, 1H), 7.99 (d, 2H), 8.16 (d, 2H), 8.42-8.34 (m, 1H), 13.63 (br s, 1H); MS: *m/z* 566.2 $(M - H)^-$.

Compound 361, sodium salt

Sodium, *N*-(4-Fluoro-3-trifluoromethylbenzyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide. To a suspension of compound **361** (4.10 g, 7.22 mmol) in water (50 mL) was added 1N NaOH (7.10 mL, 7.10 mmol) and the reaction mixture was refluxed briefly and cooled back to ambient temperature. The turbid reaction was filtered, the filtrate frozen and lyophilized to afford a fluffy product. The product was stirred with hexanes (100 mL), filtered, and the powder dried under vacuum at 50 °C to afford 4.18 g of the sodium salt of compound **361** as a cream-colored powder. ^{1}H-NMR (DMSO-d_6): δ 1.26 (s, 3H), 1.61 (s, 3H), 4.46 (d, 1H), 5.05 (s, 1H), 5.13 (d, 1H), 7.35-7.28 (m, 2H), 7.43-7.36 (m, 1H), 7.52-7.46 (m, 1H), 7.57-7.53 (m, 1H), 7.75 (d, 2H), 7.81-7.70 (m, 1H), 8.01 (d, 2H), 8.41-8.36 (m, 1H); MS: *m/z* 566.2 $(M - H)^-$.

Following the procedure described above for example 70 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 730

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-bromo-*N*-(4-fluoro-benzyl)benzene-sulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.30 (s, 3H), 4.86 (br s, 2H), 7.19-7.11 (m, 2H),

7.40-7.33 (m, 2H), 7.47-7.41 (m, 2H), 7.75-7.70 (m, 2H), 7.93-7.88 (m, 2H), 7.98-7.93 (m, 1H), 8.05-7.99 (m, 1H); MS: *m/z* 517.9 (MH^+).

Compound 731

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-bromo-*N*-(4-(trifluoromethoxy)-benzyl)benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.28 (s, 3H), 4.91 (br s, 2H), 7.33 (d, 2H), 7.49-7.42 (m, 4H), 7.75-7.70 (m, 2H), 7.93-7.88 (m, 2H), 7.98-7.93 (m, 1H), 8.05-7.99 (m, 1H); MS: *m/z* 583.9 (MH^+).

Compound 732

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(benzyl)-4-bromobenzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.28 (s, 3H), 4.86 (br s, 2H), 7.35-7.28 (m, 5H), 7.46-7.41 (m, 2H), 7.74-7.70 (m, 2H), 7.92-7.88 (m, 2H), 7.97-7.92 (m, 1H), 8.05-7.99 (m, 1H); MS: *m/z* 500.0 (MH^+).

Compound 733

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-bromo-*N*-(3-chloro-4-fluoro-benzyl)benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.37 (s, 3H), 4.88 (br s, 2H), 7.41-7.33 (m, 2H), 7.48-7.43 (m, 2H), 7.53 (dd, 1H), 7.76-7.77 (m, 2H), 7.93-7.89 (m, 2H), 7.99-7.94 (m, 1H), 8.05-7.99 (m, 1H); MS: *m/z* 552.0 (MH^+).

Compound 734

***N*-(4-Fluorobenzyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-bromo-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.17 (s, 3H), 1.63 (s, 3H), 4.34 (d, 1H), 5.11-5.02 (m, 2H), 7.22-7.04 (m, 4H), 7.38-7.27 (m, 2H), 7.84-7.76 (m, 3H), 7.90 (d, 2H), 8.44-8.36 (m, 1H); MS: *m/z* 516 $(M - OH)^+$.

Compound 735

***N*-(3-(1-Hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxybenzyl)-4-bromo-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.10 (s, 3H), 1.63 (s, 3H), 4.38 (d, 1H), 5.08 (s, 1H), 5.12 (d, 1H), 7.38-7.25 (m, 6H), 7.84-7.77 (m, 3H), 7.89 (d, 2H), 8.43-8.35 (m, 1H); MS: *m/z* 582.0 $(M - OH)^+$.

Compound 736

***N*-(Benzyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-bromo-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.09 (s, 3H), 1.64 (s, 3H), 4.33 (d, 1H), 5.12-5.03 (m, 2H), 7.17-7.09 (m, 2H), 7.37-7.20 (m, 5H), 7.84-7.75 (m, 3H), 7.89 (d, 2H), 8.43-8.36 (m, 1H); MS: *m/z* 498.0 $(M - OH)^+$.

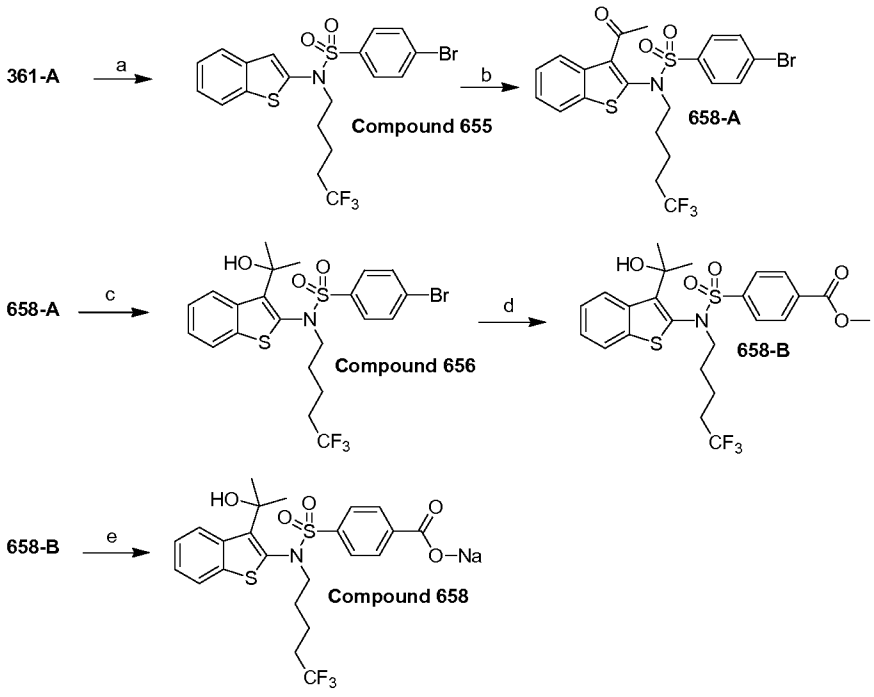
Compound 737

***N*-(3-Chloro-4-fluorobenzyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-bromo-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.33 (s, 3H), 1.63 (s, 3H), 4.97 (d, 1H), 5.02 (d, 1H), 5.11 (s, 1H), 7.20-7.12 (m, 1H), 7.39-7.25 (m, 4H), 7.84-7.76 (m, 3H), 7.90 (d, 2H), 8.43-8.35 (m, 1H); MS: *m/z* 550.0 (M - OH)$^+$.

Compound 781

Sodium, *N*-(3-(1-Hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy)benzyl-4-carboxy-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ 1.06 (s, 3H), 1.63 (s, 3H), 4.27 (d, 1H), 5.05 (s, 1H), 5.13 (d, 1H), 7.35-7.22 (m, 6H), 7.75 (d, 2H), 7.81-7.77 (m, 1H), 8.01 (d, 2H), 8.43-8.39 (m, 1H); MS: *m/z* 564.1 (M - H)$^-$.

Example 71



a) Ph_3P, DEAD, 5,5,5-trifluoropentan-1-ol, THF; b) Ac_2O, H_3PO_4; c) MeMgCl, THF; d) CO, Pd catalyst, iPr_2NEt, MeOH, DMF; e) 1. LiOH•H_2O, THF, H_2O; 2. aq HCl; 3. aq NaOH.

Compound 655

***N*-(Benzo[*b*]thiophen-2-yl)-4-bromo-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide.**

To a solution of triphenyl phosphine (1.97 g, 7.50 mmol) in THF (50 mL) was added 40% DEAD in toluene solution (3.40 mL, 7.65 mmol) and the reaction mixture was stirred for 2 min. Compound **361-A** (1.84 g, 5.00 mmol) was added, the reaction mixture stirred an additional 5 min, to which was added 5,5,5-trifluoropentan-1-ol (0.62 mL, 5.99 mmol) and the reaction mixture was stirred for 18 h. The reaction mixture was concentrated in vacuo and the crude material purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 2.19 g of compound **655** as a tan powder. ^{1}H-NMR (DMSO-d_6): δ 1.64-1.49 (m, 4H), 2.37-2.17 (m, 2H), 3.71-3.64 (m, 2H), 7.27 (s, 1H), 7.47-7.34 (m, 2H), 7.69-7.63 (m, 2H), 7.92-7.77 (m, 4H).

***N*-(3-Acetylbenzo[*b*]thiophen-2-yl)-4-bromo-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide (658-A).** To compound **655** (2.16 g, 4.39 mmol) was added acetic anhydride (50 mL) and 85% H_3PO_4 (0.50 mL) and the reaction was refluxed for 18 h, cooled, and the reaction mixture concentration under reduced pressure. The crude residue was partitioned between EtOAc (250 mL) and saturated $NaHCO_3$ (50 mL). Insoluble material was filtered, the organic layer washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 1.26 g of compound **658-A** as a thick, colorless oil. ^{1}H-NMR (DMSO-d_6): δ 1.64-1.50 (m, 2H), 1.78-1.64 (m, 2H), 2.37-2.18 (m, 2H), 2.66 (s, 3H), 3.67 (br s, 2H), 7.53-7.42 (m, 2H), 7.67-7.60 (m, 2H), 7.90-7.83 (m, 2H), 7.99-7.92 (m, 1H), 8.17-8.10 (m, 1H); MS: *m/z* 534 (MH^+).

Compound 656

4-Bromo-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide. To a solution of compound **658-A** (1.26 g, 2.35 mmol) in THF (25 mL) was added MeMgCl (3.95 mL, 3M in THF) and the reaction was stirred for 18 h. The reaction was quenched with a saturated NH_4Cl solution (10 mL), the organics were washed with brine (10 mL), dried with $MgSO_4$, filtered and evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.865 g of

compound **656** as a colorless glass. ^{1}H-NMR (DMSO-d_6): δ 1.55-1.37 (m, 3H), 1.74-1.65 (m, 4H), 1.78 (s, 3H), 2.29-2.14 (m, 2H), 3.26-3.17 (m, 1H), 3.89-3.79 (m, 1H), 5.26 (s, 1H), 7.39-7.32 (m, 2H), 7.83-7.74 (m, 3H), 7.91-7.85 (m, 2H), 8.53-8.47 (m, 1H); MS: *m/z* 532.2 $(M - OH)^+$.

***N*-(3-(1-Hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-carbomethoxy-benzenesulfonamide (658-B).** A solution of compound **656** (0.828 g, 1.50 mmol) in a 1:1 mixture of DMF and MeOH (50 mL) was treated with iPr_2NEt (0.53 mL, 3.04 mmol) and (1,1'-bis(di-tert-butylphosphino)ferrocene)palladium(II) chloride (0.050 g, 0.08 mmol) and the reaction mixture was heated at 80 °C under a pressure of 50-60 psi carbon monoxide for two days. The reaction mixture was cooled, concentrated in vacuo and the material was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.514 g of compound **658-B**. ^{1}H-NMR (DMSO-d_6): δ 1.55-1.37 (m, 3H), 1.75-1.63 (m, 4H), 1.79 (s, 3H), 2.29-2.14 (m, 2H), 3.30-3.21 (m, 1H), 3.91-3.82 (m, 1H), 3.93 (s, 3H), 5.27 (s, 1H), 7.40-7.32 (m, 2H), 7.81-7.75 (m, 1H), 8.02-7.98 (m, 2H), 8.21-8.16 (m, 2H), 8.53-8.47 (m, 1H); MS: *m/z* 512.2 $(M - OH)^+$.

Compound 658

Sodium, *N*-(3-(1-Hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-N-(5,5,5-trifluoro-pentyl)-4-carboxy-benzenesulfonamide. To compound **658-B** (0.506 g, 0.96 mmol) in a 5:1 THF/water mixture (25 mL) was added $LiOH•H_2O$ (0.084 g, 2.00 mmol) and the reaction mixture was stirred for 18 h at ambient temperature. The solvent was evaporated in vacuo, the residue dissolved in H_2O (10 mL) and acidified with 1N HCl (2.0 mL). The precipitate was filtered, washed with H_2O, and dried under vacuum to afford the 0.460 g of the carboxylic acid of compound **658**. product. Water (10 mL) was added followed by 1N NaOH (0.88 mL, 0.88 mmol), the turbid reaction filtered, and the filtrate frozen and lyophilized to afford 0.478 g of the sodium salt of compound **658** as a cream-colored powder. ^{1}H-NMR (DMSO-d_6): δ 1.58-1.36 (m, 3H), 1.76-1.62 (m, 4H), 1.80 (s, 3H), 2.31-2.11 (m, 2H), 3.21-3.09 (m, 1H), 3.91-3.78 (m, 1H), 5.27 (s, 1H), 7.38-7.29 (m, 2H), 7.70 (d, 2H), 7.82-7.75 (m, 1H), 8.00 (d, 2H), 8.56-8.47 (m, 1H); MS: *m/z* 514.2 $(M - H)^-$.

Following the procedure described above for example 71 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 504

***N*-(3-(1-Hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 1.68 (s, 3H), 1.77 (s, 3H), 2.51-2.42 (m, 1H), 2.88-2.73 (m, 1H), 3.50-3.41 (m, 1H), 3.92 (s, 3H), 4.18-4.09 (m, 1H), 5.26 (s, 1H), 7.41-7.34 (m, 2H), 7.84-7.78 (m, 1H), 7.99 (d, 2H), 8.20 (d, 2H), 8.49-8.42 (m, 1H); MS: *m/z* 484.2 $(M - OH)^+$.

Compound 505

Sodium, *N*-(3-(1-Hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carboxy-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ 1.68 (s, 3H), 1.80 (s, 3H), 2.49-2.38 (m, 1H), 2.85-2.72 (m, 1H), 3.40-3.31 (m, 1H), 4.13-4.03 (m, 1H), 5.28 (s, 1H), 7.40-7.32 (m, 2H), 7.70 (d, 2H), 7.84-7.79 (m, 1H), 8.02 (d, 2H), 8.53-8.46 (m, 1H); MS: *m/z* 486.2 $(M - H)^-$.

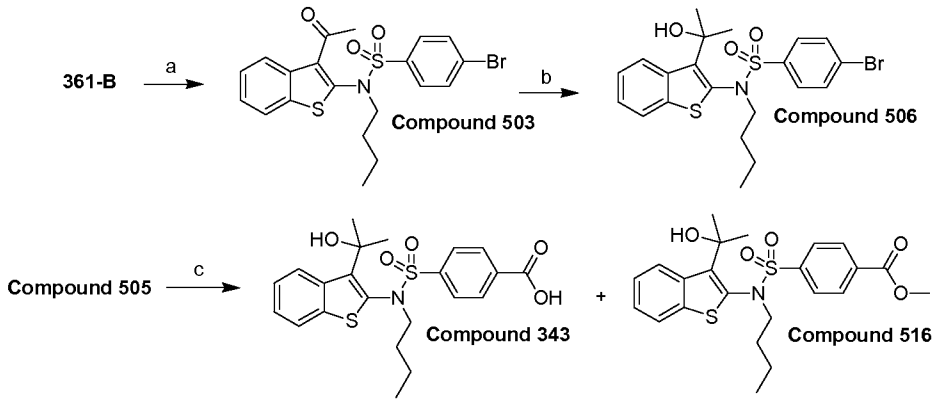
Compound 654

***N*-(Benzo[b]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-bromo-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.05-0.02 (m, 2H), 0.42-0.35 (m, 2H), 0.78-0.64 (m, 1H), 1.41 (q, 2H), 3.71 (t, 2H), 7.26 (s, 1H), 7.41-7.32 (m, 2H), 7.69-7.62 (m, 2H), 7.90-7.76 (m, 4H).

Compound 657

Sodium, *N*-(2-Cyclopropyl-ethyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide. ^{1}H-NMR (DMSO-d_6): δ -0.02- -0.16 (m, 2H), 0.40-0.31 (m, 2H), 0.68-0.56 (m, 1H), 1.27-1.08 (m, 1H), 1.66-1.52 (m, 1H), 1.70 (s, 3H), 1.79 (s, 3H), 3.24-3.11 (m, 1H), 3.93-3.80 (m, 1H), 5.28 (s, 1H), 7.38-7.30 (m, 2H), 7.68 (d, 2H), 7.83-7.75 (m, 1H), 8.01 (d, 2H), 8.56-8.48 (m, 1H); MS: *m/z* 458.2 $(M - H)^-$.

Example 72



a) 1-Bromobutane, KOH, 1-butyl-3-methyl-1*H*-imidazol-3-ium tetrafluoroborate; b) MeMgCl, THF; c) CO, Pd catalyst, iPr_2NEt, MeOH, DMF.

Compound 503

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-bromo-benzenesulfonamide.** To a suspension of compound **361-B** (0.600 g, 1.46 mmol) in 1-butyl-3-methyl-1*H*-imidazol-3-ium tetrafluoroborate (12 mL) was added powdered KOH (0.397 g, 7.08 mmol) followed by 1-bromobutane (1.00 mL, 9.27 mmol) and the reaction was heated at 150 °C for 2.5 h. Additional 1-bromobutane (0.50 mL, 4.63 mmol) was added, the reaction mixture was heated for an additional 1 h, to which was added additional KOH (0.198 g, 3.53 mmol), and the reaction mixture was heated at 150 °C for 2 days. The reaction mixture was cooled to ambient temperature, diluted with H_2O (100 mL), extracted with EtOAc (200 mL), the organic extract washed with H_2O (2x100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.347 g of compound **503** as a tan semi-solid. ^{1}H-NMR (DMSO-d_6): δ 0.86 (t, 3H), 1.35 (h, 2H), 1.60 (p, 2H), 2.66 (s, 3H), 3.63 (br s, 2H), 7.51-7.43 (m, 2H), 7.64-7.59 (m, 2H), 7.88-7.84 (m, 2H), 7.97-7.93 (m, 1H), 8.16-8.11 (m, 1H); MS: *m/z* 466.1 (MH^+).

Compound 506

***N*-(Butyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-bromo-benzenesulfonamide.** To a solution of compound **503** (0.330 g, 0.71 mmol) in THF (10 mL) was added MeMgCl (1.20 mL, 3M in THF) and the reaction mixture was stirred for 18 h. The reaction mixture was quenched with saturated NH_4Cl solution (5 mL), brine (5 mL), dried over $MgSO_4$, filtered and evaporated in vacuo. The material

was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.22 g of compound **506** as an off-white powder. ^{1}H-NMR (DMSO-d_6): δ 0.82 (t, 3H), 1.42-1.15 (m, 3H), 1.67-1.53 (m, 1H), 1.71 (s, 3H), 1.79 (s, 3H), 3.21-3.12 (m, 1H), 3.84-3.74 (m, 1H), 5.28 (s, 1H), 7.38-7.32 (m, 2H), 7.77-7.73 (m, 2H), 7.82-7.77 (m, 1H), 7.90-7.85 (m, 2H), 8.54-8.49 (m, 1H); MS: *m/z* 464 (M - OH)$^-$.

Compounds 343 and 516

***N*-(Butyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide (Cpd 343) and *N*-(Butyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide (Cpd 516).** To a solution of compound **506** (0.201 g, 0.42 mmol) in DMF (5 mL) and MeOH (2 mL) was added iPr_2NEt (0.15 mL, 0.86 mmol) followed by (1,1'-bis(diphenylphosphino)ferrocene)palladium(II) chloride (0.035 g, 0.04 mmol). The reaction mixture was degassed with argon, cooled on a dry-ice acetone bath and charged with carbon monoxide. The reaction vessel was sealed and heated at 60 °C for 18 h. The reaction was cooled to ambient temperature, iPr_2NEt (0.15 mL, 0.86 mmol) and (1,1'-bis(diphenylphosphino)ferrocene)palladium(II) chloride (0.035 g, 0.04 mmol) were added, the reaction mixture was cooled on a dry-ice acetone bath, charged with carbon monoxide, the reaction vessel sealed and heated at 60 °C for 7 h. This step was repeated once more and heated at 60 °C for 5 days. The reaction mixture was cooled, concentrated in vacuo, dissolved in MeOH, filtered, and the filtrate concentrated in vacuo. The crude residue was chromatographed reverse-phase (25-95% acetonitrile/water + 0.1% TFA) and lyophilized to afford 0.009 g of compound **343** and 0.015 g of compound **516**.

Compound 343

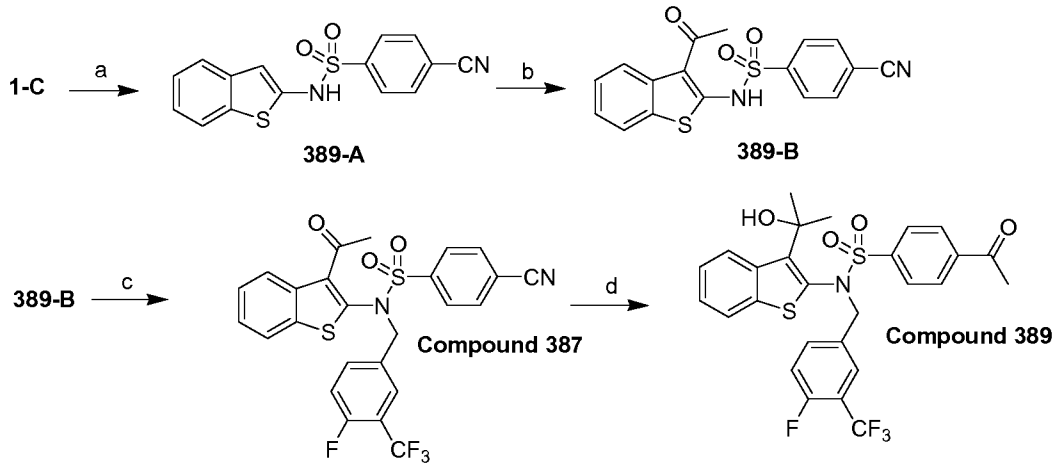
***N*-(Butyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.81 (t, 3H), 1.43-1.15 (m, 3H), 1.62-1.54 (m, 1H), 1.72 (s, 3H), 1.80 (s, 3H), 3.24-3.15 (m, 1H), 3.87-3.77 (m, 1H), 5.29 (br s, 1H), 7.39-7.32 (m, 2H), 7.80-7.75 (m, 1H), 7.95 (d, 2H), 8.17 (d, 2H), 8.55-8.48 (m, 1H), 13.58 (s, 1H); MS: *m/z* 446.3 (M - H)$^-$.

Compound 516

***N*-(Butyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 0.81 (t, 3H), 1.43-1.15 (m, 3H), 1.67-1.53 (m, 1H), 1.71 (s, 3H), 1.80 (s, 3H), 3.24-3.15 (m, 1H), 3.87-3.77 (m,

1H), 3.92 (s, 3H), 5.28 (br s, 1H), 7.39-7.32 (m, 2H), 7.80-7.74 (m, 1H), 7.97 (d, 2H), 8.19 (d, 2H), 8.54-8.48 (m, 1H); MS: *m/z* 444.3 $(M - OH)^+$.

Example 73



a) 4-Cyanobenzene-1-sulfonyl chloride, pyridine, DCM; b) AcCl, $SnCl_4$, DCM; c) 4-(bromomethyl)-1-fluoro-2-(trifluoromethyl)benzene, KO*t*Bu, 18-C-6, DMF; d) MeMgCl, THF.

***N*-(Benzo[*b*]thiophen-2-yl)-4-cyanobenzenesulfonamide (389-A).** To a stirred solution of compound **1-C** (0.927 g, 5.0 mmol) in pyridine (10 mL) and methylene chloride (5 mL), cooled on an ice bath, was added 4-cyanobenzene-1-sulfonyl chloride (1.01 g, 5.0 mmol) portion-wise over 3 min. The reaction was allowed to warm slowly to ambient temperature and allowed to stir for 72 h. The reaction mixture was concentrated under reduced pressure, the crude residue was partitioned between EtOAc (100 mL) and 1N HCl (25 mL), the layers separated, the organic phase washed with brine (25 mL), dried over $MgSO_4$, filtered and evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 1.22 g of compound **389-A** as a tan-brown powder. ^{1}H-NMR (DMSO-d_6): δ 6.91 (s, 1H), 7.33-7.21 (m, 2H), 7.69-7.64 (m, 1H), 7.82-7.76 (m, 1H), 7.99-7.93 (m, 2H), 8.11-8.05 (m, 2H), 11.49 (br s, 1H); MS: *m/z* 313.1 $(M - H)^-$.

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-cyanobenzenesulfonamide (389-B).** To a suspension of compound **389-A** (1.22 g, 3.88 mmol) in DCM (10 mL), cooled in an ice bath, was added a pre-mixed (5 min) solution of ice-cold acetyl chloride (0.36

mL, 5.06 mmol) and $SnCl_4$ (0.51 mL, 4.32 mmol) in DCM (25 mL). The reaction mixture was allowed to warm slowly to ambient temperature and stir for 18 h. The reaction mixture was quenched with a saturated NH_4Cl solution (25 mL), filtered through a pad of celite, the organics dried over $MgSO_4$, filtered and concentrated under vacuum to afford 1.62 g of compound **389-B** as a semi-pure product. ^{1}H-NMR (DMSO-d_6): δ 2.55 (s, 3H), 7.22-7.14 (m, 1H), 7.31-7.24 (m, 1H), 7.67 (d, 1H), 8.04-7.92 (m, 4H), 8.21 (d, 1H); MS: *m/z* 355.1 $(M - H)^-$.

Compound 387

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-cyano-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** To a solution of compound **389-B** (assume 3.88 mmol) in DMF (25 mL) was added a KOtBu solution (4.30 mL, 1M in THF), the reaction was stirred for 5 min, to which was added then 18-C-6 (1.03 g, 3.89 mmol) and 4-(bromomethyl)-1-fluoro-2-(trifluoromethyl)benzene (1.80 mL, 11.63 mmol). The reaction mixture was stirred for 4 days, concentrated in vacuo, and the material was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 1.59 g of compound **387** as a tan glass. ^{1}H-NMR (DMSO-d_6): δ 2.37 (s, 3H), 5.02 (br s, 2H), 7.52-7.42 (m, 3H), 7.74-7.66 (m, 2H), 8.05-7.92 (m, 4H), 8.22-8.16 (m, 2H).

Compound 389

4-Acetyl-*N*-(4-fluoro-3-trifluoromethylbenzyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-benzenesulfonamide. To a solution of compound **387** (0.267 g, 0.50 mmol) in THF (5 mL) was added MeMgCl (1.90 mL, 3M in THF), portion-wise over 5 h, and the reaction was stirred for an additional 30 min. The reaction was quenched with a saturated NH_4Cl solution (5 mL), the layers partitioned, the organic phase dried over $MgSO_4$, filtered and evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.075 g of compound **389** as a glassy yellow solid. ^{1}H-NMR (DMSO-d_6): δ 1.35 (s, 3H), 1.63 (s, 3H), 2.68 (s, 3H), 4.64 (d, 1H), 5.15-5.06 (m, 2H), 7.53-7.30 (m, 5H), 7.83-7.76 (m, 1H), 8.02 (d, 2H), 8.19 (d, 2H), 8.42-8.35 (m, 1H); MS: *m/z* 548.2 $(M - OH)^+$.

Following the procedure described above for example 73 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

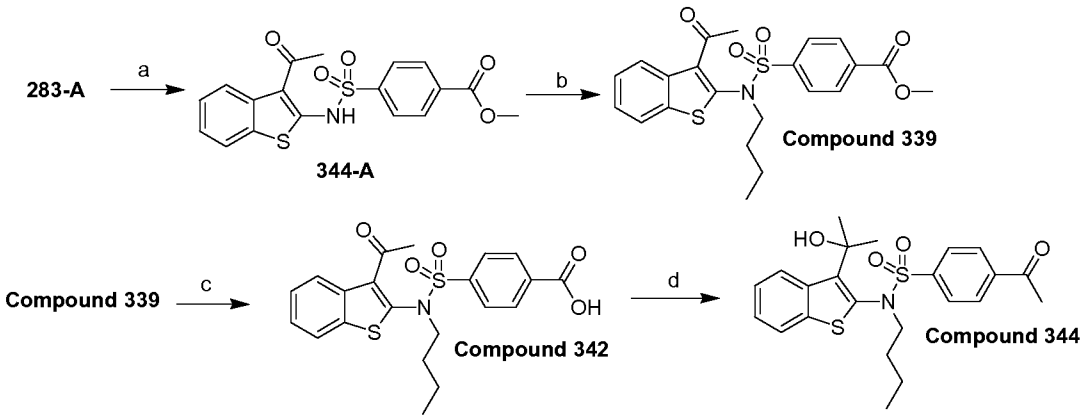
Compound 772

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-cyano-benzenesulfonamide.** ^{1}H-NMR (DMSO-d_6): δ 2.27 (s, 3H), 4.95 (s, 2H), 7.32-7.34 (d, 2H), 7.43-7.49 (m, 5H), 7.93-8.03 (m, 5H), 8.16-8.18 (m, 2H); MS: *m/z* 531.0 (MH^+).

Compound 773

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-cyano-benzenesulfonamide**. MS: *m/z* 481.0 (MH^+).

Example 74



a) AcCl, $SnCl_4$, DCM; b) Ph_3P, DEAD, butan-1-ol, THF; c) 1. $LiOH•H_2O$, THF, H_2O; 2. aq HCl; d) MeMgCl, THF.

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide (344-A).** To a suspension of compound **283-A** (1.05 g, 3.01 mmol) in DCM (4 mL), in an ice bath, was added a pre-mixed (5 min) solution of acetyl chloride (0.28 mL, 3.93 mmol) and $SnCl_4$ (0.39 mL, 3.31 mmol) in DCM (20 mL). The reaction mixture was allowed to warm slowly to ambient temperature and stir for 18 h. The reaction mixture was quenched with a saturated NH_4Cl solution (25 mL), filtered through a pad of celite, the organics dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was triturated with EtOAc (4 mL), filtered and air dried to afford 0.925 g of compound **344-A** as a tan powder. ^{1}H-NMR (DMSO-d_6): δ 2.55 (s, 3H), 3.86 (s, 3H), 7.24 (t, 1H), 7.32 (t, 1H), 7.73 (d, 1H), 7.94 (d, 2H), 8.11 (d, 2H), 8.16 (d, 1H); MS: *m/z* 390.0 (MH^+).

Compound 339

***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carbomethoxy-benzenesulfonamide.** To a solution of triphenyl phosphine (0.933 g, 3.56 mmol) in THF (30 mL) was added a 40% DEAD-toluene solution (1.60 mL, 3.60 mmol), the reaction mixture was stirred for 2 min, compound **344-A** (0.924 g, 2.37 mmol) was added, the reaction mixture was stirred for an additional 5 min, to which was added n-butanol (0.26 mL, 2.84 mmol) and the reaction was stirred for 4 days. The reaction mixture was concentrated in vacuo and the crude residue purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.624 g of compound **339** as a white foam. ^{1}H-NMR (DMSO-d_6): δ 0.86 (t, 3H), 1.35 (h, 2H), 1.61 (p, 2H), 2.67 (s, 3H), 3.65 (br s, 2H), 3.91 (s, 3H), 7.52-7.43 (m, 2H), 7.87-7.83 (m, 2H), 7.94-7.91 (m, 1H), 8.18-8.11 (m, 3H); MS: *m/z* 446.1 (MH^+).

Compound 342

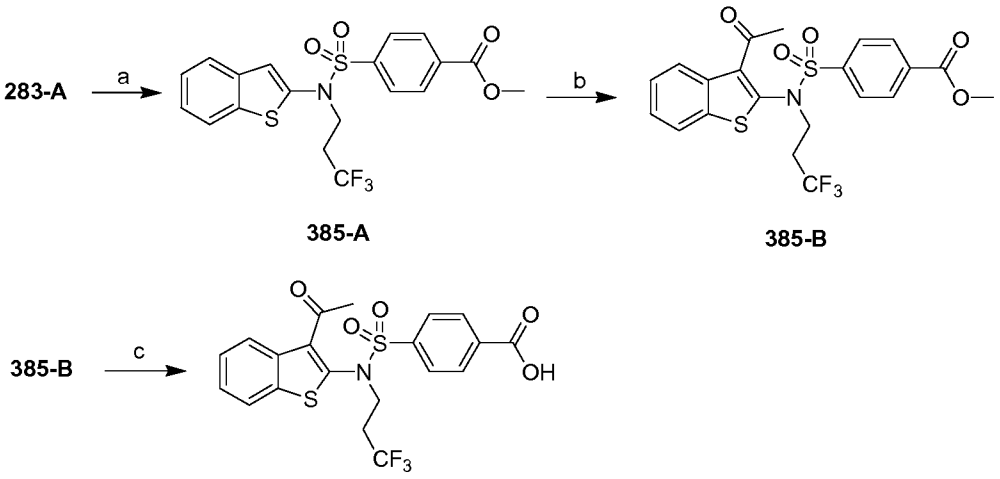
***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-4-carboxy-benzenesulfonamide.** To compound **339** (0.361 g, 0.81 mmol) in a 5:1 THF/water mixture (10 mL) was added LiOH•H_2O (0.042 g, 1.00 mmol) and the reaction mixture was stirred for 2.5 h. The solvent was evaporated in vacuo, the residue diluted with H_2O (5 mL), acidified with 1N HCl (1.0 mL), the precipitate filtered, washed with H_2O, and dried under vacuum to afford 0.334 g of compound **342** as a white powder. ^{1}H-NMR (DMSO-d_6): δ 0.86 (t, 3H), 1.35 (h, 2H), 1.61 (p, 2H), 2.67 (s, 3H), 3.65 (br s, 2H), 7.53-7.41 (m, 2H), 7.82 (d, 2H), 7.96-7.90 (m, 1H), 8.18-8.10 (m, 3H), 13.63 (s, 1H); MS: *m/z* 430.2 $(M - H)^-$.

Compound 344

***N*-(Butyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-acetyl-benzenesulfonamide.** To a solution of MeMgCl (0.37 mL, 3M in THF) in THF (2.5 mL) was added a solution of compound **342** (0.216 g, 0.50 mmol) in THF (2.5 mL), drop-wise, over was 2 min. Additional MeMgCl (0.54 mL, 3M in THF) was added in three portions over 4 h, and the reaction mixture was stirred for an additional 45 min. The reaction was quenched with a saturated NH_4Cl solution (5 mL), the organic layer were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by reverse-phase (25-95% acetonitrile/water + 0.1% TFA), the product fractions combined, treated with poly(vinylpyridine), filtered, frozen and lyophilized to afford 0.047 g of compound **344** as a cream-colored powder. ^{1}H-NMR

(DMSO-d_6): δ 0.81 (t, 3H), 1.50-1.14 (m, 3H), 1.68-1.53 (m, 1H), 1.72 (s, 3H), 1.80 (s, 3H), 2.68 (s, 3H), 3.24-3.12 (m, 1H), 3.89-3.77 (m, 1H), 5.31 (s, 1H), 7.40-7.32 (m, 2H), 7.81-7.74 (m, 1H), 7.97 (d, 2H), 8.91 (d, 2H), 8.56-8.48 (m, 1H); MS: *m/z* 428.2 $(M - OH)^+$.

Example 75



a) Ph_3P, DEAD, 3,3,3-trifluoropropan-1-ol, THF; b) Ac_2O, H_3PO_4; c) 1. $LiOH•H_2O$, THF, H_2O; 2. aq HCl.

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoropropyl)-4-carbomethoxy-benzenesulfonamide (385-A).** To a solution of triphenyl phosphine (2.27 g, 8.64 mmol) in THF (60 mL) was added a 40% DEAD-toluene solution (3.85 mL, 8.67 mmol), the reaction mixture was stirred for 2 min, compound **283-A** (2.0 g, 5.76 mmol) was added, the reaction mixture was stirred for an additional 5 min, to which was added 3,3,3-trifluoropropan-1-ol (0.61 mL, 6.90 mmol) and the reaction was stirred for 18 h. The reaction mixture was concentrated in vacuo and the crude residue purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 2.16 g of compound **385-A** as a tan solid. ^{1}H-NMR (DMSO-d_6): δ 2.68-2.50 (m, 2H), 3.90 (s, 3H), 3.97 (t, 2H), 7.28 (s, 1H), 7.42-7.34 (m, 2H), 7.84-7.76 (m, 1H), 7.94-7.86 (m, 3H), 8.18-8.11 (m, 2H); MS: *m/z* 444.1 (MH^+).

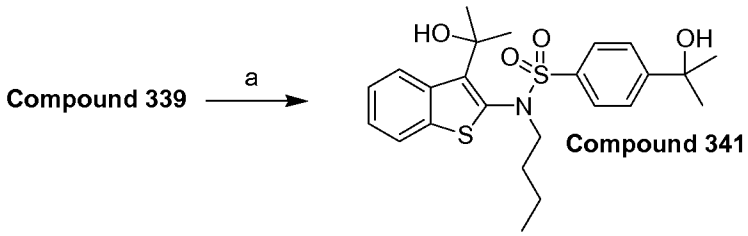
***N*-(3-Acetyl-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoropropyl)-4-carbomethoxy-benzenesulfonamide (385-B).** To compound **385-A** (0.388 g, 0.87 mmol) was added acetic anhydride (10 mL) and 85% H_3PO_4 (0.10 mL), and the

reaction was heated at 100 °C for three days. Additional acetic anhydride (10 mL) was added, the reaction mixture heated for an additional 4 more days. The reaction mixture was cooled, concentrated under vacuum, partitioned between EtOAc (100 mL) and saturated $NaHCO_3$ (50 mL), filtered, the organic layer washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash column chromatography (SiO_2) eluting with an EtOAc-heptane gradient to afford 0.197 g of compound **385-B** as a colorless oil. ^{1}H-NMR (DMSO-d_6): δ 2.64 (s, 3H), 2.91-2.72 (m, 2H), 4.01-3.87 (m, 5H), 7.54-7.43 (m, 2H), 7.87 (d, 2H), 7.99-7.92 (m, 1H), 8.19-8.08 (m, 3H); MS: *m/z* 486.1 (MH^+).

Compound 385

***N*-(3-Acetyl-benzo[b]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carboxy-benzenesulfonamide.** To compound **385-B** (0.190 g, 0.39 mmol) in a 5:1 THF/water mixture (5 mL) was added LiOH•H_2O (0.021 g, 0.50 mmol) and the reaction mixture was stirred for 18 h at ambient temperature. The solvent was evaporated in vacuo, the crude residue dissolved in warm H_2O (5 mL), acidified with 1N HCl (0.5 mL), the precipitate filtered, washed with H_2O, and dried under vacuum to afford 0.166 g of compound **385** as a white powder. ^{1}H-NMR (DMSO-d_6): δ 2.64 (s, 3H), 2.91-2.73 (m, 2H), 4.02-3.85 (m, 2H), 7.54-7.43 (m, 2H), 7.84 (d, 2H), 7.99-7.91 (m, 1H), 8.17-8.08 (m, 3H), 13.65 (s, 1H); MS: *m/z* 470.1 $(M - H)^-$.

Example 76



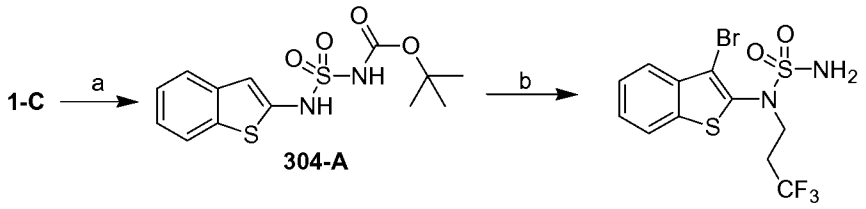
a) MeMgCl, THF.

Compound 341

***N*-(Butyl)-*N*-(3-(1-hydroxy-1-methyl-ethyl)-benzo[*b*]thiophen-2-yl)-4-(2-1-hydroxy-1-methyl-ethyl)-benzenesulfonamide.** A solution of compound **339** (0.232 g, 0.52 mmol) in THF (2.5 mL) was added to a solution of MeMgCl (0.20 mL, 3M in THF) in THF (1 mL). Additional MeMgCl (0.70 mL, 3M in THF) was added to the reaction mixture over 18 h, portion-wise, the reaction was quenched with a saturated

NH_4Cl solution (5 mL) , the layers separated, the organic layer dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by reverse-phase (25-95% acetonitrile/water + 0.1% TFA), the product fractions combined, treated with poly(vinylpyridine, filtered, frozen and lyophilized to afford 0.087 g of compound **341** as an off-white powder. ^{1}H-NMR (DMSO-d_6): δ 0.80 (t, 3H), 1.39-1.13 (m, 3H), 1.47 (s, 6H), 1.66-1.52 (m, 1H), 1.70 (s, 3H), 1.80 (s, 3H), 3.18-3.05 (m, 1H), 3.81-3.68 (m, 1H), 5.39-5.22 (br m, 2H), 7.39-7.31 (m, 2H), 7.82-7.70 (m, 5H), 8.57-8.49 (m, 1H); MS: *m/z* 444.2 $(M - OH)^+$.

Example 77



Compound 304

a) 1. DCM, pyridine; 2. $ClSO_2NCO$, t-BuOH, DCM; b) 1. Ph_3P, DEAD, 3,3,3-trifluoropropan-1-ol, THF; 2. NBS, DCE, HOAc; 3. TFA.

***tert*-Butyl *N*-(benzo[*b*]thiophen-2-yl)-sulfamoylcarbamate (304-A).** To a solution of chlorosulfonyl isocyanate (0.52 mL, 5.96 mmol) in DCM (5 mL) was added t-butanol (0.57 mL, 6.00 mmol), drop-wise over 1-2 min and the reaction mixture was stirred at ambient temperature for 2 h. A suspension of compound **1-C** (0.928 g, 5.00 mmol) in DCM (10 mL) was treated with pyridine (1 mL), the resulting solution cooled on an ice bath and the aforementioned reaction mixture was added drop-wise over 4 min. The reaction mixture was allowed to slowly warm to ambient temperature and stirred for 18 h. The reaction mixture was concentrated in vacuo, the residue dissolved in DCM (100 mL), washed with 1N HCl (25 mL), saturated $NaHCO_3$ (25 mL), brine (25 mL), the organic phase dried over $MgSO_4$, filtered, and evaporated under vacuum. The crude solid was triturated with DCM (10 mL), filtered, washed with DCM (2 mL) and air-dried to afford 0.602 g of compound **304-A** as an off-white powder. ^{1}H-NMR (DMSO-d_6): δ 1.39 (s, 9H), 6.98 (s, 1H), 7.37-7.24 (m, 2H), 7.72 (d, 1H), 7.84 (d, 1H), 11.11 (s, 1H), 11.40 (s, 1H); MS: *m/z* 351.1 (MNa^+).

Compound 304

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-sulfamide.** To a solution of Ph_3P (0.492 g, 1.88 mmol) in THF (15 mL) was added a 40% DEAD-toluene solution (0.84 mL, 1.89 mmol), the reaction mixture was stirred for 2 min, compound **304-A** (0.352 g, 1.07 mmol) was added, and the reaction mixture was then split equally into 5- portions. 3,3,3-Trifluoro-propan-1-ol (0.025 mL, 0.30 mmol) was added to one-portion of the aforementioned reaction mixture, the reaction stirred for 18 h, and the solvent evaporated in vacuo. The crude residue dissolved 1:1 dichloroethane/acetic acid (2mL), NBS (0.053 g, 0.30 mmol) was added, and the reaction mixture was stirred for 1 h. Additional NBS (0.011 g, 0.06 mmol) was added, the reaction mixture was stirred for 30 min, trifluoroacetic acid (0.50 mL) was added, and the reaction mixture was stirred for 3 days. The solvent was evaporated in vacuo, the crude residue purified by reverse-phase (25-95% acetonitrile/water + 0.1% TFA), and the product fractions frozen and lyophilized to afford 0.012 g of compound **304**. ^{1}H-NMR (DMSO-d_6): δ 2.64-2.54 (m, 2H), 3.80 (t, 2H), 7.58-7.50 (m, 2H), 7.67 (s, 2H), 7.82-7.76 (m, 1H), 8.05-8.00 (m, 1H); MS: *m/z* 403 (MH^+).

Following the procedure described above for example 77 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

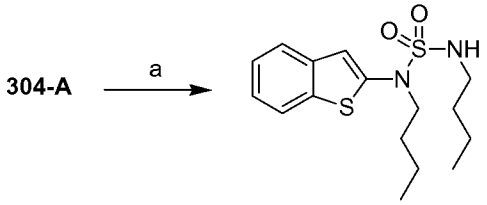
Compound 303

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(cyclopropylmethyl)-sulfamide.** MS: *m/z* 361.0 (MH^+).

Compound 849

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N,N'-bis*-butyl-sulfamide.** MS: *m/z* 419.1 (MH^+)

Example 78



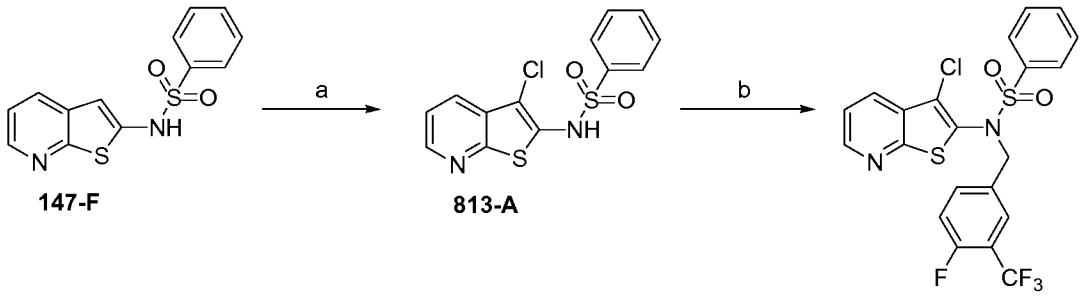
Compound 850

a) 1. Ph_3P, DEAD, butan-1-ol, THF; 2. TFA, DCM.

Compound 850

***N*-Benzo[*b*]thiophen-2-yl-*N,N'-bis*-butyl-sulfamide.** To a solution of Ph_3P (0.100 g, 1.88 mmol) in THF (3 mL) was added a 40% DEAD-toluene solution (0.17 mL, 0.38 mmol), the reaction mixture was stirred for 2 min, compound **304-A** (0.083 g, 1.07 mmol) was added, the reaction mixture stirred for 5 min, the butan-1-ol (0.027 mL, 0.29 mmol) was added, and the reaction mixture stirred for 18 h. Trifluoroacetic acid (0.50 mL) was added, the reaction mixture stirred for 1 h, and the solvent evaporated under reduced pressure. DCM (2 mL) and TFA (1 mL) were added to the residue, the reaction mixture stirred for 3 days, the solvent evaporated in vacuo, the crude residue purified by reverse-phase chromatography (25-95% acetonitrile/water + 0.1% TFA), and the product fractions frozen and lyophilized to afford 0.02 g of compound **850**. ^{1}H-NMR (DMSO-d_6): δ 0.89-0.80 (m, 6H), 1.36-1.22 (m, 4H), 1.44-1.36 (m, 2H), 1.54-1.44 (m, 2H), 2.92 (q, 2H), 3.60 (t, 2H), 7.27 (s, 1H), 7.39-7.30 (m, 2H), 7.71 (t, 1H), 7.80-7.76 (m, 1H), 7.89-7.85 (m, 1H); MS: *m/z* 341.2 (MH^+).

Example 79



Compound 813

a) NCS, DMF; b) 60% NaH, 4-fluoro-3-trifluoromethylbenzyl bromide, DMF.

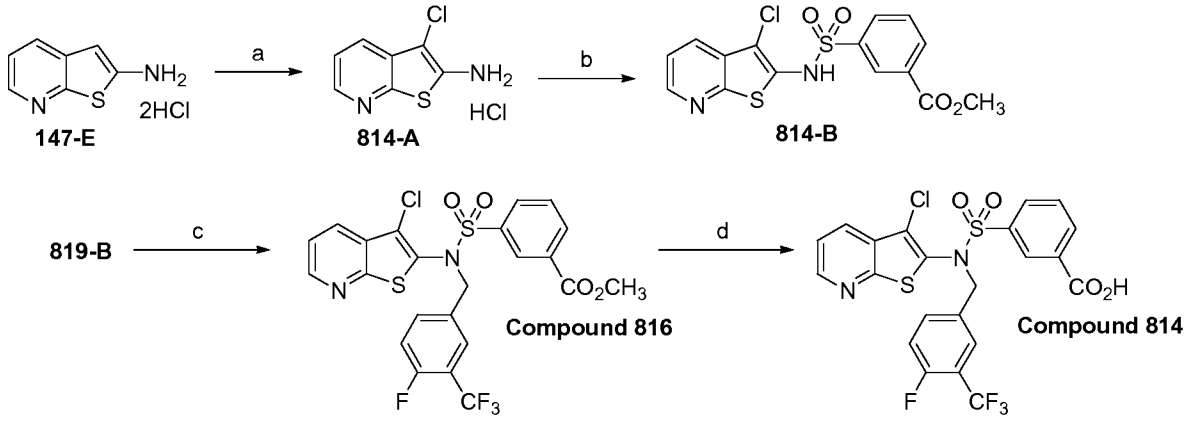
***N*-(3-Chloro-thieno[2,3-*b*]pyridin-2-yl)-benzenesulfonamide (813-A).** To compound **147-F** (0.26 g, 0.643 mmol) in DMF (1 mL) under argon at ambient temperature was added *N*-chlorosuccinimide (94.4 mg, 0.707 mmol) and the reaction mixture was stirred for 16 h. Ethyl acetate was added, the mixture washed with H_2O (2X), brine, evaporated under reduced pressure and purified by reverse phase pHPLC (C_{18}) to afford 0.072 g of compound **813-A** as a tan solid. ^{1}H-NMR (DMSO-d_6): δ 7.50

(dd, 1H), 7.56-7.65 (m, 2H), 7.65-7.74 (m, 1H), 7.81-7.89 (m, 2H), 8.00 (dd, 1H), 8.58 (dd, 1H).

Compound 813

***N*-(3-Chloro-thieno[2,3-*b*]pyridin-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide.** To a solution of compound **813-A** (72.1 mg, 0.222 mmol) in DMF (1 mL) under argon was added 60% NaH (9.3 mg, 0.233 mmol) and the reaction mixture was stirred for 15 min at ambient temperature. 4-Fluoro-3-trifluoromethylbenzyl bromide (0.034 mL, 0.222 mmol) was added and the reaction mixture was stirred for six days at ambient temperature. Saturated $NaHCO_3$ was added, the solution was extracted with EtOAc, washed with brine, dried over K_2CO_3, filtered, and evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with CH_2Cl_2, the pure fractions combined, excess 1M ethereal hydrogen chloride added, and the mixture evaporated under reduced pressure to afford 80 mg of compound **813** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 4.93 (s, 2H), 7.40-7.51 (m, 1H), 7.58 (dd, 1H), 7.63-7.78 (m, 4H), 7.80-7.90 (m, 1H), 7.95 (d, 2H), 8.15 (d, 1H), 8.65-8.76 (m, 1H); MS: *m/z* 501.04 (MH^+).

Example 80



a) NCS, DMF; b) 3-chlorosulfonyl-benzoic acid methyl ester, pyridine; c) 60% NaH, 4-fluoro-3-trifluoromethylbenzyl bromide, DMF; d) 3N NaOH, MeOH.

3-(Chloro-thieno[2,3-*b*]pyridin-2-yl)-amine (814-A). To a homogeneous solution of compound **147-E** (0.30 g, 1.34 mmol) in DMF (4 mL) under argon at ambient temperature was added *N*-chlorosuccinimide (0.22 g, 1.65 mmol), the reaction

mixture was stirred for seven days, EtOAc was added, and the precipitate filtered to afford 0.12 g of compound **814-A** as a white solid. MS: *m/z* 185 (MH^+).

3-(Chloro-thieno[2,3-*b*]pyridin-2-yl)-3-carbomethoxy-benzenesulfonamide (814-B). To a solution of comound **814-A** (0.17 g, 0.654 mmol) in pyridine (1.7 mL) under argon at ambient temperature was added 3-chlorosulfonyl-benzoic acid methyl ester (0.153 g, 0.654 mmol) and the reaction mixture was stirred at ambient temperature for 24 h. An additional portion of 3-chlorosulfonyl-benzoic acid methyl ester (0.03 g, 0.128 mmol) was added and the reaction mixture was stirred for an additional 48 h, at which time another portion of 3-chlorosulfonyl-benzoic acid methyl ester (0.043 g, 0.183 mmol) was added and the reaction mixture was allowed to stir for 18 h. The solvent was evaporated under reduced pressure and the crude residue purified by flash column chromatography (SiO_2) eluting with 1:1 heptane:CH_2Cl_2, CH_2Cl_2, and 1:3 acetone: CH_2Cl_2 to afford 0.12 g of compound **814-B**. MS: *m/z* 383.05 (MH^+).

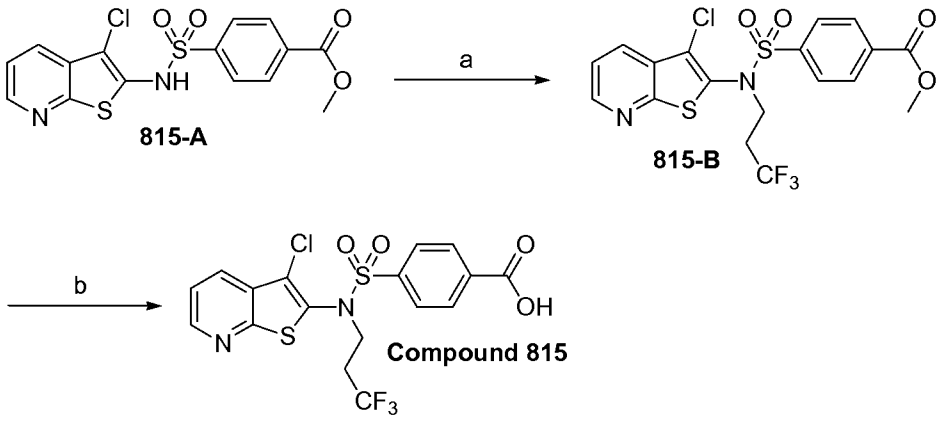
Compound 816

***N*-(3-Chloro-thieno[2,3-*b*]pyridin-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carbomethoxy-benzenesulfonamide.** To a solution of Compound **814-B** (0.12 g, 0.313 mmol) in DMF (2 mL) under argon was added 60% NaH (13.8 mg, 0.345 mmol) and the reaction mixture was stirred at ambient temperature for 15 min. 4-Fluoro-3-trifluoromethylbenzyl bromide (0.048 mL, 0.329 mmol) was added, the reaction mixture stirred for five days, water added, the solution extracted with EtOAc, washed with brine, dried with K_2CO_3, filtered, evaporated under reduced pressure, and purified by reverse phase pHPLC (C_{18}) to afford 0.06 g of compound **816** as a clear oil. MS: *m/z* 559.0 (MH^+).

Compound 814

***N*-(3-Chloro-thieno[2,3-*b*]pyridin-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-3-carboxy-benzenesulfonamide.** To a solution of compound **816** (0.055 g, 0.0983 mmol) in methanol (5.5 mL) was added 3N NaOH (0.066 ml, 0.197 mmol) and the reaction mixture was stirred at ambient temperature for six days, the solvent evaporated under reduced pressure, the residue dissolved in 0.1% TFA in acetonitrile / DMSO, and purified by reverse phase pHPLC (C_{18}) to afford 0.04 g of compound **814** as a white solid. MS: *m/z* 545.07 (MH^+).

Example 81



a) PPh_3, DEAD, 3,3,3-trifluoro-propan-1-ol, THF, toluene; b) 3N NaOH, MeOH.

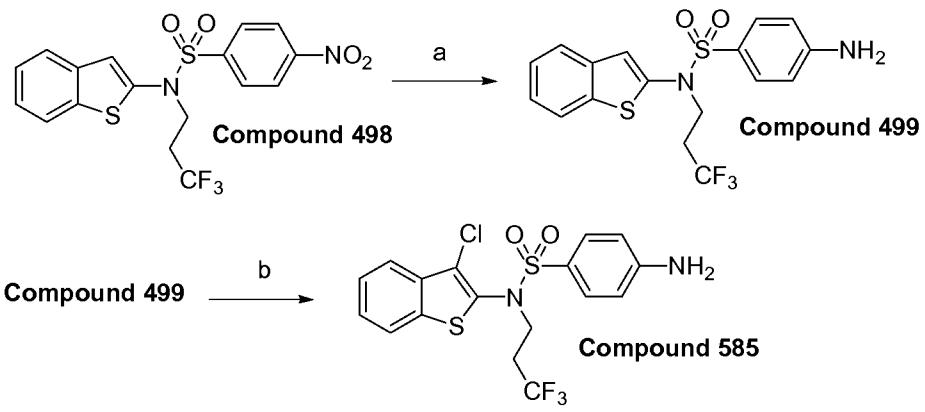
Compound **815-A** was prepared by the method used to synthesize compound **814-B** in Example 80, steps A and B.

***N*-(3-Chloro-thieno[2,3-*b*]pyridin-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carbomethoxy-benzenesulfonamide (815-B)**. To a flask under argon was added Ph_3P (0.268 g, 0.101 mmol), THF (7 mL), and 40% DEAD in toluene (0.449 mL, 0.101 mmol) and the reaction mixture was stirred for 2 min. Compound **815-A** (0.258 g, 0.674 mmol) was added, the reaction mixture stirred for five min, to which was added 3,3,3-trifluoro-propan-1-ol (0.095 g, 0.809 mmol) in THF (3 mL) and the reaction mixture stirred at ambient temperature for six days. The solvent was evaporated under reduced pressure and the residue purified by reverse phase pHPLC (C_{18}) to afford 0.167 g of compound **815-B**. MS: *m/z* 479.1 (MH^+).

Compound 815

***N*-(3-Chloro-thieno[2,3-*b*]pyridin-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-carboxy-benzenesulfonamide**. To a solution of compound **815-B** (0.167 g, 0.348 mmol) in methanol (12 mL), under argon, was added 3N NaOH (0.116 mL, 0.348 mmol) and the reaction mixture was stirred at ambient temperature 18 h. An additional portion of 3N NaOH (0.116 mL, 0.348 mmol) was added and the reaction mixture was stirred for six days. 1N HCl (0.804 mL, 0.804 mmol) was added to the reaction and the precipitate filtered to afford 0.115 g of compound **815** as a white solid. MS: *m/z* 465.0 (MH^+).

Example 82



a) 5% sulfided Pd/C, H_2, MeOH; b) NCS, DMF.

Compound 499

4-Amino-*N*-(benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide. A Paar flask containing 5% sulfided Pd/C (0.05 g, 10% w/w), compound **498** (0.49 g, 1.14 mmol) and methanol (20 mL) was reacted under hydrogen atmosphere for 3 days. The catalyst was filtered through a pad of celite and the filtrate evaporated under reduced pressure to afford 0.49 g of compound **499** as an off-white greenish solid. ^{1}H-NMR ($CDCl_3$): δ 2.48 (m, 2H), 3.78-3.87 (m, 2H), 6.63 (d, 2H), 7.14 (s, 1H), 7.30-7.40 (m, 2H), 7.48 (d, 2H), 7.65-7.75 (m, 2H); MS: *m/z* 401.19 (MH^+).

Compound 585

4-Amino-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide. To a solution of compound **499** (0.18 g, 0.450 mmol) in DMF (2.5 mL) was added *N*-chlorosuccinimide (0.084 g, 0.494 mmol) and the reaction mixture stirred at ambient temperature for 3 days. Ether was added to the reaction mixture, the organics washed with H_2O, brine, and the solvent evaporated under reduced pressure. The crude residue was purified by reverse phase pHPLC (C_{18}) to afford 0.036 g of compound **585** as an amber gum. ^{1}H-NMR ($CDCl_3$): δ 2.42-2.60 (m, 2H), 3.81-3.87 (m, 2H), 6.65-6.72 (m, 2H), 7.42-7.50 (m, 2H), 7.57-7.63 (m, 2H), 7.69-7.75 (m, 1H), 7.77-7.84 (m, 1H); MS: *m/z* 435.14 (MH^+).

Following the procedure described above for example 82 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 586

4-Amino-*N*-(benzo[*b*]thiophen-2-yl)-3-chloro-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide. ^{1}H-NMR ($CDCl_3$): δ 2.40-2.58 (m, 2H), 3.79-3.88 (m, 2H), 6.73 (d, 1H), 7.17 (s, 1H), 7.30-7.43 (m, 3H), 7.65 (d, 1H), 7.68-7.76 (m, 2H); MS: *m/z* 435.14 (MH^+).

Compound 587

4-Amino-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide. Compound **587** was prepared using the methodology in Example 82, step B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 2.43-2.61 (m, 2H), 3.80-3.89 (m, 2H), 6.65-6.73 (m, 2H), 7.42-7.50 (m, 2H), 7.58-7.65 (m, 2H), 7.70-7.76 (m, 1H), 7.77-7.83 (m, 1H); MS: *m/z* 479.23 (MH^+).

Compound 588

4-Amino-3-bromo-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide. Compound **588** was isolated as a by-product from the synthesis of compound **587**, prepared by using the methodology in Example 82, step B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 2.44-2.62 (m, 2H), 3.82-3.90 (m, 2H), 6.76 (d, 1H), 7.44-7.51 (m, 2H), 7.54 (dd, 1H), 7.72-7.77 (m, 1H), 7.78-7.84 (m, 1H), 7.91 (d, 1H); MS: *m/z* 558.92 (MH^+).

Compound 650

4-Amino-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide. Compound **650** was prepared using the methodology in Example 1, steps C and D, and Example 82, steps A and B. ^{1}H-NMR ($CDCl_3$): δ 4.78 (s, 2H), 6.65-6.74 (m, 2H), 7.01-7.10 (m, 1H), 7.36-7.44 (m, 2H), 7.45-7.56 (m, 2H), 7.59-7.69 (m, 3H), 7.70-7.74 (m, 1H); MS: *m/z* 559.08 (MH^+).

Compound 651

4-Amino-3-bromo-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide. Compound **651** was isolated as a by-product from the synthesis of compound **650**, prepared by using the methodology in Example 82, step B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 4.79 (s, 2H), 6.77 (d, 1H), 7.07 (t, 1H), 7.37-7.58 (m, 5H), 7.64-7.76 (m, 2H), 7.92 (d, 1H); MS: *m/z* 638.85 (MH^+).

Compound 653

4-Amino-*N*-(benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-benzenesulfonamide. Compound **653** was prepared using the methodology in Example 1, steps C and D, and Example 82, step A. ^{1}H-NMR ($CDCl_3$): δ 4.76 (s, 2H), 6.62-6.70 (m, 2H), 7.02 (s, 1H), 7.05-7.14 (m, 1H), 7.27-7.35 (m, 2H), 7.49-7.58 (m, 4H), 7.63 (td, 2H); MS: *m/z* 481.2 (MH^+).

Compound 666

4-Amino-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide. Compound **666** was prepared using the methodology in Example 1, step C, Example 3, step A, and Example 82, steps A and B. ^{1}H-NMR ($CDCl_3$): δ 1.52-1.75 (m, 4H), 1.96-2.15 (m, 2H), 3.61 (t, 2H), 6.64-6.71 (m, 2H), 7.40-7.49 (m, 2H), 7.55-7.63 (m, 2H), 7.66-7.74 (m, 1H), 7.76-7.84 (m, 1H); MS: *m/z* 463.11 (MH^+).

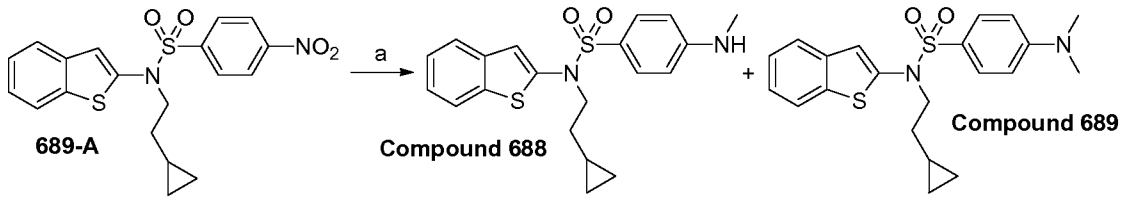
Compound 667

4-Amino-3-chloro-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide. Compound **667** was isolated as a by-product from the synthesis of compound **585**, prepared by using the methodology in Example 82, step B. MS: *m/z* 497.02 (MH^+).

Compound 668

4-Amino-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide. Compound **668** was prepared using the methodology in Example 1, step C, Example 3, step A, and Example 82, steps A and B, substituting *N*-bromosuccinimide for *N*-chlorosuccinimide. ^{1}H-NMR ($CDCl_3$): δ 1.52-1.75 (m, 4H), 1.96-2.14 (m, 2H), 3.62 (t, 2H), 6.64-6.73 (m, 2H), 7.39-7.49 (m, 2H), 7.56-7.64 (m, 2H), 7.68-7.74 (m, 1H), 7.80 (dd, 1H); MS: *m/z* 508.90 (MH^+).

Example 83



a) 10% Pd/C, H_2, MeOH/HCHO.

Compound **689-A** was prepared by the method in Example 1, step C, and Example 3, step A.

Compound 688 and Compound 689

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methylamino-benzenesulfonamide (Cpd 688) and *N*-(benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-dimethylamino-benzenesulfonamide (Cpd 689)**. A Paar flask containing 10% Pd/C (0.15 g, 24% w/w), and compound **689-A** (0.62 g, 1.54 mmol) in methanol (100 mL), contaminated with some formaldehyde, was reacted under hydrogen atmosphere for two days. The catalyst was filtered through a pad of celite and the filtrate evaporated under reduced pressure to afford 0.42 g of a mixture of compound **688** and compound **689**. The crude mixture was purified by reverse phase pHPLC (C_{18}) to afford 0.016 g of compound **688** as a white solid and 0.028 g of compound **689** as an off-white solid.

Compound 688

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methylamino-benzenesulfonamide**. MS: *m/z* 387 (MH^+).

Compound 689

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-dimethylamino-benzenesulfonamide**. MS: *m/z* 401 (MH^+).

Following the procedure described above for example 83 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 690

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methylamino-benzenesulfonamide**. Compound **690** was prepared using the methodology in Example 82, step B. ^{1}H-NMR ($CDCl_3$): δ -0.04-0.00 (m, 6H), 0.34-0.46 (m, 7H), 0.61-0.76 (m, 3H), 1.43 (q, 7H), 2.94 (s, 3H), 3.6-3.72 (m, 2H), 6.71 (d, 2H), 7.38-7.49 (m, 2H), 7.63-7.74 (m, 3H), 7.75-7.83 (m, 1H); MS: *m/z* 421.1 (MH^+).

Compound 691

3-Chloro-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methylamino-benzenesulfonamide. Compound **691** was was isolated as a by-product during the synthesis of compound **690**, prepared by using the methodology in Example

82, step B. ^{1}H-NMR ($CDCl_3$): δ 0.00-0.05 (m, 6H), 0.36-0.45 (m, 8H), 0.63-0.77 (m, 4H), 1.38-1.49 (m, 8H), 2.98 (s, 3H), 3.62-3.72 (m, 2H), 6.63 (d, 1H), 7.38-7.50 (m, 2H), 7.61 (dd, 1H), 7.76-7.84 (m, 1H); MS: *m/z* 455.09 (MH^+).

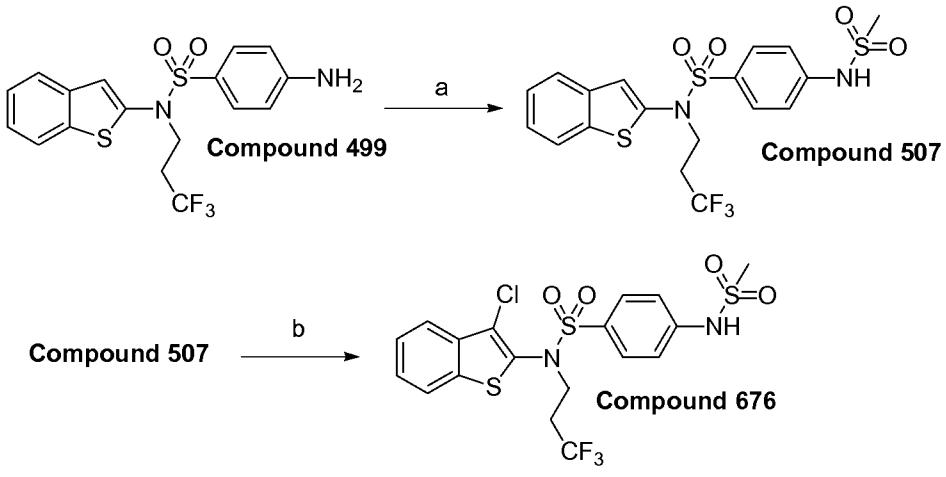
Compound 692

3-Bromo-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methylamino-benzenesulfonamide. Compound **692** was was isolated as a by-product during the synthesis of compound **693**, prepared by using the methodology in Example 82, step B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 0.00-0.04 (m, 6H), 0.37-0.45 (m, 7H), 0.61-0.78 (m, 3H), 1.38-1.51 (m, 8H), 2.98 (s, 3H), 3.63-3.73 (m, 2H), 6.60 (d, 1H), 7.38-7.49 (m, 2H), 7.65 (dd, 1H), 7.71 (dd, 1H), 7.76-7.84 (m, 1H), 7.91 (d, 1H); MS: *m/z* 544.97 (MH^+).

Compound 693

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methylamino-benzenesulfonamide**. Compound **693** was prepared using the methodology in Example 82, step B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ -0.05-0.02 (m, 9H), 0.34-0.46 (m, 2H), 0.61-0.75 (m, 1H), 1.37-1.52 (m, 2H), 2.96 (s, 3H), 3.63-3.73 (m, 2H), 6.83 (d, 2H), 7.38-7.48 (m, 2H), 7.65-7.74 (m, 3H), 7.75-7.82 (m, 1H); MS: *m/z* 465.07 (MH^+).

Example 84



a) CH_3SO_2Cl, DIEA, THF; b) NCS, DMF.

Compound 507

***N*-(Benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide**. To a flask under argon was added compound **499** (52.1 mg, 0.013 mmol), THF (3 mL), DIEA (0.027 mL, 0.016 mmol) and methanesulfonyl chloride (0.010 mL, 0.013 mmol). The reaction mixture was heated at 70 °C for seven days, the solvent evaporated under reduced pressure and the crude residue purified by flash column chromatography (SiO_2) eluting with DCM, followed by reverse phase pHPLC (C_{18}) to afford 7.2 mg of compound **507** as a yellow solid. MS: *m/z* 479.1 (MH^+).

Compound 676

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide**. To *N*-chlorosuccinimide (55.2 mg, 0.414 mmol) under argon was added compound **507** (0.22 g, 0.460 mmol) in DMF (5 mL). The reaction mixture was stirred at ambient temperature for 18 h, another portion of *N*-chlorosuccinimide (55.2 mg, 0.414 mmol) was added and the reaction mixture was stirred for an additional 18h. Ethyl acetate was added to the reaction mixture, the organics washed with water (2X), the solvent evaporated under reduced pressure and the crude residue purified by reverse phase pHPLC (C_{18}) to afford 119 mg of compound **676** as a white solid. ^{1}H-NMR ($CDCl_3$): δ 2.45-2.62 (m, 2H), 3.13 (s, 3H), 3.85-3.93 (m, 2H), 6.93 (s, 1H), 7.28-7.34 (m, 2H), 7.45-7.53 (m, 2H), 7.72-7.86 (m, 4H); MS: *m/z* 512.96 (MH^+).

Following the procedure described above for example 84 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 652

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylamino-benzenesulfonamide**. Compound **652** was prepared using the methodology in Example 1, steps C and D, and Example 82, step A, and Example 84, step A. MS: *m/z* 559.07 (MH^+).

Compound 659

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylamino-benzenesulfonamide**. Compound **659** was prepared from compound **652** using the methodology in Example 1, steps C and D, Example 82, step

A, and Example 84, steps A and B. ^{1}H-NMR ($CDCl_3$): δ 3.14 (s, 3H), 4.83 (s, 2H), 6.96 (s, 1H), 7.09 (t, 1H), 7.28-7.36 (m, 2H), 7.39-7.47 (m, 2H), 7.47-7.57 (m, 2H), 7.64-7.76 (m, 2H), 7.83 (d, 2H); MS: *m/z* 593.05 (MH^+).

Compound 660

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylamino-benzenesulfonamide**. Compound **660** was prepared from compound **652** using the methodology in Example 1, steps C and D, Example 82, step A, and Example 84, steps A and B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 3.14 (s, 3H), 4.84 (s, 2H), 7.01-7.14 (m, 2H), 7.28-7.36 (m, 2H), 7.38-7.58 (m, 4H), 7.62-7.77 (m, 2H); MS: *m/z* 639.08 (MH^+).

Compound 661

3-Bromo-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylamino-benzenesulfonamide. Compound **661** was isolated as a by-product during the synthesis of compound **660**. ^{1}H-NMR ($CDCl_3$): δ 3.14 (s, 3H), 4.86 (s, 2H), 7.10 (t, 1H), 7.19 (s, 1H), 7.45 (dd, 2H), 7.47-7.57 (m, 2H), 7.71 (ddd, 2H), 7.78-7.81 (m, 2H), 7.78-7.81 (m, 2H), 8.05 (s, 1H).

Compound 677

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(3,3,3-trifluoro-propyl)-4-methanesulfonylamino-benzenesulfonamide**. Compound **677** was prepared from compound **507** using the methodology in Example 1, steps C and D, Example 3, step A, Example 82, step A, and Example 84, steps A and B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 2.42-2.63 (m, 2H), 3.11-3.44 (m, 3H), 3.84-3.94 (m, 2H), 6.88-.24 (m, 1H), 7.30 (d, 1H), 7.36-7.44 (m, 1H), 7.45-7.52 (m, 1H), 7.64-7.97 (m, 4H); MS: *m/z* 558.93 (MH^+).

Compound 678

***N*-(Benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 1.65-1.73 (m, 4H), 1.99-2.18 (m, 2H), 3.11 (s, 3H), 3.57-3.68 (m, 2H), 6.87 (s, 1H), 7.20 (d, 2H), 7.31-7.42 (m, 2H), 7.64-7.76 (m, 4H); MS: *m/z* 507.02 (MH^+).

Compound 679

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide**. MS: *m/z* 541.02 (MH^+).

Compound 680

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide**. Compound **680** was prepared using the methodology in Example 84, steps A and B, substituting *N*-bromosuccinimide for *N*-chlorosuccinimide. MS: *m/z* 586.93 (MH^+).

Compound 681

3,5-Dichloro-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide. Compound **681** was isolated as a by-product during the synthesis of compound **676** using the methodology in Example 1, steps C and D, Example 82, step A, and Example 84, steps A and B. MS: *m/z* 580.84 (MH^+).

Compound 682

3,5-Dichloro-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(5,5,5-trifluoro-pentyl)-benzenesulfonamide. Compound **682** was isolated as a by-product during the synthesis of compound **679** using the methodology in Example 1, steps C and D, Example 82, step A, and Example 84, steps A and B. MS: *m/z* 610.79 (MH^+).

Compound 683

3-Bromo-*N*-(3-bromo-benzo[*b*]thiophen-2-yl)-4-methanesulfonylamino-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide. Compound **683** was isolated as a by-product during the synthesis of compound **677** using the methodology in Example 1, steps C and D, Example 82, step A, and Example 84, steps A and B. ^{1}H-NMR ($CDCl_3$): δ 2.47-2.65 (m, 2H), 3.11-3.45 (m, 3H), 3.87-3.96 (m, 2H), 7.18 (s, 1H), 7.46-7.54 (m, 2H), 7.73-7.84 (m, 4H), 8.04-8.09 (m, 1H).

Compound 713

***N*-(Benzo[*b*]thiophen-2-yl)-3-methanesulfonylamino-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide.** MS: *m/z* 479.00 (MH^+).

Compound 714

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-3-methanesulfonylamino-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 2.45-2.62 (m, 2H), 2.96 (s, 3H), 3.88-3.98 (m, 2H), 6.76 (s, 1H), 7.44-7.52 (m, 2H), 7.53-7.63 (m, 3H), 7.63-7.69 (m, 1H), 7.71-7.81 (m, 2H); MS: *m/z* 512.99 (MH^+).

Compound 715

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-3-methanesulfonylamino-*N*-(3,3,3-trifluoro-propyl)-benzenesulfonamide**. Compound **715** was prepared using the methodology in Example 84, steps A and B, substituting NBS for NCS. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.46-2.64 (m, 9H), 2.96 (s, 3H), 3.90-3.99 (m, 2H), 6.70 (s, 1H), 7.45-7.53 (m, 2H), 7.64-7.70 (m, 1H), 7.71-7.81 (m, 2H); MS: *m/z* 558.85 (MH^+).

Compound 716

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methanesulfonylamino-benzenesulfonamide**. ^{1}H-NMR ($CDCl_3$): δ 0.00-0.06 (m, 8H), 0.37-0.47 (m, 8H), 0.61-0.77 (m, 4H), 1.40-1.52 (m, 8H), 3.12 (s, 3H), 3.67-3.76 (m, 6H), 6.97 (s, 3H), 7.27-7.33 (m, 7H), 7.41-7.51 (m, 6H), 7.68-7.88 (m, 12H); MS: *m/z* 485.04 (MH^+).

Compound 717

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-methanesulfonylamino-benzenesulfonamide**. Compound **717** was prepared from compound **716** using the methodology in Example 84, steps A and B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 0.01-0.07 (m, 7H), 0.37-0.47 (m, 7H), 0.69 (t, 4H), 1.41-1.54 (m, 7H), 3.12 (s, 3H), 3.68-3.78 (m, 2H), 6.84 (s, 1H), 7.29 (d, 2H), 7.41-7.49 (m, 2H), 7.69-7.87 (m, 4H); MS: *m/z* 528.89 (MH^+).

Compound 718

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-4-cyclopropanesulfonylamino-*N*-(2-cyclopropyl-ethyl)-benzenesulfonamide**. MS: *m/z* 511.02 (MH^+).

Compound 719

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-4-cyclopropanesulfonylamino-*N*-(2-cyclopropyl-ethyl)-benzenesulfonamide**. Compound **719** was prepared using the methodology in Example 84, steps A and B, substituting NBS for NCS. ^{1}H-NMR ($CDCl_3$): δ 0.01-0.06 (m, 6H), 0.38-0.46 (m, 2H), 0.69 (s, 1H), 1.00-1.10 (m, 2H), 1.21-1.31 (m, 2H), 1.42-1.52 (m, 2H), 2.51-2.63 (m, 1H), 3.68-3.80 (m, 2H), 6.75 (s, 1H), 7.29-7.37 (m, 2H), 7.40-7.50 (m, 2H), 7.68-7.86 (m, 4H); MS: *m/z* 555.02 (MH^+).

Compound 743

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylamino-2-methoxy-benzenesulfonamide**. Compound **743** was

prepared using the methodology in Example 1, steps C and D, Example 82, step A, and Example 84, step A. MS: *m/z* 589.03 (MH^+).

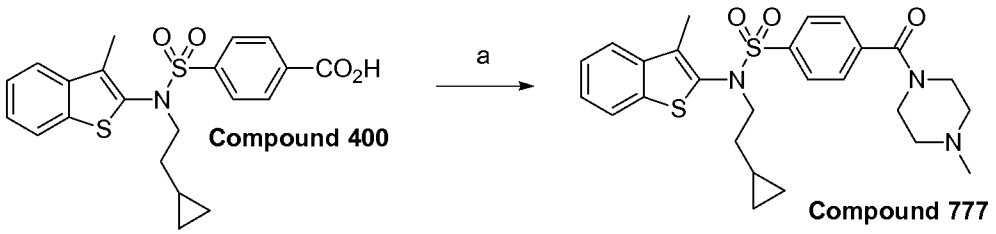
Compound 744

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylamino-2-methoxy-benzenesulfonamide.** Compound **744** was prepared from compound **743** using the methodology in Example 84, step B. MS: *m/z* 622.90 (MH^+).

Compound 766

5-Chloro-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-methanesulfonylamino-2-methoxy-benzenesulfonamide. Compound **766** was isolated as a by-product during the synthesis of compound **744**. ^{1}H-NMR ($CDCl_3$): δ 3.10 (s, 3H), 4.07 (s, 3H), 5.07 (s, 2H), 7.05 (s, 1H), 7.11 (t, 1H), 7.41 (dd, 2H), 7.47 (s, 1H), 7.53 (dd, 2H), 7.60-7.73 (m, 2H), 7.84 (s, 1H); MS: *m/z* 657.0 (MH^+).

Example 85



a) HATU, DIEA, DMF, 1-methyl-piperazine.

Compound 777

***N*-(2-Cyclopropyl-ethyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-(4-methyl-piperazine-1-carbonyl)-benzenesulfonamide.** To a solution of compound **400** (0.100 g, 0.241 mmol) in DMF (1.5 mL) was added DIEA (0.0838 mL, 0.481 mmol), 1-methyl-piperazine (0.027 mL, 0.241 mmol) and HATU (0.110 g, 0.289 mmol) and the reaction mixture stirred at ambient temperature for 18 h. Ethyl acetate was added and the organics washed with water, brine, and evaporated under reduced pressure. The crude residue was purified by reverse phase pHPLC (C_{18}) to afford 0.108 g of compound **777** as a white solid. MS: *m/z* 498.18 (MH^+).

Following the procedure described above for example 85 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

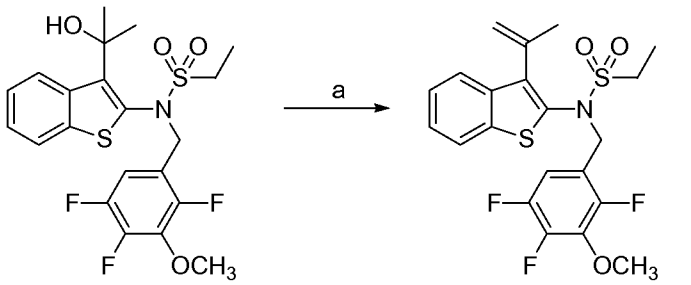
Compound 782

(*S*)-4-[(2-Cyclopropyl-ethyl)-(3-methyl-benzo[*b*]thiophen-2-yl)-sulfamoyl]-*N*-pyrrolidin-3-yl-benzamide. MS: *m/z* 484.16 (MH^+).

Compound 783

(*R*)-4-[(2-Cyclopropyl-ethyl)-(3-methyl-benzo[*b*]thiophen-2-yl)-sulfamoyl]-*N*-pyrrolidin-3-yl-benzamide. MS: *m/z* 484.16 (MH^+).

Example 86



a) 0.1% TFA in CH_3CN/H_2O.

Compound 803

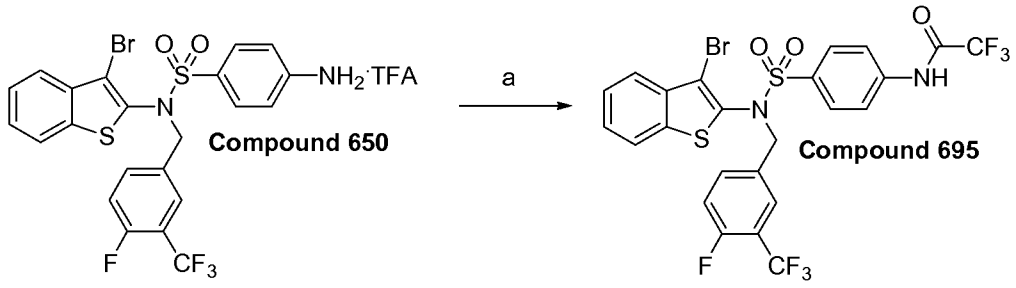
***N*-(3-Isopropenyl-benzo[*b*]thiophen-2-yl)-*N*-(2,4,5-trifluoro-3-methoxy-benzyl)-ethanesulfonamide**. Compound **802** was purified by reverse phase pHPLC (C_{18}) eluting with 0.1% TFA in CH_3CN/ H_2O. The pure fractions were lyophilized affording complete conversion of compound **802** to compound **803** as a white solid. ^{1}H-NMR ($CDCl_3$): δ 1.48 (t, 3H), 2.04 (s, 3H), 3.30 (q, 2H), 3.95 (s, 3H), 4.84 (s, 2H), 4.94 (s, 1H), 5.40 (s, 1H), 6.94 (ddd, 1H), 7.31-7.42 (m, 2H), 7.61-7.74 (m, 2H); MS: *m/z* 456.01 (MH^+).

Following the procedure described above for example 86 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 768

***N*-(4-Chloro-2-fluoro-5-methoxy-benzyl)-*N*-(3-isopropenyl-benzo[*b*]thiophen-2-yl)-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.48 (t, 3H), 2.02 (s, 3H), 3.29 (q, 2H), 3.73 (s, 3H), 4.86 (s, 2H), 4.93 (s, 1H), 5.38 (d, 1H), 6.95 (d, 1H), 7.04 (d, 1H), 7.31-7.40 (m, 2H), 7.61-7.73 (m, 2H); MS: *m/z* 454.12 (MH^+).

Example 87



a) CH_3SO_2Cl, pyridine.

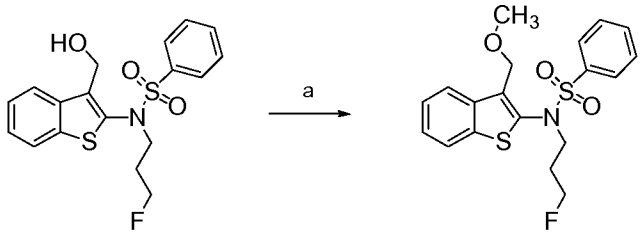
Compound 695

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-4-trifluoroacetamido-benzenesulfonamide.** To a solution of compound **650** (0.074 g, 0.136 mmol) in pyridine (1 mL), under argon, was added methanesulfonyl chloride (0.053 mL, 0.680 mmol) and the reaction mixture was stirred at ambient temperature for 18 h. The solvent was evaporated under reduced pressure and the crude residue purified by reverse phase pHPLC (C_{18}) to afford 0.029 g of compound **695** as a white solid. ^{1}H-NMR ($CDCl_3$): δ 4.85 (s, 2H), 7.04-7.14 (m, 1H), 7.38-7.57 (m, 4H), 7.63-7.74 (m, 2H), 7.76-7.82 (m, 2H), 7.85-7.93 (m, 2H), 8.12 (s, 1H); MS: *m/z* 654.9 (MH^+).

Compound 694

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(2-cyclopropyl-ethyl)-4-trifluoroacetamido-benzenesulfonamide.** MS: *m/z* 503.05 (MH^+).

Example 88



Compound 820 **Comopund 832**

a) NaH, THF, MeI.

Compound 832

***N*-(3-Fluoro-propyl)-*N*-(3-methoxymethyl-benzo[*b*]thiophen-2-yl)-benzenesulfonamide.** To a solution of compound **820** (38 mg, 0.10 mmol) in THF (3 mL), was added sodium hydride (16 mg, 0.40 mmol) followed by iodomethane (28 mg, 0.20) at room temperature and the reaction mixture was stirred for 2 h. The reaction mixture was quenched with water, extracted with EtOAc, the layers separated, and the organic phase dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with 15% ethyl acetate in hexanes, to afford 36 mg of compound **832**. MS: *m/z* 416.2 (MNa^+).

Following the procedure described above for Example 88 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

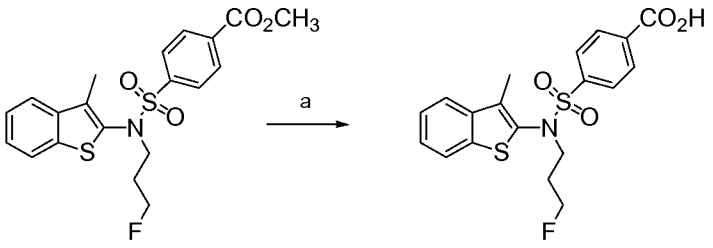
Compound 822

***N*-(3-Fluoro-propyl)-*N*-[3-(1-methoxy-ethyl)-benzo[*b*]thiophen-2-yl]-benzenesulfonamide.** MS: *m/z* 430.0 (MNa^+).

Compound 839

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-[3-(1-methoxy-ethyl)-benzo[*b*]thiophen-2-yl]-ethanesulfonamide.** ^{1}H-NMR ($CDCl_3$): δ 1.51 (t, 3H), 1.55 (s, 3H), 2.38-2.55 (br, 2H), 3.22-3.31 (br, 3H), 4.41-4.61 (br, 2H), 5.10-5.15 (br, 1H), 7.11-7.16 (m, 1H), 7.34-7.41 (m, 2H), 7.55-7.59 (m, 2H), 7.74-7.76 (m, 1H), 8.14-8.16 (m, 1H); MS: *m/z* 498.1 (MNa^+).

Example 89



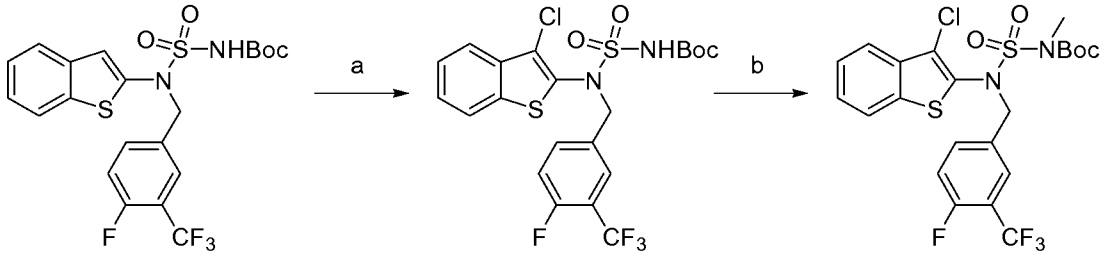
Compound 823 **Compound 824**

a) $LiOH \cdot H_2O$, THF, MeOH, H_2O.

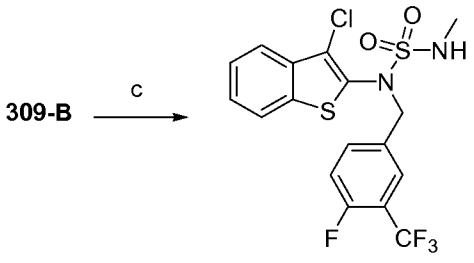
Compound 824

***N*-(3-Fluoropropyl)-*N*-(3-methyl-benzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide.** To a solution of compound **823** (100 mg, 0.237 mmol) in THF (9 mL), was added lithium hydroxide monohydrate (60 mg, 1.43 mmol) in water (3 mL), followed methanol (1 mL) at room temperature and the reaction mixture was stirred for 3 h. The reaction mixture was concentrated, triturated with 2N HCl, filtered, and the solids were washed three times with water, and the solid was dried under vacuum to afford 42 mg of compound **824**. MS: *m/z* 408.0 (MH^+).

Example 90



300-B **309-A** **309-B**



Compound 309

a) DCE, NCS; b) DMF, NaH, MeI; c) 4N HCl.

***N*-(4-Fluoro-3-trifluorobenzyl)-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-[*N*'-*tert*-butyloxycarbonyl]-sulfonamide (309-A).** To a solution of compound **300-B** (595 mg; 1.17 mmol) in DCE (6 mL), at ambient temperature, was added NCS (173 mg; 1.29 mmol), and the reaction mixture was allowed to stir at ambient temperature for 2 h. The reaction mixture was concentrated under reduced pressure and the crude residue purified by flash column chromatography (SiO_2) eluting with a heptane/EtOAc gradient to afford 528 mg of compound **309-A** as a yellow solid. ^{1}H-NMR (DMSO-d_6): δ 1.51 (s, 9H), 5.07 (s, 2H), 7.42-7.47 (q, 1H), 7.51-7.55 (m, 2H), 7.64-7.68 (m, 1H), 7.75-7.79 (m, 2H), 8.01-8.03 (m, 1H), 11.83 (s, 1H).

***N*-(4-Fluoro-3-trifluorobenzyl)-*N*-(3-chloro-benzo[*b*]thiophen-2-yl)-*N*'-methyl-*N*-(*tert*-butyloxycarbonyl)-sulfonamide (309-B).** To a solution of compound **309-A** (334 mg; 0.619 mmol) in DMF (3 mL), at ambient temperature, was added 60% NaH (31 mg; 0.805 mmol), and the suspension was allowed to stir at ambient temperature for 30 min. Methyl iodide (46 μL; 0.743 mmol) in DMF (0.1 mL), was added drop-wise, and the reaction was allowed to stir for 72 h at ambient temperature. The reaction mixture was diluted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4, filtered, and the solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (SiO_2) eluting with a heptane/EtOAc gradient to afford 303 mg of compound **309-B** as a yellow oil. ^{1}H-NMR (DMSO-d_6): δ 1.54 (s, 9H), 3.02 (s, 3H), 5.10 (s, 2H), 7.44-7.49 (q, 1H), 7.52-7.55 (m, 2H), 7.65-7.69 (m, 1H), 7.76-7.79 (m, 2H), 8.02-8.04 (m, 1H); MS: *m/z* 453.0 ((M-Boc)+H$^+$).

Compound 309

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N*'-methyl-sulfamide.** To compound **309-B** (303 mg, 0.548 mmol) was added solution of 1N HCl in dioxane (6 mL) and the reaction was stirred at ambient temperature for 18 h. The reaction mixture was evaporated under reduced pressure, the residue dried under vacuo, and purified by flash column chromatography (SiO_2) eluting with a heptane-EtOAc gradient to afford 211 mg of compound **309** as an oil. ^{1}H-NMR (DMSO-d_6): δ 2.72 (s, 3H), 4.81 (s, 2H), 7.44-7.56 (m, 3H), 7.64-7.78 (m, 3H), 7.99-8.04 (m, 2H); MS: *m/z* 453.0 (MH$^+$).

Following the procedure described above for Example 90 and substituting the appropriate reagents, starting materials and purification methods known to those skilled in the art, the following compounds of the present invention were prepared:

Compound 532

***N*-(Benzo[*b*]thiophen-2-yl)-*N*-(butyl)-*N'*-methyl-sulfamide.** MS: *m/z* 299.1 (MH^+).

Compound 533

***N*-(4-Fluoro-3-trifluoromethyl-benzyl)-*N*-(3-methylbenzo[*b*]thiophen-2-yl)-*N'*-methyl-sulfamide.** MS: *m/z* 433.0 (MH^+).

Compound 553

***N*-(3-Chloro-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-*N'*-methyl-sulfamide.** MS: *m/z* 333.0 (MH^+).

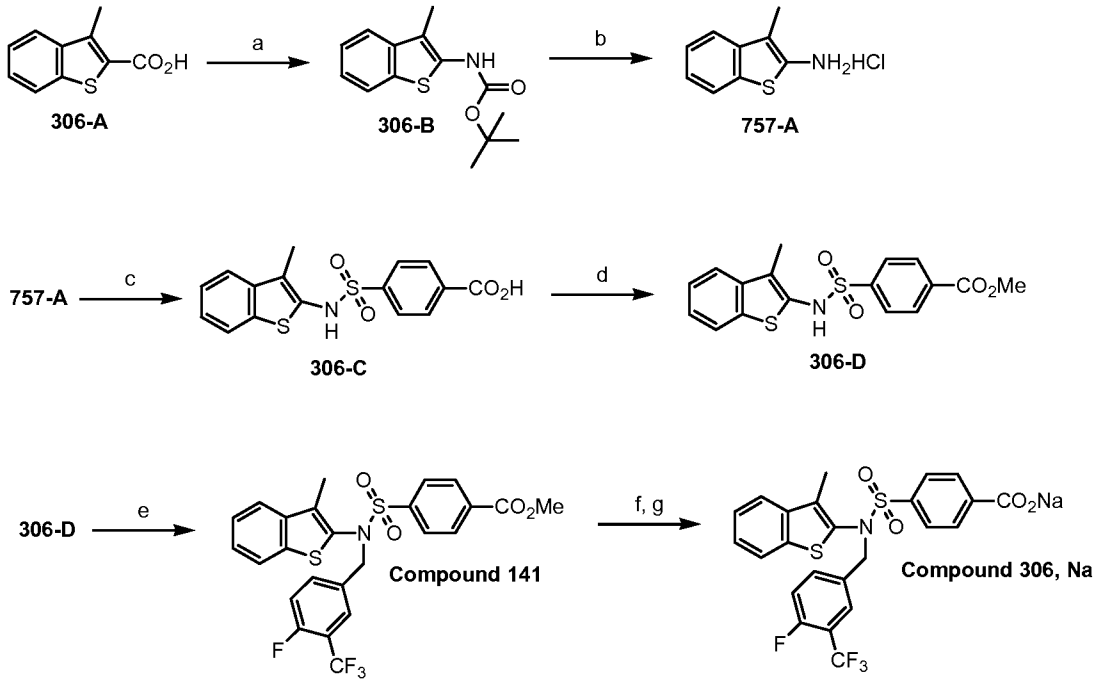
Compound 554

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(butyl)-*N'*-methyl-sulfamide.** Compound **554** was synthesized from Example 90, step C, substituting NBS for NCS. MS: *m/z* 378.9 (MH^+).

Compound 705

***N*-(3-Bromo-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl)-*N'*-methyl-sulfamide.** Compound **705** was synthesized from Example 90, step C, substituting NBS for NCS. ^{1}H-NMR (CD_3OD): δ 2.83 (s, 3H), 7.16-7.20 (m, 1H), 7.41-7.79 (m, 6H); MS: *m/z* 499.0 (MH^+).

Example 91



a) DPPA, t-BuOH; b) 4N HCl, dioxane; c) THF, pyridine, 4-chlorosulfonylbenzoic acid; d) MeOH, H_2SO_4; e) DMF, K_2CO_3, 4-fluoro-3-trifluoromethyl benzyl bromide; f) 1. MeOH, NaOH; 2. HCl; g) IPA, NaOMe, MeOH.

***tert*-Butyl-3-methylbenzo[*b*]thiophen-2-ylcarbamate (306-B).** A 5-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, reflux condenser, heating mantle and thermocouple was charged with t-butyl alcohol (2.11 L), compound **306-A** (225.0 g, 1.17 mol), and diisopropylethylamine (225 mL, 1.29 mol). Diphenylphosphorylazide (304 mL, 1.4 mol) was premixed with toluene (300 mL) and then added drop-wise over 10 min. The reaction mixture was refluxed with stirring for 21 h, cooled to 22 °C and then evaporated in vacuo. The residue was dissolved in CH_2Cl_2 (1 L), washed with 1N NaOH (500 mL), brine (500 mL), the organic layer separated, dried over $MgSO_4$, filtered, and evaporated in vacuo to afford a dark orange oil (557 g). The crude residue was purified by the flash column chromatography (SiO_2) eluting with heptane-EtOAc to afford 265 g of compound **306-B** as a pale yellow solid.

^{1}H-NMR ($CDCl_3$): δ 7.71 (d, 1H), 7.54 (d, 1H), 7.36-7.31 (m, 1H), 7.30-7.20 (m, 1H), 6.75 (br s, 1H), 2.23 (s, 3H), 1.55 (s, 9H).

3-Methylbenzo[*b*]thiophen-2-amine hydrochloride (757-A). A 5-L 3-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple was charged with 4M HCl in dioxane (3.1 L), compound **306-B** (265 g, 1.0 mol) and stirred for 18 h at 22 °C. The white precipitate was collected by filtration, washed with diethyl ether (3 x 500 mL), and dried under house vacuum at 40 °C for 48 h to afford 174 g of compound **757-A** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 8.7 (br s, 3H), 7.71 (d, 1H), 7.44 (d, 1H), 7.29 (t, 1H), 7.14 (t, 1H), 2.184 (s, 3H).

***N*-(3-Methylbenzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide (306-C).** A 12-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple was charged with THF (3.26 L) and compound **757-A** (326 g, 1.6 mol) followed by pyridine (265 mL, 3.3 mol). The reaction mixture was cooled to 5 °C using a ice bath, to which was added a solution of 4-(chlorosulfonyl)benzoic acid (396 g, 1.8 mol) dissolved in THF (2.44 L), drop-wise. The reaction was allowed to stir at ambient temperature for 72 h, diluted with EtOAc (4 L), washed with 1N HCl (1 L), brine (1 L), the organic layer dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude residue was purified by triturating with EtOAc/heptane (1:1/1L). The slurry was filtered, washed with heptane (2 x 250 mL) and dried in a vacuum oven at 40 °C for 18 h to afford 470 g of compound **306-C** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 13.51 (br s, 1H), 10.65 (br s, 1H), 8.12 (d, 2H), 7.86 (d, 2H), 7.83-7.79 (m, 1H), 7.66-7.63 (m, 1H), 7.37-7.33 (m, 1H), 2.03 (s, 3H).

***N*-(3-Methylbenzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide (306-D).** A 12-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple was charged with MeOH (7.5 L) and compound **306-C** (470 g, 1.35 mol). Sulfuric acid (24 mL, 0.45 mol) was added to the reaction mixture and the reaction was refluxed for 18 h. The reaction was cooled, diluted with EtOAc (4 L), washed with 1N NaOH (2 L), and H_2O (6 L). The aqueous layer with extracted with EtOAc (4 x 4 L), the combined organic extracts washed with brine (1 L), dried over Na_2SO_4, filtered and evaporated under reduced pressure to afford **306-D** (crude material) as a red, thick oil. ^{1}H-NMR (DMSO-d_6): δ 7.89 (d, 2H), 7.81 (d, 2H), 7.41 (d, 1H), 7.16 (d, 1H), 7.09-7.04 (m, 1H), 6.91-6.85 (m, 1H), 3.82 (s, 3H), 1.99 (s, 3H).

A 5-L 3-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple was charged with the crude residue in H_2O (4 L). The solution was acidified with 1N HCl (200 mL) until the pH = 1 and the reaction mixture allowed to stir for 30 min at ambient temperature. The solid was filtered, washed with H_2O (2 x 250 mL) and dried in a vacuum oven at 50 °C for 72 h to afford 302 g of compound **306-D** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 10.67 (br s, 1H), 8.13 (d, 2H), 8.00 (d, 2H), 7.90-7.77 (m, 1H), 7.64-7.61 (m, 1H), 7.36-7.32 (m, 2H), 3.89 (s, 3H), 2.02 (s, 3H).

Compound 141

***N*-[4-Fluoro-3-(trifluoromethyl)-benzyl]-*N*-(3-methylbenzo[*b*]thiophen-2-yl)-4-carbomethoxy-benzenesulfonamide.** A 12-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple was charged with DMF (4.9 L), compound **306-D** (245 g, 0.68 mol) and K_2CO_3 (112 g, 0.81 mol). 4-Fluoro-3-(trifluoromethyl)benzyl bromide (210 mL, 0.81 mol) was added drop-wise over 15 min and the reaction was stirred for 18 h at room temperature. The reaction mixture was poured into *cold* H_2O (10 L), stirred for 30 min, to which was added EtOAc (4 L). The layers were separated and the aqueous phase was extracted with EtOAc (2 x 1L). The combined EtOAc layers were washed with brine (1 L), dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified using flash column chromatography (SiO_2) eluting with heptane-EtOAc to afford 269 g of compound **141** as a white solid. ^{1}H-NMR (DMSO-d_6) δ 8.21 (d, 2H), 8.03 (d, 2H), 7.86-7.83 (m, 1H), 7.71-7.63 (m, 3H), 7.45-7.37 (m, 3H), 4.89 (br s, 2H), 3.93 (s, 3H), 1.94 (s, 3H).

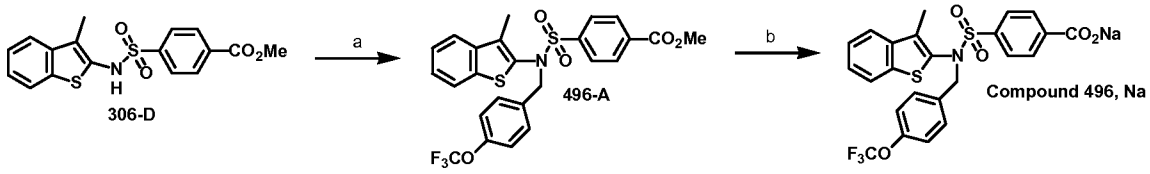
***N*-[4-Fluoro-3-(trifluoromethyl)-benzyl]-*N*-(3-methylbenzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide (not shown).** A 3-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, condenser and thermocouple was charged with MeOH (1.9 L) and compound **141** (190 g, 0.35 mol) followed by 3M NaOH (412 mL, 1.2 mol) and the reaction mixture was refluxed for 2 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (2 L) and 1N HCl (2 L), the layers separated and the aqueous phase extracted with EtOAc (2 L). The organic extracts were combined, washed with brine (1.5 L), dried over Na_2SO_4, filtered and evaporated under reduced pressure. The yellow solid was placed in vacuum oven for 18 h at 50 °C to afford 158 g of the titled compound (not shown) as a yellow solid. ^{1}H-

NMR (DMSO-d_6): δ 13.63 (s, 1H), 8.19 (d, 2H), 8.01 (d, 2H), 7.86-7.83 (m, 1H), 7.71-7.63 (m, 3H), 7.49-7.37 (M, 3H), 4.89 (br s, 1H),1.95 (s, 3H).

Compound 306, Sodium Salt

Sodium *N*-[4-Fluoro-3-(trifluoromethyl)-benzyl]-*N*-(3-methylbenzo[*b*]thiophen-2-yl)-4-carboxy-benzenesulfonamide To a 5-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple, charged with MeOH (3.1 L) and the benzoic acid (310 g, 0.59 mol), was added 0.5M NaOMe in MeOH (1.25 L, 0.62 mol), the reaction was stirred for 1 h at ambient temperature and evaporated under reduced pressure to afford the crude sodium salt as a yellow solid. A 5-L 4-neck flask equipped with overhead mechanical stirrer, N_2 inlet/outlet adapter, condenser, and thermocouple, charged with crude sodium salt and IPA (3.3 L) was refluxed for 1 h and cooled to room temperature overnight. The resulting solid was filtered, washed with cold IPA (250 mL) and dried in a vacuum oven at 60 °C for 18 h, followed by 100 °C for 72 h to afford 250 g of compound **306** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 8.04 (d, 2H), 7.85-7.82 (m, 1H), 7.76 (d, 2H), 7.69-7.63 (m, 3H), 7.48-7.41 (m, 1H), 7.40-7.35 (m, 2H), 4.83 (br s, 1H), 1.94 (s, 3H). Anal. Calcd for $C_{24}H_{16}F_4NNaO_4S_2$: C, 52.84; H, 2.96; N, 2.57; F, 13.93; S, 11.76; Na, 4.21. Found: C, 51.62; H, 2.70; N, 2.38; F, 13.73; S, 11.50; Na, 4.44; KF, 0.61.

Example 92



a) DMF, K_2CO_3, 4-trifluoromethoxy benzyl bromide; b) 1. MeOH, NaOH; 2) IPA.

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-carbomethoxy-benezenesulfonamide (496-A).** A 12-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple was charged with DMF (6.7 L), compound **306-D** (334 g, 0.92 mol) and K_2CO_3 (153 g, 1.11 mol).

1-(Bromomethyl)-4-(trifluoromethoxy)benzene (178 mL, 1.11 mol) was added drop-wise over 15 min and the reaction mixture stirred for 5 h at room temperature. The reaction mixture was poured into *cold* H_2O (13 L) and stirred for 18 h. The resultant solid was filtered, washed with heptane (3 x 1 L), dried under vacuo for 18 h at 50 °C, triturated with IPA (500 mL), filtered and dried under vacuo at 50 °C for 18 h to afford 318 g of compound **496-A** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 8.20 (d, 2H), 8.02 (d, 2H), 7.84-7.81 (m, 1H), 7.69-7.65 (m, 1H), 7.41-7.36 (m, 4H), 7.30 (d, 2H), 4.81 (br s, 2H), 3.93 (s, 3H), 1.90 (s, 3H). Anal. Calcd for $C_{25}H_{20}F_3NO_5S_2$: C, 56.07; H, 3.76; N, 2.62; F, 10.64; S, 11.97. Found: C, 55.85; H, 3.69; N, 2.72; F, 10.57; S, 11.65.

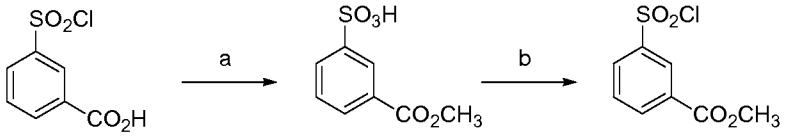
Compound 496, Sodium Salt

Sodium *N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-trifluoromethoxy-benzyl)-4-carboxy-benezenesulfonamide. To a 3-L 4-neck flask equipped with an overhead mechanical stirrer, N_2 inlet/outlet adapter, and thermocouple, charged with MeOH (1.0 L) and compound **496-A** (100 g, 0.19 mol) was added 3M NaOH (68 mL, 0.21 mol) and the reaction was stirred for 1 h at 65 °C. The reaction mixture was cooled and evaporated under reduced pressure to afford the sodium salt as a crude yellow solid. To the crude sodium salt was added IPA (250 mL) and the suspension heated (via a heat gun) until the mixture is homogeneous. The solution was allowed to cool slowly to ambient temperature, seeded with a previous batch of sodium compound **496**, the resultant solid filtered, washed with cold IPA (150 mL) and dried in a vacuum oven at 60 °C for 18 h to afford 75 g of the sodium salt of compound **496** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 8.03 (d, 2H), 7.84-7.81 (m, 1H), 7.74 (d, 2H), 7.67-7.64 (m, 1H), 7.40-7.33 (m, 4H), 7.30-7.27 (d, 2H), 4.76 (br s, 2H), 1.91 (s, 3H). Anal. Calcd for $C_{24}H_{19}F_3NNaO_6S_2$: C, 51.34; H, 3.41; N, 2.49; F, 10.15; S, 11.42; Na, 4.09; KF, 3.21. Found: C, 50.98; H, 3.10; N, 2.50; F, 9.25; S, 11.36; Na, 4.32; KF, 3.15.

Preparation of Intermediates

Example 93: Preparation of Sulfonyl Chlorides

Example 93A:



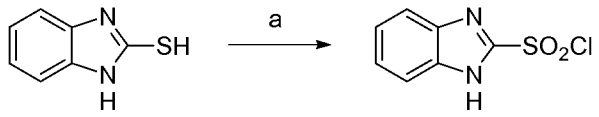
Int-1 Int-2 Int-3

a) 1. DCM, $(COCl)_2$, cat. DMF; 2) MeOH; b) C_6H_5N, $SOCl_2$.

3-Sulfo-benzoic acid methyl ester (Int-2). To a suspension of compound **Int-1** (5.09 g; 23.0 mmol) in DCM (50 mL), at ambient temperature, was added oxalyl chloride (2.41 mL; 27.6 mmol) in one-portion, followed by 1 drop of DMF and the reaction was stirred for 18 h at ambient temperature. MeOH was added to the reaction mixture and the reaction was allowed to stir for 72 h. The reaction solvent was evaporated under reduced pressure and the residue dried under vacuo to afford 4.97 grams of compound **Int-2** as an oil.

3-Chlorosulfonyl-benzoic acid methyl ester (Int-3). To compound **Int-2** (4.97 g; 23.0 mmol) was added pyridine (20 mL) and the solution was stirred under N_2 for 60 min. Thionyl chloride (4.2 mL; 57.5 mmol) was added, drop-wise at ambient temperature, and the reaction was stirred at 55 °C for 2 h. The reaction was cooled, the solvent concentrated under reduced pressure and the liquid diluted with EtOAc. The organic phase was washed with 1 N HCl (3x), H_2O, brine, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure to afford 4.89 g of compound **Int-3** as a white solid. ^{1}H-NMR (DMSO-d_6): 3.87 (s, 3H), 7.44-7.58 (m, 1H), 7.81-7.98 (m, 2H), 8.17-8.27 (m, 1H), 14.50 (s, 1H).

Example 93B:

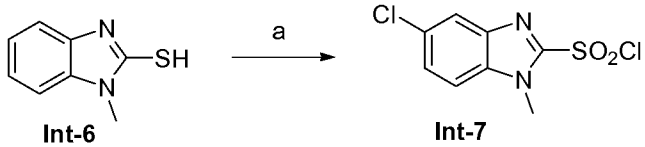


Int-4 **Int-5**

a) H_2O, AcOH, Cl_2.

***1H*-Benzimidazole-2-sulfonyl chloride (Int-5).** A suspension of 1*H*-benzimidazole-2-thiol, compound **Int-4** (1.58 g; 10.5 mmol) in 20% v/v acetic acid water (30/90 mL) was cooled to 0 °C. Chlorine gas was bubbled through the mixture until saturation, the reaction mixture was stirred for 1 h at 0 °C, filtered, washed with ice-cold water and air dried to afford 2.2 g of compound **Int-5** as an off-white solid.

Example 93C:

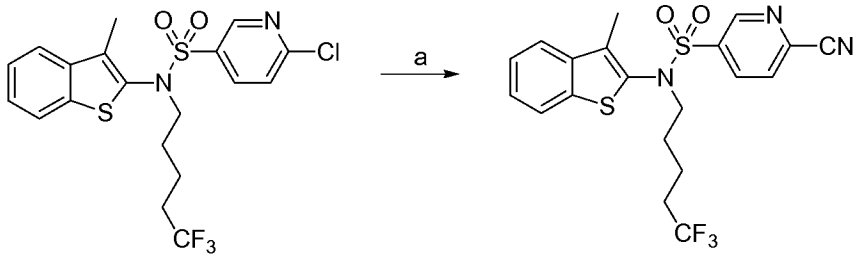


Int-6 **Int-7**

a) CCl_4, H_2O, Cl_2.

5-Chloro-1-methyl-1*H*-benzimidazole-2-sulfonyl chloride (Int-7). A suspension of 1-methyl-1*H*-benzimidazole-2-thiol, compound **Int-6** (0.538 g; 3.27 mmol) in 20% v/v CCl_4/water (30/90 mL) was cooled to 0 °C. Chlorine gas was bubbled through the mixture until saturation, the reaction mixture was stirred for 1h at 0 °C, filtered, washed with ice-cold water and air dried to afford 0.5 g of compound **Int-7** as a white solid.

Example 94: General 4-cyanopyridyl Intermediates



Int-8 **Int-9**

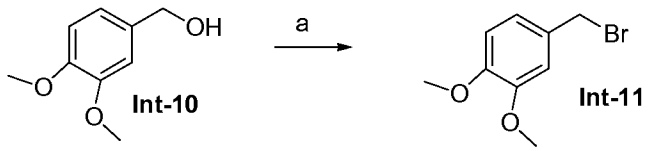
a) DMF, KCN, 18-C-6.

Compound **Int-8,** was prepared by the method used to synthesize Cpd **757** in Example 30, step A, and Example 3, step A.

***N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(5,5,5-trifluoro-pentyl)-4-cyano-pyridin-3-ylsulfonamide (Int-9).** A solution of compound **Int-8** (0.250 g, 0.54 mmol), dimethylformamide (2 mL), potassium cyanide (0.07 g, 1.08 mmol), and 18-crown-6 ether (0.006 g, 0.022 mmol) was refluxed for 4 h. The reaction mixture was cooled, poured over ice-water and extracted with EtOAc. The solvent was evaporated *in vacuo*, and the crude residue concentrated to afford 0.25 g of compound **Int-9** as a dark gum. MS: *m/z* 454.0 (MH^+).

Example 95: General Synthesis of Benzyl Bromide Intermediates

Example 95A:

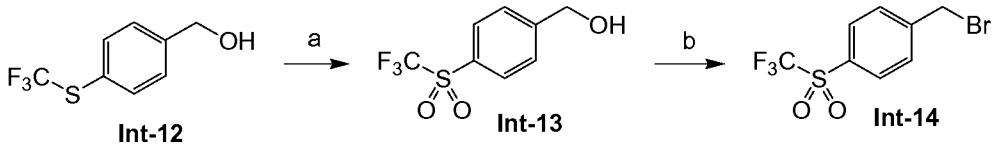


Int-10 **Int-11**

a) DCM, PBr_3.

4-Bromomethyl-1,2-dimethoxy-benzene (Int-11). To a stirred solution of **Int-10** (1.0 g, 5.95 mmol) in dichloromethane (10 mL), cooled to 0 °C, was added phosphorous tribromide (1.93 g, 7.13 mmol), drop-wise, and the reaction was stirred for 2 h. The reaction was quenched with aqueous NH_4Cl, the organic phase separated, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo* to afford 1.0 g of compound **Int-11**. ^{1}H-NMR (DMSO-d_6) δ 3.74 (s, 3H), 3.72 (s, 3H), 4.41 (d, 2H), 6.83 (d, 1H), 6.85-6.94 (m, 2H).

Example 95B:

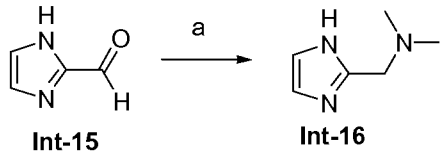


a) TFA, H_2O_2; b) PBr_3, ether.

(4-Trifluoromethanesulfonyl-phenyl)-methanol (Int-13). To a solution of compound **Int-12** (2.08 g, 10.0 mmol) in trifluoroacetic acid (25 mL) was added a 30% H_2O_2 (5 mL) solution. After stirring at ambient temperature for 5 days, the reaction mixture was diluted with ice-water (125 mL). A scoop of 10% Pd/C was added to consume the excess H_2O_2 present and allowed to stir overnight. The mixture was extracted with diethyl ether (3x50 mL), the combined organics washed times with saturated $NaHCO_3$ solution (4x50 mL) then treated with solid $NaHCO_3$ until neutralized. The layers were separated and the organic phase was washed with a 10% Na_2SO_3 solution (50 mL), brine (50 mL), dried with Na_2SO_4, filtered, and evaporated *in vacuo* to afford 2.19 g of compound **Int-13** as a white solid. ^{1}H-NMR (DMSO-d_6) δ 4.70 (s, 2H), 5.62 (br s, 1H), 7.80 (d, 2H), 8.10 (d, 2H).

1-Bromomethyl-4-trifluoromethanesulfonyl-benzene (Int-14). To a solution of compound **Int-13** (2.18 g, 9.05 mmol) in diethyl ether (25 mL) was added PBr_3 (1.3 mL, 13.7 mmol). The reaction was stirred under a nitrogen atmosphere for 3 days, diluted with diethyl ether (100 mL) and washed with H_2O (2x50 mL), saturated $NaHCO_3$ solution (50 mL), brine (50 mL), dried over Na_2SO_4, filtered and evaporated *in vacuo* to afford 2.65 g of compound **Int-14** as an off-white solid. ^{1}H-NMR ($CDCl_3$): δ 4.53 (s, 2H), 7.69 (d, 2H), 8.03 (d, 2H).

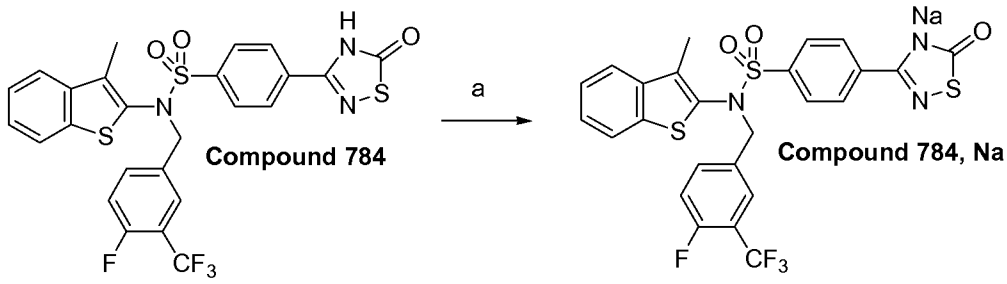
Example 96: Preparation of 1-(1*H*-imidazol-2-yl)-*N*,*N*-dimethylmethanamine Intermediate



a) MeOH, H_2O, $HN(CH_3)_2$, $NaBH_4$.

1-(1*H*-imidazol-2-yl)-*N*,*N*-dimethylmethanamine (Int-16). A solution of compound **Int-15** (5.0 g, 52.03 mmole), MeOH (10 mL), H_2O (15 mL), and dimethylamine (25 mL, 50 mmole) was stirred at 22 °C for 2 h. The reaction mixture was cooled to 0 °C, stirred for 20 min, to which was added $NaBH_4$ (5.0 g, 139.9 mmole) in one-portion and the reaction was heated at 56 °C for 3 h. The reaction mixture was cooled, quenched with brine (100 mL), extracted with CH_2Cl_2 (100 mL), dried over $MgSO_4$, filtered, and the solvent evaporated *in vacuo* to afford 4.0 g of compound **Int-16** as a yellow waxy solid. ^{1}H-NMR ($CDCl_3$): δ 2.20 (s, 6H), 3.50 (s, 2H), 6.90 (s, 2H), 10.10 (br s, 1H); MS: *m/z* 125.2 (MH^+).

Example 97: General sodium salt preparation



a) MeOH, 0.117 M NaOMe.

Compound 784, Sodium salt

Sodium, *N*-(3-Methyl-benzo[*b*]thiophen-2-yl)-*N*-(4-fluoro-3-trifluoromethyl-benzyl-4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-benzenesulfonamide. To a solution of compound **784** (335.7 mg; 0.579 mmol) suspended in MeOH (10 mL) was added a solution of 0.117 M NaOMe (5.2 mL) and the solution was stirred for 30 min. The solvent was evaporated under reduced pressure and dried under vacuo at 50 °C to afford 353.8 mg of the sodium salt of compound **784** as a white solid. ^{1}H-NMR (DMSO-d_6): δ 3.34 (s, 3H), 4.88 (br s, 2H), 7.35-7.43 (m,

2H), 7.45-7.47 (t, 1H), 7.54-7.68 (m, 4H), 7.83-7.85 (m, 3H), 8.20-8.22 (d, 2H); MS: *m/z* 580.0 (MH^+).

Using the methods described in the schemes and specific examples, and adaptations thereof, compounds of Formula (I) shown in Table 1 were prepared.

Table 1

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
1	S	H	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
2	S	methyl	1-methyl-1*H*-imidazol-4-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
3	S	H	phenyl	3-fluorophenyl methyl	H	H	H	H	CR^5	CR^6
4	S	Cl	phenyl	4-fluorophenyl methyl	H	H	H	H	CR^5	CR^6
5	S	Cl	phenyl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
6	S	Cl	phenyl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
7	S	Cl	phenyl	4-fluoro-3-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
8	S	Cl	phenyl	4-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
9	S	H	pyridin-2-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
10	S	methyl	1-methyl-1*H*-imidazol-4-yl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
11	S	methyl	1-methyl-1*H*-imidazol-4-yl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
12	S	methyl	pyridin-3-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
13	S	methyl	pyridin-3-yl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
14	S	methyl	pyridin-3-yl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
15	S	methyl	thien-3-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
16	S	methyl	thien-3-yl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
17	S	methyl	thien-3-yl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
18	S	methyl	benzo[*b*]thio phen-2-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
19	S	methyl	benzo[*b*]thio phen-2-yl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
20	S	methyl	quinolin-8-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
21	S	methyl	quinolin-8-yl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
22	S	methyl	quinolin-8-yl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
23	S	Cl	phenyl	3-fluorophenyl methyl	H	H	H	H	CR^5	CR^6
24	S	Cl	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
25	S	methyl	3-methoxyphenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
26	S	methyl	4-methoxyphenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
27	S	methyl	isoquinolin-5-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
28	S	methyl	isoquinolin-5-yl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
29	S	methyl	isoquinolin-5-yl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
30	S	methyl	quinolin-6-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
31	S	methyl	quinolin-6-yl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
32	S	methyl	quinolin-6-yl	quinolin-8-yl methyl	H	H	H	H	CR^5	CR^6
33	S	H	pyridin-3-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
34	S	H	methyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
35	S	H	ethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
36	S	H	*n*-propyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
37	S	H	*n*-butyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
38	S	methyl	thien-2-yl	4-trifluoro methyl-3-fluoro phenylmethyl	H	H	H	H	CR^5	CR^6
39	S	methyl	pyridin-3-yl	4-fluoro-3-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
40	S	methyl	ethyl	4-fluoro-3-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
41	S	methyl	ethyl	3,4-difluoro phenylmethyl	H	H	H	H	CR^5	CR^6
42	S	methyl	ethyl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
43	S	H	ethyl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
44	S	methyl	dimethyl amino	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
45	S	H	methyl	4-fluoro-3-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
46	S	H	phenyl	4-chlorophenyl methyl	H	H	H	H	CR^5	CR^6
47	S	H	phenyl	2-methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
48	S	H	phenyl	3-methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
49	S	H	phenyl	4-methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
50	S	H	phenyl	2-fluoro phenylmethyl	H	H	H	H	CR^5	CR^6
51	S	H	phenyl	3-nitro phenylmethyl	H	H	H	H	CR^5	CR^6
52	S	H	phenyl	pyridin-2-yl methyl	H	H	H	H	CR^5	CR^6
53	S	H	phenyl	pyridin-3-yl methyl	H	H	H	H	CR^5	CR^6
54	S	H	phenyl	pyridin-4-ylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
55	S	H	phenyl	2-nitrophenyl methyl	H	H	H	H	CR^5	CR^6
56	S	H	phenyl	2-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
57	S	H	phenyl	3-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
58	S	H	phenyl	4-trifluoro methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
59	S	H	phenyl	phenylmethyl	H	H	H	H	CR^5	CR^6
60	S	H	phenyl	4-fluoro-3-methoxyphenylmethyl	H	H	H	H	CR^5	CR^6
61	S	H	phenyl	4-fluoro-3-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
62	S	H	phenyl	2-methyl phenylmethyl	H	H	H	H	CR^5	CR^6
63	S	H	phenyl	3-methyl phenylmethyl	H	H	H	H	CR^5	CR^6
64	S	methyl	4-methoxy-3-fluorophenyl	4-fluoro-3-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
65	S	methyl	benzothiazol-6-yl	4-fluoro-3-trifluoro methyl phenylmethyl	H	H	H	H	CR^5	CR^6
66	S	methyl	2-oxo-2,3-dihydro-benzo oxazol-6-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
67	S	methyl	3-oxo-3,4-dihydro-2*H*-benzo[1,4] oxazin-6-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
68	S	methyl	4-methyl-3,4-dihydro-2*H*-benzo[1,4] oxazin-7-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
69	S	methyl	4-[1,2,3] thiadiazol-4-yl-phenyl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
70	S	methyl	3-phenoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
71	S	methyl	2-(methoxy carbonyl)ethyl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
72	S	methyl	2,4-dihydroxy-6-methyl-pyrimidin-5-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
73	S	methyl	2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinolin-8-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
74	S	methyl	1,3,5-trimethyl-1*H*-pyrazol-4-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
75	S	methyl	2,4-dimethyl-thiazol-5-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
76	S	methyl	2-chloro pyridin-5-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
77	S	methyl	2-chloropyridin-3-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
78	S	H	thien-3-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
79	S	methyl	1,2,3,4-tetrahydro-isoquinolin-8-yl	4-fluoro-3-trifluoro methylphenylmethyl	H	H	H	H	CR^5	CR^6
80	S	Cl	phenyl	cyclohexylmethyl	H	H	H	H	CR^5	CR^6
81	S	Cl	phenyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
82	S	Cl	phenyl	2-(2-oxo-pyrrolidin-1-yl)ethyl	H	H	H	H	CR^5	CR^6
83	S	Cl	phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
84	S	Cl	phenyl	allyl	H	H	H	H	CR^5	CR^6
85	S	Cl	phenyl	2-(phenyl)ethyl	H	H	H	H	CR^5	CR^6
86	S	Cl	phenyl	2-(*tert*-butoxycarbonyl amino)ethyl	H	H	H	H	CR^5	CR^6
87	S	Cl	phenyl	2-(dimethylamino)ethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
88	S	Cl	phenyl	2-(methanesulfonyl)ethyl	H	H	H	H	CR^5	CR^6
89	S	Cl	phenyl	(N-*tert*-butoxycarbonyl pyrrolidin-2-yl) methyl	H	H	H	H	CR^5	CR^6
90	S	Cl	phenyl	(N-*tert*-butoxycarbonyl piperidin-4-yl) methyl	H	H	H	H	CR^5	CR^6
91	S	Cl	phenyl	2-(2-oxo-imidazolidin-1-yl) ethyl	H	H	H	H	CR^5	CR^6
92	S	Cl	phenyl	2-(morpholin-4-yl)ethyl	H	H	H	H	CR^5	CR^6
93	S	methyl	phenyl	2-(methoxycarbonyl)-2(*R*)-methylethyl	H	H	H	H	CR^5	CR^6
94	S	methyl	phenyl	2-(methoxycarbonyl)-2(*S*)-methylethyl	H	H	H	H	CR^5	CR^6
95	S	methyl	phenyl	2-(morpholin-4-yl)ethyl	H	H	H	H	CR^5	CR^6
96	S	methyl	phenyl	2-(piperidin-1-yl) ethyl	H	H	H	H	CR^5	CR^6
97	S	methyl	phenyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
98	S	methyl	phenyl	2-(methylsulfanyl)ethyl	H	H	H	H	CR^5	CR^6
99	S	methyl	phenyl	2-methoxyethyl	H	H	H	H	CR^5	CR^6
100	S	methyl	phenyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
101	S	methyl	phenyl	methoxycarbonyl methyl	H	H	H	H	CR^5	CR^6
102	S	methyl	phenyl	2,2-difluoroethyl	H	H	H	H	CR^5	CR^6
103	S	methyl	phenyl	(N-*tert*-butoxycarbonyl pyrrolidin-2-yl) methyl	H	H	H	H	CR^5	CR^6
104	S	methyl	phenyl	2-phenylethyl	H	H	H	H	CR^5	CR^6
105	S	methyl	ethyl	2-methoxyethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
106	S	methyl	ethyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
107	S	methyl	ethyl	pent-3-ynyl	H	H	H	H	CR^5	CR^6
108	S	methyl	ethyl	2-(methylsulfanyl)ethyl	H	H	H	H	CR^5	CR^6
109	S	methyl	ethyl	2-oxo-pyrrolidin-5(*S*)-ylmethyl	H	H	H	H	CR^5	CR^6
110	S	methyl	ethyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
111	S	methyl	ethyl	2,2-difluoroethyl	H	H	H	H	CR^5	CR^6
112	S	methyl	ethyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
113	S	methyl	ethyl	2-(morpholin-4-yl) ethyl	H	H	H	H	CR^5	CR^6
114	S	methyl	ethyl	(N-*tert*-butoxycarbonyl pyrrolidin-2-yl) methyl	H	H	H	H	CR^5	CR^6
115	S	H	phenyl	2-phenylethyl	H	H	H	H	CR^5	CR^6
116	S	H	phenyl	allyl	H	H	H	H	CR^5	CR^6
117	S	H	phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
118	S	H	phenyl	cyclohexylmethyl	H	H	H	H	CR^5	CR^6
119	S	H	phenyl	cyclohexyl	H	H	H	H	CR^5	CR^6
120	S	H	phenyl	2-(methylsulfanyl)ethyl	H	H	H	H	CR^5	CR^6
121	S	acetyl	ethyl	*n*-butyl	H	H	H	H	CR^5	CR^6
122	S	acetyl	ethyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
123	S	acetyl	ethyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
124	S	acetyl	ethyl	2-(morpholin-4-yl) ethyl	H	H	H	H	CR^5	CR^6
125	S	methyl	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
126	S	methyl	phenylmethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
127	S	methyl	3-fluorophenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
128	S	methyl	2-fluorophenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
129	S	methyl	thien-2-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
130	S	H	1-methyl-1*H*-imidazol-4-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
131	S	H	3-fluorophenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
132	S	H	4-trifluoromethyl phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
133	S	H	methanesulfonyl methyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
134	S	H	4-methoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
135	S	H	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
136	S	H	3-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
137	S	methyl	3-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
138	S	methyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
139	S	H	2-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
140	S	Br	phenyl	4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
141	S	Br	pyridin-3-yl	3,4-difluorophenylmethyl	H	OCH_3	H	H	CR^5	CR^6
142	S	H	phenyl	3,4-difluorophenylmethyl	H	H	H	OCH_3	CR^5	CR^6
143	S	Cl	phenyl	3,4-difluorophenylmethyl	H	H	H	OCH_3	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
144	S	Cl	phenyl	3,4-difluorophenylmethyl	H	Cl	H	OCH_3	CR^5	CR^6
145a	S	Br	phenyl	3,4-difluorophenylmethyl	H	H	NA	H	N	CR^6
145b	S	Cl	phenyl	3,4-difluorophenylmethyl	H	H	NA	H	N	CR^6
146	S	H	phenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	NA	H	N	CR^6
147	S	H	phenyl	3,4-difluorophenylmethyl	H	H	H	NA	CR^5	N
148	S	Br	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
149	S	Br	pyridin-3-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
150	S	Br	1-methyl-1*H*-imidazol-4-yl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
151	S	Br	methyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
152	S	Br	ethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
153	S	Br	*n*-propyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
154	S	Br	*n*-butyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
155	S	Br	3-fluorophenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
156	S	Br	4-trifluoromethylphenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
157	S	Br	methyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
158	S	Cl	phenyl	4-chlorophenylmethyl	H	H	H	H	CR^5	CR^6
159	S	Br	phenyl	4-chlorophenylmethyl	H	H	H	H	CR^5	CR^6
160	S	Br	phenyl	2-methoxyphenylmethyl	H	H	H	H	CR^5	CR^6
161	S	Br	phenyl	5-bromo-2-methoxyphenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
162	S	Br	phenyl	3-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
163	S	Br	phenyl	2-bromo-5-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
164	S	Br	phenyl	4-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
165	S	Br	phenyl	4-methoxy-3-bromophenylmethyl	H	H	H	H	CR^5	CR^6
166	S	Br	phenyl	2-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
167	S	Br	phenyl	3-nitrophenylmethyl	H	H	H	H	CR^5	CR^6
168	S	Br	phenyl	pyridin-2-ylmethyl	H	H	H	H	CR^5	CR^6
169	S	Br	phenyl	pyridin-3-ylmethyl	H	H	H	H	CR^5	CR^6
170	S	Br	phenyl	pyridin-4-ylmethyl	H	H	H	H	CR^5	CR^6
171	S	Br	phenyl	2-nitrophenylmethyl	H	H	H	H	CR^5	CR^6
172	S	Br	phenyl	2-trifluoromethoxy phenyl methyl	H	H	H	H	CR^5	CR^6
173	S	Br	phenyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
174	S	Br	phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
175	S	Br	phenyl	phenylmethyl	H	H	H	H	CR^5	CR^6
176	S	Br	phenyl	4-fluoro-3-methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
177	S	Br	phenyl	4-fluoro-3-trifluoromethyl phenylmethyl	H	H	H	H	CR^5	CR^6
178	S	Br	phenyl	2-methylphenylmethyl	H	H	H	H	CR^5	CR^6
179	S	Br	phenyl	3-methylphenylmethyl	H	H	H	H	CR^5	CR^6
180	S	Cl	3-methoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
181	S	Cl	4-methoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
182	S	Br	4-methoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
183	S	Br	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
184	S	Br	thien-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
185	S	Br	3-methoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
186	S	Br	thien-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
187	S	Cl	thien-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
188	S	Br	pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
189	S	Cl	pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
190	S	Cl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
191	S	Cl	thien-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
192	S	Br	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
193	S	Br	3-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
194	S	Cl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
195	S	Cl	3-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
196	S	Cl	2-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
197	S	Br	2-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
198	S	cyano	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
199	S	pyrimidin-5-yl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
200	S	2-fluoro phenyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
201	S	4-fluoro phenyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
202	S	thien-3-yl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
203	S	acetyl	ethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
204	S	acetyl	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
205	S	acetyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
206	S	formyl	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
207	S	formyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
208	S	formyl	methyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
209	S	formyl	methyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
210	S	formyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
211	S	formyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
212	S	formyl	ethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
213	S	hydroxymethyl	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
214	S	hydroxymethyl	phenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
215	S	hydroxymethyl	methyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
216	S	hydroxymethyl	methyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
217	S	hydroxymethyl	ethyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
218	S	hydroxymethyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
219	S	hydroxymethyl	ethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
220	S	1-hydroxyethyl	ethyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
221	S	1-hydroxyethyl	ethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
222	S	1-hydroxyethyl	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
223	S	1-hydroxyethyl	phenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
224	S	1-hydroxy-ethyl	methyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
225	S	1-hydroxy-ethyl	methyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
226	S	1-hydroxy-1-methyl-ethyl	ethyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
227	S	1-hydroxy-1-methyl-ethyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
228	S	acetyl	methyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
229	S	acetyl	methyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
230	S	Br	phenyl	5-(ethoxycarbonyl) pentyl	H	H	H	H	CR^5	CR^6
231	S	Br	phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
232	S	Br	phenyl	cyclohexylmethyl	H	H	H	H	CR^5	CR^6
233	S	Br	phenyl	2-phenylethyl	H	H	H	H	CR^5	CR^6
234	S	Br	phenyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
235	S	Br	phenyl	2(*R*)-3-dihydroxy-propyl	H	H	H	H	CR^5	CR^6
236	S	Br	phenyl	2-(2-oxo-pyrrolidin-1-yl)ethyl	H	H	H	H	CR^5	CR^6
237	S	Br	phenyl	2-(morpholin-4-yl)ethyl	H	H	H	H	CR^5	CR^6
238	S	Br	phenyl	2-(dimethylamino)ethyl	H	H	H	H	CR^5	CR^6
239	S	Br	phenyl	2-(methanesulfonyl) ethyl	H	H	H	H	CR^5	CR^6
240	S	Br	phenyl	2-(2-oxo-imidazolidin-1-yl)-ethyl	H	H	H	H	CR^5	CR^6
241	S	Br	phenyl	*N*-methylpyrrolidin-2(*S*)-ylmethyl	H	H	H	H	CR^5	CR^6
242	S	Br	phenyl	2,2-difluoroethyl	H	H	H	H	CR^5	CR^6
243	S	Br	phenyl	methoxycarbonyl methyl	H	H	H	H	CR^5	CR^6
244	S	Br	phenyl	2(*S*)-methoxycarbonyl-2-methylethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
245	S	Br	phenyl	2(*R*)-methoxycarbonyl-2-methylethyl	H	H	H	H	CR^5	CR^6
246	S	Br	phenyl	3-phenylpropyl	H	H	H	H	CR^5	CR^6
247	S	Br	phenyl	ethyl	H	H	H	H	CR^5	CR^6
248	S	Br	phenyl	*n*-hexyl	H	H	H	H	CR^5	CR^6
249	S	Br	phenyl	adamant-1-ylmethyl	H	H	H	H	CR^5	CR^6
250	S	Br	phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
251	S	Br	phenyl	pent-3-ynyl	H	H	H	H	CR^5	CR^6
252	S	Br	phenyl	2-methoxyethyl	H	H	H	H	CR^5	CR^6
253	S	Br	phenyl	3-(methylcarbonyl) propyl	H	H	H	H	CR^5	CR^6
254	S	Br	phenyl	2-(dimethylphospho) ethyl	H	H	H	H	CR^5	CR^6
255	S	Br	phenyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
256	S	Br	phenyl	2-(piperidin-1-yl)ethyl	H	H	H	H	CR^5	CR^6
257	S	Br	phenyl	2-(2,5-dioxo-pyrrolidin-1-yl)ethyl	H	H	H	H	CR^5	CR^6
258	S	Br	phenyl	2-oxo-pyrrolidin-5(*R*)-ylmethyl	H	H	H	H	CR^5	CR^6
259	S	Br	phenyl	2-oxo-pyrrolidin-5(*S*)-ylmethyl	H	H	H	H	CR^5	CR^6
260	S	Br	phenyl	2-(methylsulfanyl)ethyl	H	H	H	H	CR^5	CR^6
261	S	Br	ethyl	*n*-butyl	H	H	H	H	CR^5	CR^6
262	S	Br	ethyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
263	S	Br	ethyl	2,2-difluoroethyl	H	H	H	H	CR^5	CR^6
264	S	Br	ethyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
265	S	Br	dimethylamino	*n*-butyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
266	S	Br	dimethylamino	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
267	S	Br	dimethylamino	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
268	S	Br	dimethylamino	2,2-difluoroethyl	H	H	H	H	CR^5	CR^6
269	S	Br	dimethylamino	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
270	S	Cl	phenyl	2-aminoethyl	H	H	H	H	CR^5	CR^6
271	S	Br	4-carboxyphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
272	S	Br	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
273	S	Br	4-carboxyphenyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
274	S	Br	4-carboxyphenyl	2-methoxyethyl	H	H	H	H	CR^5	CR^6
275	S	Br	4-carboxyphenyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
276	S	Br	4-carboxyphenyl	2,2-difluoroethyl	H	H	H	H	CR^5	CR^6
277	S	Br	4-carboxyphenyl	2-(morpholin-4-yl)ethyl	H	H	H	H	CR^5	CR^6
278	S	Br	4-carboxyphenyl	adamant-1-ylmethyl	H	H	H	H	CR^5	CR^6
279	S	Br	4-carboxyphenyl	cyclohexylmethyl	H	H	H	H	CR^5	CR^6
280	S	1-hydroxyethyl	ethyl	*n*-butyl	H	H	H	H	CR^5	CR^6
281	S	1-hydroxyethyl	ethyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
282	S	1-hydroxyethyl	ethyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
283	S	1-hydroxyethyl	ethyl	2-(*tert*-butoxy)ethyl	H	H	H	H	CR^5	CR^6
284	S	1-hydroxyethyl	ethyl	2-(morpholin-4-yl)ethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
285	S	methyl	4-hydroxyphenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
286	S	methyl	3-hydroxyphenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
287	S	H	phenyl	3-hydroxyphenylmethyl	H	H	H	H	CR^5	CR^6
288	S	Cl	3-hydroxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
289	S	Cl	4-hydroxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
290	S	Br	4-hydroxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
291	S	Br	3-hydroxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
292	S	Br	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
293	S	Br	3-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
294	S	Cl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
295	S	H	3-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
296	S	H	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
297	S	Cl	2-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
298	S	Br	2-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
299	S	formyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
300	S	H	amino	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
301	S	Br	amino	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
302	S	Cl	amino	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
303	S	bromo	amino	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
304	S	bromo	amino	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
305	S	methyl	3-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
306	S	methyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylpheny lmethyl	H	H	H	H	CR^5	CR^6
307	S	chloro	3-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
308	S	H	4-methylcarbonyl phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
309	S	chloro	methylamino	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
310	S	H	2-chloro pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
311	S	H	6-chloro-pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
312	S	bromo	4-methylcarbonyl phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
313	S	methyl carbonyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
314	S	methyl carbonyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
315	S	H	dimethylamino	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
316	S	1-hydroxy-1-methyl-ethyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
317	S	bromo	dimethylamino	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
318	S	methyl carbonyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
319	S	bromo	2-chloro pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
320	S	bromo	6-chloro-pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
321	S	chloro	2-chloro pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
322	S	bromo	pyridin-3-yl	3-fluoro-4-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
323	S	bromo	pyridin-3-yl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
324	S	bromo	pyridin-3-yl	3-chloro-6-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
325	S	trifluoro methyl	phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
326	S	methyl	5-(2-methyl-5-trifluoromethyl-2*H*-pyrazol-3-yl)-thien-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
327	S	methyl	5-methoxy carbonyl-furan-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
328	S	methyl	1-methyl-3-trifluoromethyl-1*H*-pyrazol-4-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
329	S	methyl	5-(5-trifluoromethyl-isoxazol-3-yl)-thien-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
330	S	methyl	5-bromo-6-chloro-pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
331	S	methyl	5,6-dichloro-pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
332	S	methyl	4-(pyrazol-1-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
333	S	methyl	3-(5-methyl-[1,3,4]oxadiazol-2-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
334	S	methyl	4-(oxazol-5-yl) phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
335	S	1-hydroxy-ethyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
336	S	methyl	3-chloro-4-methylcarbonylamino-phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
337	S	methyl	6-chloro-imidazo[2,1-b] thiazol-5-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
338	S	chloro	6-chloro-pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
339	S	methyl carbonyl	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
340	S	H	pyridin-3-yl	*n*-butyl	H	H	H	H	CR^5	CR^6
341	S	1-hydroxy-1-methyl-ethyl	4-(1-hydroxy-1-methyl-ethyl) phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
342	S	methyl carbonyl	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
343	S	1-hydroxy-1-methyl-ethyl	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
344	S	1-hydroxy-1-methyl-ethyl	4-methylcarbonyl phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
345	S	bromo	pyridin-3-yl	*n*-butyl	H	H	H	H	CR^5	CR^6
346	S	dimethylamino-methyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
347	S	methyl amino-methyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
348	S	*n*-propyl amino-methyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
349	S	pyrrolidin-1-yl methyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
350	S	bromo	methanesulfonyl-methyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
351	S	methyl	4-methylcarbonyl phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
352	S	methyl	4-methylcarbonyl phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
353	S	methyl	3-(2-methyl-pyrimidin-4-yl) phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
354	S	methyl	3-(2-methyl-pyrimidin-4-yl) phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
355	S	methyl	8-methoxy-quinolin-5-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
356	S	methyl	8-methoxy-quinolin-5-yl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
357	S	methyl	2-methoxy pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
358	S	methyl	2-dimethylamino pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
359	S	methyl	6-methoxy pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
360	S	methyl	6-dimethylamino-pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
361	S	1-hydroxy-1-methyl-ethyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
362	S	H	methanesulfonyl-methyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
363	S	methyl	methyl	*n*-butyl	H	H	H	H	CR^5	CR^6
364	S	methyl	methyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
365	S	methyl	methyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
366	S	methyl	methyl	2-*t*-butoxyethyl	H	H	H	H	CR^5	CR^6
367	S	methyl	methyl	3,4-difluorophenyl methyl	H	H	H	H	CR^5	CR^6
368	S	methyl	methyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
369	S	methyl	methyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
370	S	H	3-cyanophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
371	S	methyl	4-(1-hydroxy-1-methyl-ethyl)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
372	S	methyl	4-(pyridin-4-yl oxy)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
373	S	methyl	4-(pyridin-3-yl oxy)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
374	S	methyl	4-(1-hydroxy-1-methyl-ethyl) phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
375	S	methyl	3-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	F	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
376	S	methyl	3-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	F	H	H	CR^5	CR^6
377	S	methyl	2-methylthio-pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
378	S	methyl	6-methylthio pyridin-3-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
379	S	H	pyridin-3-yl	3-methoxycarbonyl phenylmethyl	H	H	H	H	CR^5	CR^6
380	S	H	pyridin-3-yl	4-methoxycarbonyl phenylmethyl	H	H	H	H	CR^5	CR^6
381	S	pyrrolidin-1-yl methyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
382	S	H	methyl	*n*-butyl	H	H	H	H	CR^5	CR^6
383	S	H	pyridin-3-yl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
384	S	methyl	2-oxo-2,3-dihydro-benzooxazol-6-yl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
385	S	methyl carbonyl	4-carboxyphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
386	S	methyl carbonyl	4-bromophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
387	S	methyl carbonyl	4-cyanophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
388	S	1-hydroxy-1-methyl-ethyl	4-bromophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
389	S	1-hydroxy-1-methyl-ethyl	4-methylcarbonyl phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
390	S	bromo	4-carboxyphenyl	ethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
391	S	bromo	4-carboxyphenyl	propyl	H	H	H	H	CR^5	CR^6
392	S	bromo	4-carboxyphenyl	pentyl	H	H	H	H	CR^5	CR^6
393	S	bromo	4-carboxyphenyl	hexyl	H	H	H	H	CR^5	CR^6
394	S	bromo	4-carboxyphenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
395	S	bromo	4-carboxyphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
396	S	bromo	4-carboxyphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
397	S	bromo	4-carboxyphenyl	3-*t*-butoxypropyl	H	H	H	H	CR^5	CR^6
398	S	methyl	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
399	S	methyl	4-carboxyphenyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
400	S	methyl	4-carboxyphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
401	S	methyl	4-carboxyphenyl	2-*t*-butoxyethyl	H	H	H	H	CR^5	CR^6
402	S	methyl	4-methoxy carbonylphenyl	ethyl	H	H	H	H	CR^5	CR^6
403	S	methyl	4-carboxyphenyl	ethyl	H	H	H	H	CR^5	CR^6
404	S	methyl	4-carboxyphenyl	propyl	H	H	H	H	CR^5	CR^6
405	S	bromo	pyridin-3-yl	3-methoxycarbonyl phenylmethyl	H	H	H	H	CR^5	CR^6
406	S	bromo	pyridin-3-yl	4-methoxycarbonyl phenylmethyl	H	H	H	H	CR^5	CR^6
407	S	bromo	pyridin-3-yl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
408	S	chloro	pyridin-3-yl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
409	S	methyl	4-carboxyphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
410	S	methyl	4-carboxyphenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
411	S	H	4-cyanophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
412	S	methyl	4-methoxy carbonylphenyl	4,4,4-trifluorobutyl	H	F	H	H	CR^5	CR^6
413	S	H	4-aminocarbonyl phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
414	S	H	4-aminocarbonyl phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
415	S	1-hydroxy-1-methyl-ethyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
416	S	methyl	4-methoxy carbonylphenyl	3-t-butoxypropyl	H	H	H	H	CR^5	CR^6
417	S	methyl amino-methyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
418	S	di methyl amino-methyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
419	S	formyl	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
420	S	di methyl amino-methyl	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
421	$S(O_2)$	H	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
422	S	methoxy	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
423	S	methoxy	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
424	S	H	4-(1*H*-tetrazol-5-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
425	S	H	4-(1*H*-tetrazol-5-yl)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
426	S	methyl	4-carboxyphenyl	4,4,4-trifluorobutyl	H	F	H	H	CR^5	CR^6
427	S	methyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	F	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
428	S	bromo	4-(1*H*-tetrazol-5-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
429	S	bromo	4-(1*H*-tetrazol-5-yl)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
430	$S(O_2)$	H	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
431	$S(O_2)$	bromo	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
432	$S(O_2)$	H	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
433	$S(O_2)$	bromo	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
434	$S(O_2)$	methoxy	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
435	$S(O_2)$	bromo	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
436	$S(O_2)$	methoxy	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
437	S	bromo	4-carboxyphenyl	cyclobutylmethyl	H	H	H	H	CR^5	CR^6
438	S	bromo	4-carboxyphenyl	cyclopentylmethyl	H	H	H	H	CR^5	CR^6
439	S	bromo	4-carboxyphenyl	bicyclo[2.2.1] hept-2-yl methyl	H	H	H	H	CR^5	CR^6
440	S	bromo	4-carboxyphenyl	tetrahydropyran-4-yl methyl	H	H	H	H	CR^5	CR^6
441	S	bromo	4-carboxyphenyl	2-(dimethylamino)ethyl	H	H	H	H	CR^5	CR^6
442	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
443	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
444	S	H	4-dimethylamino phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
445	S	H	4-(pyrrolidin-1-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
446	S	H	4-(morpholin-4-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
447	S	H	4-(1-methyl-piperazin-4-yl) phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
448	S	methyl	2-dimethylamino pyridin-3-yl	*n*-butyl	H	H	H	H	CR^5	CR^6
449	S	H	4-(1*H*-tetrazol-5-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
450	S	methyl	4-carboxyphenyl	*n*-butyl	H	F	H	H	CR^5	CR^6
451	S	H	4-carboxyphenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
452	S	bromo	4-carboxyphenyl	isobutyl	H	H	H	H	CR^5	CR^6
453	S	bromo	4-carboxyphenyl	2-(cyclohexyloxy)ethyl	H	H	H	H	CR^5	CR^6
454	S	bromo	4-carboxyphenyl	3-methoxy-3-methyl-butyl	H	H	H	H	CR^5	CR^6
455	S	methyl	3-(2*H*-tetrazol-5-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
456	S	H	4-carboxyphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
457	S	di methyl amino carbonyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
458	S	methyl amino carbonyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
459	S	amino carbonyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
460	$S(O_2)$	methyl carbonyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
461	S	H	3-dimethylamino sulfonylphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
462	S	H	3-dimethylamino sulfonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
463	$S(O_2)$	1-hydroxy-1-methyl-ethyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
464	$S(O_2)$	1-hydroxy-ethyl	phenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
465	S	amino carbonyl	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
466	S	methyl amino carbonyl	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
467	S	di methyl amino carbonyl	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
468	S	amino carbonyl	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
469	S	di methyl amino carbonyl	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
470	S	H	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathia diazol-4-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
471	S	H	4-(*N*-hydroxy-acetamidinyl) phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
472	S	H	4-(*N*-(methylcarbonyl oxy)acetamidin yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
473	S	bromo	4-(*N*-hydroxy-acetamidinyl) phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
474	S	bromo	4-(1*H*-tetrazol-5-yl)phenyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
475	S	bromo	4-(1*H*-tetrazol-5-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
476	S	H	4-bromophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
477	S	chloro	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
478	S	chloro	4-carboxyphenyl	cyclopropylmethyl	H	H	H	H	CR^5	CR^6
479	S	chloro	4-carboxyphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
480	S	chloro	4-carboxyphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
481	S	bromo	4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
482	S	H	4-(*N*-hydroxy-acetamidinyl) phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
483	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
484	S	bromo	4-(2-oxo-2,3-dihydro-2l4-[1,2,3,5]oxathia diazol-4-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
485	S	chloro	4-(2-oxo-2,3-dihydro-2l4-[1,2,3,5]oxathia diazol-4-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
486	S	methyl	4-carboxyphenyl	phenylmethyl	H	H	H	H	CR^5	CR^6
487	S	methyl	4-carboxyphenyl	4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
488	S	methyl	4-carboxyphenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
489	S	methyl	4-carboxyphenyl	3-chloro-4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
490	S	methyl	4-carboxyphenyl	4-difluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
491	S	methyl	4-carboxyphenyl	3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
492	S	methyl	4-carboxyphenyl	4-methanesulfonyl phenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
493	S	methyl	4-carboxyphenyl	pentafluorophenyl methyl	H	H	H	H	CR^5	CR^6
494	S	methyl	4-carboxyphenyl	4-trifluoromethyl sulfonylphenylmethyl	H	H	H	H	CR^5	CR^6
495	S	methyl	4-carboxyphenyl	pyridin-2-ylmethyl	H	H	H	H	CR^5	CR^6
496	S	methyl	4-carboxyphenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
497	S	methyl	4-carboxyphenyl	3-fluoro-4-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
498	S	H	4-nitrophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
499	S	H	4-aminophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
500	S	methyl carbonyl amino	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
501	S	cyclo pentyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
502	S	cyclo pentyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
503	S	methyl carbonyl	4-bromophenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
504	S	1-hydroxy-1-methyl-ethyl	4-methoxy carbonylphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
505	S	1-hydroxy-1-methyl-ethyl	4-carboxyphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
506	S	1-hydroxy-1-methyl-ethyl	4-bromophenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
507	S	H	4-(methane sulfonylamino) phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
508	S	methane sulfonyl amino	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
509	S	methyl carbonyl amino	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
510	S	methyl	2-carboxyethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
511	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
512	S	chloro	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
513	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
514	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
515	S	chloro	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
516	S	1-hydroxy-1-methyl-ethyl	4-methoxy carbonylphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
517	S	methyl	4-carboxyphenyl	3,4,5-trifluorophenylmethyl	H	H	H	H	CR^5	CR^6
518	S	methyl	4-carboxyphenyl	4-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
519	S	methyl	4-carboxyphenyl	2-fluoro-5-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
520	S	methyl	4-carboxyphenyl	2,5-dichlorophenylmethyl	H	H	H	H	CR^5	CR^6
521	S	methyl	4-carboxyphenyl	4-chloro-3-fluorophenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
522	S	methyl	4-carboxyphenyl	4-fluoro-2-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
523	S	methyl	4-carboxyphenyl	benzo[1,3]dioxol-5-yl methyl	H	H	H	H	CR^5	CR^6
524	S	methyl	4-carboxyphenyl	2,2-difluoro-benzo[1,3]dioxol-5-yl methyl	H	H	H	H	CR^5	CR^6
525	S	methyl	4-carboxyphenyl	3,4-dimethoxyphenyl methyl	H	H	H	H	CR^5	CR^6
526	S	methyl	4-carboxyphenyl	4-trifluoromethylthiophenylmethyl	H	H	H	H	CR^5	CR^6
527	S	methyl	4-carboxy thien-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
528	S	methyl	5-carboxy-3-methyl-thien-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
529	S	methyl	5-carboxy furan-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
530	S	chloro	4-methoxy carbonylphenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
531	S	chloro	4-methoxy carbonylphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
532	S	H	methylamino	*n*-butyl	H	H	H	H	CR^5	CR^6
533	S	methyl	methylamino	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
534	S	1*S**-hydroxy-ethyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
535	S	1*R**-hydroxy-ethyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
536	$S(O_2)$	dimethylamino	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
537	S	chloro	4-carboxyphenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
538	S	chloro	4-carboxyphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
539	S	methyl	4-(1*H*-tetrazol-5-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
540	S	methyl	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
541	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
542	S	methyl	4-(1*H*-tetrazol-5-yl)phenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
543	S	methyl	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
544	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
545	S	methyl	4-carboxyphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
546	S	methyl	3-cyanophenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
547	S	iso propyl	phenyl	4-fluoro-3-trifluoromethylphenylmethyl	H	H	H	H	CR^5	CR^6
548	S	iso propyl	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
549	S	methyl	3-cyanophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
550	S	methyl	3-cyanophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
551	S	methyl	3-cyanophenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
552	S	methyl	3-cyanophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
553	S	chloro	methylamino	*n*-butyl	H	H	H	H	CR^5	CR^6
554	S	bromo	methylamino	*n*-butyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
555	S	methyl	4-(hydroxyamino carbonyl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
556	S	H	4-carboxyphenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
557	S	methyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	CF_3	H	H	CR^5	CR^6
558	S	methyl	4-carboxyphenyl	*n*-butyl	H	CF_3	H	H	CR^5	CR^6
559	S	bromo	4-(morpholin-4-yl)phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
560	S	bromo	4-dimethylamino phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
561	S	chloro	4-dimethylamino phenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
562	S	chloro	4-(morpholin-4-yl)phenyl	n-butyl	H	H	H	H	CR^5	CR^6
563	S	iso propyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
564	S	iso propyl	4-methoxy carbonylphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
565	S	iso propyl	4-methoxy carbonylphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
566	S	iso propyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
567	S	iso propyl	4-carboxyphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
568	S	iso propyl	4-carboxyphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
569	S	H	4-(1*H*-tetrazol-5-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
570	S	methyl	4-(1*H*-tetrazol-5-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
571	S	H	4-(1*H*-tetrazol-5-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
572	S	methyl	4-(1*H*-tetrazol-5-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
573	S	H	3-cyanophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
574	S	H	3-cyanophenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
575	S	H	3-cyanophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
576	S	bromo	3-(1*H*-tetrazol-5-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
577	$S(O_2)$	bromo	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
578	S	chloro	3-(1*H*-tetrazol-5-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
579	S	bromo	4-(1*H*-tetrazol-5-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
580	S	chloro	4-(1*H*-tetrazol-5-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
581	S	bromo	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
582	S	chloro	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
583	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
584	S	chloro	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
585	S	chloro	4-aminophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
586	S	H	4-amino-3-chlorophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
587	S	bromo	4-aminophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
588	S	bromo	4-amino-3-bromophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
589	S	methyl	4-carboxy-2-fluorophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
590	S	methyl	4-carboxy-2-fluorophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
591	S	methyl	4-carboxy-2-fluorophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
592	S	methyl	4-carboxy-2-fluorophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
593	S	methyl	4-carboxy-2-fluorophenyl	*n*-butyl	H	H	H	H	CR^5	CR^6
594	S	bromo	4-(1*H*-tetrazol-5-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
595	S	bromo	4-(1*H*-tetrazol-5-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
596	S	H	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
597	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
598	S	methyl	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
599	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
600	S	methyl	2-(methoxy carbonyl)ethyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
601	S	methyl	2-(methoxy carbonyl)ethyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
602	S	methyl	2-(methoxy carbonyl)ethyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
603	S	methyl	2-(methoxy carbonyl)ethyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
604	S	methyl	2-carboxyethyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
605	S	methyl	2-carboxyethyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
606	S	methyl	2-carboxyethyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
607	S	bromo	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
608	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
609	S	chloro	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
610	S	H	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
611	S	methyl	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathiadiazol-4-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
612	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
613	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
614	S	methyl	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
615	S	methyl	phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
616	S	methyl	phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
617	S	methyl	phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
618	$S(O_2)$	methyl	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
619	$S(O_2)$	methyl	phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
620	$S(O_2)$	methyl	phenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
621	$S(O_2)$	methyl	phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
622	$S(O_2)$	methyl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
623	S	methyl	4-(methane sulfonylamino carbonyl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
624	S	bromo	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathia diazol-4-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
625	S	chloro	4-(2-oxo-2,3-dihydro-2λ4-[1,2,3,5]oxathia diazol-4-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
626	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol -3-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
627	S	chloro	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol -3-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
628	S	methyl	4-methoxy carbonylphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
629	S	methyl	4-methoxycarbony lphenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
630	S	methyl	4-methoxy carbonylphenyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
631	S	methyl	4-methoxy carbonylphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
632	$S(O_2)$	methyl	4-carboxyphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
633	$S(O_2)$	methyl	4-carboxyphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
634	$S(O_2)$	methyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
635	S	chloro	4-(1*H*-tetrazol-5-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
636	S	chloro	4-(1*H*-tetrazol-5-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
637	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
638	S	H	4-carboxy-2-fluorophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
639	S	H	4-carboxy-2-fluorophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
640	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
641	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
642	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
643	$S(O_2)$	di methyl amino	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
644	$S(O_2)$	methyl amino	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
645	$S(O_2)$	4-methyl-piperazin-1-yl	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
646	$S(O_2)$	amino	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
647	$S(O_2)$	piperazin-1-yl	phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
648	$S(O_2)$	methyl amino	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
649	$S(O_2)$	4-methyl-piperazin-1-yl	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
650	S	bromo	4-aminophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
651	S	bromo	4-amino-3-bromophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
652	S	H	4-methanesulfonyl aminophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
653	S	H	4-aminophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
654	S	H	4-bromophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
655	S	H	4-bromophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
656	S	1-hydroxy-1-methyl-ethyl	4-bromophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
657	S	1-hydroxy-1-methyl-ethyl	4-carboxyphenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
658	S	1-hydroxy-1-methyl-ethyl	4-carboxyphenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
659	S	chloro	4-(methane sulfonylamino) phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
660	S	bromo	4-(methane sulfonylamino) phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
661	S	bromo	3-bromo-4-(methane sulfonylamino) phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
662	S	methyl	trifluoromethyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
663	S	H	trifluoromethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
664	S	methyl	trifluoromethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
665	S	methyl	trifluoromethyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
666	S	chloro	4-aminophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
667	S	chloro	4-amino-3-chloro-phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
668	S	bromo	4-aminophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
669	S	methyl	2,2,2-trifluoroethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
670	S	methyl	2,2,2-trifluoroethyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
671	S	methyl	2,2,2-trifluoroethyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
672	S	methyl	2,2,2-trifluoroethyl	4,4,4-trifluorobutyl	H	H	H	H	CR^5	CR^6
673	S	methyl	2,2,2-trifluoroethyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
674	S	cyclo propyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
675	S	cyclo propyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
676	S	chloro	4-(methane sulfonylamino) phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
677	S	bromo	4-(methane sulfonylamino) phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
678	S	H	4-(methane sulfonylamino) phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
679	S	chloro	4-(methane sulfonylamino) phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
680	S	bromo	4-(methane sulfonylamino) phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
681	S	chloro	3,5-dichloro-4-methanesulfonyl aminophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
682	S	chloro	3,5-dichloro-4-methanesulfonyl aminophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
683	S	bromo	3-bromo-4-(methanesulfony lamino)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
684	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol -3-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
685	S	H	4-carboxy-2-fluorophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
686	S	H	4-carboxy-2-fluorophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
687	S	H	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol -3-yl)-phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
688	S	H	4-methylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
689	S	H	4-dimethylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
690	S	chloro	4-methylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
691	S	chloro	3-chloro-4-methylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
692	S	bromo	3-bromo-4-methylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
693	S	bromo	4-methylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
694	S	chloro	4-trifluoromethyl carbonylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
695	S	bromo	4-trifluoromethyl carbonylamino phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
696	S	cyclo butyl	4-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
697	S	H	2,2,2-trifluoroethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
698	S	cyclo butyl	4-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
699	S	methyl	3-hydroxypropyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
700	S	methyl	2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
701	S	methyl	4-(2-dimethylamino methyl-imidazol-1-yl)phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
702	S	bromo	2,2,2-trifluoroethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
703	S	chloro	2,2,2-trifluoroethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
704	S	hydroxy methyl	2,2,2-trifluoroethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
705	S	bromo	methylamino	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
706	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
707	S	bromo	4-carboxy-2-fluorophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
708	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
709	S	bromo	4-carboxy-2-fluorophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
710	S	bromo	4-carboxy-2-fluorophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
711	S	bromo	4-carboxy-2-fluorophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
712	S	bromo	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
713	S	H	3-methanesulfonyl aminophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
714	S	chloro	3-methanesulfonyl aminophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
715	S	bromo	3-methanesulfonyl aminophenyl	3,3,3-trifluoropropyl	H	H	H	H	CR^5	CR^6
716	S	chloro	4-methanesulfonyl aminophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
717	S	bromo	4-methanesulfonyl aminophenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
718	S	chloro	4-(cyclopropyl sulfonylamino) phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
719	S	bromo	4-(cyclopropyl sulfonylamino) phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
720	S	methyl	benzimidazol-2-yl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
721	S	methyl	quinoxalin-5-yl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
722	S	methyl	1-methyl-benzimidazol-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
723	S	methyl	quinoxalin-5-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
724	S	methyl	2-formylethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
725	S	methyl	3-hydroxy-3-methyl-butyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
726	S	methyl	benzimidazol-2-yl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
727	S	methyl	5-chloro-1-methyl-benzimidazol-2-yl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
728	S	methyl	benzimidazol-2-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
729	S	methyl	benzimidazol-2-yl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
730	S	methyl carbonyl	4-bromophenyl	4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
731	S	methyl carbonyl	4-bromophenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
732	S	methyl carbonyl	4-bromophenyl	phenylmethyl	H	H	H	H	CR^5	CR^6
733	S	methyl carbonyl	4-bromophenyl	3-chloro-4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
734	S	1-hydroxy-1-methyl-ethyl	4-bromophenyl	4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
735	S	1-hydroxy-1-methyl-ethyl	4-bromophenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
736	S	1-hydroxy-1-methyl-ethyl	4-bromophenyl	phenylmethyl	H	H	H	H	CR^5	CR^6
737	S	1-hydroxy-1-methyl-ethyl	4-bromophenyl	3-chloro-4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
738	S	methyl	4-dimethylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
739	S	methyl	4-diethylamino phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
740	S	methyl	4-(thiomorpholin-4-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
741	S	methyl	4-(morpholin-4-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
742	S	methyl	4-(piperazin-1-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
743	S	H	4-methanesulfonyl amino)-2-methoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
744	S	chloro	4-methanesulfonyl amino-2-methoxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
745	S	methyl	1-methyl-benzimidazol-2-yl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
746	S	methyl	1-methyl-benzimidazol-2-yl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
747	S	methyl	2-amino-indan-5-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
748	S	methyl	4-dimethylamino phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
749	S	methyl	4-(thiomorpholin-4-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
750	S	methyl	4-(morpholin-4-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
751	S	methyl	4-(piperidin-1-yl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
752	S	methyl	4-(piperidin-1-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
753	S	cyclo propyl	4-methoxy carbonylphenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
754	S	cyclo butyl	4-methoxy carbonylphenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
755	S	cyclo propyl	4-carboxyphenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
756	S	cyclo butyl	4-carboxyphenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
757	S	methyl	3-(methoxy carbonyl)propyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
758	S	methyl	4-hydroxybutyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
759	S	methyl	4-hydroxy-4-methylpentyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
760	S	methyl	2-(methoxy carbonyl)ethyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
761	S	methyl	methoxy carbonylmethyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
762	S	methyl	2-carboxyethyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
763	S	methyl	3-hydroxy-3-methyl-butyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
764	S	methyl	3-hydroxypropyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
765	S	methyl	3-carboxypropyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
766	S	chloro	5-chloro-2-methoxy-4-(methanesulfonylamino)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
767	S	methyl	2-methyl-1,2,3,4-tetrahydro-isoquinolin-7-yl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
768	S	isopropenyl	ethyl	4-chloro-2-fluoro-5-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
769	S	methyl	3-bromopropyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
770	S	methyl	cyclopropyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
771	S	methyl	4-bromobutyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
772	S	methyl carbonyl	4-cyanophenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
773	S	methyl carbonyl	4-cyanophenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
774	S	methyl	4-carboxy-3-fluorophenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
775	S	methyl	4-carboxy-3-fluorophenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
776	S	1-hydroxy-1-methyl-ethyl	ethyl	2-fluoro-3-methoxy phenylmethyl	H	H	H	H	CR^5	CR^6
777	S	methyl	4-(4-methyl-piperazin-1-yl carbonyl)phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
778	S	methyl	3-(imidazol-1-yl)propyl	3-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
779	S	methyl	4-(imidazol-1-yl)butyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
780	S	chloro	2-hydroxy-4-(methanesulfonylamino)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
781	S	1-hydroxy-1-methyl-ethyl	4-carboxyphenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
782	S	methyl	4-(pyrrolidin-3*S*-yl aminocarbonyl)-phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
783	S	methyl	4-(pyrrolidin-3*R*-yl aminocarbonyl)-phenyl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
784	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
785	S	methyl	4-(1*H*-tetrazol-5-yl)phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
786	S	methyl	6-dimethylamino-pyridin-3-yl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
787	S	methyl	6-(dimethylamino) pyridin-3-yl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
788	S	methyl	6-(morpholin-4-yl)pyridin-3-yl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
789	S	methyl	6-(dimethylamino) pyridin-3-yl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
790	S	methyl	6-(morpholin-4-yl)pyridin-3-yl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
791	S	methyl	methoxy carbonylmethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
792	S	methyl	carboxymethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
793	S	methyl	2-hydroxyethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
794	S	methyl	2-methoxy carbonylethyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
795	S	methyl	2-carboxyethyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
796	S	methyl	3-hydroxy-3-methyl-butyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
797	S	methyl	2-bromoethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
798	S	methyl	6-(morpholin-4-yl)pyridin-3-yl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
799	S	methyl	4-dimethylamino phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
800	S	methyl	4-(morpholin-4-yl)phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
801	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
802	S	1-hydroxy-1-methyl-ethyl	ethyl	2,4,5-trifluoro-3-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
803	S	iso propenyl	ethyl	2,4,5-trifluoro-3-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
804	S	methyl	6-(1*H*-tetrazol-5-yl)pyridin-3-yl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
805	S	methyl	6-(1*H*-tetrazol-5-yl)pyridin-3-yl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
806	S	methyl	6-(1*H*-tetrazol-5-yl)pyridin-3-yl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
807	S	methyl	6-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)pyridin-3-yl	2-(cyclopropyl)ethyl	H	H	H	H	CR^5	CR^6
808	S	methyl	6-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)pyridin-3-yl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
809	S	methyl	6-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)pyridin-3-yl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
810	S	methyl	4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl	4-trifluoromethoxy phenylmethyl	H	H	H	H	CR^5	CR^6
811	S	methyl	4-(5-oxo-4,5-dihydro-1H-[1,2,4]triazol-3-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6
812	S	methyl	4-(1-methyl-5-oxo-4,5-dihydro-1*H*-[1,2,4]triazol-3-yl)phenyl	5,5,5-trifluoropentyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
813	S	chloro	phenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	NA	CR^5	N
814	S	chloro	3-carboxyphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	NA	CR^5	N
815	S	chloro	4-carboxyphenyl	3,3,3-trifluoropropyl	H	H	H	NA	CR^5	N
816	S	chloro	3-methoxy carbonylphenyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	NA	CR^5	N
817	S	H	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
818	S	methyl	phenyl	2-fluoroethyl	H	H	H	H	CR^5	CR^6
819	S	methyl	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
820	S	hydroxy methyl	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
821	S	1-hydroxy-ethyl	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
822	S	1-methoxy-ethyl	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
823	S	methyl	4-methoxy carbonylphenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
824	S	methyl	4-carboxyphenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
825	S	methyl	3,4-difluorophenyl	phenylmethyl	H	H	H	H	CR^5	CR^6
826	S	methyl	3,4-difluorophenyl	4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6
827	S	1-hydroxy-ethyl	ethyl	4-fluoro-3-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
828	S	H	ethyl	4-fluoro-3-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
829	S	methyl	ethyl	2-fluoropyridin-4-yl methyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
830	S	1-hydroxy-1-methyl-ethyl	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
831	S	methyl	3,4-difluorophenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
832	S	methoxy methyl	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
833	S	methyl carbonyl	phenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
834	S	hydroxy methyl	2,5-dibromophenyl	3,4-difluorophenylmethyl	H	H	H	H	CR^5	CR^6
835	S	1-hydroxy-ethyl	ethyl	2-fluoro-pyridin-4-ylmethyl	H	H	H	H	CR^5	CR^6
836	S	1-hydroxy-1-methyl-ethyl	ethyl	2-fluoro pyridin-4-ylmethyl	H	H	H	H	CR^5	CR^6
837	S	methyl carbonyl	ethyl	4-fluoro-3-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
838	S	1-hydroxy-1-methyl-ethyl	ethyl	4-fluoro-3-methoxyphenyl methyl	H	H	H	H	CR^5	CR^6
839	S	1-methoxy-ethyl	ethyl	4-fluoro-3-trifluoromethylphenyl methyl	H	H	H	H	CR^5	CR^6
840	S	methyl	ethyl	2,3,5-trifluoro-pyridin-4-ylmethyl	H	H	H	H	CR^5	CR^6
841	S	methyl	3,4-difluorophenyl	2-fluoroethyl	H	H	H	H	CR^5	CR^6
842	S	H	4-methoxy carbonylphenyl	3-fluoropropyl	H	H	H	H	CR^5	CR^6
843	S	H	4-methoxy carbonylphenyl	2-fluoroethyl	H	H	H	H	CR^5	CR^6
844	S	H	phenyl	2-fluoroethyl	H	H	H	H	CR^5	CR^6
845	S	methyl	3-fluoro-4-(4-fluorophenyl methoxy)phenyl	4-fluorophenylmethyl	H	H	H	H	CR^5	CR^6

Cpd No.	G	Y	R^1	R^2	R^3	R^4	R^5	R^6	A	B
846	S	methyl	3-fluoro-4-(phenyl methoxy)phenyl	phenylmethyl	H	H	H	H	CR^5	CR^6
847	S	H	ethyl	2-fluoropyridin-4-yl methyl	H	H	H	H	CR^5	CR^6
848	S	methyl carbonyl	ethyl	2-fluoropyridin-4-yl methyl	H	H	H	H	CR^5	CR^6
849	S	bromo	*n*-butylamino	*n*-butyl	H	H	H	H	CR^5	CR^6
850	S	H	*n*-butylamino	*n*-butyl	H	H	H	H	CR^5	CR^6

Biological Examples

Example 1a

In Vitro Canine TRPM8 Functional Assay

The functional activity of compounds of the formula (I) was determined by measuring changes in intracellular calcium concentration using a Ca^{2+}-sensitive fluorescent dye. The changes in fluorescent signal were monitored by a fluorescence plate reader, either a FLIPR^{TM} (Molecular Devices) or FDSS (Hamamatsu). Increases in intracellular Ca^{2+} concentration were readily detected upon activation with icilin.

At 24 hrs prior to assay, HEK293 cells stably expressing canine TRPM8 were seeded in culture medium in black wall, clear-base poly-D-lysine coated 384-well plates (BD Biosciences, NJ, USA) and grown overnight in 5% CO_2 at 37 °C. On assay day, growth media was removed and cells were loaded with Calcium 3 Dye (Molecular Devices) for 35 min at 37 °C, under 5% CO_2 and then for 25 min at room temperature and atmosphere. Subsequently, cells were tested for agonist-induced increases in intracellular Ca^{2+} levels using FLIPR^{TM} or FDSS. Cells were challenged with a compound of the Formula (I) (at varying concentrations) and intracellular Ca^{2+} was measured for 5 min prior to the addition of icilin to all wells to achieve a final concentration that produces approximately an 80% maximal response. EC_{50} or IC_{50} values for compounds of the present invention were determined from eight-point dose-response studies. Curves were generated using the average of quadruplicate wells for each data point. The resultant data are displayed in Table 2.

Table 2

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
1	0.0240		100	426	0.0300	95	
2	0.0163*		99	427	0.0050	95	
3	0.0350		98	428	0.0100	93	
4	0.0040		97	429	0.0170	93	
5	0.0630		97	430		52	
6	0.0113*		99	431	0.0200	88	
7	0.0073*		97	432		42	
8	0.0100		99	433	0.0330	93	
9	0.0470		98	434	0.0170	90	
10	0.2290		89	435	0.0330	95	
11	0.0330		97	436	0.0040	89	
12	0.0060		97	437	0.0090	92	
13	0.0030		97	438	0.0020	90	
14	0.0189*		99	439	0.0020	86	
15	0.0050		96	440	0.0140	84	
16	0.0060		99	441		37	
17	0.0220		97	442	0.0670	81	
18	0.0810		94	443	0.0140	94	
19			58	444	0.1220	92	
20	0.0060		98	445		58	
21	0.0150		98	446	0.0960	82	
22	0.0320		98	447		19	
23	0.0260		99	448	0.0120	102	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
24	0.0088*		100	449	0.0880	97	
25	0.0210		99	450	0.0290	101	
26	0.0200		98	451	0.0680	97	
27	0.0200		99	452	0.0180	101	
28	0.0320		100	453	0.0020	101	
29	0.0330		99	454	0.0040	101	
30	0.0120		100	455	0.0360	101	
31	0.0220		100	456		67	
32	0.0370		100	457	0.0470	93	
33	0.0574		100	458	0.0120	102	
34	0.1841		98	459	0.0090	102	
35	0.0608		100	460	0.0080	102	
36	0.0771		98	461		30	
37	0.0983		96	462		22	
38	0.0030		97	463	0.0260	101	
39	0.0039		101	464	0.0070	102	
40	0.0137		97	465	0.0630	90	
41	0.0054		99	466		66	
42	0.0106		100	467	0.0200	100	
43	0.0250		94	468		16	
44	0.0070		98	469		13	
45	0.0520	97		470		15	
46	0.0840		99	471	0.0590	97	
47	0.1120		97	472	0.0400	88	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
48	0.0790		98	473	0.0090	102	
49	0.1700		90	474	0.0080	101	
50	0.0660		99	475	0.0020	102	
51	0.0780		98	476		39	
52	0.1160		99	477	0.0120	100	
53	0.1640		97	478	0.0250	99	
54			65	479	0.0080	100	
55	0.0655		99	480	0.0130	100	
56	0.1031		99	481		69	
57	0.1080		100	482	0.0240	100	
58	0.0455*		98	483	0.0090	101	
59	0.0445		98	484	0.0210	100	
60	0.0283		97	485	0.0210	96	
61	0.0524		95	486	0.0040	100	
62	0.0581		98	487	0.0020	101	
63	0.0740		98	488	0.0010	101	
64	0.0190	96		489	0.0006	101	
65	0.0170	97		490	0.0010	101	
66	0.0040	96		491	0.0010	101	
67	0.0550	77		492	0.0620	91	
68	0.0020	99		493	0.0008	101	
69	0.0030	96		494	0.0009	101	
70	0.0070	99		495	0.0550	98	
71	0.0180	98		496	0.0008	101	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
72	0.0260	99		497	0.0004	101	
73		24		498		41	
74	0.0210	97		499	0.0150	101	
75	0.0180	98		500		15	
76	0.0210	95		501		31	
77	0.0220	97		502	0.0100	100	
78	0.0225	102		503	0.0470	96	
79		69		504	0.0180	101	
80	0.0290		98	505	0.0240	98	
81	0.0150		99	506	0.0310	100	
82	0.3190		87	507	0.0340	92	
83	0.0480		101	508		47	
84	0.0350		100	509	0.0320	100	
85	0.0240		100	510	0.0110	102	
86	0.0530		101	511	0.0030	101	
87	0.1700		94	512	0.0040	102	
88	0.2610		88	513	0.0210	101	
89	0.2050		96	514	0.0460	100	
90	0.0210		99	515		49	
91			33	516	0.0190	102	
92	0.0682	79		517	0.0020	102	
93	0.0110	98		518	0.0007	101	
94	0.0180	98		519	0.0060	102	
95	0.0060	97		520	0.0090	102	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
96	0.0040	98		521	0.0020	101	
97	0.0140	96		522	0.0040	101	
98	0.0150	97		523	0.0020	101	
99	0.0180	99		524	0.0020	102	
100	0.0068	103		525	0.0060	101	
101	0.0305	101		526	0.0010	102	
102	0.0402	98		527	0.0050	101	
103	0.0908	80		528	0.0160	102	
104	0.0089	98		529		35	
105		20		530		54	
106	0.0190	93		531	0.0460	88	
107		72		532		19	
108		71		533	0.0320	102	
109		14		534	0.0020	102	
110	0.0072	97		535	0.0010	102	
111	0.0920	68		536	0.0770	89	
112	0.0302	95		537	0.0082	104.64	
113		19		538	0.0049	104.55	
114	0.0511*	93		539	0.0067	104.91	
115	0.0795		95	540	0.0122	104.6	
116	0.1017		98	541	0.0108	104.57	
117	0.0537		99	542	0.0023	104.93	
118	0.0480		100	543	0.0072	104.46	
119	0.1336		93	544	0.0018	105.04	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
120	0.1560	75		545	0.0019	104.78	
121	0.0350	86		546	0.0683	85.683	
122		23		547	0.0074	104.86	
123		60		548	0.0289	102.47	
124		14		549	0.0159	103.68	
125	0.0050*		99	550	0.0188	103.79	
126			45	551	0.0886	94.385	
127	0.0080		98	552	0.0251	101.3	
128	0.0090		99	553		38.688	
129	0.0028*		101	554		52.301	
130	0.1040		98	555	0.0219	102.49	
131	0.0480		95	556	0.0482	99.314	
132			56	557		39.483	
133	0.0600		97	558	0.0994	80.935	
134		30		559	0.0032	104.59	
135		18		560	0.0657	104.01	
136		40		561	0.0284	103.38	
137	0.0080	98		562	0.0331	102.74	
138	0.0130	83		563	0.0493	94.006	
139	0.0620	91		564		57.717	
140	0.0020		98	565	0.1170	74.399	
141		18		566	0.0018	104.33	
142			60	567	0.0103	104.13	
143			48	568	0.0024	103.99	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
144			62	569	0.0350	88	
145	0.0141		100	570	0.0066	101	
146	0.0480		97	571		14	
147	0.0782		96	572	0.0166	101	
148	0.0021*		98	573		28	
149	0.0071*	102	101	574		16	
150	0.0154		100	575		15	
151	0.0167		96	576	0.0191	100	
152	0.0026		95	577	0.0078	101	
153	0.0188		97	578	0.0267	91	
154	0.0362		96	579	0.0088	102	
155	0.0040		99	580	0.0221	101	
156			65	581	0.0251	100	
157	0.0140	100		582	0.0503	96	
158	0.0104		94	583	0.0079	100	
159	0.0134		98	584	0.0159	100	
160	0.0358		97	585	0.0064	101	
161	0.0554		95	586	0.0346	100	
162	0.0045		101	587	0.0039	100	
163	0.0639		92	588	0.0121	101	
164	0.0319		97	589	0.0042	100	
165	0.0037		98	590	0.0061	101	
166	0.0114		94	591	0.0042	101	
167	0.0104		101	592	0.0018	101	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
168	0.0142		96	593	0.0076	101	
169	0.0214		98	594	0.0060	101	
170	0.0445		97	595	0.0190	101	
171	0.0193		100	596		17	
172	0.0111		98	597		25	
173	0.0084		99	598	0.0307	101	
174	0.0025		99	599	0.0161	101	
175	0.0046		97	600	0.0089	101	
176	0.0028		97	601	0.0241	100	
177	0.0057		96	602	0.0221	101	
178	0.0355		96	603	0.0103	101	
179	0.0036		98	604		13	
180	0.0430	96		605		18	
181	0.0840	95		606	0.0905	75	
182	0.0100		99	607	0.0368	101	
183	0.0140		99	608	0.0181	101	
184	0.0039		97	609	0.0537	99	
185	0.0064	102		610		55	
186	0.0037	103		611	0.0146	101	
187	0.0060	100		612	0.0537	97	
188	0.0122*	99	101	613	0.0066	101	
189	0.0116	100		614	0.0074	101	
190	0.0152	101		615	0.0073	101	
191	0.0060	105		616	0.0128	101	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
192	0.0600	82		617	0.0074	101	
193	0.0145	101		618	0.0104	101	
194		45		619	0.0398	101	
195	0.0473	88		620	0.0234	101	
196	0.0080	99		621	0.0110	101	
197	0.0070	99		622	0.0313	89	
198	0.0100	95		623	0.0070	101	
199	0.0130	91		624	0.0134	103	
200		29		625	0.0204	103	
201		14		626	0.0074	103	
202		32		627	0.0086	103	
203	0.0150		93	628	0.0233	103	
204	0.0060		96	629	0.0262	103	
205	0.0030		96	630	0.0356	103	
206	0.0130	98		631	0.0263	103	
207	0.0160	98		632		12	
208	0.0120	96		633		17	
209	0.0320	98		634		55	
210	0.0080	91		635	0.0074	101	
211	0.0300	80		636	0.0460	103	
212	0.0114	101		637	0.0122	104	
213	0.0014	95		638	0.0600	100	
214	0.0021	97		639	0.1280	84	
215	0.0060	101		640	0.0110	103	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
216	0.0140	100		641	0.0140	103	
217	0.0030	88		642	0.0410	90	
218	0.0010	90		643	0.0050	103	
219	0.0078	101		644		63	
220	0.0012*	98	99	645		20	
221	0.0050	92		646		55	
222	0.0017	95		647		21	
223	0.0023	96		648		62	
224	0.0010	100		649		26	
225	0.0040	98		650	0.0040	102	
226	0.0020	99		651	0.0060	103	
227	0.0006*	101		652	0.0850	102	
228	0.0060	101		653	0.0130	102	
229	0.0210	99		654		56	
230	0.0129	100		655		55	
231	0.0290		95	656	0.0537	98	
232	0.0740		94	657	0.0075	101	
233	0.0220		93	658	0.0043	101	
234	0.0100		93	659	0.0141	100	
235			51	660	0.0112	100	
236			68	661	0.0141	100	
237	0.0248*	87	92	662		50.122	
238	0.0930		96	663		17.113	
239	0.0920		96	664		53.117	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
240			43	665		27.939	
241	0.1060		97	666	0.0081	102.6	
242	0.0382	95		667	0.0301	102.96	
243	0.0380	98		668	0.0050	102.88	
244	0.0122	100		669	0.0512	96.422	
245	0.0142	102		670	0.0390	99.074	
246	0.0088	102		671	0.0345	100.03	
247	0.0255	99		672	0.0749	75.3	
248	0.0083	98		673	0.0738	94.378	
249	0.0009	97		674	0.0776	85.377	
250	0.0127	102		675	0.0024	100	
251	0.0387	95		676	0.0259	102.32	
252	0.0171	102		677	0.0246	101.48	
253	0.0273	101		678		60.964	
254	0.1250	58		679	0.0579	100.43	
255	0.0860	89		680	0.0561	96.235	
256	0.0300	87		681	0.0674	93.318	
257		62		682	0.0317	101.01	
258		25		683	0.0258	100.57	
259		24		684	0.1448	73.142	
260	0.0500	86		685	0.0119	102.25	
261	0.0126	97		686	0.0047	104.94	
262	0.0670	94		687	0.0569	74.496	
263	0.2030	52		688	0.0602	99	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
264	0.0341	99		689	0.0528	86	
265	0.0220	90		690	0.0161	101.25	
266	0.0390	86		691	0.0160	101.81	
267	0.0100	96		692	0.0072	101.48	
268		67		693	0.0252	103.39	
269	0.0160	94		694		42	
270	0.3380		75	695	0.0170	101	
271	0.0117*	98		696	0.0230	97	
272	0.0062*	97		697	0.0640	92	
273	0.0180*	96		698	0.0020	102	
274	0.0360	94		699	0.0060	103	
275	0.0030*	97		700		37	
276	0.0710	76		701	0.0325	95	
277	0.0390	91		702	0.0230	99	
278	0.0010*	98		703	0.0510	80	
279	0.0013	97		704	0.0150	102	
280	0.0380	87		705	0.0190	101	
281		62		706	0.0140	102	
282	0.0700	86		707	0.0030	102	
283	0.0920	82		708	0.0130	102	
284		15		709	0.0060	102	
285	0.0025		100	710	0.0070	102	
286	0.0070		99	711	0.0020	102	
287	0.0298		96	712	0.0040	102	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
288	0.0200	90		713		47	
289	0.0270	92		714	0.0290	96	
290	0.0053	103		715	0.0240	101	
291	0.0058	101		716	0.0090	101	
292	0.0008*	98	100	717	0.0050	102	
293	0.0078*	101	101	718	0.0390	96	
294	0.0018	99		719	0.0230	100	
295	0.0330	81		720		52	
296	0.0020	96		721	0.0042	102	
297		21		722		28	
298		18		723	0.0180	102	
299	0.0030	90		724	0.0053	102	
300		21		725	0.0078	102	
301		63		726	0.0903	69	
302		50		727		16	
303		56		728		44	
304		29		729	0.0962	75	
305	0.0120	97		730	0.0236	100	
306	0.0008	102		731	0.0444	87	
307	0.0151	101		732	0.0133	100	
308	0.0698	92		733	0.0134	100	
309	0.0550	93		734	0.0097	102	
310		69		735	0.0268	101	
311	0.1480	82		736	0.0172	101	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
312	0.0110	102		737	0.0299	101	
313	0.0210	102		738	0.0089	102	
314	0.0100	102		739	0.0232	90	
315	0.0640	99		740		57	
316	0.0100	101		741	0.0173	101	
317	0.0170	102		742		66	
318	0.0150	101		743		32	
319	0.0240	100		744	0.0573	99	
320	0.0100	100		745	0.0849	74	
321	0.0700	81		746		31	
322	0.0100	99		747		48	
323	0.0100	102		748	0.0053	101	
324	0.0150	100		749		64	
325	0.0050	102		750	0.0092	101	
326		14		751		54	
327	0.0370	97		752		65	
328	0.0350	94		753	0.0272	69	
329		17		754	0.0164	82	
330	0.0880	80		755	0.0009	101	
331	0.0900	71		756	0.0014	101	
332	0.0070	100		757	0.0108	101	
333	0.0090	101		758	0.0051	101	
334	0.0060	98		759	0.0183	101	
335	0.0010	101		760	0.0459	94	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
336	0.0150	101		761	0.0400	79	
337	0.0190	101		762	0.0253	101	
338	0.0290	95		763	0.0277	102	
339	0.0262	94		764	0.0221	101	
340		52		765	0.0136	101	
341	0.0140	96		766	0.0078	101	
342	0.0130	100		767	0.0892	77	
343	0.0190	98		768	0.0188	93	
344	0.0127	99		769	0.0440	85	
345	0.0265	99		770	0.0072	95	
346	0.0438	95		771	0.0072	96	
347	0.0571	95		772	0.0057	95	
348		60		773	0.0167	94	
349		42		774	0.0013	95	
350		48		775	0.0016	95	
351	0.0212	97		776	0.0067	95	
352	0.0086	96		777		56	
353	0.0094	98		778	0.1069	87	
354	0.1064	87		779	0.0487	79	
355	0.0296	92		780	0.1450	72	
356	0.0416	93		781	0.0030	102	
357	0.0190	95		782		33	
358	0.0120	92		783		38	
359	0.0170	93		784	0.0033	102	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
360	0.0410	92		785	0.0022	102	
361	0.0008	93		786	0.0154	102	
362		67		787	0.0149	102	
363	0.0510	84		788	0.0259	100	
364	0.0440	77		789	0.0117	102	
365		38		790	0.0220	101	
366	0.0400	85		791	0.0231	95	
367	0.0100	91		792		23	
368	0.0180	96		793	0.0155	102	
369	0.0180	98		794	0.0294	101	
370		29		795	0.0246	100	
371	0.0090	94		796	0.0242	101	
372	0.0270	91		797	0.0048	102	
373	0.1230	77		798	0.0359	102	
374	0.0040	89		799	0.0039	102	
375	0.0370	79		800	0.0068	102	
376	0.0260	85		801	0.0028	102	
377		65		802	0.0080	101	
378	0.0970	85		803	0.0308	101	
379		54		804	0.0111	102	
380		24		805	0.0022	103	
381		20		806	0.0130	102	
382		17		807	0.0060	103	
383		49		808	0.0007	102	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
384	0.0170	96		809	0.0069	103	
385		54		810	0.0010	102	
386	0.0128	100.87		811	0.0037	103	
387	0.0310	98		812	0.0076	103	
388	0.0190	97		813	0.0280	90	
389	0.0100	97		814	0.1380	80	
390		69		815		44	
391	0.0470	93		816		15	
392	0.0070	93		817	0.0730	80	
393	0.0050	95		818	0.0620	92	
394	0.0090	101		819	0.0210	98	
395	0.0030	101		820	0.0280	102	
396	0.0050	101		821	0.0090	102	
397	0.0080	95		822	0.0490	97	
398	0.0060	101		823	0.0220	102	
399	0.0360	93		824	0.0380	98	
400	0.0050	102		825	0.0250	89	
401	0.0050	91		826	0.0240	97	
402		38		827	0.0066	101	
403		52		828	0.0427	88	
404	0.0530	96		829	0.0230	100	
405	0.0360	95		830	0.0150	102	
406		66		831	0.0500	91	
407	0.0430	96		832	0.0880	76	

Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)	Cpd No.	IC_{50} (μM)	%Inh @ 0.2 (μM)	%Inh @ 0.5 (μM)
408	0.1220	78		833	0.0130	102	
409	0.0100	101		834	0.1230	87	
410	0.0170	96		835	0.0551	89	
411		43		836	0.0240	96	
412		13		837	0.0150	103	
413	0.0460	93		838	0.0041	101	
414		33		839	0.0159	101	
415	0.0050	92		840	0.0981	71.105	
416	0.0120	95		841		55	
417	0.0620	93		842		63	
418	0.0690	90		843		31	
419	0.3450	74		844		31	
420		48		845		24	
421	0.0640	90		846		28	
422	0.0180	97		847		33	
423	0.0070	93		848		68	
424	0.0070	95		849		25	
425	0.0790	86		850		28	

*IC_{50} values are listed as an average of two or more determinations

Example 1b

In Vitro Rat and Human TRPM8 Functional Assay

HEK293 cells are routinely grown as monolayer in Dulbecco's minimum essential medium supplemented with 10% FBS, 1mM L-glutamine, 100 units/ mL penicillin and 100ug/ mL streptomycin. Cells are maintained in 5% CO2 at 37 °C.

For functional expression of TRPM8, the full-length cDNA encoding human and rat TRPM8 are subcloned into pCI-NEO mammalian expression vectors. The expression constructs are transiently transfected into HEK293 cells according to the FuGENE 6 transfection reagent® (ROCHE) instructions. Within twenty-four hours, transiently trasfected cells are harvested and either seeded directly into assay plate or cryopreserved for future usage.

Transfected cells may be either cryopreserved or freshly transfected and plated into clearbase poly-D-lysine coated 384-well plates (BD Biosciences, NJ, USA) at a density of 10,000 cells per well in culture medium and grown overnight. The following day, all medium is removed and the cells are incubated with 52 μL of 0.5 X Calcium 3 Dye (Molecular Devices) prepared in complete assay buffer containing 20mM HEPES, 0.1% BSA, and 2.5mM probenecid at 37 °C for thirty five minutes. The cells are then incubated for an additional fifteen minutes at room temperature before initiating experiments. Following incubation, plates are inserted into a FDSS instrument, where cells were challenged with compounds of the formula (I) (at varying concentrations) and intracellular Ca2+ are measured for 5 min prior to the addition of icilin at the EC_{80} concentration. IC50 values for compounds of the formula (I) are determined from eight point dose-response studies.

Maximal fluorescence intensity (FI) achieved upon addition of icilin is exported from the FDSS and further analyzed using GraphPad Prism 3.02 (Graph Pad Software Inc., CA, U.S.A.) where data is normalized to percent of maximal response. The dose response curves from the average of quadruplicate wells for each data point are analyzed by using nonlinear regression of either sigmoidal dose response or sigmoidal dose response (variable slope). Finally, the IC50 values are calculated with the best-fit dose curve determined by Prism. Results are shown in Table 3.

Table 3

Cpd No	Cell preparation	rTRPM8 IC_{50}, nM	hTRPM8 IC_{50}, nM
306	Freshly transfected	5.0	4.0
496	Cryopreserved	1.8	1.4

Example 2

TRPM8 patch clamp assays

For patch clamp experiments, HEK293 cells are stably transfected with canine TRPM8 and cultured in DMEM supplemented with 10% fetal bovine serum, 100 units/ml penicillin, 100 μg/ml streptomycin and 1 mg/ml G418. Cells are maintained at 37 °C and in 5% CO_2.

The extracellular solution contains (in mM): NaCl, 132; EGTA, 1; KCl, 5.4; $MgCl_2$, 0.8; HEPES, 10; glucose, 10; pH=7.4. Recordings are performed using the conventional whole-cell patch clamp technique, 1-2 days after plating cells onto glass coverslips at densities appropriate for single cell recording. Currents are amplified by a patch clamp amplifier and filtered at 2 kHz (Axopatch 200B, Molecular Devices, Union City, CA). Menthol (100 μM) is applied to the cell at 0.5 ml/min via a gravity-fed perfusion system. Recordings involving menthol activation are performed at 22 °C.

In experiments where temperatures are varied, temperature ramps are generated by cooling the perfusate in an in-line cooler (Model SC-20, Warner Instruments, Hamden, CT) controlled by a temperature controller (Model CL-100, Warner Instruments). The temperature in the vicinity of the recorded cell is measured with a custom-made miniature thermo-microprobe connected to a monitoring thermometer (Model TH-8, Physitemp, Clifton, NJ), and sampled using Digidata 1322A and pClamp 9.0 (Molecular Devices), as are the currents concurrently measured in the whole-cell patch clamp mode. The current is continuously sampled (at 100 Hz) at a holding potential of -60 mV.

Compounds of the formula (I) are diluted from 10 mM DMSO stocks (stored at -20 °C) into an extracellular solution either containing 100 μM menthol or subjected to cooling. Increasing concentrations of a compound are applied to a cell in a cumulative manner and concentration-dependent responses are measured after steady-state activation is achieved by either 100 μM menthol or cooling to 10 °C. A saturating concentration of a reference antagonist is applied at the end of an experiment (either in the presence of 100 μM menthol or 10 °C temperature) to establish the baseline from which all the other measurements are subtracted.

Percentage inhibition by a compound is calculated as follows:

$100\times(1-I_{comp}/I_0)$; where I_{comp} and I_0 are steady-state current amplitudes in either the presence or absence of a concentration of compounds of the formula (I). Concentration-response data are fitted to a logistic function as follows: $R = 100/(1+c/IC_{50})^p$; where, R is the percentage inhibition, p is the Hill coefficient and c is the concentration of compounds of the formula (I). Results are shown in Table 4.

Table 4

Cpd	Mode of stimulation	[μM]	%inh	n	IC_{50} (nM)
284	Cold	0.003 0.01	24.0 71.0	2 3	8.0
306	menthol	0.0003 0.001 0.003 0.01	11.6 47.3 78.0 94.9	3 3 3 3	1.1
306	cold	0.001 0.003 0.01 0.03	22.4 60.1 86.2 97.3	3 3 3 3	2.3

Cpd	Mode of stimulation	[μM]	%inh	n	IC_{50} (nM)
496	menthol	0.0001	27.5	3	0.183
		0.0003	68.6	3	
		0.001	95.8	3	
		0.003	99.6	3	
496	cold	0.0003	21.6	3	0.554
		0.001	77.7	3	
		0.003	96.4	3	

In Vivo Models

Example 3

Inhibition of icilin-induced behaviors in rodents

Icilin was initially developed as a "super-cooling" compound by Delmar Chemicals Ltd. Subsequently it was shown to be one of the most potent known agonists of TRPM8 (McKemy DD, et al. Nature **2002**, 416(6876): 52-8), having an EC_{50} = 0.2 μM in stimulating calcium ion influx into TRPM8 transfected cells (Behrendt HJ et al. Brit J Pharmacol **2004**, 141(4): 737-45). Initial in vivo testing of icilin showed it to cause "wet-dog" shakes in rats. Similar shaking or jumping behavior was also evident in mice, rabbits, cats, dogs and monkeys. In humans, icilin produced a sensation of coolness on contact with mucous membranes, cold prickling when 0.1 mg was dropped on the tongue and coldness in the mouth, pharynx and chest lasting 30-60 minutes when 5-10 mg was ingested orally (Wei ET, Seid DA, J Pharm Pharmacol. **1983,** 35, 110). The inhibition or reversal of icilin-induced shaking behaviors in rodents provides evidence for the utility of TRPM8 antagonists of the formula (I) in treating or preventing a disease, syndrome, disorder, or condition in a subject in which the disease, syndrome, disorder or condition is affected by the modulation of TRPM8 receptors.

Example 3a

Inhibition of icilin-induced "wet –dog" shakes in rats

Male Sprague Dawley rats (220-450 g, Charles River Labs, n= 6-9/ treatment) were used to evaluate the ability of selected compounds of the formula (I) to block icilin-induced "wet-dog" shakes (WDS). Compounds of the formula (I) were administered in an appropriate vehicle, such as hydroxypropyl-β-cyclodextrin (HPβCD), methocellulose, 10% Solutol, or H_2O, or the like, by the appropriate route, i.p. or p.o., 30 – 120 minutes before icilin. Icilin was administered in PEG-400 or 10% solutol/H_2O, at 1.0 or 3.0 mg/kg, i.p. and spontaneous "wet-dog" shakes were counted 10-20 minutes post-icilin. Results are presented as a percent inhibition of shakes, which was calculated as [1-(test compound WDS count / vehicle WDS count)] x 100. Results are shown in Table 5.

Table 5

Cpd	Form	Dose	Route	Vehicle	Pre-icilin min	% Inhibition	ED50, mg/kg
271	$CO_2^-Na^+$	30	p.o.	Water	30	65	
271	$CO_2^-Na^+$	1 3 10 30	p.o.	Water	30	28 35 46 88	5.7
272	CO_2^-H	3 10 30	p.o.	methocel	30	26 23 43	
272	CO_2^-H	30	p.o.	HPbCD	30	37	
272	$CO_2^-Na^+$	10 30	p.o.	HPbCD	30	0 72	

Cpd	Form	Dose	Route	Vehicle	Pre-icilin min	% Inhibition	ED50, mg/kg
272	$CO_2^-Na^+$	3 10 30 100	p.o.	HPbCD	30	0 29 74 75	22
273	$CO_2^-Na^+$	30	p.o.	HPbCD	30	39	
273	$CO_2^-Na^+$	10 30 100	p.o.	HPbCD	30	17 25 71	53
283	$CO_2^-Na^+$	30	p.o.	HPbCD	30	65	
283	$CO_2^-Na^+$	3 10 30 100	p.o.	HPbCD	30	13 -19 13 43	
283	$CO_2^-Na^+$	30	p.o.	Water	30	71	
296	$CO_2^-Na^+$	30	p.o.	HPbCD	30	27	
306	$CO_2^-Na^+$	30	p.o.	HPbCD	60	99	
306	$CO_2^-Na^+$	3 10 30	p.o.	HPbCD	60	63 99 100	
306	$CO_2^-Na^+$	0.3 1 3 10	p.o.	HPbCD	60	39 9 64 98	2.5
306	$CO_2^-Na^+$	10	p.o.	HPbCD	60	99	
307	CO_2H	30	p.o.	HPbCD	30	13	
309	CO_2H	30	p.o.	HPbCD	30	23	
361	CO_2H	30	p.o.	HPbCD	30	87	

Cpd	Form	Dose	Route	Vehicle	Pre-icilin min	% Inhibition	ED50, mg/kg
361	$CO_2^-Na^+$	3 10 30	p.o.	Water	120	38 74 98	4.5
394	$CO_2^-Na^+$	30	p.o.	HPbCD	30	63	
395	$CO_2^-Na^+$	30	p.o.	HPbCD	30	100	
395	$CO_2^-Na^+$	1 3 10 30	p.o.	Water	60	15 26 55 88	7.6
396	$CO_2^-Na^+$	30	p.o.	HPbCD	30	99	
398	$CO_2^-Na^+$	30	p.o.	HPbCD	30	7	
400	$CO_2^-Na^+$	30	p.o.	HPbCD	30	84	
409	$CO_2^-Na^+$	30	p.o.	HPbCD	30	16	
427	$CO_2^-Na^+$	30	p.o.	Water	30	82	
429	1*H*, Na tetrazole	30	p.o.	HPbCD	30	41	
429	1*H*, Na tetrazole	30	p.o.	HPbCD	60	36	
435	$CO_2^-Na^+$	30	p.o.	Water	30	41	
479	$CO_2^-Na^+$	30	p.o.	HPbCD	60	77	
480	$CO_2^-Na^+$	30	p.o.	HPbCD	60	39	
483	1*H*, Na oxadiazole	30	p.o.	Water w/NaOH	30	19	
486	$CO_2^-Na^+$	10	p.o.	HPbCD	60	18	
487	$CO_2^-Na^+$	30	p.o.	HPbCD	60	99	
488	$CO_2^-Na^+$	10	p.o.	HPbCD	60	73	
489	$CO_2^-Na^+$	30	p.o.	Water	60	99	

Cpd	Form	Dose	Route	Vehicle	Pre-icilin min	% Inhibition	ED50, mg/kg
490	$CO_2^-Na^+$	10	p.o.	HPbCD	60	84	
496	$CO_2^-Na^+$	30	p.o.	Water	60	99	
496	$CO_2^-Na^+$	1 3 10 17.8	p.o.	HPbCD	120	74 100 99 100	
496	$CO_2^-Na^+$	0.1 0.3 1 3	p.o.	HPbCD	120	43 34 79 98	2.5
497	$CO_2^-Na^+$	30	p.o.	Water	60	96	
502	$CO_2^-Na^+$	10	p.o.	HPbCD	60	14	
505	$CO_2^-Na^+$	30	p.o.	HPbCD	60	72	
519	$CO_2^-Na^+$	10	p.o.	HPbCD	60	-6	
524	$CO_2^-Na^+$	10	p.o.	HPbCD	60	82	
537	$CO_2^-Na^+$	30	p.o.	HPbCD	60	42	
567	$CO_2^-Na^+$	10	p.o.	HPbCD	60	55	
623	$C(O)NNaSO_2CH_3$	10	p.o.	HPbCD	60	38	
627	1*H*, Na oxadiazole	30	p.o.	HPbCD	60	0	
635	1*H*, Na tetrazole	3 10 30 56	p.o.	HPbCD	60	31 -8 53 72	
640	1*H*, Na oxo-thiadiazole	30	p.o.	HPbCD	60	20	
657	$CO_2^-Na^+$	10	p.o.	HPbCD	60	32	

Cpd	Form	Dose	Route	Vehicle	Pre-icilin min	% Inhibition	ED50, mg/kg
658	$CO_2^-Na^+$	10	p.o.	HPbCD	60	63	
755	$CO_2^-Na^+$	10	p.o.	HPbCD	60	99	
756	$CO_2^-Na^+$	10	p.o.	HPbCD	60	100	
784	1*H*, Na oxo-thiadiazole	30	p.o.	HPbCD	60	79	

Example 3b

Reversal of icilin-induced behaviors in rats

Male Sprague Dawley rats (225–450 g, Charles River Labs, n=4-6/ treatment) were used to evaluate the ability of selected compounds of the formula (I) to reverse icilin-induced "wet-dog" shakes. Icilin was administered in PEG-400 or 10% solutol/H_2O, at 1.0 or 3.0 mg/kg, i.p. and spontaneous "wet-dog" shakes (WDS) were counted 10-20 minutes post-icilin. Animals that exhibited 10 or more shakes were randomized into treatment groups and immediately administered compounds of the formula (I) in an appropriate vehicle, such as hydroxypropyl-β- cyclodextrin (HP β CD), methocellulose, 10% Solutol, or H_2O, or the like, and by the appropriate route, such as i.p. or p.o. Spontaneous "wet-dog" shakes were counted 60-70 minutes after compound administration. Results are presented as a percent inhibition of shakes, which was calculated as [1-(test compound WDS count/ vehicle WDS count)] x 100. Results are shown in Table 6.

Table 6

Cpd No.	Dose (mg/kg)	Route	Post-icilin	% Inhibition
2	30	p.o.	1 h	18
7	30	p.o.	1 h	65
13	30	p.o.	1 h	28
14	30	p.o.	1 h	-16
15	30	p.o.	1 h	-18
125	30	p.o.	1 h	39
148	30	p.o.	1 h	33
149	30	p.o.	1 h	-3
168	30	p.o.	1 h	-29
174	30	p.o.	1 h	45
177	30	p.o.	1 h	66
	3	p.o.	1 h	15
	10	p.o.	1 h	53
	16.6	p.o.	1 h	54
	30	p.o.	1 h	52
	100	p.o.	1 h	52
188	30	p.o.	1 h	7

Example 3c

Rightward Shift of Icilin Dose Effect Curve in Rats

Male Sprague Dawley rats (200–400 g, Charles River Labs, n=6-9/ treatment) were administered icilin in a suitable vehicle (e.g. PEG-400, 10% Solutol) at 0.1 – 30

mg/kg, i.p. Spontaneous "wet-dog" shakes were counted 10-20 minutes post-icilin in order to generate a icilin dose-effect curve. A compound of the present invention was administered orally in hydroxypropyl-β-cyclodextrin 60 minutes before icilin challenge to assess the compound's ability to inhibit spontaneous "wet-dog" shakes (WDS) produced by a range of icilin doses. The ED_{50} of the icilin dose-effect curve generated in the presence of TRPM8 antagonist may be compared to that generated in the presence of vehicle to determine the magnitude of rightward shift as shown below in Table 7.

Table 7

Cpd	Dose (mg/kg)	Route	Pre-icilin	Icilin ED50, mg/kg, i.p., no pretreatment	Icilin ED50, mg/kg, i.p., compound pretreatment
306	3	p.o.	60	0.75	2.96

Example 4

In vivo model of subacute inflammatory pain: carrageenan-induced hyperalgesia

Intraplantar injection of carrageenan into the hind paw of rats causes a robust acute inflammatory response characterized by reddening, swelling and hypersensitivity of the paw to thermal and mechanical stimuli typically peaking 3-6 hours following application and subsiding over the 12-24 hours.

Example 4a

Rat Carrageenan-induced Radiant Heat Hypersensitivity

To assess the effect of test compounds of the formula (I) on inflammatory hyperalgesia radiant heat response latencies were evaluated 3 hours following intraplantar carrageenan (Lambda, Type IV, 200 uL) injection into a single hind paw in male Sprague-Dawley rats. The test compound was administered either 2 hours prior to or 1 hour following carrageenan injection.. The intent was to determine whether the compound would prevent or retard the hypersensitivity associated with this inflammogen. Baseline thermal response latencies were determined prior to any treatment and again 3 hours after carrageenan injection. Percent reversal of

hyperalgesia relative to vehicle treatment (%R) was calculated for both compound treatment paradigms according to the following formula and is depicted in Table 8:

%R = (Post compound latency – Post vehicle latency)/ ((Baseline latency – Post vehicle latency) x 100%

Table 8

Cpd No.	Salt Form	Dose	Route	Vehicle	Treatment Time, hours relative to Cg	Percent Reversal, relative to vehicle
306	$CO_2^-Na^+$	30	p.o.	HPbCD	-2 1	64 100
496	$CO_2^-Na^+$	30	p.o.	HPbCD	-2 1	74 106

Example 5

In vivo model for of chronic inflammatory pain: complete Freund's adjuvant (CFA)-induced hyperalgesia

Intraplantar injection of complete Freund's adjuvant (CFA) in rodents results in a long-lasting inflammatory reaction, characterized by a pronounced hypersensitivity to both thermal and mechanical stimuli. This hypersensitivity peaks between 24-72 hours following injection and can last for several weeks. To assess whether test compounds of the formula (I) reverse established hypersensitivity, a 100 μL intraplantar injection of CFA (suspended in a 1:1 emulsion of saline and heat-killed *Mycobacterium tuberculosis* in mineral oil) can be injected into a single hind paw of Sprague-Dawley rats (typically males ranging from 150-350 g). This paradigm also may be conducted with a multiple dosing or a prophylactic dosing regime designed to alter the course of hyperalgesia development. This test predicts the analgesic, anti-allodynic and antihyperalgesic effect of numerous effective clinical agents, including acetaminophen, NSAIDS such as aspirin and ibuprofen, and opioids, such as morphine.

Example 5a

CFA-induced paw radiant heat hypersensitivity

Each rat is placed in a test chamber on a warm glass surface and allowed to acclimate for approximately 10 minutes. A radiant thermal stimulus (beam of light) is then focused through the glass onto the plantar surface of each hind paw in turn. The thermal stimulus is automatically shut off by a photoelectric relay when the paw is moved or when the cut-off time is reached (20 seconds for radiant heat at ~5 Amps). An initial (baseline) response latency to the thermal stimulus is recorded for each animal prior to the injection of CFA. Twenty-four hours following intraplantar CFA injection, the response latency of the animal to the thermal stimulus is then re-evaluated and compared to the animal's baseline response time. Only rats that exhibit at least a 25% reduction in response latency (i.e. hyperalgesia) are included in further analysis. Immediately following the post-CFA latency assessment, test compound or vehicle (usually Solutol, hydroxypropyl methylcellulose, hydroxypropyl beta-cyclodextrin or PEG-400) is administered i.p. or p.o. to rats. Post-compound treatment withdrawal latencies are assessed at fixed time intervals, typically 30, 60 and 120 minutes. The percent reversal (%R) of hypersenstivitiy is calculated according to the following formula:

% Reversal =

(Treatment Response-CFA Response)/(Baseline Response-CFA Response) x 100.

Table 9

Cpd No.	Salt Form	High Dose	Route	Vehicle	Treatment Time, min	Percent Reversal	ED50
306	$CO_2^-Na^+$	10	p.o.	HPbCD	100	91	
306	$CO_2^-Na^+$	3 5.6 10 30	p.o.	HPbCD	100	31 76 93 59	4
361	$CO_2^-Na^+$	10	p.o.	HPbCD	100	28	
496	$CO_2^-Na^+$	10	p.o.	HPbCD	60	79	

Cpd No.	Salt Form	High Dose	Route	Vehicle	Treatment Time, min	Percent Reversal	ED50
496	$CO_2^-Na^+$	1 3 5.6 10 30	p.o.	HPbCD	60	9 -10 10 24 30	
496	$CO_2^-Na^+$	10	p.o.	HPbCD	60	52	

Example 5b

CFA-induced paw cold hypersensitivity

Prior to intraplantar CFA injection, mice or rats are placed individually in elevated observation chambers having wire mesh floors. Through the mesh floor a series of three applications of acetone (0.04 –0.10 mL/application) is sprayed onto the bottom of the paw using a multidose syringe device. A positive response takes the form of an abrupt withdrawal and licking of the paw. The cumulative duration of licking is recorded for each of the three trials which are then averaged to give the individual's response. Twenty-four hours following CFA injection acetone licking durations are markedly elevated implying a hypersensitivity to cooling. Test compounds of the formula (I) can be assessed for its ability to return acetone-evoked paw licking durations to pre-CFA levels (typically near zero) following systemic administration. Percent inhibition is calculated as follows

%Inhibition = [1-(treatment licking duration / vehicle licking duration)] x 100.

Example 6

Chemically-induced abdominal irritant models of visceral pain

A chemical irritant (such as acetic acid, kaolin, bradykinin, phenyl-p-(benzo) quinine, bromo-acetylcholine, or zymosan) is injected in mice intraperitoneally, causing a contraction of the abdominal musculature, which is characterized by an elongation of the body extending through to the hind limbs. The number of such responses is quantitated and is reduced by pretreatment of analgesic agents, thus forming the basis

for a screening test (Collier HO et al. Br J Pharmacol Chemother **1968**, 32(2): 295-310). This type of abdominal irritant test has been used to predict the analgesic effect of numerous clinically effective agents, the potency of which in the abdominal irritant test parallels the magnitude of the dose needed in the relief of clinical pain. Such agents include acetaminophen, NSAIDS such as aspirin and ibuprofen, opioids, such as morphine and codeine, and other centrally acting analgesics, such as tramadol.

One modification of the chemically-induced abdmonial irritant model of visceral pain is to pretreat animals with agents known to induce inflammatory responses following intraperitoneal injection (such as LPS, zymosan, or thioglycolate). A small intraperitoneal dose of such an inflammogen, administered hours or days before the acute chemical irritant challenge, has been shown to increase the number of abdominal contractions observed (Ribeiro RA, et al. Eur J Pharmacol **2000**, 387(1): 111-8). While some analgesic agents are effective at mitigating acute viscerochemical nociception, others, particularly those dependent upon receptor induction are more effective at preventing or reversing the enhancement of behavioral responses caused by a preconditioning inflammatory stimulus. Because of the up-regulation of the TRPM8 receptor in inflammation, TRPM8 antagonists that are effective at reducing the mean number of contractions are predicted to provide analgesic action in human clinical use.

The ability of compounds of the formula (I) to mitigate chemical irritant – induced abdominal contractions following a pre-conditioning inflammatory stimulus can be studied as follows. Thioglycolate (3 %, w/v, 2-3mL *i.p.*) is injected into male CD1 mice (20-40 g, Charles River Labs), at a maximum dosage volume of 80 mL/ kg, to induce peritoneal inflammation. Following a twenty-four hour pre-inflammation period these mice are dosed orally with compounds of the formula (I) (30 mg/kg; n=10) or vehicle (HPMC with 2% Tween80; n=9) and then one hour later subjected to an abdominal irritant challenge of acetic acid (1%, 10 mL/ kg, i.p.). Immediately following injection of acetic acid, mice are placed individually in glass bell jars (approximately 15 cm in diameter) for counting of abdominal contractions over the next 15 minutes. The total number of abdominal contractions is summed for each treatment group and employed in the following formula to calculate Percent Inhibition (%I):

$$\%I = [1-(\text{test compound contractions} / \text{vehicle contractions})] \times 100.$$

Example 7

In vivo models of neuropathic pain

The sciatic nerve is the major sensorimotor innervation of the (hind) leg and foot. Injury to the sciatic nerve or its constituent spinal nerves often results in pain-related behaviors. In rats and mice, tight ligation of the L5 spinal nerve with silk suture, partial tight ligation of the sciatic nerve with silk suture or loose ligation of the sciatic nerve with chromic gut suture each result in behaviors reminiscent of neuropathic pain in humans. These lesions (one per animal) are performed surgically in anesthetized rodents. Both the spinal nerve and sciatic nerve lesions result in allodynia, a painful response to normally innocuous stimuli, and hyperalgesia, an exaggerated response to normally noxious stimuli. It is important to note that both of these pain-related behaviors are evoked by the testing procedures and that normal use of the paw (e.g., walking) is relatively uncompromised, apart from occasional "guarding" of the paw. Subsequent to the surgery, the subjects' behaviors, such as grooming, feeding, and weight gain, are normal, except for hypersensitivity (as defined above) of the affected paw.

In addition to induction by nerve damage resulting from accidental trauma or surgical procedures, neuropathic pain can also be induced by diabetes (Fox, A et al., *Pain* 81:307-316, 1999) or by treatment with chemotherapeutic agents, such as paclitaxel or vincristine (Yaksh, TL et al., *Pain* 93:69-76, 2001).

Agents that attenuate neuropathic pain in the clinic also are effective in rodent neuropathic pain models. These agents include the recently approved Cymbalta (Duloxetine, Iyengar, S., et al., *JPET* **2004** 311:576-584), morphine (Suzuki, R et al., *Pain* **1999** 80:215-228) and gabapentin (Hunter, JC et al., *Eur J Pharmacol* **1997** 324:153-160). The dual TRPV1/TRPM8 receptor antagonist BCTC reduced mechanical hyperalgesia and tactile allodynia in the chronic constriction injury rodent neuropathic pain model (Pomonis, JD et al., *JPET* **2003** 306:387-393; Behrendt, H et al., *Brit J Pharm* **2004** 141:737). Cold allodynia is a particularly debilitating symptom of neuropathic pain conditions (Jorum E et al. *Pain* **2003** 101: 229-235). The antiallodynic effect of compounds of the formula (I) in this rodent model is predictive of clinical effect for these novel agents.

Example 7a

Chronic constriction injury (CCI)-induced model of neuropathic pain – acetone-induced hypersensitivity

Male Sprague Dawley rats (225-450 g; n=5-8/ treatment) were used to evaluate the ability of selected compounds of the formula (I) to reverse CCI-induced cold hypersensitivity. Four loose ligatures of 4-0 chromic gut were surgically placed around the left sciatic nerve under inhalation anesthesia as described by Bennett et al (Bennett GJ, Xie YK. *Pain* **1988**, 33(1): 87-107). Fourteen to 35 days following CCI surgery, subjects were placed in elevated observation chambers containing wire mesh floors and five applications of acetone (0.05 mL/application separated by approximately 5 minutes) were spritzed onto the plantar surface of the paw using a multidose syringe. An abrupt withdrawal or lifting of the paw was considered a positive response. The number of positive responses was recorded for each rat over the five trials. Following baseline withdrawal determinations, compounds of formula (I) are administered in an appropriate vehicle, such as hydroxypropyl-β- cyclodextrin (HP β CD), methylcellulose, Methocel, 10% Solutol, or H_2O, or the like, by the appropriate route, i.p. or p.o. The number of withdrawals were redetermined 1 to 3 h after compound administration. Results are presented as a percent inhibition of shakes, which was calculated for each subject as [1-(test compound withdrawals / pre-test withdrawals)] x 100 and then averaged by treatment. Results are shown in Table 10.

Table 10

Cpd No.	Salt Form	Dose, mg/kg	Route of Administration	Vehicle	Pretreatment Time, hr	Percent Inhibition	ED50, mg/kg
7	CO_2H	30	p.o.	10% Solutol	1	47	
		30	i.p.	10% Solutol	2	66	
177	CO_2H	3 10 30 100	p.o.	10% Solutol	1	23 49 46 70	

Cpd No.	Salt Form	Dose, mg/kg	Route of Administration	Vehicle	Pretreatment Time, hr	Percent Inhibition	ED50, mg/kg
		30	i.p.	10% Solutol	3	60	
292	CO_2^- Na^+	30	p.o.	Water	2	60	
292	CO_2^- Na^+	3 10 30 100	p.o.	Water	3	7 16 21 67	70
272	CO_2^- Na^+	30	p.o.	HPbCD	1	31	
273	CO_2^- Na^+	30	p.o.	HPbCD	0.5	49	
271	CO_2^- Na^+	30	p.o.	HPbCD	1	77	
271	CO_2^- Na^+	10 30 100	p.o.	HPbCD	1	24 44 56	
306	CO_2^- Na^+	30	p.o.	HPbCD	6	69	
306	CO_2^- Na^+	3 10 17.8 30 56 100	p.o.	HPbCD, Water	4	20 38 57 68 77 77	15
361	CO_2^- Na^+	30	p.o.	Water	4	74	
361	CO_2^- Na^+	3 10 30	p.o.	Water	2	9 17 91	13

Cpd No.	Salt Form	Dose, mg/kg	Route of Administration	Vehicle	Pretreatment Time, hr	Percent Inhibition	ED50, mg/kg
395	$CO_2^- Na^+$	30	p.o.	Water	2	23	
395	$CO_2^- Na^+$	30	p.o.	Water	2	38	
396	$CO_2^- Na^+$	30	p.o.	Water	4	50	
400	$CO_2^- Na^+$	30	p.o.	Water	1	40	
400	$CO_2^- Na^+$	30	p.o.	Water	3	25	
487	$CO_2^- Na^+$	30	p.o.	HPbCD	3	66	
487	$CO_2^- Na^+$	10	p.o.	HPbCD	3	43	
488	$CO_2^- Na^+$	30	p.o.	HPbCD	2	43	
489	$CO_2^- Na^+$	30	p.o.	Water	3	86	
489	$CO_2^- Na^+$	10 17.8 30 56	p.o.	Water	4	13 60 57 70	23
490	$CO_2^- Na^+$	30	p.o.	HPbCD	1	23	
496	$CO_2^- Na^+$	30	p.o.	Water	2	74	
496	$CO_2^- Na^+$	10 17.8 30 56	p.o.	Water	4	76 64 72 68	

Cpd No.	Salt Form	Dose, mg/kg	Route of Administration	Vehicle	Pretreatment Time, hr	Percent Inhibition	ED50, mg/kg
496	CO_2^- Na^+	0.3 1 3 5.6 10	p.o.	HPbCD	4	28 32 23 72 71	3.5
497	CO_2^- Na^+	30	p.o.	Water	4	60	
505	CO_2^- Na^+	30	p.o.	HPbCD	1	11	
524	CO_2^- Na^+	30	p.o.	HPbCD	3	46	

Example 7b

Chronic constriction injury (CCI)-induced model of neuropathic pain – cold plate-induced hypersensitivity

In male SD rats (175- 325g), four loose ligatures of 4-0 chromic gut are surgically placed around the left sciatic nerve under inhalation anesthesia as described by Bennet et al (Bennett GJ, Xie YK. *Pain* 1988, 33(1): 87-107). Seven to 21 days following sciatic chronic constriction injury (CCI) surgery, the subjects can be placed onto a commercial cold plate device cooled by peltier elements such that the surface temperature is held at 1°C. Each subject can undergo a 6 minute conditioning period followed by a 3 minute assessment period during which the total duration of hind paw lifting is recorded. This procedure is repeated at several intervals prior to and following systemic drug administration. Compounds of the formula (I) can be assessed for their ability to return duration of paw lifting back to pre-lesion levels. The duration of paw lifting during the 3 minute test period following administration of test compound is taken as a percentage of the duration of paw lifting during the 3 minute test period prior to test compound treatment.

Example 7c

Chronic constriction injury (CCI)-induced model of neuropathic pain – Mechanical Allodynia (von Frey Test)

In male SD rats (175- 325g), four loose ligatures of 4-0 chromic gut are surgically placed around the left sciatic nerve under inhalation anesthesia as described by Bennet et al (Bennett GJ, Xie YK. *Pain* 1988, 33(1): 87-107). Seven to 21 days following sciatic chronic constriction injury (CCI) surgery, the subjects can be placed onto an elevated rack of plexigas chambers having wire mesh or another type of perforated flooring. The measurement of mechanical allodynia can be performed using the von Frey hairs (Semmes-Weinstein Monofilaments, Stoelting Co., IL) wherein the rats can be habituated to the wire mesh bottom cages before the start of the experiment. Static allodynia can be tested in the unrestrained rats by touching the plantar surface of the hind paw with von Frey hairs in ascending order of force (1.2, 1.5, 2.0, 3.6, 5.5, 8.5, 12,

15, 29, and 76 g) for up to 6 s or until a paw withdrawal response can be elicited. The lowest amount of force required to elicit a response can be recorded as the withdrawal threshold in log g. This procedure is repeated at several intervals prior to and following systemic drug administration. Compounds of the formula (I) can be assessed for their ability to return the threshold force which elicits paw lifting back to pre-lesion levels.

Example 8

Inflammatory agent-induced models of pyresis / antipyresis

Compounds of the formula (I) can be tested in animal models of pyresis, according to previously documented and validated methods, such as those described by Kozak et al (Kozak W, Fraifeld V. *Front Biosci* 2004, 9: 3339-55). Fever is a frequent accompaniment of inflammatory disease. Animal models make use of the pyretic properties of yeast and other inflammatory agents, injecting a yeast suspension or other agent subcutaneously (Tomazetti J et al. *J Neurosci Methods* 2005, 147(1): 29-35); Van Miert AS, Van Duin CT. *Eur J Pharmacol* 1977, 44(3): 197-204). For example, Male Wistar rats (75–100 g) can be housed in groups of four to a cage at controlled temperature (23 ± 1 ˚C) with a 12 h light:12 h dark cycle (lights on at 07:00 h) and with standard lab chow and tap water ad libitum. All measured temperatures can be taken between 08:00 and 19:00 h. Each animal can be used in only one study. Rectal temperature (TR) can be measured by inserting a lubricated thermistor probe (external diameter: 3 mm) 2.8 cm into the rectum of the animal. The probe can be linked to a digital device, which displayed the temperature at the tip of the probe with a 0.1˚C precision and logs the values over time. Immediately after measuring the initial basal rectal temperature, the animals can be injected with commercially available dried baker yeast (Saccharomyces cerevisiae) suspended in pyrogen-free 0.9% NaCl (0.05–0.25 g/kg, i.p.) or 0.9% NaCl (10 ml/kg). TR changes can be recorded every hour up to 12 h, and expressed as the difference from the basal value. Since it has been previously reported that handling and temperature measuring-related stress alter rectal temperature, these animals can be habituated to the injection and measuring procedure for 2 days before experiments are carried out. In these sessions, the animals can be

subjected to the same temperature measuring procedure described above, and can be injected intraperitoneally (i.p.) with 0.9% NaCl (10 ml/kg).

To assess the effect of potential antipyretic compounds on basal rectal temperature study animals can have their TR measured for 4 h, and after the fourth TR measurement they can be subcutaneously (s.c.) injected with vehicle (such as 10% Solutol in sterile water 5 ml/kg) or compounds of the formula (I) prepared in vehicle. TR can then be recorded every hour up to 8 h after the compound injections. To assess the effect of compounds of the formula (I) on baker yeast-induced hyperthermia, study animals can have their basal TR measured and then be injected with a pyrogenic dose of baker yeast (for example, 0.135 g/kg). TR changes can be recorded every hour up to 4 h, when potential antipyretics agents such as those compounds of the formula (I) are administered. Rectal temperature can then be monitored over the following 8 h. Basal rectal temperature and changes in rectal temperature can be expressed as means ± S.E.M. of the differences from TR at 07:00 h. Data can be analyzed by two-way analysis of variance (ANOVA), with time of measures treated as within subject factor, depending on the experimental design. Post hoc analysis can be carried out by the F-test for simple effect and the Student–Newman–Keuls test, when appropriate. A value of $P < 0.05$ would be considered statistically significant.

The modification of the subsequent pyretic response by therapeutic agents can also be monitored by rectal telemetry or other measurements of body temperature. Several clinically relevant agents such as acetaminophen, aspirin and ibuprofen, reduce fever in these models. The antipyretic effect of TRPM8 antagonists, such as compounds of the formula (I), in these tests would also be predictive of their clinical effect.

Example 9

CFA-induced model of rheumatoid arthritis

Compounds of the formula (I) can be tested in animal models of rheumatoid arthritis, according to previously documented and validated methods, such as those described by Nagakura et al (Nagakura Y, et al. *J Pharmacol Exp Ther* 2003, 306(2): 490-7). For example, arthritis can be induced by the CFA inoculation in the rats (Male

Lewis rats150–225 g; Charles River). Briefly, 100 mg of Mycobacterium butyricum (Difco, Detroit, MI) can be thoroughly mixed with 20 mL of paraffin oil. Then mixture can be autoclaved for 20 min at 120°C. Each rat can be injected in the right footpad (hind paw) with the mixture in a 0.1-mL volume under inhalation anesthesia. The rats serving as controls can be injected with 0.1 mL of saline. Pain and other disease development parameters can be measured in the CFA- or saline-treated rats just before inoculation and up to 28 days post-inoculation. The measurement for pain parameters can be conducted for both mechanical and thermal (hot or cold) endpoints. The measurement of mechanical allodynia can be performed using the von Frey hairs (Semmes-Weinstein Monofilaments, Stoelting Co., IL) wherein the rats can be habituated to wire mesh bottom cages before the start of the experiment. Static allodynia can be tested in the unrestrained rats by touching the plantar surface of the hind paw with von Frey hairs in ascending order of force (1.2, 1.5, 2.0, 3.6, 5.5, 8.5, 12, 15, 29, and 76 g) for up to 6 s or until a paw withdrawal response can be elicited. The lowest amount of force required to elicit a response can be recorded as the withdrawal threshold in log g. Thermal hyperalgesia can be assessed using the radiant heat test wherein a mobile radiant heat source can be located under a glass surface upon which the rat is placed. The beam of light can be focused on the hind paw, and the paw withdrawal latencies are defined as the time taken by the rat to remove its hind paw from the heat source. The measurement of joint hyperalgesia can be performed by a modification of the previously reported method (Rupniak NMJ et al. *Pain* 1997, 71: 89–97). The torso of each rat can be held from the back with the left palm, and the bending and extension (one after the other and five times in each direction) of the ankle within its limits of range of motion can be performed with the right fingers. The total number of vocalizations emitted after the manipulation (the bending and extension, five times in each direction) can be recorded for each paw (the maximum score is 10 for each paw).

The scoring of mobility can be performed by modifying the evaluation scale reported by Butler et al. (Butler SH et al *Pain* 1992, 48: 73–81): score 6, walks normally; score 5, walks being protective toward the ipsilateral hind paw (touches the ipsilateral hind paw fully on the floor); score 4, walks being protective toward the ipsilateral hind paw (touches only the toe of the ipsilateral hind paw on the floor); score 3, walks being protective toward both hind paws (touches the contralateral hind paw

fully on the floor); score 2, walks being protective toward both hind paws (touches only the toe of the contralateral hind paw on the floor); score 1, crawls only using the fore paws; and score 0, does not move. Paw volumes can be measured by volume displacement of electrolyte solution in a commercially available plethysmometer device. The hind paw can be immersed to the junction of the hairy skin, and the volumes can be read on a digital display. The scoring of joint stiffness can be performed as follows: the body of rats can be held from the back with the left palm, and the bending and extension (once in each direction) of the ankle within its limits of range of motion can be performed with the right fingers. It can be confirmed beforehand that there is no restriction of ankle joint movement in the bending and extension manipulations in naive rats, and the scoring can be performed according to the evaluation scale reported by Butler (Butler SH et al *Pain* 1992, 48: 73–81): score 2, there are restrictions of full range of movement of the ankle in both bending and extension; score 1, there is a restriction of full range of movement of the ankle in bending or extension; and score 0, no restriction. The measurements for paw volume and joint stiffness can be conducted for both hind paws.

Compounds of the formula (I) can be assessed for antihyperalgesic efficacy as follows: thirty-two rats (8 rats per dose and four doses per compound) that are be treated with the CFA and another eight rats as naive controls can be used for each drug evaluation. The analgesic effects can be evaluated on post-inoculation day 9, when mechanical allodynia, thermal hyperalgesia, joint hyperalgesia, and joint stiffness in the ipsilateral paw reached almost the maximum, although those parameters in the contralateral paw changed only slightly and the systemic disturbance shown by the change of mobility score is small. On the day before evaluation, body weight, mechanical allodynia, thermal hyperalgesia, and joint hyperalgesia can be measured for the 32 rats that are to be used for compound evaluation. The rats are allocated to four groups (eight rats per group) such that the differences in the averages of those parameters among the groups became small. All the analgesic effect evaluations and behavioral observations can be carried out by the observer who is blind to the drug treatment.

Data can be expressed as the mean +/- S.E.M. The time-course curves for mechanical allodynia, thermal hyperalgesia, joint hyperalgesia, body weight, and paw

volume can be subjected to two-way repeated measures analysis of variance with post hoc t test. In experiments for evaluation of compounds of formula (I), the difference in scores between the vehicle-treated and naive control groups can be analyzed by Student's t test to confirm significant changes in the pain parameters in the ipsilateral paw. The analgesic effects can be analyzed by Dunnett's t test, and in each case the drug-treated groups can be compared with the vehicle-treated group. In each statistical analysis, the comparison can be conducted for paws on the corresponding side. $P < 0.05$ is considered statistically significant. In this model, the centrally acting analgesics morphine and tramadol fully relieved pain, whereas the NSAIDs, indomethacin and diclofenac are partially effective, evidencing the model's clinical predictability. The analgesic effect of compounds of the formula (I) in this test would predict their clinical usefulness in treating arthritis.

Example 10

In vivo model for arthritis: inflammogen- induced hyperalgesia of the knee joint

Compounds of the formula (I) can be tested in animal models of osteoarthritis, according to previously documented and validated methods, such as those described by Sluka et al (Sluka KA, Westlund KN. *Pain* 1993, 55(3): 367-77). For example, male Sprague-Dawley rats (Harlan, Indianapolis, IN) weighing 225 to 350 g can be briefly anesthetized with vaporized halothane and then injected with a mixture of 3% carrageenan and 3% kaolin (100 µL in 0.9% sterile saline) into the joint cavity of one knee. After the injection, the animals can be returned to their cages until the time of testing. For behavioral testing animals can be placed in individual clear plastic cages on top of an elevated wire mesh surface that restricted movement. The animals should be allowed to acclimate for approximately 1 hour before testing. Von Frey filaments, as described above, can then be used to test for enhanced responses to mechanical stimuli. The filaments can be successively applied through the wire mesh perpendicularly to the plantar surface in between the pads of the third and fourth phalanges. The response threshold to mechanical stimuli can be determined before inflammation of the knee joint; 4 hours after inflammation to confirm the development of hyperalgesia; immediately after the administration of test compound such as those of Formula (I) i.e. 5 hours after inflammation; and at 8, 12, and 24 hours after inflammation.

The Kruskal-Wallis test, a nonparametric test, can be used to analyze the effects for frequency, intensity, and group for response to mechanical stimuli at baseline, 4 hours after inflammation, and after compound treatment (5 hours, 8 hours, 12 hours, and 24 hours after inflammation). Further post hoc testing between groups can be executed by using the Mann-Whitney signed rank test. The data can be presented as median with 25th and 75th percentiles. Significance is $P \leq .05$.

Additionally, the gait of the animal or other pain-related behavior can be scored as the dependent measure of the painful effect of the arthritis on the animal's activity (Hallas B, Lehman S, Bosak A, et al. *J Am Osteopath Assoc* 1997, 97(4): 207-14). The effect of test drug on the animal's normal behavior can be quantified from zero, meaning no response, to three for incapacitating impairment. Effective analgesic treatment includes the clinically used indomethacin (Motta AF, et al. *Life Sci* 2003, 73(15): 1995-2004). Thus the benefit of compounds of the formula (I) in this model would predict their clinical relevance.

Example 11

Sarcoma cell-induced models of bone cancer pain

Compounds of the formula (I) can be tested in animal models of bone cancer pain, according to previously documented and validated methods, such as those described in the scientific literature (El Mouedden M, Meert TF. *Pharmacol Biochem Behav* 2005, 82(1): 109-19; Ghilardi JR, et al. *J Neurosci* 2005, 25(12): 3126-31). In preparation for cell inoculation and tumor induction, osteolytic murine sarcoma cells (NCTC 2472, American Type Culture Collection (ATCC), Rockville, MD, USA) can be cultured in NCTC 135 medium (Invitrogen) containing 10% horse serum (Gibco) and passaged 2 times weekly according to ATCC guidelines. For their administration, cells can be detached by scraping and then centrifuged at 1000x g. The pellet can be suspended in fresh NCTC 135 medium ($2.5x10^6$ cells/20 µL) and then used for intramedullary femur inoculation. Male C3H/HeNCrl mice (25–30 g, Charles River Labs) can be used in such experiments. After induction of general anesthesia with xylazine (10 mg/kg i.p.) and ketamine (100 mg/kg i.p.) the left hind paw can be shaved and disinfected with povidone–iodine followed by 70% ethanol. A superficial incision of 1 cm can then be made over the knee overlaying the patella. The patellar ligament can then be cut, exposing the condyles of the distal femur. A 23-gauge needle can be

inserted at the level of the intercondylar notch and the intramedullary canal of the femur to create a cavity for injection of the cells. Twenty microliters of media (sham animals) or media containing tumor cells (approximately $2.5x10^6$ cells) can then be injected into the bone cavity using a syringe. To prevent leakage of cells outside the bone, the injection site can be sealed with dental acrylic and the wound closed with skin stitches.

Pain behaviors can be evaluated in separate groups (n =6) of sham and bone tumor mice with confirmed hyperalgesia as assessed by spontaneous lifting behavior. Animals can be behaviorally tested during a 3-week period prior to and after tumor inoculation. Body weight of the mice can be recorded throughout the experimental period to help monitor general health status. To measure the spontaneous lifting, the animals can be habituated in a transparent acrylic cylinder of 20 cm diameter put on an horizontal surface and thereafter observed during 4 min for spontaneous lifting behavior of the left hind paw. After spontaneous lifting behavior assessment, animals can be immediately placed on a mouse rotarod (e.g. ENV-575M\, Med Associates Inc., GA, USA) at a speed of 16 rpm for 2 min wherein limb-use during forced ambulation is scored: 4=normal; 3=limping; 2=partial non-use of left hind paw; 1=substantial non-use of left hind paw; 0=non-use of left hind paw. Assessment of cold allodynia may be made by exposing the ipsilateral hind paw of the mouse to 5 repeated applications of acetone (20 µL) and quantifying the lift/licking frequency and/or duration. Post-mortem evaluation of bone destruction can be assessed by ACT processing followed by scanning using a system such as the Skyscan 1076 microtomograph system for small animal imaging (Skyscan 1076\, Skyscan, Aartselaar, Belgium). Measured histomorphometry parameters of bone destruction can be subsequently correlated with behavioral endpoints.

The antihyperalgesic, antiallodynic and disease modifying effects of compounds of the formula (I) can be tested in this murine model of bone cancer pain in separate groups (n =6 per dose group). Animals with confirmed hyperalgesia, as assessed by spontaneous or acetone-evoked lifting, can be behaviorally tested, for example, on days 15 and 22 after distal femur tumor inoculation before and 1 h after systemic administration of vehicle (e.g. 20% HPbCD in sterile water) or compounds of the formula (I). The statistical analysis can be performed by one-way ANOVA to compare behavioral measurements and bone parameters among the experimental groups. To

compare behavioral measurements and bone parameters between sham and tumor-bearing animals, a Mann–Whitney U test can be used. Results are considered statistically significant at P <0.05 (two-tailed). Data are expressed as mean+/- S.E.M.

Bone cancer causes intense pain in humans, mimicked in animal models of bone cancer pain in rodents such as that described above. Analgesic treatments that are effective in this model include COX-2 inhibitors (Sabino MA, Ghilardi JR, Jongen JL, et al. *Cancer Res* 2002, 62(24): 7343-9) and high doses of morphine (Luger NM et al. *Pain* 2002, 99(3): 397-406), agents used clinically for pain relief in patients experiencing bone cancer pain. Because this model so closely mimics the human disease state, the finding that cold allodynia is a prominent symptom (Lee, Seong et al. *Yonsei Med J* 2005, 46(2): 252-9) strongly supports the concept that TRPM8 antagonists of the present invention will provide relief of pain associated with human bone cancer.

Example 12

Respiratory irritant-induced models of cough

Compounds of the formula (I) can be tested in animal models of antitussive activity, according to previously documented and validated methods, such as those described by: Tanaka, M. and Maruyama, K. *J Pharmacol. Sci* 2005, 99(1), 77-82; Trevisani, M. et al., *Throax* 2004, 59(9), 769-72; and Hall, E. et al., *J Med. Microbiol* 1999, 48: 95-98. Testing is conducted in transparent ventilated chambers with a constant airflow of 400 mL/min. The tussive agent (citric acid 0.25 M or capsaicin 30 mM) can be nebulised via a miniultrasonic nebuliser with an output of 0.4 mL/min. The appearance of cough can be detected by means of a tie clip microphone and confirmed by the characteristic posture of the animal. The cough sounds can be recorded and digitally stored. A blinded observer subsequently counts the number of elicited cough efforts. In some cases, animals can be sensitized by pre-exposure to certain agents such as ovalbumin. A test compound can be administered to at the peak of irritant-induced cough to evaluate the antitussive effects of the compound. In addition, prophylactic or multiple dosing regimes can be utilized to evaluate the test compound for modulation of the onset and duration of irritant-induced cough. Variations of these tests predict the antitussive effects of effective clinical agents, including NMDA antagonists such as dextrorphan and dextromethorphan, opioids such

as codeine, beta 2 agonists such as salbutamol and antimuscarinics such as ipratropium (Bolser, D.C. et al., *Eur J Pharmacol* 1995, 277(2-3), 159-64; Braga, P.C. *Drugs Exper Clin Res* 1994, 20,199-203). The antitussive action of menthol in both guinea pig and humans Eccles R. *Curr Allergy Asthma Rep* 2003, 3(3): 210-4; Laude EA, et al. *Pulm Pharmacol* 1994, 7(3): 179-84; Morice AH, et al. *Thorax* 1994, 49(10): 1024-6) is predictive of the clinical utility of compounds of the formula (I) as antitussive agents.

Example 13

Chemical irritant-induced models of itch, contact dermatitis, eczema and other manifestations of dermal allergy, hypersensitivity and/or inflammation

Compounds of the formula (I) can be tested in animal models of contact dermatitis or itch, according to previously documented and validated methods, such as those described in the scientific literature (Saint-Mezard P et al. *Eur J Dermatol* 2004, 14(5): 284-95; Thomsen J.S., et al. *J Exp Dermatol* 2002, 11(4): 370-5; Weisshaar E, et al. Arch Dermatol Res 1998, 290(6): 306-11; Wille JJ, et al. *Skin Pharmacol Appl Skin Physiol* 1999, 12(1-2): 18-27). Mice (or species such as guinea pig or rat) can be sensitized with 25 mL of 0.5% dinitrofluorobenzene solution (DNFB diluted 4:1 in acetone:olive oil immediately before application or other haptens, such as 12-myristate-13 acetate, picryl chloride, oxazolone, capsaicin, arachidonic acid, lactic acid, trans-retinoic acid or sodium lauryl sulfate) painted to the shaved dorsal skin or untreated (controls). Five days later, 10 mL of 0.2% DNFB a nonirritant dose) can be applied onto both sides of the right ear and the same amount of solvent alone onto the left ear. Ear thickness can be monitored daily using a caliper. Compounds of the formula (I) can be administered at the peak of inflammation to evaluate the anti-allergy activity of compounds. In addition, prophylactic or multiple dosing regimes can be utilized to evaluate the test compound for modulation of the onset and duration of anti-allergy activity. Variations of these tests can predict the anti-allergy and itch activity of effective clinical agents. The ability of these models to predict the therapeutic effect of compounds in human dermal conditions is supported by the cross-species ability of serotonin to induce itch (Weisshaar E, Gollnick H. Skin Therapy Lett 2000, 5(5): 1-2,5). Additionally, the contact sensitizing property of commercially important drugs and the ability of ion channel modulators to prevent and treat skin sensitization in these

models (Kydonieus A, et al., *Proceedings of the International Symposium on Controlled Release of Bioactive Materials* 24th:23-24, 1997) demonstrate the therapeutic utility of compounds of the formula (I) in dermal sensitization.

Example 14

Chemical irritant-induced models of rhinitis and other manifestations of nasal hypersensitivity and/or inflammation

Compounds of the formula (I) can be tested in animal models of rhinitis, according to previously documented and validated methods, such as those described in the scientific literature (Hirayama Y, et al. *Eur J Pharmacol* 2003, 467(1-3): 197-203; Magyar T, et al *Vaccine* 2002, 20(13-14): 1797-802; Tiniakov RL, et al. *J Appl Physiol* 2003, 94(5): 1821-8). Testing can be conducted in mouse, guinea pig, dog or human in response to intranasal challenge with one or more irritants such as cold air, capsaicin, bradykinin, histamine, pollens, dextran sulfate, 2,4-tolylene diisocyanate, Bordetella bronchiseptica, Pasteurella multodica or acetic acid. In some cases, animals can be sensitized by pre-exposure to certain agents including, but not limited to, ragweed or ovalbumin. Prior to or following irritant administration, the test subject can receive, respectively, the prophylactic or therapeutic administration one or more times of compounds of the formula (I), or vehicle control, by the enteral or parenteral route. Significant differences indicative of nasal rhinitis or sensitization for the test compound-treated subjects compared with vehicle-treated subjects can be taken as evidence of anti-rhinitis activity. Independent variables include dose, frequency and route of administration, time interval between prophylactic or therapeutic test compound administration and irritant challenge as well as sex and non-sex genotype of the test subject. The intimate role of neurogenic inflammation in these hypersensitivity states demonstrates that compounds of the formula (I) desensitize or block the sensitization underlying these disease states.

Example 15

Conflict-induced models of anxiety, panic disorder and other non-adaptive stressful or phobic responses

Compounds of the formula (I) can be tested in animal models of anxiety, panic disorders and other non-adaptive responses, according to previously documented and validated methods, such as those described by Cryan and Holmes (Cryan JF, Holmes A. *Nat Rev Drug Discov* 2005, 4(9): 775-90) or Braw et.al. (Y. Braw et al. *Behav Brain Res* 2006, 167: 261–269). Specifically, for studies in rats, the following apparati may be utilized: an open-field arena (62 cm×62 cm) enclosed by opaque walls (30 cm high) and plus-maze consists of two open arms, 50 cm×10 cm, and two enclosed arms, 50 cm×10 cm×40 cm with an open roof, arranged such that the two arms of each type are opposite each other. The maze is elevated to a height of 70 cm. The walls of the enclosed arms are made from black Plexiglas, while the floors from white Plexiglas. Videotape recordings can be analyzed using the 'Observer' system (Noldus Information Technology). A subject rat can be removed from its home cage, weighed and placed gently in the center of the open-field arena. The rat can be allowed to explore the open-field freely while its behavior is videotaped for 5 min. Afterwards, it can be transferred to the plus-maze and placed at the center, facing a closed arm. The rat's behavior can again be videotaped for 5 min, after which it can be returned to its home cage. The apparatus can cleaned using a 70% ethanol solution between rats.

Open-field and plus-maze measures can be grouped into two behavioral classes, namely 'anxiety-like behaviors' and 'activity'. Open-field behavioral measures may include 1) Anxiety measures: % time in center square, % number of entries to center square (from total squares entered), % time freezing, latency to first freezing (freezing is scored when the subject is in an immobile state for at least 3 seconds; and 2) Activity measures: Total squares entered, number of rearings (standing on two hind legs), latency for first rearing. Plus-maze measures may include 1) Anxiety: % time in open arms, % number of entries to open arms (from total entries), number of unprotected head dips, latency to enter open arm; and 2) Activity: Total entries to all arms. Anxiety-like behaviors and activity can be analyzed by one-way ANOVA's on each of the measures, for each the between-subject comparisons. Plus-maze analyses can be conducted in a similar fashion.

Testing may also be conducted in mouse or rat in this fashion in order to measure avoidance of other aversive environmental stimuli such as Geller or Vogel anticonflict tests, the light/dark test and the hole-board test (see Cryan JF, Holmes A. *Nat Rev Drug Discov* 2005, 4(9): 775-90). Prior to environmental exposure, the test subject can receive the prophylactic administration one or more times of compounds of the formula (I), or vehicle control (e.g. 10% Solutol in sterile water), by the enteral or parenteral route. The cumulative time or number of times spent engaged in the aversive behavior can be measured. Significant differences in one or more of these measures for the test compound-treated subjects compared with vehicle-treated subjects can be taken as evidence of anxiolytic activity. Because these models are pharmacologically validated by the effectiveness of clinically useful anxiolytics (Cryan JF, Holmes A. *Nat Rev Drug Discov* 2005, 4(9): 775-90), they will be useful for the detection of anxiolytic compounds of the formula (I).

Example 16

Bladder pressure- and hypertrophy-induced models of urinary incontinence

Compounds of the formula (I) can be tested in animal models of urinary incontinence according to previously documented and validated methods, such as those described by in the scientific literature (Kaiser S, Plath T, (Metagen Pharmaceuticals GmbH, Germany DE Patent 10215321; McMurray G, et al. *Br J Pharmacol* 2006, 147 Suppl 2: S62-79). TRPM8 is expressed in human prostate, testicle, seminiferous tubules, scrotal skin and inflamed bladder (Stein RJ, et al. *J Urol* 2004, 172(3): 1175-8; Stein RJ, et al. *J Urol* 2004, 172(3): 1175-8; Mukerji et al. *BMC Urology* 2006, 6:6). Excitation of TRPM8 receptors through cooling or application of menthol causes contraction in the bladder and a decrease in micturation threshold volume (Tsukimi Y, Mizuyachi K, et al. *Urology* 2005, 65(2): 406-10). To assess compounds of the formula (I) for potential urinary incontinence activity, Sprague-Dawley rats are surgically implanted with bladder catheters allowing for the delivery of fluid (typically saline) and the monitoring of pressure (using a pressure transducer). Cystometry recordings can be monitored with a polygraph to evaluate voiding interval, threshold pressure, bladder capacity, bladder compliance, and the number of spontaneous bladder contractions. For example, the bladder catheter can be connected to a Harvard infusion

pump, and bladders perfused overnight with saline at 2 mL/h. The next morning the bladder catheter can be attached (using a "T" connector) to a Statham pressure transducer (Model P23Db) and to a Harvard infusion pump. A plastic beaker attached to a force displacement transducer (Grass FTO3) can be placed under the rat's cage to collect and record urine volume. The cystometric evaluation of bladder function can be started by infusing saline (20 mL/h) and after the first micturition the infusion is maintained for 20 min. Two hours after the first cystometry period, the rats can be dosed orally with compounds of the formula (I) and a second cystometry is performed between 30 min and 4 h after administration of test compound. The appropriate vehicle (e.g. 10% Solutol in sterile water) can be similarly administered to groups of rats that served as controls and the cystometry can be performed at the same respective time points.

Compounds of the formula (I) can also be evaluated under conditions of bladder hypertrophy and instability. Under anesthesia, a silk ligature is tied around the proximal urethra of rodents producing a partial outlet obstruction and subsequent hypertrophied bladder development within 6-9 weeks (Woods M. et al., *J Urology* 2001, 166:1142-47). Cystometry recordings can then be evaluated as described above. Such preclinical procedures are sensitive to compounds having clinical utility for the treatment of urinary incontinence (Soulard C, et al. *J Pharmacol Exp Ther* 1992, 260(3): 1152-8), and the activity of compounds of the formula (I) in this model would be predictive of clinical utility.

Example 17

In vivo model for cold-enhanced central pain states

Injury to the brain or spinal cord, such as that caused by trauma, interrupted blood flow or neurodegenerative diseases, often precipitates a central pain condition. Examples of such injuries characterized, in part by, a hypersensitivity to cold stimuli include multiple sclerosis (Morin C, et al. *Clin J Pain* 2002, 18(3): 191-5; Svendsen KB, et al. *Pain* 2005, 114(3): 473-81), stroke or cerebral ischemia (Greenspan JD, et al. Pain. 2004, 109(3): 357-66) and spinal cord injury (Defrin R, Ohry A, Blumen N, Urca G. *Pain* 2001, 89(2-3): 253-63; Defrin R, et al. *Brain* 2002, 125(Pt 3): 501-10; Finnerup NB, et al. *Anesthesiology* 2005, 102(5): 1023-30). Each of these conditions may be readily modeled in animals for assessment of the ability of compounds of the

formula (I) to mollify the hypersensitive state. For example, a spinal cord injury (SCI) can be performed in adult Sprague–Dawley rats having a body weight of 150–200 g at time of surgery (Erichsen et al. *Pain* 2005, 116: 347-358). The rats can be anaesthetized with chloral hydrate (300 mg/kg, i.p., Sigma, USA) and a catheter can be inserted into the jugular vein. A midline skin incision can then be made along the back to expose the T11-L2 vertebrae. The animals can be positioned beneath a tunable argon ion laser (Innova model 70, Coherent Laser Products Division, CA, USA) operating at a wavelength of 514 nm with an average power of 0.17 W. The laser light can be focused into a thin beam covering the single T13 vertebra, which can be irradiated for 10 min. Immediately before the irradiation, erythrosin B (Aldrich, 32.5 mg/kg dissolved in 0.9% saline) can be injected intravenously via the jugular catheter. Due to rapid metabolism of erythrosin B, the injection can be repeated after 5 min in order to maintain adequate blood concentrations. During irradiation, the body core temperature can be maintained at 37-38 °C by a heating pad. After irradiation the wound can be closed in layers and the skin sutured together.

SCI rats can be routinely tested for the presence of pain-like behaviors from 3–4 weeks after surgery. The fur of the animals can be shaved at least a day prior to examination of the cutaneous pain threshold to avoid sensitization of the skin receptors. During testing, the rats can be gently held in a standing position by the experimenter and the flank area and hindlimbs can be examined for hypersensitivity to sensory stimulation. On the day of drug testing, SCI rats can be administered drug according to the experimental schedule and the time course of pain-like behaviors can be measured. To test for the presence of cold allodynia, ethyl chloride or acetone can be sprayed onto the skin of the animals, often that which has been previously determined to be sensitive to mechanical stimulation by von Frey filament testing. The subsequent response to cold stimulation can be observed and classified according to the following scale: 0, no visible response; 1, localized response (skin twitch) without vocalization; 2, transient vocalization; 3, sustained vocalization. Kruskal Wallis ANOVA on ranks can be used to analyze the overall effects of non-parametric data obtained in response to cold stimulation following pretreatment with either compounds of the formula (I) or vehicle.

Example 18

In vivo model for post-anesthetic shivering

Spontaneous post-anesthetic tremor that resembles shivering is common during recovery from anesthesia. Risks to postoperative patients include an increase in metabolic rate of up to 400%, hypoxemia, wound dehiscence, dental damage, and disruption of delicate surgical repairs. The etiology of spontaneous post-anesthetic tremor is most commonly attributed to normal thermoregulatory shivering in response to intraoperative hypothermia. In most operating and recovery rooms, shivering is controlled by the use of humidifiers, warming blankets, and inhalation of humidified heated oxygen. However, pharmacological control is an effective alternate treatment modality (Bhatnagar S, et al. *Anaesth Intensive Care* 2001, 29(2): 149-54; Tsai YC, Chu KS. *Anesth Analg* 2001, 93(5): 1288-92). Compounds of the formula (I) may be assessed for their ability to mitigate post-ansethetic induced-shaking by using animal models such as that described by Nikki et al (Nikki P, Tammisto T. *Acta Anaesthesiol Scand* 1968, 12(3): 125-34) and Grahn (Grahn, DA, et al. *J Applied Physiology* 1996, 81: 2547-2554). For example, Wistar rats (males, weighing 250-450 g) may be surgically implanted with an EEG/EMG recording array to assess post anesthetic tremor activity. The EEG electrodes are located bilaterally 2 mm off midline and adjacent to bregma and lamda. Following a one-week recovery period, frontal-occipital EEG, raw EMG, and integrated EMG activities, as well as three temperatures (skin, rectal, and water blanket temperatures during anesthesia), and ambient temperature post-anesthesia can be monitored throughout the experiment using copper-constantin thermocouples. The EEG and EMG signals can be recorded on polygraph paper (5 mm/s, Grass model 7E polygraph) and, during recovery from anesthesia, the EEG is computer scored in 10 second epochs as either synchronized: high amplitude (.100 μV), low frequency (1-4 Hz dominated) activity characteristic of slow-wave sleep (SWS-like) or desynchronized: low amplitude (75 μV), high frequency (5-15 Hz dominated), characteristic of waking and rapid-eye-movement sleep (W-like). The EMG activity can be quantified as the averaged summed voltage/time interval by processing the raw EMG signal through an integrator (Grass model 7P3, 0.5 s time constant). On the day of an experiment, the animal can be placed in a small acrylic box (15 x 15 x 15 cm) and exposed to a halothane vapor-air mixture (4% halothane). Immediately after the

induction of anesthesia, the animal can be removed from the enclosure and subsequently anesthetized through a nose cone. Following cessation of anesthesia, two stages of recovery can be judged: emergence from anesthesia and restoration of behavioral activity (behavioral recovery). Emergence from anesthesia may be defined as an increase in tonic EMG activity and a change in the EEG from a SWS-like pattern to a W-like pattern. Behaviorally, recovery has occurred when the animal rises from a prone position and initiated coordinated movements. The time intervals from termination of anesthesia to emergence and behavioral recovery can be measured in all animals. Time interval data can be subjected to a repeated measure analysis of variance, and the Scheffe's method can be employed for testing differences between pairs of means.

Example 19

Cold-evoked cardiovascular pressor responses

Compounds of the formula (I) can be tested in animals and humans for their ability to mitigate cardiovascular pressor responses evoked by cold exposure. Seasonal environmental cooling is directly associated with elevated blood pressure and an increased incidence of coronary events in human populations worldwide (Barnett, AG et al. *J Epidemiol Community Heath* 2005, 59 551-557). Cold-evoked pulmonary hypertention and cold aggravation of chronic obstructive pulmonary disease are clinical indications succeptible to heightened cardiopulmonary sensitivity to cold (Marno P et al. Eur Respiratory Review 2006, 15 (101): 185.; Acikel M et al Int J of Cardiol (2004) 97: 187– 192). The clinical cold pressor test assesses changes in blood pressure (BP) and cold pain perception during a 2-3 minute immersion of one hand into ice water. This test may be utilized to characterize analgesic compounds (Koltzenberg M et al. *Pain* 2006, 126(1-3): 165-74) and to assess cold hypersensitivity (Desmeules JA et al. *Arthritis Rheum* 2003, 48(5): 1420-9). Compounds of the formula (I) can be studied in an anesthetized rat cold pressor paradigm to determine whether TRPM8 antagonism would interfere with the blood pressure pressor response to cold stimulation of the forepaws. Male Sprague-Dawley rats (300 -450g) anesthetized with sodium pentobarbital are instrumented with a jugular catheter and an indwelling carotid artery cannula connected to a pressure transducer. Vehicle (e.g. 20% HPbCD in sterile water) or test compound is infused (1 mL/kg) over one minute through the intravenous

catheter. Ten minutes later both forelimbs are packed in crushed ice for 5 minutes. Alternatively, the test compound and vehicle treatments may be administered orally at an appropriated time prior to the surgical cannulations and cold challenge. Percent changes in mean arterial pressure in response to this cold stimulus are calculated for vehicle and test compound pretreatments. Percent inhibition attributed to treatment with test compound is then determined using the following formula: % Inhibition = [1-(cold evoked % change in BP post-test compound / cold evoked % change in BP post-vehicle)] x 100. Results are shown in Table 11

Table 11

Cpd No.	Salt Form	Dose	Route	Vehicle	Treatment Time, hours relative to Cold Challenge	Percent Inhibition, relative to vehicle
306	$CO_2^-Na^+$	1 3 10 30	p.o.	HPbCD	1.5	16 41 62 75

Example 20

Cold-Induced Vasoconstriction: Ramifications for Tissue Perfusion

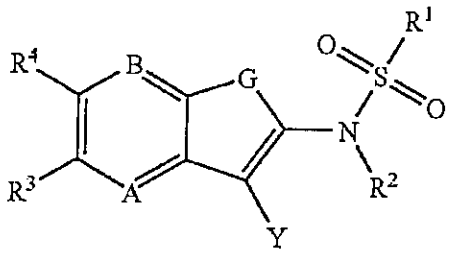
Damage may occur to a bodily tissue when blood flow is compromised or interrupted. Reasons for vascular compromise include peripheral vascular disease (Lamah M et al, European journal of vascular and endovascular surgery (1999), 18(1), 48-51), prior traumatic or frostbite injury, Raynaud's syndrome (Lutolf, O et al Microvascular research (1993), 46(3), 374-82), diabetic neuropathy (Forst T et al, Clinical science (London, England : 1979) (1998), 94(3), 255-61.), surgical intervention and autonomic dysregulation (Gherghel D et al, Investigative ophthalmology & visual science (2004), 45(10), 3546-54). In the case of marginal resting perfusion, vasoconstriction as enchanced by cool temperature may aggravate symptoms and potentiate tissue injury (Cankar K et al,The Journal of hand surgery (2000), 25(3), 552-8; Lutolf O et al Microvascular research (1993), 46(3), 374-82.). Several of these conditions may be readily modeled in animals to assess of the ability of TRPM8 antagonists such as compounds of the formula (I) to preserve tissue

perfusion in the face of local cooling. For example, laser Doppler assessment of skin blood flow may be studied in the paws of anesthetized rats (Hord A H et al, Anesthesia and analgesia (1999), 88(1), 103-8), wherein the paw is subject to a series of decreasing temperatures steps as applied by physical contact with a Peltier cooling element under computer control. The laser Doppler measures skin perfusion in the face of cooling–induced vasoconstriction thereby generating a temperature x perfusion relationship. Systemic administratin of a TRPM8 antagonist is anticipated to shift this curve toward preserving perfusion at reduced temperatures relative to vehicle pretreatment. This activity is envisioned to be therapeutic in protecting tissue from hypo-perfusion and ischemia thereby minimizing the associated symptoms (e.g. pain) and potential tissue damage.

While the foregoing specification teaches the principles of the present invention, with examples provided for the purpose of illustration, it will be understood that the practice of the invention encompasses all of the usual variations, adaptations and/or modifications as come within the scope of the following claims and their equivalents.

We claim:

1. A compound of the formula (I)



(I)

wherein

A is CR^5;

B is CR^6;

G is S;

Y is

(i) H;

(ii) isopropenyl;

(iii) C_{1-6} alkylcarbonyl optionally substituted with 1 to 3 fluoro substituents;

(iv) C_{3-6} cycloalkylcarbonyl;

(v) phenylcarbonyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, fluoro, or chloro;

(vi) phenylcarbonyl substituted with trifluoromethyl and optionally one additional substituent selected from trifluoromethyl, chloro, fluoro, or C_{1-4} alkyl;

(vii) heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkyl, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

(viii) benzo-fused heteroaryl optionally substituted with one to two substituents independently selected from chloro, fluoro, bromo, trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-3} alkylamino, or di(C_{1-3})alkylamino;

(ix) bromo;
(x) chloro;
(xi) fluoro;
(xii) iodo;
(xiii) cyano;
(xiv) formyl;
(xv) C_{1-6} alkyl optionally substituted with 1 to 3 substituents independently selected from hydroxy, fluoro, or chloro;
(xvi) $C(OH)(C_{1-3}$ alkyl$)_2$;
(xvii) C_{3-6} cycloalkyl;
(xviii) C_{1-2} alkyl substituted with 1 substituent independently selected from C_{1-4} alkoxycarbonyl, cyano, C_{1-3} alkylthio, C_{1-4} alkoxy, or NR^7R^8 wherein R^7 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^8 is hydrogen or C_{1-4} alkyl; or R^7 and R^8 are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur;
(xix) C_{1-4} alkoxycarbonyl;
(xx) C_{1-3} alkoxy;
(xxi) hydroxy;
(xxii) C_{6-10} aryl optionally substituted with one to three substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkoxy, hydroxy, C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, or C_{1-6} alkyl optionally substituted with one to three halogen substituents; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-3} alkoxycarbonyl, C_{1-3} alkylthio, cyano, amino, C_{1-2} alkylamino, di(C_{1-2})alkylamino, and C_{1-6} alkyl substituted with one to three halogen substituents;
(xxiii) NR^9R^{10} wherein R^9 is hydrogen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^{10} is hydrogen or C_{1-4} alkyl, or R^9 and R^{10} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said 5 or 6 membered ring

is optionally substituted with a C_{1-4} alkyl substituent; with the proviso that when G is S and R^{10} is hydrogen, R^9 is other than hydrogen and C_{1-4} alkyl;

(xxiv) aminocarbonyl;

(xxv) methylaminocarbonyl;

(xxvi) dimethylaminocarbonyl; or

(xxvii) arylhydroxy(C_{1-3})alkyl;

R^1 is

(i) CF_3;

(ii) C_{1-6} alkyl optionally substituted with 1 substituent selected from C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, formyl, hydroxy, carboxy, trifluoromethyl, C_{1-4} alkoxy, C_{1-3} alkylthio, bromo, cyano, R^{11}, or R^{12};

(iii) aryl(C_{1-2} alkyl) wherein the ring of the aryl group is optionally substituted with 1 to 3 substituents independently selected from C_{1-4} alkyl, fluoro, chloro, trifluoromethyl, hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, or carboxy; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxycarbonyl, and carboxy;

(iv) C_{3-8} cycloalkyl; or cyclohexyl substituted at the 4-position with one substitutent selected from the group consisting of cyano, C_{1-4} alkoxycarbonyl, carboxy, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3} alkyl)aminocarbonyl, amino-methyl, methylamino-methyl, dimethylamino-methyl, R^{11}, and R^{12};

(v) benzo-fused C_{5-6}cycloalkyl attached at the benzo portion of the ring system, and wherein the C_{5-6}cycloalkyl portion of benzo-fused C_{5-6}cycloalkyl is optionally substituted with amino, (C_{1-3} alkyl)amino, or di(C_{1-3} alkyl)amino;

(vi) phenyl substituted with 3- or 4-imidazolyl, wherein the point of attachment of the imidazolyl is through a nitrogen heteroatom; and wherein the imidazolyl is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, 2-cyano, chloro, bromo, amino-C_{1-2} alkyl,

(C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl) amino-C_{1-2} alkyl; wherein di(C_{1-3} alkyl) is optionally taken together with the nitrogen atom to which it is attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein the ring formed by di(C_{1-3} alkyl)amino is optionally substituted with C_{1-3}alkyl; with the proviso that not more than one of the substituents is amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, or di(C_{1-2} alkyl)amino-C_{1-2} alkyl;

(vii) phenyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl optionally substituted with one to three chloro or fluoro substituents or one hydroxy substituent, chloro, fluoro, bromo, C_{1-4} alkoxy, trifluoromethoxy, 3- or 4-phenyloxy, 3- or 4-heteroaryloxy wherein the heteroaryl ring is a 6 membered ring containing carbon ring members and 1 or 2 nitrogen heteroatom ring members, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, hydroxy, carboxy, cyano, nitro, 3- or 4-heteroaryl wherein said heteroaryl is other than imidazolyl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonylaminocarbonyl, di(C_{1-3})alkylaminosulfonyl, $P(O)(OC_{1-3}$ alkyl$)_2$, $P(O)(OH)_2$, SO_3H, C(O)NHOH, $C(=N)NH_2$, $C(=NOH)NH_2$, C(=N (methylcarbonyloxy))NH_2, or SO_2NH_2; with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethoxy, 3- or 4-substituted phenyloxy, 3- or 4-heteroaryloxy, C_{1-3} alkylsulfonyl, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, carboxy, cyano, 3- or 4-heteroaryl, C_{1-3} alkylcarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3}) alkylaminocarbonyl, C_{1-3} alkylsulfonylaminocarbonyl, di(C_{1-3}) alkylaminosulfonyl, and $P(O)(OC_{1-3}$ alkyl$)_2$ and not more than one of the substituents is selected from the group consisting of —$P(O)(OH)_2$, —SO_3H, carboxy, C(O)NHOH, $C(=N)NH_2$, $C(=NOH)NH_2$, $C(=N(C_{1-3}$alkylcarbonyloxy))NH_2, and —SO_2NH_2; wherein the phenyloxy is optionally substituted with one to two substituents independently selected from the group consisting of methyl and fluoro; and wherein the heteroaryl substituent is optionally independently substituted with

one to two substituents selected from the group consisting of C_{1-3} alkyl, trifluoromethyl, trifluoromethoxy, cyano, amino, methylamino, dimethylamino, chloro, bromo, carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino-C_{1-2} alkyl; with the proviso that not more than one of the substituents is selected from the group consisting of carboxy, C_{1-2} alkoxycarbonyl, C_{1-2} alkoxycarbonylmethyl, carboxymethyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl) amino-C_{1-2} alkyl;

(viii) naphthyl optionally substituted with one substituent selected from the group consisting of hydroxy, chloro, fluoro, bromo, C_{1-4} alkoxycarbonyl, and carboxy;

(ix) C_{6-10} aryl substituted with phenyl optionally substituted with one to two substituents selected from chloro, fluoro, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, carboxy, hydroxy, or C_{1-3} alkyl;

(x) phenyl substituted with R^{11} or R^{12} at the 3 or 4 position; and optionally one additional substituent selected from fluoro, chloro, or C_{1-3} alkyl;

(xi) a ring that is phenyl, wherein said ring is substituted with $NR^{15}R^{16}$; wherein R^{15} is hydrogen, C_{1-4} alkyl, C_{1-4} alkylcarbonyl, trifluoromethylcarbonyl, trifluoromethylsulfonyl, C_{3-6} cycloalkylsulfonyl, or C_{1-3} alkylsulfonyl; and R^{16} is hydrogen or C_{1-4} alkyl; or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur optionally substituted with one or two oxo substituents; and wherein the ring formed by $NR^{5}R^{16}$ is optionally substituted with C_{1-3}alkyl, C_{1-2} alkoxycarbonyl, or carboxy; and wherein said phenyl is optionally substituted with one to two additional substituents independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, fluoro, chloro, and bromo;

(xii) phenyl substituted with $C(O)NR^{17}R^{18}$ wherein R^{17} is hydrogen, C_{1-4} alkyl, C_{1-4} alkylcarbonyl, pyrrolidin-3-yl, or C_{1-3} alkylsulfonyl; and R^{18} is hydrogen or C_{1-4} alkyl; or R^{17} and R^{18} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said ring is optionally substituted with C_{1-3}alkyl;

(xiii) phenyl substituted with 4 or 5 fluoro substituents;

(xiv) phenyl substituted at the 4-position with —Q—$C(R^xR^y)$—$(CH_2)_{0-1}CO_2H$ wherein Q is a bond or O; and wherein R^x and R^y are independently hydrogen or methyl; or R^x and R^y are taken together with the carbon atom to which they are both attached to form a cyclopropyl ring;

(xv) amino;

(xvi) C_{1-6} alkylamino; or

(xvii) di(C_{1-6} alkyl)amino;

R^2 is

(i) C_{3-6} cycloalkyl;

(ii) C_{1-2} alkyl substituted with adamantyl or norbornanyl;

(iii) C_{1-6} alkyl substituted with two C_{6-10} aryl groups wherein one of said aryl groups is optionally substituted with 1 to 3 substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3}) alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl; and the other of said aryl groups is optionally

substituted with 1 substituent selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl;

(iv) C_{1-6} alkyl substituted with one C_{6-10} aryl group and optionally one additional substituent selected from hydroxy or oxo, wherein said C_{6-10} aryl group is optionally substituted with 1 to 3 substituents independently selected from chloro, fluoro, bromo, C_{1-4} alkyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, hydroxy, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, trifluoromethylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3})alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, or C_{1-3} alkylcarbonyl; with the proviso that not more than two of the substituents are selected from the group consisting of C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-4} alkoxycarbonyl, C_{1-3} alkylthio, trifluoromethylthio, cyano, trifluoromethyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3}) alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, nitro, amino, C_{1-3} alkylamino, di(C_{1-3})alkylamino, and C_{1-3} alkylcarbonyl;

(v) C_{1-6} alkyl substituted with phenyl, wherein phenyl is substituted with 4 or 5 fluoro substituents; or phenyl is substituted with methoxy and 3 to 4 fluoro substituents; or

(vi) C_{2-6} alkyl optionally substituted with 1 to 2 substituents independently selected from cyano, trifluoromethyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, amino, C_{1-3} alkylamino, di(C_{1-3}) alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, fluoro, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-4} alkoxycarbonylamino, $P(O)(OC_{1-3})_2$, C_{3-6} cycloalkyloxy, C_{3-4}

cycloalkyl, or C_{5-8} cycloalkyl optionally substituted with one to three substituents independently selected from the group consisting of halogen, oxo and C_{1-4} alkyl optionally substituted with one to three substituents independently selected from halogen or hydroxy; with the proviso that not more than one of the substituents on the C_{1-4} alkyl of the C_{1-4} alkyl substituted C_{5-8} cycloalkyl is hydroxy, and not more than two of the substituents on the C_{5-8} cycloalkyl are oxo;

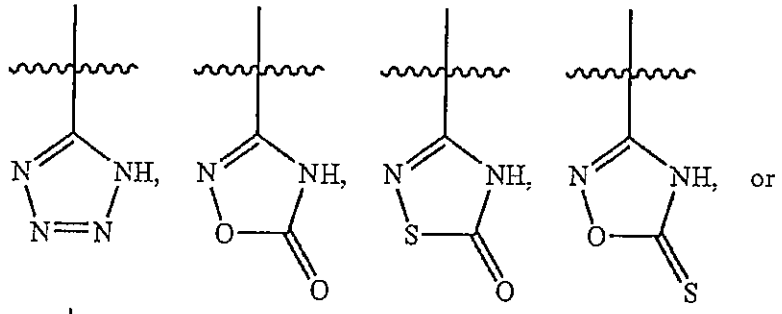
R^3 is
(i) hydrogen,
(ii) C_{1-6} alkyl,
(iii) trifluoromethyl,
(iv) C_{1-4} alkoxy,
(v) bromo,
(vi) chloro,
(vii) fluoro, or
(viii) hydroxy;

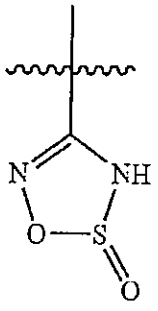
R^4 is
(i) hydrogen,
(ii) fluoro,
(iii) chloro, or
(iv) methyl;

R^5 is hydrogen;

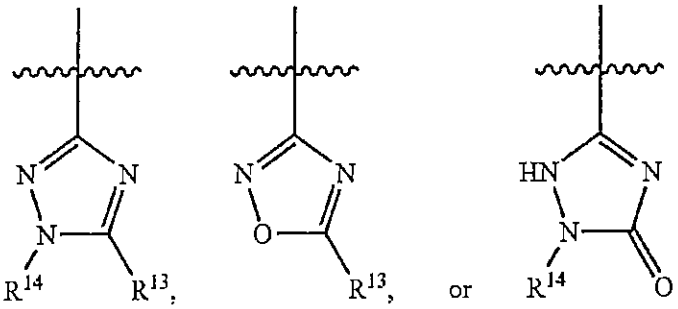
R^6 is hydrogen,

R^{11} is selected from





R^{12} is selected from



wherein R^{13} is H, —C_{1-4} alkyl, —$CH_2CO_2CH_3$, —$CH_2NH(C_{1-3}alkyl)$, —$CH_2N(C_{1-3}alkyl)_2$, or —CH_2CO_2H; and R^{14} is —C_{6-10} aryl, —C_{1-6} alkyl, —C_{1-3} alkyl-OH, or —C_{1-3} alkylCO_2H;

with the proviso that when R^1 is C_{6-10} aryl, wherein C_{6-10} aryl is phenyl, substituted with carboxy at the 2 position, Y is not hydrogen;

with the proviso that when R^2 is C_{1-6} alkyl substituted with at least one $P(O)(OCH_3)_2$ substituent, R^1 is optionally substituted C_{6-10} aryl;

with the proviso that when R^2 is C_{1-6} alkyl substituted with at least one C_{1-6} alkoxycarbonyl substituent, R^1 is optionally substituted C_{6-10} aryl;

with the proviso that when Y is unsubstituted phenyl, and R^1 is ethyl, R^2 is not 4-fluoro-3-trifluoromethyphenylmethyl;

with the proviso that Formula (I) is other than

a compound wherein G is S, Y is H, R^1 is 4-cyanophenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is 1-hydroxyethyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methyl, R^1 is 4-piperazin-1-ylcarbonylphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylcarbonylamino, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-aminocarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylaminocarbonyl, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is 4-methyl-piperazin-1-ylcarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is bromo, R^1 is 4-(1-hydroxyethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6, are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is dimethylaminomethyl, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 3-fluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; and

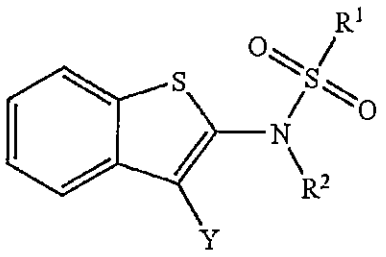
a compound wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-fluoroethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound wherein G is S, Y is H, R^1 is 3-(1H-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

or an enantiomer, diastereomer, or pharmaceutically acceptable salts thereof.

2. A compound of claim **1** of the formula II:

(II)



or an enantiomer, diastereomer, or pharmaceutically acceptable salts thereof.

3. A compound of any one of claim **1** or **2** wherein when R^1 is C_{6-10} aryl, wherein C_{6-10} aryl is phenyl, substituted with carboxy at the 2 position, and Y is chloro.

4. A compound of claim **1** wherein Y is hydrogen, isopropenyl, formyl, methyl, isopropyl, trifluoromethyl, methoxy, chloro, acetyl, hydroxymethyl, 1-hydroxyethyl, 1-methoxyethyl, 1-hydroxy-1-methyl-ethyl, methylamino-methyl, dimethylamino-methyl, n-propylamino-methyl, pyrrolidin-1-yl-methyl, 4-methyl-piperazin-1-yl, piperazin-1-yl; cyclopropyl, cyclobutyl, cyclopentyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, methylcarbonyl, methanesulfonylamino, bromo, pyrimidin-5-yl, thien-3-yl, 2-fluorophenyl, or 4-fluorophenyl.

5. A compound of claim 1 wherein Y is hydrogen, methyl, isopropyl, isopropenyl, trifluoromethyl, methoxy, chloro, acetyl, hydroxymethyl, 1-hydroxyethyl, 1-methoxyethyl, 1-hydroxy-1-methyl-ethyl, methylamino-methyl, dimethylamino-methyl, cyclopropyl, cyclobutyl, cyclopentyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, methylcarbonyl, or bromo.

6. A compound as in claim 1 wherein R^1 is phenyl substituted with 3- or 4-imidazolyl, wherein the point of attachment of the imidazolyl is through a nitrogen heteroatom; and wherein the imidazolyl is optionally independently substituted with one to two substituents selected from the group consisting of C_{1-3} alkyl, amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, and di(C_{1-2} alkyl)amino-C_{1-2} alkyl; wherein di(C_{1-3} alkyl) is optionally taken together with the nitrogen atom to which it is attached to form a pyrrolidinyl or piperadinyl ring; with the proviso that not more than one of the substituents is amino-C_{1-2} alkyl, (C_{1-2} alkyl)amino-C_{1-2} alkyl, or di(C_{1-2} alkyl)amino-C_{1-2} alkyl.

7. A compound of as in claim 1 wherein R^1 is phenyl optionally substituted with one to three substituents independently selected from hydroxyl, fluoro, chloro, bromo, cyano, nitro, 3- or 4-heteroaryl, 3- or 4-phenyloxy, 3- or 4-heteroaryloxy, C_{1-3} alkylsulfonylaminocarbonyl, di(C_{1-3})alkylaminosulfonyl, C(=NOH)NH_2, C(O)NHOH, C(C=N(C_{1-3} alkylcarbonyloxy))NH_2, aminocarbonyl, C_{1-4} alkyl subsitituted with one to three chloro or fluoro substitituents or one hydroxyl substituent, C_{1-3}alkylcarbonyl, C_{1-3} alkoxycarbonyl, C_{1-3} alkoxy, or carboxy; wherein the phenyloxy is optionally substituted with one to two substituents independently selected from the group consisting of methyl and fluoro.

8. A compound as in claim 1 wherein R^1 is phenyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, ydroxyl, fluoro, bromo, cyano, nitro, thiadazolyl, pyrazol-1-yl, 2-methyl-pyrimidin-4-yl, oxazol-5-yl, 1H-tetrazol-5-yl, 2H-tetrazol-5-yl, 1H-tetrazol-5-yl, 3- or 4-phenyloxy, 3- or 4-pyridinyloxy, methanesulfonylaminocarbonyl, di(methyl)aminosulfonyl, C(=NOH)NH_2, C(O)NHOH, C(C=N(methylcarbonyloxy))NH_2, trifluoromethyl, methoxycarbonyl, aminocarbonyl, methoxy, or

carboxy; wherein the C_{1-4} alkyl is optionally substituted with one hydroxyl substituent and the phenyloxy is optionally substituted with a fluoro substituent.

9. The compound of claim 8 wherein the R^1 is phenyl, 3-cyanophenyl, 4-cyanophenyl, 2,5-dibromophenyl, 4-bromophenyl, 4-(1-hydroxy-1-methyl-ethyl)phenyl, phenyl, 4-hydroxy-3-fluorophenyl, 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, 4-(2-oxo-3H-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, 4-(5-oxo-4,5-dihydro-1H-[1,2,4]triazol-3-yl)phenyl, 4-(1-methyl-5-oxo-4,5-dihydro-1H-[1,2,4]triazol-3-yl)-phenyl, 3-(5-methyl-[1,3,4]oxadiazol-2-yl)phenyl, 3-fluoro-4-(phenylmethoxy)phenyl, 3-fluoro-4-(4-fluorophenylmethoxy)phenyl, 4-pyridin-3-yloxyphenyl, 4-pyridin-4-yloxyphenyl, 4-methoxycarbonylphenyl, 4-methylcarbonylphenyl, 3-dimethylaminosulfonylphenyl, 4-(methanesulfonylaminocarbonyl)phenyl, 4-fluorophenyl, 3,4-difluorophenyl, 4-carboxyphenyl, 3-carboxyphenyl, 4-(2-dimethylaminomethyl-imidazol-1-yl)phenyl, 4-(N-hydroxy-acetamidinyl)phenyl, 4-hydroxyaminocarbonylphenyl, 4-(N-(methylcarbonyloxy)acetamidinyl)phenyl, 4-(pyrazol-1-yl)phenyl, 3-(2-methyl-pyrimidin-4-yl)phenyl, 4-(oxazol-5-yl)phenyl, 3-(1H-tetrazol-5-yl)phenyl, 3-(2H-tetrazol-5-yl)phenyl, 4-(1H-tetrazol-5-yl)phenyl, or 3-methoxyphenyl.

10. A compound of claim 1 wherein R^1 is phenyl substituted with R^{11} or R^{12} at the 3 or 4 position; and optionally one additional substituent selected from fluoro, chloro, or C_{1-3} alkyl.

11. A compound of claim 1 wherein R^1 is phenyl wherein said phenyl is substituted with $NR^{15}R^{16}$; wherein R^{15} is hydrogen, C_{1-4} alkyl, methylcarbonyl, trifluoromethylcarbonyl, cyclopropylsulfonyl, or C_{1-3} alkylsulfonyl; and R^{16} is hydrogen or C_{1-4} alkyl; or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form morpholin-4-yl, piperazin-1-yl, piperadin-1-yl, thiomorpholin-4-yl, or pyrrolidin-1-yl; and wherein the ring formed by $NR^{15}R^{16}$ is optionally substituted with C_{1-3}alkyl; and wherein said phenyl is optionally substituted with one to two additional substituents independently selected from the group consisting of methoxy, hydroxy, chloro, and bromo.

12. A compound of claim 1 wherein R^1 is phenyl substituted with $C(O)NR^{17}R^{18}$ wherein R^{17} is hydrogen, C_{1-4} alkyl, or C_{1-3} alkylsulfonyl; and R^{18} is hydrogen; or R^{17} and R^{18} are taken together with the nitrogen atom to which they are attached to form 4-methyl-piperazin-1-yl.

13. A compound of claim 1 wherein R^2 is C_{1-2} alkyl substituted with phenyl, wherein phenyl is substituted with 4 or 5 fluoro substituents; or phenyl is substituted with methoxy and 3 to 4 fluoro substituents.

14. A compound of claim 1 wherein R^2 is C_{1-6} alkyl substituted with- phenyl optionally substituted with one to three substituents independently selected from C_{1-4} alkyl, trifluoromethyl, C_{1-4} alkoxy optionally substituted with 1 to 3 fluoro substituents, C_{1-3} alkylthio, trifluoromethylthio, C_{1-3} alkoxycarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3}) alkylaminocarbonyl, C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, chloro, fluoro, bromo, or nitro with the proviso that not more than two of the substituents are selected from the group consisting of trifluoromethyl, C_{1-4} alkoxy substituted with 1 to 3 fluoro substituents, C_{1-3} alkylthio, trifluoromethylthio, C_{1-3} alkoxycarbonyl, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3}) alkylaminocarbonyl; C_{1-3} alkylsulfonyl optionally substituted with 1 to 3 fluoro substituents, and nitro.

15. A compound of claim 14 wherein the R^2 is C_{1-6} alkyl substituted with phenyl optionally substituted with one to two substituents independently selected from methoxy, fluoro, nitro, trifluoromethoxy, trifluoromethyl, methylthio, trifluoromethylthio, methoxycarbonyl, methylsulfonyl, trifluoromethylsulfonyl, methyl, chloro, or bromo.

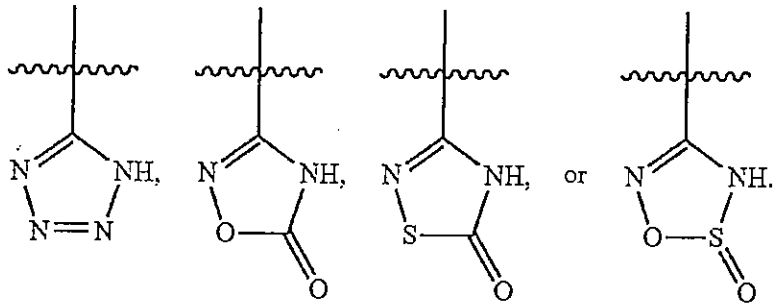
16. A compound of claim 15 wherein the R^2 is 3-methoxyphenylmethyl, 4-methoxyphenylmethyl, 2-fluorophenylmethyl, 3-fluorophenylmethyl, 4-fluorophenylmethyl, 3,4,5-trifluorophenylmethyl, 3,4-difluorophenylmethyl, 2-nitrophenylmethyl, 2-trifluoromethoxyphenylmethyl, 3-trifluoromethoxyphenylmethyl, 4-trifluoromethoxyphenylmethyl, 4-difluoromethoxyphenylmethyl, 4-chloro-2-fluoro-5-methoxyphenylmethyl, phenylmethyl, 4-fluoro-3-trifluoromethylphenylmethyl, 4-fluoro-2-trifluoromethylphenylmethyl, 2-methylphenylmethyl, 3-methylphenylmethyl, 2,5-dichlorophenylmethyl, 3-chloro-4-fluorophenylmethyl, 4-chloro-3-fluorophenylmethyl, 2-(phenyl)ethyl, 4-chlorophenylmethyl, 2-methoxyphenylmethyl, 5-bromo-2-methoxyphenylmethyl, 3-methoxyphe-

nylmethyl, 4-fluoro-3-methoxyphenylmethyl, 2-bromo-5-methoxyphenylmethyl, 4-methoxy-3-bromophenylmethyl, 3-nitrophenylmethyl, 3-methoxycarbonylphenylmethyl, 4-methoxycarbonylphenylmethyl, 4-trifluoromethylthiophenylmethyl, 4-trifluoromethylsulfonylphenylmethyl, or 3-hydroxyphenylmethyl.

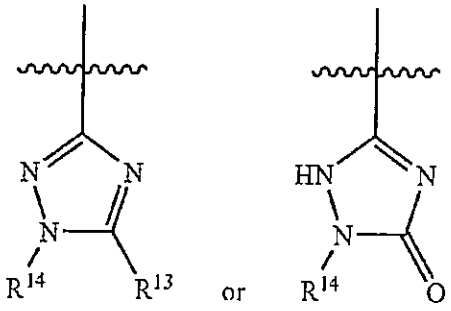
17. A compound of claim 1 wherein the R^2 is C_{1-6} alkyl substituted with one substituent selected from benzo[1,3] dioxol-5-ylmethyl, or 2,2-difluoro-benzo[1,3]dioxol-5-ylmethyl.

18. A compound of claim 17 wherein the R^2 is benzo[1,3] dioxol-5-ylmethyl, or 2,2-difluoro-benzo[1,3]dioxol-5-ylmethyl.

19. A compound of claim 1 wherein R^{11} is selected from



20. A compound of claim 1 wherein R^{12} is selected from



wherein R^{13} is H, —C_{1-4} alkyl, —$CH_2NH(C_{1-3}alkyl)$, —$CH_2NH(C_{1-3}alkyl)_2$, or —CH_2CO_2H; and R^{14} is —C_{1-2} alkyl, —C_{1-3} alkyl-OH, or —$C_{1-3}alkylCO_2H$.

21. A compound of claim 1 that is

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; or

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; or a pharmaceutically acceptable salt thereof.

22. A pharmaceutical composition comprising a compound of claim 1 and at least one of a pharmaceutically acceptable carrier, pharmaceutically acceptable excipient, and a pharmaceutically acceptable diluent.

23. The pharmaceutical composition of claim 22, wherein the composition is a solid oral dosage form.

24. The pharmaceutical composition of claim 22, wherein the composition is a syrup, an elixor, or a suspension.

25. A compound of claim 1 wherein R^1 is C_{1-4} alkyl optionally substituted with 1 substituent selected from the group consisting of C_{1-3} alkylsulfonyl, C_{1-3} alkoxycarbonyl, hydroxy, carboxy, formyl, trifluoromethyl, bromo, and a 5 to 6 membered heteroaryl optionally substituted with C_{1-4} alkyl, aminomethyl, methylamino-methyl, or dimethylamino-methyl.

26. A compound of claim 1 wherein R^1 is unsubstituted cyclopropyl or cyclohexyl substituted at the 4-position with one substituent selected from the group consisting of C_{1-4} alkoxycarbonyl, carboxy, aminocarbonyl, C_{1-3} alkylaminocarbonyl, di(C_{1-3} alkyl)aminocarbonyl, aminomethyl, methylamino-methyl, dimethylamino-methyl, R^{11}, and R^{12}.

27. A compound of claim 1 wherein R^1 is methyl, ethyl, propyl, butyl, phenylmethyl, carboxymethyl, methoxycarbonylmethyl, 2-(methoxycarbonyl)ethyl, 2,2,2-trifluoroethyl, 2-bromoethyl, 2-hydroxyethyl, 2-formylethyl, 2-carboxyethyl, 3-bromopropyl, 3-hydroxypropyl, 3-(methoxycarbonyl)propyl, 3-(imidazol-1-yl)propyl , 4-(imidazol-1-yl)butyl, 3-hydroxy-3-methyl-butyl, 4-bromobutyl, 4-hydroxybutyl, 4-(4-methyl-piperazin-1-yl)butyl, 4-hydroxy-4-methylpentyl, or methanesulfonylmethyl.

28. A compound of claim 1 wherein R^1 is amino, methylamino, or dimethylamino.

29. A compound of claim 1 wherein R^1 is CF_3.

30. A compound of claim 1 wherein R^2 is cyclohexyl.

31. A compound of claim 1 wherein R^2 is C_{1-6} alkyl substituted with one substituent selected from cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

32. A compound of claims 1 wherein R^2 is cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, 2-(cyclopropyl) ethyl, or cyclohexylmethyl.

33. A compound as in claim 1 wherein Y is hydrogen; isopropenyl; pyrimidinyl; thienyl; bromo; chloro; fluoro; iodo; cyano; formyl; aminocarbonyl; methylaminocarbonyl; dimethylaminocarbonyl; C_{1-6} alkylcarbonyl; C_{3-6} cycloalkyl; C_{1-3} alkoxy; C_{1-2} alkyl optionally substituted with 1 substituent selected from C_{1-4} alkoxy or NR^7R^8 wherein R^7 is hydro-

gen, C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^8 is hydrogen or C_{1-4} alkyl or R^7 and R^8 are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; C_{1-2} alkyl optionally substituted with 1 to 3 groups independently selected from hydroxy, fluoro, or chloro; NR^9R^{10} wherein R^9 is C_{1-4} alkyl, C_{1-3} alkylcarbonyl, or C_{1-3} alkylsulfonyl and R^{10} is hydrogen or C_{1-4} alkyl, or R^9 and R^{10} are taken together with the nitrogen atom to which they are attached to form a 5 or 6 membered ring optionally containing one additional heteroatom selected from nitrogen, oxygen, or sulfur; and wherein said 5 or 6 membered ring is optionally substituted with a C_{1-4} alkyl substituent; with the proviso that when G is S and R^{10} is hydrogen, R^9 is other than hydrogen and C_{1-4} alkyl; or C_{6-10} aryl optionally substituted with 1 to three groups independently selected from chloro, fluoro, or bromo.

34. A compound of claim 1 that is

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is adamant-1-ylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-carboxyphenyl, R_2 is adamant-1-ylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is phenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is phenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 4-fluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is phenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is phenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 4-trifluoromethoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is 4-hydroxyphenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is ethyl, R_2 is 3,4-difluorophenyl methyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 4-fluoro-3-methoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is formyl, R_1 is 4-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 3-methyl phenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 4-methoxy-3-bromophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 4-fluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 3-fluorophenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is methyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 3-methoxyphenyl methyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is phenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is ethyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is phenyl, R_2 is 3,4-difluoro phenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-hydroxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is ethyl, R_2 is 3,4-difluorophenyl methyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 3-hydroxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is acetyl, R_1 is phenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is acetyl, R_1 is methyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is methyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-carboxyphenyl, R_2 is n-butyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 3-methoxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is phenyl, R_2 is 2-(tert-butoxy)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is 3-phenoxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is dimethylamino, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 2-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is 3-hydroxyphenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is ethyl, R_2 is 2-(tert-butoxy)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is ethyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 3-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is 3-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is 2-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is 3-fluorophenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is formyl, R_1 is ethyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is n-hexyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 3-trifluoromethoxy phenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 3-phenylpropyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is phenyl, R_2 is 2-phenylethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is 2-fluorophenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-(tert-butoxy)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is dimethylamino, R_2 is 2-(tert-butoxy)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 4-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-methoxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is cyano, R_1 is ethyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 3-nitrophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 4-chlorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is ethyl, R_2 is 4-trifluoromethoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is phenyl, R_2 is 2-(methoxycarbonyl)-2-methylethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-trifluoromethoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 4-trifluoromethoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-fluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is formyl, R_1 is ethyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-carboxyphenyl, R_2 is 3,3,3-trifluoropropyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is formyl, R_1 is methyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2(S)-methoxycarbonyl-2-methylethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is ethyl, R_2 is n-butyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 3,3,3-trifluoropropyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 5-(ethoxycarbonyl) pentyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is 4-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is formyl, R_1 is phenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 4-chlorophenyl methyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is ethyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is ethyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is methyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R_1 is methyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2(S)-methoxycarbonyl-2-methylethyl R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 3-methoxycarbonyl phenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is acetyl, R_1 is ethyl, R_2 is 3,4difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 2-(tert-butoxy)ethyl R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is ethyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6; or

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is trifluoromethyl, R^1 is phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(pyrazol-1-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(5-methyl-[1,3,4]oxadiazol-2-yl)phenyl, R^2 is

4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(oxazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-chloro-4-methylcarbonylamino-phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-(1-hydroxy-1-methyl-ethyl) phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methylcarbonylphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 3,4-difluoro-phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1-hydroxy-1-methyl-ethyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is pentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is hexyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 3-t-butoxypropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-t-butoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 3-t-butoxypropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methoxy, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is cyclobutylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is cyclopentylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 2-cyclohexyloxy-ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 3-methoxy-3-methyl-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylaminocarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is aminocarbonyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(N-hydroxy-acetamidinyl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,4-difluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3-chloro-4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-difluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is pentafluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethylsulfonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3-fluoro-4-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-aminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopentyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,4,5-trifluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2-fluoro-5-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2,5-dichlorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-chloro-3-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 2,2-difluoro-benzo[1,3]dioxol-5-ylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 3,4-dimethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl; R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethylthiophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1S*-hydroxy-ethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1R*-hydroxy-ethyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(2-oxo-3H-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5 and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(2-oxo-3H-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl,

R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(morpholin-4-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-aminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-aminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-amino-3-bromophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-2-fluorophenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-(methoxycarbonyl)ethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(2-oxo-3H-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(methanesulfonylaminocarbonyl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(2-oxo-3H-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-aminophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-amino-3-bromophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-aminophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 3-bromo-4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-aminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-aminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopropyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 3-bromo-4-methylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclobutyl, R^1 is 4-carboxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxypropyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is hydroxymethyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-formylethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-hydroxy-3-methyl-butyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is phenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-bromophenyl, R^2 is 3-chloro-4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is 4-fluorophenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-dimethylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-dimethylaminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(morpholin-4-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopropyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclobutyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-(methoxycarbonyl)propyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-hydroxybutyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-carboxypropyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 5-chloro-2-methoxy-4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is cyclopropyl, R^2 is 3-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-bromobutyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-cyanophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-3-fluorophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxy-3-fluorophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is ethyl, R^2 is 2-fluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-carboxyphenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-hydroxyethyl, R^2 is 4-fluoro-3-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-bromoethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-dimethylaminophenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(morpholin-4-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 4-trifluoromethoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is ethyl, R^2 is 2,4,5-trifluoro-3-methoxyphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; or a pharmaceutically acceptable salt thereof.

35. A compound of claim 1 that is

a compound of formula (I) wherein G is S, Y is Cl, R_1 is 3-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is n-butyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 3-fluorophenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-(methylsulfanyl)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is methyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 2-(tert-butoxycarbonylamino)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is n-butyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 5-bromo-2-methoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 2-methylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is methanesulfonylmethyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is ethyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 2-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-bromo-5-methoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 2-nitrophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 2-fluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is ethyl, R_2 is 3,3,3-trifluoropropyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-carboxyphenyl, R_2 is 2,2-difluoroethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 3-methylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is n-propyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 3-nitrophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 3-methoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 2-phenylethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 4-chlorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is 4-methoxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-(methanesulfonyl)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is ethyl, R_2 is 2,2-difluoroethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is ethyl, R_2 is 2-(tert-butoxy)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-(dimethylamino)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is n-butyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 2-trifluoromethoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 3-trifluoromethoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 2-methoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2-(dimethylphospho)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is cyclohexyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is methylamino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is dimethylamino, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylamino-methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylamino-methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (1) wherein G is S, Y is methyl, R^1 is methyl, R^2 is 2-t-butoxyethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-pyridin-3-yloxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 6-methylthiopyridin-3-yl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is propyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylamino-methyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylamino-methyl, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-dimethylaminophenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-morpholin-4-yl-phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is aminocarbonyl, R^1 is 4-methoxycarbonylphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(N-hydroxy-acetamidinyl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is 4-methanesulfonylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is $S(0_2)$, Y is dimethylamino, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 3-cyanophenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^4 is trifluoromethyl, R^3, R^5, and R^6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-dimethylaminophenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(2-oxo-3H-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxy-2-fluorophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methanesulfonylaminophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is 1-hydroxy-1-methyl-ethyl, R^1 is 4-bromophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2,2,2-trifluoroethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopropyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(methanesulfonylamino)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 3,5-dichloro-4-(methanesulfonylamino)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]thiadiazol-3-yl)-phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 2,2,2-trifluoroethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-methanesulfonylamino-2-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 2-hydroxy-4-(methanesulfonylamino)phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; or a pharmaceutically acceptable salt thereof.

36. A compound of claim 1 that is

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 2-methylsulfanylethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is phenyl, R_2 is 4-methoxyphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 2-(dimethylamino)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is methyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is ethyl, R_2 is 2,2-difluoroethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 2-(methanesulfonyl)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is phenyl, R_2 is 2-aminoethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is ethyl, R_2 is 2-(methylsulfanyl)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is dimethylamino, R_2 is 2,2-difluoroethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is amino, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 1-hydroxyethyl, R_1 is ethyl, R_2 is cyclopropylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is acetyl, R_1 is ethyl, R_2 is 2-(tert-butoxy)ethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is amino, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is 4-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 3-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 4-methoxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 2-fluorophenyl, R_1 is ethyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is amino, R_2 is 4-fluoro-3-trifluoromethylphenyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Cl, R_1 is 2-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is ethyl, R_2 is 2-methoxyethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 2-carboxyphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 4-methoxycarbonylphenyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is 4-fluorophenyl, R_1 is ethyl, R_2 is 4-fluoro-3-trifluoromethylphenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is 4-trifluoromethylphenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is H, R_1 is 4-trifluoromethylphenyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is Br, R_1 is phenyl, R_2 is 2,3-dihydroxypropyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is methyl, R_1 is phenylmethyl, R_2 is 3,4-difluorophenylmethyl, R_3, R_4, R_5, and R_6 are hydrogen, A is CR_5, and B is CR_6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is amino, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is n-propylamino-methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is n-propylamino-methyl, R^1 is ethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methylcarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonyl, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-carboxyphenyl, R^2 is ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-cyanophenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^4 is fluoro, R^3, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-aminocarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is formyl, R^1 is 4-methoxycarbonylphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylamino-methyl, R^1 is 4-methoxycarbonylphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-carboxyphenyl, R^2 is 2-dimethylamino-ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-pyrrolidin-1-ylphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1-methyl-piperazin-4-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-carboxyphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-dimethylaminosulfonylphenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-dimethylaminosulfonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylaminocarbonyl, R^1 is 4-methoxycarbonylphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is aminocarbonyl, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is dimethylaminocarbonyl, R^1 is 4-carboxyphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(2-oxo-3H-[1,2,3,5]oxathiadiazol-4-yl)phenyl R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5 and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-bromophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is 4-(5-thioxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-nitrophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methylcarbonylamino, R^1 is 4-methoxycarbonylphenyl, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is cyclopentyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methanesulfonylamino, R^1 is phenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)-phenyl, R^2 is 4,4,4-trifluoro-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-methoxycarbonylphenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is methylamino, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is methylamino, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is bromo, R^1 is methylamino, R^2 is n-butyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-carboxyphenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is isopropyl, R^1 is 4-methoxycarbonylphenyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(1H-tetrazol-5-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-cyanophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(2-oxo-2,3-dihydro-2 . 4-[1,2,3,5]oxathiadiazol-4-yl) phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(5-oxo-4,5-dihydro-[1,2,4]oxadiazol-3-yl)phenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 2-carboxyethyl, R^2 is 4,4,4-trifluorobutyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-(2-oxo-2,3-dihydro-2 4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-bromophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (1) wherein G is S, Y is H, R^1 is 4-bromophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is trifluoromethyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (1) wherein G is S, Y is H, R^1 is trifluoromethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is trifluoromethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is trifluoromethyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methanesulfonylaminophenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is chloro, R^1 is 4-trifluoromethylcarbonylaminophenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 3-methanesulfonylaminophenyl, R^2 is 3,3,3-trifluoropropyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(thiomorpholin-4-yl)phenyl, R^2 is 2-(cyclopropyl) ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(piperazin-1-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is H, R^1 is 4-methanesulfonylamino-2-methoxyphenyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(thiomorpholin-4-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(piperidin-1-yl)phenyl, R^2 is 2-(cyclopropyl)ethyl R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(piperidin-1-yl)phenyl, R^2 is 5,5,5-trifluoropentyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

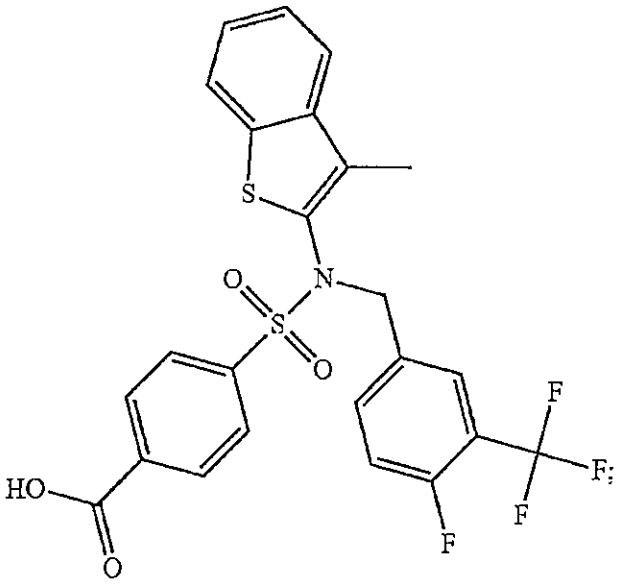
a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(4-methyl-piperazin-1-ylcarbonyl)phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(pyrrolidin-3S-ylaminocarbonyl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is 4-(pyrrolidin-3R-ylaminocarbonyl)-phenyl, R^2 is 2-(cyclopropyl)ethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6;

a compound of formula (I) wherein G is S, Y is methyl, R^1 is carboxymethyl, R^2 is 4-fluoro-3-trifluoromethylphenylmethyl, R^3, R^4, R^5, and R^6 are hydrogen, A is CR^5, and B is CR^6; or a pharmaceutically acceptable salt thereof.

37. A compound selected from the group consisting of



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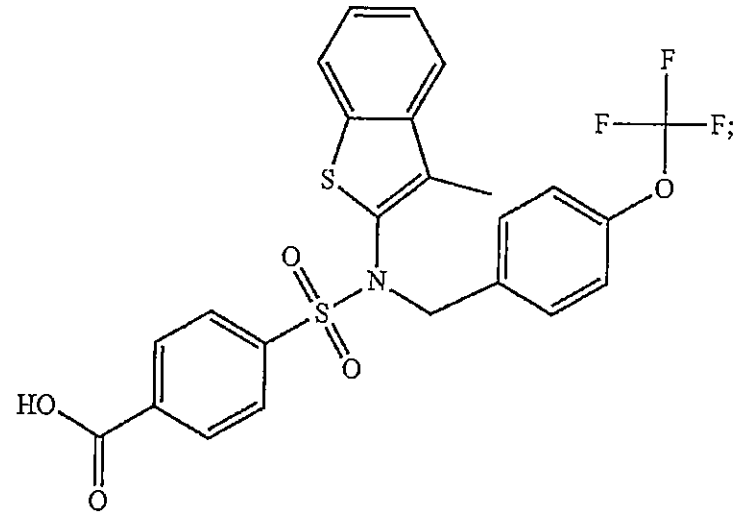

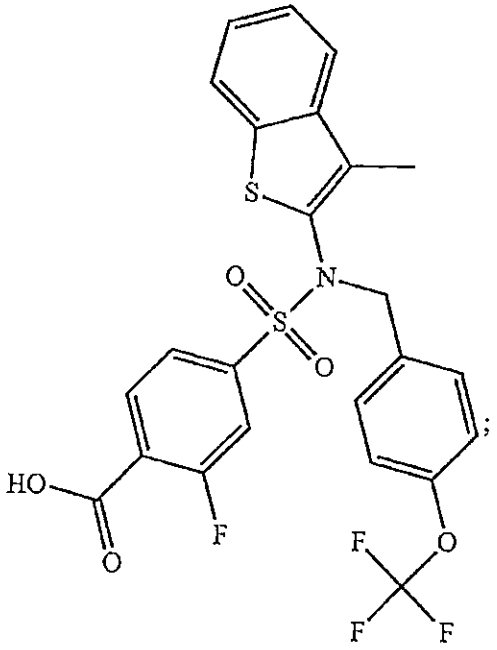

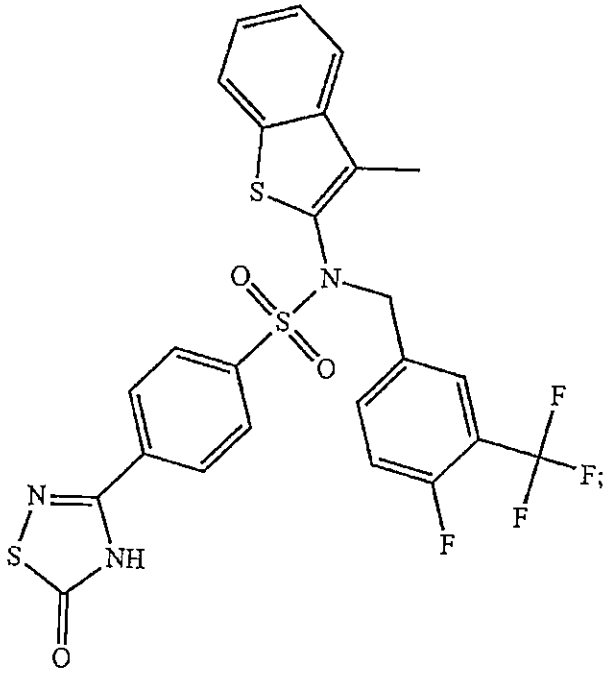

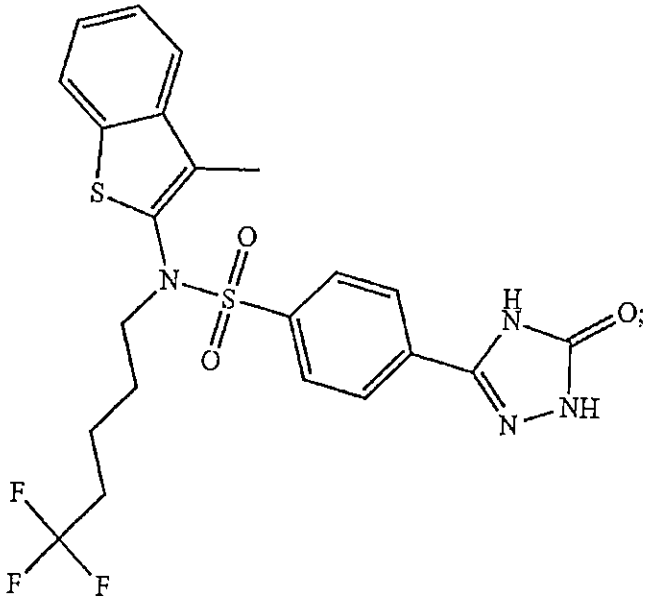

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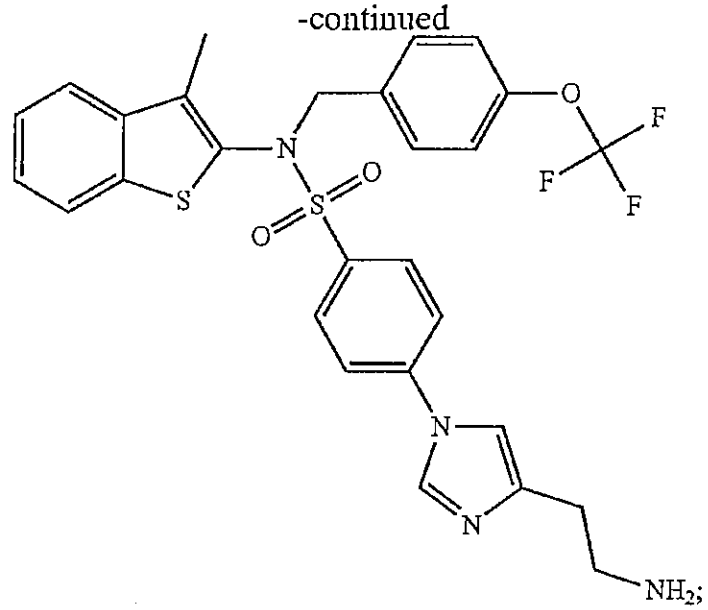

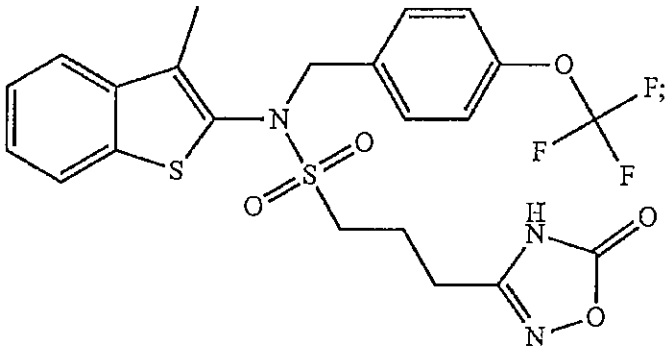

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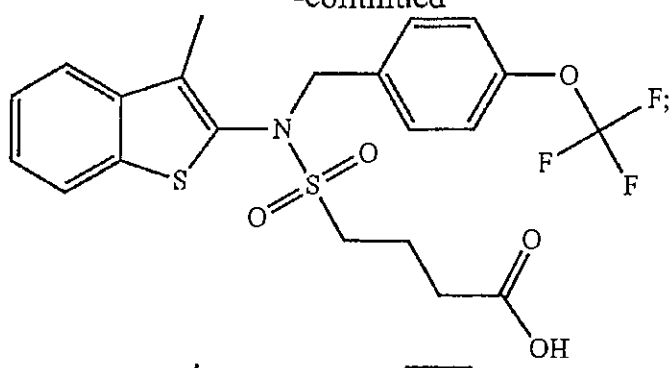

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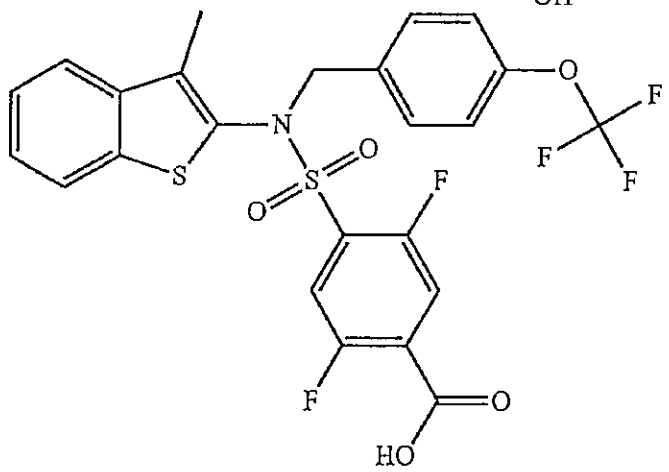

or a pharmaceutically acceptable salt thereof.