SUBSTITUTED OXOAZAHETEROCYCLYL FACTOR Xa INHIBITORS

FIELD OF THE INVENTION

This invention is directed to oxoazaheterocycyl compounds which inhibit factor Xa, to pharmaceutical compositions comprising these compounds, to intermediates useful for preparing these compounds and to a method of inhibiting factor Xa.

BACKGROUND OF THE INVENTION

Factor Xa and Factor Xa assembled in the prothrombinase complex (Factor Xa, Factor Va, calcium and phospholipid) activates prothrombin to generate thrombin. Factor Xa is strategically located at the intersection of extrinsic and intrinsic pathways of the blood coagulation system. Thus, an inhibitor of Factor Xa inhibits the formation of thrombin and therefore is useful for preventing or treating disorders related to blood coagulation in mammals.

Anticoagulant therapy is indicated for the treatment and prophylaxis of a variety of thrombotic conditions of both the venous and arterial vasculature. In the arterial system, abnormal thrombus formation is primarily associated with arteries of the coronary, cerebral and peripheral vasculature. The diseases associated with thrombotic occlusion of these vessels principally include acute myocardial infarction (AMI), unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy and percutaneous transluminal coronary angioplasty (PTCA), transient ischemic attacks, stroke, intermittent claudication and bypass grafting of the coronary (CABG) or peripheral arteries. Chronic anticoagulant therapy may also be beneficial in preventing the vessel luminal narrowing (restenosis) that often occurs following PTCA and CABG, and in the maintenance of vascular access patency in long-term hemodialysis patients. With respect to the venous vasculature, pathologic thrombus formation frequently occurs in the veins of the lower extremities following abdominal, knee and hip surgery (deep vein thrombosis, DVT). DVT further predisposes the patient to a higher risk of pulmonary thromboembolism. A systemic, disseminated intravascular coagulopathy (DIC) commonly occurs in both vascular systems during septic shock, certain viral infections and cancer. This condition is characterized by a rapid consumption of coagulation factors and their plasma inhibitors resulting in the formation of life-threatening clots throughout the microvasculature of several organ systems.

In addition to their use in anticoagulant therapy, Factor Xa inhibitors are useful in the treatment or prevention of other diseases in which the generation of thrombin has been implicated as playing a physiologic role. For example, thrombin has been proposed to contribute to the morbidity and mortality of such chronic and degenerative diseases as arthritis, cancer, atherosclerosis and Alzheimer's disease by

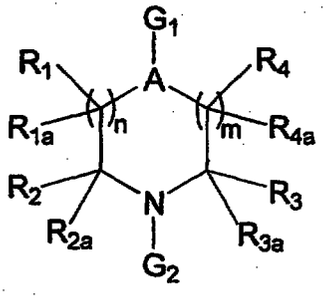
virtue of its ability to regulate many different cell types through specific cleavage and activation of a cell surface thrombin receptor, mitogenic effects, diverse cellular functions such as cell proliferation, for example, abnormal proliferation of vascular cells resulting in restenosis or angiogenesis, release of PDGF and DNA syntheses. Inhibition of Factor Xa will effectively block thrombin generation and therefore neutralize any physiologic effects of thrombin on various cell types.

The representative indications discussed above include some, but not all, of the possible clinical situations amenable to treatment with a Factor Xa inhibitor.

Oxoazaheterocyclyl Factor Xa inhibitors are disclosed in International Patent Numbers PCT/US98/07158, published Oct. 22, 1998; PCT/US98/07159, published Oct. 22, 1998; PCT/US98/07160, published Oct. 22, 1998; PCT/US98/07161, published Oct. 22, 1998; and PCT/US96/09290, published Dec. 19, 1996. Oxoazaheterocyclyl fibrinogen antagonists are disclosed in International Patent Application Number PCT/US92/09467, published May 13, 1993.

SUMMARY OF THE INVENTION

This invention is directed to a compound of formula I



I

or a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof

wherein

G_1 and G_2 are L_1-Cy_1 or L_2-Cy_2, provided that when R_1 and R_{1a} or R_4 and R_{4a} taken together form O or S, then G_1 is L_2-Cy_2 and G_2 is L_1-Cy_1, or when R_2 and R_{2a} or R_3 and R_{3a} taken together form O or S, then G_1 is L_1-Cy_1 and G_2 is L_2-Cy_2;

Cy_1 and Cy_2 are independently selected from optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted

heterocyclyl, optionally substituted heterocyclenyl, optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkenyl, optionally substituted fused arylheterocyclyl, optionally substituted fused arylheterocyclenyl, optionally substituted fused heteroarylcycloalkyl, optionally substituted fused heteroarylcycloalkenyl, optionally substituted fused heteroarylheterocyclyl and optionally substituted fused heteroarylheterocyclenyl;

L_1 is O, NR_5, $-S(O)_p-$, $-S(O)_pNR_5-$, $-C(X)Y-$ or $-L_3-Q-L_4-Q'-L_5-$,

L_3 and L_5 are independently absent, optionally substituted alkylene, optionally substituted alkenylene or optionally substituted alkynylene;

L_4 is optionally substituted alkylene, optionally substituted alkenylene, or optionally substituted alkynylene;

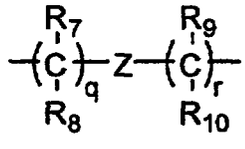
Q and Q' are independently absent, O, S, NR_5, $-S(O)_p-$, $-S(O)_pNR_5-$ or $-C(X)Y-$;

A is CH or N;

R_1, R_{1a}, R_2, R_{2a}, R_3, R_{3a}, R_4 and R_{4a} are independently selected from hydrogen, carboxy, alkoxycarbonyl, Y^1Y^2NCO, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl and optionally substituted heteroaralkyl, or R_1 and R_{1a}, R_2 and R_{2a}, R_3 and R_{3a}, or R_4 and R_{4a} taken together form O or S;

m and n are independently 0, 1 or 2, provided that m and n are not both 0 and further provided that when R_1 and R_{1a} taken together form O or S, n is 1 and when R_4 and R_{4a} taken together form O or S, m is 1;

L_2 is absent or a group of formula



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R_5 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted heteroaralkyl, $R_6O(CH_2)_v$-, $R_6O_2C(CH_2)_x$-, $Y^1Y^2NC(O)(CH_2)_x$-, or $Y^1Y^2N(CH_2)_v$-;

R_6 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl or optionally substituted heteroaralkyl;

Y^1 and Y^2 are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a monocyclic heterocyclyl;

R_7, R_8, R_9 and R_{10} are independently selected from hydrogen, hydroxy, alkoxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl and optionally substituted heteroaralkyl, provided that only one of R_7 and R_8 or one of R_9 and R_{10} is hydroxy or alkoxy, and further provided when R_7, R_8, R_9 and R_{10} is hydroxy or alkoxy, then the hydroxy or alkoxy is not α substituted to a N, O or S in Z;

X is O or S;

Y is absent or is selected from O, S and NR_5;

Z is absent or is selected from optionally substituted lower alkenylene, optionally substituted lower alkynylene, O, $S(O)_p$, NR_5, $-NR_5C(O)-$ and $-C(O)NR_5$-;

x is 1, 2, 3 or 4;

v is 2, 3 or 4;

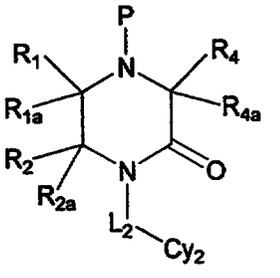
p is 1 or 2; and

q and r are independently 0, 1, 2 or 3, provided that q and r are not both 0.

In another aspect, this invention is directed to a pharmaceutical composition comprising a therapeutically effective amount of the compound of formula I and a pharmaceutically acceptable carrier.

In another aspect, this invention is directed to a method of treating a physiological disorder capable of being modulated by inhibiting Factor Xa comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I.

In another aspect, this invention is directed to a compound of formula II



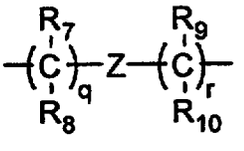
II

wherein

P is H or a nitrogen protecting group;

R_1, R_{1a}, R_2, R_{2a}, R_3, R_{3a}, R_4 and R_{4a} are independently selected from hydrogen, carboxy, alkoxycarbonyl, Y^1Y^2NCO, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl and optionally substituted heteroaralkyl;

L_2 is a group of formula



Cy_2 is selected from optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclenyl, optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkenyl, optionally substituted fused arylheterocyclyl, optionally substituted fused arylheterocyclenyl, optionally substituted fused heteroarylcycloalkyl, optionally substituted fused heteroarylcycloalkenyl, optionally substituted fused heteroarylheterocyclyl and optionally substituted fused heteroarylheterocyclenyl;

R_5 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted heteroaralkyl, $R_6O(CH_2)_v$-, $R_6O_2C(CH_2)_x$-, $Y^1Y^2NC(O)(CH_2)_x$-, or $Y^1Y^2N(CH_2)_v$-;

R_6 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl or optionally substituted heteroaralkyl;

Y^1 and Y^2 are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a monocyclic heterocyclyl;

R_7, R_8, R_9 and R_{10} are independently selected from hydrogen, hydroxy, alkoxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl and optionally substituted heteroaralkyl, provided that only one of R_7 and R_8 or one of R_9 and R_{10} is hydroxy or alkoxy, and further provided when R_7, R_8, R_9 and R_{10} is hydroxy or alkoxy, then the hydroxy or alkoxy is not α substituted to a N, O or S in Z;

Z is absent or is selected from optionally substituted lower alkenylene, optionally substituted lower alkynylene, O, $S(O)_p$, NR_5, $-NR_5C(O)-$ and $-C(O)NR_5-$;

x is 1, 2, 3 or 4;

v is 2, 3 or 4; and

q and r are independently 0, 1, 2 or 3, provided that q and r are not both 0,
which is an intermediate useful in the preparation of the compound of formula I.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

As used above, and throughout the description of the invention, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

"Patient" includes both human and other mammals.

"Alkyl" means an aliphatic hydrocarbon group which may be straight or branched having about 1 to about 20 carbon atoms in the chain. Preferred alkyl groups have 1 to about 12 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl are attached to a linear alkyl chain. "Lower alkyl" means about 1 to about 4 carbon atoms in the chain which may be

straight or branched. The alkyl may be substituted with one or more "alkyl group substituents" which may be the same or different, and include halo, cycloalkyl, hydroxy, alkoxy, amino, carbamoyl, acylamino, aroylamino, carboxy, alkoxycarbonyl, aralkyloxycarbonyl and heteroaralkyloxycarbonyl. Representative alkyl groups include methyl, trifluoromethyl, cyclopropylmethyl, cyclopentylmethyl, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, n-pentyl, 3-pentyl, methoxyethyl, carboxymethyl, methoxycarbonylethyl, benzyloxycarbonylmethyl, and pyridylmethyloxycarbonylmethyl.

"Alkenyl" means a straight or branched aliphatic hydrocarbon group containing a carbon-carbon double bond and having about 2 to about 15 carbon atoms in the chain. Preferred alkenyl groups have 2 to about 6 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl are attached to a linear alkenyl chain. "Lower alkenyl" means about 2 to about 4 carbon atoms in the chain which may be straight or branched. The alkenyl group may be substituted by one or more alkyl group substituents as defined herein. Representative alkenyl groups include ethenyl, propenyl, n-butenyl, i-butenyl, 3-methylbut-2-enyl, n-pentenyl, heptenyl, octenyl, decenyl, and the like.

"Alkylene" means a straight or branched bivalent hydrocarbon chain having from 1 to about 20 carbon atoms. The preferred alkylene groups are the lower alkylene groups having from 1 to about 6 carbon atoms. Alkylene may be substituted with 1 or more alkyl group substituents as defined herein. Representative alkylene groups include methylene, ethylene, and the like.

"Alkenylene" means a bivalent group derived from a straight or branched chain hydrocarbon containing at least one carbon-carbon double bond. The preferred alkenylene groups are the lower alkenylene groups having from 1 to about 6 carbon atoms. Alkenylene may be substituted by one or more alkyl group substituents as defined herein. Representative alkenylene include -CH=CH-, -CH_2CH=CH-, -$C(CH_3)$=CH-, -CH_2CH=$CHCH_2$-, and the like.

"Alkynylene" means a bivalent group derived from a straight or branched chain hydrocarbon containing at least one carbon-carbon double bond. Preferred alkynylene groups are the lower alkynylene groups having from 1 to about 6 carbon atoms. Alkynylene may be substituted by one or more alkyl group substituents as defined herein. Representative akynylene include —CH≡CH—, —CH≡CH-CH_2—, —CH≡CH-$CH(CH_3)$—, and the like.

"Amidino" or "amidine" means a group of formula $-C(=NR_{11})-NHR_{12}$ wherein R_{11} is selected from hydrogen, R_6O_2C-, R_6O-, $R_6C(O)$-, cyano, optionally substituted lower alkyl, nitro or Y^1Y^2N- and R_{12} is selected from hydrogen, optionally substituted lower alkyl, optionally substituted aralkyl and optionally substituted heteroaralkyl. Preferred amidino groups are those in which R_{11} is hydrogen, R_6O, or optionally substituted lower alkyl and R_{12} is as defined above. Most preferred amidino groups are those in which R_{11} and R_{12} are hydrogen.

"Basic nitrogen atom" means an sp^2 or sp^3 hybridized nitrogen atom having a non-bonded pair of electrons which is capable of being protonated. Examples of basic nitrogen atoms, which may be optionally substituted where possible, include those in heteroaryl, heterocyclyl, heterocyclenyl, fused arylheterocyclyl, fused arylheterocyclenyl, fused heteroarylcycloalkyl, fused heteroarylcycloalkenyl, fused heteroarylheterocyclyl, fused heterocyclylheterocyclenyl, imino, amino and amidino groups.

"Cycloalkyl" means a non-aromatic mono- or multicyclic hydrocarbon ring system of about 3 to about 10 carbon atoms. Representative monocyclic cycloalkyl rings include cyclopentyl, cyclohexyl, cycloheptyl, and the like. Representative multicyclic cycloalkyl rings include decalinyl, norbornyl, adamantyl, and the like. The cycloalkyl group is optionally substituted with one or more cycloalkyl group substituents which may be the same or different, where "cycloalkyl group substituent" includes oxo, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, acylamino, aroylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, amidino, amino, carbamoyl, or sulfamoyl. Preferred cycloalkyl group substituents are amino and amidino.

"Cycloalkenyl" means a non-aromatic monocyclic or multicyclic hydrocarbon ring system containing a carbon-carbon double bond and having about 3 to about 10 carbon atoms. The cycloalkenyl group is optionally substituted by one or more cycloalkyl group substituents as defined herein. Representative monocyclic cycloalkenyl rings include cyclopentenyl, cyclohexenyl or cycloheptenyl, and the like. A representative multicyclic cycloalkenyl ring is norbornylenyl. Preferred cycloalkenyl group substituents are amino and amidino.

"Heterocyclyl" means a non-aromatic saturated monocyclic or multicyclic ring system of about 3 to about 10 ring atoms wherein the ring system contains one or more element(s) other than carbon. "Azaheterocyclyl" means heterocyclyl wherein one or more of the atoms in the ring system is/are nitrogen. Preferred heterocyclyl comprise about 5 to about 6 ring atoms wherein one or two of the ring atoms is/are independently selected from oxygen, nitrogen or sulfur. "Aza", "oxo" or "thia", when used as a prefix before heterocyclyl means that the ring system contains at lease one nitrogen, oxygen or sulfur atom. The heterocyclyl is optionally substituted with one or more heterocyclyl group substituents which may be the same or different, where " heterocyclyl group substituent" includes oxo, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, carboxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aralkoxycarbonyl, acylamino, aroylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, amino, carbamoyl, or sulfamoyl. Preferred heterocyclyl group substituents include amino, amidino, halogen, hydroxy, alkoxycarbonylalkyl and carboxyalkyl. Representative heterocyclyl include piperidyl,

pyrrolidinyl, piperazinyl, pyrazolidinyl, imidazolinyl, tetrahydrofuryl, morpholinyl, thiomorpholinyl, thiazolidinyl, 1,3-dioxolanyl, 1,4-dioxanyl, 1,4-dithianyl, 1,3,5-triathianyl, tetrahydrothienyl, tetrahydrothiopyranyl, quinuclidinyl, and the like. The thio or nitrogen moiety of the heterocyclyl may also be optionally oxidized to the corresponding S-oxide, S,S-dioxide or N-oxide.

"Heterocyclenyl" means a heterocyclyl as defined herein which contains at least one carbon-carbon or carbon-nitrogen double bond. "Aza", "oxo" or "thia", when used as a prefix before heterocyclenyl means that the ring system contains at lease one nitrogen, oxygen or sulfur atom. The heterocyclenyl is optionally substituted with one or more heterocyclyl group substituents as defined herein. Representative heterocyclenyl include 2H-pyrrolyl, 2-pyrrolinyl, 3-pyrrolinyl, 2-imidazolinyl, 2-pyrazolinyl, 2H-pyranyl, 1,2-dihydropyridyl, 1,4-dihydropyridyl, 1,2,3,4- tetrahydropyridyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, and the like. Preferred heterocyclyl group substituents include amino, amidino, halogen, hydroxy, alkoxycarbonylalkyl and carboxyalkyl. The thio or nitrogen moiety of the heterocyclyl may also be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide.

"Aryl" means a 6 to 10 membered aromatic monocyclic or multicyclic hydrocarbon ring system. The aryl is optionally substituted with one or more aryl group substituents which may be the same or different, where "aryl group substituent" includes hydrogen, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, aryldiazo, heteroaryldiazo, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, acylamino, aroylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, arylazo, heteroarylazo, amino, alkylamino, carbamyl and sulfamyl. Preferred aryl groups are optionally substituted phenyl or optionally substituted naphthyl. Preferred aryl group substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino.

"Heteroaryl" means about a 5- to about a 10- membered aromatic monocyclic or multicyclic ring system wherein one or more of the atoms in the ring system is/are element(s) other than carbon. Preferred heteroaryl contain one to about 4 heteroatoms selected from oxygen, nitrogen and sulfur. "Aza", "oxo" or "thia", when used as a prefix before heteroaryl means that the ring system contains at lease one nitrogen, oxygen or sulfur atom. The heteroaryl is optionally substituted with one or more aryl group substituents as defined herein. Representative heteroaryl groups include pyrrolyl, pyrazinyl, furyl, thienyl, pyridyl, pyrimidyl, pyridazinyl, isoxazolyl, isothiazolyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, oxadiazolyl, thiadiazolyl, thienopyridyl, pyrrolopyridyl, furanopyridyl, furazanyl, quinoxalinyl, quinazolinyl, quinolizinyl, imidazo[1,2-a]pyridyl, phthalazinyl, imidazo[2,1-b]thiazolyl, benzofuranyl, indolyl, isoindolyl, indolizinyl, indazolyl, azaindolyl, benzimidazolyl, benzothienyl, benzisoxazolyl,

benzothiazolyl, purinyl, benzotriazolyl, 1,8-naphthyridinyl, pteridinyl, quinolinyl, imidazolyl, isoquinolinyl, cinnolinyl, triazinyl, benzotriazinyl, and the like. Preferred heteroaryl group substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino. When heteroaryl contains a nitrogen atom, the nitrogen atom may be oxidized to the N-oxide.

"Fused arylcycloalkyl" means a fused aryl and cycloalkyl as defined herein. Preferred fused arylcycloalkyls are those wherein the aryl thereof is phenyl and the cycloalkyl consists of about 5 to about 6 carbon atoms. Representative fused phenylcycloalkyl groups include 1,2,3,4-tetrahydronaphthyl, indanyl, and the like. The fused arylcycloalkyl is optionally substituted with one or more fused arylcycloalkyl group substituents selected from, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, aryldiazo, heteroaryldiazo, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, acylamino, aroylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, arylazo, heteroarylazo, amino, alkylamino, carbamyl and sulfamyl. The cycloalkyl moiety is further optionally substituted with oxo. Preferred fused phenylcycloalkyl group substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino.

"Fused arylcycloalkenyl" means a fused aryl and cycloalkenyl as defined herein. Preferred fused arylcycloalkyenl are those wherein the aryl thereof is phenyl and the cycloalkenyl consists of about 5 to about 6 carbon atoms. The fused arylcycloalkenyl is optionally substituted with one or more fused arylcycloalkyl group substituents as defined herein. Representative fused phenylcycloalkenyls include 1,2-dihydronaphthylenyl, indenyl, and the like. The cycloalkyl moiety is further optionally substituted with oxo. Preferred substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino.

"Fused arylheterocyclyl" means a fused aryl and heterocyclyl as defined herein. Preferred fused arylheterocyclyl are those wherein the aryl thereof is phenyl and the heterocyclyl consists of about 5 to about 6 ring atoms wherein one or two of the ring atoms is/are independently selected from oxygen, nitrogen and sulfur. "Aza", "oxo" or "thia", when used as a prefix before the heterocyclyl portion of the fused arylheterocyclyl means that the heterocyclyl contains at lease one nitrogen, oxygen or sulfur atom. Representative preferred fused phenylheterocyclyl ring systems include indolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 1H-2,3-dihydroisoindolyl, 2,3-dihydrobenz[f]isoindolyl, 1,2,3,4-tetrahydrobenz[g]isoquinolinyl, and the like. The fused phenylheterocyclyl is optionally substituted with one or more fused phenylcycloalkyl group substituents

as defined herein. The heterocyclyl moiety is further optionally substituted with oxo. Preferred substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino. The nitrogen or sulphur atom of the heterocyclyl may also be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide.

"Fused arylheterocyclenyl" means a fused aryl and heterocyclenyl as defined herein. "Aza", "oxo" or "thia", when used as a prefix before the heterocyclenyl portion of the fused arylheterocyclenyl means that the heterocyclenyl contains at lease one nitrogen, oxygen or sulfur atom. Preferred fused arylheterocyclyl are those wherein the aryl thereof is phenyl and the heterocyclyl consists of about 5 to about 6 ring atoms wherein one or two of the ring atoms is/are independently selected from oxygen, nitrogen and sulfur. Representative preferred fused arylheterocycloalkenyl ring systems include 3H-indolinyl, 1H-2-oxoquinolyl, 2H-1-oxoisoquinolyl, and the like. The fused arylheterocyclenyl is optionally substituted with one or more fused arylcycloalkyl group substituents as defined herein. The heterocyclyl moiety is further optionally substituted with oxo. Preferred substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino. The nitrogen or sulphur atom of the heterocyclenyl is optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide.

"Fused heteroarylcycloalkyl" means a fused heteroaryl and cycloalkyl as defined herein. "Aza", "oxo" or "thia", when used as a prefix before the heteroaryl portion of the fused heteroarylcycloalkyl means that the heteroaryl contains at lease one nitrogen, oxygen or sulfur atom. Preferred fused heteroarylcycloalkyls are those wherein the heteroaryl thereof consists of about 5 to about 6 ring atoms in which one or two of the ring atoms are independently selected from oxygen, nitrogen and sulfur and the cycloalkyl consists of about 5 to about 6 ring atoms. Representative preferred fused heteroarylcycloalkyl include 5,6,7,8-tetrahydroisoquinolyl, 5,6,7,8-tetrahydroquinoxalinyl, 5,6,7,8-tetrahydroquinazolyl, 4,5,6,7-tetrahydro-1H-benzimidazolyl, 4,5,6,7-tetrahydrobenzoxazolyl, 1H-4-oxa-1,5-diazanaphthalen-2-onyl, 1,3-dihydroimidizole-[4,5]-pyridin-2-onyl, and the like. The fused heteroarylcycloalkyl is optionally substituted with one or more fused phenylcycloalkyl group substituents as defined herein. The cycloalkyl moiety is further optionally substituted with oxo. Preferred substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino. The nitrogen atom of the heteroaryl portion of the fused heteroarylcycloalkyl is optionally oxidized to the N-oxide.

"Fused heteroarylcycloalkenyl" means a 5- or 6-membered heteroaryl fused with a cycloalkenyl ring. "Aza", "oxo" or "thia", when used as a prefix before the heteroaryl portion of the fused heteroarylcycloalkenyl means that the cycloalkenyl contains at lease one nitrogen, oxygen or sulfur

atom. Preferred fused heteroarylcycloalkenyls are those wherein the heteroaryl thereof consists of about 5 to about 6 ring atoms in which one or two of the ring atoms are independently selected from oxygen, nitrogen and sulfur and the cycloalkenyl consists of about 5 to about 6 ring atoms. Representative preferred fused heteroarylcycloalkenyl include 5,6-dihydroisoquinolyl, 5,6-dihydroquinoxalinyl, 5,6-dihydroquinazolinyl, 4,5-dihydro-1H-benzimidazolyl, 4,5-dihydrobenzoxazolyl, and the like. The fused heteroarylcycloalkenyl is optionally substituted with one or more fused phenylcycloalkyl group substituents as defined herein. The cycloalkenyl moiety is further optionally substituted with oxo. Preferred substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino. The nitrogen atom of the heteroaryl portion of the fused heteroarylcycloalkyl is optionally oxidized to the N-oxide.

"Fused heteroarylheterocyclyl" means a fused heteroaryl and heterocyclyl as defined herein. "Aza", "oxo" or "thia", when used as a prefix before the heteroaryl or heterocyclyl portion of the fused heteroarylheterocyclyl means that the heteroaryl or heterocyclyl contains at lease one nitrogen, oxygen or sulfur atom. Preferred fused heteroarylheterocyclyls are ring systems wherein one or two of the ring atoms of the heteroaryl are independently selected from oxygen, nitrogen and sulfur and the heterocyclyl portion consists of about 5 to about 6 ring atoms in which one or two of the ring atoms are independently selected from oxygen, nitrogen and sulfur. Representative fused heteroarylheterocyclyl include 2,3-dihydro-1H pyrrol[3,4-b]quinolin-2-yl, 1,2,3,4-tetrahydrobenz [b][1,7]naphthyridin-2-yl, 1,2,3,4-tetrahydrobenz [b][1,6]naphthyridin-2-yl, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indol-2yl, 1,2,3,4-tetrahydro-9H-pyrido[4,3-b]indol-2yl, 2,3,-dihydro-1H-pyrrolo[3,4-b]indol-2-yl, 1H-2,3,4,5-tetrahydroazepino[3,4-b]indol-2-yl, 1H-2,3,4,5-tetrahydroazepino[4,3-b]indol-3-yl, 1H-2,3,4,5-tetrahydroazepino[4,5-b]indol-2 yl, 5,6,7,8-tetrahydro[1,7]napthyridinyl, 1,2,3,4-tetrhydro[2,7]naphthyridyl, 2,3-dihydro[1,4]dioxino[2,3-b]pyridyl, 2,3-dihydro[1,4]dioxino[2,3-b]pyridyl, 3,4-dihydro-2H-1-oxa-4,6-diazanaphthalenyl, 4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyridyl, 6,7-dihydro-5,8-diazanaphthalenyl, and the like. The fused heteroarylheterocyclyl is optionally substituted with one or more fused arylcycloalkyl group substituents as defined herein. The heterocyclyl moiety is further optionally substituted with oxo. Preferred substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino. The nitrogen atom of the heteroaryl portion is optionally oxidized to the N-oxide. The nitrogen or sulphur atom of the heterocyclyl is optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide.

"Fused heteroarylheterocyclenyl" means a fused heteroaryl and heterocyclenyl as defined herein. "Aza", "oxo" or "thia", when used as a prefix before the heteroaryl or heterocyclenyl portion of the fused heteroarylheterocyclenyl means that the heteroaryl or heterocyclenyl contains at lease one nitrogen,

oxygen or sulfur atom. Preferred fused heteroarylcycloalkenyls are ring systems wherein the heteroaryl portion thereof consists of about 5 to about 6 ring atoms in which one or two of the ring atoms are independently selected from oxygen, nitrogen and sulfur and the heterocyclenyl portion consists of about 5 to about 6 ring atoms in which one or two of the ring atoms are independently selected from oxygen, nitrogen and sulfur. Representative fused heteroarylheterocyclenyl include 7,8-dihydro[1,7]naphthyridinyl, 1,2-dihydro[2,7]naphthyridinyl, 6,7-dihydro-3H-imidazo[4,5-c]pyridyl, and the like. The fused heteroarylheterocyclenyl is optionally substituted with one or more fused arylcycloalkyl group substituents as defined herein. The heterocyclenyl moiety is further optionally substituted with oxo. Preferred substituents include hydrogen, alkyl, aryl, heteroaryl, hydroxy, acyl, aroyl, halo, nitro, cyano, alkoxycarbonyl, acylamino, alkylthio, alkylamino, amino, carbamyl, thiocarbamyl and amidino. The nitrogen atom of the heteroaryl portion is optionally oxidized to the N-oxide. The nitrogen or sulphur atom of the heterocyclenyl is optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide.

"Aralkyl" means an aryl-alkyl- group in which the aryl and alkyl are as defined herein. Preferred aralkyls contain a lower alkyl moiety. Representative aralkyl groups include benzyl, 2-phenethyl and naphthlenemethyl.

"Heteroaralkyl" means a heteroaryl-alkyl- group in which the heteroaryl and alkyl are as defined herein. Preferred heteroaralkyls contain a lower alkyl moiety. Representative heteroaralkyl groups may contain thienylmethyl, pyridylmethyl, imidazolylmethyl and pyrazinylmethyl.

"Aralkenyl" means an aryl-alkenyl- group in which the aryl and alkenyl are as defined herein. Preferred aralkenyls contain a lower alkenyl moiety. An representative aralkenyl group is 2-phenethenyl.

"Heteroaralkenyl" means a heteroaryl-alkenyl- group in which the heteroaryl and alkenyl are as defined herein. Preferred heteroaralkenyls contain a lower alkenyl moiety. Representative heteroaralkenyl groups may contain thienylethenyl, pyridylethenyl, imidazolylethenyl and pyrazinylethenyl.

"Hydroxyalkyl" means a HO-alkyl- group in which alkyl is defined herein. Preferred hydroxyalkyls contain lower alkyl. Representative hydroxyalkyl groups include hydroxymethyl and 2-hydroxyethyl.

"Acyl" means an H-CO- or alkyl-CO- group in which alkyl is defined herein. Preferred acyls contain a lower alkyl. Representative acyl groups include formyl, acetyl, propanoyl, 2-methylpropanoyl, butanoyl and palmitoyl.

"Aroyl" means an aryl-CO- group in which aryl is defined herein. Representative aroyl groups include benzoyl and 1- and 2-naphthoyl.

"Aryldiazo" means an aryl-N=N- group in which aryl is defined herein. Representative aryldiazo groups include phenyldiazo and naphthyldiazo.

"Heteroaroyl" means an means a heteroaryl-CO- group in which heteroaryl is defined herein. Representative heteroaryl groups include thiophenoyl and pyridinoyl.

"Heteroaryldiazo" means a heteroaryl-N=N- group in which heteroaryl is defined herein. Representative heteroaryldiazo groups include pyridyldiazo and thienyldiazo.

"Alkoxy" means an alkyl-O- group in which alkyl is defined herein. Representative alkoxy groups include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy and heptoxy.

"Aryloxy" means an aryl-O- group in which aryl is defined herein. Representative aryloxy groups include phenoxy and naphthoxy.

"Aralkyloxy" means an aralkyl-O- group in aralkyl is defined herein. Representative aralkyloxy groups include benzyloxy and 1- or 2-naphthalenemethoxy.

"Alkylthio" means an alkyl-S- group in which alkyl is defined herein. Representative alkylthio groups include methylthio, ethylthio, i-propylthio and heptylthio.

"Arylthio" means an aryl-S- group in which the aryl group is defined herein. Representative arylthio groups include phenylthio and naphthylthio.

"Aralkylthio" means an aralkyl-S- group in which aralkyl is defined herein. A representative aralkylthio group is benzylthio.

"Amino" means a group of formula Y^1Y^2N- wherein Y^1 and Y^2 are defined herein. Preferred amino groups include amino (H_2N-), methylamino, dimethylamino, diethylamino, benzylamino, or phenethylamino.

"Aminoalkyl" means a Y^1Y^2N-alkylene- group wherein Y^1, Y^2 and alkylene are defined herein.

"Alkoxycarbonyl" means an alkyl-O-CO- group wherein alkyl is defined herein. Representative alkoxycarbonyl groups include methoxycarbonyl, ethoxycarbonyl, or t-butyloxycarbonyl.

"Alkoxycarbonylalkyl" means an alkyl-O-CO-alkylene- group wherein alkyl and alkylene are defined herein.

"Aryloxycarbonyl" means an aryl-O-CO- group wherein aryl is defined herein. Representative aryloxycarbonyl groups include phenoxycarbonyl and naphthoxycarbonyl.

"Aralkoxycarbonyl" means an aralkyl-O-CO- group wherein aralkyl is defined herein. A representative aralkoxycarbonyl group is benzyloxycarbonyl.

"Carbamyl" means a group of formula Y^1Y^2NCO- wherein Y^1 and Y^2 are defined herein. Representative carbamyl groups are carbamyl (H_2NCO-) and dimethylaminocarbamyl (Me_2NCO-).

"Sulfamyl" means a group of formula $Y^1Y^2NSO_2$- wherein Y^1 and Y^2 are defined herein. Representative sulfamyl groups are aminosulfamoyl (H_2NSO_2-) and dimethylaminosulfamoyl (Me_2NSO_2-).

"Acylamino" means an acyl-NH- group wherein acyl is defined herein.

"Aroylamino" means an aroyl-NH- group wherein aroyl is defined herein.

"Alkylsulfonyl" means an alkyl-SO_2- group wherein alkyl is defined herein. Preferred alkylsulfonyl groups are those in which the alkyl group is lower alkyl.

"Alkylsulfinyl" means an alkyl-SO- group wherein alkyl is defined herein. Preferred alkylsulfinyl groups are those in which the alkyl group is lower alkyl.

"Arylsulfonyl" means an aryl-SO_2- group wherein aryl is defined herein.

"Arylsulfinyl" means an aryl-SO- group wherein aryl is defined herein.

"Halo" or "halogen" means fluoro, chloro, bromo, or iodo. Preferred are fluoro, chloro or bromo, and more preferred are fluoro or chloro.

"Nitrogen protecting group" means an easily removable group which is known in the art to protect an amino group against undesirable reaction during synthetic procedures and to be selectively removable. The use of N-protecting groups is well known in the art for protecting groups against undesirable reactions during a synthetic procedure and many such protecting groups are known, CF, for example, T.H. Greene and P.G.M. Wuts, Protective Groups in Organic Synthesis, 2nd edition, John Wiley & Sons, New York (1991), incorporated herein by reference. Preferred N-protecting groups are acyl, including formyl, acetyl, chloroacetyl, trichloroacetyl, o-nitrophenylacetyl, o-nitrophenoxyacetyl, trifluoroacetyl, acetoacetyl, 4-chlorobutyryl, isobutyryl, o-nitrocinnamoyl, picolinoyl, acylisothiocyanate, aminocaproyl, benzoyl and the like, and acyloxy including methoxycarbonyl, 9-fluorenylmethoxycarbonyl, 2,2,2-trifluoroethoxycarbonyl, 2-trimethylsilylethxoycarbonyl, vinyloxycarbonyl, allyloxycarbonyl, t-butyloxycarbonyl (BOC), 1,1-dimethylpropynyloxycarbonyl, benzyloxycarbonyl (CBZ), p-nitrophenylsulfinyl, p-nitrobenzyloxycarbony, 2,4-dichlorobenzyloxycarbonyl, allyloxycarbonyl (Alloc), and the like.

"Oxo" means a carbonyl (>C=O) group.

"Compounds of the invention", and equivalent expressions, are meant to embrace compounds of general formula (I) as hereinbefore described, which expression includes the prodrugs, the pharmaceutically acceptable salts, and the solvates, e.g. hydrates, where the context so permits. It is understood that the activity of individual compounds of formula (I) will vary depending on the individual compound and assay employed. Compounds of the invention as used herein includes all compounds of formula (I) having an in-vitro activity of greater than 10% at 3.9 μM in the Factor Xa in vitro enzyme assay described herein. Similarly, reference to intermediates, whether or not they themselves are

claimed, is meant to embrace their salts, and solvates, where the context so permits. For the sake of clarity, particular instances when the context so permits are sometimes indicated in the text, but these instances are purely illustrative and it is not intended to exclude other instances when the context so permits.

"Prodrug" means a form of the compound of formula I which may or may not itself be biologically active but which may be converted, for example by metabolic, solvolytic, or other physiological means, to a biologically active chemical entity, and is suitable for administration to a patient without undue toxicity, irritation, allergic response, and the like, and effective for their intended use, including ketal, ester and zwitterionic forms. A prodrug is transformed in vivo to yield the parent compound of the above formula, for example by hydrolysis in blood. A thorough discussion is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A. C. S. Symposium Series, and in Edward B. Roche, ed., Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference.

"Solvate" means a physical association of a compound of this invention with one or more solvent molecules. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. "Solvate" encompasses both solution-phase and isolable solvates. Representative solvates include ethanolates, methanolates, and the like. "Hydrate" is a solvate wherein the solvent molecule(s) is/are H_2O.

Where the compound of this invention is substituted with a basic moiety, acid addition salts may be formed. The acids which can be used to prepare the acid addition salts include preferably those which produce, when combined with the free base, pharmaceutically acceptable salts, that is, salts whose anions are non-toxic to the patient in pharmaceutical doses of the salts, so that the beneficial effects inherent in the free base are not vitiated by side effects ascribable to the anions. Although pharmaceutically acceptable salts of said basic compounds are preferred, all acid addition salts are useful as sources of the free base form even if the particular salt, per se, is desired only as an intermediate product as, for example, when the salt is formed only for purposes of purification, and identification, or when it is used as intermediate in preparing a pharmaceutically acceptable salt by ion exchange procedures. Pharmaceutically acceptable salts within the scope of the invention are those derived from the following acids: mineral acids such as hydrochloric acid, sulfuric acid, phosphoric acid and sulfamic acid; and organic acids such as acetic acid, citric acid, lactic acid, tartaric acid, malonic acid, methanesufonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, cyclohexylsulfamic acid, quinic acid, and the like. The corresponding acid addition salts comprise the following: hydrohalides, e.g. hydrochloride and hydrobromide, sulfate, phosphate, nitrate, sulfamate, acetate, citrate, lactate, tartarate, malonate, oxalate, salicylate, propionate, succinate, fumarate, maleate,

methylene-bis-β-hydroxynaphthoates, gentisates, mesylates, isethionates and di-p-toluoyltartratesmethanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, cyclohexylsulfamate and quinate, respectively.

Acid addition salts of the compounds of this invention are prepared by reaction of the free base with the appropriate acid by the application or adaptation of known methods. For example, the acid addition salts of the compounds of this invention are prepared either by dissolving the free base in aqueous or aqueous-alcohol solution or other suitable solvents containing the appropriate acid and isolating the salt by evaporating the solution, or by reacting the free base and acid in an organic solvent, in which case the salt separates directly or can be obtained by concentration of the solution.

The acid addition salts of the compounds of this invention can be regenerated from the salts by the application or adaptation of known methods. For example, parent compounds of the invention can be regenerated from their acid addition salts by treatment with an alkali, e.g. aqueous sodium bicarbonate solution or aqueous ammonia solution.

Where the compound of the invention is substituted with an acidic moiety, base addition salts may be formed. The bases which can be used to prepare the base addition salts include preferably those which produce, when combined with the free acid, pharmaceutically acceptable salts, that is, salts whose cations are non-toxic to the animal organism in pharmaceutical doses of the salts, so that the beneficial effects inherent in the free acid are not vitiated by side effects ascribable to the cations. Pharmaceutically acceptable salts, including for example alkali and alkaline earth metal salts, within the scope of the invention are those derived from the following bases: sodium hydride, sodium hydroxide, potassium hydroxide, calcium hydroxide, aluminum hydroxide, lithium hydroxide, magnesium hydroxide, zinc hydroxide, ammonia, trimethylammonia, triethylammonia, ethylenediamine, n-methylglucamine, lysine, arginine, ornithine, choline, N,N'-dibenzylethylenediamine, chloroprocaine, diethanolamine, procaine, n-benzylphenethylamine, diethylamine, piperazine, tris(hydroxymethyl)aminomethane, tetramethylammonium hydroxide, and the like.

Metal salts of compounds of the present invention may be obtained by contacting a hydride, hydroxide, carbonate or similar reactive compound of the chosen metal in an aqueous or organic solvent with the free acid form of the compound. The aqueous solvent employed may be water or it may be a mixture of water with an organic solvent, preferably an alcohol such as methanol or ethanol, a ketone such as acetone, an aliphatic ether such as tetrahydrofuran, or an ester such as ethyl acetate. Such reactions are normally conducted at ambient temperature but they may, if desired, be conducted with heating.

Amine salts of compounds of the present invention may be obtained by contacting an amine in an aqueous or organic solvent with the free acid form of the compound. Suitable aqueous solvents include water and mixtures of water with alcohols such as methanol or ethanol, ethers such as

tetrahydrofuran, nitriles such as acetonitrile, or ketones such as acetone. Amino acid salts may be similarly prepared.

The base addition salts of the compounds of this invention can be regenerated from the salts by the application or adaptation of known methods. For example, parent compounds of the invention can be regenerated from their base addition salts by treatment with an acid, e.g. hydrochloric acid.

As well as being useful in themselves as active compounds, salts of compounds of the invention are useful for the purposes of purification of the compounds, for example by exploitation of the solubility differences between the salts and the parent compounds, side products and/or starting materials by techniques well known to those skilled in the art.

Compounds of this invention may exhibit stereoisomerism by virtue of the presence of one or more asymmetric or chiral centers in the compounds. The present invention contemplates the various stereoisomers and mixtures thereof. Desired enantiomers are obtained by chiral synthesis from commercially available chiral starting materials by methods well known in the art, or may be obtained from mixtures of the enantiomers by resolution using known techniques.

Compounds of this invention may also exhibit geometrical isomerism. Geometrical isomers include the cis and trans forms of compounds of the invention having alkenyl or alkenylenyl moieties. The present invention comprises the individual geometrical isomers and stereoisomers and mixtures thereof.

Preferred Embodiments

Compounds contemplated as falling within the scope of this invention, include, but are not limited to

4-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxo-piperazine-1-ylmethyl]benzamidine,

4-[4-(4-Methoxy-benzenesulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(5-Chloro-thieno[3,2-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[2-Oxo-4-(thieno[2,3-c]pyridine-2-sulfonyl)-piperazin-1-ylmethyl]-benzamidine,

4-[4-(7-Chloro-thieno[2,3-c]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(4-Chloro-thieno[3,2-c]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[2-Oxo-4-(toluene-4-sulfonyl)-piperazin-1-ylmethyl]-benzamidine,

4-[4-(Benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-Amino-3-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[2-Oxo-4-(toluene-4-sulfonyl)-piperazin-1-ylmethyl]-benzamidine,

3-[4-(6-Fluoro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(4-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(5-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(6-Methoxy-naphthalene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-{4-[5-(5-Nitro-pyridine-2-sulfonyl)-thiophene-2-sulfonyl]-2-oxo-piperazin- 1-ylmethyl}-benzamidine,

3-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]- benzamidine,

3-{4-[2-(3-Chloro-phenyl)-ethenesulfonyl]-2-oxo-piperazin-1-ylmethyl}- benzamidine,

3-[2-Oxo-4-(4-phenylazo-benzenesulfonyl)-piperazin-1-ylmethyl]-benzamidine,

3-[4-(Benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]- benzamidine,

4-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-{4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-2-oxopiperazin-1-ylmethyl}benzamidine,

3-{4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-2-oxopiperazin-1-ylmethyl}benzamidine,

3-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

1-(2-Aminoquinolin-6-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)piperazin-2-one,

6-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]-1H-quinolin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[2,3-c]pyridin-3-ylmethyl-piperazin-2-one,

1-(2-Amino-quinoxalin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[2,3-c]pyridin-2-ylmethyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[3,2-c]pyridin-2-ylmethyl-piperazin-2-one,

1-(2-Amino-quinolin-6-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-hydroxy-isoquinolin-6-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-chloro-isoquinolin-6-ylmethyl)-piperazin-2-one,

7-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-2H-isoquinolin-1-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-chloro-isoquinolin-7-ylmethyl)-piperazin-2-one,

1-(7-Amino-thieno[2,3-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(2-chloro-quinolin-6-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-quinolin-6-ylmethyl-piperazin-2-one,

7-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-1H-quinolin-2-one,

1-(2-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1,2,3,4-tetrahydro-isoquinolin-6-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-isoquinolin-6-ylmethyl-piperazin-2-one,

1-(2-Amino-quinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(decahydro-isoquinolin-6-ylmethyl)-piperazin-2-one,
1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(decahydro-isoquinolin-7-ylmethyl)-piperazin-2-one,
1-(1-Amino-isoquinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,
1-(4-Amino-thieno[3,2-c]pyridin-3-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,
(+/-)-[1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-4-thieno[3,2-c]pyridin-2-ylmethyl-piperazin-2-yl]-acetic acid,
(+/-)-[1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-4-thieno[2,3-c]pyridin-2-ylmethyl-piperazin-2-yl]-acetic acid,
1-(1-Amino-isoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,
1-(1-Amino-isoquinolin-6-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,
(3S)-1-(7-Chloro-isoquinolin-3-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-methoxymethyl-piperazin-2-one,
(3S)-1-(7-Chloro-isoquinolin-3-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3-methoxymethyl-piperazin-2-one,
(S)-4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-3-ethyl-1-(4-hydroxy-quinolin-7-ylmethyl)-piperazin-2-one,
1-(2-Amino-quinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,
1-(2-Aminoquinolin-6-ylmethyl)-4-(4-methoxybenzyl)piperazin-2-one,
1-(2-Aminoquinolin-6-ylmethyl)-4-6-chlorobenzo[b]thiophen-2-ylmethyl)piperazin-2-one,
1-(2-Aminoquinolin-6-ylmethyl)-4-(5-methoxy-1H-benzoimidazol-2-ylmethyl)piperazin-2-one,
1-(2-Aminoquinolin-6-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)piperazin-2-one,
1-(2-Aminoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,
1-(2-Aminoquinolin-6-ylmethyl)-4-[3-(3,5-dibromo-4-methoxy-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]piperazin-2-one,
3-[4-(2-Aminoquinolin-6-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-fluoro-1H-quinolin-2-one,
1-(2-Aminoquinolin-6-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one,
3-(4-Biphenyl-3-ylmethyl-3-oxo-piperazin-1-ylmethyl)-benzamidine,
4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-piperazin-2-one,
1,4-Bis-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-benzamidine,

4-(4-Cyclohexylmethyl-2-oxo-piperazin-1-ylmethyl)-benzamidine,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-3-(S)-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-1-[4-(6-oxo-1,6-dihydro-pyridin-3-yl)-benzyl]-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-3-methoxymethyl-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-3-methyl-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-sulfonyl)piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid 3-chloro-benzylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid 4-chloro-benzylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-isoxazol-3-yl-thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid [2-(3-chloro-phenyl)-ethyl]-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid [2-(4-chloro-phenyl)-ethyl]-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-(3-Amino-benzenesulfonyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-methyl-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-methyl-piperazin-2-one,

(+/-)-[4-(4-Amino-quinazolin-7-ylmethyl)-1-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-piperazin-2-yl]-acetic acid,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-hydroxy-quinazolin-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-hydroxy-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(5-oxy-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1-methyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(3-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorothieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Bromobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

2-[3-Oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazine-1-sulfonyl]-benzo[b]thiophene-6-carbonitrile,

4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-[2-(4-Chlorophenyl)ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl} acetic acid,

4-(5-Pyridin-4-ylthiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl} acetic acid ethyl ester,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-[1-(2-methoxyethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]piperazin-2-one,

4-(6-Chlorothieno[3,2-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[2,3-c]pyridin-1-yl} acetic acid methyl ester,

2-[3-Oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazine-1-sulfonyl]benzo[b]thiophene-5-carbonitrile,

4-(5-Aminomethylbenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

2-{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl}acetamide,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-[1-(2-hydroxyethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]piperazin-2-one,

4-(6-Chloro-1H-benzoimidazole-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(1H-Benzoimidazole-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Aminomethyl-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethanesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(2-Benzo[b]thiophen-2-yl-ethenesulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[2-(5-Chloro-4-methoxy-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-furo[3,2-c]pyridin-2-ylmethyl-piperazin-2-one,

4-(6-Fluoro-benzo[b]thiophene-2-sulfonyl)-1-furo[3,2-c]pyridin-2-ylmethyl-piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorothieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-pyrrolo[2,3-c]pyridin-1-yl}-acetic acid methyl ester,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-b]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-(±)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(-)-1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(+)-1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid amide,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[2-(4-Chloro-phenyl)-ethenesulfonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-ylmethyl)piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzothioazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzooxazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzothioazol-2-ylmethyl)-piperazin-2-one,

3-[4-(4-Aminoquinazoline-7-ylmethyl)-3-oxopiperazin-1-ylmethyl]-7-chloro-1H-quinolin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-(E)-enyl]-piperazin-2-one ditrifluoroacetate,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-2-methyl-(E)-allyl]-piperazin-2-one ditrifluoroacetate,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-furan-2-yl)-(E)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-methoxy-pyridin-3-yl)-(E)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-allyl]-4-oxy-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-prop-2-ynyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-prop-2-ynyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-2-yl-prop-2-ynyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yloxy)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1-methyl-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-4-methyl-thiophen-2-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzofuran-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-5-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,7-dichloro-1H-indol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-p-tolyl-prop-2-ynyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-m-tolyl-prop-2-ynyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-4-yl-prop-2-ynyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4,5-dibromo-thiophen-2-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-3-yl-prop-2-ynyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2,5-dichloro-thiophen-3-yl)-prop-2-ynyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-propyl]-piperazin-2-one,
1,4-Bis-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-nitro-thiophen-2-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-pyridin-3-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(5-methyl-thiophen-2-yl)-penta-2,4-dienyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophen-5-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-methyl-thiophen-2-yl)-allyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-methoxy-thiophen-2-yl)-allyl]-piperazin-2-one,
4-(1-Amino-7-chloro-isoquinolin-3-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,
2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-N-(5-chloro-thiophen-2-yl)-acetamide,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenyl)-2-(S)-hydroxy-ethyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenylsulfanyl)-ethyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-methylene-1,1-dioxo-2,3-dihydro-1H-1l 6-benzo[b]thiophen-3-yl)-piperazin-2-one ,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-nitro-phenyl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophen-6-ylmethyl)-piperazin-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-N-(4-chloro-phenyl)-acetamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(4-chloro-phenyl)-pyrrolidin-3-yl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-propyl]-piperazin-2-one,

2-[4-(4-Aminoquinazoline-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-3-(4-chlorophenyl)-acrylic acid,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-1-hydroxy-isoquinolin-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-isoquinolin-3-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(3-chloro-phenyl)-pyrrolidin-3-yl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1,7-dichloro-isoquinolin-3-ylmethyl)-piperazin-2-one,

4-(2-Amino-7-chloro-quinolin-3-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophene-2-ylmethyl)piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(4-chloro-phenylsulfanyl)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(6-chloro-benzo[b]thiophen-2-yl)-ethyl]-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-[2-(4-chloro-phenoxy)-ethyl]-piperazine-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-4H-benzo[1,4]thiazin-3-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,7-dichloro-quinolin-3-ylmethyl)-piperazin-2-one,

2-[[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-(4-chloro-phenyl)-methyl]-acrylic acid ethyl ester,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-3-(4-chloro-phenyl)-acrylic acid ethyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-allyl]-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-fluoro-1H-quinolin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-1H-quinoxalin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1-methyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-3H-quinazolin-4-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-thiophen-2-yl-propyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-quinolin-3-ylmethyl)-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-5,7-dichloro-1H-quinolin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6,7-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-5-chloro-1H-quinolin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-[2,3']bithiophenyl-5'-ylmethyl)-piperazin-2-one,
4-(6-Amino-benzo[b]thiophen-2-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-quinolin-6-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-bromo-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-nitro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(3-chloro-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-3-methoxy-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-1H-quinolin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-trifluoromethyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3,3'-dimethyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3,5-dibromo-4-methoxy-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3'-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-bromo-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-oxazol-2-ylmethyl]-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,6-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(4,5-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzooxazol-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-5-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-5-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thieno[3,2-b]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,6-dichloro-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-benzooxazol-2-yl-benzyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(4-chloro-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-methyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2,2']bithiophenyl-5-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-fluoro-benzo[b]thiophene-2-ylmethyl)piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(1-methyl-5-trifluoro-methyl-1H-pyrazol-3-yl)-thiophen-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3,4-dimethyl-thieno[2,3-b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-3-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-3-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(2-methyl-5-trifluoromethyl-2H-pyrazol-3-yl)thiophen-2-ylmethyl] piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(3-nitro-phenyl)-furan-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thieno[3,2-b]pyridin-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(4-methoxy-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-hydroxy-2-pyridin-2-yl-pyrimidin-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-fluoro-phenoxy)-benzyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(4-chloro-phenyl)-thiazol-4-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-bromo-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-benzo[b]thiophen-2-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3,5-bis-trifluoromethyl-benzyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-biphenyl-4-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-naphthalen-2-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-thiophene-2-carbonyl)-piperazin-2-one,

4-[3-(3-Amino-4-chloro-phenyl)-(E)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

5-Chloro-thiophene-2-carboxylic acid {2-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-2-oxo-ethyl}-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indole-2-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

5-Chloro-thiophene-2-carboxylic acid {2-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-1-methyl-2-oxo-ethyl}-amide,

5-Chloro-thiophene-2-carboxylic acid {3-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-3-oxo-propyl}-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-2-methyl-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-(E)-acryloyl]-piperazin-2-one,

N-[2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-1-(5-chloro-thiophen-2-ylmethyl)-2-oxo-ethyl]-benzamide,

N-[1-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-2-(5-chloro-thiophen-2-yl)-vinyl]-benzamide,

N-[1-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-2-(5-chloro-thiophen-2-yl)-vinyl]-acetamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-(E)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yl)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-piperazin-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-6-chloro-4H-benzo[1,4]thiazin-3-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-benzo[b]thiophen-2-yl)-acetyl]-piperazin-2-one,

4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid 4-chloro-benzylamide,
4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid (5-chloro-thiophen-2-ylmethyl)amide,
4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (3-amino-4-chloro-phenyl)-amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-methoxy-phenyl)-amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (3,4-dichloro-phenyl)-amide,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid 5-chloro-thiophen-2-ylmethyl ester,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-carboxylic acid 6-chloro-benzooxazol -2-ylmethyl ester,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid 1-(3-chloro-phenyl)-pyrrolidin-3-yl ester,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methyl-piperazin-2-one,
4-(4-Amino-quinazolin-7-ylmethyl)- 4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enyl]-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-benzoimidazol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-2-ylmethyl)-3-(R)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(R)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enoyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-(S)-3-ethyl-piperazin-2-one,

2-(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetamide,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,3-dichloro-benzo[b]thiophene-6-carbonyl)-(S)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophene-6-carbonyl)-(S)-3-ethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid ethyl ,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-thiophen-2-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid methyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-(3S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(4-chloro-phenyl)-1H-pyrrole-2-carbonyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenylsulfanyl)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enoyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indole-2-carbonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-propionyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-ethyl-4-[3-(4-methoxy-phenyl)-propionyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-5-methoxy-phenoxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yloxy)-ethyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(R)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)- methoxymethyl-piperazin-2-one,

4-[3-(4-Amino-phenyl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-3H-imidazol-4-yl-acryloyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

(1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thiophene-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-bromo-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)--methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-5-methoxy-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-fluoro-thiophen-2-yloxy)-acetyl]-3-(S)- methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-fluoro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenoxy)-propionyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-4-[(4-trifluoromethylsulfanyl-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-ylsulfanyl)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

2-(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophene-6-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,3-dichloro-benzo[b]thiophene-6-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid methyl ester,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid ethyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,3-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-fluoro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-2-methyl-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,4-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

(1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(R)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-ethoxymethyl-4-[(3-fluoro-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[(4-chloro-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-propyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-isopropyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-(2-methoxy-ethyl)-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-(2-methoxy-ethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-(2-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-(2-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-6-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-6-(R)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

(1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-(S)-3-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-(S)-3-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-4-fluoro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2,5-dichloro-phenyl)-acryloyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-2-methyl-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methoxymethyl-6-methyl-piperazin-2-one,

(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-6-methyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2(S)-(2-methoxy-ethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-butyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-3-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(S)-2-propyl-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (3-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(2S)-propyl-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(S)-2-propyl-piperazine-1-carboxylic acid (5-chloro-2-methoxy-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-2-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-trifluoromethoxy-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-fluoro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (2,4-dichloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (2,4-difluoro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (3-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(2S)-propyl-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (6-chloro-pyridin-3-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-5-(R,S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-ethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-ethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-4-methoxy-thiophen-2-yl)-amide,

(3S, 5RS)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

(3S,5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-sulfonyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

(3S, 5S)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

(3S, 5S)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

1-(4-Aminoquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-methyl-piperazin-2-one,

(3S,5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(3S,5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(S,R)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

(S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(5-chlorothiophen-2-yl)-allyl]-3-methylpiperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-methyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-methyl-piperazin-2-one,

(3S,5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

(3S,5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-(S)-3-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-(S)-3-((R)-1-methoxy-ethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-methoxymethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-methyl-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-1-[4-(2-hydroxy-ethylamino)-quinolin-7-ylmethyl]-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-ethylamino-quinolin-7-ylmethyl)-3-methyl-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-ethylamino-quinolin-7-ylmethyl)-3-methoxymethyl-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-3-methyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-3-methoxymethyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-methyl-4-oxy-piperazin-2-one,

(S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)acryloyl]-3-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-(S)-3-ethyl-1-(4-hydroxyamino-quinolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one,
(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methyl-piperazin-2-one,
1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-piperazin-2-one,
(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methoxymethyl-piperazin-2-one,
(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one,
(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-ethyl-piperazin-2-one,
(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-methoxymethyl-6-methyl-piperazin-2-one,
1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-(S)-3-(1-(R)-methoxy-ethyl)-piperazin-2-one,
1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)-acryl-oyl]-3-(S)-(1-(R)-methoxyethyl)-piperazin-2-one trifluoroacetate,
1-(4-Aminoquinolin-7-ylmethyl)-4-[(5-chlorothiophen-2-yloxy-acetyl]-3-(S)-(1-(R)-methoxyethyl)-piperazin-2-one trifluoroacetate,
(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one,
1-(4-Aminocinnolin-7-ylmethyl)-4-[2-(5-chlorothiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,
4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(methyl-pyridin-4-yl-amino)-ethyl]-piperazin-2-one,
4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(3-methyl-pyridin-4-ylamino)-ethyl]-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,
1-[2-(Pyridin-4-ylamino)-ethyl]-4-(thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,
4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,
1-[2-(Pyridin-4-ylamino)-ethyl]-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one,
4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,
4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(methylpyridin-4-ylamino)-ethyl]-piperazin-2-one,
4-(2-Benzo[b]thiophen-2-yl-ethenesulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(3-methyl-pyridin-4-ylamino)-ethyl]-piperazin-2-one,
4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(2-pyrrolo[3,2-c]pyridin-1-yl-ethyl)-piperazin-2-one,
1-[2-(2-Amino-3-chloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,
1-[2-(2-Amino-5-chloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(2,3,5,6-tetrachloro-pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-[2-(2-Amino-3,5,6-trichloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(pyridazin-4-yl-amino)-ethyl]-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propenyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propenyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-allyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-allyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-[2-(5-Chlorothiophen-2-yl)-ethenesulfonyl]-1-(2-pyrrolo[3,2-c]pyridin-1-ylethyl)-piperazin-2-one,

4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-naphthalen-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(7-Chloro-isoquinolin-3-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester,

1-(5-Chloro-1H-indol-2-ylmethyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester,

1-[(5-Chloro-thiophen-2-yloxy)-acetyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-(6-Chloro-benzo[b]thiophene-2-carbonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(3-Phenyl-prop-2-ynyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-prop-2-ynyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(4-Chloro-phenyl)-(E)-acryloyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(S)-2-Methoxymethyl-3-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

(S)-4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-[3-(6-Chloro-benzo[b]thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indole-2-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[4-(6-Methoxy-pyridin-3-yl)-benzoyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(4-Pyridin-3-yl-benzoyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(4-Bromo-thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-propionyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[(5-Chloro-3-methyl-benzo[b]thiophen-2-yl)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[2-(4-Chloro-phenyl)-2-methyl-propionyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(3,4-Dichloro-phenyl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[(4-Chloro-phenyl)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(4-Chloro-phenyl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methyl ester,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid benzylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid (2-hydroxy-ethyl)-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid bis-(2-hydroxy-ethyl)-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylcarbamoylmethyl-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-(4-methyl-piperazine-1-carbonyl)-piperazin-2-one,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethyl ester,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid,

4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

2-Amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile,

4-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzamidine,

1-(4-Amino-quinazolin-7-ylmethly)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperidin-2-one,

4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-1-(2,4-diamino-quinazolin-7-ylmethyl)-piperidin-2-one,

1-(4-Amino-2-methyl-quinazolin-7-ylmethly)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperidin-2-one,

(3S, 5R)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine,

(3S,5S)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-{4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl}-benzamidine,

(3R,5S)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine,

820. 2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-4-yl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-3-ylmethyl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-piperidin-4-yl-acetamide,

N-(1-Carbamimidoyl-piperidin-4-yl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

5-(2-{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetylamino}-ethyl)-imidazole-1-carboxylic acid ethyl ester,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyrimidin-4-yl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-phenyl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(9H-purin-6-yl)-acetamide,

N-(4-Amino-2-methyl-pyrimidin-5-ylmethyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(1-methyl-1H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-4-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(3-methyl-3H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-2-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-3-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-imidazol-1-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(1-methyl-1H-pyrrol-2-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(5-methyl-1H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(4-dimethylamino-[1,3,5]triazin-2-yl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-pyridin-4-yl-acetamide,

N-[2-(2-Amino-pyridin-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(4-methyl-thiazol-5-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-thiazol-4-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-guanidino-propyl)-acetamide trifluoroacetic acid salt,

N-(3-Amino-propyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-mercapto-1H-imidazol-4-yl)-ethyl]-acetamide,

N-[2-(2-Amino-thiazol-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-(2-pyridin-4-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-methylsulfanyl-1H-imidazol-4-yl)-ethyl]-acetamide,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[3-(3H-imidazol-4-yl)-propyl]-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-piperidine-1-carboxamidine,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-piperazin-1-yl-propyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-pyridin-4-yl-propyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-piperidin-4-yl-butyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(2-piperidin-4-yl-ethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-piperidin-4-yl-propyl)-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

4'-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-biphenyl-2-carbonitrile,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-chloro-3-hydroxy-benzyl)-piperazin-2-one,

1-Benzyl-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-chloro-benzyl)-piperazin-2-one,

4-[(4-Chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-3-(S)-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methyl-1-[4-(6-oxo-1,6-dihydro-pyridin-3-yl)-benzyl]-piperazin-2-one,

1-Biphenyl-4-ylmethyl-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-(S)-methyl-3,6-dioxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-(R)-methyl-3,6-dioxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2,5-dioxo-piperazin-1-ylmethyl]-benzamidine and

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2,5-dioxo-piperazin-1-ylmethyl]-benzamidine.

Preferred compounds have formula I wherein Cy_2 contains at least one nitrogen atom and when Cy_2 is optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted fused phenylcycloalkyl or optionally substituted fused phenylcycloalkenyl, then said nitrogen atom is a basic nitrogen atom.

Other preferred compounds have formula I wherein Z is absent or is selected from O, $S(O)_p$ and NR_5.

Other preferred compounds have formula I wherein Z is $-NR_5C(O)-$ or $-C(O)NR_5-$.

Preferred compounds wherein Z is $-NR_5C(O)-$ or $-C(O)NR_5-$ are selected from

2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-4-yl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-3-ylmethyl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-piperidin-4-yl-acetamide,

N-(1-Carbamimidoyl-piperidin-4-yl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

5-(2-{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetylamino}-ethyl)-imidazole-1-carboxylic acid ethyl ester,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyrimidin-4-yl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-phenyl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(9H-purin-6-yl)-acetamide,

N-(4-Amino-2-methyl-pyrimidin-5-ylmethyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(1-methyl-1H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-4-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(3-methyl-3H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-2-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-3-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-imidazol-1-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(1-methyl-1H-pyrrol-2-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(5-methyl-1H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(4-dimethylamino-[1,3,5]triazin-2-yl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-pyridin-4-yl-acetamide,

N-[2-(2-Amino-pyridin-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(4-methyl-thiazol-5-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-thiazol-4-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-guanidino-propyl)-acetamide trifluoroacetic acid salt,

N-(3-Amino-propyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-mercapto-1H-imidazol-4-yl)-ethyl]-acetamide,

N-[2-(2-Amino-thiazol-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-(2-pyridin-4-yl-ethyl)-acetamide, or

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-methylsulfanyl-1H-imidazol-4-yl)-ethyl]-acetamide,

or a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

Other preferred compounds have formula I wherein m is 1; and n is 1.

Other preferred compounds have formula I wherein A is N.

Other preferred compounds have formula I wherein R_3 and R_{3a} taken together are O; and R_1, R_{1a}, R_2, R_{2a}, R_4 and R_{4a} are hydrogen.

Other preferred compounds have formula I wherein R_3 and R_{3a} taken together are O; R_1, R_{1a}, R_2, R_{2a} and R_4 are hydrogen; and R_{4a} is optionally substituted alkyl.

Other preferred compounds have formula I wherein R_3 and R_{3a} taken together are O; R_1, R_{1a}, R_2 and R_4 are hydrogen; and R_{2a} and R_{4a} are optionally substituted alkyl.

Other preferred compounds have formula I wherein R_3 and R_{3a} taken together are O; R_1, R_2, R_{2a} and R_4 are hydrogen; and R_{1a} and R_{4a} are optionally substituted alkyl.

Other preferred compounds have formula I wherein R_3 and R_{3a} taken together are O; R_1, R_2, R_{2a}, R_4 and R_{4a} are hydrogen; and R_{1a} is carboxy, alkoxycarbonyl, Y^1Y^2NCO or optionally substituted alkyl.

Other preferred compounds have formula I wherein R_3 and R_{3a} taken together are O; and R_1, R_{1a}, R_2, R_4 and R_{4a} are hydrogen; and R_{2a} is carboxy, alkoxycarbonyl, Y^1Y^2NCO or optionally substituted alkyl.

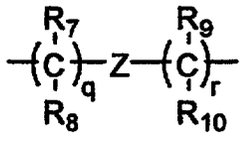
Other preferred compounds have formula I wherein L_1 is $-S(O)_p-$, -C(X)Y- or -L3-Q-L4-Q'-L5-.

Other preferred compounds have formula I wherein Cy_1 is optionally substituted aryl or optionally substituted heteroaryl.

More preferred compounds have formula I wherein L_2 is alkylene of one to three carbon atoms.

Other more preferred compounds have formula I wherein L_2 is $-CH_2-$.

Other more preferred compounds have formula I wherein L_2 is a group of formula



wherein Z is NR_5; q is 2; r is 0; R_5 is hydrogen or optionally substituted alkyl; and R_7 and R_8 are hydrogen.

Other more preferred compounds have formula I wherein R_5 is hydrogen.

Other more preferred compounds have formula I wherein Cy_2 is optionally substituted aryl or optionally substituted heteroaryl.

Other more preferred compounds have formula I wherein L_1 is $-S(O)_2-$.

Other more preferred compounds have formula I wherein L_1 is -C(X)Y-; X is O; and Y is NH.

Other more preferred compounds have formula I wherein L_1 is -L3-Q-L4-Q'-L5-; Q is $-S(O)_2-$ or -C(O)-; and L_4 is optionally substituted alkenylene.

Other more preferred compounds have formula I wherein L_1 is -L3-Q-L4-Q'-L5-; and L_4 is optionally substituted alkylene.

Other more preferred compounds have formula I wherein L_1 is -L3-Q-L4-Q'-L5-; Q is -C(O)-; Q' is O; and L_4 is optionally substituted alkylene.

Other more preferred compounds have formula I wherein L_1 is -L3-Q-L4-Q'-L5-; L_3 is optionally substituted alkylene; and L_4 is optionally substituted alkenylene.

Other more preferred compounds have formula I wherein Cy_1 is optionally substituted phenyl, optionally substituted thienyl, optionally substituted benzothienyl, optionally substituted isoquinolinyl, optionally substituted indolyl, optionally substituted thienopyridyl, optionally substituted furanyl, optionally substituted pyridyl, or optionally substituted benzimidazolyl.

Other more preferred compounds have formula I wherein Cy_2 is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted imidazolyl, optionally substituted quinolinyl, optionally substituted isoquinolinyl, optionally substituted quinazolinyl, optionally substituted cinnolinyl, optionally substituted azaindolyl, or optionally substituted thienopyridyl.

Still more preferred compounds are selected from

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(1-Amino-isoquinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-4-oxy-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-4-oxy-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-((S)-1-(R)-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(R)-carboxylic acid ethyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-chloro-1H-quinolin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-butyl-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-piperazin-2-one,

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methyl-piperazin-2-one,

(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-ethyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-piperidine-1-carboxamidine,

4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,
4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,
4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-2-(S)-propyl-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,
4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,
1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,
1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-sulfonyl)-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[1-(2-hydroxy-ethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]-piperazin-2-one,
4-(6-Bromo-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-methyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,
1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3, 5-dimethyl-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(R)-carboxylic acid methyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(S)-carboxylic acid methyl ester,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-(R)-hydroxymethyl-3-(S)-methoxymethyl-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)- propyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid amide

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide,

4-[4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)- propyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)- propyl-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)- propyl-piperazin-2-one,

1-(4-Amino-cinnolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(S)-carboxylic acid ethyl ester,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3, 5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3, 5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(S)-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-5 3-chloro-1-aza-inden-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid (2-hydroxy-ethyl)-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,
or a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

Still yet more preferred compounds are selected from
1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,
4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,
4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,
1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,
4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one and
4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-propyl-piperazin-2-one,
or
a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

Preferred intermediates according to this invention have formula II wherein Cy_2 contains at least one nitrogen atom and when Cy_2 is optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted fused phenylcycloalkyl or optionally substituted fused phenylcycloalkenyl, then said nitrogen atom is a basic nitrogen atom.

Other preferred intermediates according to this invention have formula II wherein Z is absent.

Other preferred intermediates according to this invention have formula II wherein R_1, R_{1a}, R_2, R_{2a}, R_4 and R_{4a} are hydrogen.

More preferred intermediates according to this invention are selected from
(2S, 6RS)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester,

(3S,5RS)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(2S, 6R)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester,

(3S, 5S)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one,

(3S, 5R)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one,

4-(2-Oxopiperazin-1-ylmethyl)benzamidine,

1-(2-Aminoquinolin-6-ylmethyl)piperazin-2-one,

1-(1-Aminoisoquinolin-6-ylmethyl)piperazin-2-one,

2-(2-Oxopiperazin-1-ylmethyl)pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester,

2-(5-(±)-Methoxycarbonyl-2-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester,

2-(2-(±)-Methoxycarbonyl-6-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester,

1-(4-Aminoquinazoline-7-ylmethyl)piperazine-2-one,

1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-piperazin-2-one,

4-[3-(2-Oxo-piperazin-1-yl)-propyl]-piperidine-1-carboxylic acid tert-butyl ester,

1-(4-Amino-quinazoline-7-ylmethyl)-3-methoxymethyl-piperazine-2-one,

1-(4-Aminoquinazoline-7-ylmethyl)-3-butyl-piperazine-2-one,

1-(4-Aminoquinazoline-7-ylmethyl)-3-ethyl-piperazine-2-one,

1-(4-Aminoquinazoline-7-ylmethyl)-3-propyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-ethoxymethyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-methyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-benzyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-(1-methoxyethyl)-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3,3-dimethyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-isopropyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-isobutyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-(2-methoxyethyl) l-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-methoxymethyl-6-methyl-piperazine-2-one,

(3S,5RS)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

1-(4-Chloroquinolin-7-ylmethyl)-piperazin-2-one,

1-(4-Chlorocinnolin-7-ylmethyl)-piperazin-2-one,

1-(4-Chloroquinolin-7-ylmethyl)-3-(S)-methylpiperazin-2-one,

1-[2-(Pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-[2-{(Methyl)-(pyridin-4-yl)-amino}-ethyl]-piperazin-2-one trifluroacetate,

1-[2-(3-Methylpyridin-4-yl-amino)-ethyl]-piperazin-2-one,

1-[2-(Pyridazin-4-ylamino)-ethyl]-piperazin-2-one,

4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propenyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester,

4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester

4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester.

4-(Benzyloxycarbonyl)-1-(2-pyrrolo[3,2-c]pyridin-1-ylethyl)-piperazin-2-one,

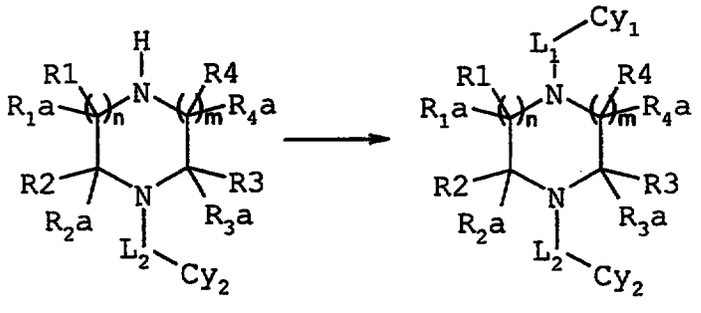
(±)-1-(3-Amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester and

(±)-1-(3-Amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid.

Preparation of the Compounds of the Invention

A general route to the compounds of this invention wherein A is N and R_1, R_{1a}, R_2, R_{2a}, R_3, R_{3a}, R_4, R_{4a}, L_1, L_2, Cy_1, Cy_2, m and n are defined herein is outlined in Scheme 1.

Scheme 1



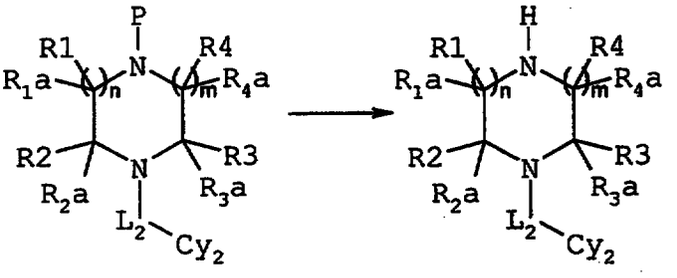
II I

As shown in Scheme 1, coupling of a compound of formula II with a sulfonyl chloride, an alkyl halide, an acid or an activated derivative thereof such as an anhydride or acid chloride, an isocyanate, chloroformate or activated sulfamyl ester in an appropriate solvent generates the compound of formula I

in which the L_1-Cy_1 portion is a sulfonamide, alkyl amine, amide, urea, carbamate or sulfamyl urea respectively. Sulfonamide formation is accomplished with a base such as a trialkylamine in an inert solvent such as dichloromethane, THF or acetonitrile at about 0 °C to about 100 °C in the presence or absence of an activating agent such as dimethylaminopyridine (DMAP). Alkyl amine formation can be achieved with a suitable base such as K_2CO_3 or trialkylamine in an appropriate solvent such as DMF or acetonitrile at about 0 °C to about 100 °C. Amide, urea, carbamate and sulfamyl urea formation can be conducted with acids and coupling reagents such as EDC or TBTU or with any variant of reactive acid derivatives and the use of an appropriate base additive such as triethylamine, N-methylmorpholine or diisopropylethylamine.

The preparation of the compound of formula II wherein R_1, R_{1a}, R_2, R_{2a}, R_3, R_{3a}, R_4, R_{4a}, L_2, Cy_2, m and n are defined herein is outlined in Scheme 2.

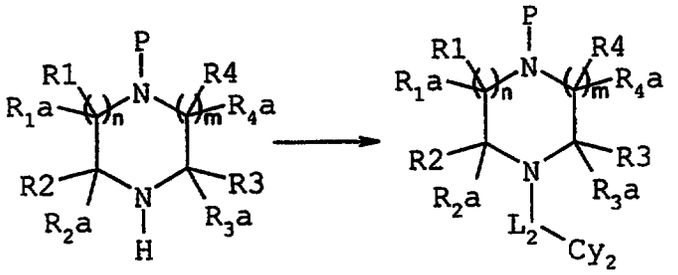
Scheme 2



As shown in Scheme 2, the compound of formula II is prepared by removing a nitrogen protecting group P from the compound of formula 1. In a preferred aspect, P is an alkyl, aralkyl or aryl carbamate moiety which is removed using strong acid, strong base or catalytic hydrogenation in an appropriate solvent such as methanol or ethanol.

The preparation of the compound of formula 1 wherein R_1, R_{1a}, R_2, R_{2a}, R_3, R_{3a}, R_4, R_{4a}, L_1, L_2, Cy_1, Cy_2, m and n and P are defined herein is outlined in Scheme 3.

Scheme 3

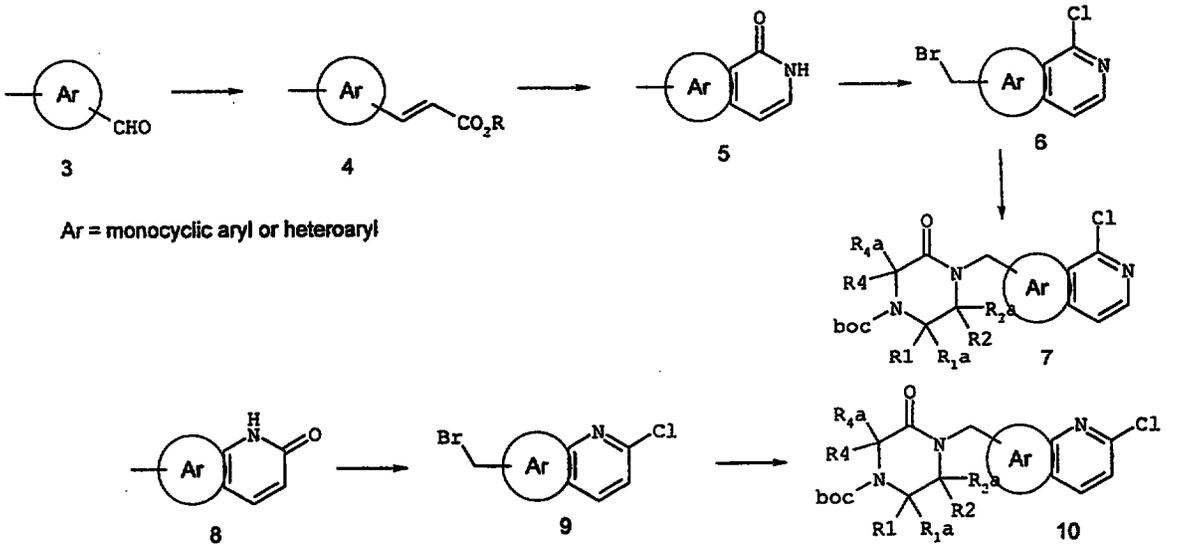


2 1

As shown in Scheme 3, the compound of formula 1 is obtained by coupling a compound of formula 2 with an appropriate Cy_2-L_2-LG group wherein LG is a leaving group such as chloro, bromo, iodo, or optionally substituted lower alkylsulfonyloxy or arylsulfonyloxy in an inert organic solvent such as THF, Et_2O or DMF in the presence of a strong base such as NaH, lithium hexamethyldisilylazide or lithium diisopropylamine. In a preferred aspect, P is an alkyl, aralkyl or aryl carbamate group.

The preparation of intermediate compounds of formula 7 and 10 are outlined in Scheme 4.

Scheme 4



Ar = monocyclic aryl or heteroaryl

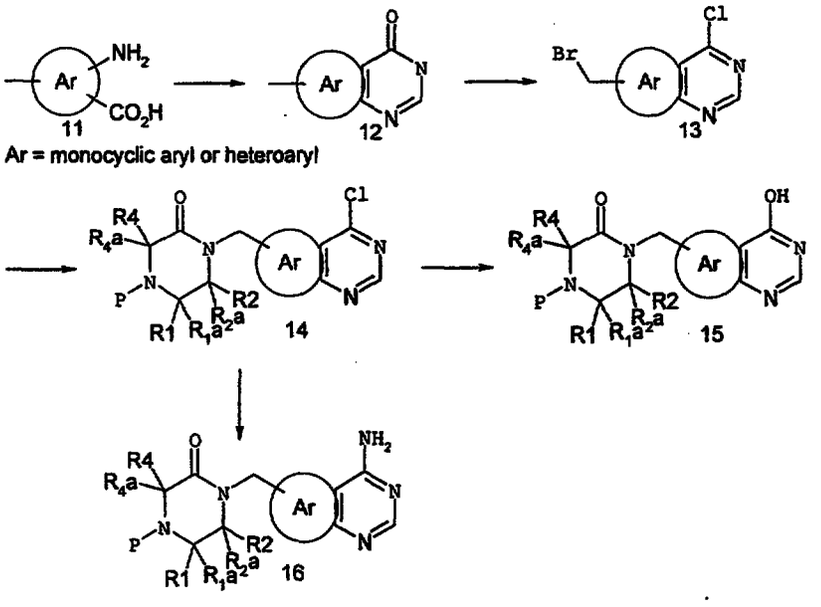
As shown in Scheme 4, reacting a compound of formula 3 with an appropriate malonic acid in a polar solvent such as pyridine or ethanol and a base such as piperidine or pyridine at reflux provides a compound of formula 4 wherein R is H. Alternatively, a compound of formula 3 may be reacted with a suitable Wittig or Horner-Emmons reagent in an inert solvent such as THF to give a compound of formula 4 wherein R is lower alkyl. When R is lower alkyl, the ester is hydrolyzed to the corresponding carboxylic acid (R is H) by an appropriate strong acid or alkali base. The corresponding acid is

converted to the acid chloride using standard methods such as thionyl chloride or is converted to the mixed anhydride in a polar solvent such as acetone or THF to form an activated acyl compound. The activated acyl compound is then treated with a solution of NaN_3 in water at about -10 °C to about 25 °C to yield the corresponding acyl azide. The acyl azide compound is then heated slowly in an inert solvent such as benzene or toluene at about 60 °C to about 110 °C then concentrated in vacuo and heated in a higher boiling inert solvent such as 1,2-dichlorobenzene or phenyl ether at about 180 °C to about 240 °C with a catalyst such as iodine or tributylamine to obtain a compound of formula 5. Alternatively the acyl azide compound can be added directly to a high boiling inert solvent such as phenyl ether at about 190 °C to about 240 °C with a catalyst such as iodine or tributylamine to obtain the compound of formula 5.

A compound of formula 8, prepared as described in Syn., 739 (1975), which is incorporated herein by reference, or formula 5 above may be chlorinated using standard methods such as $POCl_3$ or $POCl_3/PCl_5$ and halogenated using standard conditions such as N-halosuccinimide and benzoyl peroxide in an inert solvent such as carbon tetrachloride to give the corresponding chloro-halomethyl compounds 6 and 9, respectively.

The preparation of aminoquinazoline, quinazolinone or amino-thienopyrimidine intermediates is outlined in Scheme 5.

Scheme 5

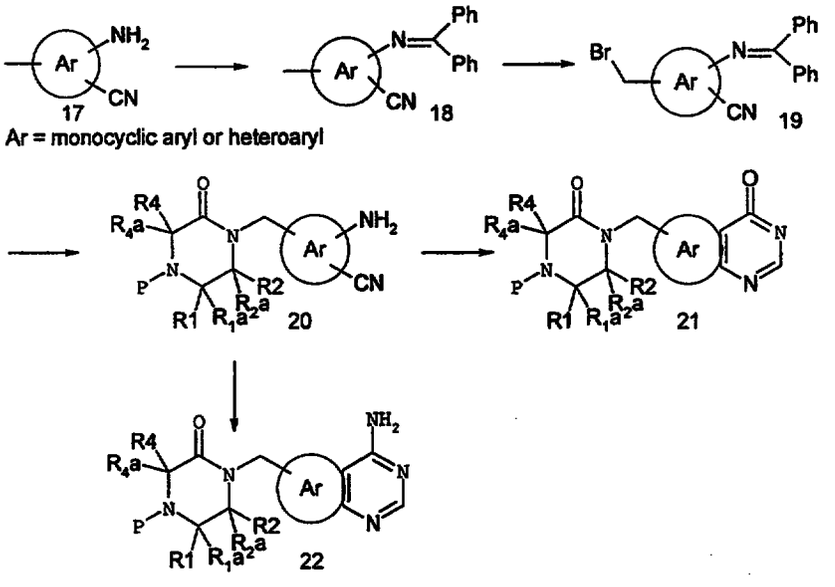


As shown in Scheme 5, an aminoheteroaryl carboxylic acid or an aminoarylcarboxylic acid 11 in which the amino and carboxylic acid are adjacent is treated with formamidine under heat to form the corresponding quinazolinone or thienopyrimidinone 12. The quinazolinone or thienopyrimidinone 12 is

then converted to the chloroquinazoline or chlorothienopyrimidine using a chlorinating reagent such as $P(O)Cl_3$ and heat. The chloroquinazoline or chlorothienopyrimidine is brominated at the benzylic carbon using radical bromination conditions. Alternatively, a chloroquinazoline or chlorothienopyrimidine, containing a hydroxy-methylene group is converted to the corresponding bromide using CBr_4/PPh_3; or PBr_3 conditions. The bromide 13 is then reacted with the anion of the ring nitrogen of compounds of formula 2, formed using NaH, $LiN(SiMe_3)_3$, $NaN(SiMe_3)_3$, LDA, lithium alkoxides, sodium alkoxides or an appropriate base, in an inert solvent such as THF, DMF, ether, or DME. This yields compounds of formula 14 in which Cy_2 is a chloro-quinazoline or a chloro-thienopyrimidine. The chloro group is converted to an amino group using NH_3 in ethanol in the presence of a catalytic acid source. Alternatively, the chloro group is converted to a substituted amino using a primary or secondary amine in a solvent. Alternatively, the chloro group is converted to a hydroxy group using acetic acid in water with heating or using a hydroxide source. Alternatively, the chloro is converted to an alkoxy group using an alcoholic solvent with heated in the presence of a base.

An alternative synthesis of quinazolines and thienoquinazolines is outlined in Scheme 6.

Scheme 6.

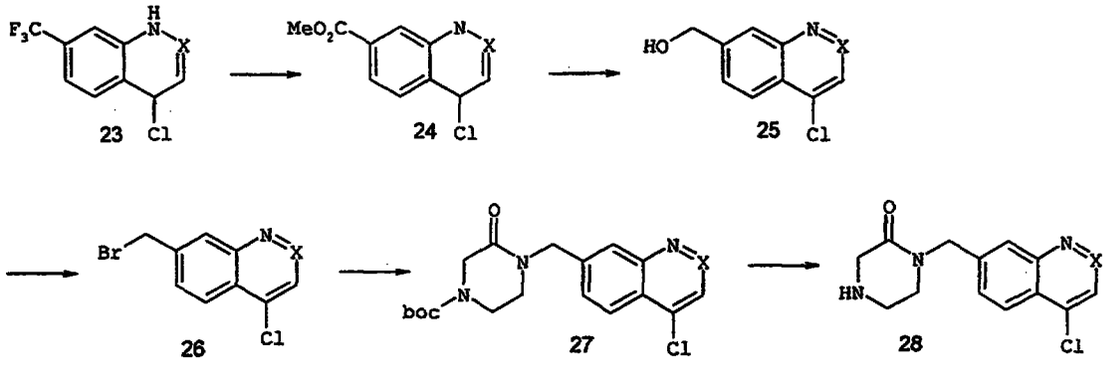


As shown in Scheme 6, an amino-aryl nitrile or an amino heteroaryl nitrile 17 is treated with an aldehyde or ketone under imine forming conditions. The corresponding aryl or heteroaryl imine is brominated using radical bomination with NBS. The bromide is then reacted with the anion of the ring nitrogen of compounds of formula 2, formed using NaH, $LiN(SiMe_3)_3$, $NaN(SiMe_3)_3$, LDA, lithium alkoxides, sodium alkoxides or an appropriate base, in an inert solvent such as THF, DMF, ether, or DME. This yields compounds of formula 20 in which Cy_2 is an imino-aryl nitrile or an imino heteroaryl

nitrile. The imine is deprotected using an acid such as HCl to give the corresponding aniline. The aniline-aryl-nitrile or the aniline-heteroaryl nitrile is converted to the amino-quinazoline or thienopyrimidine using triazine or formamidine. The quinazolinone or thienopyrimidinone 21 is formed using formamide.

The preparation of cinnoline (X = N) and quinoline (X = CH) intermediates is outlined in Scheme 7.

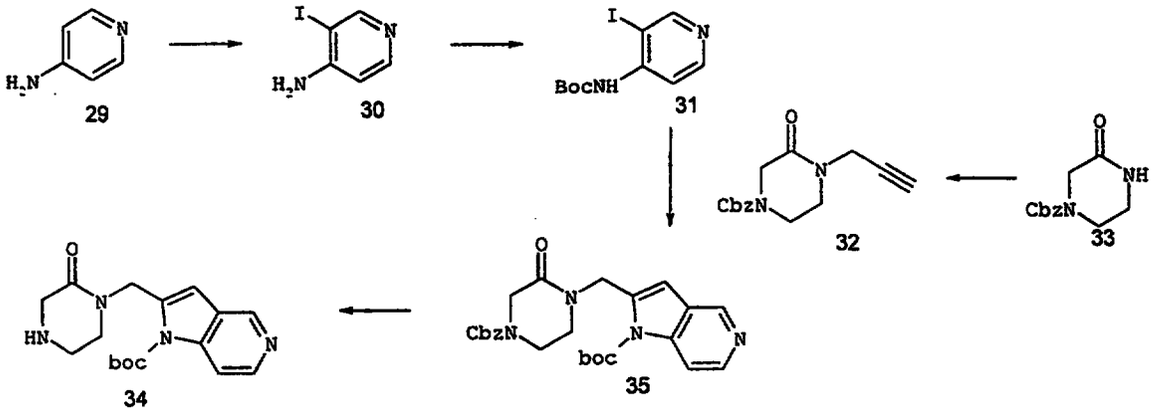
Scheme 7



As shown in Scheme 7, halogenated azaarenes exemplified by 4-chloro-7-trifluoromethylquinoline or cinnoline are treated with H_2SO_4 (70 -95 %) at 180-220 °C for about 16 to 48 hours in a sealed reaction vessel. The solution is cooled, poured into water and neutralized with base to pH ~ 3-4. The product is dissolved in aqueous base and precipitated by acidification to yield 7-carboxy-4-chloroquinoline or cinnoline. This material is converted to the alkyl ester (such as methyl or ethyl) by standard methods. 7-Alkyloxycarbonyl-4-chloroquinoline or cinnoline is dissolved in an anhydrous, aprotic solvent (THF or ether). The solution is cooled (-60 to -95 °C) and treated with a reducing agent such as lithium aluminum hydride. The solution is warmed (approximately -40 to -50 °C) for about 15 to 30 minutes and quenched with a solvent such as ethyl acetate. Standard workup gives the product 7-hydroxymethyl-4-chloroquinoline or cinnoline. This material is treated with 45-50 % HBr and heated to about 100-140 °C for about 45 to 90 minutes. After cooling and standard workup 7-bromomethyl-4-chloroquinoline or cinnoline is obtained.

The preparation of pyrrolopyridine derivatives is outlined in Scheme 8.

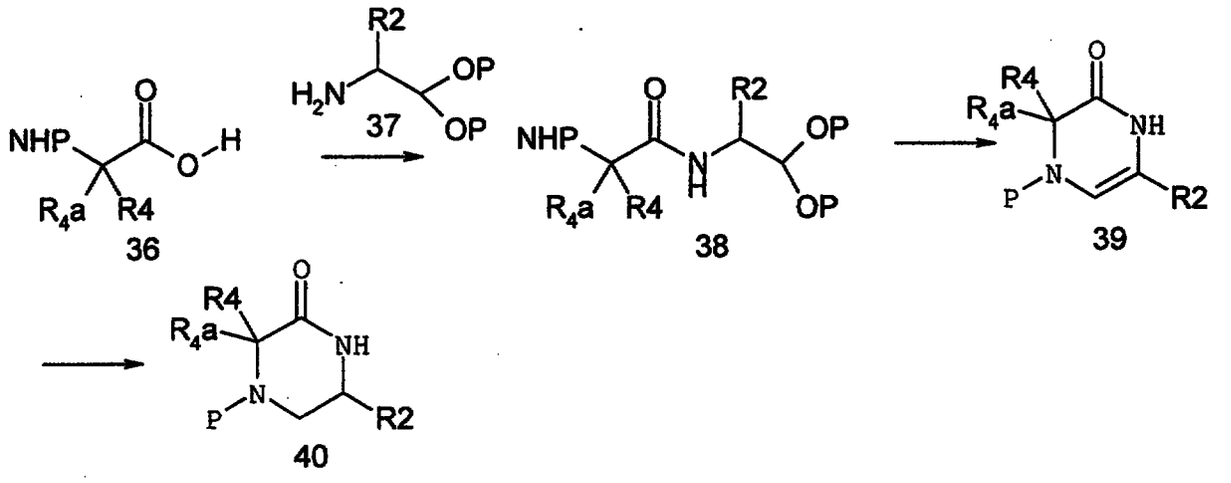
Scheme 8



As shown in Scheme 8 pyrrolopyridine derivatives are prepared by alkylation of a suitably protected oxopiperazine with propargyl bromide in the presence of a base such as sodium hydride. The resulting alkyne is heated (100-120 °C) with a halopyridine optionally substituted with hydroxy, alkoxycarbonylamino, or sulfhydryl, a catalyst such as $Pd(PPh_3)_2Cl_2$, copper iodide and triethylamine in a suitable solvent such as acetonitrile in a sealed vessel or in DMF for 2-20 hours. When the pyridine is substituted with a hydroxyl moiety furopyridines are isolated directly. If the pyridine is substituted with an alkoxycarbonylamino moiety, additional treatment with DBU at about 60 °C in DMF yields pyrrolopyridines. Subsequent carbamate deprotection using transfer hydrogenation conditions such as Pd black in formic acid yields the desired oxopiperazine furopyridines or pyrrolopyridine-1-carboxylic acid alkyl ester derivatives. After further reaction with the L_1-Cy_1 group, an additional deprotection step such as Boc removal using, for example, TFA, HCl is required for generating the oxopiperazine pyrrolopyridines.

The preparation of the compound of formula 40 are shown in Scheme 9.

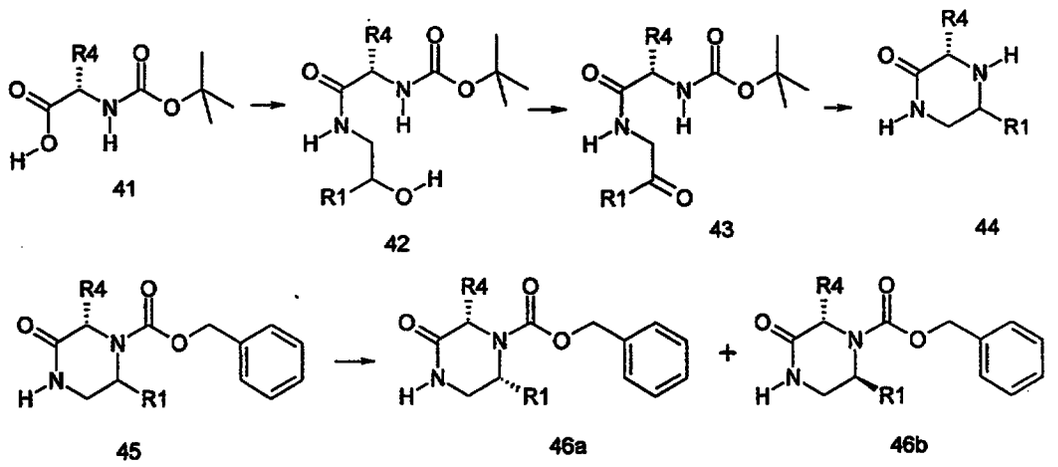
Scheme 9



As shown in Scheme 9, compounds of formula 40 are prepared from an appropriately protected mono- or di- substituted amino-acid. To this is added an amino-acetaldehyde, protected as an acetal derivative, under standard peptide coupling procedures, employing activating reagents such as EDC, TBTU, or BOP. The resulting dipeptidyl moiety is subjected to conditions which remove the acetal, such as acidic conditions (TsOH). The resulting cyclic material is reduced using hydrogenating conditions to yield compounds of formula 40. This reduction, alternatively can be carried out using a reagent which acts as a hydride source.

The preparation of compounds of formula 46a and b is shown scheme 10.

Scheme 10.

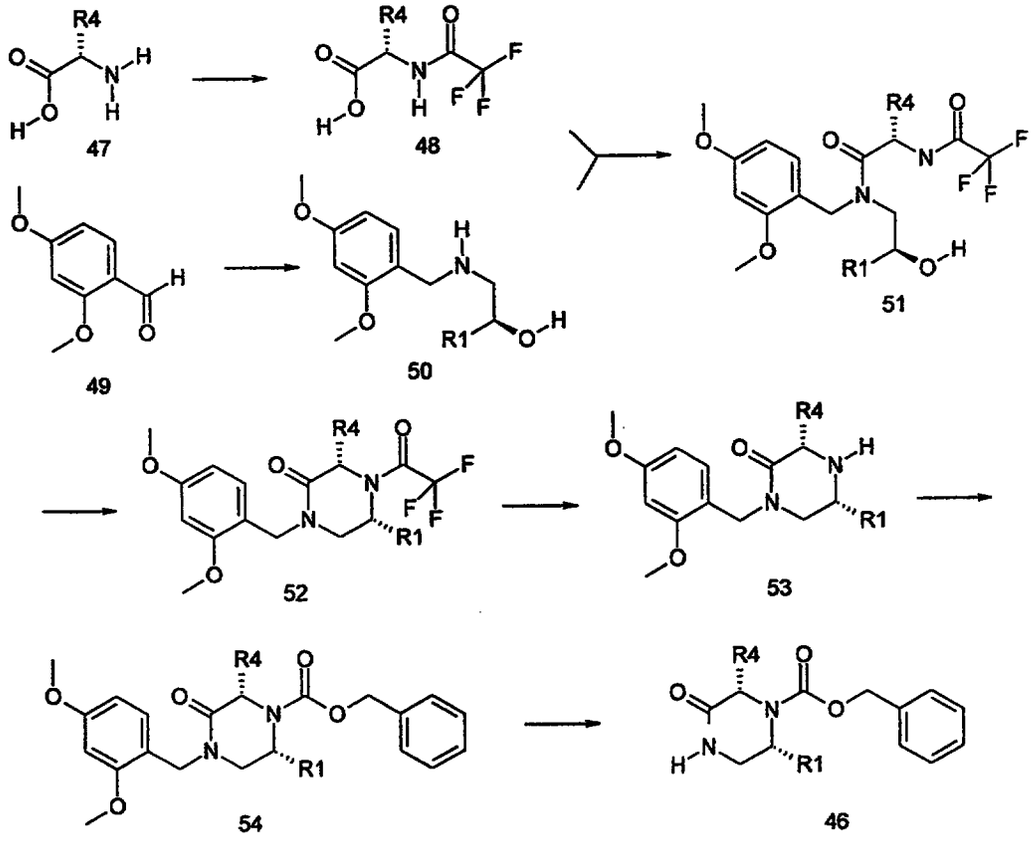


As shown in Scheme 10, a protected amino acid is coupled to a beta-aminoalcohol using standard peptide coupling procedures as describe above. The alcohol is then oxidized to a ketone using, for example, Swern oxidation conditions. The protecting group is removed and the resulting compound

is reduced under hydrogenation conditions to give the 2-piperidinone. The free amine can be reprotected and diastereomers are separated by chromatographic methods, or in some cases by recrystallization.

A chiral synthesis of compounds of formula 46 is shown in Scheme 11.

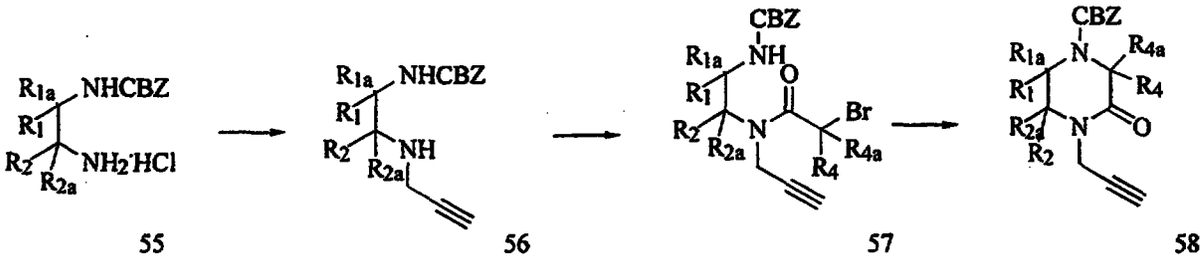
Scheme 11



As shown in Scheme 11, an amino acid is protected as its trifluoroacetate derivative using trifluoroacetic anhydride and a base. An amino-alcohol is derivatized via reductive amination conditions using a benzaldehyde derivative, such as 2,4-dimethoxybenzaldehyde. The resulting secondary amine is then coupled to an amino-acid protected as a trifluoroacetate using standard peptide coupling procedures. Ring closure is then accomplished by utilizing Mitsinobu conditions. The trifluoroacetate group is removed under basic conditions, and the amide of the ring is deproteced using an aqueous solution of potassium persulfate and sodium phosphate and heat. All possible enantiomers of piperazin-2-one can be made from the corresponding amino-alcohol and amino acid as shown in scheme 2c.

The preparation of the compound of formula 58 wherein R_1, R_2, R_{2a} ,R_4 and R_{4a} are hydrogen and R_{1a} is carbomethoxy, methoxymethyl, or a protected hydroxymethyl group is shown in Scheme 12.

Scheme 12

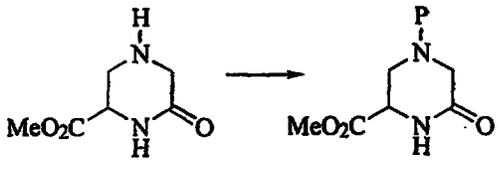


55 56 57 58

As shown in Scheme 12, alkylating a compound of formula 55 with propargyl bromide in the presence of an amine base such as triethylamine provides the compound of formula 56. Coupling with bromoacetic acid using a standard reagent such as DCC gives the compound of formula 57 which can be cyclized using a non-nucleophilic strong base such as NaH in a solvent such as THF to yield the desired compound of formula 58.

The preparation of a compound of formula 59 is outlined in Scheme 13.

Scheme 13

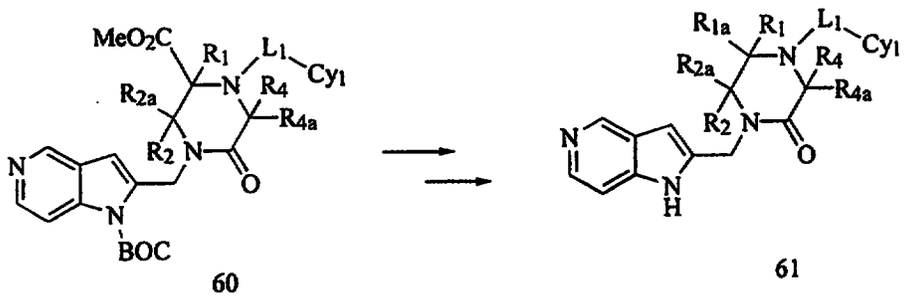


59

As shown in Scheme 13, protection of methyl 6-oxopiperazine-2-carboxylate (Aebischer, B., Helv. Chim. Acta 1989, 72, 1043-1051) using, for example, benzyl chloroformate or allyl chloroformate under standard conditions provides compound 59. Alkylation of 59 with propargyl bromide using a strong base such as NaH in polar solvents as THF or DMF provides the compound of formula 58.

The preparation of a compound of formula 61 wherein R_1, R_2, R_4, R_{4a}, L_1 and Cy_1 are defined as above and R_{1a} or R_{2a} are independently carboxy, acetamido or hydroxymethyl is outlined in Scheme 14.

Scheme 14

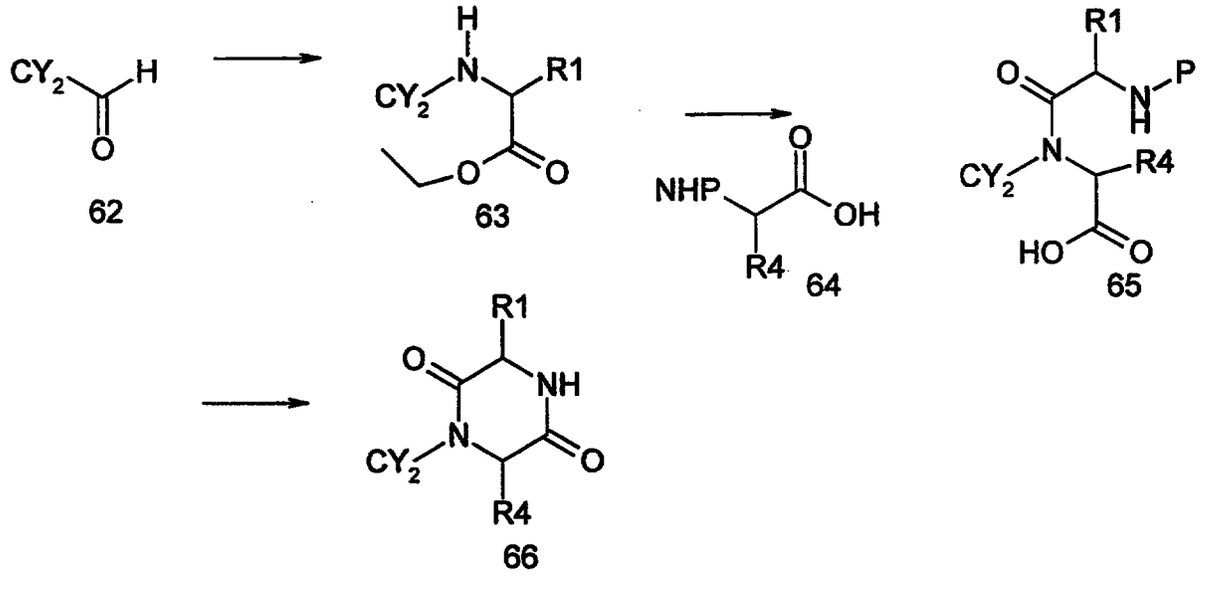


60 61

As shown in Scheme 14, the compound of formula 61 is prepared by hydrolysis of the ester using a base such as NaOH or LiOH to yield the acid, coupling the corresponding acid with a primary or secondary amine or ammonia using standard coupling reagents such as TBTU or EDC and reduction of the ester using a reducing agent such as $NaBH_4$ to yield hydroxymethyl.

The preparation of diketopiperazine compounds formula 66 in which R_1 and R_{1a} together and R_3 and R_{3a} together are oxygen are prepared as outlined in Scheme 15.

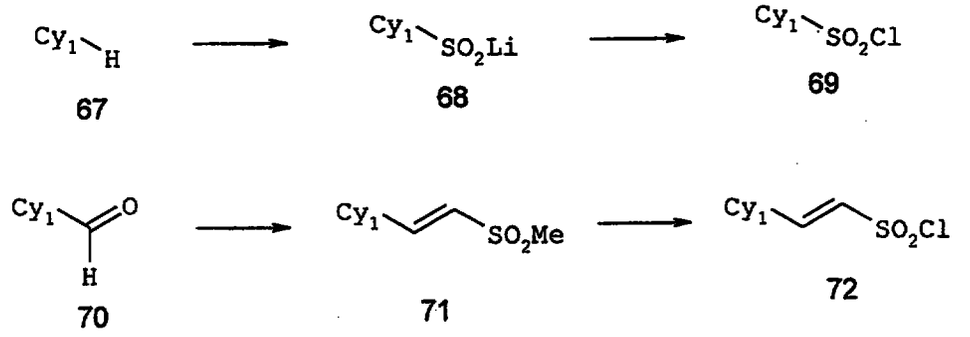
Scheme 15



As shown in Scheme 15, an aldehyde containing the Cy_2 group is condensed with an amino acid ester under reductive amination conditions. The resulting secondary amine is then coupled to an N-protected amino acid. The resulting dipeptide is deprotected which in general results in cyclization to the Cy_2 diketopiperazine. Alternatively for cases which do not cyclize, diketopiperazine formation can be achieved using a peptide coupling reagent such as EDC, TBTU, or BOP.

The preparation of sulfonyl chloride intermediates is outlined in Scheme 16.

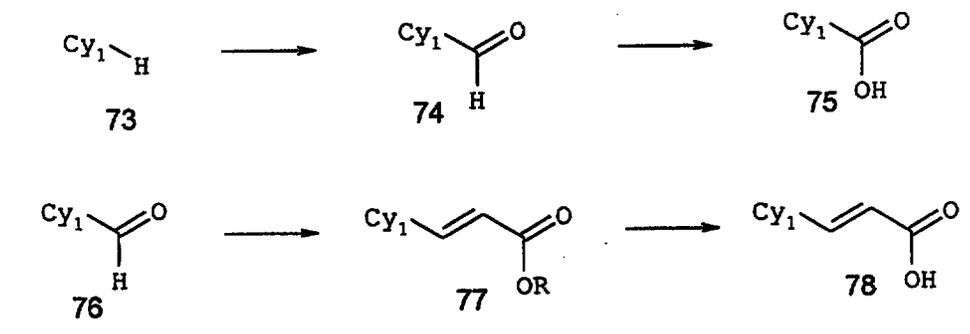
Scheme 17



As shown in Scheme 16, Cy_1 substituted sulfonyl chlorides are prepared by treatment of the appropriate aryl and heteroaryl compounds with a strong base such as n-BuLi at -78 °C followed by the addition of SO_2 gas and treatment of the lithium heteroaryl sulfonate with a chlorinating agent such as NCS or SO_2Cl_2 or, alternately, by homologation of the appropriate aryl and heteroaryl aldehydes using, for example, ethylmethanesulfonate and ethylchlorophosphonate.

The preparation of intermediate compounds of formula Cy_1-CO_2H is outlined in Scheme 17.

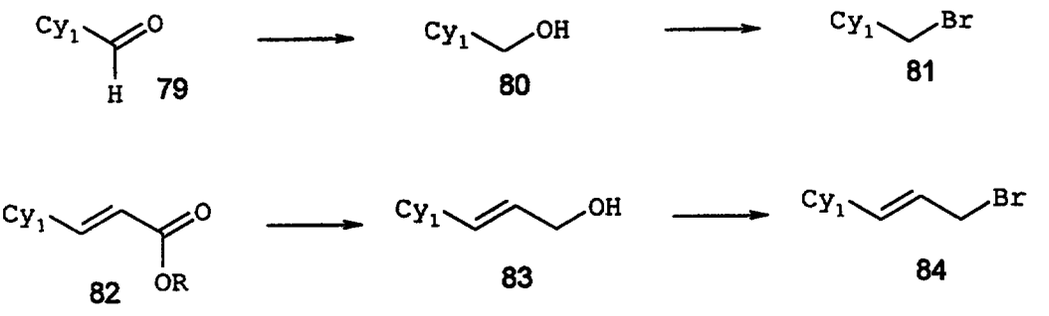
Scheme 17



As shown in Scheme 17, the requisite Cy_1 acids as defined above can be obtained by oxidation of the corresponding alcohols or the aldehydes using, for example, MnO_2, PDC or $AgNO_3$ in an appropriate solvent such as CH_2Cl_2 or H_2O/EtOH. The Cy_1 substituted aryl and heteroaryl groups can be functionalized by deprotonation methods using an appropriate non-nucleophilic base such as n-BuLi in an appropriate solvent such as Et_2O or THF and quenching with an appropriate carbonyl electrophile such as DMF, CO_2 or alkyl chloroformate. Alternatively, the acids can also be generated by hydrolysis of the corresponding esters using, for example, NaOH or LiOH. For example, in the acrylic esters, the Cy_1-(alkenylene)- groups as defined above are generated by homologation of the Cy_1 aldehydes using the usual Wittig type or Horner-Emmons type reagents in an appropriate solvent such as CH_2Cl_2 or THF.

The preparation of Cy_1 alkyl and alkenyl halides is outlined in Scheme 18.

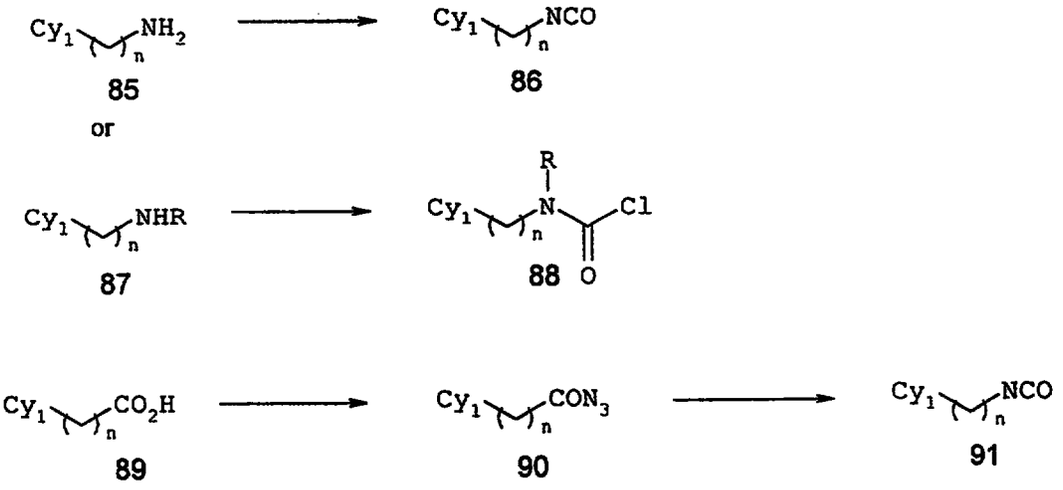
Scheme 18



As shown in Scheme 18, Cy_1 alkyl and alkenyl halides as defined above can be prepared by halogenation of the corresponding alcohols using either NBS, CBr_4 or PBr_3 under standard solvent conditions. The alcohols are generated by reduction of the corresponding aldehydes or esters using $NaBH_4$ or DIBAL in an appropriate solvent.

The preparation of Cy_1 isocyanate intermediates is outlined in Scheme 19.

Scheme 19

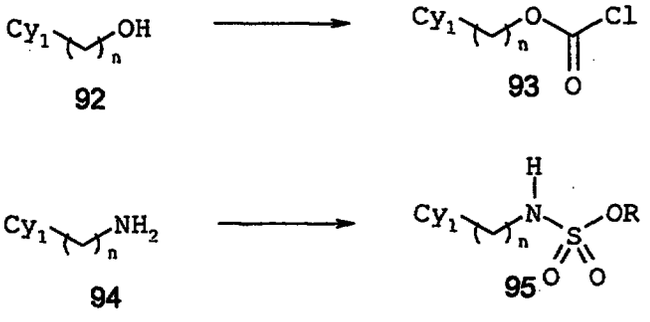


As shown in Scheme 19, Cy_1 isocyanates are obtained by chlorocarbonylation methods using phosgene or triphosgene in an appropriate solvent such as CH_2Cl_2 with an appropriate base additive such as triethylamine or pyridine on the corresponding primary or secondary amines. Alternatively, the isocyanates can also be generated by Curtius rearrangement in an appropriate solvent such as toluene, p-dioxane or DMF of the corresponding Cy_1 carbonyl azides. The carbonyl azides, in turn, are derived

from the corresponding carboxylic acids using either DPPA reagent or by proceeding through the mixed anhydride via an alkyl chloroformate reagent in an appropriate solvent such as DMF or acetone and using an appropriate base additive such as treithylamine.

The preparation of Cy_1 chloroformate intermediates is outlined in Scheme 20.

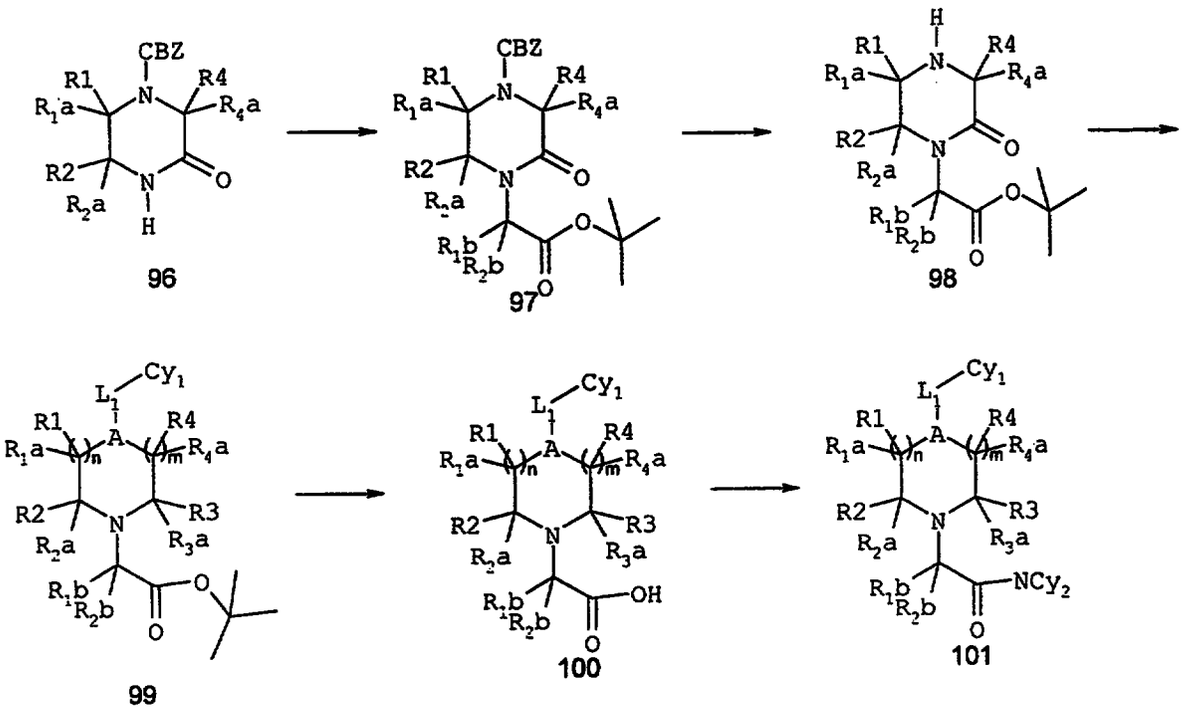
Scheme 20



As shown in Scheme 20, Cy_1 chloroformates are obtained by chlorocarbonylation methods using reagents such as phosgene, triphosgene or 1,1'-carbonyldiimidazole in an appropriate solvent such as CH_2Cl_2 on the corresponding alcohols. Activated sulfamyl esters are prepared from the corresponding amines using catechol sulfate in an appropriate solvent.

The preparation of acetamido compounds of this invention is outlined in Scheme 21.

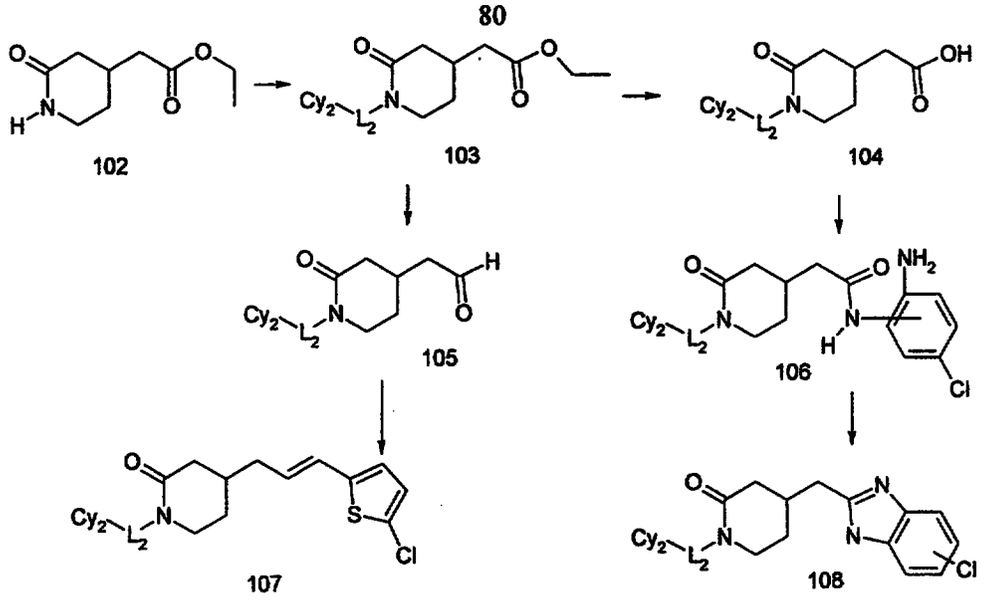
Scheme 21



As shown in Scheme 21, alkylation of piperazin-2-one 96 is achieved with a strong base such as NaH and a t-butyl ester of haloacetic acid to give the acetate 97. Pd-catalyzed hydrogenation effectes removal of the CBZ group from the acetate 97 to give amine 98 which is converted to the compound 99 as described in Scheme 1 above. Hydrolysis of t-butyl ester 99 is accomplished using, for example, TFA/CH_2Cl_2. The resulting acid 100 is coupled with the optionally protected amine $HNCy_2$ under typical amide bond formation conditions to give the acetamide 101.

The preparation of compounds of this invention wherein Cy_1 is benzimidazol-2-yl is outlined in Scheme 22.

Scheme 22



Piperidin-2-one 102 is alkylated as described above to give the ester 103 which is hydrolyzed to give the acid 104 or reduced to give aldehyde 105. Coupling of the acid 104 and amines affords amide 106 which is cyclized with acetic anhydride to give the compound 108. Wittig-coupling of aldehyde 105 produces compound 107.

This invention is further exemplified but not limited by the following examples which further illustrate the preparation of the compounds of this invention. The starting materials and intermediates are prepared by the application or adaptation of known methods, for example methods described herein or their obvious equivalents.

EXAMPLE 1. 6-Chlorobenzo[b]thiophene-2-sulfonyl chloride.

A. 1-Chloro-3-(2,2-dimethoxyethylsulfanyl)benzene.

To a solution of 3-chlorothiophenol (2.4 g, 16.6 mmol) in THF (200 mL) at 0°C is added bromoacetaldehyde dimethyl acetal (2.8 g, 16.6 mmol). To the solution is added sodium hydride (60% mineral oil dispersion, 0.70 g, 17.4 mmol). The reaction is stirred for 16 hours, and then is quenched by the addition of saturated NH_4Cl (aq.). The solution is diluted with EtOAc. The organic layer is washed with a saturated NaCl (aq.). The organic layer is dried over $MgSO_4$, filtered and concentrated. The crude product is purified by column chromatography eluting with hexanes. The title compound (3.7 g, 15.9 mmol) is obtained as an oil. ^1H NMR ($CDCl_3$, 300MHz) δ 7.32 (m, 1H), 7.25 (m, 1H), 7.12 (m, 1H), 4.47 (m, 1H), 3.07 (s, 3H), 3.02 (s, 3H).

B. 4-Chlorobenzo[b]thiophene and 6-Chlorobenzo[b]thiophene.

A solution containing polyphosphoric acid (8 g) and chlorobenzene (50 mL) is heated at reflux. A solution containing 1-chloro-3-(2,2-dimethoxyethylsulfanyl)benzene (2.7 g, 11.6 mmol) in chlorobenzene (5 mL) is added dropwise to the refluxing polyphosphoric acid solution. After 6 hours, the solution is cooled to ambient temperature. The solution is diluted with CH_2Cl_2 and washed with water and saturated NaCl (aq.). The organic layer is dried over $MgSO_4$, filtered and concentrated. The crude product is purified by column chromatography eluting with hexanes to yield the title compounds (2.4 g, 9.0 mmol) as a 1:1 isomeric mixture. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.88 (m, 1H), 7.75 (m, 2H), 7.42 (m, 2H). MS (EI): m/z 168, 170 (M+), Cl pattern.

C. 4-Chlorobenzo[b]thiophene-2-sulfonyl chloride and 6-Chlorobenzo[b]thiophene-2-sulfonyl chloride.

To a solution of 4-chloro-benzo[b]thiophene and 6-chlorobenzo[b]thiophene (11.8 g, 88.1 mmol), in 400 mL of THF at -78°C is added n-BuLi (55 mL of a 1.6M solution in hexanes, 88.1 mmol). After 15 minutes, the solution is added by cannula to a precooled (-78°C) solution of SO_2 (200 g) in 100 mL of THF. After addition, the solution is allowed to warm to ambient temperature. After 0.5 hour, the solution is concentrated. The residue is suspended in hexanes (400 mL) and is cooled to 0°C. To the solution is added SO_2Cl_2 (12.5 g, 92.5 mmol). After stirring for 15 minutes, the solution is concentrated. The residue is dissolved in EtOAc. The organic solution is washed with saturated NH_4Cl (aq.), H_2O and saturated NaCl (aq.). The organic layer is dried over $MgSO_4$, filtered and concentrated. The crude product is dissolved in CH_2Cl_2 and filtered through a plug of silica gel. The crude product is purified by column chromatography eluting with hexanes to yield the title compound as well as 4-chlorobenzo[b]thiophene-2-sulfonyl chloride as white solids.

4-Chlorobenzo[b]thiophene-2-sulfonyl chloride: ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.32 (m, 1H), 7.81 (m, 1H), 7.53 (m, 2H).

6-Chlorobenzo[b]thiophene-2-sulfonyl chloride: ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.11 (s, 1H), 7.88 (m, 2H), 7.50 (m, 1H).

EXAMPLE 2. 5'-Chloro-[2,2']bithiophenyl-5-sulfonyl chloride.

A. 5-Chloro-[2,2']bithiophene.

The title compound is prepared from 2-chloro-thiophene according to the procedure described in Bull. Chem. Soc. Japan, 1979, 1126. The crude product is purified by column chromatography eluting with a gradient of 5% EtOAc/hexanes to 10% EtOAc/hexanes to afford a white solid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.24 (m, 1H), 7.11 (d, 1H), 7.03 (dd, 1H), 6.94 (d, 1H), 6.83 (d, 1H). MS (EI) [M+]= 200, 202, Cl pattern.

B. 5'-Chloro-[2,2']bithiophenyl-5-sulfonyl chloride.

The title compound is prepared as described in Example 1, Part C using 5-chloro-[2,2']bithiophene in place of 6-chloro-benzo[b]thiophene. The crude product is purified by column chromatography eluting with a gradient of 5% EtOAc/hexanes to 10% EtOAc/hexanes to give a white solid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.76 (d, 1H), 7.14 (d, 1H), 7.09 (d, 1H), 6.92 (d, 1H). MS (EI): m/z 298, 300 (M+), Cl pattern.

EXAMPLE 3. 2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl chloride.

A. 2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid ethyl ester.

n-Butyllithium (53.1 mL, 2.5M solution in hexanes) is added dropwise to a solution of ethylmethanesulfonate (12.9 mL, 0.12 mol) in THF (300 mL) at -78°C. The reaction mixture is stirred for 15 min then ethylchlorophosphonate (9.9 mL, 0.07 mol) is added dropwise. The solution is stirred at -78°C for 30 minutes and then heated to 50°C for 1 hour. The reaction mixture is then cooled to -78°C and stirred for 1 h then 5-chlorothiophenecarboxaldehyde (7.1 mL, 0.07 mol) is added dropwise. The reaction mixture is allowed to slowly warm to RT overnight. Water (30 mL) is added to the mixture and stirred for 15 min then concentrated in vacuo. The residue is taken up in CH_2Cl_2 and washed with water, brine, dried over $MgSO_4$, filtered and concentrated to dryness. The crude product is purified by column chromatography eluting with 5% EtOAc/hexanes to give title product (11.3 g, 0.04 mol) as an oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.51 (d, 1H), 7.10 (d, 1H), 6.91 (d, 1H), 6.42 (d, 1H), 4.20 (q, 2H), 1.40 (t, 3H).

B. 2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl chloride.

Tetrabutylammonium iodide (16.3 g, (44.2 mmol) is added to a solution of 2-(5-chloro-thiophen-2-yl)-ethenesulfonic acid ethyl ester (11.3 g, 40.2 mmol) in acetone (100 mL) at room temperature. The mixture is heated to reflux and stirred overnight then cooled to RT and conconcentrated in vacuo. The residue is taken up in CH_2Cl_2 then washed with water and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated to dryness to give an oil (18.74 g, 40.2 mmol) which is taken on to the next step without further purification. Sulfuryl chloride (7.1 mL, 88.5 mmol) is added to a solution of triphenylphosphine (21.0 g, 86.42 mmol) in CH_2Cl_2 at 0°C . The ice bath is then removed and the product (18.74 g, 40.2 mmol) from the above reaction is added. After 2 h, the reaction mixture is concentrated in vacuo and the product purified by column chromatography eluting with 10% EtOAc/Hexanes to give the title compound (6.4 g, 26.3 mmol) as an off-white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70 (d, 1H), 7.23 (d, 1H), 7.00 (d, 1H), 6.91 (d, 1H).

EXAMPLE 4. 3-Chlorobenzyl sulfamyl catechol.

To a solution of 3-chlorobenzylamine (0.14 g, 1.0 mmol) in 3 mL of DMF is added Et_3N (0.10 g, 1.5 mmol). The solution is cooled to 0°C. Catechol sulfate (0.172 g, 1.0 mmol) is added. The solution is warmed to ambient temperatures. After 2.5 h, 30 mL of EtOAc is added. The solution is washed with 5% HCl, H_2O and saturated NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated to give the title compound (0.30 g, 0.97 mmol). ^1H NMR (d6-DMSO, 300 MHz) δ 9.94 (s, 1H), 8.82 (m, 1H), 7.41 (m, 4H), 7.19 (d, 1H), 7.10 (m, 1H), 6.95 (d, 1H), 6.79 (m, 1H), 4.32 (AB, 2H).

EXAMPLE 5. 2-Bromomethyl-6-chlorobenzo[b]thiophene.

A. 6-Chlorobenzo[b]thiophene-2-carboxaldehyde.

To a solution of 6-chlorobenzo[b]thiophene (1.0 g, 5.93 mmol) in THF (60 mL) at -78°C is added a 1.6 M solution of n-BuLi in THF (3.9 mL, 6.23 mmol). After 10 minutes, 0.5 mL of DMF is added. The solution is stirred for 0.5 hours, then allowed to warm to ambient temperature. The solution is poured into a solution of saturated NH_4Cl. The solution is diluted with ether and the layers are separated. The organic layer is washed with H_2O and saturated NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated. The title compound is obtained as a white solid. MS (EI): m/z 196 (M+).

B. 6-Chlorobenzo[b]thiophen-2-yl)methanol.

To a solution of 6-chlorobenzo[b]thiophene-2-carboxaldehyde in THF at 0°C is added $NaBH_4$. After 1 hour, the solution is diluted with saturated NH_4Cl and ether. The organic layer is washed with H_2O and saturated NaCl, dried over $MgSO_4$, filtered and concentrated. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.82 (s, 1H), 7.60 (d, 1H), 7.40 (m, 2H), 4.91 (AB, 2H).

C. 2-Bromomethyl-6-chlorobenzo[b]thiophene.

To a solution of 6-chlorobenzo[b]thiophen-2-yl)-methanol (0.2 g, 1.01 mmol) in THF (10 mL) is added triphenyl phosphine (0.34 g, 1.31 mmol) followed by CBr_4 (0.42g, 1.26 mmol). After 3 hours, the solution is concentrated. The product is purified by column chromatography eluting in a gradient of 5% EtOAc/hexanes to 10% EtOAc/hexanes. The product is obtained as a white solid (0.25 g, 0.53 mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.82 (s, 1H), 7.62 (d, 1H), 7.40 (m, 2H), 4.76 (s, 2H).

EXAMPLE 6. 5-Bromomethyl-5'-chloro-[2,2']bithiophenyl.

A. (5'-Chloro-[2,2']bithiophenyl-5-yl)-methanol.

To a solution of 5-chloro-[2,2']bithiophenyl (3.00 g, 14.9 mmol) in 30 mL of THF at 0°C is added n-BuLi (9.8 mL of a 1.6M solution in hexanes, 15.7 mmol) dropwise. DMF (2.30 mL, 30 mmol) is added dropwise and the resulting solution is heated at reflux for 1 hour. The solution is diluted with H_2O and extracted with Et_2O. The organic layer is washed with H_2O and saturated NaCl solution, then dried over $MgSO_4$, filtered and concentrated. The crude aldehyde is dissolved in 40 mL of anhydrous MeOH and sodium borohydride (0.85 g, 22.5 mmol) is added portionwise. The mixture is stirred at room temperature for 10 min, then quenched with water. The mixture is diluted with Et_2O and the layers separated. The organic layer is washed with H_2O, then dried over $MgSO_4$, filtered and concentrated to yield the title compound (2.23 g, 9.66 mmol) which is used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300MHz) δ 6.95 (d, 1H), 6.90 (m, 2H), 6.86 (d, 1H), 4.82 (s, 2H), 1.88 (bs, 1H).

B. 5-Bromomethyl-5'-chloro-[2,2']bithiophenyl.

To a solution of (5'-chloro-[2,2']bithiophenyl-5-yl)-methanol (2.23 g, 9.66 mmol) in 65 mL of CH_2Cl_2 is added bromotrimethylsilane (3.82 mL, 29.0 mmol). After 4 h, the solution is concentrated in vacuo. The crude product is stirred in hot hexanes and filtered. The filtrate is concentrated and the title compound (1.67 g, 5.69 mmol) is obtained as a green solid. ^1H NMR ($CDCl_3$, 300MHz) δ 7.00 (d, 1H), 6.94 (m, 2H), 6.85 (d, 2H), 4.71 (s, 2H).

EXAMPLE 7. 7-Bromomethyl-4-chloroquinazoline.

A. 7-Methyl-3H-quinazolin-4-one.

A solution of 2-amino-4-methylbenzoic acid (31.6 g, 206 mmol) in formamide (60mL) is heated to 130°C for 1 hour, then at 175°C for 3 hours. The solution is poured into 500 mL of ice water. The resulting solid is collected by filtration and further dried under reduced pressure. The title compound (26.2 g, 170 mmol) is obtained as a white solid. MS (EI): m/z 159 (M+).

B. 4-Chloro-7-methyl-quinazoline.

To a solution of 7-methyl-3H-quinazolin-4-one (10.6 g, 69 mmol) in toluene (350mL) is added triethylamine (17.5 g, 173 mmol) followed by phosphorous oxychloride (12.3 g, 80 mmol). The resulting solution is heated to 80°C. After 4 hours, the solution is cooled to ambient temperature. The reaction mixture is poured into 500 mL of water. The layers are separated and the organic layer is washed with H_2O, saturated $NaHCO_3$, and saturated NaCl, dried over $MgSO_4$, filtered and concentrated. The resulting crude product is purified by recrystallization from EtOAc. The title compound is obtained

as a white solid (10g, 56 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.02 (s, 1H), 8.16 (d, 1H), 7.87 (s, 1H), 7.55 (d, 1H), 2.62 (s, 3H).

C. 7-Bromomethyl-4-chloroquinazoline.

To a solution of 4-chloro-7-methylquinazoline (7.0 g, 39 mmol) in carbon tetrachloride (140 mL) is added N-bromosuccinimide (8.0 g, 45 mmol), and benzoyl peroxide (0.8 g, 3.3 mmol). The solution is refluxed for 8 hours. After this time, the solution is filtered. The filtrate is concentrated and the residue is stirred with ether to give the title compound as an off-white solid (5.1 g, 20 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.10 (s, 1H), 8.30 (d, 1H), 8.10 (s, 1H), 7.82 (d, 1H), 4.68 (s, 2H). MS (EI): m/z 237 (M+).

EXAMPLE 8. 3-Bromomethyl-7-chloro-1H-quinolin-2-one.

A. N-(3-Chlorophenyl)-2-methyl-3-phenylacrylamide.

To a solution of 3-chloroaniline (0.98 mL, 9.3 mmol) in CH_2Cl_2 (25 mL) at 0°C is added pyridine (0.78mL, 9.5 mmol). To the resulting solution is added dropwise a solution of α-methyl cinnamic acid chloride (1.6 g, 9.3 mmol) in CH_2Cl_2 (8 mL). After 3 hours, the solution is concentrated. The crude product is purified by column chromatography eluting with 5%EtOAc/hexanes to 10%EtOAc/hexanes. The title compound is obtained as a solid (2.5 g, 9.2 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.95 (m, 1H), 7.73 (s, 1H), 7.46 (m, 1H), 7.33 (m, 6H), 7.22 (m, 1H), 7.03 (m, 1H), 2.13 (s, 3H).

B. 7-Chloro-3-methyl-1H-quinolin-2-one.

To a solution of N-(3-chlorophenyl)-2-methyl-3-phenylacrylamide (2.5 g, 9.2 mmol) in chlorobenzene (50 mL) is added $AlCl_3$ (6.2 g, 46 mmol). The solution is heated to 120°C. After 4 hours, the solution is poured onto ice. The solution is filtered. The organic layer is washed with 1N HCl, H_2O and saturated NaCl. The crude product is purified by column chromatography eluting with 2% MeOH/CH_2Cl_2. The title compound is obtained as a white solid (1.5 g, 7.74 mmol). ^{1}H NMR (d6-DMSO, 300 MHz) δ 11.82 (bs, 1H), 7.73 (s, 1H), 7.52 (m, 1H), 7.21 (m, 2H), 2.08 (s, 3H).

C. 3-Bromomethyl-7-chloro-1H-quinolin-2-one.

The title compound is prepared as described in Example 7, Part C, substituting 7-chloro-3-methyl-1H-quinoline-2-one for 7-methyl-4-chloroquinazoline. The title compound is obtained as a white solid. ^{1}H NMR (d6-DMSO, 300 MHz) δ 12.00 (bs, 1H), 8.17 (s, 1H), 7.72 (d, 1H), 7.29 (m, 2H), 4.58 (s, 2H).

EXAMPLE 4. 6-Bromomethyl-2-chloro-quinoline.

A. 6-Methyl-1H-quinolin-2-one.

The title compound is prepared from p-toluidine and cinnamoyl chloride according to the procedure described in Synthesis 1975, 739. The crude product obtained is triturated in Et_2O/hexanes and filtered to give the title compound as a beige solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 11.60 (bs, 1H), 7.82 (d, 1H), 7.41 (s, 1H), 7.30 (d, 1H), 7.18 (d, 1H), 6.45 (d, 1H), 2.30 (s, 3H).

B. 2-Chloro-6-methylquinoline.

6-Methyl-1H-isoquinolin-2-one (14.6 g, 91.7 mmol) in phosphorus oxychloride (160 mL) is heated at 60°C for 17 hours. The mixture is cooled to room temperature, then concentrated to a beige residue. The residue is diluted with ice water and the pH is adjusted to about 8 by slow addition of 10 N NaOH. The crude product is precipitated out during neutralization of the aqueous solution and the solid is filtered, washed with water and dried. The solid is recrystallize from MeOH to afford the title compound (12.0 g, 67.5 mmol) as a beige solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.02 (d, 1H), 7.92 (d, 1H), 7.60 (s, 1H), 7.58 (d, 1H), 7.33 (d, 1H), 2.53 (s, 3H).

C. 6-Bromomethyl-2-chloro-quinoline.

N-Bromosuccinimide (12.9 g, 72.5 mmol) and benzoyl peroxide (0.33 g, 1.30 mmol) are added to a solution of 2-chloro-6-methyl-quinoline (12.0 g, 67.5 mmol) in carbon tetrachloride (300 mL). The mixture is heated at reflux for 6 hours. At this time, the resulting mixture is cooled to room temperature, filtered, washed with CH_2Cl_2 and concentrated in vacuo. The crude residue is recrystallized from 50% EtOAc/hexanes to yield the title compound (8.80 g, 34.3 mmol) as a beige crystalline solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, 1H), 8.02 (d, 1H), 7.83 (s, 1H), 7.77 (dd, 1H), 7.40 (d, 1H), 4.65 (s, 2H). MS (EI): m/z 256, 258 (M+), Cl pattern.

EXAMPLE 10. 3-Bromomethyl-1,7-dichloro-2H-isoquinoline.

A. 3-(4-Chlorophenyl)-2-methyl-acryloyl azide.

To a solution of 3-(4-chlorophenyl)-2-methyl-acrylic acid (11.2 g, 57 mmol) in 500 mL of acetone at 0°C is added triethyl amine (9.6 mL, 68 mmol) followed by ethyl chloroformate (6.2 mL, 63 mmol). The solution is allowed to warm to ambient temperatures. After 2 h, sodium azide (5.6 g, 86 mmol) in 35 mL of H_2O is added. After addition, the solution is stirred for 2 hours. The solution is diluted with H_2O (100 mL). The resulting solid is collected by filtration giving the title compound as a white solid (11.1 g, 50mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.67 (s, 1H), 3.38 (m, 4H), 2.10 9s, 3H).

B. 7-Chloro-3-methyl-2H-isoquinoline-1-one.

3-(4-Chlorophenyl)-2-methyl-acryloyl azide (11.0 g, 50 mmol) is dissolved in 80 mL of diphenyl ether. The solution is added dropwise to a solution of tributyl amine (11.8 mL, 50mmol) in 170 mL of diphenyl ether at 210°C. After 4 hours., the solution is cooled 50°C and diluted with 1.5 L of hexanes. The resulting solid is collected by filtration giving the title compound as a white solid (7.2 g, 37 mmol). ^{1}H NMR (d6-DMSO, 300 MHz) δ 11.4 (bs, 1H), 8.02 (s, 1H), 7.67 (d, 1H), 7.55 (d, 1H), 6.34 (s, 1H), 2.18 (s, 3H).

C. 1,7-Dichloro-3-methyl-isoquinoline.

A solution of 7-chloro-3-methyl-2H-isoquinoline-1-one (7.1 g, 36.7 mmol) in 100 mL of phosporous oxychloride is heated to 100°C. After 5 h, the solution is concentrated to dryness. The residue is dissolved in CH_2Cl_2. The solution is washed with H_2O. The organic layer is dried over $MgSO_4$, filtered and concentrated. The crude product is purified by column chromatography eluting with a gradient of 3%EtOAc/hexanes to 5% EtOAc/hexanes. The title compound is obtained as a white solid (6.0g, 28 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.23 (s, 1H), 7.68 (m, 1H), 7.63 (m, 1H), 7.40 (s, 1H), 2.64 (s, 3H).

D. 3-Bromomethyl-1,7-dichloro-2H-isoquinoline.

The title compound is prepared as described in Example 7, part C, substituting 1,7-dichloro-3-methyl-isoquinoline for 4-chloro-7-methylquinazoline. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.29 (s, 1H), 7.82 (m, 1H), 7.76 (m, 2H), 4.68 (s, 2H).

EXAMPLE 11. 3-Bromomethyl-7-chloroisoquinoline.

A. 7-Chloro-3-methyl-isoquinoline.

To a solution of 1,7-dichloro-3-methyl-isoquinoline (0.50 g, 2.36 mmol), Example 10, part C, in 5.5 mL of 9:1 acetic acid:H_2O at 75°C is added zinc (0.23 g, 3.54 mmol) After 75 minutes, the solution is cooled to ambient temperatures. The solution is diluted with a 4:1 EtOAc:CH_2Cl_2 solution. To the solution is added 100mL of a 1N NaOH solution. The aqueous solution is extracted with 4:1 EtOAc:CH_2Cl_2. The combined organic layers are washed with a saturated NaCl solution. The organic layer is dried over $MgSO_4$, filtered and concentrated. The crude product is purified by column chromatography eluting with a gradient of 5%EtOAc/hexanes to 15% EtOAc/hexanes. The title compound is obtained as a white solid (0.36 g, 1.97 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.09 (s, 1H), 7.89 (s, 1H), 7.61 (d, 1H), 7.55 (d, 1H), 7.44 (s, 1H) 2.68 (s, 3H). MS (EI): m/z 177, 179 (M+), Cl pattern.

B. 3-Bromomethyl-7-chloroisoquinoline.

The title compound is prepared as described in Example 7, part C, substituting 7-chloro-3-methyl-isoquinoline for 4-chloro-7-methylquinazoline. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.18 (s, 1H), 7.97 (s, 1H), 7.75 (m, 2H), 7.67 (m, 1H), 4.71 (s, 2H).

EXAMPLE 12. 2-Bromomethyl-6-chloronaphthalene.

A. 6-Chloro-3,4-dihydro-1H-naphthalene-2-one.

To a solution of (4-chlorophenyl)-acetyl chloride (17.3 g, 92 mmol) in 50 mL of CH_2Cl_2 at -20°C is added a solution of $AlCl_3$ (24.4 g, 184 mmol) in 200 mL CH_2Cl_2 dropwise. After 20 minutes, ethylene (g) is bubbled through the solution for 30 minutes. The solution is stirred at -10°C for 15 minutes. The reaction mixture is poured into 300 g of ice. The layers are separated. The organic layer is washed with H_2O, saturated $NaHCO_3$ and saturated NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated. The resulting solid is triturated with pentane (2x20mL). The solid is then dried to give the title compound as a solid (15.2 g, 84.2 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28 (m, 2H), 7.06 (m, 1H), 3.52 (s, 2H), 3.04 (m, 2H), 2.56 (m, 2H).

B. 6-Chloro-2-methyl-1,2,3,4-tetrahydronaphthalene-2-ol.

To a solution of $TiCl_4$ (95 mL, 1M in toluene) at -45°C is added a solution of CH_3MgBr (4.2 mL 3M in THF). The solution is stirred for 20 minutes. After this time, 6-chloro-3,4-dihydro-1H-naphthalene-2-one (11.3 g, 63 mmol) in 80 mL of CH_2Cl_2 is added dropwise over 15 minutes. The reaction is stirred for an additional 15 min at -45°C. The solution is warmed to 0°C. After 2 h, the solution is diluted with H_2O and CH_2Cl_2. The organic layer is dried over $MgSO_4$, filtered and concentrated. The title compound is obtained as an oil (11.3 g, 57.5 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.10 (m, 2H), 6.97 (m, 1H), 3.02 (m, 2H), 2.80 (s, 3H), 1.85 (m, 2H), 1.80 (m, 2H).

C. 2-Chloro-6-methyl naphthalene.

A solution of 6-chloro-2-methyl-1,2,3,4-tetrahydronaphthalene-2-ol (11.3 g, 57.5 mmol) and Ph_3COH (16.5 g, 63 mmol) in 80 mL of TFA is stirred for 2.5 days. After this time, the solution is concentrated to dryness. The residue is dissolved in CH_2Cl_2. The organic layer is washed with H_2O, saturated $NaHCO_3$, and saturated NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated. The crude product is purified by column chromatography eluting with hexanes. The title compound is obtained as a white solid (4.05 g, 22.9 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.78 (s, 1H), 7.69 (m, 2H), 7.58 (s, 1H), 7.50 (m, 2H), 2.49 (s, 3H).

D. 2-Bromomethyl-6-chloronaphthalene.

The title compound is prepared as described in Example 7, part C, substituting 2-chloro-6-methyl naphthalene for 4-chloro-7-methylquinazoline. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.82 (m, 2H), 7.78 (s, 1H), 7.76 (m, 2H), 7.52 (d, 1H), 7.42 (d, 1H), 4.62 (s, 2H).

EXAMPLE 13. 2-(Benzhydrylidene-amino)-4-bromomethyl-benzonitrile.

A. 2-(Benzhydrylidene-amino)-4-methyl-benzonitrile.

To a solution of 2-amino-4-methyl benzonitrile (20 g, 151 mmol) in 1000mL of dichloroethane is added benzophenone imine (30g, 166mmol). The solution is refluxed for 48 hours After this time, the solution is cooled to ambient temperatures. The solution is washed with sat. $NaHCO_3$, water and sat. NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated under vacuum. The product is further purified by recrystallization from t-butyl ether. The title compound (25.5g, 118mmol) is obtained as a yellow solid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.88 (m, 2H), 7.42 (m, 3H), 7.32 (m, 7H), 6.79 (d, 1H), 6.58 (s, 1H), 2.23 (s, 3H).

B. 2-(Benzhydrylidene-amino)-4-bromomethyl-benzonitrile.

To a solution of 2-(benzhydrylidene-amino)-4-methyl-benzonitrile (11.2g, 37.8mmol) in 500mL of CCl_4 is added N-bromosuccinimide (7.06g, 39.7mmol), and benzoyl peroxide (0.92g, 3.8mmol). The solution is heated to reflux for 16 hours. After this time, the solution is filtered and the organic solution is concentrated under vacuum. The residue is purified by column chromatography eluting with a gradient of 20%t-butyl ether/hexanes to 25% t-butyl ether/hexanes. The product is obtained as an oil containing a mixture of the desired monobromide, dibromide and unreacted starting material. The mixture is assayed by proton NMR and is found to have a purity between 60-75%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.82 (m, 2H), 7.42 (m, 9H), 6.92 (d, 1H), 6.81 (s, 1H), 4.29 (s, 2H).

EXAMPLE 14. 7-Bromomethyl-4-chloroquinoline.

A. 7-Methyloxycarbonyl-4-chloroquinoline.

4-Chloro-7-trifluoromethylquinoline (5.0 g, 21.6 mmol) in 100 mL 80% H_2SO_4 is heated to 200°C for 24 hours in a sealed tube. The solution is cooled, poured into water and neutralized with sodium hydroxide to pH ~ 3-4. The precipitated solid is collected, washed with water and dissolved in 2 N sodium hydroxide. The aqueous solution is washed with ethyl acetate then acidified to pH~3-4. The precipitate is collected, washed with water and dried in a vacuum oven overnight to yield 7-carboxy-4-

chloroquinoline as a solid (5.1 g, 24.6 mmol). A portion of this material (2.0 g, 9.6 mmol) is treated with anhydrous THF (200 mL) and DMF (2 mL) and 2 M oxalyl chloride in methylene chloride (14.5 mL, 29 mmol). The resulting suspension is stirred at room temperature for 2 h then treated with methanol (10 mL). After stirring 30 minutes the solution is concentrated and the residue is taken up in methylene chloride. The solution is washed with saturated sodium bicarbonate and dried (sodium sulfate) and concentrated to yield the title compound as a solid (2.1 g, 9.5 mmol). MS m/z: $M^+ = 221$; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.6 (s, 1H), 8.2 (s, 1H), 7.9 (d, 1H), 7.65 (d, 1H), 7.45 (s, 1H), 3.95 (s. 3H).

B. 7-Hydroxymethyl-4-chloroquinoline.

7-Methyloxycarbonyl-4-chloroquinoline (2.1 g, 9.5 mmol) is dissolved in anhydrous THF (25 mL) and anhydrous ether (200 mL). The solution is cooled in a dry ice/acetone bath and treated 1M lithium aluminum hydride in THF (11.0 mL, 11 mmol). The solution is warmed (approximately -45°C) for 20 minutes and quenched with ethyl acetate. The solution is diluted with ether (100 mL) and treated with water (36 mL), 15% NaOH (36 mL) and water (36 mL) in succession. The mixture is filtered and evaporated to yield the title compound as a residue (2.0 g, 9.7 mmol) which is dried under vacuum and used without further purification. MS m/z: $M^+ = 193$; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.65 (d, 1H), 8.15 (d, 1H), 8.0 (d, 1H), 7.6 (d, 1H), 7.45 (d, 1H), 4.8 (s, 2H).

C. 7-Bromomethyl-4-chloroquinoline.

7-Hydroxymethyl-4-chloroquinoline (0.2 g, 0.97 mmol) is treated with 48 % HBr and heated to 120°C for 1 hours. The resulting solution is cooled with ice, diluted with water and treated with ethyl acetate and sodium bicarbonate until basic to pH paper. The layers are separated and the organic layer is washed with water, dried (Na_2SO_4) and concentrated to give 7-bromomethyl-4-chloroquinoline (0.23 g, 0.9 mmol). MS m/z: $M^+ = 255$; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.75 (d, 1H), 8.25 (d, 1H), 8.1 (s, 1H), 7.7 (d, 1H), 7.5 (d, 1H), 4.7 (s. 2H).

EXAMPLE 15. 7-Bromomethyl-4-chlorocinnoline.

A. 4-methyl-2-nitrophenylethanone.

4-Fluro-3-nitrotoluene (7.5 g, 48.4 mmol) is treated with a solution of nitroethane (15.2 mL, 200 mmol) in ethyl acetate (100 mL) and DBU (21 mL, 145 mmol) and stirred overnight at ambient temperature. The solution is concentrated under vacuum, diluted with methanol, treated with 30% H_2O_2 (25 mL) and 10% sodium bicarbonate (25 ml) and stirred overnight at ambient temperature. The reaction mixture is concentrated in vacuo, acidified with 5% HCl and extracted with methylene chloride. The organic layer is dried (sodium sulfate) and chromatographed (35% ethyl acetate/hexane) to give the

title compound (7.2 g, 40.2 mmol). MS m/z: $M^+ = 279$; ^1H NMR ($CDCl_3$, 300MHz) δ 7.8 (s, 1H), 7.48 (d, 1H), 7.32 (d, 1H), 2.5 (s, 3H), 2.4 (s, 3H).

B. 2-Amino-4-methylphenylethanone.

A solution of 4-methyl-2-nitrophenylethanone (5.0 g, 28 mmol) in methanol (100 mL) is treated with ammonium formate (9.6 g, 140 mmol) and 5% palladium on carbon (1.5 g). The mixture is heated to 60°C for 6 h then stirred at ambient temperature for 16 hours. The reaction mixture is filtered through Celite and the filtrate is concentrated in vacuo. The concentrate is treated with sodium bicarbonate and partitioned between water and ethyl acetate. The organic layer is separated, dried with sodium sulfate and concentrated to give crude title compound (4.5 g, 30.2 mmol) which is used without further purification. MS m/z:$M^+ = 149$; ^1H NMR ($CDCl_3$, 300MHz) δ 8.05 (d, 1H), 7.4 (d, 1H), 7.25 (s, 1H), 2.8 (s, 3H), 2.45 (s, 3H).

C. 7-Methyl-1-H-cinnolin-4-one.

A solution of 2-amino-4-methylphenylethanone (5.0 g, 33.6 mmol) in concentrated HCl (100 mL) is treated, in portions, with a solution of sodium nitrite (5.7 g, 82.6 mmol) in water (~ 10 mL). The resulting solution is stirred at 60°C for 2 hr, cooled to ambient temperature and diluted with a saturated solution of sodium acetate (~ 200 mL). Solid sodium acetate is added portionwise until the solution tested basic to pH paper. Upon stirring, the title compound precipitated as a white solid which is collected and air dried (2.3 g, 14.3 mmol). MS m/z: $[M+H]^+ = 161$; ^1H NMR ($CDCl_3$, 300MHz) δ 8.1 (d, 1H), 7.85 (s, 1H), 7.45 (s, 1H) 7.3 (d, 1H), 2.55 (s, 3H).

D. 4-Chloro-7-methylcinnoline.

7-Methyl-1-H-cinnolin-4-one (1.3 g, 8.1 mmol) is treated with about 80 mL of chlorobenzene and heated until the solid dissolves. The resulting solution is cooled and treated with pyridine (0.16 mL, 2 mmol) and $POCl_3$ (1.13 mL, 12.2 mmol). The solution is heated to reflux for 1 h then concentrated to dryness. The residue is chromatographed (20 % ethyl acetate/hexane) to yield the title compound as a tan solid (~ 1 g, 5.6 mmol). MS m/z (M+=178); ^1H NMR ($CDCl_3$, 300MHz) δ 9.3 (s, 1H), 8.35 (s, 1H), 8.1 (d, 1H), 7.7 (d, 1H), 2.68 (s, 3H).

E. 7-Bromomethyl-4-chlorocinnoline.

A solution of 4-chloro-7-methylcinnoline (0.6 g, 3.37 mmol) in carbon tetrachloride (30 mL) is treated with N-bromosuccinimide (0.64 g, 3.4 mmol) and a catalytic amount of 70 % benzoyl peroxide (0.22 g, 0.63 mmol). The solution is heated to 80 °C overnight, then filtered. The filtrate is concentrated in vacuo and the resulting residue is chromatographed (20 % ethyl acetate/ methyl chloride) to give the

title compound (0.3 g, 1.2 mmol) and some unreacted starting material (0.1 g, 0.56 mmol). MS m/z: $[M+H]^+ = 257$; ^1H NMR ($CDCl_3$, 300MHz) δ 9.35 (s, 1H), 8.55 (s, 1H), 8.2 (d, 1H), 8.85 (d, 1H), 4.75 (s, 2H).

EXAMPLE 16. 6-Bromomethyl-3-chloro-1-(toluene-4-sulfonyl)-1H-indole.

A. 1H-Indole-6-carboxylic acid methyl ester.

To a solution of 6-indole carboxylic acid (0.91 g, 5.67 mmol) in 33 mL of 2:1 THF/MeOH is added (trimethylsilyl)diazomethane (5.0 mL of a 2.0M solution in hexanes, 10.0 mmol). The mixture is stirred for 3 h and concentrated in vacuo to give the title compound (0.87 g, 4.97 mmol). The crude product is used in the next step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.70 (bs, 1H), 8.20 (s, 1H), 7.82 (dd, 1H), 7.67 (d, 1H), 7.45 (m, 1H), 6.60 (m, 1H), 3.95 (s, 3H).

B. 3-Chloro-1H-indole-6-carboxylic acid methyl ester.

To a solution of 1H-indole-6-carboxylic acid methyl ester (5.86 g, 33.5 mmol) in 30 mL of CH_2Cl_2 is added N-chlorosuccinimide (0.58, 4.33 mmol) portionwise over 1.5 hours. The mixture is stirred for 2 h, then diluted with water. The layers are separated and the organic phase is washed with water and saturated NaCl solution. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo to give the title compound (5.74 g, 27.3 mmol). The crude product is used in the next step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.46 (bs, 1H), 8.19 (s, 1H), 7.90 (dd, 1H), 7.69 (d, 1H), 7.36 (d, 1H), 3.97 (s, 3H).

C. 3-Chloro-1-(toluene-4-sulfonyl)-1H-Indole-6-carboxylic acid methyl ester.

To a solution of 3-chloro-1H-indole-6-carboxylic acid methyl ester (3.00 g, 17.1 mmol) in 40 mL of THF at -78°C is added LDA(8.55 mL of a 2.0M solution in hexanes, 17.1 mmol) dropwise. The solution is stirred at -78°C for 30 minutes p-Toluenesulfonyl chloride (3.43 g, 18.0 mmol) in 15 mL of THF is added dropwise and the resulting solution is stirred at -78°C for 3 hours. The mixture is warmed to 0°C , quenched with saturated $NaHCO_3$ solution and diluted with H_2O and Et_2O. The layers are separated. The organic phase is washed with saturated $NaHCO_3$ solution, H_2O and saturated NaCl solution, then dried over $MgSO_4$, filtered and concentrated. The crude residue is purified via flash column chromatography eluting with a gradient of 10% EtOAc/hexanes to 30% EtOAc/hexanes to provide the title compound (3.64 g, 10.0 mmol). ^1H NMR ($CDCl_3$, 300MHz) δ 8.70 (s, 1H), 8.01 (dd, 1H), 7.80 (d, 2H), 7.70 (s, 1H), 7.60 (d, 1H), 7.38 (m, 2H), 4.00 (s, 3H), 2.49 (s, 3H).

D. [3-Chloro-1-(toluene-1-sulfonyl)-1H-indol-6-yl]-methanol.

To a solution of 3-chloro-1-(toluene-4-sulfonyl)-1H-Indole-6-carboxylic acid methyl ester (3.10 g, 8.53 mmol) in 50 mL of toluene at -78°C is added DIBAL (13.8 mL of a 1.5M solution in toluene, 20.8 mmol) dropwise. The mixture is stirred at -78°C for 2 h, then warmed to room temperature and stirred for 2 hours. The reaction mixture is quenched by the addition of MeOH and washed with saturated disodium tartrate solution. The aqueuos layer is extracted with Et_2O. The combined organics are washed with saturated disodium tartrate solution, water and saturated NaCl solution. The organic phase is then dried over anhydrous $MgSO_4$, filtered and concentrated to give the title compound (2.88 g). The crude product is used in the next step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.01 (s, 1H), 7.79 (d, 2H), 7.56 (s, 1H), 7.53 (d, 1H), 7.31 (d, 1H), 7.25 (d, 2H), 4.84 (s, 2H), 2.37 (s, 3H), 1.88 (bs, 1H).

E. 6-Bromomethyl-3-chloro-1-(toluene-4-sulfonyl)-1H-indole.

To a solution of [3-chloro-1-(toluene-1-sulfonyl)-1H-indol-6-yl]-methanol (0.45 g, 1.34 mmol) in 13 mL of Et_2O at 0°C is added phosphorous tribromide (0.04 mL, 0.40 mmol). The mixture is stirred at 0°C for 15 min, then at room temperature for 2 hours. The mixture is quenched by the addition of water/ice and diluted with Et_2O. The layers are separated and the organic phase is washed with saturated $NaHCO_3$ solution, water and saturated NaCl solution. The organic layer is dried over anhydrous $MgSO_4$, filtered and concentrated to provide the title compound (0.47 g, 1.18 mmol) as an oil. The crude product is used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.09 (s, 1H), 7.79 (d, 2H), 7.59 (s, 1H), 7.50 (d, 1H), 7.35 (d, 1H), 7.27 (m, 2H), 4.66 (s, 2H), 2.39 (s, 3H).

EXAMPLE 17. 2-(3-Bromo-(E)-propenyl)-5-chloro-thiophene.

A. 3-(5-Chloro-thiophen-2-yl)-(E)-acrylic acid methyl ester.

To a solution of 5-chloro-2-thiophene-carboxaldehyde (5.10 g, 34.8 mmol) in 100 mL of dry CH_2Cl_2 is added methyl (triphenylphosphoranylidene)acetate (11.8 g, 35.3 mmol). The resulting brown-green mixture is stirred for 19 h at room temperature. The mixture is filtered through a Celite pad, concentrated in vacuo and triturated with hexane. The white precipitate (triphenylphosphine oxide) is filtered off and the filtrate is concentrated. The crude residue is purified via flash column chromatography eluting with a gradient of 5% EtOAc/hexanes to 10% EtOAc/hexanes to provide the title compound (6.20 g, 30.6 mmol) as a yellow solid. ^1H NMR ($CDCl_3$, 300MHz) δ 7.65 (d, 1H), 7.05 (d, 1H), 6.89 (d, 1H), 6.10 (d, 1H), 3.80 (s, 3H).

B. 3-(5-Chloro-thiophen-2-yl)-prop-2-(E)-en-1-ol.

To a solution of 3-(5-chloro-thiophen-2-yl)-(E)-acrylic acid methyl ester (5.00 g, 24.7 mmol) in 80 mL of CH_2Cl_2 at 0°C is added slowly a solution of DIBAL (36.2 mL of a 1.5M solution in toluene, 54.3 mmol). The mixture is stirred at 0°C for 15 min, then quenched by the addition of 6 mL of MeOH. The mixture is allowed to warm to room temperature, diluted with water/ice and stirred for 15 minutes. The mixture is filtered through a pad of Celite and washed with CH_2Cl_2. The layers are separated and the aqueous layer is extracted with CH_2Cl_2. The combined organics are washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue is purified via flash column chromatography eluting with a gradient of 15% EtOAc/hexanes to 25% EtOAc/hexanes to afford the title compound (4.18 g, 23.9 mmol) as an oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.77 (d, 1H), 6.71 (d, 1H), 6.60 (d, 1H), 6.10 (m, 1H), 4.30 (d, 2H), 1.79 (bs, 1H).

C. 2-(3-Bromo-(E)-propenyl)-5-chloro-thiophene.

To a solution of 3-(5-chloro-thiophen-2-yl)-prop-2-(E)-en-1-ol (4.18 g, 23.9 mmol) in 140 mL of Et_2O at 0°C is added phosphorous tribromide (1.34 mL, 14.3 mmol) in 10 mL of Et_2O. The mixture is stirred at 0°C for 45 min, then at room temperature for 1.5 hours. The mixture is quenched by the addition of water/ice and diluted with Et_2O. The layers are separated and the organic phase is washed with water until neutral (3x) and once with saturated NaCl solution. The organic layer is dried over anhydrous $MgSO_4$, filtered and concentrated to provide the title compound (5.46 g, 23.0 mmol) as an oil. The crude material solidified upon storage in the freezer and can be used in the subsequent step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.80 (m, 2H), 6.65 (d, 1H), 6.10 (m, 1H), 4.10 (d, 2H).

EXAMPLE 18. 3-(4-Bromo-furan-2-yl)-(E)-propenal.

To a solution of 4-bromo-2-furfuraldehyde (0.5 g, 2.86 mmol) in 30 mL of dry CH_2Cl_2 is added (triphenylphosphoranylidene)acetaldehyde (0.87 g, 2.86 mmol). The resulting mixture is stirred for 16 h at room temperature. The crude mixture is concentrated in vacuo and the residue is purified via flash column chromatography eluting with CH_2Cl_2 to provide the title compound (0.15 g, 0.75 mmol) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.62(d, 1H), 7.59 (s, 1H), 7.18 (d, 1H), 6.81 (s, 1H), 6.60 (m, 1H).

EXAMPLE 19. Acetic acid 3-(6-methoxy-pyridin-3-yl)-(E)-allyl ester.

To a solution of 3-(6-methoxy-pyridin-3-yl)-prop-2-(E)-en-1-ol (0.39 g, 2.36 mmol, prepared as described in PREPARATION MB from 6-methoxy-pyridine-3-carbaldehyde (J. Org. Chem. 1990, 72)) in 8 mL of CH_2Cl_2 at 0°C is added triethylamine (0.66 mL, 4.72 mmol), DMAP (0.05 g, 0.40 mmol) and Ac_2O (0.33 mL, 3.54 mmol). The mixture is stirred at 0°C for 45 min, then at room temperature for 16

hours. The mixture is diluted with Et_2O and washed with 1N HCl, water, saturated $NaHCO_3$ solution and saturated NaCl solution. The organic layer is dried over anhydrous $MgSO_4$, filtered and concentrated. The residue is purified via flash column chromatography eluting with a gradient of 10% EtOAc/hexanes to 20% EtOAc/hexanes to afford the title compound (0.25 g, 1.21 mmol) as an oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.12 (d, 1H), 7.68 (dd, 1H), 6.72 (d, 1H), 6.60 (d, 1H), 6.18 (dt, 1H), 4.73 (d, 2H), 3.95 (s, 3H), 2.10 (s, 3H).

EXAMPLE 20. 2-(3-Bromo-prop-1-ynyl)-5-chloro-thiophene.

A. 3-(5-Chloro-thiophen-2-yl)-prop-2-yn-1-ol.

Nitrogen (g) is bubbled through a solution of 5-bromo-2-chloro-thiophene (1.00 g, 5.06 mmol) in 8 mL of piperidine. After 5 min, propargyl alcohol (0.32 mL, 5.56 mmol), tetrakis(triphenylphosphine) palladium(0) (0.06 g) and CuI (catalytic amount) are added to the solution. The mixture is heated at 80°C for 1 h in a sealed glass vessel. At this time, the mixture is cooled and diluted with EtOAc/Et_2O. The organic layer is washed 3N HCl, water, saturated $NaHCO_3$ solution and saturated NaCl solution. The organic layer is dried, filtered and concentrated. The crude residue is purified via flash column chromatography eluting with a gradient of 10% EtOAc/hexanes to 20% EtOAc/hexanes to give the title compound (0.8 g, 0.46 mmol) as an oil. ^1H NMR (DMSO-d_6, 300 MHz) δ 6.99 (d, 1H), 6.80 (d, 1H), 4.49 (s, 2H), 1.90 (bs, 1H). EI MS, $[M]^+$=172, 174 (Cl pattern).

B. 2-(3-Bromo-prop-1-ynyl)-5-chloro-thiophene.

The title compound is prepared as described in EXAMPLE 17, Part C, using 3-(5-chloro-thiophen-2-yl)-prop-2-yn-1-ol in place of 3-(5-chloro-thiophen-2-yl)-prop-2-(E)-en-1-ol. The crude product is used in the subsequent step without further purification.

^1H NMR ($CDCl_3$, 300 MHz) δ 7.04 (d, 1H), 6.80 (d, 1H), 4.98 (d, 2H).

EXAMPLE 21. 2-Bromomethyl-5-chloro-indole-1-carboxylic acid tert-butyl ester.

A. 5-Chloro-2-methyl-indole-1-carboxylic acid tert-butyl ester.

A solution containing 5-chloro-2-methylindole (4.0 g, 24.1 mmol) and DMAP (295 mg, 2.42 mmol) in anhydrous THF (100 mL) is cooled to 0°C. A solution containing $(Boc)_2O$ (5.27 g, 24.1 mmol) in anhydrous THF (100 mL) is then added over a 20 min period. The reaction mixture is stirred for 2 h at 0°C and then at ambient temperature for 16 hours. The reaction mixture is concentrated and the crude residue is purified by flash silica gel chromatography (2% EtOAc/hexane to 5% EtOAc/hexane) to provide 5.2 g (81%) of title compound as a pale yellow solid. ^1H NMR (300 MHz, $CDCl_3$) δ 1.67 (s,

9H), 2.57 (s, 3H), 6.24 (t, J = 0.9 Hz, 1H), 7.16 (dd, J = 8.8, 2.1 Hz, 1H), 7.38 (d, J = 2.1 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H) ppm; MS (EI): m/z 265 (M+).

B. 2-Bromomethyl-5-chloro-indole-1-carboxylic acid tert-butyl ester.

A solution containing 5-chloro-2-methyl-indole-1-carboxylic acid tert-butyl ester (3.0 g, 11.3 mmol), NBS (1.33 g, 11.3 mmol), and benzoyl peroxide (0.4 g, 1.13 mmol) in CCl_4 (100 mL) is heated at 80°C for 3 hours. An additional portion of NBS (0.65 g, 5.65 mmol), and benzoyl peroxide (0.2 g, 0.56 mmol) is then added and the reaction mixture is heated for an additional 3 hours. After cooling to ambient temperature, the reaction mixture is filtered. The filtrate is concentrated to a brown oil which is triturated with hexane to remove residual succinimide, filtered, and concentrated. The resultant oil (4.5 g, >100%) is used directly in the next reaction without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.72 (s, 9H), 4.88 (s, 2H), 6.63 (s, 1H), 7.27 (dd, J = 9.0, 2.0 Hz, 1H), 7.46 (d, J = 2.0 Hz, 1H), 8.09 (d, J = 9.0 Hz, 1H) ppm; MS (EI): m/z 343 (M+).

EXAMPLE 22. 3-Bromomethyl-5-iodo-2-methoxy-pyridine

A. 5-Iodo-3-methyl-2-methoxy-pyridine.

To a solution containing 2-bromo-5-iodo-3-methyl-pyridine (4.80 g, 16.0 mmol) in DMSO (15 mL) is added methanolic NaOMe (3.33 M, 5.3 mL, 17.7 mmol) at 0 °C. The solution is allowed to warm to ambient temperature and then heated at 70°C for 1 hour. The reaction mixture is diluted with diethyl ether (300 mL) and water (200 mL) and the layers are separated. The organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product is purified by silica gel flash column chromatography (hexane/diethyl ether, 19:1) to provide 2.86 g (71%) of the title compound as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12 (s, 3H), 3.90 (s, 3H), 7.60 (d, J = 2.1 Hz, 1H), 8.14 (d, J = 2.1 Hz, 1H) ppm; MS (EI): m/z 249 (M+).

B. 3-Bromomethyl-5-iodo-2-methoxy-pyridine.

A solution containing 5-iodo-3-methyl-2-methoxy-pyridine (1.00 g, 4.00 mmol) and NBS (0.78 g, 4.40 mmol) in CCl_4 (20 mL) is warmed to reflux. AIBN is added in 5 mg portions (0.03 mmol) every hour. After 3 h, the reaction mixture is cooled and then concentrated in vacuo. The residue is dissolved in EtOAc (150 mL) and washed successively with aqueous $Na_2S_2O_3$ (100 mL), water (100 mL), brine then dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product ispurified by silica gel flash column chromatography (hexane/diethyl ether, 19:1) to provide 0.72 g (55%) of the title compound as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3H), 4.38 (s, 2H), 7.83 (d, J = 2.2 Hz, 1H), 8.27 (d, J = 2.2 Hz, 1H) ppm; MS (EI): m/z 327 (M+).

EXAMPLE 23. 5-Bromomethyl-6-methoxy -nicotinic acid methyl ester.

A. 6-Methoxy-5-methyl-nicotinic acid methyl ester.

A solution containing 5-iodo-3-methyl-2-methoxy-pyridine (10.0 g, 40.0 mmol), Et_3N (8.0 g, 80.0 mmol), and $(Ph_3P)_4PdCl_2$ (2.80 g, 4.00 mmol) in 1:1 DMF/MeOH (100 mL) is cooled to 0°C. Carbon monoxide is bubbled into the cooled solution for approx. 5 min at which time the reaction mixture is sealed under a balloon of CO. The reaction mixture is allowed to warm to ambient temperature and then stirred for 16 hours. The reaction mixture is concentrated in vacuo and the residue is partitioned between water (300 mL) and EtOAc (300 mL) and the layers are separated. The organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product is purified by silica gel flash column chromatography (hexane/diethyl ether, 19:1) to provide 4.10 g (57%) of the title compound as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 2.20 (s, 3H), 3.88 (s, 3H), 4.00 (s, 2H), 7.96 (d, J = 2.2 Hz, 1H), 8.65 (d, J = 2.2 Hz, 1H) ppm; MS (ISP loop): m/z 182 (M+H).

B. 5-Bromomethyl-6-methoxy -nicotinic acid methyl ester.

A solution containing 6-methoxy-5-methyl-nicotinic acid methyl ester (4.00 g, 22.1 mmol), NBS (5.11 g, 28.7 mmol), and AIBN (0.90 g, 5.5 mmol) in CCl_4 (100 mL) is warmed to reflux. After 5 h, the reaction mixture is cooled and then concentrated in vacuo. The residue is dissolved in EtOAc (500 mL) and washed successively with aqueous $Na_2S_2O_3$ (300 mL), water (100 mL), brine then dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product is purified by silica gel flash column chromatography (hexane/diethyl ether, 9:1) to provide 3.10 g (54%) of the title compound as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 3.90 (s, 3H), 4.07 (s, 3H), 4.46 (s, 2H), 8.19 (d, J = 2.2 Hz, 1H), 8.79 (d, J = 2.2 Hz, 1H) ppm; MS (EI): m/z 259 (M+).

EXAMPLE 24. 5-Chloro-2-thienyloxyacetic acid.

A. 2-Hydroxy-thiophene.

Thiophene (42g, 500mmol) is dissolved in ether (250mL). To the solution is added n-BuLi (200mL of a 2.5N solution in hexanes, 500mmol) at a rate which maintains a gentle reflux. After addition, the solution is stirred for 0.5 hour. The solution is then cooled to -78°C and triethyl borate (102 g, 700mL) is added dropwise. The solution is stirred for 3 hours. The cold bath is removed and 130mL of a 30% H_2O_2 is added dropwise with rapid stirring. After addition, the solution is allowed to refluxed for an additional 20 minutes. The solution is then cooled to 0°C and acidified to pH=3 with 6N HCl. The resulting solution is extracted with ether. The organic solution is washed with 10% ferric

ammonium sulfate, water and saturated NaCl. The solution is dried over $MgSO_4$, filtered and concentrated under vacuum. The title compound (32g, 320mmol) is obtained as an oil. ^1H NMR ($CDCl_3$, 300MHz) δ 7.60 (m, 1H),6.35 (m, 1H), 4.12 (d, 2H).

B. Ethyl 2-thienyloxyacetate.

To a solution of 2-hydroxy-thiophene (32g, 320 mmol) in $CHCl_3$ (500mL) is added ethyl bromoacetate (53.4 g, 320 mmol). To the resulting solution is added a solution containing n-Bu_4NHSO_4 (25g, 74mmol) and NaOH (15.8g, 394 mmol) in water (500mL). After addition, the solution is stirred vigorously using mechanical stirring. The reaction is stirred for 12 hours. After this time, the layers are separated. The aqueous layer is extracted with $CHCl_3$. The combined organic layers are washed with water and saturated NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated under vacuum. The resulting crude product is purified by column chromatography eluting with a gradient of 30%CH_2Cl_2:hexanes to 60%CH_2Cl_2:hexanes. The title compound (11.5g, 62mmol) is obtained as an oil. ^1H NMR ($CDCl_3$, 300MHz) δ 6.68 (dd, 1H), 6.60 (d, 1H), 6.22 (d, 1H), 4.62 (s, 2H), 4.30 (q, 2H), 1.31 (t, 3H).

C. Ethyl 5-chloro-2-thienyloxyacetate.

To a solution of ethyl 2-thienyloxyacetate (1.1g, 5.9mmol) in acetic acid (15mL) is added N-chlorosuccinimide (0.78g, 5.9mmol). The solution is stirred for 1.5 hour. After this time the solution is concentrated. The resulting oil is dissolved in ether and washed with 1N NaOH, water and sat. NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated under vacuum. The title compound (1.26g, 5.7mmol) is obtained as an oil. ^1H NMR ($CDCl_3$, 300MHz) δ 6.52 (d, 1H), 6.06 (d, 1H), 4.60 (s, 2H), 4.24 (q, 2H), 1.31 (t, 3H).

D. 5-Chloro-2-thienyloxyacetic acid.

To a solution of ethyl 5-chloro-2-thienyloxyacetate (0.39g, 1.77mmol) in 9mL of a 1:1:1 mixture of CH_3OH:THF:water is added LiOH (0.38g, 9.0 mmol). The solution is stirred for 16 hours. After this time, the solution is concentrated to 1/3 its volume. The resulting solution is acidified to pH=3 with 1N HCl. The aqueous solution is extracted with CH_2Cl_2. The organic layer is dried over $MgSO_4$, filtered and concentrated under vacuum. The title compound (0.32g, 1.66mmol) is obtained as a white solid. ^1H NMR ($CDCl_3$, 300MHz) δ 6.50 (d, 1H), 6.07 (d, 1H), 4.66 (s, 2H).

EXAMPLE 25. 3-(5-Chloro-thiophen-2-yl)-(E)-acrylic acid.

To a mixture of 3-(5-chloro-thiophen-2-yl)-(E)-acrylic acid methyl ester (0.60 g, 2.96 mmol) in 15 mL of 1:1:1 THF/MeOH/H_2O at 0°C is added lithium hydroxide monohydrate (0.62 g, 14.7 mmol).

The mixture is stirred at 0°C for 1 h, then at room temperature for 1 h and concentrated in vacuo. The residue is diluted with EtOAc and washed with 1N HCl. The aqueous layer is extracted with EtOAc and the combined organics are washed with water (2x), dried, filtered and concentrated to provide the title compound (0.54 g, 2.86 mmol) as a white solid. The crude material can be used in the subsequent step without further purification. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.65 (d, 1H), 7.05 (d, 1H), 6.90 (d, 1H), 6.10 (d, 1H).

EXAMPLE 26. 3-(4-Chloro-thiophen-2-yl)-(E)-acrylic acid.

A. 4-Chloro-2-thiophene-carboxaldehyde.

To a solution of 2-thiophene-carboxaldehyde (6.33 g, 56.4 mmol) in 100 mL of $CHCl_3$ at 0°C is added aluminum trichloride (16.8 g, 126 mmol) portionwise over a few minutes. In a separate vessel, chlorine gas (4.00 g) is bubbled for about 2 min into 100 mL of CCl_4 at 0°C and then added to the former mixture slowly at 0°C . The resulting mixture is stirred at 0°C for 45 min, then allowed to warm to room temperature and stirred overnight. After 16 h, the reaction mixture is poured slowly into 6N HCl at 0°C , then stirred at room temperature for 2 hours. The layers are separated. The aqueous layer is extracted with $CHCl_3$. The combined organic layers are washed with H_2O and saturated NaCl solution, then dried over $MgSO_4$, filtered and concentrated. The crude product is purified by column chromatography eluting with 10% EtOAc/hexanes to yield the title compound (6.70 g, 45.9 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.87 (s, 1H), 7.64 (s, 1H), 7.63 (s, 1H).

B. 3-(4-Chloro-thiophen-2-yl)-(E)-acrylic acid methyl ester.

The title compound is prepared as described in EXAMPLE 1, Part A from 4-chloro-2-thiophene-carboxaldehyde. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, 1H), 7.15 (s, 1H), 7.11 (s, 1H), 6.25 (d, 1H), 3.82 (s, 3H).

C. 3-(4-Chloro-thiophen-2-yl)-(E)-acrylic acid.

The title compound is prepared as described in EXAMPLE 1, Part B from 3-(4-chloro-thiophen-2-yl)-(E)-acrylic acid methyl ester. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (d, 1H), 7.19 (d, 2H), 6.25 (d, 1H).

EXAMPLE 27. (5-Chloro-thiophen-2-yl)-acetic acid.

A. [2-(5-Chloro-thiophen-2-yl)-1-dimethylaminovinyl]phosphonic acid diethyl ester.

To a suspension of sodium hydride (0.25 g, 6.25 mmol, 60% mineral oil dispersion) in 10 mL of THF is added slowly a solution of tetraethyl dimethylaminomethylenediphosphonate (2.03 g, 6.14 mmol, prepared according to the procedure described in Psaume, Montury, and Cosmetic Comm. 1982, 12, 415) in 10 mL of THF. After stirring 1 h, a solution of 5-chloro-2-thiophene carboxaldehyde (0.90 g, 6.14 mmol) in 10 mL of THF is added. The resulting mixture is heated at reflux for 1 h, then cooled to room temperature. The reaction mixture is partitioned between Et_2O and water. The organic layer is washed sequentially with 1N HCl, water and saturated NaCl, then dried over $MgSO_4$, filtered and concentrated. The crude product is purified via flash column chromatography eluting with a gradient of 40% EtOAc/hexanes to 50% EtOAc/hexanes to afford the title compound (1.52 g, 4.69 mmol) as an oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, 1H), 6.95 (d, 1H), 6.82 (d, 1H), 4.15 (m, 4H), 2.62 (s, 6H), 1.60 (t, 6H).

B. (5-Chloro-thiophen-2-yl)-acetic acid.

A mixture of [2-(5-chloro-thiophen-2-yl)-1-dimethylaminovinyl]phosphonic acid diethyl ester (1.52 g, 4.69 mmol) and 30 mL of 6N HCl is heated at reflux for 2 hours. After cooling to room temperature, ice water is added and the mixture is partitioned between Et_2O and water. The organic layer is washed with water (2x), dried over $MgSO_4$, filtered and concentrated to give the title compound (0.62 g, 3.51 mmol) as a brown solid. The crude material can be used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.30 (bs, 1H), 7.79 (d, 1H), 6.71 (d, 1H), 3.81 (s, 2H).

EXAMPLE 28. 3-(5-Chloro-thiophen-2-yl)-propionic acid.

A. 3-(5-Chloro-thiophen-2-yl)-propionaldehyde.

To a mixture of $Pd(OAc)_2$ (0.12 g, 0.53 mmol), $NaHCO_3$ (0.52 g, 6.19 mmol) and NaI (0.28 g, 1.87 mmol) in 5 mL of HMPA is added 5-bromo-2-chloro-thiophene (1.00 g, 5.06 mmol) and allyl alcohol (1.03 mL, 15.2 mmol). The mixture is heated to 90°C and stirred for 16 hours. The reaction mixture is cooled to room temperature, diluted with Et_2O and washed with water. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue is purified by flash column chromatography eluting with a gradient of 10% Et_2O/hexanes to 20% Et_2O/hexanes to provide the product (0.18 g, 1.03 mmol) as an oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 9.81 (s, 1H), 6.71 (d, 1H), 6.58 (d, 1H), 3.07 (t, 2H), 2.81 (t, 2H).

B. 3-(5-Chloro-thiophen-2-yl)-propionic acid.

Silver nitrate (117 mg, 0.69 mmol) in 1 mL of H_2O is added to 1.36 mL of 1N NaOH at 0°C and stirred for 5 minutes. To the brown suspension is added 3-(5-chloro-thiophen-2-yl)-propionaldehyde (60

mg, 0.34 mmol) and the resulting mixture is allowed to warm to room temperature over 2 hours. The precipitate is filtered and washed with hot water (2x). The combined aqueous layers are acidified with 6 N HCl and extracted with EtOAc (2x). The combined organic layers are washed with water (2x), then dried over $MgSO_4$, filtered and concentrated in vacuo to give the title compound (50 mg, 0.26 mmol) as a beige solid. The crude material can be used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 6.72 (d, 1H), 6.60 (d, 1H), 3.07 (t, 2H), 2.71 (t, 2H).

EXAMPLE 29. 3-Fluorophenoxy-acetic acid.

A. 3-Fluorophenoxy-acetic acid ethyl ester.

To a solution of 3-fluorophenol (1.2g, 11.8mmol) in 20mL of DMF at 0°C is added sodium hydride (0.47g, 10.7mmol). After stirring for 10 minutes Ethyl bromoacetate (1.2g, 10.7 mmol) is added dropwise. The reaction is allowed to warm to ambient temperatures and is stirred for 16 hours. To the reaction is added a saturated solution NH_4Cl (aq.). The resulting mixture is diluted with EtOAc and H_2O. The layers are separted. The organic layer is washed with H_2O and a saturated solution NaCl (aq.). The organic layer is dried over $MgSO_4$, filtered and concentrated to give the product (2g, 10mmol) as an oil. ^1H NMR ($CDCl_3$, 300MHz) δ 7.22 (m, 1H), 6.65 (m, 3H), 4.61 (s, 2H), 4.27 (q, 2H), 1.24 (t, 3H).

B. 3-Fluorophenoxy-acetic acid.

To a solution of ethyl 3-fluorophenoxy-acetate (2g, 10mmol) in 24mL of a 1:1:1 solution of MeOH:H_2O:THF is added lithium hydroxide monohydrate (2.25g, 54mmol). The solution is stirred for 16 hours. After this time, the solution is concentrated under reduced pressure to 1/3 of its volume. The remaining solution is acidified to pH=3 with 1N HCl (aq.). The aqueous solution is extracted with EtOAc. The organic layer is washed with a saturated solution NaCl (aq.). The organic layer is dried over $MgSO_4$, filtered and concentrated to give the product (1.65g, 9.7mmol) as a white solid. ^1H NMR ($CDCl_3$, 300MHz) δ 9.8 (bs, 1H), 7.28 (m, 1H), 6.69 (m, 3H), 4.70 (s, 2H).

EXAMPLE 30. 2-Chloropyrdin-3-ylamino-acetic acid.

To a solution of 3-amino-2-chloropyridine (1.0g, 7.8mmol) in 20mL of MeOH is added glyoxylic acid (0.86mL of a 50% by weight solution in H_2O, 7.8mmol). After stirring for 10 minutes, $NaCNBH_3$ (1.54 g, 23mmol) is added. The reaction is stirred for 16 hours., then is concentrated under reduced pressure. The resulting residue is dissolved in H_2O. The solution is acidified to pH=3 with 1N HCl (aq.). The solution is extracted with EtOAc/CH_2Cl_2 (2:1). The organic layer is dried over $MgSO_4$, filtered and concentrated. The resulting product is obtained as a white solid (0.95g, 5.1mmol). ^1H NMR

(d6-DMSO, 300MHz) δ 12.7 (bs, 1H), 7.62 (m, 1H), 7.44 (m, 1H), 6.90 (m, 1H), 5.8 (bs, 1H), 3.95 (AB, 2H).4.70 (s, 2H).

EXAMPLE 31. 5-Chlorothiophen-2-yl-sulfanyl acetic acid.

A. Thiophen-2-yl-sulfanyl acetic acid ethyl ester.

To a solution of thiophene-2-thiol (1.49g, 116mmol) in 40mL of CH_3CN is added ethyl bromoacetate (2.14g, 167mmol) followed by K_2CO_3 (3.54g, 138mmol). The solution is stirred for 16 hours. After this time, the solution is filtered. The solvent is evaporate to give the product as an oil (2.4g, 118mmol). ^1H NMR ($CDCl_3$, 300MHz) δ 7.37 (m, 1H), 7.21 (m, 1H), 6.94 (m, 1H), 4.15 (q, 2H), 3.48 (s, 2H), 1.20 (t, 3H). MS (EI): m/z 202 (M+).

B. 5-Chlorothiophen-2-yl sulfanyl acetic acid.

To a solution of thiophen-2-yl-sulfanyl acetic acid ethy (0.52g, 2.6mmol) in 25 mL of CH_2Cl_2 is added N-chlorosuccinimide (0.35g, 2.6mmol). The solution is stirred for 10 minutes. After this time, 1 drop of TFA is added. The solution is stirred for 16 hours. The reaction mixture is then diluted with 25 mL of CH_2Cl_2. The resulting solution is washed with 1N NaOH and a saturated NaCl solution. The organic layer is dried over $MgSO_4$, filtered and concentrated. The resulting product is obtained as an oil which is determined to contain 45% of the desired product. The oil is then dissolved in 60 mL of 1:1:1 THF:MeOH:H_2O. To the solution is added lithium hydroxide monohydrate (1.26g, 30mmol). The solution is stirred for 16 hours. After this time, the solution is acidified to pH=3 with 1N HCl. The aqueous solution is washed with H_2O and saturated NaCl solution. The solution is extracted with EtOAc/CH_2Cl_2 (2:1). The organic layer is dried over $MgSO_4$, filtered and concentrated. The resulting crude product is purified by column chromatography eluting with 20% MeOH:Et_2O to give the product as a white solid (0.4g, 1.9mmol). MS (EI): m/z 208, 210 (M+), Cl pattern.

EXAMPLE 32. 5'-Chloro-[2,2']bithiophenyl-5-carboxylic acid.

A. 5'-Chloro-[2,2']bithiophenyl-5-carbaldehyde.

To a solution of 5-chloro-[2,2']bithiophene (1.06 g, 5.28 mmol) in 12 mL of THF at -78°C is added n-BuLi (4.4 mL of a 1.6M solution in hexanes, 6.99 mmol). After 15 minutes, DMF (0.97 mL, 14 mmol) is added and the resulting solution is allowed to warm to 0°C. After 15 min, the solution diluted with EtOAc and quenched with saturated $NaHCO_3$ solution. The organic solution is washed with H_2O and saturated NaCl solution, then dried over $MgSO_4$, filtered and concentrated. The crude product is purified by flash column chromatography eluting with a gradient of 10% Et_2O/hexanes to 20%

Et_2O/hexanes to yield the title compound (0.89 g, 3.89 mmol) as a white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 9.87 (s, 1H), 7.70 (d, 1H), 7.20 (d, 1H), 7.15 (d, 1H), 6.91 (d, 1H).

B. 5'-Chloro-[2,2']bithiophenyl-5-carboxylic acid.

The title compound is prepared as described in EXAMPLE 28, Part B using 5'-chloro-[2,2']bithiophenyl-5-carbaldehyde. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, 1H), 7.09 (d, 1H), 7.06 (d, 1H), 6.89 (d, 1H). EI MS, $[M]^+$=243,245 (Cl pattern).

EXAMPLE 33. 7-Chloro-isoquinoline-3-carboxylic acid.

A. 7-Chloro-isoquinoline-3-carbaldehyde.

A 20mL of 80% H_2SO_4 is added 7-chloro-3,3-dibromomethyl isoquinoline (0.69g, 2.06mmol) is heated to 150°C for 16 hours. The solution is then cooled to ambient temperatures and diluted with 40 mL of H_2O. The resulting solution is basified to pH=11 with 1N NaOH. The aqueous solution is extracted with CH_2Cl_2. The organic solution is washed with H_2O and a saturated NaCl solution. The organic layer is dried over $MgSO_4$, filtered and concentrated to give the product as an oil (0.25g, 1.3 mmol). ^1H NMR ($CDCl_3$, 300MHz) δ 10.0 (s, 1H), 9.30 (s, 1H), 8.36 (s, 1H), 8.07 (s, 1H), 7.95 (d, 1H), 7.78 (d, 1H). MS (EI): m/z 191, 193 (M+), Cl pattern.

B. 7-Chloro-isoquinoline-3-carboxylic acid.

To 4.5 mL of a 1N NaOH solution at 0°C is added a solution of $AgNO_3$ (0.31g, 1.8mmol) in 3 mL of H_2O, followed by a solution of of 7-chloro-isoquinoline-3-carbaldehyde (0.25g, 1.3mmol) in 3 mL of EtOH. The solution is stirred at 0°C for 10 minutes, then at room temp. For 3 hours. The solution is acidified to pH=3 with 1H HCl. The resulting solution is extracted with $CHCl_3$. The organic layer is dried over $MgSO_4$, filtered and concentrated to give the product as a white solid (0.2g, 0.96mmol). ^1H NMR (CD_3OD, 300MHz) δ 9.18 (s, 1H), 8..63 (s, 1H), 8.18 (m, 1H), 7.80 (m, 2H). 6.94 (m, 1H), 4.15 (q, 2H), 3.48 (s, 2H), 1.20 (t, 3H). MS (EI): m/z 208, 210 (M+), Cl pattern.

EXAMPLE 34. 2-Acetylamino-3-(5-chloro-thiophen-2-yl)-acrylic acid.

A. 4-(5-Chloro-thiophen-2-ylmethylene)-2-methyl-4H-oxazol-5-one.

A mixture consisting of 5-chlorothiophene-2-carboxaldehyde (1.00 g, 6.82 mmol), N-acetylglycine (0.96 g, 8.18 mmol), NaOAc (0.67 g, 8.18 mmol) in Ac_2O (5 mL) is warmed at reflux for 16 hours. The reaction mixture is cooled to ambient temperature and diluted with dilute aqueous NaOH (0.5 M, 100 mL) and CH_2Cl_2 (100 mL). The layers are separated and the organic phase is washed with

aqueous $NaHCO_3$, brine, dried over anhydrous Na_2SO_4, filtered and concentrated to provide 1.5 g (100%) of the title compound as a colorless oil which is used without further purification in the next reaction. ^1H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 6.94 (d, J = 4.0 Hz, 1H), 7.21 (s, 1H), 7.26 (d, J = 4.0 Hz, 1H) ppm.

B. 2-Acetylamino-3-(5-chloro-thiophen-2-yl)-acrylic acid.

To a solution containing 4-(5-chloro-thiophen-2-ylmethylene)-2-methyl-4H-oxazol-5-one (1.5 g, 6.82 mmol) in MeOH (18 mL) is added 1.0 M NaOH (12.0 mL, 12 mmol) at ambient temperature. After 3 h, the reaction mixture is diluted with water (100 mL) and CH_2Cl_2 (100 mL) and the layers are separated. The basic, aqueous layer is washed with CH_2Cl_2 and then acidified using 1.0 M HCl (20 mL) to provide a crude solid which is collected on a Buchner funnel. Drying in vacuo provided 1.2 g (75%) of the title compound as a pale brown solid which is used without further purification. ^1H NMR (300 MHz, DMSO-d_6) δ 2.00 (s, 3H), 7.14 (d, J = 4.01 Hz, 1H), 7.38 (d, J = 4.01 Hz, 1H), 7.63 (s, 1H), 9.28 (s, 1H), 12.73 (br s, 1H) ppm; MS (EI): m/z 245 (M+).

EXAMPLE 35. 2-Acetylamino-3-(5-chloro-thiophen-2-yl)-propionic acid.

To a solution containing 2-acetylamino-3-(5-chloro-thiophen-2-yl)-acrylic acid (1.00 g, 4.08 mmol) and K_2CO_3 (1.70 g, 12.1 mmol) in DMF (20 mL) is added MeI (0.87 g, 6.12 mmol) at ambient temperature. After 2 h, the reaction mixture is diluted with water (100 mL) and EtOAc (100 mL) and the layers are separated. The aqueous layer is extracted with EtOAc (50 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to provide 0.92 g (83%) of the methyl ester which is used without further purification. ^1H NMR (300 MHz, $CDCl_3$) δ 2.19 (s, 3H), 3.77 (s, 3H), 6.86 (d, J = 4.02 Hz, 1H), 6.99 (m, 1H), 7.05 (d, J = 4.02 Hz, 1H), 7.64 (s, 1H) ppm.

A small Parr® vessel is charged with the crude ester (0.85 g, 3.13 mmol) and $(Ph_3P)_3RhCl$ (0.10 g, 0.10 mmol) in MeOH (50 mL). The vessel is pressurized to 50 PSI H_2 pressure and agitated for 7 h at ambient temperature. The reaction mixture is then filtered and concentrated to provide the desired compound, which is used without further purification. MS (EI): m/z 261 (M+).

The above-prepared saturated ester is dissolved in a 1:1:1 solution of water/THF/MeOH (15 mL). LiOH monohydrate (0.14 g, 3.23 mmol) is added and the heterogeneous mixture is stirred for 16 hours. The reaction mixture is diluted with water (100 mL) and EtOAc (100 mL) and the layers are separated. The aqueous layer is extracted with EtOAc (50 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to provide 0.62 g (81%) of the title compound as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 2.02 (s, 3H), 3.30 (m, 2H), 4.81 (m, 1H), 6.45 (br d, J = 6.45 Hz, 1H), 6.58 (d, J = 3.68 Hz, 1H), 6.71(d, J = 3.68 Hz, 1H), 9.79 (br s, 1H) ppm; MS (EI): m/z 247 (M+).

EXAMPLE 36. 3-(6-Amino-pyridin-3-yl)-acrylic acid.

A. N-(5-Bromo-pyridin-2-yl)-acetamide.

Triethylamine(17.7mL, 75 mmol) is added to a mixture of 2-amino-5-bromopyridine (5.0 g, 29 mmol) and acetic acid (7.1 mL, 75 mmol). The solution is heated to reflux for 48 hours. After this time, the solution is concentrated. The reside is dissolved in water and the pH is adjusted to 10 with 1N NaOH. The solids are collected by filtration. The crude product is recrystallized from boiling water to give the title compound (2.6 g 12.0 mmol) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.62 (1H, bs), 8.42 (s, 1H), 8.01 (m, 2H), 2.05 (s, 3H).

B. 3-(6-Acetylamino-pyridin-3-yl)-acrylic acid

To a mixture of N-(5-bromo-pyridin-2-yl)-acetamide (1.26 g, 5.86 mmol) and tri-n-butylamine in xylenes (10 mL)is added $Pd(OAc)_2$ (1.4 mg, 0.006 mmol) and triphenyl phosphine (15.4mg, 0.06 mmol). Acrylic acid (0.48 mL, 7.03 mmol) is then added dropwise over 5 minutes. The mixture is heated to reflux for 5 hours. The solution is cooled to ambient temperatures. The mixture is diluted with water and the pH is adjusted to 4 with 1N HCl. The solution is extracted with EtOAc/CH_2Cl_2 (2:1). The resulting suspension is filtred to give the title compound (0.80 g, 3.88 mmol) as a white solid. MS (ion spray) 207, (M+H).

C. 3-(6-Amino-pyridin-3-yl)-acrylic acid

To 3-(6-acetylamino-pyridin-3-yl)-acrylic acid (0.80 g, 3.88 mmol) in ethanol (10 mL) is added 1N NaOH (20mL). The solution is heated to reflux. After 16 h, the solution is concentrated to 1/3 its volume. The aqueous solution is diluted with water and acidified to pH=2 with 6N HCl. The solution is concentrated to dryness. The residue is dissolved in methanol. The solution is filtered. The organic solution is concentrated. The crude product is purified by RP-HPLC eluting with a gradient of 5%CH3CN/H2O (0.1% TFA) to 30% CH3CN/H2O (0.1%TFA) to give the product as a white solid (0.54 g, 1.93 mmol). ^{1}H NMR (300 MHz, CD_3OD) δ 8.34 (d, 1H), 8.07 (s, 1H), 7.54 (d, 2H), 7.06 (d, 1H), 6.47 (d, 1H). MS (ion spray) 165, (M+H).

EXAMPLE 37. 4-Chloro-benzyl isocyanate.

To a solution of triphosgene (0.54 g, 1.85 mmol) in 10 mL of dry CH_2Cl_2 at 0°C is added 4-chloro-benzylamine (0.61 mL, 5.00 mmol) dropwise as a white precipitate forms. Et_3N (1.39 mL, 10.0 mmol) in 5 mL of CH_2Cl_2 is added immediately and the resulting mixture is stirred at 0°C for 5 min, then at room temperature for 3 hours. The mixture is concentrated in vacuo and triturated with EtOAc.

The white precipitate (triethylamine hydrochloride) is filtered off and the filtrate is concentrated. The title compound (6.20 g, 30.6 mmol) is isolated as a crude yellow residue and used in the subsequent step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35 (d, 2H), 7.25 (d, 2H), 4.50 (s, 2H).

EXAMPLE 38. 5-Chloro-thiophene-2-carbonyl azide.

To a solution of 5-chloro-2-thiophene-carboxylic acid (5.00 g, 30.7 mmol) in 130 mL of acetone is added Et_3N (4.29 mL, 30.7 mmol). The mixture is cooled to 0°C and ethyl chloroformate (3.23 mL, 33.8 mmol) is added. The mixture is stirred at 0°C for 1h and sodium azide (3.40 g, 52.3 mmol) is added. The mixture is stirred at 0°C for 2 h, then poured into 300 mL of ice water and the aqueous layer is extracted with CH_2Cl_2 (2x). The combined organics are washed with water (2x) and brine, then dried, filtered and concentrated. The crude residue is purified via flash column chromatography eluting with 10% EtOAc/hexanes to provide the title compound (3.00 g, 16.0 mmol) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.67 (d, 1H), 6.99 (d, 1H).

EXAMPLE 39. 4-Nitro-2,3,5,6-tetrachloropyridine.

Pentachloropyridine (80 g, 320 mmol) is treated with benzyl amine (104 mL, 96 mmol), dissolved in dioxane (1 L) and refluxed for 16 hours. The reaction mixture is cooled to ambient temperature and the precipitated white solid is removed by filtration. The filtrate is concentrated to a brown residue and triturated with 4 % ethyl acetate in hexane (3 X 250 mL) to give 4-benzylamino-2,3,5,6-tetrachloropyridine as an off-white solid (40 g, 124 mmol). This material is dissolved in chloroform (400 mL), cooled in an ice bath and treated with trifluoroacetic acid (500 mL) and 30% hydrogen peroxide (100 mL). The reaction mixture is warmed to room temperature overnight and treated with additional trifluoroacetic acid (500 mL) and 30% hydrogen peroxide (100 mL). After stirring 24 hours the reaction is treated with water (1L). The lower organic layer is separated and the aqueous layer is extracted with chloroform. The combined organic layers are concentrated to a solid residue and redissolved in ethyl acetate/hexane (30 mL). The suspended orange solid is removed and the filtrate is loaded on a silica flash column. The column is eluted with hexane and the title compound is collected as a white solid (15.6 g, 60 mmol). EI MS m/z 260, 262, 264 [M+].

EXAMPLE 40. 4-(tert-Butyloxycarbonyl)-piperazin-2-one

4-(Benzyloxycarbonyl)-piperazin-2-one (2.2 g, 9.4 mmol) and Boc anhydride (2.5 g, 11.3 mmol) are dissolved in methanol (100 mL), treated with 5% Pd /C and shaken 16 h under hydrogen gas (30 PSI). The reaction vessel contents are filtered through Celite and the filtrate is concentrated to yield 4-(tert-Butyloxycarbonyl)-2-oxopiperazine (1.9 g, 9.4 mmol) which is used without further purification. EI

MS m/z 200, M^+; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.17 (br, 1H), 4.20 (s, 2H), 3.55 (t, 2H), 3.38 (m, 2H), 1.48 (s, 9H).

EXAMPLE 41. 2-Methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

A. N-Cbz-O-methylserine-aminoacetaldehyde dimethyl acetal.

To a solution of N-Cbz-O-methylserine (10.8g, 41.8mmol) in 500mL of CH_2Cl_2 is added Et_3N (12.7 g, 125mmol). The solution is cooled to 0°C and TBTU (13.5g, 42mmol) and aminoacetaldehyde dimethyl acetal (4.83g, 46mmol) are added. The solution is stirred for 16 hours. The solution is diluted with 500mL of ether. The resulting solution is washed with water, 1N $KHSO_4$, and sat. NaCl. The title compound (13.7g, 41.8mmol) is obtained as a white foam. ^1H NMR ($CDCl_3$, 300MHz) δ 7.40 (m, 5H),6.55 (bs, 1H), 5.66 (bs, 1H), 5.32 (m, 1H), 5.13 (s, 2H), 4.32 (m, 2H), 3.79 (dd, 1H), 3.44 (m, 2H), 3.40 (m, 9H).

B. N-Cbz-2-Oxo-3-(S)-methoxymethyl-(4,5-dihydro)piperazine.

To a solution of N-Cbz-O-methylserine-aminoacetaldehyde dimethyl acetal (13.7g, 41.8mmol) in 300mL of toluene is added TsOH.H2O (0.80g, 4.2mmol). The solution is heated to 60°C. After 5h, the solution is diluted with ether. The resulting organic solution is washed with water, sat. NaHCO3, and sat. NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated under vacuum. The resulting crude product is purified by column chromatography eluting with a gradient of 10%EtOAc:CH_2Cl_2 to 20%EtOAc:CH_2Cl_2. The title compound (10.7g, 38mmol) is obtained as a white solid. ^1H NMR ($CDCl_3$, 300MHz) δ 7.36 (m, 5H), 6.45 and 6.30 (d, 1H rotational isomers), 5.61 and 5.50 (d, 1H rotational isomers), 5.20 (s, 2H), 4.92 and 4.83 (bs, 1H rotational isomers), 3.63 (m, 3H), 3.32 and 3.20 (s, 1H rotational isomers).

C. 2-Methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

To a solution of N-Cbz-2-oxo-3-(S)-methoxymethyl-(4,5-dihydro)piperidine (10.7g, 38mmol) in 50mL of methanol is added Pt/C (1gm, 10% by weight). The atmosphere above the reaction is replaced by hydrogen. After 24h, the solution is filtered and the filtrate is washed with methanol. The collected organic solutions are concentrated under vacuum. The resulting crude product is purified by column chromatography eluting with a gradient of 2%MeOH/CH_2Cl_2 to 5%MeOH/CH_2Cl_2. The title compound (6.0g, 22mmol) is obtained as a white solid. ^1H NMR ($CDCl_3$, 300MHz) δ 7.35 (m, 5H),6.42 (bs, 1H), 5.20 (AB, 2H), 4.58 (m, 1H), 4.18 (m, 1H), 3.95 (m, 1H), 3.50 (m, 4H), 3.27 (s, 3H).

EXAMPLE 42. 2-Butyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-norleucine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300mHz) δ 7.32 (m, 5H), 5.13 (AB, 2H), 4.60 (m, 1H), 4.13 (m, 1H), 3.38 (m, 2H), 3.23 (m, 2H), 1.90 (m, 1H), 1.66 (m, 1H), 1.29 (m, 4H), 0.89 (m, 3H). MS (ion spray) m/z 291, (M+H).

EXAMPLE 43. 2-Ethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-2-amino-butric acid for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300mHz) δ 7.37 (m, 5H), 6.55 (bs, 1H), 5.10 (AB, 2H), 4.57 (m, 1H), 4.24 (m, 1H), 3.42 (m, 1H), 3.26 (m, 2H), 2.20 (m, 1H), 1.81 (m, 1H), 0.96 (m, 3H).

EXAMPLE 44. 2-Propyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-norvaline for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300mHz) δ 7.32 (m, 5H), 7.00 (bs, 1H), 5.12 (AB, 2H), 4.58 (m, 1H), 4.21 (m, 1H), 3.40 (m, 1H), 3.19 (m, 2H), 1.88 (m, 1H), 1.73 (m, 1H), 1.37 (m, 2H), 0.91 (m, 3H). MS (ion spray) m/z 277, (M+H).

EXAMPLE 45. 2-Ethoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-O-ethyl-serine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.32 (m, 5H),6.96 (bs, 1H), 5.17 (AB, 2H), 4.58 (m, 1H), 4.18 (m, 1H), 4.03 (m, 1H), 3.66 (m, 2H), 3.44 (m, 3H), 3.27 (s, 1H), 1.06 (m, 3H). MS (ion spray) m/z 293, (M+H).

EXAMPLE 46. 2-Methyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-alanine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.34 (m, 5H),7.02 (bs, 1H), 5.17 (AB, 2H), 4.65 (m, 1H), 4.17 (m, 1H), 3.42 (m, 1H), 3.23 (m, 2H), 1.41 (d, 3H). MS (EI) m/z 248, (M+).

EXAMPLE 47. 2-Benzyl-3-oxo-piperazine-1-carboxylic acid benzyl ester

The title compound is prepared as in EXAMPLE 41, substituting Cbz-phenylalanine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.22 (m, 10H), 7.00 (bs, 1H), 5.10 (AB, 2H), 4.10 (m, 1H), 3.27 (m, 2H), 3.10 (m, 2H), 2.55 (m, 2H). MS (EI) m/z 324, (M+).

EXAMPLE 48. 2-(1-Methoxyethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-O-methyl-threonine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.52 (bs, 1H), 7.22 (m, 5H), 5.12 (AB, 2H), 4.33

(m, 1H), 4.05 (m, 2H), 3.60 (m, 1H), 3.14 (s, 3H), 3.10 (m, 1H), 2.82 (m, 1H), 1.10 (d, 3H). MS (ion spray) m/z 293, (M+H).

EXAMPLE 49. 2,2-Dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-2-amino-isobutryic acid for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.36 (m, 5H),6.52 (bs, 1H), 5.12 (s, 2H), 3.72 (m, 2H), 3.33 (m, 2H), 1.68 (s, 3H), 1.64 (s, 3H). MS (EI) m/z 262, (M+).

EXAMPLE 50. 2-Isopropyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-valine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.36 (m, 5H),5.88 (bs, 1H), 5.10 (s, 2H), 4.35 (m, 1H), 3.44 (m, 1H), 3.27 (m, 2H), 2.31 (m, 1H), 1.00 (d, 3H), 0.94 (d, 2H).

EXAMPLE 51. 2-Isobutyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-leucine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.35 (m, 5H), 6.50 (m, 1H), 5.15 (s, @H), 4.18 (m, 1H), 3.42 (m, 2H), 3.21 (m, 2H), 1.50 (m, 3H), 0.90 (m, 6H).

EXAMPLE 52. 2-(2-Methoxyethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting Cbz-O-methyl-homo-serine for Cbz-O-methyl-serine. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.32 (m, 5H), 6.85 (bs, 1H), 5.14 (s, 2H), 4.75 (m, 2H), 4.20 (m, 2H), 3.42 (m, 1H), 3.21 (m, 3H), 2.12 (m, 4H).

EXAMPLE 53. 2-Methoxymethyl-5-methyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as in EXAMPLE 41, substituting 2-amino-propionaldehyde dimethyl acetal for aminoacetaldehyde dimethyl acetal. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.42 (m, 5H), 6.96 (bs, 1H), 5.12 (AB, 2H), 4.52 (m, 1H), 4.21 (m, 1H), 3.92 (m, 1H), 3.58 (m, 2H), 3.22 (s, 3H), 3.10 (m, 1H), 0.95 (m, 3H).

EXAMPLE 54. 3-(R)-(tert-Butyl-dimethyl-silanyloxymethyl)-5-oxo-piperazine-1-carboxylic acid benzyl ester.

A. 2-tert-Butoxycarbonylamino-3-(tert-butyl-dimethyl-silanyloxy)-propionic acid.

tert-Butyldimethylchlorosilane (32.3 g, 0.214 mol) in THF (50 mL) is added dropwise via cannula to a solution of BOC serine (20.0g, 0.098 mol) and imidazole (15.3 g, 0.224 mol) in THF (360

mL) at RT. The resulting slurry is stirred for 2.5 h then the solvent is removed in vacuo. The crude product is dissolved in MeOH (180 mL) and 5N NaOH (58 mL) is slowly added at RT. The mixture is stirred for 3 h then diluted with water (180 mL) after which time the aqueous layer is washed with ether (180 mLx2). The aqueous layer is acidified to pH 4-5 with 2N HCl and extracted with diethyl ether. The organic layer is washed with saturated $NaHCO_3$ and brine then dried over $MgSO_4$, filtered and concentrated to dryness. The crude product (12.67g, 0.040 mol) is used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.35 (bs, 1H), 4.30 (bs, 1H), 4.13 (dd, 1H), 3.80 (dd, 1H), 1.45 (s, 9H), 0.98 (s, 9H), 0.10 (s, 6H). EI MS, $[M+H]^+$=320.

B. [2-(tert-Butyl-dimethyl-silanyloxy)-1-(methoxy-methyl-carbamoyl)-ethyl]-carbamic acid tert-butyl ester.

N,N-Dimethylaminopyridine (2.60 g, 21.3 mmol) and BOP reagent (18.15 g, 41.0 mmol) are added to a solution of 2-tert-butoxycarbonylamino-3-(tert-butyl-dimethyl-silanyloxy)-propionic acid (12.37 g, 38.7 mmol), diisopropylethylamine (8.1 mL, 46.4 mmol) and N,O-dimethylhydroxylamine hydrochloride (4.53 g, 46.4 mmol) in THF (260 mL) at RT. The resulting suspension is stirred at RT overnight then concentrated to dryness. The residue is diluted with EtOAc and washed with saturated NH_4Cl, saturated $NaHCO_3$ and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo to give the crude product which is purified by flash chromatography eluting with 10-30% EtOAc/Hexanes to yield the title compound (11.86 g, 30.37 mmol) as an oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.35 (bd, 1H), 4.71 (bs, 1H), 3.78-3.85 (m, 2H), 3.72 (s, 3H), 3.20 (s, 3H), 1.42 (s, 9H), 0.90 (s, 9H), 0.05 (s, 6H).

C. [1-(tert-Butyl-dimethyl-silanyloxymethyl)-2-oxo-ethyl]-carbamic acid tert-butyl ester.

A solution of [2-(tert-butyl-dimethyl-silanyloxy)-1-(methoxy-methyl-carbamoyl)-ethyl]-carbamic acid tert-butyl ester (11.86, 30.37 mmol) in Et_2O (100 mL) is added dropwise to a 1.0M solution of LAH in ether (35.5 mL) at -5°C-0°C . The resulting mixture is stirred for 2.5 h then an aqueous solution of $KHSO_4$ is slowly added. The reaction mixture is stirred for 30 minutes and then washed with saturated NH_4Cl, saturated $NaHCO_3$ and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo to give the crude product which is purified by flash chromatography eluting with 30% EtOAc/Hexanes to yield the title compound (6.04 g, 19.9 mmol) as an oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 9.65 (s, 1H), 5.30 (bs, 1H), 4.20 (m, 1H), 3.65 (4.90 (m, 2H), 1.48 (s, 9H), 0.90 (s, 9H), 0.05 (s, 6H). Ion spray MS, $[M+H]^+$=304.

D. [2-tert-Butoxycarbonylamino-3-(tert-butyl-dimethyl-silanyloxy)-propylamino]-acetic acid methyl ester.

Sodium cyanoborohydride (2.63 g, 41.9 mmol) is added to a solution of [1-(tert-butyl-dimethyl-silanyloxymethyl)-2-oxo-ethyl]-carbamic acid tert-butyl ester (6.04 g, 19.9 mmol) and glycine methyl ester hydrochloride (2.75 g, 32.9 mmol) in MeOH (500 mL). The mixture is stirred for 2 days at RT then concentrated to dryness. The crude product is purifed by flash chromatography eluting with 1-5% MeOH/CH_2Cl_2 to yield the title compound (3.06, 8.12 mmol) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.00 (bs, 1H), 3.75 (s, 3H), 3.60-3.70 (m, 4H), 3.40 (d, 1H), 2.80 (dd, 1H), 2.68 (dd, 1H), 1.40 (s, 9H), 0.90 (s, 9H), 0.05 (s, 6H). Ion spray MS, $[M+H]^+$=377.

E. (Benzyloxycarbonyl-[2-tert-butoxycarbonylamino-3-(tert-butyl-dimethyl-silanyloxy)-propyl]-amino)-acetic acid methyl ester.

Benzylchloroformate (1.4 mL, 9.81 mmol) is added dropwise to a solution of N,N-dimethylaminopyridine (1.09 g, 8.93 mmol) and [2-tert-butoxycarbonylamino-3-(tert-butyl-dimethyl-silanyloxy)-propylamino]-acetic acid methyl ester (3.06 g, 8.12 mmol) in CH_2Cl_2 at RT. The resulting mixture is stirred overnight then concentrated to dryness. The crude product is purifed by flash chromatography eluting with 1% MeOH/CH_2Cl_2 to yield the title compound (3.52 g, 6.89 mmol) as a colorless oil. Ion spray MS, $[M+H]^+$=511.

F. 3-(tert-Butyl-dimethyl-silanyloxymethyl)-5-oxo-piperazine-1-carboxylic acid benzyl ester

(Benzyloxycarbonyl-[2-tert-butoxycarbonylamino-3-(tert-butyl-dimethyl-silanyloxy)-propyl]-amino)-acetic acid methyl ester (3.52 g, 6.89 mmol) is stirred in 50% TFA/CH_2Cl_2 (40 mL) at RT for 40 minutes. The reaction mixture is concentrated in vacuo and the crude product is purifed by flash chromatography eluting with 1% MeOH/CH_2Cl_2 to yield the title compound (1.1 g, 2.9 mmol) as a colorless oil. Ion spray MS, $[M+H]^+$=379.

EXAMPLE 55. 5-Oxo-piperazine-1,3(R or S)-dicarboxylic acid 1-benzyl ester 3-methyl ester.

N,N-Dimethylaminopyridine (0.43 g, 3.5 mmol) and benzylchloroformate (0.55 g, 3.8 mmol) are added to a solution of methyl 6-oxopiperazine-2-carboxylate (0.50 g, 3.2 mmol) (Aebischer, B., Helv. Chim. Acta 1989, 72, 1043-1051) in CH_2Cl_2 at RT. After 1 h, the reaction mixture is poured into EtOAc and washed with saturated $NaHCO_3$ and brine then dried over $MgSO_4$, filtered and concentrated to dryness to give a solid (0.90 g, 3.1 mmol) which is used in subsequent reactions without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40 (bs, 5 H), 6.32 (bs, 1H), 5.15 (s, 2H), 4.00-4.30 (m, 3H), 4.23 (s, 3H), 3.70-3.80 (m, 2H). MS (EI) m/z 292 (M+).

EXAMPLE 56. (S)-5-Oxo-piperazine-1,3-dicarboxylic acid 1-allyl ester 3-methyl ester.

To a solution containing methyl (S)-6-oxopiperazine-2-carboxylate (1.32 g, 8.35 mmol), prepared by the method of Aebischer, in anhydrous dichloromethane (30 mL) at 0 °C is added triethylamine (1.26 g, 12.5 mmol) followed by allylchloroformate (1.20 g, 10.0 mmol). After 1 h, the reaction mixture is poured onto a 1:1 mixture of CH_2Cl_2/water (200 mL), acidified using 1 N HCl and the layers are separated. The organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is chromatographed on silica gel (CH_2Cl_2 to 1% MeOH/CH_2Cl_2) to provide 1.22 g (60%) of EXAMPLE 35 as a viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.43 (bs, 1H), 5.90 (m, 1H), 5.26 (m, 2H), 4.61 (m, 2H), 4.05-4.26 (m, 3H), 3.80 (s, 3H), 3.72 (m, 2H); MS (ISP loop): m/z 243 (M+H).

EXAMPLE 57. (2S, 6R)-4-(2,6-dimethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester.

and

EXAMPLE 58. (2S, 6S)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

A. (2RS, 1S)-[1-(2-hydroxy-propylcarbamyl)-ethyl]-carbamic acid tert-butyl ester

N-(tert-Butoxycarbonyl)-L-alanine (10.0 g, 52.8 mmol) is dissolved in 150 mL of THF. Once the triethylamine (11.0 ml, 79.2 mmol) is added, the solution is cooled to 0°C . Isopropyl chloroformate in toluene (1M) (52.8 ml, 52.8 mmol) is added slowly followed by the addition of (2RS) 1-amino-2-propanol (6.1 ml, 79.2 mmol). After stirring overnight, the mixture is washed with 1N sodium hydroxide and 1N hydrochloric acid. Concentration of the organic solvent afforded (2RS, 1S)-[1-(2-hydroxy-propylcarbamyl)-ethyl]-carbamic acid tert-butyl ester (9.92 g, 76% yield) as a clear oil.

B. (1S)-[1-(2-oxo-propylcarbamoyl)-ethyl]-carbamic acid tertbutyl ester

Dimethylsulfoxide (7.16 ml, 100.8 mmol) is added to a solution of oxalyl chloride (4.41 ml, 50.4 mmol) in 126 mL of methylene chloride at -78 °C . The mixture is left to stir for fifteen minutes, and a solution of (2RS, 1S)-[1-(2-hydroxy-propylcarbamyl)-ethyl]-carbamic acid tert-butyl ester (9.92 g, 40.32 mmol) in 100 mL of CH_2Cl_2 is added dropwise. After stirring for 15 minutes at -78 °C , the reaction is quenched with triethylamine (28 mL, 381 mmol), and the temperature is allowed to rise to room temperature. The volatile solvents are removed, and the residue is purified by flash column (SiO_2, 60% EtOAc/Hexane). The product (1S)-[1-(2-oxo-propylcarbamoyl)-ethyl]-carbamic acid tertbutyl ester (5.93 g, 60 %) is isolated as a white solid. MS $C_{11}H_{20}N_2O_4$ MS m/z: 245.

C: (3S, 5RS)-3,5-dimethyl-piperazin-2-one.

(1S)-[1-(2-oxo-propylcarbamoyl)-ethyl]-carbamic acid tertbutyl ester (5.93 g, 24.3 mmol) is stirred in a solution of 30 % trifluoroacetic acid in methylene chloride (100 mL) for three hours. The

solvents are removed in vacuo. The residue is dissolved in 50 mL of MeOH and transferred to a par bottle. Palladium on carbon (10 % , 1.0 g) is added, and the mixture is hydrogenated under pressure for 24 hours. The catalyst is filtered off ; the MeOH is removed in vacuo to afford (3S, 5RS)-3,5-dimethyl-piperazin-2-one which is directly protected with a benzyl carbamate without further purification.

D: (2S, 6RS)-2,6-Dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

To a solution of (3S, 5RS)-3,5-dimethyl-piperazin-2-one (24.3 mmol) in 100 mL of methylenechloride is added triethylamine (8.45 mL, 60.75 mmol) and N-(benzyloxycarbonyloxy)succinimide (12.1 g, 48.6 mmol). After stirring overnight, the CH_2Cl_2 is removed, and the crude mixture is chromatographed (50 % EtOAc/Hexane). (2S, 6RS)-2,6-Dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (3.3 g, 52 % yield over three steps) is isolated as a white powder. MS $C_{14}H_{18}N_2O_3$ MS m/z: 263.

E. (2S, 6R)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester and (2S, 6S)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester

The two single enantiomers [(2S, 6R)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester and (2S, 6S)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester] can be seperated by column chromatography from (2S, 6RS)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, which can also be used directly in combination or separation of its derivatives as shown below.

EXAMPLE 59. (2S, 6R)-4-(2,4-Dimethoxy-benzyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

A. (2S, 2S)-N-(2, 4-dimethoxy-benzyl)-N-(2-hydroxy-propyl)-2-(2,2,2-trifluoroacetylamino)-propionamide.

To a slurry of (2S)-2-(2,2,2-trifluoroacetylamino)-propionic acid (15.3 g, 53.4 mmol) in 120 mL of methylene chloride is added triethylamine (5.6 mL, 40.0 mmol). The heterogeneous mixture is cooled to 0°C and isopropyl chloroformate (27 mL, 27.0 mmol) is added slowly. After stirring for 20 minutes at room temperature, a solution of the (2S)-1-(2,4-dimethoxy-benzylamino)-propan-2-ol (6.0 g, 26.7 mmol, obtained from the reductive amination of the corresponding aldehyde and aminoalcohol) in 5mL of methylene chloride is added. The resulting mixture is left to stir overnight. Ethyl acetate (500 mL) is added, and the organic solution is washed with 1N hydrochloric acid (50 mL) and 1N sodium hydroxide (50 mL). The ethyl acetate is dried with magnesium sulfate, filtered and condensed. The resulting residue is chromatographed on silica gel (25% ethyl acetate/hexane) to give (2S, 2S)-N-(2,4-dimethoxy-benzyl)-N-(2-hydroxy-propyl)-2-(2,2,2-trifluoroacetylamino)-propionamide (6.29g, 60% yield) as a clear oil. MS $C_{17}H_{23}F_3N_2O_5$ MS m/z: 393.

B. (3S, 5R)-1-(2,4-dimethoxy-benzyl)-3,5-dimethyl-4-trifluoroacetyl-piperazin-2-one.

(2S, 2S)-N-(2,4-Dimethoxy-benzyl)-N-(2-hydroxypropyl)-2-(2,2,2-trifluoroacetylamino)-propionamide (3.64 g, 9.29 mmol) is dissolved in 25 mL of tetrahydrofuran. Triphenylphosphate (3.65 g, 14.0 mmol) is added, and the resulting mixture is cooled to 0 °C before diethyl azodicarboxylate (2.2 mL, 14 mmol) is added slowly. The resulting mixture is left to stir overnight. The reaction mixture is condensed, and the residue is purified by column chromatography (SiO_2, 25% ethyl acetate/hexane). The desired product, (3S, 5R)-1-(2,4-dimethoxy-benzyl)-3,5-dimethyl-4-trifluoroacetyl-piperazin-2-one (1.5 g, 43% yield), is isolated as a clear oil.

C. (3S, 5R)-1-(2,4-Dimethoxy-benzyl)-3,5-dimethyl-piperazin-2-one.

(3S, 5R)-1-(2,4-Dimethoxy-benzyl)-3,5-dimethyl-4-trifluoroacetyl-piperazin-2-one (575 mg, 1.54 mmol) is dissolved in 30 mL of methanol and 3 mL of H_2O. Potassium carbonate (883 mg, 6.4 mmol) is added to the solution, and the reaction is refluxed for one and half hours before concentration. Ethyl acetate (3x 50 mL) is used to extract the aqueous layer. Removal of Ethyl acetate afforded the crude amine (387 mg, 91% yield) as a clear oil. $C_{15}H_{22}N_2O_3$ MS m/z: 279.

D. (2S, 6R)-4-(2,4-dimethoxy-benzyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

Triethylamine (0.4 mL, 2.8 mmol) and N-(benzyloxycarbonyloxy)-succinimide (1.04 g, 4.2 mmol) is added to a solution of the above crude amine (387 mg, 1.4 mmol) in 15 mL of methylene chloride. The reaction mixture is left to stir overnight. The residue after concentration is chromatographed on silica gel (30% ethyl acetate/hexane) to give (2S, 6R)-4-(2,4-dimethoxy-benzyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (450 mg, 78 % yield) as a clear oil.

E. (2S, 6R)-2,6-Dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

(2S,6R)-4-(2,4-Dimethoxy-benzyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (1.13 g, 2.74 mmol) is dissolved in 20 mL of acetonitrile. An aqueous solution of potassium persulfate (2.2 g, 8.23 mmol) and sodium phosphate (2.3 g, 16.5 mmol) in 12 mL of H_2O is added, and the resulting mixture is heated to 95-100 °C for two hours. After cooling to room temperature, ethyl acetate (200 mL) is used to extract the aqueous layer and dried over magnesium sulfate. The residue after filtration and concentration is chromatographed (SiO_2, 60% ethyl acetate/hexane) to give (2S, 6R)-2,6-Dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (480 mg, 67 % yield) as a yellow oil.

EXAMPLE 60. (2S, 6RS)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

(2S,6RS)-2,6-Dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (380 mg, 1.45 mmol) is dissolved in 10 mL of THF and 1mL of DMF. Sodium hydride (60%, 72 mg, 3.14 mmol) is added at 0 °C and left to stir at room temperature for thirty minutes before 7-bromomethyl-4-chloro-quinoline (257 mg, 1.0 mmol) is added. The reaction is stirred for four hours. Ethyl acetate is added to the mixture, and the reaction is quenched with 3 mL of H_2O. The two layers are separated and ethyl acetate (2x 30 ml) is used to extract before dried over magnesium sulfate. The residue after filtration and concentration is chromatographed on silica gel (60% EtOAc/Hexane) to give (2S, 6RS)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (417 mg, 95 % yield).$C_{22}H_{20}ClN_3O_3$ MS m/z: 438, 440.

EXAMPLE 61. (3S,5RS)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

and

EXAMPLE 62. (3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

and

EXAMPLE 63 (3S, 5S)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

(2S, 6RS)-4-(4-Chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (417 mg, 1.0 mmol) is taken up in 7 mL of acetonitrile, and iodotrimethyl- silane (0.43 mL, 3.0 mmol) is added. The resulting mixture is stirred for one hour at room temperature before quenched with methanol (1 mL). The residue after concentration is taken up in 2N hydrochloric acid (3 mL) and is extracted with ether (2x 30 mL). The aqueous layer is condensed to dryness and the residue is recrystalized from isopropanol and ether to give a mixture (1:4 ratio) of (3S, 5RS)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one as a yellow solid (290 mg). The two epimers are separated using a flash column (SiO_2, 1% triethylamine/3% methanol/methylene chloride). $C_{16}H_{18}ClN_3O$ MS m/z: 304, 306. The minor isomer (3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.is (3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one while the major isomer is (3S, 5S)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one. Alternatively, (3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one and (3S, 5S)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one can be made via the same chemistry shown below from pure (2S, 6S)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester and (2S, 6RS)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, respectively.

Alternative synthesis of (3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

A. (2S, 6R)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

(2S, 6R)-2,6-Dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (750 mg, 2.86 mmol) is dissolved in 20 mL of THF and 2 mL of DMF. Sodium hydride (60%, 142.6 mg, 6.20 mmol) is added at 0 °C , and the reaction is left to stir at room temperature for thirty minutes at which time the 7-bromomethyl-4-chloro-quinoline (952 mg, 3.72 mmol) is added. The reaction is complete after stirring for four hours. Ethyl acetate (200 mL) is added to the mixture, and the reaction is quenched with 3 mL of H_2O . The two layers are separated, and ethyl acetate (2x 30 mL) is used to extract and dried over magnesium sulfate. The residue after filtration and concentration is chromatographed on silica gel (60% EtOAc/Hexane) to give (2S,6R)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (1.04 g, 83 %).

B. (3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

A 33 % solution of hydrogen bromide in acetic acid (10 mL) is added to (2S,6R)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (1.04 g, 2.38 mmol). The reaction is left to stir at room temperature for one hour. The reaction mixture is diluted with ethyl acetate and stirred vigorously to force the product to precipitate out of solution. The ethyl acetate is decanted off and the precipitate is purified on a silica gel column (1 % triethylamine/3 % methanol/methylene chloride) to 582 mg (81% yield) of (3S,5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one as a white solid.

EXAMPLE 64. (3S, 5S)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one.

and

EXAMPLE 65. (3S, 5R)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one.

The crude (3S,5RS)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one (69 mg, 0.20 mmol) obtained from above is dissolved in 1 mL of DMF. Potassium carbonate (76 mg, 0.60 mmol) is added followed by the addition of 2-(3-bromopropenyl)-5-chloro-thiophene (56 mg, 0.24 mmol). The reaction is left to stir overnight. The potassium carbonate is filtered off, and the crude material is purified. The two epimers are separated at this stage by preparative thin layer chromatography (80 % EtOAc/hexane) to give a major epimer (3S, 5R)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one (25 mg, 26% yield) and a minor epimer (3S, 5S)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one (7 mg, 7.5% yield).

EXAMPLE 66. 4-(2-Oxopiperazin-1-ylmethyl)benzamidine.

A. 4-(4-Cyanobenzyl)-3-oxopiperazine-1-carboxylic acid benzyl ester.

To a solution of 3-oxo-piperazine-1-carboxylic acid benzyl ester (3.0 g, 12.8 mmol) and 4-bromomethyl tolylnitrile (2.76 g, 14.1 mmol) in 135 mL of THF and 15 mL of DMF at 0°C is added a 60% dispersion in mineral oil of NaH (0.49 g, 12.8 mmol). After 5 hours, the solution is diluted with saturated NH_4Cl and EtOAc. The organic layer is washed with H_2O and saturated NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated. The crude product is purified by column chromatography over silcia gel eluting with 20% EtOAc/CH_2Cl_2. The title compound is obtained as a white solid (4.01 g, 11.4 mmol). ^1H NMR ($CDCl_3$, 300MHz) δ 7.62 (d, 2H), 7.39 (m, 7H), 5.14 (s, 2H), 4.68 (s, 2H), 4.27 (s, 2H), 3.73 (m, 2H), 3.30 (m, 2H).

B. 4-(4-Carbamimidoylbenzyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester.

A solution of 4-(4-cyanobenzyl)-3-oxopiperazine-1-carboxylic acid benzyl ester (2.4 g, 6.87 mmol) in 30mL of pyridine and 3 ml of Et_3N is saturated with H_2S. The resulting mixture is sealed and stirred for 16 hours. After this time, the solution is concentrated. The residue is dissolved in 30 mL of acetone and methyl iodide (19.4 g, 137 mmol) is added. The solution is refluxed for 2 hours. After this time, the solution is concentrated. The residue is dissolved in MeOH (40 mL) and NH_4OAc (5.0 g, 65 mol) is added. The solution is reluxed for 3 hours. After this time, the solution is concentrated. The crude product is purified by RP-HPLC eluting in a gradient of CH_3CN to 60% CH_3CN/H_2O(0.1%TFA). The appropriate collected fractions are lyophilized to give the product as a white foam. MS (FAB) m/z 367, (M+H).

C. 4-(2-Oxopiperazin-1-ylmethyl)benzamidine.

To a solution of 4-(4-carbamimidoylbenzyl)-3-oxopiperazine-1-carboxylic acid benzyl ester (2.0 g, 5.0 mmol) in 40 mL of MeOH and 4 mL of AcOH is added 10% Pd/C (0.4 g). The atmosphere above the reaction is replaced by hydrogen. After 4hours, the solution is filtered through a pad of Celite. The organic layer is concentrated. The resulting crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1%TFA) to 40% CH_3CN/H_2O (0.1% TFA). The title compound is obtained as a white foam. ^1H NMR (d^6-DMSO, 300 MHz) δ 9.3 (bs, 4H), 9.1 (bs, 2H), 7.83 (d, 2H), 7.42 (d, 2H), 4.78 (s, 2H), 3.80 (s, 2H), 3.44 (m, 2H), 3.32 (m, 2H).

EXAMPLE 67. 1-(2-Aminoquinolin-6-ylmethyl)piperazin-2-one.

A. 4-(2-Chloro-quinolin-6-ylmethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester.

To a solution of 3-oxopiperazine-1-carboxylic acid benzyl ester (4.65 g, 19.8 mmol) and 6-bromomethyl-2-chloroquinoline (5.40 g, 21.0 mmol) in 80 mL of a 3:1 mixture of THF:DMF at 0°C is added sodium hydride (0.81 g, 20.2 mmol, 60% mineral oil dispersion). The resulting mixture is stirred for 1 hour at 0°C then at room temperature for 18 hours. The reaction mixture is quenched with saturated NH_4Cl solution, then diluted with EtOAc. The organic layer is washed sequentially with 1N HCl, water, saturated $NaHCO_3$ and saturated NaCl, then dried over $MgSO_4$, filtered and concentrated. The crude product is triturated in Et_2O/hexanes/EtOAc and filtered to afford the title compound (6.96 g, 17.0 mmol) as a white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, 1H), 8.00 (d, 1H), 7.69 (s, 1H), 7.63 (dd, 1H), 7.41 (d, 1H), 7.35 (s, 5H), 5.15 (s, 2H), 4.78 (s, 2H), 4.28 (s, 2H), 3.70 (m, 2H), 3.32 (bs, 2H).

B. 4-(2-Phenoxyquinolin-6-ylmethyl)-3-oxopiperazine-1-carboxylic acid benzyl ester.

A mixture of phenol (15.1 g, 160 mmol) and 4-(2-chloroquinolin-6-ylmethyl)-3-oxopiperazine-1-carboxylic acid benzyl ester (6.60 g, 16.1 mmol) is melted together at 70°C until a homogeneous mixture is obtained. Potassium hydroxide (3.15 g, 56.1 mmol) is added and the resulting mixture is heated overnight at 120°C. After 24 hours, the brown/black residue is cooled to room temperature, diluted with CH_2Cl_2 and stirred with 1N NaOH (100 mL) for 30 minutes. The two layers are separated and the aqueous layer is extracted with CH_2Cl_2. The combined organic layers are washed with 1N NaOH, saturated NaCl, dried over Na_2SO_4, filtered and concentrated. The crude title compound (6.92 g, 14.8 mmol) is obtained as a beige foam and used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.07 (d, 1H), 7.76 (d, 1H), 7.63 (s, 1H), 7.50 (dd, 1H), 7.42 (m, 2H), 7.34 (m, 6H), 7.25 (m, 2), 7.09 (d, 1H), 5.14 (s, 2), 4.75 (s, 2H), 4.27 (s, 2H), 3.66 (m, 2H), 3.30 (bs, 2H).

C. 4-(2-Aminoquinolin-6-ylmethyl)-3-oxopiperazine-1-carboxylic acid benzyl ester

A mixture of ammonium acetate (18.7 g, 242 mmol) and 4-(2-phenoxyquinolin-6-ylmethyl)-3-oxopiperazine-1-carboxylic acid benzyl ester (6.92 g, 14.8 mmol) is heated overnight at 150°C. After 21 hours, an additional 3 g of ammonium acetate is added and the heating is continued. After 5 hours, the mixture is cooled to room temperature, diluted with CH_2Cl_2 and stirred with 1N NaOH (100 mL) for 30 minutes. The two layers are separated and the aqueous layer is extracted with CH_2Cl_2. The combined organic layers are washed with 1N NaOH, saturated NaCl, dried over Na_2SO_4, filtered and concentrated. The crude mixture of the title compounds (5.50 g, 14.1 mmol) is obtained as a beige foam and used in the subsequent step without further purification.

Major component (4-(2-aminoquinolin-6-ylmethyl)-3-oxopiperazine-1-carboxylic acid benzyl ester): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.86 (d, 1H), 7.63 (d, 1H), 7.48 (d, 1H), 7.45 (d, 1H), 7.35 (s, 5H), 6.74 (d, 1H), 5.14 (s, 2H), 4.79 (bs, 2H), 4.71 (s, 2H), 4.26 (s, 2H), 3.66 (s, 2H), 3.30 (s, 2H).

Minor component (3-oxo-4-(2-oxo-1,2-dihydroquinolin-6-ylmethyl)piperazine-1-carboxylic acid benzyl ester): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.75 (d, 1H), 7.48 (m, 2H), 7.37 (m, 6H), 6.70 (d, 1H), 5.14 (s, 2H), 4.66 (s, 2H), 4.26 (s, 2H), 3.66 (s, 2H), 3.30 (s, 2H).

D. 1-(2-Aminoquinolin-6-ylmethyl)piperazin-2-one.

To a solution of a mixture of 4-(2-aminoquinolin-6-ylmethyl)-3-oxopiperazine-1-carboxylic acid benzyl ester and 3-oxo-4-(2-oxo-1,2-dihydro-quinolin-6-ylmethyl)piperazine-1-carboxylic acid benzyl ester (5.50 g, 14.1 mmol) in 100 mL of 10:1 MeOH/HOAc is added a catalytic amount of 10% palladium on activated carbon. The heterogenous mixture is hydrogenated at room temperature under a balloon of H_2 for 18 hours. The reaction mixture is filtered through a pad of Celite, washed with MeOH, and the filtrate is concentrated in vacuo. The crude mixture of products is purified by RP-HPLC eluting in a gradient of 2% CH_3CN/H_2O (0.1% TFA) to 20% CH_3CN/H_2O(0.1% TFA) and the appropriate product fractions are concentrated in vacuo to provide 1-(2-aminoquinolin-6-ylmethyl)-piperazin-2-one ditrifluoroacetate (2.64 g, 5.45 mmol) as the major product in the form of a white solid. ^{1}H NMR (d^6-DMSO, 300 MHz) δ 8.78 (bs, 2H), 8.31 (d, 1H), 7.80 (s, 1H), 7.66 (m, 2H), 7.08 (d, 1H), 4.70 (s, 2H), 3.84 (s, 2H), 3.46 (bs, 4H). MS m/z 256, [M+]. Elemental analysis calculated with 0.25 mol of H_2O cal. C=44.25%, H=3.82%, N=11.47%, found C=44.23%, H=3.76%, N=11.23%.
The minor by-product 6-(2-oxo-piperazin-1-ylmethyl)-1H-quinolin-2-one(0.62 g, 1.28 mmol) is also isolated from the RP-HPLC separation as a white solid ^{1}H NMR (d^6-DMSO, 300 MHz) δ 11.76 (bs, 1H), 9.30 (bs, 2H), 7.85 (d, 1H), 7.55 (s, 1H), 7.42 (d, 1H), 7.28 (d, 1H), 6.50 (d, 1H), 4.60 (s, 2H), 3.80 (s, 2H), 3.38 (bs, 4H). MS m/z 257, [M+]. Elemental analysis calculated with 0.5 mol of H_2O cal. C=43.72%, H=3.68%, N=8.50%, found C=43.70%, H=3.62%, N=8.61%.

EXAMPLE 68. 1-(1-Aminoisoquinolin-6-ylmethyl)piperazin-2-one.

The title compound is prepared as described in EXAMPLE 67 substituting 6-bromomethyl-1-chloroisoquinoline for bromomethyl-2-chloroquinoline. ^{1}H NMR (d6-DMSO, 300 MHz) δ (9.18 (bs, 2H), 8.53 (d, 1H), 7.81 (s, 1H), 7.63 (m, 2H), 7.14 (d, 1H), 4.77 (s, 2H), 3.88 (s, 2H), 3.50 (m, 4H).

EXAMPLE 69. 2-(2-Oxopiperazin-1-ylmethyl)pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester.

A. 3-Iodopyridin-4ylamine.

A solution of potassium iodide (19.48 g, 117.4 mmol) and iodine (18.37 g, 72.3 mmol) in water (77 mL) is added dropwise via an addition funnel to a refluxing solution of 4-aminopyridine (9.21 g, 97.8 mmol) and sodium carbonate (6.12 g, 57.7 mmol) in water (35 mL). Upon complete addition the mixture is stirred for 2 hours at reflux then cooled to room temperature and extracted with ethyl acetate. The combined organic layers are washed with saturated sodium thiosulfate solution (3x) and brine then dried

over $MgSO_4$, filtered and concentrated to give the title product (8.37 g, 38.0 mmol) and a trace of the di-iodo compound as an yellow/orange solid. This material is used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.70 (s, 1H), 8.10 (d, 1H), 6.55 (d, 1H), 4.60 (bs, 2H).

B. (3-Iodopyridin-4-yl)-carbamic acid tert-butyl ester.

Di-tert-butyl dicarbonate (20.7 g, 94.8 mmol) is added to a solution of 3-iodopyridin-4-ylamine (19.0 g, 86.4 mmol) in THF (86 mL). The resulting solution is stirred for 2 hours at room temperature then concentrated. The residue is diluted with ethyl acetate and washed with saturated sodium bicarbonate solution and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated. The residue is purified by column chromatography eluting with 1% EtOAc/CH_2Cl_2 to give the title product and a small amount of the BOC-protected di-iodo compound. Trituration of the mixture with ether/hexane removes the undesired compound leaving the title product in the solution. Filtration of the solid and concentration of the filtrate yields the title product (18.95 g, 59.2 mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 8.75 (s, 1H), 8.35 (d, 1H), 8.1 (d, 1H), 7.0 (bs, 1H), 1.55 (s, 9H).

C. 3-Oxo-4-prop-2-ynylpiperazine-1-carboxylic acid benzyl ester.

Sodium hydride (0.82 g, 23.0 mmol, 60% mineral oil dispersion) is added to a solution of 4-benzyloxycarbonylpiperazin-2-one (5.13 g, 21.9 mmol) in THF/DMF (75 mL, 3/1 v/v) at 0°C . The mixture is stirred for 5 minutes, then propargyl bromide (3.7 mL, 41.5 mmol) is added dropwise. The resulting solution is stirred for 1 hour then brought to room temperature and stirred for 2 hours. The reaction is quenched with saturated ammonium chloride solution then diluted with ethyl acetate and washed with water (4x) and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated to dryness. The residue is purified by column chromatography eluting with 5% MeOH/CH_2Cl_2 to give the product (5.96 g, 21.9 mmol) as a white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.3 (m, 5H), 5.12 (s, 2H), 4.25 (s,2H), 4.16 (s, 2H), 3.75 (m, 2H), 3.47 (m, 2H), 2.22 (s, 1H).

D. 2-(4-Benzyloxycarbonyl-2-oxopiperazin-1-ylmethyl)pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester.

$Pd(PPh_3)_2Cl_2$ (0.29 g, 0.41 mmol), CuI (0.05 g, 0.25 mmol) and triethylamine (4.6 mL, 32.9 mmol) is added to a solution of 3-oxo-4-prop-2-ynylpiperazine-1-carboxylic acid benzyl ester (2.24 g, 8.23 mmol) and (3-iodopyridin-4-yl)-carbamic acid tert-butyl ester (2.63 g, 8.23 mmol) in DMF (30 mL) at room temperature. The mixture is heated to 100°C and stirred for 1.5 hours. The reaction mixture is then cooled to 50°C and DBU (2.5 mL, 16.5 mmol) is added. After 30 minutes the solution is cooled to room temperature, diluted with ethyl acetate and washed with saturated ammonium chloride, water and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting solid is

purified by column chromatography eluting with a gradient of 2% MeOH/$CH_2Cl_2$to 5% MeOH/ $CH_2Cl_2$to give the product (2.93 g, 6.31 mmol) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.75 (s, 1H), 8.4 (d, 1H), 7.85 (d, 1H), 7.35 (m, 5H), 6.38 (s, 1H), 5.2 (s, 2H), 5.00 (s, 2H), 4.29 (s, 2H), 3.85 (m, 2H), 3.52 (m, 2H), 1.7 (s, 9H). Ion spray MS, $[M+H]^+$= 465.

E. 2-(2-Oxopiperazin-1-ylmethyl)pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester.

Palladium black (1.1 g, 10.3 mmol) is added to a solution of 2-(4-benzyloxycarbonyl-2-oxo-piperazin-1-ylmethyl)pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester (1.7 g, 3.7 mmol) in HCO_2H/MeOH (45 mL, 4.4% solution). After 40 minutes the catalyst is filtered through Celite and washed with MeOH. The filtrate is concentrated in vacuo to remove methanol then the resulting solution is diluted with methylene chloride and washed with saturated sodium bicarbonate, and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated to dryness. The resulting solid is purified by column chromatography eluting with a gradient of 5% MeOH/CH_2Cl_2 to 10% MeOH/CH_2Cl_2 to give the product (0.8 g, 2.5 mmol) as a pale yellow foamy solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.78 (s, 1H), 8.40 (d, 1H), 7.9 (d, 1H), 6.48 (s, 1H), 4.98 (s, 2H), 3.7 (s, 2H), 3.51 (t, 2H), 3.40 (t, 2H), 1.91 (bs, 1H), 1.70 (s, 9H).

EXAMPLE 70. 2-(5-(±)-Methoxycarbonyl-2-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

A. 2-Benzyloxycarbonylamino-3-(prop-2-ynylamino)-propionic acid methyl ester.

Propargyl bromide (1.6 mL, 14.4 mmol) is added to a solution of 3-amino-2-benzyloxycarbonylamino-propionic acid methyl ester hydrochloride (4.0 g, 13.9 mmol) and triethylamine (4.1 mL, 29.4 mmol) in THF (46 mL). The resulting mixture is heated to 50°C and stirred overnight then cooled to RT and concentrated in vacuo. The crude residue is diluted with methylene chloride, washed with saturated $NaHCO_3$ and brine then the organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material (4.0 g) is taken on to the subsequent step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25-7.30 (m, 5H), 5.75 (bs, 1H), 5.20 (s, 2H), 4.45 (bs, 1H), 3.80 (s, 3H), 3.75 (m, 1H), 3.31 (s, 2H), 3.08 (dd, 1H), 2.98 (dd, 1H), 2.20 (t, 1H). EI MS, $[M+H]^+$=291.

B. 2-Benzyloxycarbonylamino-3-(bromoactyl-prop-2-ynyl-amino)-propionic acid methyl ester.

DCC (2.27 g, 11.0 mmol) and bromoacetic acid (1.48 g, 10.7 mmol) is added to a solution of 2-benzyloxycarbonylamino-3-(prop-2-ynylamino)-propionic acid methyl ester (3.10 g, 10.7 mmol) in CH_2Cl_2 at RT. The mixture is stirred overnight then diluted with ether. The white solid which precipitates out is filtered and the filtrate is concentrated to give a yellow oil. The crude product is

purified by chromatography eluting with a gradient of 40% EtOAc/hexanes to 50% EtOAc/hexanes to yield the title product (2.1g, 5.12 mmol) as an oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (m, 5H), 5.70 (d, 1H), 5.10 (s, 2H), 4.63 (m, 1H), 4.15 (d, 2H), 4.00 (m, 1H), 3.80 (s, 3H), 3.75 (s, 2H), 3.70 (dd, 1H), 2.27 (bs, 1H). Ion spray MS, $[M+H]^+$=411, 413, Br pattern.

C. 5-Oxo-4-prop-2-ynyl-piperazine-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester.

Sodium hydride (0.20 mg, 4.9 mmol) is added to a solution of 2-benzyloxycarbonylamino-3-(bromoactyl-prop-2-ynyl-amino)-propionic acid methyl ester (2.0 g, 4.8 mmol) in THF (50 mL) at 0°C. The solution is stirred for 40 minutes then quenched with saturated NH_4Cl solution. The reaction mixture is concentrated in vacuo then diluted with CH_2Cl_2 and washed with brine. The organic layer is dried over , filtered and concentrated in vacuo. The crude product is purified by chromatography eluting with 50% EtOAc/hexanes to give the title product (1.4 g, 4.1 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (m, 5H), 5.20 (s, 2H), 5.10 (m, 1H), 4.30 (dd, 1H), 4.25 (d, 2H), 4.08 (m, 1H), 4.00 (dd, 1H), 3.78 (dd, 1H), 3.78 (s, 3H), 2.25 (t, 1H).

D. 2-(5-(±)-Methoxycarbonyl-2-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.75 (s, 1H), 8.41 (d, 1H), 7.90 (d, 1H), 6.42 (s, 1H), 5.00 (AB, 2H), 3.85-3.93 (m, 2H), 3.78 (s, 3H), 3.70-3.81 (m, 3H), 1.65 (s, 9H). Ion spray MS, $[M+H]^+$=389.

EXAMPLE 71. 2-(2-(±)-Methoxycarbonyl-6-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.81 (s, 1H), 8.43 (d, 1H), 7.90 (d, 1H), 6.48 (s, 1H), 5.63 (d, 1H), 4.40 (d, 1H), 4.20 (m, 1H), 3.78 (s, 3H), 3.70 (d, 1H), 3.52 (d, 1H), 3.33 (dd, 1H), 2.92 (s, 1H), 1.55 (s, 9H). Ion spray MS, $[M+H]^+$=389.

EXAMPLE 72. 1-(4-Aminoquinazoline-7-ylmethyl)piperazine-2-one.

A. 4-(4-Chloroquinazoline-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid tert-butyl ester.

To a solution of 3-oxopiperazine-1-carboxylic acid tert-butyl ester (3.93 g, 19.6 mmol) and 7-bromomethyl-4-chloroquinazoline, EXAMPLE 7, (5.0 g, 19.6 mmol) in 150 mL of THF and 15 mL of DMF at 0°C is added a 60% dispersion in mineral oil of NaH (0.79 g, 19.6 mmol). The solution is stirred at 0°C for 0.5 hours and then is allowed to warm to ambient temperature. After 4 hours, the solution is poured into a saturated solution of NH_4Cl. The layers are separated and the organic layer is washed with

H_2O, and saturated NaCl, dried over $MgSO_4$, filtered and concentrated. The title compound is obtained as a white solid (5.1 g, 13.4 mmol). MS (FAB) m/z 377, 379, (M+H), chlorine pattern.

B. 4-(4-Aminoquinazoline-7-ylmethyl-3-oxopiperazine-1-carboxylic acid tert-butyl ester.

A solution of 4-(4-chloroquinazoline-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid tert-butyl ester (1.84 g, 4.9 mmol) in 120 mL of ethanol is saturated with NH_3 gas. To the resulting solution is added acetic acid (0.03 mL). The solution is heated to reflux. After 16 hours, the solution is concentrated. The resulting solid is dissolved in CH_2Cl_2 and the inorganic salts are filtered off. The organic solution is concentrated. The resulting solid is triturated with EtOAc. The title compound is obtained a a white solid (1.59 g, 4.5 mmol). MS (FAB) m/z 356, (M+H).

C. 1-(4-Aminoquinazoline-7-ylmethyl)piperazine-2-one.

A solution of 4-(4-aminoquinazoline-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid tert-butyl ester (1.92 g, 5.4 mmol) in EtOAc (200 mL) at 0 °C is saturated with HCl gas. The solution is stirred at 0°C for 4 hours. After this time, the solution is concentrated. The title compound is obtained as a white solid (1.79 g, 5.4 mmol). ^{1}H NMR (d^6-DMSO, 300 MHz) δ 9.9 (bs, 3H), 9.7 (bs, 2H), 8.8 (s, 1H), 8.46 (d, 1H), 7.72 (s, 1H), 7.61 (d, 1H), 4.78 (s, 2H), 3.83 (s, 2H), 3.4 (m, 4H).

Example 73. 1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-piperazin-2-one.

A. 1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-3-oxo-piperazine-1-carboxylic acid tert-butyl ester.

The title compound is prepared as described in EXAMPLE 72, Part A, substituting 6-bromomethyl-4-chlorothieno[2,3-d]pyrimidine. for 7-bromomethyl-4-chloroquinazoline. Followed by treatment as described in EXAMPLE 72, Part B, the title compound is obtained. ^{1}H NMR (CD_3OD, 300 MHz) δ 8.22 (s, 1H), 7.35 (s, 1H), 5.48 (s, 2H), 4.10 (s, 2H), 3.60 (m, 2H), 3.40 (m, 2H), 1.45 (s, 9H). MS (ion spray), 364, (M+H).

B. 1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-piperazin-2-one.

The title compound is obtained by treatment of 1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-3-oxo-piperazine-1-carboxylic acid tert-butyl ester as described in EXAMPLE 72, Part C. MS (EI), 2634, (M+).

EXAMPLE 72. 4-[3-(2-Oxo-piperazin-1-yl)-propyl]-piperidine-1-carboxylic acid tert-butyl ester.

A. 4-[3-(1-tert-butoxycarbonyl-piperidin-4-yl)-propyl]-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared as described in EXAMPLE 72, Part A, substituting 3-oxopiperazine-1-carboxylic acid benzyl ester for 3-oxopiperazine-1-carboxylic acid tert-butyl ester and 4-(3-bromopropyl)-piperidine-1-carboxylic acid tert-butyl ester for 7-bromomethyl-4-chloroquinazoline. The title compound is obtained as a white foam. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.38 (m, 5H), 5.12 (s, 2H), 4.18 (m, 4H), 3.73 (m, 2H), 3.33 (m, 4H), 2.66 (m, 2H), 1.58 (m, 6H), 1.42 (s, 9H), 1.38 (m, 3H).

B. 4-[3-(2-Oxo-piperazin-1-yl)-propyl]-piperidine-1-carboxylic acid tert-butyl ester.

4-[3-(1-tert-butoxycarbonyl-piperidin-4-yl)-propyl]-3-oxo-piperazine-1-carboxylic acid benzyl ester is treated as described in EXAMPLE 67, Part D, to give the title compound as an oil.

EXAMPLE 75. 1-(4-Amino-quinazoline-7-ylmethyl)-3-methoxymethyl-piperazine-2-one.

A. 2-Methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

To a solution of 2-oxo-3-(S)-methoxymethylpiperidine (5.36g, 19.3mmol), EXAMPLE 41, in 200mL of 10:1 THF:DMF is added 2-(benzhydrylidene-amino)-4-bromomethyl-benzonitrile (12.6g, 60%purity, 19.3mmol), prepared as in EXAMPLE 13. The solution is cooled to 0°C. To the solution is added NaH (0.77g of a 60% dispersion in mineral oil, 19.3mmol). The solution is stirred for 16 hours. After this time, 1N HCl is added until the pH=1. The solution is stirred for 1 hour. After this time, the solution is diluted with EtOAc. The organic layer is washed with water and sat. NaCl. The organic layer is dried over $MgSO_4$, filtered and concentrated under vacuum. The resulting crude product is purified by column chromatography eluting with a gradient of 20%EtOAc/CH_2Cl_2 to 40%EtOAc/CH_2Cl_2. The title compound (6.8g, 16.7mmol) is obtained as a white solid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.34 (m, 5H), 6.61 (m, 2H),5.13 (AB, 2H), 4.76 (m, 1H), 4.40 (AB, 2H), 4.08 (m, 5H), 3.74 (m, 2H), 3.32 (m, 1H), 3.30 (s, 3H), 3.10 (m, 1H).

B. 4-(4-Amino-quinazolin-7-ylmethyl)-2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

To a solution of 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (6.8g, 16.7mmol) in 100mL of ethanol is added triazine (2.2g, 26.4mmol) and acetic acid (1.6g,26.4mmol). The solution is heated to a reflux. After 36h, the solution is concentrated. The resulting crude product is purified by column chromatography eluting with a gradient of 2%MeOH/CH_2Cl_2 to 5% MeOH/CH_2Cl_2. The title compound (5.8g, 13.3mmol) is obtained as a white solid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.55 (s, 1H), 7.72 (m, 2H), 7.48 (m, 1H), 7.35 (m, 5H), 6.40 (bs, 2H), 5.16 (AB, 2H), 5.06 (m, 1H),4.72 (m, 1H), 4.59 (m, 1H), 4.09 (m, 2H), 3.74 (m, 2H), 3.44 (m, 1H), 3.30 (s, 3H), 3.12 (m, 1H). MS (ion spray) m/z 436, (M+H).

C. 1-(4-Amino-quinazoline-7-ylmethyl)-3-methoxymethyl-piperazine-2-one.

To a solution of 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (5.8g, 13.3mmol) in 50mL of acetic acid is added dropwise, 20mL of a 30%HBr in AcOH solution. The solution is stirred for 1 hour. After this time, the solution is concentrated. The resulting crude product is purified by column chromatography eluting with CH_2Cl_2:MeOH:NH_4OH (20:5:1). The title compound (2.0g, 6.6mmol) is obtained as a white solid. ^1H NMR (d^6-DMSO, 300MHz) δ 8.60 (s, 1H), 7.72 (m, 2H),7.48 (d, 1H), 5.60 (bs, 2H), 4.72 (AB, 2H), 3.87 (m, 2H), 3.71 (m, 1H), 3,42 (m, 1H), 3.40 (s, 3H), 3.19 (m, 2H), 3.02 (m, 1H). MS (ion spray) m/z 302, (M+H).

EXAMPLE 76. 1-(4-Aminoquinazoline-7-ylmethyl)-3-butyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-butyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 42, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^1H NMR (CD_3OD, 300MHz) δ 8.35 (s, 1H), 8.09 (d, 1H), 7.54 (s, 1H), 7.41 (d, 1H), 4.74 (s, 2H), 3.43 (m, 2H), 3.28 (m, 1H), 3.09 (m, 1H), 2.95 (m, 1H), 1.92 (m, 1H), 1.70 (m, 1H), 1.39 (m, 4H), 0.93 (m, 3H). MS (ion spray) m/z 314, (M+H).

EXAMPLE 77. 1-(4-Aminoquinazoline-7-ylmethyl)-3-ethyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-ethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester r, Example 43, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^1H NMR (CD_3OD, 300MHz) δ 8.36 (s, 1H), 8.11 (d, 1H), 7.57 (s, 1H), 7.42 (d, 1H), 4.78 (s, 2H), 3.40 (m, 2H), 3.29 (m, 1H), 3.11 (m, 1H), 2.98 (m, 1H), 2.00 (m, 1H), 1.77 (m, 1H), 1.20 (m, 3H). MS (ion spray) m/z 286, (M+H).

EXAMPLE 78. 1-(4-Aminoquinazoline-7-ylmethyl)-3-propyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-propyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 44, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^1H NMR (CD_3OD, 300MHz) δ 8.36 (s, 1H), 8.13 (d, 1H), 7.60 (s, 1H), 7.47 (d, 1H), 4.78 (s, 2H), 3.44 (m, 2H), 3.30 (m, 1H), 3.11 (m, 1H), 2.97 (m, 1H), 1.98 (m, 1H), 1.72 (m, 1H), 1.50 (m, 2H), 0.97 (m, 3H). MS (ion spray) m/z 300, (M+H).

EXAMPLE 79. 1-(4-Amino-quinazoline-7-ylmethyl)-3-ethoxymethyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-ethoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 45, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^1H NMR (CD_3OD, 300MHz) δ 8.34 (s, 1H), 8.07 (d, 1H), 7.53 (s, 1H),

7.40 (d, 1H), 4.79 (AB, 2H), 3.90 (m, 1H), 3.72 (m, 1H), 3.68 (m, 1H), 3.52 (m, 2H), 3.36 (m, 2H), 3.20 (m, 1H), 3.00 (m, 1H), 1.92 (m, 3H). MS (ion spray) m/z 316, (M+H).

EXAMPLE 80. 1-(4-Amino-quinazoline-7-ylmethyl)-3-methyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-methyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 46, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^{1}H NMR (CD_3OD, 300MHz) δ 8.36 (s, 1H), 8.11 (d, 1H), 7.57 (s, 1H), 7.44 (d, 1H), 4.79 (AB, 2H), 3.58 (m, 1H), 3.47 (m, 1H), 3.31 (m, 1H), 3.12 (m, 1H), 3.00 (m, 1H), 1.41 (d, 3H). MS (ion spray) m/z 272, (M+H).

EXAMPLE 81. 1-(4-Amino-quinazoline-7-ylmethyl)-3-benzyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-benzyl-3-oxo-piperazine-1-carboxylic acid benzyl, Example 47, ester for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^{1}H NMR (CD_3OD, 300MHz) δ 8.35 (s, 1H), 8.09 (d, 1H), 7.57 (s, 1H), 7.38 (d, 1H), 7.27 (m, 5H), 4.74 (AB, 2H), 3.76 (m, 1H), 3.47 (m, 1H), 3.30 (m, 3H), 3.08 (m, 1H), 2.96 (m, 1H). MS (ion spray) m/z 348, (M+H).

EXAMPLE 82. 1-(4-Amino-quinazoline-7-ylmethyl)-3-(1-methoxyethyl)-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-(1-methoxyethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 48, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. This compound is isolated as the bis hydrobromide salt. ^{1}H NMR (CD_3OD, 300MHz) δ 8.70 (s, 1H), 8.40 (d, 1H), 7.88 (s, 1H), 7.71 (d, 1H), 4.94 (AB, 2H), 4.30 (m, 2H), 3.76 (m, 1H), 3.68 (m, 3H), 3.36 (s, 3H), 1.42 (d, 3H). MS (ion spray) m/z 316, (M+H).

EXAMPLE 83. 1-(4-Amino-quinazoline-7-ylmethyl)-3,3-dimethyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2,2-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 49, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^{1}H NMR (d^6-DMSO, 300MHz) δ 8.34 (s, 1H), 8.12 (d, 1H), 7.72 (bs, 2H), 7.41 (s, 1H), 7.26 (d, 1H), 4.60 (s, 2H), 3.33 (m, 2H), 2.98 (m, 2H), 1.27 (s, 6H).

EXAMPLE 84. 1-(4-Amino-quinazoline-7-ylmethyl)-3-isopropyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-isopropyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 50, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^{1}H NMR (d^6-DMSO, 300MHz) δ 8.32 (s, 1H), 8.12 (d, 1H), 7.66 (bs, 2H),

7.42 (s, 1H), 7.27 (d, 1H), 4.60 (AB, 2H), 3.23 (m, 2H), 3.05(m, 1H), 2.79 (m, 1H), 2.34 (m, 1H), 0.92 (s, 3H), 0.80 (s, 3H).

EXAMPLE 85. 1-(4-Amino-quinazoline-7-ylmethyl)-3-isobutyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-isobutyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 51, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^{1}H NMR (d^6-DMSO, 300MHz) δ 8.65 (s, 1H), 7.70 (m, 2H), 7.48 (m, 1H), 5.61 (m, 2H), 4.82 (m, 1H), 4.65 (m, 1H), 3.52 (dd, 1H), 3.37 (m, 1H), 3.18 (m, 2H), 2.98 (m, 1H), 1.92 (m, 1H), 1.76 (m, 1H), 1.59 (m, 2H), 0.95 (m, 6H).

EXAMPLE 86. 1-(4-Amino-quinazoline-7-ylmethyl)-3-(2-methoxyethyl) l-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-(2-methoxyethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 52, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^{1}H NMR (d^6-DMSO, 300MHz) δ 8.32 (s, 1H), 8.13 (d, 1H), 7.70 (bs, 2H), 7.42 (s, 1H), 7.28 (m, 1H), 4.60 (m, 2H), 3.32 (m, 8H), 3.11 (m, 1H), 2.95 (m, 1H), 2.78 (m, 1H), 2.07 (m, 1H), 1.72 (m, 1H).

EXAMPLE 87. 1-(4-Amino-quinazoline-7-ylmethyl)-3-methoxymethyl-6-methyl-piperazine-2-one.

The title compound is prepared as described in EXAMPLE 75, substituting 2-methoxymethyl-5-methyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, Example 53, for 2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester. ^{1}H NMR (CD_3OD, 300MHz) δ 8.72 (s, 1H), 8.32 (d, 1H), 7.78 (m, 2H), 5.11 (m, 1H), 4.81 (m, 1H), 4.42 (m, 1H), 4.13 (m, 1H), 4.04 (m, 1H), 3.74 (m, 2H), 3.52 (m, 1H), 3.43 (s, 3H), 1.34 (d, 3H).

EXAMPLE 88. (3S,5RS)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

A. (2S,6RS)-4-[3-(benzhydryl-amino)-4-cyano-benzyl]-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

To a solution of the (2S,6RS)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (1.98 g, 7.56 mmol in 20 mL of tetrahydrofuran and 2 mL of DMF is added sodium hydride (60%, 289 mg, 12.6 mmol) at 0°C. The reaction is stirred for one hour at room temperature and the 2-benzhydrylidene-amino)-4-bromomethyl-benonitrile (4.24 mg, 11.34 mmol), Example 13, is added. After stirring at room temperature overnight, the tetrahydrofuran is removed. The residue is taken up in ethyl acetate. Excess sodium hydride is quenched with 5 mL of water, and normal aqueous work-up followed. The crude product is chromatographed on silica gel (50% EtOAc/Hexane) to give (2S,6RS)-

4-[3-(benzhydryl-amino)-4-cyano-benzyl]-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (2.6 g, 65%). $C_{35}H_{32}N_4O_3$ MS m/z: 557.

B. (2S,6RS)-4-(3-amino)-4-cyano-benzyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

(2S,6RS)-4-[3-(Benzhydryl-amino)-4-cyano-benzyl]-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (2.6 g, 5.21 mmol) is dissolved in 100 mL of ethyl acetate and cooled to 0°C. A 12N solution of hydrochloric acid (0.5 ml, 6.0 mmol) is added dropwise. The deprotection is complete in thirty minutes. The reaction mixture is washed with 10 % sodium bicarbonate. The ethyl acetate layer is dried with magnesium sulfate, filtered and condensed. The resulting residue is purified by flash column (SiO_2, 60 % ethyl acetate/hexane) to give the product (2S,6RS)-4-(3-amino)-4-cyano-benzyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (2.03 g, 99 %).

C. (2S,6RS)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

Glacial acetic acid (0.9 ml, 15.54 mmol) and 1,3,5-triazine (840 mg, 10.36 mmol) is added to a solution of (2S,6RS)-4-(3-amino-4-cyano-benzyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (2.03 g, 5.18 mmol) in ethanol. The resulting mixture is heated to reflux overnight. Replaced the ethanol with ethyl acetate and washed with saturated sodium bicarbonate (5 mL). The ethyl acetate layer is dried with magnesium sulfate, filtered and condensed. The resulting residue is purified by flash column (SiO_2, 20% methanol/methylene chloride) to give the product (2S,6RS)-4-(4-amino-quinazolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (1.85 g, 85%) as a yellow solid. $C_{23}H_{25}N_5O_3$ MS m/z: 420.

D. (3S,5RS)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

Palladium on carbon (10 %, 700 mg) is added to a solution of (2S,6RS)-4-(4-amino-quinazolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester (1.62 g, 3.87 mmol) in 20 mL of methanol and 2 mL of acetic acid. The reaction mixture is left to stir in an atmosphere of hydrogen for eight hours. The palladium is filtered off, and the volitale solvents are removed on the rotovap. The crude product (1.7 g, 95 %) is isolated as a white solid. The two epimers are separated on silica gel (1% triethylamine/15% methanol/methylene chloride). The minor epimer is assigned as (3S,5R)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one and the major epimer is assigned as (3S,5S)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one.

EXAMPLE 89. 1-(4-Chloroquinolin-7-ylmethyl)-piperazin-2-one.

4-(Benzyloxycarbonyl)-piperazin-2-one (1.1 g, 4.6 mmol) is dissolved in THF (50 mL), cooled in an ice bath and treated with tretrabutylammonium iodide (0.18 g, mmol) and 60% sodium hydride (0.24 g, 6.0 mmol). The reaction mixture is stirred at 0 C for 30 minutes then treated dropwise with a solution of 7-bromomethyl-4-chloroquinoline (1.2 g, 4.6 mmol), Example 14, in THF (50 mL). The resulting solution is stirred at 0 C for 2 h then quenched with ammonium chloride solution and concentrated. Dilution with ethyl acetate is followed by a water wash; the organic layer is dried (sodium sulfate) and concentrated. The residue is chromatographed (4% methanol/methylene chloride) to yield solid 4-(benzyloxycarbonyl)-1-(4-chloroquinolin-7-ylmethyl)-piperazin-2-one (1.2 g, 2.9 mmol). A portion of this material (0.75 g, 1.8 mmol) is dissolved in acetonitrile (20 mL) and treated with iodo trimethylsilane (0.78 mL, 5.4 mmol) at room temperature for 3 hours. The reaction is quenched with methanol and concentrated to dryness. Methanol addition and concentration is repeated four times. The final residue is taken up is 2M aqueous HCl; the solution is washed with ether and concentrated. The residue is recrystallized from isopropanol and ether to yield the title compound (0.63 g, 2.3 mmol) MS m/z: M^+ = 275; ^{1}HNMR (CD_3OD, 300 MHz) δ 9.1 (d, 1H), 8.5 (d, 1H), 8.2-8.3 (m, 2H), 8.0 (d, 1H), 5.2 (s, 2H), 4.1 (s, 2H), 3.7-3.8 (m, 2H), 3.6-3.7 (m, 2H).

EXAMPLE 90. 1-(4-Chlorocinnolin-7-ylmethyl)-piperazin-2-one.

4-(t-Butyloxycarbonyl)-piperazin-2-one (0.6 g, 3.0 mmol), EXAMPLE 40, is dissolved in THF (80 mL), cooled in an ice bath and treated with tretrabutylammonium iodide (0.23 g, 0.62 mmol) and 60% sodium hydride (0.12 g, 3.0 mmol). The reaction mixture is stirred at °C for 40 minutes then treated dropwise with a solution of 7-bromomethyl-4-chlorocinnoline (10.7g, 2.7 mmol), Example 15, in THF (20 mL). The resulting solution is warmed to ambient temperature over 2 hours. The solution is evaporated to dryness and the residue is taken up in ethyl acetate and 10 % aqueous sodium bicarbonate solution. The organic layer is separated, washed with water, dried (sodium sulfate) and concentrated. The residue is chromatographed (ethyl acetate) to yield the title compound (0.6 g, 1.6 mmol). A portion of this material (0.21 g, 1.26 mmol) is dissolved in THF (~ 4 mL) and treated with a saturated solution of HCl in ethyl acetate (50 mL) at room temperature for 2 hours. The solution is filtered and concentrated to a residue (0.14 g, 0.4 mmol). MS m/z: M^+ = 275; ^{1}H NMR (CD_3OD, 300 MHz) δ 9.15 (d, 1H), 8.5 (d, 1H), 8.25 (s, 1H), 8.15 (d, 1H), 8.0 (d, 1H), 5.0 (s, 2H), 4.1 (s, 2H), 3.7-3.8 (m, 2H), 3.6-3.7 (m, 2H).

EXAMPLE 91. 1-(4-Chloroquinolin-7-ylmethyl)-3-(S)-methylpiperazin-2-one.

4-(Benzyloxycarbonyl)-3-(S)-methylpiperazin-2-one (1.0 g, 4.0 mmol), EXAMPLE 46, is dissolved in THF (60 mL), cooled in an ice bath and treated with tretrabutylammonium iodide (0.10 g, 0.27 mmol) and 60% sodium hydride (0.18 g, 4.4 mmol). The reaction mixture is stirred at 0°C for 30

minutes then treated dropwise with a solution of 7-bromomethyl-4-chloroquinoline (1.12 g, 4.4 mmol), EXAMPLE 14, in THF (5 mL). The resulting solution warmed to room temperature over approximately 1 h then quenched with sodium bicarbonate solution and concentrated. The residue is partitioned between ethyl acetate and water; the organic layer is dried (sodium sulfate) and concentrated. The residue is chromatographed (5 % methanol/methylene chloride) to yield solid 4-(Benzyloxycarbonyl)-1-(4-chloroquinolin-7-ylmethyl)-3-(S)-methyl-piperazin-2-one (1.32 g, 3.1 mmol). A portion of this material (0.10 g, 0.23 mmol) is dissolved in acetonitrile (6 mL) and treated with iodotrimethyl-silane (0.1 mL, 0.75 mmol) at room temperature for 2 hours. The reaction is quenched with methanol and concentrated to dryness. Methanol addition and concentration is repeated six times. The final residue is taken up is 2M aqueous HCl; the solution is washed with ether and concentrated to yield the title compound. MS m/z: $M^+ = 289$; ^{1}H NMR (CD_3OD, 300 MHz) δ 9.2 (d, 1H), 8.6 (d, 1H), 8.2-8.3 (m,2H), 8.0 (d, 1H), 5.1 (q, 1H), 4.3-4.4 (m, 1H), 3.8-4.0 (m, 2H), 3.6-3.8 (m, 3H), 1.75 (d, 3H).

EXAMPLE 92. 1-[2-(Pyridin-4-ylamino)-ethyl]-piperazin-2-one.

A. 4-(tert-Butyloxycarbonyl)-1-(2-aminoethyl)-piperazin-2-one.

4-(tert-Butyloxycarbonyl)-piperazin-2-one (8.0 g, 40 mmol), EXAMPLE 40, is dissolved in THF (160 mL), cooled in an ice bath and treated with 60 % sodium hydride (1.9 g, 48 mmol). The reaction mixture is stirred 40 minutes, then treated with tetra-butylammonium iodide (0.35 g, 0.95 mmol) and bromoacetonitrile (3.4 mL, 48 mmol). After 2 h the reaction is quenched with water, concentrated to a small volume and extracted with methylene chloride (3 X). The combined organic extracts are concentrated and the residue is chromatographed (50 % ethyl acetate/hexane) to give 4-(tert-butyloxycarbonyl)-1-cyanomethyl-piperazin-2-one (5.2 g, 21.7 mmol). This material is dissolved in ethanol (140 mL) and treated with platinum oxide (0.83 g) at 50 PSI of hydrogen gas for 24 hours. The catalyst is removed by filtration and the solution is concentrated to yield 4-(tert-butyloxycarbonyl)-1-(2-aminoethyl)-piperazin-2-one (5.2 g, 21.6 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.08 (s, 2H), 3.62 (m, 2H), 3.44 (t, 2H), 3.38 (t, 2H), 2.89 (t, 2H).

B. 4-(tert-Butyloxycarbonyl)-1-[2-(2,3,5,6-tetrachloropyridin-4-ylamino)-ethyl]- piperazin-2-one.

4-(tert-Butyloxycarbonyl)-1-(2-aminoethyl)-piperazin-2-one (4.0 g, 16 mmol) is dissolved in methylene chloride (150 mL) and treated with 4-nitro-2,3,5,6-tetrachloro-pyridine (4.8 g, 18 mmol) and N-methylmorpholine (4.0 mL, 36 mmol). The reaction mixture is stirred for 5 h, concentrated and the residue is purified by chromatography (50% ethyl acetate/hexane) to give the title compound (4.8 g, 10.5 mmol). Fab MS m/z: 457, 469, 461, $[M+1]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.00 (t, 1H), 4.10 (s, 2H), 3.97 (m, 2H), 3.66 (m, 2H), 3.38 (m, 2H).

C. 1-[2-(Pyridin-4-ylamino)-ethyl]-piperazin-2-one.

4-(tert-Butyloxycarbonyl)-1-[2-(2,3,5,6-tetrachloropyridin-4-ylamino)-ethyl-piperazin-2-one (3.5 g, 7.6 mmol) is dissolved in methanol (20 mL) and 0.5 M sodium methoxide in methanol (150 mL, 75 mmol). The solution is treated with Pd/C (0.5 g) and agitated under 50 PSI of hydrogen gas for 16 hours. The solvent is removed and the residue is extracted with methylene chloride which is filtered. The filtrate is concentrated and loaded onto a silica flash column. The column is eluted with 5% MeOH/CH_2Cl_2 followed by NH_4OH/MeOH/CH_2Cl_2 (1:5:95) and NH_4OH/MeOH/ CH_2Cl_2 (1:10:70) to yield 4-(tert-Butyloxycarbonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one as a white foam (1.5 g, 4.7 mmol). This material (1.5 g, 4.7 mmol) is treated with 20% trifluoroacetic acid in methylene chloride (110mL) at ambient temperature for 2 hours. The solution is concentrated and the residue is treated with saturated bicarbonate solution and ammonium hydroxide until a basic solution is obtained. The solution is applied to a silica column and eluted with NH_4OH/MeOH/CH_2Cl_2 (1:10:60) and 1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one is isolated as a mixture of desired product and inorganic salts (estimate 25 % by weight) EI MS m/z: 220, M^+; ^1H NMR (CD_3OD, 300 MHz) δ 8.07 (d, 2H), 6.96 (d, 2H), 3.77 (s, 2H), 3,65 (m, 6H), 3.44 (t, 2H).

EXAMPLE 93. 1-[2-{(Methyl)-(pyridin-4-yl)-amino}-ethyl]-piperazin-2-one trifluroacetate.

4-(tert-Butyloxycarbonyl)-1-[2-(2,3,5,6-tetrachloropyridin-4-ylamino)-ethyl]-piperazin-2-one (0.19 g, 0.41 mmol), Example 92, Part B, is dissolved in DMF (3 ml) and treated with 60 % NaH (20 mg, 0.5 mmol). After 10 minutes methyl iodide (0.025 ml, 0.40 mmol) is added and the yellow solution is stirred at r.t. overnight. The solution is diluted with EtOAc and washed with H_2O (6 X). The organic layer is dried (MgSO4) and concentrated to a residue (0.19 g, 0.40 mmol). The residue is dissolved in methanol (2 ml) and treated with 0.5 M NaOMe in MeOH (8 ml, 4.0 mmol)). The solution is treated with Pd/C and agitated under 60 PSI of hydrogen gas overnight and filtered. The filtrate is concentrated and extracted several times with CH_2Cl_2; removal of solvent in vacuo gives 4-(tert-Butyloxycarbonyl)-1-[2-{(methyl)-(pyridin-4-yl)-amino}-ethyl]-piperazin-2-one as an amorphous residue (0.16 g). EI MS m/z: 335, $[M+1]^+$; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.21 (d, 2H), 6.56 (d, 2H), 3.99 (s, 2H), 3.60 (t, 2H), 3.53 (t, 2H), 3.47 (t, 2H), 3.28 (t, 2H), 2.98 (s, 3H), 1.46 (s, 9H). Treatment of the above product with 20% TFA/CH_2Cl_2 (10 mL) at r.t. for 1 h gives, after concentration, the title compound as a residue which is used without further purification. ^1H NMR (CD_3OD, 300 MHz) δ 8.14 (d, 2H), 7.30 (br, 1H), 7.00 (br, 1H), 3.88-3.67 (m, 8H), 3.53 (t, 2H), 2.26 (s, 3H).

EXAMPLE 94. 1-[2-(3-Methylpyridin-4-yl-amino)-ethyl]-piperazin-2-one.

A. 4-[2-(3-Methylpyridin-4-ylimino)-ethyl]-3-oxo-piperazine-1-carboxlic acid benzyl ester.

4-(Benzyloxycarbonyl)-piperazin-2-one (4.7 g, 20 mmol) is dissolved in THF (50 mL) and treated with 1.5M LDA (20 mL, 30 mmol) at 0°C. The reaction mixture is treated with condensed ethylene oxide (3 mL, 40 mmol) and stirred at r.t. overnight. The mixture is neutralized with 2N HCl, concentrated, and extracted with EtOAc. The EtOAc layer is washed with H_2O and concentrated to a crude residue. Further extraction of the crude with Et_2O and concentration of the ethereal layer gives an oil (1.5 g). The above oil is dissolved in CH_2Cl_2 (25 mL) and added to the solution of 2M oxalyl chloride (7.5 mL, 15 mmol) and DMSO (2.3 mL, 29.7 mmol) in CH_2Cl_2 (25 mL) at -60°C. After 15 minutes, Et_3N (2.1 ml, 15 mmol) is added. The mixture is stirred at -50 °C for 10 minutes then warmed to r.t for 10 minutes. The reaction is quenched with 0.5 N HCl and extracted with CH_2Cl_2. The CH_2Cl_2 layer is washed with 0.5 N HCl, brine (2 X), H_2O, and concentrated to a residue. The residue is purified by chromatography (2% MeOH/CH_2Cl_2) to give 4-amino-3-methyl pyridine as an oil (0.5 g, 1.6 mmol). A solution of the oil (0.2 g, 2 mmol), and (1R)-(-)-10-camphorsulfonic acid (15 mg) in toluene (100 ml) is refluxed with a Dean Stark set up overnight. The mixture is concentrated and the residue is purified by chromatography (2-4% MeOH/CH2Cl2) to give the title imine as a white foam (0.20 g, 0.54 mmol). Ion spray MS m/z: 367, $[M+1]^+$; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.20 (d, 1H), 8.14 (s, 1H), 7.35 (s, 5H), 6.60 (d, 1H), 6.18 (dd, 1H), 5.15 (s, 2H), 4.97 (d, 1H), 4.30 (s, 2H), 3.78 (t, 2H), 3.50 (bm, 2H), 2.15 (s, 3H).

B. 1-[2-(3-Methylpyridin-4-yl-amino)-ethyl]-piperazin-2-one.

4-[2-(3-Methylpyridin-4-ylimino)-ethyl]-3-oxo-piperazine-1-carboxlic acid benzyl ester (0.20 g, 0.54 mmol) is dissolved in anhydrous ethanol (20 mL) and hydrogenated at 50 PSI with 10% Pd/C overnight. After filtration, the filtrate is concentrated. The residue is treated with Pd black in 5% HCO_2H/CH_2Cl_2 (10 ml) for 10 minutes. Filtration and concentration gives crude residue, which is purified by chromatography using NH_4OH/MeOH/CH_2Cl_2 (1:5:95) to give the title compound as a clear syrup (0.078 g, 0.33 mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 8.17 (d, 1H), 8.03 (s, 1H), 7.35 (s, 5H), 6.36 (d, 1H), 5.30 (b, 1H), 3.74 (t, 2H), 3.53 (s, 2H), 3.38 (m, 4H), 3.08 (t, 2H), 2.02 (s, 3H).

EXAMPLE 95. 1-[2-(Pyridazin-4-ylamino)-ethyl]-piperazin-2-one.

1-(2-Aminoethyl)-4-(tert-butyloxycarbonyl)-piperazin-2-one from EXAMPLE 92, Part A (1.0 g, 4.1 mmol) is treated with 3,4,5-trichloropyridazine (0.81 g, 4.1 mmol), triethylamine (0.57 mL, 4.1 mmol), THF (25 mL) and heated to 120°C in a sealed tube for 3 hours. Upon cooling, the solution is diluted with ethyl acetate and washed with aqueous sodium bicarbonate (25 mL), water and dried over sodium sulfate. The organic layer is concentrated and chromatographed (5% methanol/methylene chloride) to give a mixture of isomers (0.8 g, 20 mmol). The mixture is dissolved in 0.5 M sodium methoxide in methanol (200 mL), treated with 10% Pd/C (0.5 g) and agitated under 50 PSI of hydrogen

for 20 hours. The reaction mixture is filtered; the filtrate is concentrated to a residue which is chromatographed (NH_4OH/H_2O/MeOH/EtOAc, 1:1:2:90) to give crude 4-(tert-butyloxycarbonyl)-1-[2-(pyridazin-4-ylamino)-ethyl]-piperazin-2-one. This material is dissolved in a minimal amount of THF and treated with a saturated solution of HCl in ethyl acetate (50 mL). The solution is stirred at ambient temperature for 2 h and diluted with diethyl ether (50 mL). The precipitated title compound is collected and air dried (0.5 g, 1.7 mmol). MS m/z: 367, $[M+1]^+$; ^1H NMR (CD_3OD, 300 MHz) δ 8.8 (d, 1H), 8.5 (s, 1H), 7.4 (d, 1H), 4.1 (s, 2H), 3.5-3.8 (m, 8H).

EXAMPLE 96. 4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propenyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester and 4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester.

A. 1-Allyl-4-(tert-butyloxycarbonyl)-piperazin-2-one.

4-(tert-Butyloxycarbonyl)-piperazin-2-one (1.0 g, 5.0 mmol), EXAMPLE 40, is alkylated with allyl bromide (0.48 ml, 5.5 mmol) in THF (20 ml) using the procedure described in Example 92, PartA. The title compound (0.92 g, 3.8 mmol) is obtained as a colorless liquid after chromatographed (50 % ethyl acetate/hexane). EI MS m/z 240 (M+); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.80-5.68 (m, 1H), 5.23-5.15 (m, 2H), 4.09 (s, 2H), 4.03 (d, 2H), 3.63 (t, 2H), 3,30 (t, 2H), 1.45 (s, 9H).

B. 4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propenyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester and 4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester

1-Allyl-4-(tert-butyloxycarbonyl)-piperazin-2-one (0.49 g, 2.0 mmol) is treated with (3-iodo-pyridin-4-yl)-carbamic acid tert-butyl ester (0.64 g, 2.0 mmol), $Pd(OAc)_2$ (14 mg, 0.06 mmol), $P(o\text{-}tol)_3$ (37 mg, 0.12 mmol), and Et_3N (0.56 mmol) in a seal tube. The mixture is stirred at 100 °C overnight, then diluted with CH_2Cl_2 and washed H_2O (2 X). The CH_2Cl_2 layer is concentrated and the residue is chromatographed (5% MeOH/CH_2Cl_2) to give a mixture of two isomers (0.40 g, 0.92 mmol). The mixture is separated into its constituent isomers upon further chromatography (EtOAc) to give 4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-propenyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester (90 mg, 0.21 mmol, higher R_f value) and 4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester (0.24 g, 0.56 mmol, lower R_f value). For the former: MS m/z 433 (M+1); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.38 (d, 1H), 8.28 (s, 1H), 7.93 (d, 1H), 7.48 (d, 1H), 6.67 (s, 1H), 5.10 (m, 1H), 4.15 (s, 2H), 3.70 (t, 2H), 3,46 (t, 2H), 3.39 (d, 2H), 1.48 (s, 9H), 1.45 (s, 9H). For the latter: MS m/z 433 (M+1); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.39 (s, 1H), 8.37 (d, 1H), 7.98 (d, 1H), 6.77 (s,

1H), 6.52 (d, 1H), 6.07 (m, 1H), 4.23 (d, 2H), 4.12 (s, 2H), 3,69 (t, 2H), 3.40 (t, 2H), 1.52 (s, 9H), 1.45 (s, 9H).

EXAMPLE 97. 4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester

A mixture of the two isomers from EXAMPLE 96, Part B. (0.11 g, 0.25 mmol) is dissolved in MeOH (7 ml), treated with with 10% Pd/C and is stirred under a balloon of hydrogen for 4 hours. Filtration and concentration gives a white foam (80 mg, 0.18 mmol). EI MS m/z 434 (M+); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.33 (d, 1H), 8.30 (s, 1H), 8.05 (d, 1H), 4.08 (s, 2H), 3.64 (t, 2H), 3.50 (t, 2H), 3.35 (t, 2H), 2.58 (t, 2H), 1.90 (m, 2H), 1.57 (s, 9H), 1.48 (s, 9H).

EXAMPLE 98. 4-(Benzyloxycarbonyl)-1-(2-pyrrolo[3,2-c]pyridin-1-ylethyl)-piperazin-2-one

4-(Benzyloxycarbonyl)-1-(2-hydroxyethyl)-piperazin-2-one, prepared as described in EXAMPLE 94, part A. (0.26 g, 0.94 mmol) in methylene chloride (6 mL) is treated with triphenyl phosphine (0.60 g, 2.3 mmol), imidazole (0.16 g, 2.3 mmol), and iodine (0.47 g, 1.9 mmol) for 0.5 h at 0 °C. The reactin mixture is partitioned between water and methylene chloride; the organic layer is concentrated and the residue is chromatographed (15 % EtOAc/ methylene chloride) to give 4-(benzyloxycarbonyl)-1-(2-iodoethyl)-piperazin-2-one (0.24 g, 0.62 mmol). Pyrrolo[3,2-c]pyridine (0.073 g, g, 0.62 mmol) is dissolved in DMF (3 mL) and treated with 60 % sodium hydride (0.03 g, 0.74 mmol) and all of the 4-(benzyloxycarbonyl)-1-(2-iodoethyl)-piperazin-2-one from the previous step; the reaction mixture is stirred at r.t. for 16 g. The reaction mixture is concentrated to dryness and the residue is partitioned between water and methylene chloride. The organic layer is concentrated and subjected to chromatography (2-5 % MeOH/methylene chloride) to yield the title compound (0.028 g, 0.074 mmol) Ion Spray MS m/z: 379, $[M+1]^+$.

EXAMPLE 99. (±)-1-(3-Amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester.

A. (±)-1-[3-(Benzhydrylidene-amino)-4-cyano-benzyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester

A solution containing (±)-1-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-6-oxo-piperazine-2-carboxylic acid methyl ester (55 mg, 0.12 mmol) in CH_2Cl_2 (1 mL) is cooled to 0°C. DIPEA (24 mg, 0.18 mmol) is then added followed by the addition of 6-chloro-benzo[b]thiophene-2-sulfonyl chloride (32 mg, 0.12 mmol), EXAMPLE 1. The reaction mixture is warmed to ambient temperature. After 16 h, the reaction mixture is absorbed directly onto silica gel and chromatographed (CH_2Cl_2 to 2% MeOH/

CH_2Cl_2) to provide 60 mg (73%) of the title compound. ^1H NMR (300 MHz, $CDCl_3$) δ 2.77 (dd, J = 12.3, 3.4 Hz, 1H), 3.50-3.72 (m, 3H), 3.79 (s, 3H), 4.15 (dd, J = 12.3, 1.4 Hz, 1H), 4.24 (d, J = 16.9 Hz, 1H), 5.41 (d, J = 15.3 Hz, 1H), 6.50 (s, 1H), 6.76 (dd, J = 7.9, 1.4 Hz, 1H), 7.11-7.86 (m, 15H) ppm; MS (ISP loop): m/z 683 (M+H).

B. (±)-1-(3-Amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester

Concentrated HCl (12M, one drop) is added at 0°C to a mixture containing (±)-1-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester (60 mg, 0.08 mmol) in MeOH (5 mL). Added THF (2 mL) followed by a second drop of 12M HCl and warmed reaction mixture to ambient temperature. The reaction is quenched by pouring the reaction mixture onto a 1:1 mixture of CH_2Cl_2/aqueous $NaHCO_3$ and the layers are separated. The aqueous phase is washed with CH_2Cl_2 and then the combined organic phase is washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude residue is chromatographed on silica gel (CH_2Cl_2 to 4% MeOH/ CH_2Cl_2) to provide 42 mg (93%) of the title compound. ^1H NMR (300 MHz, $CDCl_3$) δ 2.98 (dd, J = 12.5, 3.5 Hz, 1H), 3.60 (d, J = 16.8 Hz, 1H), 3.69 (d, J = 15.3 Hz, 1H), 3.79 (s, 3H), 3.98 (m, 1H), 4.21-4.31 (m, 2H), 4.44 (br s, 2H), 5.36 (d, J = 15.3 Hz, 1H), 6.47 (dd, J = 8.0, 1.4 Hz, 1H), 6.54 (s, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.45 (dd, J = 8.5, 1.8 Hz, 1H), 7.80-7.86 (m, 3H) ppm; MS (ISP loop): m/z 519 (M+H).

EXAMPLE 100. (±)-1-(3-Amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid.

Water (5 drops) is added to a solution containing (±)-1-(3-amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester (30 mg, 0.05 mmol), EXAMPLE 99, in a 1:1 mixture of THF/MeOH (2 mL). At ambient temperature, LiOH monohydrate (7 mg, 1.66 mmol) is then added. After 16 h, the reaction mixture is diluted with water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 10 mg (34%) of the title compound as a white solid. ^1H NMR (300 MHz, d_6-DMSO) δ 3.18 (dd, J = 12.1, 3.5 Hz, 1H), 3.61 (d, J = 16.0 Hz, 1H), 3.77 (d, J = 16.0 Hz, 1H), 3.95 (d, J = 16.0 Hz, 1H), 4.06 (d, J = 12.1 Hz, 1H), 4.14 (m, 1H), 6.40 (d, J = 8.0 Hz, 1H), 6.54 (s, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.57 (dd, J = 8.6, 1.9 Hz, 1H), 8.06 (d, J = 8.6 Hz, 1H), 8.18 (s, 1H), 8.33 (s, 1H) ppm; MS (ISP loop): m/z 505 (M+H).

EXAMPLE 101. 4-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxo-piperazine-1-ylmethyl]benzamidine.

To a solution of 4-(2-oxopiperazin-1-ylmethyl)benzamidine bistrifluoroacetate (0.38 g, 0.83mmol), EXAMPLE 66, in CH_2Cl_2 (5 mL) is added Et_3N (0.35 mL, 2.6 mmol) and 6-chloro-benzo[b]thiophene-2-sulfonyl chloride (0.23 g, 0.85 mmol, EXAMPLE 1. After 6 hours, the solution is concentrated. The product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O(0.1% TFA) to 70% CH_3CN/H_2O(0.1% TFA). The appropriate collected fractions are lyophilized to afford the title compound as a white solid (0.37 g, 0.65 mmol). ^1H NMR (d^6-DMSO, 300MHz) δ 9.33 (bs, 2H), 8.96 (bs, 2H), 8.30 (s, 1H), 8.18 (s, 1H), 8.04 (d, 1H), 7.70 (m, 2H), 7.50 (m, 1H), 7.28 (m, 2H), 4.55 (s, 2H), 3.86 (s, 2H), 3.44 (m, 2H), 3.22 (m, 2H).

The following compounds are prepared from 1-(4-Aminoquinazoline-7-ylmethyl)-3-ethyl-piperazine-2-one, Example 77, and the appropriate sulfonyl chloride using the method of Example 101.

Example #	Name	m/z (M+H)
102	4-[4-(4-Methoxy-benzenesulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	403
103	4-[4-(5-Chloro-thieno[3,2-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	463, 465
104	4-[4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	464, 466 Cl pattern
105	4-[2-Oxo-4-(thieno[2,3-c]pyridine-2-sulfonyl)-piperazin-1-ylmethyl]-benzamidine	430
106	4-[4-(7-Chloro-thieno[2,3-c]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	464, 466 Cl pattern
107	4-[4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	495, 497 Cl pattern
108	4-[4-(4-Chloro-thieno[3,2-c]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	464, 466 Cl pattern
109	4-[2-Oxo-4-(toluene-4-sulfonyl)-piperazin-1-ylmethyl]-benzamidine	387
110	4-[4-(Benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	429
111	4-Amino-3-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	478, 480 Cl pattern
112	3-[2-Oxo-4-(toluene-4-sulfonyl)-piperazin-1-ylmethyl]-	387

	benzamidine	
113	3-[4-(6-Fluoro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	447
114	3-[4-(4-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	463, 465 Cl pattern
115	3-[4-(5-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	463, 465 Cl pattern
116	3-[4-(6-Methoxy-naphthalene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	453
117	3-{4-[5-(5-Nitro-pyridine-2-sulfonyl)-thiophene-2-sulfonyl]-2-oxo-piperazin- 1-ylmethyl}-benzamidine	565
118	3-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]- benzamidine	463, 465 Cl pattern
119	3-{4-[2-(3-Chloro-phenyl)-ethenesulfonyl]-2-oxo-piperazin-1-ylmethyl}- benzamidine	433, 435 Cl pattern
120	3-[2-Oxo-4-(4-phenylazo-benzenesulfonyl)-piperazin-1-ylmethyl]-benzamidine	477
121	3-[4-(Benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	429

EXAMPLE 122. 4-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine.

Hydrogen chloride gas is bubbled into an ice-cooled solution of 4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzonitrile (100 mg, 0.264 mmol), (prepared by deprotecting 4-(4-cyanobenzyl)-3-oxopiperazine-1-carboxylic acid benzyl ester, EXAMPLE 66, Part A, followed by alkylation with 6-chloro-2-chloromethylbenzimidazole) in 15 mL of methanol. The solution contained 3Å molecular sieves. The reaction mixture is stored at -30°C. The methanol is removed on the rotovap. Fresh methanol (20 ml) is added folowed by a stream of ammonia gas. The resulting mixture is heated to reflux for three hours. The reaction mixture is filtered at room temperature. The mother liquor is condensed and the resulting residue is purified by reverse phase HPLC (0-50 % ACN/H_2O). The product is isolated as a white solid with a melting point of 91-95°C . MS $C_{20}H_{21}ClN_6O$ m/z: 397, 399. Anal. cald. for $C_{20}H_{21}ClN_6O \cdot 3C_2HF_3O_2$: C, 42.26; H, 3.27; N, 11.37. Found C, 42.20; H, 3.44; N, 11.36.

EXAMPLE 123. 4-{4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-2-oxopiperazin-1-ylmethyl}benzamidine.

To a solution of 4-(2-oxopiperazin-1-ylmethyl)benzamidine bistrifluoroacetate (75 mg, 0.16 mmol), EXAMPLE 66, in 1.5 mL of DMF is added N,N-diisopropylethylamine (0.14 mL, 0.80 mmol). After stirring 10 min at room temperature, 3-(5-chloro-thiophen-2-yl)-(E)-acrylic acid (32 mg, 0.17 mmol), EXAMPLE 25, is added, followed by 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU) (55 mg, 0.17 mmol). The resulting mixture is stirred at room temperature for 16 h and the solution is concentrated. The crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 70% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to provide the title compound (77 mg, 0.15 mmol) as a white solid. ^1H NMR (d6-DMSO, 300 MHz) δ 9.27 (bs, 2H), 9.10 (bs, 2H), 7.77 (d, 2H), 7.65 (d, 1H), 7.49 (dd, 2H), 7.39 (m, 1H), 7.15 (d, 1H), 6.89 (d, 1H), 4.65 (s, 2H), 4.45, 4.21 (m, 2H, rotamers), 3.80 (m, 2H), 3.35 (m, 2H). ESI MS, $[M+H]^+$=403,405 (Cl pattern).

EXAMPLE 124. 3-{4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-2-oxopiperazin-1-ylmethyl}benzamidine.

The title compound is prepared as described in EXAMPLE 123 using 3-(5-chloro-thiophen-2-yl)-(E)-acrylic acid (EXAMPLE 25) and 3-(2-oxopiperazin-1-ylmethyl)benzamidine bistrifluoroacetate (prepared from 3-bromomethyl toluylnitrile as described in EXAMPLE 66). ^1H NMR (DMSO-d_6, 300 MHz) δ 9.32 (bs, 2H), 9.16 (bs, 2H), 7.65 (m, 5H), 7.39 (m, 1H), 7.15 (d, 1H), 6.89 (d, 1H), 4.64 (s, 2H), 4.44, 4.21 (m, 2H, rotamers), 3.93, 3.79 (m, 2H, rotamers), 3.36 (m, 2H). ESI MS, $[M+H]^+$=403,405 (Cl pattern).

EXAMPLE 125. 3-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine.

A white solid (13.0 mg, 13%). $C_{20}H_{21}ClN_6O$ MS m/z: 397, 399 Anal. cald. for $C_{20}H_{21}ClN_6O \cdot 3C_2HF_3O_2$: C, 42.26; H, 3.27; N, 11.37. Found C, 43.70; H, 3.71; N, 11.95.

EXAMPLE 126. 1-(2-Aminoquinolin-6-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)piperazin-2-one.

The title compound is prepared as described in Example 101 using 1-(2-aminoquinolin-6-ylmethyl)piperazin-2-one, EXAMPLE 67, and 5'-chloro-[2,2']bithiophenyl-5-sulfonyl chloride, EXAMPLE 2. The crude product is triturated in CH_2Cl_2 and filtered to provide the title compound as a white solid. ^1H NMR (d_6-DMSO, 300 MHz) δ 7.82 (d, 1H), 7.68 (d, 1H), 7.42 (m, 3H), 7.36 (d,1H),

7.25 (d, 1H), 7.20 (d, 1H), 6.70 (d, 1H), 6.43 (bs, 2H), 4.53 (s, 2H), 3.78 (s, 2H), 3.31 (m, 4H). MS (ion spray) m/z 519, 521, (M+H), Cl pattern.

EXAMPLE 127. 6-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]-1H-quinolin-2-one.

The title compound is prepared as described in EXAMPLE 101,using 6-(2-oxopiperazin-1-ylmethyl)-1H-quinolin-2-one, minor product from EXAMPLE 67, Part D, and 6-chlorobenzo[b]thiophene-2-sulfonyl chloride, EXAMPLE 1. The crude product is triturated in CH_2Cl_2 and filtered to provide the title compound as a white solid. ^1H NMR (d_6-DMSO, 300 MHz) δ 11.72 (bs, 1H), 8.33 (s, 1H), 8.18 (s, 1H), 8.07 (d,1H), 7.78 (d,1H), 7.58 (dd, 1H), 7.45 (s, 1H), 7.30 (dd, 1H), 7.18 (d, 1H), 6.46 (d, 1H), 4.52 (s, 2H), 3.86 (s, 2H), 3.43 (m, 2H), 3.31 (m, 2H). MS (ion spray) m/z 488, 490, (M+H), Cl pattern.

The following compounds are prepared using starting materials prepared as described in Examples 67, 68 and 73 and the appropriate carboxylic acid according to the method of Example 123.

Example #	Name	m/z (M+H)
128	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[2,3-c]pyridin-3-ylmethyl-piperazin-2-one	478, 480 Cl pattern
129	1-(2-Amino-quinoxalin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	
130	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[2,3-c]pyridin-2-ylmethyl-piperazin-2-one	478, 480 Cl pattern
131	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[3,2-c]pyridin-2-ylmethyl-piperazin-2-one	478, 480 Cl pattern
132	1-(2-Amino-quinolin-6-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one	488, 490 Cl pattern
133	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-hydroxy-isoquinolin-6-ylmethyl)-piperazin-2-one	488, 490 Cl pattern
134	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-chloro-isoquinolin-6-ylmethyl)-piperazin-2-one	506, 508 Cl pattern
135	7-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-2H-isoquinolin-1-one	488, 490 Cl pattern
136	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-chloro-	506, 508

	isoquinolin-7-ylmethyl)-piperazin-2-one	Cl pattern
137	1-(7-Amino-thieno[2,3-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	493, 495 Cl pattern
138	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(2-chloro-quinolin-6-ylmethyl)-piperazin-2-one	506, 508 Cl pattern
139	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-quinolin-6-ylmethyl-piperazin-2-one	472, 474 Cl pattern
140	7-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-1H-quinolin-2-one	488, 490 Cl pattern
141	1-(2-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	487, 489 Cl pattern
142	1-(4-Amino-thieno[3,2-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	493, 495 Cl pattern
143	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1,2,3,4-tetrahydro-isoquinolin-6-ylmethyl)-piperazin-2-one	475, 477 Cl pattern
144	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-isoquinolin-6-ylmethyl-piperazin-2-one	472, 474 Cl pattern
145	1-(2-Amino-quinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	487, 489 Cl pattern
146	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(decahydro-isoquinolin-6-ylmethyl)-piperazin-2-one	482, 484 Cl pattern
147	1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	487, 489 Cl pattern
148	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(decahydro-isoquinolin-7-ylmethyl)-piperazin-2-one	482, 484 Cl pattern
149	1-(1-Amino-isoquinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	487, 489 Cl pattern
150	1-(4-Amino-thieno[3,2-c]pyridin-3-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	493, 495 Cl pattern
151	(+/-)-[1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-4-thieno[3,2-c]pyridin-2-ylmethyl-piperazin-2-yl]-acetic acid	536, 538 Cl pattern
152	(+/-)-[1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-4-thieno[2,3-c]pyridin-2-ylmethyl-piperazin-2-yl]-acetic acid	536, 538 Cl pattern
153	1-(1-Amino-isoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-	471, 473

	(E)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	Cl pattern
154	1-(1-Amino-isoquinolin-6-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	475, 477 Cl pattern
155	(3S)-1-(7-Chloro-isoquinolin-3-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-methoxymethyl-piperazin-2-one	494, 496, 498, Cl_2 pattern
156	(3S)-1-(7-Chloro-isoquinolin-3-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3-methoxymethyl-piperazin-2-one	490, 492, 494, Cl_2 pattern
157	(S)-4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-3-ethyl-1-(4-hydroxy-quinolin-7-ylmethyl)-piperazin-2-one	456, 458 Cl pattern
158	1-(2-Amino-quinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one	427, 429 Cl pattern

The following compounds are prepared from starting materials prepared as described in Example 67 and the appropriate aryl-methyl bromide or allyl-methyl bromide using a K_2CO_3-mediated alkylation reaction.

Example #	Name	m/z (M+H)
159	1-(2-Aminoquinolin-6-ylmethyl)-4-(4-methoxybenzyl)piperazin-2-one	377
160	1-(2-Aminoquinolin-6-ylmethyl)-4-6-chlorobenzo[b]thiophen-2-ylmethyl)piperazin-2-one	436, 438 Cl pattern
161	1-(2-Aminoquinolin-6-ylmethyl)-4-(5-methoxy-1H-benzoimidazol-2-ylmethyl)piperazin-2-one	417
162	1-(2-Aminoquinolin-6-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)piperazin-2-one	469, 471 Cl pattern
163	1-(2-Aminoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one	413, 415 Cl pattern
164	1-(2-Aminoquinolin-6-ylmethyl)-4-[3-(3,5-dibromo-4-methoxy-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]piperazin-2-one	601, 603, 605 Br_2 pattern
165	3-[4-(2-Aminoquinolin-6-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-fluoro-1H-quinolin-2-one	431

166	1-(2-Aminoquinolin-6-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one	430

The following compounds are prepared from starting materials prepared as described in Examples 66, 67, 68 and 73 and the appropriate aryl-methyl bromide or allyl-methyl bromide using a K_2CO_3-mediated alkylation reaction.

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Example #	Name	m/z (M+H)
167	3-(4-Biphenyl-3-ylmethyl-3-oxo-piperazin-1-ylmethyl)-benzamidine	399
168	4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-piperazin-2-one	439, 441 Cl pattern
169	1,4-Bis-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one	427
170	1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one	439, 441 Cl pattern
171	1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	444, 446 Cl pattern
172	1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one	420, 422 Cl pattern
173	1-(3-Amino-1H-indazol-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one	401
174	1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	426
175	1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	443
176	4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine	413, 415 Cl pattern
177	4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-benzamidine	413, 415 Cl pattern
178	4-(4-Cyclohexylmethyl-2-oxo-piperazin-1-ylmethyl)-benzamidine	329
179	1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	437, 439 Cl pattern
180	1-(1-Amino-isoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-	457, 459

	yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one	Cl pattern
181	4-[3-(5-Chloro-thiophen-2-yl)-allyl]-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-3-(S)-methyl-piperazin-2-one	468
182	4-[3-(5-Chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-1-[4-(6-oxo-1,6-dihydro-pyridin-3-yl)-benzyl]-piperazin-2-one	454
183	(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-3-methoxymethyl-piperazin-2-one	483
184	(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-3-methyl-piperazin-2-one	453

EXAMPLE 185. 1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-sulfonyl)piperazin-2-one.

The title compound is prepared as described in EXAMPLE 101, substituting 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one bishydrochloride, EXAMPLE 72, for 4-(2-oxopiperazin-1-ylmethyl)-benzamidine. The product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 70% CH_3CN/H_2O (0.1% TFA). The appropriate collected fractions are lyopholized to afford the title compound as a white solid. MS (ion spray) m/z 488, 490, (M+H). ^1H NMR (d_6-DMSO, 300 MHz) δ 9.65 (s, 2H), 8.80 (s, 1H), 8.30 (m, 2H), 8.20 (s, 1H), 8.05 (d, 1H), 7.60 (m, 3H), 4.70 (s, 2H), 3.85 (s, 2H), 3.50-3.20 (m, 4H).

EXAMPLE 186. 4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid 3-chloro-benzylamide.

To a solution of 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one bishydrochloride, EXAMPLE 72, (0.10g, 0.30mmol) is 9 mL of DMF is added 3-chlorobenzyl sulfamyl catechol (0.09g, 0.30mmol), EXAMPLE 4, Et_3N (0.08g, 0.75 mmol) and DMAP (0.001 g, 0.12 mmol). The solution is heated to 60°C. After 16 h, the solution is concentrated. The crude product is purified by RP-HPLC eluting with a gradient of 10% CH_3CN/H_20 (0.1%TFA) to 100% CH_3CN. The product fractions are lyophilized to give the title compound (0.077g, 0.17 mmol) as the TFA salt. ^1H NMR (d_6-DMSO, 300 MHz) δ 9.82 (bs, 2H), 8.98 (s, 1H), 8.52 (d, 1H), 8.32 (d, 1H), 7.60 (m, 2H), 7.35 (m, 4H), 4.69 (AB, 2H), 4.11 (m, 2H), 3.77 (s, 2H), 3.38 (m, 2H), 3.27 (m, 2H). MS (ion spray) m/z 461, 463, (M+H), Cl pattern.

The following compounds are prepared from the compound of Example 72 and the appropriate sulfonyl choride using the method of Example 101.

Example #	Name	m/z (M+H)
187	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one	489, 491 Cl pattern
188	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-piperazin-2-one	520, 522 Cl pattern
189	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid 4-chloro-benzylamide	460
190	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-isoxazol-3-yl-thiophene-2-sulfonyl)-piperazin-2-one	471
191	1-(4-Amino-quinazolin-7-ylmethyl)-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one	455
192	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid [2-(3-chloro-phenyl)-ethyl]-amide	474
193	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid [2-(4-chloro-phenyl)-ethyl]-amide	474
194	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-sulfonyl)-piperazin-2-one	472
195	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	464, 466 Cl pattern
196	4-(3-Amino-benzenesulfonyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one	413

The following compounds are prepared from starting materials obtained as described in Examples 75-88 and the appropriate sulfonyl chloride using the method of Example 101.

Example #	Name	m/z (M+H)
197	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3-(S)-ethyl-piperazin-2-one	492, 494 Cl pattern
198	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-ethyl-piperazin-2-one	516, 518 Cl pattern
199	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-ethyl-piperazin-2-one	548, 550 Cl pattern
200	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-methyl-piperazin-2-one	534, 536 Cl pattern

201	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-methyl-piperazin-2-one	502, 504 Cl pattern
202	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-methyl-piperazin-2-one	502, 504 Cl pattern
203	(+/-)-[4-(4-Amino-quinazolin-7-ylmethyl)-1-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-piperazin-2-yl]-acetic acid	546, 548 Cl pattern

The following compounds are prepared from starting materials obtained as described in Examples 72 and 73 and the appropriate sulfonyl chloride according to the method of Example 101 or the appropriate carboxylic acid according to the method of Example 123.

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Example #	Name	m/z (M+H)
204	1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	470, 472 Cl pattern
205	1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	493, 495 Cl pattern
206	1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	494, 496 Cl pattern
207	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-hydroxy-quinazolin-6-ylmethyl)-piperazin-2-one	489, 491 Cl pattern
208	1-(4-Amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	494, 496 Cl pattern
209	1-(4-Amino-quinazolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	488, 490 Cl pattern
210	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-hydroxy-quinazolin-7-ylmethyl)-piperazin-2-one	489, 491 Cl pattern
211	1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-piperazin-2-one	478, 480 Br pattern
212	1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one	434, 436 Cl pattern

EXAMPLE 213. 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.

A. 2-{4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-2-oxopiperazin-1-ylmethyl}pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

To a solution of 2-(2-oxopiperazin-1-ylmethyl)pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester (0.71 g, 2.1 mmol), EXAMPLE 69, in CH_3CN (7 mL) is added triethylamine (0.60 mL, 4.3 mmol) followed by 2-(5-chloro-thiophen-2-yl)-ethenesulfonyl chloride, EXAMPLE 3, (0.57 g, 2.1 mmol). The mixture is stirred overnight, then concentrated to dryness. The residue is diluted with CH_2Cl_2 and washed with saturated sodium bicarbonate and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo to give the title compound (1.2 g, 2.1 mmol) as a light yellow solid. The crude material can be used in the subsequent step without further purification. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.80 (s, 1H), 8.42 (d, 1H), 7.88 (d, 1H), 7.55 (d, 1H), 7.14 (d, 1H), 6.98 (d, 1H), 6.41 (s, 1H), 6.36 (d, 1H), 5.00 (s, 2H), 3.98 (s, 2H), 3.61 (m, 4H), 1.71 (s, 9H). Ion spray MS, $[M+H]^+$= 537, 539, Cl pattern.

B. 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.

Trifluoroacetic acid (2.2 mL, 28.6 mmol) is added dropwise to a slurry of 2-[4-(6-chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (1.32 g, 2.4 mmol) in CH_2Cl_2 (25 mL) at 0°C. After 1.5 hours, the ice bath is removed and the solution stirred at room temperature for 4 hours. The reaction mixture is diluted with methylene choride and washed with saturated sodium bicarbonate and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo to give the title compound as the free base. The crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 100% CH_3CN and the appropriate product fractions are lyophilized to provide the title compound (1.29 g, 2.2 mmol) as a white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 14.90 (bs, 1H), 12.81 (s, 2H), 9.12 (s, 1H), 8.41 (d, 1H), 7.89 (d, 1H), 7.60 (d, 1H), 7.50 (d, 1H), 7.20 (d, 1H), 7.12 (d, 1H), 6.95 (s, 1H), 4.80 (s, 2H), 3.98 (s, 2H), 3.48 (s, 4H). Ion spray MS, $[M+H]^+$= 437, 439, Cl pattern.

EXAMPLE 214. 4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.

A. 2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

^1H NMR ($CDCl_3$, 300 MHz) δ 8.7 (s, 1H), 8.41 (d, 1H), 7.9-7.8 (m, 3H), 7.45 (d, 1H), 7.25 (d, 1H), 6.31 (s, 1H), 4.95 (s, 2H), 3.98 (s, 2H), 3.65 (m, 2H), 3.55 (m, 2H), 1.68 (s, 9H). Ion spray MS, $[M+H]^+$= 561, 563, Cl pattern.

B. 4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one trifluoroacetate.

^{1}H NMR (d6-DMSO, 300 MHz) δ 14.68 (bs, 1H), 12.6 (s, 1H), 9.1 (s, 1H), 8.36 (d, 1H), 8.29 (d, 1H), 8.17 (s, 1H), 8.05 (d, 1H), 7.82 (d, 1H), 7.56 (m, 2H), 6.83 (s, 1H), 4.1 (s, 2H), 3.84 (s, 2H), 3.38 (m, 4H). Ion spray MS, $[M+H]^+$= 461,463, Cl pattern.

EXAMPLE 215. 4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(5-oxy-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one (0.06 g, 0.13 mmol) is dissolved in anhydrous methylene chloride (20 ml), treated with m-chloroperbenzoic acid (0.03 g, mmol) and stirred at room temperature for 4 hours. The solution is diluted with methylene chloride, washed with $NaHCO_3$, dried (Na_2SO_4) and concentrated. The residue is purified by flash chromatography (5-10 % MeOH/CH_2Cl_2) and converted to the TFA salt to provide the title compound (0.015 g, 0.032 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.14 (bs, 1H), 8.95 (d, 1H), 7.8- 7.87 (m, 3H), 7.57 (d, 1H), 7.48 (dd, 1H), 6.87 (s, 1H), 4.90 (s, 2H), 3.95 (s, 2H), 3.86 (s, 3H), 3.49 (s, 3H). EI MS, $[M^+]$ = 474, 476, Cl pattern.

EXAMPLE 216. 4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1-methyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one (0.59 g, 1.28 mmol), EXAMPLE 214, is dissolved in anhydrous DMF (30 ml), cooled in an ice bath, treated with 60 % sodium hydride (0.061 g, 1.53 mmol) and stirred at room temperature for 30 minutes. The solution is treated with methyl iodide (83 mL, 1.33 mmol) and warmed to room temperature over 4 hours. The reaction is quenched with ammonium chloride solution, diluted with ethyl acetate and separated. The organic layer is washed with brine (3x), dried (Na_2SO_4) and concentrated. The residue is purified by flash chromatography (5-10 % MeOH/CH_2Cl_2) to provide the title compound (0.31 g, 0.65 mmol). ^{1}H NMR (CD_3OD, 300 MHz) δ 8.55 (d, 1H), 7.99 (dd, 1H), 7.82 (m, 3H), 7.49 (dd, 1H), 7.43 (d, 1H), 6.55 (s, 1H), 4.75 (s, 2H), 3.96 (s, 2H), 3.52 (m, 4H), 3.86 (s, 3H), 3.49 (s, 3H). Ion Spray MS, $[M+H]^+$=477.

The following compounds are prepared from starting materials obtained as described in Example 69 and the appropriate sulfonyl chlorides according to the method of Example 101.

Example #	Name	m/z (M+H)

217	4-(3-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one	460
218	4-(6-Chlorothieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.	462, 464 Cl pattern
219	4-(6-Bromobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one	505
220	2-[3-Oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazine-1-sulfonyl]-benzo[b]thiophene-6-carbonitrile	452
221	4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one	493
222	4-[2-(4-Chlorophenyl)ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one	431
223	{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl} acetic acid	519, 521 Cl pattern
224	4-(5-Pyridin-4-ylthiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one	454
225	{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl} acetic acid ethyl ester	547, 549 Cl pattern
226	4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-[1-(2-methoxyethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]piperazin-2-one	519, 520
227	4-(6-Chlorothieno[3,2-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one	462, 464
228	{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[2,3-c]pyridin-1-yl} acetic acid methyl ester	533, 535
229	2-[3-Oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazine-1-sulfonyl]benzo[b]thiophene-5-carbonitrile	452
230	4-(5-Aminomethylbenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one	456
231	2-{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl}acetamide	518, 520
232	4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-[1-(2-hydroxyethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]piperazin-2-one	505
233	4-(6-Chloro-1H-benzoimidazole-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	445, 447

234	4-(1H-Benzoimidazole-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	411
235	4-(6-Aminomethyl-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	456
236	1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one	428
237	1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one	428
238	4-[2-(5-Chloro-thiophen-2-yl)-ethanesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	439, 441 Cl pattern
239	4-(2-Benzo[b]thiophen-2-yl-ethenesulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	453
240	4-[2-(5-Chloro-4-methoxy-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	467, 469
241	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-furo[3,2-c]pyridin-2-ylmethyl-piperazin-2-one	462, 464
242	4-(6-Fluoro-benzo[b]thiophene-2-sulfonyl)-1-furo[3,2-c]pyridin-2-ylmethyl-piperazin-2-one	446
243	4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)piperazin-2-one	460, 462 Cl pattern
244	4-(6-Chlorothieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)piperazin-2-one	462, 464 Cl pattern
245	{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-pyrrolo[2,3-c]pyridin-1-yl}-acetic acid methyl ester	533, 535 Cl pattern
246	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-b]pyridin-2-ylmethyl)-piperazin-2-one	461, 463 Cl pattern

EXAMPLE 247. 1-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)piperazin-2-one.

A. (2-Chloro-pyridin-4-yl)-carbamic acid tert-butyl ester.

NaHMDS (61.7 mL, 1.0M solution in THF) is rapidly added to a solution of 2-chloro-pyridin-ylamine (4.0 g, 30.9 mmol) amd BOC anhydride (6.74 g, 30.9 mmol) in THF (28 mL) at RT. The reaction mixture is cooled in an ice water bath (0°C) for 1h then stirred for 3 hr at RT. The gelatinous mixture is concentrated in vacuo and diluted with ethyl acetate and saturated NH_4Cl solution. The

organic layer is washed with 0.1N HCl, saturated $NaHCO_3$ and brine. The organic layer is then dried over $MgSO_4$, filtered and concentrated to dryness. The crude product is chromatographed eluting with 1% MeOH/CH_2Cl_2 to yield the title product (5.57 g, 24.4 mmol) as a yellow solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.18 (d, 1H), 7.48 (d, 1H), 7.12 (dd, 1H), 1.60 (s, 9H). EI MS $[M]^+$=228.

B. (2-Chloro-3-iodo-pyridin-4-yl)-carbamic acid tert-butyl ester.

tert-Butyllithium (36.3 mL, 1.7M in pentane) is added dropwise to a solution of (2-chloro-pyridin-4-yl)-carbamic acid tert-butyl ester (6.00 g, 26.2 mmol) in THF (46 mL) at -78 °C under Ar. The yellow/orange mixture is stirred for 2 h at -78°C then warmed to -40 °C for 1 h then cooled to -78°C before dropwise addition of I_2 (15.65 g, 61.7 mmol) in THF (49 mL). The reaction mixture is stirred for 1.5 h at -78°C then at -10°C for 30 minutes. The reaction is quenched with saturated NH_4Cl solution then diluted with CH_2Cl_2 and washed with saturated NH_4Cl, saturated sodium thiosulfate, water then brine. The organic layer is dried over $MgSO_4$, filtered and concentrated to dryness. The crude product is chromatographed eluting with 1-2% MeOH/CH_2Cl_2 to yield the title product (7.96 g, 22.5 mmol) as a bright yellow solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.14 (d, 1H), 8.02 (d, 1H), 7.32 (bs, 1H), 1.60 (s, 9H). EI MS $[M]^+$=354, 356, Cl pattern.

C. 4-(4-Chloro-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester.

Trifluoroacetic acid (10 mL) is added to a solution of 2-(4-benzyloxycarbonyl-2-oxo-piperazin-1-ylmtheyl)-4-chloro-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (5.66 g, 11.3 mmol, prepared in the same manner as described previously) in CH_2Cl_2 (10 mL). The solution is stirred overnight then diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated to dryness. The crude product is chromatographed eluting with 1-5% MeOH/CH_2Cl_2 to yield the title product (3.81 g, 9.56 mmol) as a foamy yellow solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 9.43 (bs, 1H), 8.08 (d, 1H), 7.38 (s, 5H), 7.18 (d, 1H), 6.51 (s, 1H), 5.15 (s, 2H), 4.58 (s, 2H), 4.20 (s, 2H), 3.71 (m, 2H), 3.50 (m, 2H). Ion spray $[M+H]^+$= 399, 401, Cl pattern.

D. 4-(1-Benzenesulfonyl-4-chloro-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester.

Powdered NaOH (0.96 g, 23.9 mmol) followed by nBu_4NHSO_4 (0.32 g, 0.96 mmol) and benzene sulfonyl chloride (1.8 mL, 14.1 mmol) is added to a solution of 4-(4-chloro-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester (3.81 g, 9.56 mmol) in CH_2Cl_2 (32 mL) at RT. The resulting slurry is stirred for 3.5 h then diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated to dryness. The crude product is chromatographed eluting with 1-5% MeOH/CH_2Cl_2 to yield the title product (5.06 g, 9.38 mmol). ^1H

NMR ($CDCl_3$, 300 MHz) δ 8.23 (d, 1H), 7.97 (d, 1H), 7.84 (d, 2H), 7.61 (d, 1H), 7.51 (m, 2H), 7.38 (s, 5H), 6.50 (s, 1H), 5.18 (s, 2H), 5.03 (s, 2H), 4.29 (s, 2H), 4.29 (s, 2H), 3.80 (m, 2H), 3.51 (m, 2H). Ion spray $[M+H]^+$= 539, 541, Cl pattern.

E. 1-(1-Benzenesulfonyl-4-chloro-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

TMSI (2.7 mL, 19.0 mmol) is added to a solution of 4-(1-benzenesulfonyl-4-chloro-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester (5.06 g, 9.38 mmol) in CH_3CN (134 mL) at 0°C. The reaction mixture is warmed to RT and stirred for 5 hours. The reaction mixture is concentrated to dryness and the red residue is diluted with MeOH and concentrated to dryness (this is repeated twice). The mixture is diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated to dryness. The crude product is chromatographed eluting with 1-5% MeOH/CH_2Cl_2 to yield the title product (0.70 g, 1.74 mmol) and unreacted starting material (3.58 g, 6.64 mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 8.20 (d, 1H), 7.93 (d, 1H), 7.85 (d, 2H), 7.60 (d, 1H), 7.51 (m, 2H), 6.50 (s, 1H), 5.01 (s, 2H), 3.45 (m, 2H), 3.18 (m, 2H). Ion spray $[M+H]^+$= 405, 407, Cl pattern.

F. 1-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-sulfonyl)piperazin-2-one.

Anhydrous ammonium acetate (0.56 g, 7.2 mmol), phenol (0.45 g, 4.8 mmol) and 1-(1-benzenesulfonyl-4-chloro-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one (0.31 g, 0.48 mmol, prepared as described previously) are heated to 100°C for 3.5 days. The mixture is cooled to RT then the crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 100% CH_3CN then the appropriate product fractions are lyophilized to provide the title compound (1.29 g, 2.2 mmol) as a white solid (22.4 mg, 0.038 mmol). ^1H NMR (DMSO-d_6, 300 MHz) δ 12.40 (bs, 1H), 12.00 (bs, 1H), 8.31 (d, 1H), 8.20 (s, 1H), 8.06 (d, 1H), 8.02 (bs, 2H), 7.57 (dd, 1H), 7.48 (m, 1H), 6.89 (d, 1H), 6.81 (s, 1H), 4.60 (s, 2H), 3.81 (s, 2H), 3.40 (m, 4H). LR-FAB MS, $[M+H]^+$=476, 478.

EXAMPLE 248. 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-(±)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. 2-{4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-2-(±)-hydroxymethyl-6-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

Sodium borohydride (0.005 g, 0.13 mmol) is added to a solution of 2-{4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-2-(±)-methoxycarbonyl-6-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-

carboxylic acid tert-butyl ester (0.04 g, 0.07 mmol), (prepared from 2-(2-(±)-methoxycarbonyl-6-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester, EXAMPLE 71, and 2-(5-chloro-thiophen-2-yl)-ethenesulfonyl chloride, EXAMPLE 3, using the procedure described in EXAMPLE 214, Part A) in MeOH (3 mL) at RT. The reaction mixture is stirred for 6 h then quenched with water and concentrated in vacuo. The crude product (0.04 g) is taken onto the next step without further purification.

B. 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-(±)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

Trifluoroacetic acid (1.8 mL) is added to a solution of 2-{4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-2-(±)-hydroxymethyl-6-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (0.04 g) in CH_2Cl_2 (4.2 mL) at RT. The reaction mixture is stirred for 4 h then concentrated in vacuo. The title compound is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 100% CH_3CN and lyophilizing the appropriate product fractions. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.10 (s, 1H), 8.46 (d, 1H), 7.82 (d, 1H),7.50 (d, 1H) 7.43 (d, 1H), 7.14 (d, 1H), 7.01 (d, 1H), 6.94 (s, 1H), 5.12 (bs, 1H), 4.80 (AB, 2H), 3.98 (d, 2H0, 3.90 (m, 1H), 3.40-3.50 (m, 4H). APCI MS, $[M+H]^+$=467, 469.

The following compounds are prepared from starting materials obtained using the methods of Examples 69, 70 and 71 and the appropriate sulfonyl chorides according to the method of Example 101.

Example #	Name	m/z
249	1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester	519, 521 Cl pattern
250	1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester	495, 497 Cl pattern
251	1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid	505, 507 Cl pattern
252	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-(±)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	491, 493 Cl pattern

The following enantiomerically pure compounds are obtained by chiral resolution on a CHIRACEL OD prep column.

Example #	Name	%ee	m/z
253	1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(-)-carboxylic acid methyl ester	99% (-)	495, 497 Cl pattern
254	1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(+)-carboxylic acid methyl ester	95% (+)	495, 497 Cl pattern

EXAMPLE 255. 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. 6-(R)-(tert-Butyl-dimethyl-silanyloxymethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

Trifluoroacetic acid (0.25 mL) is added to a solution of 2-{2-(R)-(tert-butyl-dimethyl-silanyloxymethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (0.025 g, 0.037 mmol) in CH_2Cl_2 (0.5 mL) at room temperature. The reaction mixture is stirred for 2 h then concentrated to dryness. The residue is diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product (0.019 g, 0.033 mmol) is used in the subsequent step without further purification.

B. 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

Glacial acetic acid (3 mL, 0.046 mmol) and tetrabutylammonium fluoride (92 mL, 0.092 mmol) is added to a solution of 6-(R)-(tert-butyl-dimethyl-silanyloxymethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one (0.019 g, 0.033 mmol) in THF (0.5 mL). The resulting solution is stirred for 4 h then concentrated in vacuo. The crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 100% CH_3CN and the appropriate product fractions are lyophilized to provide the title compound (0.009 g, 0.016 mmol) as a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 14.50 (bs, 1H), 12.60 (bs, 1H), 9.18 (s, 1H), 8.38 (d, 1H), 7.89 (d, 1H), 7.61 (d, 1H), 7.50 (d, 1H), 7.21 (d, 1H), 7.08 (d, 1H), 6.90 (s, 1H), 5.03 (s, 2H), 4.63 (d, 2H), 3.70-3.90 (AB, 2H), 3.75 (m, 1H), 3.21 (m, 2H). Ion spray MS, $[M+H]^+$=467, 469, Cl pattern.

The following compounds are prepared from starting materials obtained as described in Examples 69, 70 and 71 and the appropriate sulfonyl chloride according to the method of Example 101.

Example #	Name	m/z
256	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	491, 493
257	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester	495, 497 Cl pattern
258	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester	519, 521 Cl pattern
259	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid	481, 483 Cl pattern
260	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid	505, 507 Cl pattern
261	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-(±)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	491, 493 Cl pattern
262	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(±)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	467, 469 Cl pattern
263	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid amide	504, 506 Cl pattern
264	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	481, 483
265	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	505, 507
266	4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	537, 539
267	4-[2-(4-Chloro-phenyl)-ethenesulfonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	475, 477

EXAMPLE 268. 1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-ylmethyl)piperazin-2-one.

To a solution of 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one bishydrochloride (1.84 g, 5.73 mmol), EXAMPLE 72, in DMF (20 mL) is added 2-bromomethyl-6-chloro-benzo[b]thiophene, EXAMPLE 5, (1.5 g, 5.73 mmol) and K_2CO_3 (4.0 g, 28.7 mmol). The solution is stirred for 16 hours. After this time, the solution is diluted with water. The solution is acidified with trifluoroacetic acid. The product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 50% CH_3CN/H_2O (0.1% TFA). The appropriate collected fractions are lyopholized to afford the title compound as a white solid. ^{1}H NMR (d^6-DMSO, 300MHz) δ 9.78 (bs, 3H), 8.82 (s, 1H), 8.34 (d, 1H), 8.07 (s, 1H), 7.81 (d, 1H), 7.63 (d, 1H), 7.51 (s, 1H), 7.32 (m, 2H), 4.71 (s, 2H), 3.95 (s, 2H), 3.28 (m, 4H), 2.80 (m, 2H).

EXAMPLE 269. 1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)piperazin-2-one.

A mixture of 1-(4-aminoquinazolin-7-ylmethyl)piperazin-2-one (50 mg, 0.15 mmol), EXAMPLE 72, 6-chloro-2-chloromethylbenzimidazole (30.5 mg, 0.15 mmol) and potassium carbonate (83 mg, 0.6 mmol) in 2 mL of DMF is stirred at ambient temperature overnight. The mixture is purified on reverse phase HPLC (CH_3CN/H_2O/TFA) to give the trifluoroacetic acid salt of 1-(4-aminoquinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)piperazin-2-one (25 mg) as a solid. ^{1}H NMR (CD_3OD, 300 MHz) δ 8.69 (s, 1H), 8.33 (d, 1H), 7.79 (s, 1H), 7.75-7.69 (m, 3H), 7.57-7.54 (m, 1H), 4.86 (s, 2H), 4.22 (s, 2H), 3.31 (m, 4H), 2.99 (m, 2H). MS m/z 422 (M+H).

EXAMPLE 270. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzothioazol-2-ylmethyl)-piperazin-2-one.

To a solution of 1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one (76 mg, 0.23 mmol), EXAMPLE 72, in 2 mLof DMF is added potassium carbonate (127 mg, 0.92 mmol) followed by 6-chloro-2-chloromethyl-benzothiazole (prepared according to the procedure of B.L.Mylari, Synthesis Comm. 1989, 16, 2921) (50 mg, 0.23 mmol). The resulting mixture is stirred overnight at room temperature. The undissolved potassium carbonate is removed by filtration and the mother liquor is purified by reverse phase HPLC (10-100% CH_3CN/H_2O). The desired is product is obtained as a white solid with a melting point of 123-126°C. $C_{21}H_{19}ClN_6OS$ MS m/z: 439, 441. Anal. cald. for $C_{21}H_{19}ClN_6OS \cdot 2C_2HF_3O_2$: C, 45.02; H, 3.17 N, 12.60. Found C, 44.15; H, 3.19; N, 11.79.

EXAMPLE 271. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzooxazol-2-ylmethyl)-piperazin-2-one.

The desired product (10.0 mg, 7 %) is isolated as a white solid. $C_{21}H_{19}ClN_6O_2$ MS m/z: 423, 425.

EXAMPLE 272. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzothioazol-2-ylmethyl)-piperazin-2-one.

The desired product (19.0 mg, 22%) is obtained as a white solid. $C_{21}H_{19}ClN_6OS$ MS m/z: 438,440. Anal. cald. for $C_{21}H_{19}ClN_6OS \cdot 2C_2HF_3O_2$: C, 45.02; H, 3.17 N, 12.60. Found C, 43.35; H, 3.26; N, 12.65.

EXAMPLE 273. 3-[4-(4-Aminoquinazoline-7-ylmethyl)-3-oxopiperazin-1-ylmethyl]-7-chloro-1H-quinolin-2-one.

The title compound is prepared as described in EXAMPLE 268, substituting 3-bromomethyl-7-chloro-1H-quinoline-2-one, EXAMPLE 8, for 2-bromomethyl-6-chlorobenzo[b]thiophene. The product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O(0.1% TFA) to 50% CH_3CN/H_2O(0.1% TFA). The appropriate collected fractions are lyopholized to afford the title compound as a white solid. ^1H NMR (d^6-DMSO, 300MHz) δ 12.18 (bs, 1H), 9.75 (m, 1H), 8.86 (s, 1H), 8.40 (m, 1H), 8.11 (d, 1H), 8.10 (s, 1H), 7.78 (m, 1H), 7.69 (m, 2H), 7.37 (m, 1H), 4.80 (s, 2H), 4.10 (m, 2H), 3.47 (m, 4H), 3.30 (m, 2H). MS (ion spray) m/z 449, (M+H).

EXAMPLE 274. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-piperazin-2-one.

A. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1-(toluene-4-sulfonyl)-1H-indol-6-ylmethyl)-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 268 using 6-bromomethyl-3-chloro-1-(toluene-4-sulfonyl)-1H-indole, EXAMPLE 16, in place of 2-bromomethyl-6-chloro-benzo[b]thiophene. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 80% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to give a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.75 (bs, 2H), 8.82 (s, 1H), 8.40 (d, 1H), 7.64 (m, 2H), 7.60 (m, 2H), 7.40 (d, 1H), 7.23 (m, 1H), 7.19 (m, 2H), 6.99 (d, 2H), 5.09 (s, 2H), 4.78 (s, 2H), 4.10 (m, 2H), 3.40 (m, 4H), 2.49 (s, 3H).

B. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-piperazin-2-one.

To a solution of 1-(4-amino-quinazolin-7-ylmethyl)-4-(3-chloro-1-(toluene-4-sulfonyl)-1H-indol-6-ylmethyl)-piperazin-2-one ditrifluoroacetate (31 mg, 0.04 mmol) in 2 mL of MeOH is added 0.3 mL of 1N NaOH solution. The solution is heated at 100°C for 3 hours. After this time, the solution is diluted with water/acetonitrile and neutralized with trifluoroacetic acid. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 60% CH_3CN/H_2O (0.1% TFA) and

the appropriate product fractions are combined and lyopholized to give the title compound (21 mg, 0.03 mmol) as a white solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.71 (bs, 2H), 8.81 (s, 1H), 8.40 (d, 1H), 7.63 (m, 3H), 7.53 (d, 1H), 7.50 (s, 1H), 7.20 (d, 1H), 4.78 (s, 2H), 4.30-3.10 (m, 8H). ESI MS, $[M+H]^+$=421, 423 (Cl pattern).

EXAMPLE 275. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-allyl]-piperazin-2-one.

To a solution of 1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one bishydrochloride (100 mg, 0.31 mmol), EXAMPLE 72, in 3 mL of DMF is added 2-(3-bromo-(E)-propenyl)-5-chloro-thiophene (73 mg, 0.31 mmol), prepared as described in EXAMPLE 17., and K_2CO_3 (0.21 g, 1.54 mmol). The solution is stirred at room temperature for 16 hours. After this time, the solution is diluted with water/acetonitrile and neutralized with trifluoroacetic acid. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 60% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to give the title compound (80 mg, 0.12 mmol) as a white solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.76 (bs, 2H), 8.81 (s, 1H), 8.40 (d, 1H), 7.70 (s, 1H), 7.62 (dd, 1H), 7.10 (m, 2H), 6.90 (d, 1H), 6.05 (dt, 1H), 4.80 (s, 2H), 3.77 (m, 4H), 3.50 (m, 2H), 3.37 (m, 2H). ESI MS, $[M+H]^+$=414,416 (Cl pattern). Anal. ($C_{20}H_{20}ClN_5OS \cdot 2.0TFA \cdot 1.1H_2O$) C, H, N.

EXAMPLE 276. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-(E)-enyl]-piperazin-2-one ditrifluoroacetate.

^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.70 (bs, 2H), 8.82 (s, 1H), 8.40 (d, 1H), 7.68 (s, 1H), 7.61 (d, 1H), 7.10 (m, 2H), 5.88 (t, 1H), 4.79 (s, 2H), 3.75 (m, 4H), 3.49 (m, 2H), 3.29 (m, 2H), 2.09 (s, 3H). EI MS, $[M+H]^+$=427, 429 (Cl pattern).

EXAMPLE 277. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-2-methyl-(E)-allyl]-piperazin-2-one ditrifluoroacetate.

^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.80 (bs, 2H), 8.85 (s, 1H), 8.41 (d, 1H), 7.70 (s, 1H), 7.68 (d, 1H), 7.06 (d, 1H), 7.05 (d, 1H), 6.70 (bs, 1H), 4.80 (s, 2H), 4.30 (bs, 2H), 3.45 (m, 4H), 3.10 (m, 2H), 1.99 (s, 3H). ESI MS, $[M+H]^+$=428, 430 (Cl pattern).

EXAMPLE 278. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-furan-2-yl)-(E)-allyl]-piperazin-2-one.

To a solution of 1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one (50 mg, 0.20 mmol), EXAMPLE 72.in 3 mL of acetonitrile is added 3-(4-bromo-furan-2-yl)-(E)-propenal (43 mg, 0.22 mmol), prepared as described in EXAMPLE 18, 2 drops of HOAc and sodium triacetoxyborohydride (62

mg, 0.29 mmol). The solution is stirred at room temperature for 16 hours. After this time, the solution is diluted with water/acetonitrile. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 80% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to give the title compound (48 mg, 0.07 mmol) as a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.75 (bs, 2H), 8.85 (s, 1H), 8.60 (d, 1H), 7.95 (s, 1H), 7.69 (s, 1H), 7.62 (d, 1H), 6.80 (s, 1H), 6.65 (d, 1H), 6.19 (dt, 1H), 4.80 (s, 2H), 3.70 (m, 4H), 3.50 (m, 2H), 3.28 (m, 2H). ESI MS, $[M+H]^+$=441,443 (Br pattern).

EXAMPLE 279. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-methoxy-pyridin-3-yl)-(E)-allyl]-piperazin-2-one.

Nitrogen (g) is bubbled through a solution of 1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one (100 mg, 0.39 mmol), EXAMPLE 72, in 2 mL of CH_3CN. After 5 min, acetic acid 3-(6-methoxy-pyridin-3-yl)-(E)-allyl ester (75 mg, 0.36 mmol, prepared as described in EXAMPLE 19 in 2 mL of CH_3CN, palladium(II) acetate (catalytic amount), triphenylphosphine (catalytic amount), 2 mL of H_2O and 0.5 mL of triethylamine are added to the solution. The mixture is heated at 80°C for 1 hours. At this time, the mixture is cooled, filtered and concentrated in vacuo. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 60% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to give the title compound (44 mg, 0.07 mmol) as a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.86 (s, 1H), 9.79 (s, 1H), 8.83 (s, 1H), 8.40 (d, 1H), 8.25 (s, 1H), 7.95 (d, 1H), 7.75 (s, 1H), 7.63 (d, 1H), 6.86 (d, 1H), 6.82 (d, 1H), 6.32 (dt, 1H), 4.78 (s, 2H), 3.98 (s, 2H), 3.93 (m, 2H), 3.85 (s, 3H), 3.53 (m, 4H). ESI MS, $[M+H]^+$=405.

EXAMPLE 280. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-allyl]-4-oxy-piperazin-2-one.

To a solution of 1-(4-amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-allyl]-piperazin-2-one ditrifluoroacetate (0.60 g, 0.94 mmol), prepared as described in EXAMPLE 275, in 25 mL of CH_2Cl_2 is added m-chloroperoxybenzoic acid (0.30 g, 0.96 mmol, 55% pure grade). The mixture is stirred at room temperature for 3 h and then concentrated in vacuo. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 60% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to give the title compound (0.5 mg, 0.76 mmol) as a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.68 (bs, 2H), 8.79 (s, 1H), 8.39 (d, 1H), 7.68 (s, 1H), 7.60 (d, 1H), 7.17 (d, 1H), 7.12 (d, 1H), 7.06 (d, 1H), 6.17 (dt, 1H), 4.84 (s, 2H), 4.53 (m, 2H), 4.50 (AB, 2H), 4.04 (m, 2H), 3.78 (m, 1H), 3.60 (m, 1H). ESI MS, $[M+H]^+$=430,432 (Cl pattern). Anal. ($C_{20}H_{20}ClN_5O_2S \cdot 2.0TFA \cdot 1.4H_2O$) C, H, N.

EXAMPLE 281. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-prop-2-ynyl]-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 275 using 2-(3-bromo-prop-1-ynyl)-5-chloro-thiophene (prepared as described in EXAMPLE 20) in place of 2-(3-bromo-(E)-propenyl)-5-chloro-thiophene. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 70% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to give the title compound as a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.77 (bs, 2H), 8.83 (s, 1H), 8.38 (d, 1H), 7.63 (d, 1H), 7.58 (s, 1H), 7.25 (d, 1H), 7.13 (d, 1H), 4.74 (s, 2H), 3.74 (s, 2H), 3.32 (m, 4H), 2.85 (m, 2H). ESI MS, $[M+H]^+$=412, 414 (Cl pattern).

EXAMPLE 282. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-piperazin-2-one

The title compound is prepared as described in EXAMPLE 278 using 3-(5-chloro-thiophen-2-yl)-propionaldehyde (EXAMPLE 28, Part A) in place of 3-(4-bromo-furan-2-yl)-(E)-propenal. The crude material is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 60% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to give the title compound as a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.77 (bs, 2H), 8.81 (s, 1H), 8.39 (d, 1H), 7.71 (s, 1H), 7.60 (d, 1H), 6.95 (d, 1H), 6.77 (d, 1H), 4.78 (s, 2H), 3.88 (m, 2H), 3.50 (m, 2H), 3.42 (m, 2H), 3.05 (m, 2H), 2.80 (t, 2H), 1.96 (m, 2H). ESI MS, $[M+H]^+$=416,418 (Cl pattern).

EXAMPLE 283. 1-(4-Amino-quinazolin-7-ylmethyl)-4-prop-2-ynyl-piperazin-2-one.

A. 1-(4-Amino-quinazolin-7-ylmethyl)-4-prop-2-ynyl-piperazin-2-one.

Propargyl bromide (0.29 g, 1.95 mmol) is added to a solution containing 1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one (0.5 g, 1.95 mmol), EXAMPLE 72, and K_2CO_3 (0.40 g, 2.93 mmol) in DMSO (10 mL) at ambient temperature. After 15 min, the reaction mixture is partitioned between aqueous $NaHCO_3$ (100 mL) and CH_2Cl_2 (100 mL) and the layers are separated. The aqueous phase is subsequently saturated with NaCl and extracted three times with $CHCl_3$ (50 mL). The combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue is purified by flash silica gel chromatography (CH_2Cl_2 to 10% MeOH/CH_2Cl_2) to provide 390 mg (68%) of the title compound as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 2.68 (m, 1H), 3.13-3.37 (m, 6H), 4.07 (app q, J = 5.2 Hz, 1H), 4.63 (s, 2H), 7.28 (dd, J = 8.4, 1.4 Hz, 1H), 7.42 (s, 1H), 7.72 (br s, 2H), 8.14 (d, J = 8.4 Hz, 1H), 8.34 (s, 1H) ppm; MS (ISP loop): m/z 296 (M+H).

EXAMPLE 284. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-2-yl-prop-2-ynyl)-piperazin-2-one.

A solution containing 1-(4-amino-quinazolin-7-ylmethyl)-4-prop-2-ynyl-piperazin-2-one (50 mg, 0.17 mmol), EXAMPLE 283, 2-bromobiphenyl (44 mg, 0.19 mmol), Et_3N (69 mg, 0.68 mmol), $(Ph_3P)_4PdCl_2$ (6 mg, 0.008 mmol), and CuI (1 mg, 0.005 mmol) in anhydrous DMF (2 mL) is warmed at 80°C for 1 hours. The reaction mixture is cooled to 50 °C and the solvent is removed over 16 h under a stream of nitrogen. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 10% MeOH CH_2Cl_2) to afford a colorless gum which is triturated with ethyl alcohol to provide 4 mg (5%) of the title compound as a white solid. ^1H NMR (300 MHz, d_6-DMSO) δ 3.03 (s, 2H), 3.14 (m, 2H), 3.31 (m, 2H), 3.50 (s, 2H), 7.21-7.55 (m, 11H), 7.76 (br s, 2H), 8.18 (d, J = 8.6 Hz, 1H), 8.36 (s, 1H) ppm; MS (ion spray): m/z 448 (M+H).

EXAMPLE 285. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. (3-{3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-prop-1-ynyl}-pyridin-4-yl)-carbamic acid tert-butyl ester.

A solution containing 1-(4-amino-quinazolin-7-ylmethyl)-4-prop-2-ynyl-piperazin-2-one (100 mg, 0.34 mmol), EXAMPLE 283, (3-iodo-pyridin-4-yl)-carbamic acid tert-butyl ester, EXAMPLE 69, Part B, (108 mg, 0.34 mmol), Et_3N (140 mg, 1.36 mmol), $(Ph_3P)_4PdCl_2$ (12 mg, 0.017 mmol), and CuI (2 mg, 0.01 mmol) in anhydrous DMF (5 mL) is stirred at ambient temperature. After 5 h, the reaction mixture is diluted with EtOAc (50 mL) and water (50 mL) and the layers are separated. The aqueous layer is extracted twice with EtOAc (25 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 10% MeOH CH_2Cl_2) to provide 59 mg (36%) of SC34 as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 1.49 (s, 9H), 2.84 (m, 2H), 3.35 (m, 2H), 3.44 (s, 2H), 3.71 (s, 2H), 4.75 (s, 2H), 6.19 (br s, 2H), 7.24 (d, J = 5.5 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.66 (s, 1H), 7.79 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 5.5 Hz, 1H), 8.37 (s, 1H), 8.49 (s, 1H), 8.58 (s, 1H) ppm; MS (ISP loop): m/z 488 (M+H).

B. 2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

1,8-Diazabicyclo[5.4.0]undec-7-ene (37 mg, 0.24 mmol) is added to a suspension containing (3-{3-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-prop-1-ynyl}-pyridin-4-yl)-carbamic acid tert-butyl ester (59 mg, 0.12 mmol) in anhydrous CH_3CN (5 mL) and the mixture is warmed to 50 °C. Dimethylformamide (1 mL) is added to solubilize and the homogeneous solution is maintained for 5 h at 50°C. The reaction mixture is diluted with EtOAc (50 mL) and water (50 mL) and the layers are

separated. The aqueous layer is extracted twice with EtOAc (25 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to provide 50 mg of the product as a crude solid which is used directly without further purification. ^1H NMR (300 MHz, $CDCl_3$) δ 1.64 (s, 9H), 2.78 (m, 2H), 3.30 (m, 2H), 3.37 (s, 2H), 3.95 (s, 2H), 4.74 (s, 2H), 6.24 (br s, 2H), 6.63 (s, 1H), 7.40 (dd, J = 8.5, 1.6 Hz, 1H), 7.64 (s, 1H), 7.81 (d, J = 5.8 Hz, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.99 (s, 1H), 8.39 (d, J = 5.8 Hz, 1H), 8.58 (s, 1H), 8.77 (s, 1H) ppm.

C. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

To a solution containing 2-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (50 mg, 0.12 mmol) in CH_2Cl_2 (5 mL) is added TFA (1 mL) at ambient temperature. After 16 h, the reaction mixture is concentrated to dryness, diluted with water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 45% B over 30 min] to provide 34 mg (73%, two steps) of the title compound as a white, lyophilized solid. ^1H NMR (300 MHz, $CDCl_3$) δ 2.77 (s, 3H), 3.23 (s, 2H), 3.31 (m, 2H), 3.89 (s, 2H), 4.00 (br s, 3H), 4.71 (s, 2H), 6.94 (s, 1H), 7.60 (m, 2H), 7.84 (d, J = 6.5 Hz, 1H), 8.36 (m, 2H), 8.81 (s, 1H), 9.18 (s, 1H), 9.73 (br s, 2H), 12.87 (s, 1H) ppm; MS (ion spray): m/z 388 (M+H).

The following compounds are prepared from the compound of Example 72 using the procedures described above.

Example #	Name	m/z (M+H)
286	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yloxy)-ethyl]-piperazin-2-one	418, 420 Cl pattern
287	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1-methyl-1H-indol-2-ylmethyl)-piperazin-2-one	435, 437 Cl pattern
288	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-piperazin-2-one	414, 416 Cl pattern
289	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-allyl]-piperazin-2-one	464, 466 Cl pattern
290	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-4-methyl-thiophen-2-yl)-allyl]-piperazin-2-one	428, 430 Cl pattern
291	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzofuran-2-ylmethyl)-piperazin-2-one	422, 424 Cl pattern

292	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-5-ylmethyl)-piperazin-2-one	421, 423 Cl pattern
293	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one	421, 423 Cl pattern
294	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,7-dichloro-1H-indol-2-ylmethyl)-piperazin-2-one	455, 457 Cl pattern
295	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-indol-2-ylmethyl)-piperazin-2-one	421, 423 Cl pattern
296	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-p-tolyl-prop-2-ynyl)-piperazin-2-one	386
297	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-m-tolyl-prop-2-ynyl)-piperazin-2-one	386
298	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one	406, 408 Cl pattern
299	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one	406, 408 Cl pattern
300	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one	406
301	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-4-yl-prop-2-ynyl)-piperazin-2-one	448
302	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4,5-dibromo-thiophen-2-yl)-allyl]-piperazin-2-one	536, 538, 540 Br_2 pattern
303	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-3-yl-prop-2-ynyl)-piperazin-2-one	448
304	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2,5-dichloro-thiophen-3-yl)-prop-2-ynyl]-piperazin-2-one	446, 448 Cl pattern
305	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-propyl]-piperazin-2-one	410, 412 Cl pattern
306	1,4-Bis-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one	415
307	1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-piperazin-2-one	388
308	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-nitro-thiophen-2-yl)-allyl]-piperazin-2-one	425
309	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-pyridin-3-	409, 411

	yl)-allyl]-piperazin-2-one	Cl pattern
310	1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	388
311	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-allyl]-piperazin-2-one	414, 416 Cl pattern
312	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-allyl]-piperazin-2-one	442, 444 Br pattern
313	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(5-methyl-thiophen-2-yl)-penta-2,4-dienyl]-piperazin-2-one	420
314	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophen-5-ylmethyl)-piperazin-2-one	438, 440 Cl pattern
315	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-methyl-thiophen-2-yl)-allyl]-piperazin-2-one	394
316	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-methoxy-thiophen-2-yl)-allyl]-piperazin-2-one	410
317	4-(1-Amino-7-chloro-isoquinolin-3-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one	448, 450 Cl pattern
318	2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-N-(5-chloro-thiophen-2-yl)-acetamide	431
319	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one	433, 435 Cl pattern
320	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenyl)-2-(S)-hydroxy-ethyl]-piperazin-2-one	412, 414 Cl pattern
321	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenylsulfanyl)-ethyl]-piperazin-2-one	428, 430 Cl pattern
322	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-methylene-1,1-dioxo-2,3-dihydro-1H-11 6-benzo[b]thiophen-3-yl)-piperazin-2-one	470
323	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-nitro-phenyl)-allyl]-piperazin-2-one	419
324	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophen-6-ylmethyl)-piperazin-2-one	438, 440 Cl pattern
325	2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-N-(4-chloro-phenyl)-acetamide	425, 427 Cl pattern
326	1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(4-chloro-phenyl)-	437, 439

	pyrrolidin-3-yl]-piperazin-2-one	Cl pattern
327	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethyl]-piperazin-2-one	402, 404 Cl patten
328	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-propyl]-piperazin-2-one	410, 412 Cl pattern
329	2-[4-(4-Aminoquinazoline-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-3-(4-chlorophenyl)-acrylic acid	452, 454 Cl pattern
330	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-1-hydroxy-isoquinolin-3-ylmethyl)-piperazin-2-one	449, 451 Cl pattern
331	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one	432, 434 Cl pattern
332	1-(4-Amino-quinazolin-7-ylmethyl)-4-isoquinolin-3-ylmethyl-piperazin-2-one	399
333	1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(3-chloro-phenyl)-pyrrolidin-3-yl]-piperazin-2-one	437, 439 Cl pattern
334	1-(4-Amino-quinazolin-7-ylmethyl)-4-(1,7-dichloro-isoquinolin-3-ylmethyl)-piperazin-2-one	467, 469 Cl pattern
335	4-(2-Amino-7-chloro-quinolin-3-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one	448, 450 Cl pattern
336	1-(4-Aminoquinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophene-2-ylmethyl)piperazin-2-one.	438, 440 Cl pattern
337	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(4-chloro-phenylsulfanyl)-ethyl]-piperazin-2-one	428, 430 Cl pattern
338	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(6-chloro-benzo[b]thiophen-2-yl)-ethyl]-piperazin-2-one	452, 454 Cl pattern
339	1-(4-Aminoquinazolin-7-ylmethyl)-4-[2-(4-chloro-phenoxy)-ethyl]-piperazine-2-one	412, 414 Cl pattern
340	2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-4H-benzo[1,4]thiazin-3-one	469, 471 Cl pattern
341	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,7-dichloro-quinolin-3-ylmethyl)-piperazin-2-on	467, 469 Cl_2 pattern
342	2-[[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-(4-chloro-phenyl)-methyl]-acrylic acid ethyl ester	480, 482 Cl pattern
343	2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-	480, 482

	ylmethyl]-3-(4-chloro-phenyl)-acrylic acid ethyl ester	Cl pattern
344	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-allyl]-piperazin-2-one	408, 410 Cl pattern
345	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-allyl]-piperazin-2-one	408, 410 Cl pattern
346	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-allyl]-piperazin-2-one	458, 460 Br pattern
347	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-allyl]-piperazin-2-one	458, 460 Br pattern
348	3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-fluoro-1H-quinolin-2-one	433
349	3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-1H-quinoxalin-2-one	450, 452 Cl pattern
350	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1-methyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one	436, 438 Cl pattern
351	2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-3H-quinazolin-4-one	492, 494 Cl pattern
352	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-thiophen-2-yl-propyl)-piperazin-2-one	382
353	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-quinolin-3-ylmethyl)-piperazin-2-one	432, 434 Cl pattern
354	3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-5,7-dichloro-1H-quinolin-2-one	483, 485 Cl pattern
355	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6,7-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	472, 474 Cl_2 pattern
356	3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-5-chloro-1H-quinolin-2-one	449, 451 Cl pattern
357	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-[2,3']bithiophenyl-5'-ylmethyl)-piperazin-2-one	470, 472 Cl pattern
358	4-(6-Amino-benzo[b]thiophen-2-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one	419
359	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-quinolin-6-ylmethyl)-piperazin-2-one	433, 435 Cl pattern
360	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-bromo-1H-	466, 468

	benzoimidazol-2-ylmethyl)-piperazin-2-one	Br pattern
361	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-nitro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	449
362	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(3-chloro-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one	464, 466
363	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-3-methoxy-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	468, 470 Cl pattern
364	3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-1H-quinolin-2-one	449, 451 Cl pattern
3653	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-trifluoromethyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one	456
366	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one	450
367	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	418
368	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3,3'-dimethyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one	498, 500 Cl pattern
369	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3,5-dibromo-4-methoxy-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-piperazin-2-one	602, 604, 606 Br_2 pattern
370	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	418
371	1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	418
372	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	438, 440 Cl pattern
373	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3'-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one	484, 486 Cl pattern
374	1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-benzoimidazol-2-ylmethyl)-piperazin-2-one	388
375	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-bromo-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one	514, 516 Br pattern
376	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-oxazol-2-ylmethyl]-piperazin-2-one	473
377	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,6-dichloro-	472, 474

	benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	Cl pattern
378	1-(4-Amino-quinazolin-7-ylmethyl)-4-(4,5-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	472, 474 Cl pattern
379	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzooxazol-2-ylmethyl)-piperazin-2-one	423, 425 Cl pattern
380	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-5-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	456, 458 Cl pattern
381	1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-5-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	456, 458 Cl pattern
382	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one	484, 486 Cl pattern
383	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thieno[3,2-b]pyridin-2-ylmethyl)-piperazin-2-one	439, 441 Cl pattern
384	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,6-dichloro-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one	456
385	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-benzooxazol-2-yl-benzyl)-piperazin-2-one	464
386	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(4-chloro-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one	464, 466 Cl pattern
387	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-methyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one	402
388	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2,2']bithiophenyl-5-ylmethyl-piperazin-2-one	435
389	1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	422
390	1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-fluoro-benzo[b]thiophene-2-ylmethyl)piperazin-2-one.	422
391	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(1-methyl-5-trifluoro-methyl-1H-pyrazol-3-yl)-thiophen-2-ylmethyl]-piperazin-2-one	501
392	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3,4-dimethyl-thieno[2,3-b]thiophen-2-ylmethyl)-piperazin-2-one	438
393	1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-3-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	452, 454 Cl pattern
394	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-3-methyl-	452, 454

	benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	Cl pattern
395	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(2-methyl-5-trifluoromethyl-2H-pyrazol-3-yl)thiophen-2-ylmethyl] piperazin-2-one	502
396	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(3-nitro-phenyl)-furan-2-ylmethyl]-piperazin-2-one	459
397	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thieno[3,2-b]pyridin-6-ylmethyl)-piperazin-2-one	439, 441 Cl pattern
398	1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(4-methoxy-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one	460
399	1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-hydroxy-2-pyridin-2-yl-pyrimidin-5-ylmethyl)-piperazin-2-one	443
400	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-fluoro-phenoxy)-benzyl]-piperazin-2-one	458
401	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(4-chloro-phenyl)-thiazol-4-ylmethyl]-piperazin-2-one	465, 467 Cl pattern
402	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-bromo-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	482, 484 Br pattern
403	1-(4-Amino-quinazolin-7-ylmethyl)-4-benzo[b]thiophen-2-ylmethyl-piperazin-2-one	404
404	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one	470, 472 Cl pattern
405	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3,5-bis-trifluoromethyl-benzyl)-piperazin-2-one	488
406	1-(4-Amino-quinazolin-7-ylmethyl)-4-biphenyl-4-ylmethyl-piperazin-2-one	423 (M+)
407	1-(4-Amino-quinazolin-7-ylmethyl)-4-naphthalen-2-ylmethyl-piperazin-2-one	397 (M+)
408	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-3-ylmethyl)-piperazin-2-one	438, 440 Cl pattern
409	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-piperazin-2-one	438, 440 (M+), Cl pattern

EXAMPLE 410. 1-(4-Aminoquinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]piperazin-2-one.

The title compound is prepared as described in EXAMPLE 123 using 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one bishydrochloride, EXAMPLE 72, in place of 4-(2-oxopiperazin-1-ylmethyl)benzamidine bistrifluoroacetate. ^{1}H NMR (d6-DMSO, 300 MHz) δ 9.77 (bs, 2H), 8.83 (s, 1H), 8.40 (dd, 1H), 7.68 (d, 1H), 7.65 (s, 1H), 7.58 (d, 2H), 7.15 (d, 2H), 4.80 (s, 2H), 4.33, 4.15 (m, 2H, rotamers), 3.70 (m, 2H), 3.49 (m, 2H). ESI MS, $[M+H]^+$=456, 458 (Br pattern).

The following compounds are prepared from the compound of Example 72 using the methods described above.

Example #	Name	m/z [M+H]
411	1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-thiophene-2-carbonyl)-piperazin-2-one	402, 404 Cl pattern
412	4-[3-(3-Amino-4-chloro-phenyl)-(E)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one	437, 439 Cl pattern
413	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-piperazin-2-one	435, 437 Cl pattern
414	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]piperazin-2-one	432, 434 Cl pattern
415	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one	472, 474 Br pattern
416	5-Chloro-thiophene-2-carboxylic acid {2-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-2-oxo-ethyl}-amide	459, 461 Cl pattern
417	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one	428, 430 Cl pattern
418	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indole-2-carbonyl)-piperazin-2-one	435, 437 Cl pattern
419	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one	478, 480 Cl pattern
420	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one	472, 474 Br pattern
421	5-Chloro-thiophene-2-carboxylic acid {2-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-1-methyl-2-oxo-ethyl}-amide	473, 475 Cl pattern

422	5-Chloro-thiophene-2-carboxylic acid {3-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-3-oxo-propyl}-amide	473, 475 Cl pattern
423	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-piperazin-2-one	426, 428 Cl pattern
424	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-2-methyl-phenoxy)-acetyl]-piperazin-2-one	440, 442 Cl pattern
425	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-carbonyl)-piperazin-2-one	484, 486 Cl pattern
426	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-piperazin-2-one	430, 432 Cl pattern
427	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-(E)-acryloyl]-piperazin-2-one	422, 424 Cl pattern
428	N-[2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-1-(5-chloro-thiophen-2-ylmethyl)-2-oxo-ethyl]-benzamide	428, 430 Cl pattern
429	N-[1-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-2-(5-chloro-thiophen-2-yl)-vinyl]-benzamide	549, 550 Cl pattern
430	N-[1-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-2-(5-chloro-thiophen-2-yl)-vinyl]-acetamide	485, 487 Cl pattern
431	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-(E)-acryloyl]-piperazin-2-one	422, 424 Cl pattern
432	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yl)-acetyl]-piperazin-2-one	415, 417 Cl pattern
433	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-piperazin-2-one	451, 453 Cl pattern
434	2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-6-chloro-4H-benzo[1,4]thiazin-3-one	483, 485 Cl pattern
435	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-benzo[b]thiophen-2-yl)-acetyl]-piperazin-2-one	466, 468 Cl pattern

EXAMPLE 436. 4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid 4-chloro-benzylamide.

To a solution of 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one (25 mg, 0.097 mmol), EXAMPLE 72, in 1 mL of DMF is added 4-chloro-benzyl isocyanate (22 mg, 0.13 mmol, prepared as described in EXAMPLE 37). After stirring 1 h at room temperature, the solution is concentrated. The crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 80%

CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to provide the title compound (36 mg, 0.067 mmol) as a white solid. ^1H NMR (d6-DMSO, 300 MHz) δ 9.76 (bs, 2H), 8.83 (s, 1H), 8.38 (d, 1H), 7.64 (d, 1H), 7.60 (s, 1H), 7.34 (d, 2H), 7.31 (m, 1H), 7.26 (d, 2H), 4.75 (s, 2H), 4.22 (d, 2H), 4.08 (s, 2H), 3.60 (m, 2H), 3.35 (m, 2H). ESI MS, $[M+H]^+$=425,427 (Cl pattern).

EXAMPLE 437. 4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid (5-chloro-thiophen-2-ylmethyl)amide.

To a solution of (5-chloro-thiophen-2-yl)-acetic acid (0.18 g, 1.04 mmol), prepared as described in EXAMPLE 27 in 6 mL of dry CH_2Cl_2 is added Et_3N (0.15 mL g, 1.04 mmol) and diphenylphosphoryl azide (0.24 mL, 1.04 mmol). The mixture is stirred at room temperature for 2.5 h, then heated at 50°C for 2 hours. To the solution is added 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one (0.10 g, 0.41 mmol), EXAMPLE 72, and Et_3N (0.15 mL g, 1.04 mmol) and the mixture is heated at 50°C for 2 h, then stirred at room temperature for 16 hours. The resulting mixture is concentrated. The crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 60% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to provide the title compound (10 mg, 0.02 mmol) as a white solid. ^1H NMR (d6-DMSO, 300 MHz) δ 9.69 (bs, 2H), 8.80 (s, 1H), 8.48 (d, 1H), 7.61 (d, 1H), 7.60 (s, 1H), 7.41 (t, 1H), 6.90 (d, 1H), 6.80 (d, 1H), 4.77 (d, 2H), 4.30 (d, 2H), 4.10 (s, 2H), 3.61 (m, 2H), 3.38 (m, 2H). ESI MS, $[M+H]^+$=431,433 (Cl pattern).

EXAMPLE 438. 4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)amide.

A mixture of 5-chloro-thiophene-2-carbonyl azide (55 mg, 0.29 mmol, prepared as described in EXAMPLE 38) and 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one (50 mg, 0.20 mmol), EXAMPLE 72, in 3 mL of dry toluene is heated at 105°C for 1 hours. The resulting mixture is concentrated in vacuo. The crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 60% CH_3CN/H_2O (0.1% TFA) and the appropriate product fractions are combined and lyopholized to provide the title compound (35 mg, 0.02 mmol) as a white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 10.04 (s, 1H), 9.71 (bs, 2H), 8.81 (s, 1H), 8.38 (dd, 1H), 7.64 (d, 1H), 7.61 (s, 1H), 6.77 (d, 1H), 6.42 (d, 1H), 4.76 (s, 2H), 4.21 (s, 2H), 3.73 (m, 2H), 3.40 (m, 2H). ESI MS, $[M+H]^+$=417,419 (Cl pattern).

The following compounds are prepared from the compound of Example 72 using the methods described above.

Example #	Name	m/z [M+H]
439	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide	417, 419 Cl pattern
440	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide	461, 463 Br pattern
441	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (3-amino-4-chloro-phenyl)-amide	426, 428 Cl pattern
442	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide	455, 457 Br pattern
443	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	411, 413 Cl pattern
444	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-methoxy-phenyl)-amide	407
445	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (3,4-dichloro-phenyl)-amide	445, 447 Cl_2 pattern

EXAMPLE 446. 4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid 5-chloro-thiophen-2-ylmethyl ester.

To a solution of 5-chloro-2-thiophene-methanol (0.10 g, 0.67 mmol, prepared by $NaBH_4$ reduction of 5-chloro-2-thiophene-carboxaldehyde) in 6 mL of CH_2Cl_2 is added 1,1'-carbonyldiimidazole (0.11 g, 0.67 mmol). The mixture is stirred at room temperature for 3 hours. Then 1-(4-aminoquinazoline-7-ylmethyl)piperazine-2-one (0.17 g, 0.67 mmol, EXAMPLE 72) and a catalytic amount of DMAP is added to the solution and the resulting mixture is heated at 35°C for 18 hours. The mixture is dissolved in water/MeOH and the crude product is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 100% CH_3CN. The appropriate fractions are combined and lyopholized to provide the title compound as a white solid. ESI MS, $[M+H]^+$=432,434 (Cl pattern).

The following compounds are prepared from the compound of Example 72 using the methods described above.

Example #	Name	m/z [M+H]
447	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-carboxylic acid 6-chloro-benzooxazol -2-ylmethyl ester	467, 469 Cl pattern
448	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic	481, 483

	acid 1-(3-chloro-phenyl)-pyrrolidin-3-yl ester	Cl pattern

EXAMPLE 449. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methyl-piperazin-2-one.

To a solution of 1-(4-amino-quinazoline-7-ylmethyl)-3-methyl-piperazine-2-one, EXAMPLE 80, (0.06g, 0.2mmol) in 2 mL of DMF is added 3-bromomethyl-7-chloroisoquinoline, EXAMPLE 11, 0.052g, 0.20mmol), and K_2CO_3 (0.08 g, 0.06 mmol). After 16 h, the reaction mixture is concentrated to dryness. The crude product is purified by RP-HPLC eluting with a gradient of 5%CH_3CN/H_2O (0.1% TFA) to 50%CH_3CN/H_2O (0.1% TFA). The product fractions are lyophilized to give the title compound as a tristrisfluoroacetic acid salt (0.06g, 0.08 mmol) as a white solid. ^{1}H NMR (d6-DMSO, 300 MHz) δ 9.79 (bs, 2H), 9.40 (s, 1H), 8.73 (s, 1H), 8.33 (d, 1H), 8.25 (s, 1H), 8.06 (s, 1H), 8.00 (d, 1H), 7.79 (d, 1H), 7.60 (m, 2H), 4.80 (AB, 2H), 4.72 (AB, 2H), 4.28 (m, 1H), 3.54 (m, 4H), 1.96 (d, 3H). MS (ion spray) 447, 449, (Cl pattern). Elemental analysis $C_{28}H_{25}ClF_6N_6O_6 \cdot 3CF_3CO_2H \cdot 0.28H_2O$, cal C=45.38%, H=3.35%, N=10.58%; found C=45.38, H=3.35%, N=10.63%.

EXAMPLE 450. 4-(4-Amino-quinazolin-7-ylmethyl)- 4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 274 using 1-(4-amino-quinazoline-7-ylmethyl)-3-methyl-piperazine-2-one, EXAMPLE 80. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.79 (bs, 2H), 8.82 (s, 1H), 8.39 (d, 1H), 7.61 (m, 3H), 7.57 (d, 1H), 7.52 (d, 1H), 7.49 (d, 1H), 7.20 (d, 1H), 7.10 (d, 1H), 4.75 (AB, 2H), 4.57 (m, 1H), 4.23 (m, 1H), 3.97 (m, 1H), 3.50 (m, 3H), 1.65 (d, 3H). ESI MS, $[M+H]^+$= 435,437 (Cl pattern). Anal. ($C_{23}H_{23}ClN_6O \cdot 2.15TFA \cdot 0.25H_2O$) C, H, N.

The following compounds are prepared from the compound of Example 80 using the methods described above.

Example #	Name	m/z [M+H]
451	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one	428, 430 Cl pattern
452	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one	478, 480 Cl pattern
453	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-methyl-piperazin-2-one	429, 431 Cl pattern
454	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-	435, 437

	ylmethyl)-3-(S)-methyl-piperazin-2-one	Cl pattern
455	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enyl]-3-(S)-methyl-piperazin-2-one	442, 444 Cl pattern
456	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methyl-piperazin-2-one	483 (M+) (EI)
457	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-benzoimidazol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one	536, 538 Cl pattern
458	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one	428, 430 Cl pattern
459	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one	446, 448 Cl pattern
460	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-3-(S)-methyl-piperazin-2-one	453, 455 Cl pattern
461	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one	452, 454 Cl pattern
462	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one	452, 454 Cl pattern
463	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-2-ylmethyl)-3-(R)-methyl-piperazin-2-one	452, 454 Cl pattern
464	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(R)-methyl-piperazin-2-one	452, 454 Cl pattern

EXAMPLE 465 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 123, using 1-(4-amino-quinazoline-7-ylmethyl)-3-methyl-piperazine-2-one, EXAMPLE 80, and 3-(4-chloro-thiophen-2-yl)-(E)-acrylic acid, EXAMPLE 26. ^{1}H NMR (d6-DMSO, 300 MHz) δ 9.74 (bs, 2H), 8.82 (s, 1H), 8.40 (d, 1H), 7.62 (m, 5H), 7.05 (d, 1H), 4.92 (m, 1H), 4.80 (m, 2H), 4.73 (m, 1H), 4.50 (m, 1H), 3.40 (m, 2H), 1.42 (m, 3H). ESI MS, $[M+H]^+$= 442, 444 (Cl pattern).

The following compounds are prepared from the compound of Example 80 using the methods described above.

Example #	Name	m/z [M+H]

466	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one	446, 448 Cl pattern
467	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one	446, 448 Cl pattern
468	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one	486, 488 Br pattern
469	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-3-(S)-methyl-piperazin-2-one	449, 451 Cl pattern
470	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-methyl-piperazin-2-one	461, 463 Cl pattern
471	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one	446, 448 Cl pattern
472	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one	486, 488 Br pattern
473	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-methyl-piperazin-2-one	440, 442 Cl pattern
474	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-carbonyl)-3-(S)-methyl-piperazin-2-one	498, 500 Cl pattern
475	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enoyl]-3-(S)-methyl-piperazin-2-one	456, 458 Cl pattern
476	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methyl-piperazin-2-one	466, 468 Cl pattern
477	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one	442, 444 Cl pattern

EXAMPLE 478. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-ethyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 278 using 1-(4-aminoquinazoline-7-ylmethyl)-3-ethyl-piperazine-2-one, EXAMPLE 77 and 3-(5-chloro-thiophen-2-yl)-propionaldehyde, EXAMPLE 28. ^{1}H NMR (d6-DMSO + 1 drop TFA, 300 MHz) δ 9.80 (bs, 2H), 8.79 (s, 1H), 8.32 (d, 1H), 7.58 (m, 2H), 6.88 (d, 1H), 6.70 (d, 1H), 4.72 (AB, 2H), 4.00 (m, 1H), 3.72 (m, 1H), 3.48 (m, 2H), 3.23 (m, 3H), 2.72 (m, 2H), 1.96 (m, 4H), 0.98 (m, 3H). MS (ion spray), m/z, (M+H) = 444, 446 (Cl pattern).

The following compounds are prepared from the compound of Example 77 using the methods described above.

Example #	Name	m/z [M+H]
479	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-3-(S)-ethyl-piperazin-2-one	442, 444 Cl pattern
480	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enyl]-3-(S)-ethyl-piperazin-2-one	456, 458 Cl pattern
481	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-ethyl-piperazin-2-one	461, 463 Cl pattern
482	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-ethyl-piperazin-2-one	442, 444 Cl pattern
483	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one	460, 462 Cl pattern
484	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one	466, 468 Cl pattern
485	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one	467, 469 Cl pattern

EXAMPLE 486. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 123, using 1-(4-aminoquinazoline-7-ylmethyl)-3-ethyl-piperazine-2-one, EXAMPLE 77 and 3-(5-chloro-thiophen-2-yl)-(E)-acrylic acid, EXAMPLE 25. ^{1}H NMR (d6-DMSO + 1 drop TFA, 300 MHz) δ 9.78 (bs, 2H), 8.79 (s, 1H), 8.37 (d, 1H), 7.65 (m, 2H), 7.50 (s, 1H), 7.41 (m, 1H), 7.11 (d, 1H), 6.98 (d, 1H), 4.88 (m, 2H), 4.60 (m, 1H), 4.31 (m, 1H), 3.52 (m, 1H), 3.30 (m, 2H), 1.96 (m, 2H), 0.88 (m, 3H). MS (ion spray), m/z, (M+H) = 456, 458 (Cl pattern). Elemental analysis, cal $C_{22}H_{22}ClN_5O_2S \cdot 1.5C_2HF_3O_2$ %C=47.89, %H=3.78, %N=11.17; found %C=47.34, %H=4.00, %N=11.12.

The following compounds are prepared from the compound of Example 77 using the methods described above.

Example #	Name	m/z [M+H]
487	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-	460, 462

	yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one	Cl pattern
488	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one	460, 462 Cl pattern
489	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-(S)-3-ethyl-piperazin-2-one	456, 458 Cl pattern
490	2-(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetamide	517, 519 Cl pattern
491	(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid	518, 520 Cl pattern
492	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,3-dichloro-benzo[b]thiophene-6-carbonyl)-(S)-3-ethyl-piperazin-2-one	514, 516, 518 Cl_2 pattern
493	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophene-6-carbonyl)-(S)-3-ethyl-piperazin-2-one	480, 482 Cl pattern
494	(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid ethyl ester	546, 548 Cl pattern
495	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-thiophen-2-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one	494, 496 Cl pattern
496	(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid methyl ester	532, 534 Cl pattern
497	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-(3S)-ethyl-piperazin-2-one	463, 465
498	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-ethyl-piperazin-2-one	475, 477 Cl pattern
499	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-piperazin-2-one	460, 462 Cl pattern
500	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one	500, 502 Br pattern
501	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one	456, 458 Cl pattern
502	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one	500, 502 Br pattern

503	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-3-(S)-ethyl-piperazin-2-one	458, 460 Cl pattern
504	1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(4-chloro-phenyl)-1H-pyrrole-2-carbonyl]-3-(S)-ethyl-piperazin-2-one	489, 491 Cl pattern
505	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenylsulfanyl)-acetyl]-3-(S)-ethyl-piperazin-2-one	470, 472 Cl pattern
506	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enoyl]-3-(S)-ethyl-piperazin-2-one	470, 472 Cl pattern
507	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-ethyl-piperazin-2-one	454, 456 Cl pattern
508	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-acryloyl]-3-(S)-ethyl-piperazin-2-one	450, 452 Cl pattern
509	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indole-2-carbonyl)-3-(S)-ethyl-piperazin-2-one	463, 465 Cl pattern
510	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-propionyl]-3-(S)-ethyl-piperazin-2-one	452, 454 Cl pattern
511	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-ethyl-4-[3-(4-methoxy-phenyl)-propionyl]-piperazin-2-one	448
512	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-ethyl-piperazin-2-one	480, 482 Cl pattern

EXAMPLE 513. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 123, using 1-(4-aminoquinazoline-7-ylmethyl)-3-propyl-piperazine-2-one, EXAMPLE 78 and 5-chloro-2-thienyloxyacetic acid, EXAMPLE 24. ^{1}H NMR (d6-DMSO, 300 MHz) δ 9.78 (bs, 2H), 8.81 (s, 1H), 8.35 (d, 1H), 7.60 (m, 2H), 7.51 (s, 1H), 6.69 (m, 1H), 6.21 (d, 1H), 4.91 (AB, 2H), 4.72 (m, 2H), 3.84 (m, 1H), 3.52 (m, 2H), 3.23 (m, 1H), 1.80 (m, 2H), 1.24 (m, 2H), 0.82 (m, 3H). MS (ion spray), m/z, 474, 476, (M+H) (Cl pattern). Elemental analysis, cal $C_{22}H_{22}ClN_5O_2S \cdot C_2HF_3O_2 \cdot 1.15H_2O$ %C=47.31, %H=4.52, %N=11.50; found %C=47.39, %H=4.140, %N=11.19.

EXAMPLE 514. 4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-propyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 123, using 1-(4-aminoquinazoline-7-ylmethyl)-3-propyl-piperazine-2-one, EXAMPLE 78 and 3-(6-amino-pyridin-3-yl)-acrylic acid,

EXAMPLE 36. ^{1}H NMR (d6-DMSO, 300 MHz) δ 9.73 (bs, 2H), 8.81 (s, 1H), 8.36 (m, 2H), 8.22 (m, 3H), 7.62 (d, 1H), 7.52 (m, 1H), 7.39 (m, 1H), 7.21 (m, 1H), 6.91 (d, 1H), 5.00 (m, 1H), 4.78 (m, 1H), 4.60 (m, 2H), 4.34 (m, 1H), 3.30 (m, 2H), 1.87 (m, 2H), 1.24 (m, 2H), 0.90 (m, 3H). MS (ion spray), m/z, 446, 448 (M+H), (Cl pattern).

The following compounds are prepared from the compound of Example 78 using the methods described above.

Example #	Name	m/z [M+H]
515	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one	508, 509, 511, Cl_2 pattern
516	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one	474, 476 Cl pattern
517	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one	514, 516 Br pattern
518	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one	470, 472 Cl pattern
519	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-propyl-piperazin-2-one	468, 470 Cl pattern
520	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one	474, 476 Cl pattern
521	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-5-methoxy-phenoxy)-acetyl]-3-(S)-propyl-piperazin-2-one	498, 500 Cl pattern
522	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one	470, 472 Cl pattern
523	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one	470, 472 Cl pattern

EXAMPLE 524. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 278 using 1-(4-amino-quinazoline-7-ylmethyl)-3-methoxymethyl-piperazine-2-one, EXAMPLE 75 and 2-(3-bromo-(E)-propenyl)-5-chloro-thiophene EXAMPLE 17. ^{1}H NMR (d6-DMSO, 300 MHz) δ 9.74 (bs, 2H), 8.80 (s, 1H), 8.38 (d, 1H), 7.69 (m, 2H), 7.02 (dd, 1H), 6.84 (d, 1H), 6.02 (m, 1H), 4.76 (AB, 2H), 3.86 (m, 4H), 3.30 (s, 3H), 3.23 (m, 2H), 3.02 (m, 2H). MS (ion spray), m/z, 458, 460, (M+H) (Cl pattern). Elemental analysis, cal

$C_{22}H_{24}ClN_5O_2S \cdot 2C_2HF_3O_2 \cdot 1.45H_2O$ %C=43.85, %H=4.09, %N=9.83; found %C=43.92, %H=3.61, %N=9.63.

The following compounds are prepared from the compound of Example 75 using the methods described above.

Example #	Name	m/z [M+H]
525	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one	465, 467
526	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yloxy)-ethyl]-3-(S)-methoxymethyl-piperazin-2-one	446, 448 Cl pattern
527	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one	446, 448 Cl pattern
528	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(R)-methoxymethyl-piperazin-2-one	477, 479 Cl pattern
529	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one	477, 479 Cl pattern
530	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one	476, 478 Cl pattern
531	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one	482, 484 Cl pattern

EXAMPLE 532. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one.

To a solution of 4-(4-amino-quinazoline-7-ylmethyl)-2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, EXAMPLE 75, (0.69g, 2.29mmol) in 9mL of DMF is added N,N-diisopropylethyl amine (0.89g, 6.87mmol), TBTU (0.76g, 2.36mmol), and 5-chloro-2-thienyloxyacetic acid, EXAMPLE 24, (0.40g, 2.08mmol). The solution is stirred for 16 hours. After this time the solution is concentrated. The crude material is purified by RP-HPLC eluting with a gradient of 10%CH_3CN/H_2O (0.1%TFA) to 80%CH_3CN/H_2O (0.1%TFA). The product fractions are lyophilized to give the product as a white solid (1.0g, 1.57mmol). ^1H NMR (d6-DMSO, 300MHz) δ 9.70 (bs, 2H), 8.78 (s, 1H), 8.29 (m, 1H), 7.55 (m, 2H), 6.72 (m, 1H), 6.22 (m, 1H), 4.80 (m, 4H),3.78 (m, 4H), 3.59 (m, 3H), 3.31and 3.2 (s, 3H rotational isomers).MS (ion spray) M+H=476.Elemental Analysis: C21H22ClN5O4S·1.4CF3CO2H cal: C=45.03%, H=3.68%, N=11.04%; found C=44.98%, H=3.71%, N=11.02%.

EXAMPLE 533. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one.

To a solution of 4-(4-amino-quinazoline-7-ylmethyl)-2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester, EXAMPLE 75, (20 mg, 0.066 mml) in 1.5 mL of DMF is added TBTU (923.4 mg, 0.073 mmol), diisopropylethylamine (0.013 ml, 0.073 mmol) and 6-chloro-1H-benzoimidazole-2-carboxylic acid (prepared from literature in Eur.J.med.Chem. 1993, 28, 71) (14.3 mg, 0.073 mmol). The resulting mixture is left to stir at room temperature overnight. The crude mixture is directly purified by reverse phase HPLC (10-70% ACN/H_2O). The product (30.1 mg, 55%) is isolated as a white powder. $C_{23}H_{22}ClN_7O_3$ MS m/z: 480, 481. Anal. cald. for $C_{23}H_{22}ClN_7O_3 \cdot 2C_2HF_3O_2$: C, 45.81; H, 3.42; N, 13.85. Found C, 45.19; H, 3.59; N, 13.76.

The following compounds are prepared from the compound of Example 75 using the methods described above.

Example #	Name	m/z [M+H]
534	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)- methoxymethyl-piperazin-2-one	476, 478 Cl pattern
535	4-[3-(4-Amino-phenyl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one	447
536	1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-3H-imidazol-4-yl-acryloyl)-3-(S)-methoxymethyl-piperazin-2-one	
537	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	510, 512, Cl_2 pattern
538	(1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one	480, 482 Cl pattern
539	1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thiophene-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one	446, 448 Cl pattern
540	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	500, 502 Br pattern
541	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	510, 512 Br pattern
542	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	466, 468 Cl pattern

543	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-bromo-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	576, 578 Br pattern
544	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	466, 468 Cl pattern
545	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	576, 578 Br pattern
546	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)--methoxymethyl-piperazin-2-one	476, 478 Cl pattern
547	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	471, 473 Cl pattern
548	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	471, 473 Cl pattern
549	4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one	448
550	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-5-methoxy-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	500, 502 Cl pattern
551	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	472, 474 Cl pattern
552	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	504, 506, 508 Cl_2 pattern
553	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-fluoro-thiophen-2-yloxy)-acetyl]-3-(S)- methoxymethyl-piperazin-2-one	460
554	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-fluoro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	453
555	1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenoxy)-propionyl]-3-(S)-methoxymethyl-piperazin-2-one	484, 486 Cl pattern
556	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	471, 473 Cl pattern
557	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-4-[(4-trifluoromethylsulfanyl-phenoxy)-acetyl]-piperazin-2-one	536
558	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	469, 471 Cl pattern
559	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	469, 471 Cl pattern

560	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	471, 473 Cl pattern
561	(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid	534, 536 Cl pattern
562	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-ylsulfanyl)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	492, 494 Cl pattern
563	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	470, 472 Cl pattern
564	2-(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-	533, 535 Cl pattern
565	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophene-6-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one	496, 498 Cl pattern
566	1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,3-dichloro-benzo[b]thiophene-6-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one	530, 532, 534 Cl_2 pattern
567	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	510, 512, 514 Cl_2 pattern
568	(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid methyl ester	548, 550 Cl pattern
569	(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid ethyl ester	562, 564 Cl pattern
570	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	470, 472 Cl pattern
571	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,3-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	504, 506, 508 Cl_2 pattern
572	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-fluoro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	454
573	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-2-methyl-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	484, 486 Cl pattern

574	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,4-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	504, 506, 508 Cl_2 pattern
575	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one	491, 493 Cl pattern
576	(1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	516, 518 Br pattern
577	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	472, 474 Cl pattern
578	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(R)-methoxymethyl-piperazin-2-one	472, 474 Cl pattern
579	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one	472, 474 Cl pattern
580	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one	496, 498 Cl pattern
581	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one	470, 472 Cl pattern

EXAMPLE 582. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 123, using 1-(4-aminoquinazoline-7-ylmethyl)-3-ethoxymethyl-piperazine-2-one, EXAMPLE 79 and, (6-chloro-pyridin-3-yloxy)-acetic acid, prepared similary to the procedure descibed in EXAMPLE 29. ^{1}H NMR (d6-DMSO, 300 MHz) δ 9.73 (bs, 2H), 8.81 (s, 1H), 8.37 (m, 1H), 8.10 (m, 1H), 7.61 (m, 2H), 7.40 (m, 2H), 4.98 (m, 2H), 4.65 (m, 2H), 4.50 (m, 1H), 3.91 (m, 1H), 3.75 (m, 1H), 3.59 (m, 2H), 3.31 (m, 2H), 1.07 (m, 3H). MS (ion spray), m/z, 485, 487 (M+H), (Cl pattern).

The following compounds are prepared from the compound of Example 79 using the methods described above.

Example #	Name	m/z [M+H]
583	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-ethoxymethyl-4-[(3-fluoro-phenoxy)-acetyl]-piperazin-2-one	454
584	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-	486, 488

	acryloyl]-3-(S)-ethoxymethyl-piperazin-2-one	Cl pattern
585	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one	484, 486 Cl pattern
586	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one	484, 486 Cl pattern
587	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one	490, 492 Cl pattern

The following compounds are prepared from the compounds of Examples 81-85 using the methods described above.

Example #	Name	m/z [M+H]
588	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one	518, 520 Cl pattern
589	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-piperazin-2-one	542, 544 Cl pattern
590	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one	504, 506 Cl pattern
591	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one	528, 530 Cl pattern
592	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[(4-chloro-phenoxy)-acetyl]-piperazin-2-one	516, 518 Cl pattern
593	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one	522, 524 Cl pattern
594	1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-propyl]-piperazin-2-one	506, 508 Cl pattern
595	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one	490, 492 Cl pattern
596	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one	472, 474 Cl pattetn
597	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one	486, 488 Cl pattern
598	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one	530, 532 Br pattern

599	1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one	491, 493 Cl pattern
600	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-isopropyl-piperazin-2-one	480, 482 Cl, pattern
601	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,3-dimethyl-piperazin-2-one	466. 468 Cl pattern
602	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,3-dimethyl-piperazin-2-one	442, 444 Cl pattern
603	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3,3-dimethyl-piperazin-2-one	456, 458 Cl pattern
604	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3,3-dimethyl-piperazin-2-one	480, 482 Cl pattern
605	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-(2-methoxy-ethyl)-piperazin-2-one	490, 492 Cl pattern
606	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-(2-methoxy-ethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	469, 471 Cl pattern
607	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-(2-methoxy-ethyl)-piperazin-2-one	490, 492 Cl pattern
608	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-(2-methoxy-ethyl)-piperazin-2-one	510, 512 Cl pattern

EXAMPLE 609. 1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-6-(S)-methyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 268, using 1-(4-amino-quinazoline-7-ylmethyl)-3-methoxymethyl-6-methyl-piperazine-2-one, EXAMPLE 87, and 2-bromomethyl-6-chloronaphthalene, EXAMPLE 12. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (s, 1H), 7.79 (d, 1H), 7.70-7.12 (m, 3H), 7.68-7.67 (m, 2H), 7.55 (d, 1H), 7.39 (d, 1H), 4.78 (d, 2H), 3.98 (d, 2H), 3.44 (s, 3H), 3.38 (t, 1H), 2.64 (m, 2H), 1.26 (d, 3H). MS (ISP) 490, 492, (M+H), Cl pattern.

The following materials are prepared from starting materials obtained as described in Example 87 using the methods described above.

Example #	Name	m/z [M+H]
610	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-	458, 460

	propyl]-3-(S)-ethyl-6-methyl-piperazin-2-one	Cl pattern
611	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-6-(R)-methyl-piperazin-2-one	490, 492 Cl pattern
612	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one	472, 474 Cl pattern
613	(1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methoxymethyl-6-methyl-piperazin-2-one	490, 492 Cl pattern
614	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-6-dimethyl-piperazin-2-one	491, 493 Cl pattern
615	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-6-methyl-piperazin-2-one	442, 446 Cl pattern
616	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-methyl-piperazin-2-one	428, 430 Cl pattern

EXAMPLE 617. 1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one.

The title compound is prepared as described in EXAMPLE 123 using 1-(4-amino-quinazoline-7-ylmethyl)-3-methoxymethyl-6-methyl-piperazine-2-one, EXAMPLE 87, and 5-chloro-2-thienyloxyacetic acid, EXAMPLE 24. ^{1}H NMR (CD_3OD300 MHz) δ 8.68 (s, 1H), 8.27 (d, 1H), 7.62 (m, 2H), 6.54 (d, 1H), 6.18 (m, 1H), 7.39 (d, 1H), 4.94 (m, 4H), 4.15 (m, 2H), 3.76 (m, 2H), 3.44 (s, 3H), 3.10 (m, 2H), 1.28 (d, 3H).

The following compounds are prepared from compounds obtained as described Examples 75-87 using the methods described above.

Example #	Name	m/z [M+H]
618	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-(S)-3-methoxymethyl-6-methyl-piperazin-2-one	490, 492 Cl pattern
619	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-(S)-3-methoxymethyl-6-methyl-piperazin-2-one	490, 492 Cl_2 pattern
620	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-4-fluoro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one	502, 504 Cl_2 pattern
621	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one	502, 504 Cl pattern

622	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2,5-dichloro-phenyl)-acryloyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one	514
623	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-2-methyl-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one	498, 500 Cl_2 pattern
624	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one	518
625	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one	484
626	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-3(S)-ethyl-6-methyl-piperazin-2-one	472, 474 Cl pattern
627	1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3(S)-ethyl-6-methyl-piperazin-2-one	474
628	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one	514, 516 Br pattern
629	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one	470, 472 Cl pattern
630	(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methoxymethyl-6-methyl-piperazin-2-one	486, 488 Cl pattern
631	(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-methoxymethyl-6-methyl-piperazin-2-one	530, 532 Br pattern
632	1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3(S)-6-dimethyl-piperazin-2-one	480 Cl pattern
633	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3(S)-6-dimethyl-piperazin-2-one	500, 502 Br pattern
634	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-6-dimethyl-piperazin-2-one	456, 458 Cl pattern
635	1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-6-methyl-piperazin-2-one	442, 444 Cl pattern

EXAMPLE 636. 4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide.

The title compound is prepared as described in EXAMPLE 436 using 1-(4-amino-quinazoline-7-ylmethyl)-3-methoxymethyl-piperazine-2-one, EXAMPLE 75, and 4-chlorophenyl isocyanate. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.77 (bs, 2H), 8.81 (s, 1H), 8.70 (s, 1H), 8.40 (d, 1H), 7.64 (d, 1H), 7.61 (s, 1H),

7.49 (d, 2H), 7.28 (d, 2H), 4.88 (m, 1H), 4.80 (AB, 2H), 4.19 (m, 1H), 3.96 (m, 1H), 3.74-3.42 (m, 4H), 3.28 (s, 3H). ESI MS, $[M+H]^+$=455,457 (Cl pattern). Anal. ($C_{22}H_{23}ClN_6O_3 \cdot TFA \cdot 1.5H_2O$) C, H, N.

EXAMPLE 637. 4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide.

The title compound is prepared as described in EXAMPLE 438 using 1-(4-amino-quinazoline-7-ylmethyl)-3-methyl-piperazine-2-one (EXAMPLE 80) and 5-chloro-thiophene-2-carbonyl azide (EXAMPLE 38). ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.01 (s, 1H), 9.73 (bs, 2H), 8.83 (s, 1H), 8.39 (d, 1H), 7.65 (d, 1H), 7.58 (s, 1H), 6.79 (d, 1H), 6.44 (d, 1H), 4.85 (d, 1H), 4.71 (m, 1H), 4.69 (d, 1H), 4.17 (d, 1H), 3.50 (m, 3H), 1.45 (d, 3H). ESI MS, $[M+H]^+$=431,433 (Cl pattern). Anal. ($C_{19}H_{19}ClN_6O_2S \cdot TFA \cdot 1.9H_2O$) C, H, N.

EXAMPLE 638. 4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide.

The title compound is prepared as described in EXAMPLE 439 using 1-(4-amino-quinazoline-7-ylmethyl)-3-methoxymethyl-piperazine-2-one (EXAMPLE 75) and 5-chloro-thiophene-2-carbonyl azide (EXAMPLE 38). ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.00 (s, 1H), 9.73 (bs, 2H), 8.82 (s, 1H), 8.40 (d, 1H), 7.65 (d, 1H), 7.60 (s, 1H), 6.80 (d, 1H), 6.42 (d, 1H), 4.86 (d, 1H), 4.80 (m, 1H), 4.70 (d, 1H), 4.18 (d, 1H), 3.96 (dd, 1H), 3.60 (m, 4H), 3.30 (s, 3H). ESI MS, $[M+H]^+$=461,463 (Cl pattern). Anal. ($C_{20}H_{21}ClN_6O_3S \cdot TFA \cdot 1.1H_2O$) C, H, N.

The following compounds are prepared using the methods described above.

Example #	Name	m/z [M+H]
639	4-(4-Amino-quinazolin-7-ylmethyl)-2(S)-(2-methoxy-ethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	469
640	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-butyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	467, 469 Cl pattern
641	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide	505, 507
642	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-3-yl)-amide	461, 463
643	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide	461

644	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(S)-2-propyl-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	453, 455 Cl pattern
645	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (3-bromo-phenyl)-amide	499
646	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(2S)-propyl-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide	459, 461
647	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(S)-2-propyl-piperazine-1-carboxylic acid (5-chloro-2-methoxy-phenyl)-amide	483, 485 Cl pattern
648	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-2-chloro-phenyl)-amide	533, 535
649	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-trifluoromethoxy-phenyl)-amide	505
650	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-fluoro-phenyl)-amide	439
651	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (2,4-dichloro-phenyl)-amide	489, 491
652	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (2,4-difluoro-phenyl)-amide	457
653	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (3-chloro-phenyl)-amide	455
654	4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(2S)-propyl-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide	459, 460 Cl pattern
655	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (6-chloro-pyridin-3-yl)-amide	426, 428
656	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide	499, 501
657	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide	486, 488
658	4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-5-(R,S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	469, 471
659	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-ethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide	483, 485
660	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	425, 427

661	4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-ethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	439, 441
662	4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-4-methoxy-thiophen-2-yl)-amide	491, 493 Cl pattern

EXAMPLE 663. (3S, 5RS)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one.

(3S,5RS)-1-(4-Amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one (260 mg, 0.56 mmol), EXAMPLE 88, is dissolved in 5 mL of DMF. Potassium carbonate (193.4 mg, 1.4 mmol) is added followed by the addition of 2-bromomethyl-6-chloro-benzo[b]thiophene (218 mg, 0.84 mmol), EXAMPLE 5. Reaction is left to stir overnight. The crude mixture is purified by reverse phase HPLC (10 -70% ACN/H_2O) to afford the product (27 mg, 6%) as a clear wax with a melting point of 130-131 °C . $C_{24}H_{24}ClN_5OS$ MS m/z: 466, 468.

EXAMPLE 664. (3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one.

and

EXAMPLE 665. (3S,5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one.

(3S,5RS)-1-(4-Amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one (60 mg, 0.13 mmol) is dissolved in 1 mL of DMF. Potassium carbonate (53 mg, 0.39 mmol) is added followed by the addition of 3-bromoallyl-5-chloro-thiophene (75 mg, 0.32 mmol). Reaction is left to stir overnight. The two epimers are separated by reverse phase HPLC (10 -70% ACN) in 43% yield.

The major epimer is assigned as (3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5 -dimethyl-piperazin-2-one trifluoroacetic acid salt (30.8 mg) and is isolated as a yellow solid with a melting point of 69-72 °C . $C_{22}H_{24}ClN_5OS$ MS m/z: 442, 444.

The minor epimer is assigned as (3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one trifluoroacetic acid salt (13.1 mg) with a melting point of 67-70 °C . $C_{22}H_{24}ClN_5OS$ MS m/z: 442, 444. 1H NMR (CD_3OD) δ: 8.67 (s, 1H); 8.31 (d, 1H, J = 8.56 Hz); 7.83 (s, 1H); 7.74 (d, 2H, J = 8.56 Hz); 7.14 (d, 1H, J = 15.6 Hz); 6.92 (d, 1H, J = 3.74 Hz); 6.10-6.03 (m, 1H); 5.0-4.74 (m, 2H); 4.25-3.63 (m, 6 H); 1.78 (d, 3H, J = 7.03 Hz); 1.50 (d, 3H, J = 6.47 Hz).

EXAMPLE 666. (3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one.

(3S,5R)-1-(4-Amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one (43 mg, 0.123 mmol), minor epimer fromEXAMPLE 88, Part D, is taken up in methylene chloride to this is added triethylamine (0.034 ml, 0.25 mmol) followed by 2-(5-chloro-thiophen-2-yl)-ethenesulfonyl chloride (40 mg, 0.16 mmol), EXAMPLE 3. The reaction is stirred overnight, and the crude material is purified by preparative thin layer chromatography (15 % methanol/CH_2Cl_2). The product (1.4 mg, 2.3%) is isolated as a yellow wax. $C_{21}H_{22}ClN_5O_3S_2$ MS m/z: 492, 494. 1H NMR (CD_3OD) δ 8.36 (s, 1H); 8.03 (d, 1H, J = 7.5 Hz); 7.61 (s, 1H); 7.49-7.44 (m, 2H); 7.19 (d, 1H, J = 3.83 Hz); 6.98 (d, 1H, J = 3.75 Hz); 6.76 (d, 1H, J = 15.1 Hz); 4.86-4.71 (m, 2H); 4.45-4.39 (m, 1H); 4.13-4.09 (m, 1H); 3.64-3.7 (m, 2H); 1.63 (d, 3H, J = 7.09 Hz); 1.33 (d, 3H, J = 6.80 Hz).

EXAMPLE 667. (3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one.

The product (7 mg, 9.4 %) is isolated as a yellow solid with a melting point of 218-221 °C . $C_{21}H_{22}ClN_5O_3S_2$ MS m/z: 492, 494. 1H NMR (CD_3OD) δ 8.37 (s, 1H); 8.10 (d, 1H, J = 8.57 Hz); 7.61-7.45 (m, 3H); 7.24 (d, 1H, J = 3.94 Hz); 6.98 (d, 1H, J = 3.85 Hz); 6.71 (d, 1H, J = 15.1 Hz); 4.76 (s, 2H); 4.32 (m, 1H); 3.71 (m, 1H); 3.36 (m, 2H); 1.62 (d, 3H, J = 7.06 Hz); 1.20 (d, 3H, J = 6.63 Hz).

EXAMPLE 668. (3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-sulfonyl)-3,5-dimethyl-piperazin-2-one.

The desired product (5.4 mg, 8.5 %) is isolated as yellow solid with a melting point of 224-226° C. $C_{23}H_{22}ClN_5O_3S_2$ MS m/z: 516, 518.

EXAMPLE 669. (3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3,5-dimethyl-piperazin-2-one.

To a solution of (3S,5S)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one (42 mg, 0.147 mmol), major epimer from EXAMPLE 88, Part D, in 2 mL of DMF is added TBTU (52 mg, 0.162 mmol), triethylamine (0.02 mL, 0.162 mmol) and 3-(5-chloro-thiophen-2-yl)-acrylic acid (28 mg, 0.15 mmol), EXAMPLE 25. After stirring for two hours, the reaction mixture is directly purified by reverse phase HPLC (10-70 % ACN/H_2O). The product (35.5 mg, 36%) is isolated as a yellow solid with a melting point of 116-120°C. $C_{22}H_{22}ClN_5O_2S$: MS m/z: 456, 458. Anal. calcd. for $C_{22}H_{22}ClN_5O_2S \bullet C_2HF_3O_2$: C, 50.57; H, 4.07; N, 12.29. Found: C, 46.48; H, 3.64; N, 11.04.

EXAMPLE 670. (3S, 5R)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide.

4-Bromo-phenyl isocyanate (20.8 mg, 0.105 mmol) is added to solution of (3S,5R)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one (30 mg, 0.105 mmol), minor epimer from EXAMPLE 88, Part D, in 1 mL of DMF. The reaction is stirred for two hours at room temperature. The product (21.4 mg, 33%) is isolated from reverse phase HPLC (10 -70% ACN/H_2O) as white solid. The melting of the compound is 142-144 °C . $C_{22}H_{23}BrN_6O_2$ MS m/z: 483, 485. Anal. cald.for $C_{22}H_{23}BrN_6O_2$ •$2C_2HF_3O_2$: C, 43.90; H, 3.54; N, 11.81. Found: C, 44.52; H, 3.86; N, 12.44.

EXAMPLE 671. (3S, 5S)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide.

The desired product (35 mg, 47%) is isolated as a white solid with a melting point of 142-144°C . $C_{22}H_{23}BrN_6O_2$ MS m/z: 483, 485. Anal. cald.for $C_{22}H_{23}BrN_6O_2$•$2C_2HF_3O_2$: C, 43.90; H, 3.54; N, 11.81. Found: C, 44.73; H, 3.59; N, 12.38.

EXAMPLE 672. (3S, 5S)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide.

The product (24.7 mg, 50%) is obtained as a white solid with a melting point of 123-125 °C . $C_{22}H_{23}ClN_6O_2$ MS m/z: 439, 441. Anal. cald.for $C_{22}H_{23}ClN_6O_2$•$2C_2HF_3O_2$: C, 46.82; H, 3.78; N, 12.60. Found: C, 47.69; H, 4.33; N, 13.32.

EXAMPLE 673. 1-(4-Aminoquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one.

A. 1-(4-Chloroquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one.

1-(4-chloroquinolin-7-ylmethyl)-3-(S)-methylpiperazin-2-one hydrochloride (0.49 g, 1.4 mmol), EXAMPLE 89, is treated with acetonitrile (20 mL), triethyl amine (1.2 ml, 8.4 mmol) and a solution of 6-chlorobenzo[b]thiophen-2-sulfonyl chloride (0.41 g, 1.54 mmol), EXAMPLE 1, in acetonitrile (10 mL) at 0°C. After 2 h the solution is poured into water and extracted with ethyl acetate. The organic layer is washed with water, dried over sodium sulfate and concentrated to yielded the title compound (0.45 g, 0.95 mmol). MS m/z: 506, $[M+1]^+$; ^1H NMR (CD_3OD, 300 MHz) δ 8.8 (d, 1H), 8.15 (d, 1H), 7.9 (d, 2H), 7.85 (s, 1H), 7.4-7.5 (m, 2H), 6.8 (s, 1H), 4.8 (s, 2H), 4.0 (s, 2H), 3.4-3.45 (m, 4H).

B. 1-(4-Azidoquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one

1-(4-Chloroquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one (0.52 g, 1.03 mmol) is dissolved in DMF (15 mL), treated with sodium azide (0.52 g, 8.0 mmol), tetrabutyl ammonium chloride (0.1 g, 0.36 mmol) and heated to 65 °C overnight. The reaction mixture is cooled,

poured into water and extracted with ethyl acetate. The organic layer is washed with water, dried (sodium sulfate) and concentrated to give the title compound (0.5 g, 1.04 mmol). ^{1}H NMR (CD_3OD, 300 MHz) δ 9.0 (d, 1H), 8.2 (d, 1H),8.0 (s, 1H), 7.9 (d, 2H), 7.8 (d,1H), 7.6 (d,1H), 7.5 (d,1H),6.9 (s, 1H), 4.85 (s, 2H), 4.0 (s, 2H), 3.5-3.7 (m, 4H).

C. 1-(4-Aminoquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one.

A suspension of 1-(4-azidoquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one (0.50 g, 1.04 mmol) in 100 mL of acetic acid/methanol (~ 1:10) is treated with 10% Pd/C (0.15 g) and stirred under hydrogen for 1.5 hours. The resulting solution is filtered through Celite and the filtrate is evaporated in vacuo. The organic layer is concentrated and the residue is purified by reverse phase HPLC (gradient elution of 30 % of 0.1 % aqueous TFA/acetonitrile to 100 % acetonitrile) and lyopholized to give the title compound (0.39 g, 0.86 mmol). MS (ISP) m/z 487, 489, (M+H), Cl pattern.

The following compounds are prepared from the compound of Example 89 or 91 using the methods described above.

Example #	Name	m/z [M+H]
674	1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	463, 465
675	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-methyl-piperazin-2-one	501, 503
676	(3S,5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one	491, 493
677	(3S,5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one	491, 493
678	(S,R)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid	531, 533
679	1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide	544
680	1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide	558
681	1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide	558

682	1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one	600

EXAMPLE 683. (S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(5-chlorothiophen-2-yl)-allyl]-3-methylpiperazin-2-one.

A. (S)-1-(4-Chloroquinolin-7-ylmethyl)-4-[3-(5-chlorothiophen-2-yl)-allyl]-3-methylpiperazin-2-one.

(S)-1-(4-chloroquinolin-7-ylmethyl)-3-methylpiperazin-2-one hydrochloride (0.25 g, 1.0 mmol), EXAMPLE 91, is treated with 2-(3-Bromo-(E)-propenyl)-5-chloro-thiophene (0.35 g 1.2 mmol), EXAMPLE 17, and potassium carbonate (0.5 g, 3 mmol). The resulting suspension is sonicated for 10 minutes then stirred vigorously for 16 h at ambient temperature. The reaction mixture is poured into water and extracted with ethyl acetate (2 X 150 mL). The organic layer is washed with water (4 X 200 mL), dried over sodium sulfate and concentrated. The residue is chromatographed (3 % methanol/methylene chloride) to give the title compound (0.31 g, 0.73 mmol).

B. (S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(5-chlorothiophen-2-yl)-allyl]-3-methylpiperazin-2-one.

(S)-1-(4-Chloroquinolin-7-ylmethyl)-4-[3-(5-chlorothiophen-2-yl)-allyl]-3-methylpiperazin-2-one (0.35 g, 0.82 mmol) is treated with phenol (2 g) and ammonium acetate (0.7 g, 9.1 mmol) and heated to 120 °C in a sealed vessel for 1 hour. Upon cooling, the solution is partitioned between 2 N NaOH and ethyl acetate. The organic layer is separated and washed with fresh 2 N NaOH (3 X 100 mL) and water. The organic layer is concentrated and the residue is purified by reverse phase HPLC to give the title compound as a white solid (0.15 g, 0.35 mmol). MS (ISP) m/z 427, 429, (M+H), Cl pattern.

The following compounds are prepared from starting materials prepared as described in Examples 61-64, 89 or 91 using the methods described above.

Example #	Name	m/z [M+H]
684	1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one	413, 415
685	(3S, 5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one	465, 467
686	(3S, 5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one	464
687	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-	446,448

	ylmethyl)-3-methyl-piperazin-2-one	
688	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-methyl-piperazin-2-one	444
689	(3S,5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one	441, 443
690	(3S,5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one	441, 443
691	1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one	420, 422
692	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-ethyl-piperazin-2-one	458
693	1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-(S)-3-((R)-1-methoxy-ethyl)-piperazin-2-one	470
694	1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-(S)-3-((R)-1-methoxy-ethyl)-piperazin-2-one	489
695	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-methoxymethyl-piperazin-2-one	464, 466
696	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-methyl-piperazin-2-one	434, 436
697	4-(5-Chloro-1H-indol-2-ylmethyl)-1-[4-(2-hydroxy-ethylamino)-quinolin-7-ylmethyl]-piperazin-2-one	464
698	(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-ethylamino-quinolin-7-ylmethyl)-3-methyl-piperazin-2-one	462
699	(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-ethylamino-quinolin-7-ylmethyl)-3-methoxymethyl-piperazin-2-one	492
700	(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-3-methyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one	448
701	(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-3-methoxymethyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one	478
702	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-methyl-4-oxy-piperazin-2-one	443

EXAMPLE 703. (S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)acryloyl]-3-methyl-piperazin-2-one.

A. (S)-1-(4-Chloroquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)acryloyl]-3-methyl piperazin-2-one.

(S)-1-(4-chloroquinolin-7-ylmethyl)-3-methylpiperazin-2-one hydrochloride (0.35 g, 1.4 mmol), EXAMPLE 91, is treated with DMF (20 mL), 3-(4-bromothiophen-2-yl)-(E)-acrylic acid (0.32 g, 1.4 mmol), prepared according to EXAMPLE 26, using 4-bromothiophene-2-carboxaldehyde, triethyl amine (0.21 ml, 1.4 mmol) and 2-(1H-benzotriazol-1-yl)1,1,3,3-tertamethyluronium tetrafluoroborate (0.45 g, 1.4 mmol) and heated to 50 °C for 5 minutes. The reaction mixture is stirred at ambient temperature for 16 h then partitioned between ethyl acetate and water. The organic layer is concentrated and the residue is chromatographed (5% methanol/methylene chloride) to give crude title compound (0.5 g , 0.9 mmol). MS m/z: $[M+H]^+ = 504$. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.9 (d, 1H), 8.2-8.3(m, 2H), 8.0 (s, 1H), 7.7-7.8 (m, 1H), 7.4 (s, 1H), 7.3-7.4 (m, 1H), 6.7-6.8 (m, 1H), 6.6 (d, 1H), 5.1-5.2 (m, 1H), 4.6-4.7 (m, 2H), 3.4-3.6 (m, 2H), 3.0-3.3 (m, 2H), 1.5 (d, 3H).

B. (S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)acryloyl]-3-methyl-piperazin-2-one.

(S)-1-(4-Chloroquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)acryloyl]-3-methyl piperazin-2-one (0.50 g, 0.9 mmol) is treated with phenol (~ 2 g) and ammonium acetate (0.5 g, 6.4 mmol) and heated to 120 °C in a sealed vessel for 1 hour. Upon cooling, the solution is partitioned between 2 N NaOH and ethyl acetate. The organic layer is separated and washed with fresh 2 N NaOH (3 X 100 mL) and water. The organic layer is concentrated and the residue is purified by reverse phase HPLC (gradient elution of 10 % of 0.1 % aqueous TFA/acetonitrile to 100 % acetonitrile) to give the title compound (0.22 g, 0.56 mmol). MS m/z: $[M+H]^+ = 485, 487$, Cl pattern. ^1H NMR (CD_3OD, 300 MHz) δ 8.2-8.4 (m, 2H), 7.7-7.8 (m, 2H), 7.6 (d, 1H), 7.5 (s, 1H), 7.3 (s, 1H), 6.9-7.0 (m, 1H), 6.7 (d, 1H), 5.0-5.1 (m, 1H), 4.9 (q, 2H), 4.3-4.4 (m, 1H), 3.5-3.7 (m, 2H), 3.3-3.4 (m, 2H), 1.5 (d, 3H).

The following compounds are prepared from starting materials prepared as described in Examples 75-87 using the methods described above.

Example #	Name	m/z [M+H]
704	1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one	469 Cl pattern
705	4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-(S)-3-ethyl-1-(4-hydroxyamino-quinolin-7-ylmethyl)-piperazin-2-one	471, 473
706	1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-	427, 429

	acryloyl]-piperazin-2-one	
707	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one	454
708	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methyl-piperazin-2-one	441, 443
709	1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-piperazin-2-one	471, 473
710	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methoxymethyl-piperazin-2-one	470
711	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one	498
712	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-ethyl-piperazin-2-one	458
713	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-methoxymethyl-6-methyl-piperazin-2-one	488
714	1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-(S)-3-(1-(R)-methoxy-ethyl)-piperazin-2-one	484
715	1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)-acryloyl]-3-(S)-(1-(R)-methoxyethyl)-piperazin-2-one trifluoroacetate	528
716	1-(4-Aminoquinolin-7-ylmethyl)-4-[(5-chlorothiophen-2-yloxy-acetyl]-3-(S)-(1-(R)-methoxyethyl)-piperazin-2-one trifluoroacetate	488
717	(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one	454

EXAMPLE 718. 1-(4-Aminocinnolin-7-ylmethyl)-4-[2-(5-chlorothiophen-2-yl)-ethenesulfonyl]-piperazin-2-one.

A. 1-(4-Chlorocinnolin-7-ylmethyl)-4-[2-(5-chlorothiophen-2-yl)-ethenesulfonyl]-piperazin-2-one

1-(4-chlorocinnolin-7-ylmethyl)-piperazin-2-one hydrochloride (0.14 g, 0.4 mmol), EXAMPLE 90, is treated with acetonitrile (20 mL), triethylamine (2 mL, 14 mmol) and 2-(5-chlorothiophen-2-yl)ethene-sulfonyl chloride (0.097 g, 0.4 mmol), EXAMPLE 3, at 0°C. The solution is warmed to ambient temperature over 1.5 h and diluted with ethyl acetate. The solution is washed with 10 % sodium bicarbonate solution and water, dried (sodium sulfate) and concentrated to yield the title compound (0.17 g, 0.35 mmol). MS m/z: $[M+H]^+ = 483$; ^1H NMR ($CDCl_3$, 300 MHz) δ 9.4 (s, 1H), 8.4 (s, 1H), 8.3 (d,

1H) 7.85 (d, 1H), 7.7 (d, 1H), 7.1 (d, 1H), 6.95 (d, 1H), 6.35 (d, 1H), 4.9 (s, 2H), 4.0 (s, 2H), 3.4-3.5 (m, 4H).

B. 1-(4-Aminocinnolin-7-ylmethyl)-4-[2-(5-chlorothiophen-2-yl)-ethenesulfonyl]-piperazin-2-one

1-(4-Chlorocinnolin-7-ylmethyl)-4-[2-(5-chlorothiophen-2-yl)-ethenesulfonyl]-piperazin-2-one (0.06 g, 0.12 mmol) is treated with phenol (0.20 g) and ammonium acetate (0.2 g, 2.6 mmol) and heated to 120 °C for 45 minutes. The reaction mixture is cooled, diluted with ethyl acetate and washed with 1 N NaOH (3 X 100 mL) and water. The organic layer is concentrated and the residue is purified by reverse phase HPLC (20 % aqueous TFA (0.1 %)/acetonitrile to 100 % acetonitrile). Fractions containing the desired product are lyophilized to obtain the title compound (0.02 g, 0.043 mmol). MS m/z: $[M+H]^+$ = 464; ^{1}H NMR (CD_3OD, 300 MHz) δ 8.6 (s, 1H), 8.4 (d, 1H), 7.75 (d, 1H), 7.65 (d, 1H), 7.35 (d, 1H), 7.1 (d,1H), 6.8 (d, 1H), 4.9 (s, 2H), 4.05 (s, 2H), 3.6 (m, 4H).

EXAMPLE 719. 4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one.

1-[2-(Pyridin-4-ylamino)-ethyl]-piperazin-2-one (0.20 mmol), EXAMPLE 90, is dissolved in MeCN (5 mL) and treated with 4-methylmorphorline (0.055 ml, 0.50 mmol). 6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl chloride (54 mg, 0.20 mmol) in MeCN (2 mL) is added dropwise. The reaction mixture is stirred at r.t. for 1.5 h, then subjected to HPLC purification, to give the title compound as white solid (0.021 g, 0.037 mmol). MS m/z 452, 454 (M+1); ^{1}H NMR (CD_3OD, 300 MHz) δ 8.37 (d, 1H), 8.30 (b, 1H), 8.12 (d, 1H), 8.02 (s, 1H), 7.97 (d, 1H), 7.57 (d. 1H), 6.98 (d, 1H), 6.88 (d, 2H), 3.73 (s, 2H), 3.60-3.48 (m, 8H).

EXAMPLE 720. 4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(methyl-pyridin-4-yl-amino)-ethyl]-piperazin-2-one.

A portion (~50%) of the crude 1-[2-{(Methyl)-(pyridin-4-yl)-amino}-ethyl]-piperazin-2-one, EXAMPLE 93 is reacted with 6-chloro-benzo[b]thiophene-2-sulfonyl chloride (54 mg, 0.20 mmol), EXAMPLE 1, using same procedure as described in EXAMPLE 719. The residue obtained after HPLC purification is subjected to silica gel chromatography using NH_4OH/MeOH/CH_2Cl_2 (1:4:95) as eluant to give title compound (30 mg, 0.064 mmol) as a white solid. MS m/z 465, 457 (M+1); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.15 (d, 2H), 7.88 (s, 1H), 7.85 (d, 1H), 7.79 (s, 1H), 7.47 (d, 1H), 6.47 (d. 2H), 3.80 (s, 2H), 3.50 (m, 4H), 3.43 (d, 2H), 3.30 (d, 2H), 2.98 (s, 3H).

EXAMPLE 721. 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(3-methyl-pyridin-4-ylamino)-ethyl]-piperazin-2-one.

1-[2-(3-Methylpyridin-4-yl-amino)-ethyl]-piperazin-2-one (38 mg, 0.16 mmol), EXAMPLE 94, is reacted with 2-(5-chloro-thiophen-2-yl)-ethenesulfonyl chloride (40 mg, 0.16 mmol), EXAMPLE 3, using the same procedure as described in EXAMPLE 719. Reverse phase HPLC purification gives the title compound (29 mg, 0.052 mmol) as a white solid. MS m/z 441, 443 (M+H); ^{1}H NMR (CD_3OD, 300 MHz) δ 8.08 (d, 1H), 7.98 (s, 1H), 7.56 (d, 1H), 7.30 (d, 1H), 7.02 (s, 1H), 7.00 (d. 1H), 6.78 (d, 1H), 3.87 (s, 2H), 3.70-3.50 (m, 8H), 2.15 (s, 3H).

The following compounds are prepared from starting materials obtained as described in Examples 92-97 using the methods described above.

Example #	Name	m/z [M+H]
722	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one	520 (M+)
723	1-[2-(Pyridin-4-ylamino)-ethyl]-4-(thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one	417
724	4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one	483,485
725	1-[2-(Pyridin-4-ylamino)-ethyl]-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one	418
726	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one	427,429
727	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(methylpyridin-4-ylamino)-ethyl]-piperazin-2-one	441
728	4-(2-Benzo[b]thiophen-2-yl-ethenesulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one	443
729	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(3-methyl-pyridin-4-ylamino)-ethyl]-piperazin-2-one	465, 467
730	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(2-pyrrolo[3,2-c]pyridin-1-yl-ethyl)-piperazin-2-one	450, 452
731	1-[2-(2-Amino-3-chloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	476, 478
732	1-[2-(2-Amino-5-chloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	476, 478
733	4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(2,3,5,6-	563, 565,

	tetrachloro-pyridin-4-ylamino)-ethyl]-piperazin-2-one	567, 569
734	1-[2-(2-Amino-3,5,6-trichloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	544, 546, 548
735	4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one	391, 393

EXAMPLE 736. 4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(pyridazin-4-yl-amino)-ethyl]-piperazin-2-one.

1-[2-(Pyridazin-4-ylamino)-ethyl]-piperazin-2-one hydrochloride (0.5 g, 1.7 mmol), EXAMPLE 95, is reacted with 6-chloro-benzo[b]thiophene-2-sulfonyl chloride (0.40 g, 1.5 mmol), EXAMPLE 1, using essentially the same procedure as described in EXAMPLE 719. Reverse phase HPLC purification gives the title compound (0.34 g, 0.75 mmol) as a white solid. MS m/z (M+H= 452); ^{1}H NMR (CD_3OD, 300 MHz) δ 8.6 (d, 1H), 8.4 (d, 1H), 8.05 (s, 1H), 8.05 (s, 1H), 7.9 (d, 1H), 7.5 (d, 1H), 7.2 (d, 1H), 3.8 (s,2H), 3.4-3.7 (m, 8H).

EXAMPLE 737. 1-[3-(4-Amino-pyridin-3-yl)-propenyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one.

4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propenyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester from EXAMPLE 96, Part B (45 mg, 0.10 mmol) is dissolved in 20% TFA/ CH_2Cl_2 and stirred at r.t. for 2 hours. The solution is concentrated to residue. The residue is dissolved in MeCN (2.5 ml) and treated with 4-methylmorphorline (0.027 ml, 0.25 mmol). 2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl chloride (24 mg, 0.10 mmol), EXAMPLE 3, in MeCN (1 mL) is then added dropwise. The reaction mixture is stirred at r.t. for 1 h, then subjected to reverse phase HPLC purification, to give the title compound as white solid (0.040 g, 0.037 mmol). MS m/z 439, 441 (M+H); ^{1}H NMR (CD_3OD, 300 MHz) δ 8.20 (br, 1H), 8.10 (s, 1H), 8.08 (d, 1H), 7.60 (d, 1H), 7.53 (d. 1H), 7.35 (d, 1H), 7.21 (d, 1H), 7.07 (d,1H), 6.82 (d, 1H), 5.27 (m, 1H), 3.88 (s, 2H), 3.60-3.50 (m, 4H), 3.30 (d, 2H).

The following compounds are prepared from starting materials obtained as described in Examples 92-97 using the methods described above.

Example #	Name	m/z [M+H]
738	1-[3-(4-Amino-pyridin-3-yl)-propenyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	463, 465
739	1-[3-(4-Amino-pyridin-3-yl)-allyl]-4-(6-chloro-benzo[b]thiophene-2-	463, 465

	sulfonyl)-piperazin-2-one	
740	1-[3-(4-Amino-pyridin-3-yl)-allyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	439, 441
741	1-[3-(4-Amino-pyridin-3-yl)-propyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	465, 467
742	1-[3-(4-Amino-pyridin-3-yl)-propyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one	441, 443

EXAMPLE 743. 4-[2-(5-Chlorothiophen-2-yl)-ethenesulfonyl]-1-(2-pyrrolo[3,2-c]pyridin-1-ylethyl)-piperazin-2-one.

4-(Benzyloxycarbonyl)-1-(2-pyrrolo[3,2-c]pyridin-1-ylethyl)-piperazin-2-one (0.028 g, 0.074 mmol), EXAMPLE 98, is treated with 4 % HCO_2H/MeOH (5 mL) and a catalytic amount of Pd black for 5 minutes. The reaction mixture is filtered washed with methanol and the filtrate is concentrated to a residue. The residue is treated with acetonitrile (3 mL) excess N-methylmorpholine (0.04 mL) and 2-(5-chlorothiophen-2-yl)ethene-sulfonyl chloride (0.018 g, 0.074 mmol), EXAMPLE 3, and processed as usual (EXAMPLE 719). Further chromatographic purification (NH_4OH/MeOH/CH_2Cl_2:1/4/95) yields the title compound: MS m/z 451, 453 (M+H); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.93 (bs, 1H), 8.24 (bs, 1H), 7.41 (d, 1H), 7.23 (d, 1H), 7.14 (m, 2H), 6.94 (d, 1H), 6.68 (d. 1H), 6.18 (d, 1H), 4.43 (t, 2H), 3.67 (t, 2H), 2.88 (t, 2H), 2.66 (t, 2H).

EXAMPLE 744. 4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. 2-(2-Oxo-4-prop-2-ynyl-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

A solution containing 2-(2-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (4.3 g, 13.0 mmol), EXAMPLE 69, in CH_3CN (250 mL) is cooled to 0°C. Potassium carbonate (1.98 g, 14.3 mmol) is added to the reaction mixture followed by propargyl bromide (1.55g, 13.0 mmol). The mixture is slowly warmed to ambient temperature and maintained until complete consumption of starting material is observed by TLC (approx. 8 h). The mixture is concentrated to dryness and then partitioned between aqueous $NaHCO_3$ (200 mL) and CH_2Cl_2 (200 mL) and the layers are separated. The aqueous phase is extracted twice with CH_2Cl_2 (100 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 5% MeOH/CH_2Cl_2) to provide 3.38 g (70%) of the title compound as a pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.69 (s, 9H), 2.34 (t, J = 2.4 Hz, 1H), 2.89 (m, 2H), 3.42 (s, 2H), 3.45 (d, J = 2.4 Hz, 2H), 3.52 (m, 2H), 4.95 (d, J = 1.4 Hz, 2H), 6.42

(br s, 1H), 7.88 (dd, J = 5.8, 0.8 Hz, 1H), 8.41 (d, J = 5.8 Hz, 1H), 8.78 (d, J = 0.8 Hz, 1H) ppm; MS (EI): m/z 368 (M+).

B. 4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

To a solution containing 2-(2-oxo-4-prop-2-ynyl-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (1.3 g, 3.53 mmol) in CH_2Cl_2 (100 mL) is added TFA (20 mL) at 0 °C. After 6 h, the reaction mixture is concentrated to dryness and then partitioned between aqueous $NaHCO_3$ (500 mL) and CH_2Cl_2 (200 mL) and the layers are separated. The aqueous phase is extracted four times with CH_2Cl_2 (100 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 10% MeOH/CH_2Cl_2) to provide 616 mg (65%) of the title compound as a pale yellow solid. ^1H NMR (300 MHz, $CDCl_3$) δ 2.27 (app t, J = 2.4 Hz, 1H), 2.76 (m, 2H), 3.33 (s, 2H), 3.83 (d, J = 2.4 Hz, 2H), 3.45 (m, 2H), 4.57 (s, 2H), 6.47 (s, 1H), 7.23 (d, J = 5.7 Hz, 1H), 8.28 (d, J = 5.7 Hz, 1H), 8.85 (d, J = 0.9 Hz, 1H), 9.34 (br s, 1H) ppm; MS (EI): m/z 268 (M+).

EXAMPLE 745. 1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. 2-{4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-prop-2-ynyl]-2-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

A solution containing 2-(2-oxo-4-prop-2-ynyl-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (100 mg, 0.27 mmol), EXAMPLE 743, (3-iodo-pyridin-4-yl)-carbamic acid tert-butyl ester (87 mg, 0.27 mmol), EXAMPLE 69, Part B, Et_3N (110 mg, 1.08 mmol), $(Ph_3P)_4PdCl_2$ (10 mg, 0.013 mmol), and CuI (1 mg, 0.008 mmol) in anhydrous DMF (5 mL) is stirred at ambient temperature. After 5 h, the reaction mixture is diluted with EtOAc (50 mL) and water (50 mL) and the layers are separated. The aqueous layer is extracted twice with EtOAc (25 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 10% MeOH CH_2Cl_2) to provide 77 mg (51%) of SC41 as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$, ~2:1mixture of rotamers) major rotamer: δ 1.53 (s, 9H), 1.69 (s, 9H), 2.98 (m, 2H), 3.49 (s, 2H), 3.56 (m, 2H), 3.78 (s, 2H), 4.98 (s, 2H), 6.43 (s, 1H), 7.89 (m, 1H), 8.09 (m, 2H), 8.34 (m, 1H), 8.41 (m, 1H), 8.75 (m, 1H) ppm; MS (ISP loop): m/z 561 (M+H).

B. 2-[4-(1-tert-Butoxycarbonyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

1,8-Diazabicyclo[5.4.0]undec-7-ene (42 mg, 0.27 mmol) is added to a suspension containing 2-{4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-prop-2-ynyl]-2-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (SC41, 77 mg, 0.14 mmol) in anhydrous CH_3CN (10 mL) and the mixture is warmed to 50 °C. After 4 h, the reaction mixture is concentrated to dryness and the residue is partitioned between CH_2Cl_2 (50 mL) and water (50 mL) and the layers are separated. The aqueous layer is extracted twice with CH_2Cl_2 (25 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to provide 85 mg of the title compound as a crude solid which is used directly without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.68 (s, 9H), 1.70 (s, 9H), 2.91 (m, 2H), 3.41 (s, 2H), 3.49 (m, 2H), 4.26 (s, 2H), 4.95 (d, J = 1.1 Hz, 2H), 6.39 (d, J = 0.7 Hz, 1H), 6.68 (d, J = 0.7 Hz, 1H), 7.86 (m, 1H), 8.41 (m, 1H), 8.76 (br s, 1H), 8.82 (br s, 1H) ppm; MS (EI): m/z 561 (M+H).

C. 1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

To a solution containing 2-[4-(1-tert-Butoxycarbonyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (85 mg, 0.14mmol) in CH_2Cl_2 (5 mL) is added TFA (1 mL) at 0°C and the solution is allowed to slowly warm to ambient temperature. After 16 h, the reaction mixture is concentrated to dryness, diluted with water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 45% B over 30 min] to provide 35 mg (36%, two steps) of SC43 as a pale yellow, lyophilized solid. ^{1}H NMR (300 MHz, d_6-DMSO) δ 2.80 (m, 2H), 3.25 (s, 2H), 3.37 (m, 2H), 3.93 (s, 2H), 4.76 (s, 2H), 6.88 (s, 1H), 6.94 (s, 1H), 7.85 (d, J = 6.6 Hz, 1H), 7.89 (d, J = 6.6 Hz, 1H), 8.37 (d, J = 6.7 Hz, 1H), 8.38 (d, J = 6.7 Hz, 1H), 9.17 (s, 1H), 9.19 (s, 1H), 12.80 (s, 1H), 12.96 (s, 1H), 14.91 (br s, 2H) ppm; MS (ion spray): m/z 361 (M+H). $C_{23}H_{25}ClN_4OS$ MS m/z: 441,443.

The following compounds are prepared from starting materials obtained as described in Examples 69-71 using the methods described above.

Example #	Name	m/z [M+H]
746	4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	395, 397
747	4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	443, 445
748	4-[3-(5-Chloro-thiophen-2-yl)-allyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	386, 388
749	4-(5-Chloro-1H-indol-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-	394, 396

	ylmethyl)-piperazin-2-one	
750	4-(6-Chloro-naphthalen-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	405, 407
751	4-(7-Chloro-isoquinolin-3-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	406, 408
752	4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester	501, 503
753	1-(5-Chloro-1H-indol-2-ylmethyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester	452, 454
754	1-[(5-Chloro-thiophen-2-yloxy)-acetyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester	463, 465
755	1-(6-Chloro-benzo[b]thiophene-2-carbonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester	483, 485
756	1-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester	554, 556
757	1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-piperazin-2-one	361
758	4-(3-Phenyl-prop-2-ynyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	345
759	4-[3-(5-Chloro-thiophen-2-yl)-prop-2-ynyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	384

The following compounds are prepared from 3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one using the procedures described above.

Example #	Name	m/z [M+H]
760	4-[3-(5-Chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	431, 433
761	4-(5-Chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	438, 440
762	4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methoxymethyl-	487, 489

	1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	
763	4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	469, 471
764	4-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	540, 542
765	4-[3-(4-Chloro-phenyl)-(E)-acryloyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	439, 441
766	(S)-2-Methoxymethyl-3-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide	428, 430
767	(S)-4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	445, 447

EXAMPLE 768. 4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.

A. 2-[4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-2-oxopiperazin-1-ylmethyl]-(pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester.

The title compound is prepared as described in EXAMPLE 123 using 6-chloro-benzo[b]thiophene-2-carboxylic acid, EXAMPLE 1 and 2-(2-oxopiperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester EXAMPLE 69. The mixture is stirred overnight, then concentrated to dryness. The residue is diluted with CH_2Cl_2 and washed with saturated sodium bicarbonate and brine. The organic layer is dried over $MgSO_4$, filtered and concentrated in vacuo to give the title compound as a solid. The crude material can be used in the subsequent step without further purification.

B. 4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one.

Trifluoroacetic acid (0.5 mL) is added dropwise to a solution of 2-[4-(6-chloro-benzo[b]thiophene-2-carbonyl)-2-oxopiperazin-1-ylmethyl]-(pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester (0.14 g, 0.27 mmol) in 6 mL CH_2Cl_2 at 0°C. After 1 h, the ice bath is removed and the solution stirred at room temperature for 2 hours. The reaction mixture is concentrated in vacuo. The crude residue is purified by RP-HPLC eluting in a gradient of 10% CH_3CN/H_2O (0.1% TFA) to 100% CH_3CN and the appropriate product fractions are combined and lyophilized to provide the title compound (0.07 g, 0.13 mmol) as a white solid. ESI MS, $[M+H]^+$=425, 427 (Cl pattern).

The following compounds are prepared using starting materials obtained as described in Example 69 using the methods described above.

Example #	Name	m/z [M+H]
769	4-[3-(6-Chloro-benzo[b]thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	451, 453
770	4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	405, 407
771	4-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	497, 499
772	4-(5'-Chloro-[2,2']bithiophenyl-5-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	457, 459
773	4-(5-Chloro-1H-indole-2-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	364, 366
774	4-[4-(6-Methoxy-pyridin-3-yl)-benzoyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	442
775	4-(4-Pyridin-3-yl-benzoyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	412
776	4-[3-(4-Bromo-thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	446
777	4-[3-(5-Chloro-thiophen-2-yl)-propionyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	403, 405
778	4-[(5-Chloro-3-methyl-benzo[b]thiophen-2-yl)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	453, 455
779	4-[2-(4-Chloro-phenyl)-2-methyl-propionyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	411, 413
780	4-[3-(3,4-Dichloro-phenyl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	431, 433
781	4-[(4-Chloro-phenyl)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	383, 385
782	4-[3-(4-Chloro-phenyl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one	395, 397
783	4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-	400, 402

	c]pyridin-2-ylmethyl)-piperazin-2-one	

EXAMPLE 784. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methyl ester.

A. (±)-4-[3-(Benzhydrylidene-amino)-4-cyano-benzyl]-5-oxo-piperazine-1,3-dicarboxylic acid 1-allyl ester 3-methyl ester.

To a solution containing (S)-5-oxo-piperazine-1,3-dicarboxylic acid 1-allyl ester 3-methyl ester (0.43 g, 1.77 mmol), EXAMPLE 56, and 2-(benzhydrylidene-amino)-4-bromomethyl-benzonitrile (0.66 g, 1.77 mmol), EXAMPLE 13, in anhydrous DMF (5 mL) at 0°C is added 60% NaH (78 mg, 1.95 mmol). After 30 min, the reaction mixture is warmed to ambient temperature and maintained for 6 hours. The reaction mixture is carefully quenched with water and then diluted with water and diethyl ether. The layers are separated and the organic phase is washed twice with water, brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is chromatographed on silica gel (2:1 hexane/ethyl acetate to 1:1 hexane/ethyl acetate) to provide 0.37 g (39%) of the title compound as a glassy solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.01-3.22 (m, 2H), 3.58 (m, 2H), 3.73 (s, 3H), 3.86-3.92 (m, 1H), 4.42-4.58 (m, 4H), 5.25 (m, 2H), 5.93 (m, 1H), 6.57 (br s, 1H), 6.85 (d, J = 8.2 Hz, 1 H), 7.17-7.51 (m, 9H), 7.76 (m, 2H) ppm; MS (ion spray): m/z 537 (M+H).

B. (±)-1-[3-(Benzhydrylidene-amino)-4-cyano-benzyl]-6-oxo-piperazine-2-carboxylic acid methyl ester.

Tetrakis(triphenylphosphine)palladium(0) (237 mg, 0.2 mmol) is added to a solution containing (±)-4-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-5-oxo-piperazine-1,3-dicarboxylic acid 1-allyl ester 3-methyl ester (1.10 g, 2.05 mmol) and morpholine (894 mg, 10.2 mmol) in CH_2Cl_2 (30 mL). After ~5 min, the reaction mixture is absorbed onto silica gel and chromatographed (CH_2Cl_2 to 10% MeOH/ CH_2Cl_2) to provide 900 mg (97%) of the title compound as a viscous yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.83 (br s, 1H), 2.95 (dd, J = 13.5, 4.3 Hz, 1H), 3.27 (br d, J = 13.5 Hz, 1H), 3.46-3.72 (m, 4H), 3.73 (s, 3H), 5.40 (d, J = 15.3 Hz, 1H), 6.57 (br s, 1H), 6.83 (dd, J = 8.0, 1.2 Hz, 1H), 7.17-7.50 (m, 9H), 7.75-7.77 (m, 2H) ppm; MS (ion spray): m/z 453 (M+H).

C. (±)-2-{4-[3-(Benzhydrylidene-amino)-4-cyano-benzyl]-3-methoxycarbonyl-5-oxo-piperazin-1-ylmethyl}-5-chloro-indole-1-carboxylic acid tert-butyl ester.

To a mixture of (±)-1-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-6-oxo-piperazine-2-carboxylic acid methyl ester (630 mg, 1.39 mmol) and K_2CO_3 (380 mg, 2.78 mmol) in anhydrous CH_3CN (5 mL) at 0 °C is added 2-bromomethyl-5-chloro-indole-1-carboxylic acid tert-butyl ester (720 mg, 2.09

mmol), EXAMPLE 21, in CH_3CN (4 mL). The reaction mixture is allowed to warm to ambient temperature then maintained for 16 hours. The reaction mixture is diluted with diethyl ether/water and the layers are separated. The organic phase is washed twice with water, brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is chromatographed on silica (CH_2Cl_2 to 2% MeOH/ CH_2Cl_2) to provide 550 mg (55%) of the title compound which is used directly in the next reaction without further characterization.

D. (±)-2-[4-(3-Amino-4-cyano-benzyl)-3-methoxycarbonyl-5-oxo-piperazin-1-ylmethyl]-5-chloro-indole-1-carboxylic acid tert-butyl ester.

Partially-purified (±)-2-{4-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-3-methoxycarbonyl-5-oxo-piperazin-1-ylmethyl}-5-chloro-indole-1-carboxylic acid tert-butyl ester (550 mg, 0.76 mmol) is suspended in reagent grade MeOH (20 mL). To the heterogeneous mixture is added 12M HCl (5 drops) and the reaction mixture is maintained at ambient temperature until homogeneous (~30 min). The reaction mixture is partitioned between diethyl ether and water containing excess $NaHCO_3$ (500 mL). The layers are separated and the organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is chromatographed on silica gel (CH_2Cl_2 to 2% MeOH/ CH_2Cl_2) to provide 400 mg (94%) of the title compound which is used directly in the next reaction. MS (ISP loop): 532 (M+H).

E. (±)-2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-methoxycarbonyl-5-oxo-piperazin-1-ylmethyl]-5-chloro-indole-1-carboxylic acid tert-butyl ester.

A solution containing (±)-2-[4-(3-amino-4-cyano-benzyl)-3-methoxycarbonyl-5-oxo-piperazin-1-ylmethyl]-5-chloro-indole-1-carboxylic acid tert-butyl ester (100 mg, 0.18 mmol), 1,3,5-triazine (146 mg, 1.81 mmol), and glacial HOAc (99 mg, 1.81 mmol) in absolute EtOH (10 mL) is maintained at reflux for 16 hours. A second portion of 1,3,5-triazine (146 mg, 1.81 mmol) and glacial HOAc (99 mg, 1.81 mmol) is added and the reaction mixture is maintained at reflux for an additional 16 hours. The reaction mixture is concentrated in vacuo and the crude product is diluted with water/CH_3CN and purified by reverse-phase HPLC [Buffer A: water w/0.1% TFA; Buffer B: CH_3CN w/0.1% TFA; Gradient: 0%B to 60%B over 30 min] to provide 26 mg (20%) of the title compound as a white solid which is used directly in the next reaction without further characterization.

F. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methyl ester.

To a solution containing (±)-2-[4-(4-amino-quinazolin-7-ylmethyl)-3-methoxycarbonyl-5-oxo-piperazin-1-ylmethyl]-5-chloro-indole-1-carboxylic acid tert-butyl ester (26 mg, 0.03 mmol) in CH_2Cl_2

(4 mL) is added trifluoroacetic acid (1mL) at ambient temperature. After 4 h, the reaction mixture is concentrated in vacuo and then dissolved in water/CH_3CN and purified by reverse-phase HPLC [Buffer A: water w/0.1% TFA; Buffer B: CH_3CN w/0.1% TFA; Gradient: 0%B to 60%B over 30 min] to provide 10 mg (47%) of the title compound as a white solid. ^1H NMR (300 MHz, d_6-DMSO) δ 2.62 (m, 1H), 3.05-3.51 (m, 4H), 3.59 (s, 3H), 3.81 (d, J = 14.0 Hz, 1H), 4.26 (m, 1H), 4.69 (ABq, Δ_{AB} = 310 Hz, J_{AB} = 16.4 Hz, 2H), 6.26 (s, 1H), 7.02 (dd, J = 8.6, 2.0 Hz, 1H), 7.31 (d, J = 8.6 Hz, 1H), 7.49 (d, J = 2.0 Hz, 1H), 7.52 (s, 1H), 7.61 (d, J = 8.7 Hz, 1H), 8.30 (d, J = 8.6 Hz, 1H), 8.47 (s, 1H), 8.77 (s, 1H), 9.69 (br s, 2H), 11.17 (s, 1H) ppm; MS (ion spray): m/z 479 (M+H).

EXAMPLE 785. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid.

A. (±)-1-(3-Amino-4-cyano-benzyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid.

LiOH monohydrate (380 mg, 9.06 mmol) is added at ambient temperature to a solution containing (±)-2-[4-(3-amino-4-cyano-benzyl)-3-methoxycarbonyl-5-oxo-piperazin-1-ylmethyl]-5-chloro-indole-1-carboxylic acid tert-butyl ester (1.0 g, 1.81 mmol), EXAMPLE 784, Part E, in 1:1:1 THF/MeOH/water (30 mL). After 16 h, HOAc (0.5 mL) is added and the reaction mixture is concentrated in vacuo. The residue is dissolved in CH_3CN/water and purified by reverse-phase HPLC [Buffer A: water w/0.1% TFA; Buffer B: CH_3CN w/0.1% TFA; Gradient: 0%B to 60%B over 30 min] to provide 378 mg (48%) of the title compound as a white solid. ^1H NMR (300 MHz, d_6-DMSO) δ 3.03 (m, 1H), 3.48 (m, 1H), 3.51 (ABq, Δ_{AB} = 69.2 Hz, J_{AB} = 16.4 Hz, 2H), 3.78 (d, J = 15.9 Hz, 1H), 4.05-4.09 (m, 2H), 5.04 (d, J = 15.9 Hz, 1H), 6.41 (m, 2H), 6.58 (s, 1H), 7.04 (dd, J = 8.6, 2.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.6 Hz, 1H), 7.51, d, J = 2.0 Hz, 1H) ppm; MS (ISP loop): m/z 438 (M+H).

B. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid

A solution containing (±)-1-(3-amino-4-cyano-benzyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid (200 mg, 0.30 mmol), 1,3,5-triazine (244 mg, 3.00 mmol), and glacial HOAc (180 mg, 3.00 mmol) in absolute EtOH (20 mL) is maintained at reflux for 16 hours. The reaction mixture is cooled to ambient temperature and the solid is collected on a Buchner funnel and washed with EtOH followed by diethyl ether. Oven-drying in vacuo provided 13 mg (76%) of the title compound as an off-white solid. ^1H NMR (300 MHz, d_6-DMSO) δ 2.63 (m, 1H), 3.06 (d, J = 16.4 Hz, 1H), 3.24-3.42 (m, 4H), 3.68 (ABq, Δ_{AB} = 34.5 Hz, J_{AB} = 14.1 Hz, 2H), 3.96 (m, 1H), 4.63 (ABq, Δ_{AB} = 400 Hz, J_{AB} =

15.8 Hz, 2H), 6.27 (s, 1H), 6.99 (dd, J = 8.6, 2.0 Hz, 1H), 7.29 (d, J = 8.5 Hz, 2H), 7.40 (s, 1H), 7.46 (s, 1H), 7.69 (br s, 2H), 8.10 (d, J = 8.5 Hz, 1H), 8.32 (s, 1H), 11.20 (s, 1H) ppm; MS (ion spray): m/z 465 (M+H).

EXAMPLE 786. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylamide

To a solution containing (±)-1-(4-amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid (25 mg, 0.03 mmol), EXAMPLE 785, and N-methylmorpholine (36 mg, 0.36 mmol) in anhydrous DMF (1 mL) is added methylamine hydrochloride (10 mg, 0.14 mmol) followed by HATU (40 mg, 0.10 mmol) at ambient temperature. After 3 h, the solvent is removed under high vacuum and the residue is dissolved in CH_3CN/water and purified by reverse-phase HPLC [Buffer A: water w/0.1% TFA; Buffer B: CH_3CN w/0.1% TFA; Gradient: 0%B to 60%B over 30 min] to provide 22 mg (88%) of the title compound as a white solid. ^1H NMR (300 MHz, d_6-DMSO) δ 2.57 (d, J = 4.4 Hz, 3H), 2.70 (m, 1H), 3.0 (m, 1H), 3.66 (d, J = 14.2 Hz, 1H), 3.77 (d, J = 14.2 Hz, 1H), 3.85 (m, 1H), 4.03 (d, J = 16.3 Hz, 1H), 5.18 (d, J = 16.3 Hz, 1H), 6.28 (s, 1H), 7.02 (dd, J = 8.5, 2.0 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 7.49 (d, J = 2.0 Hz, 1H), 7.51 (s, 1H), 7.58 (d, J = 8.6 Hz, 1H), 7.97 (m, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.79 (s, 1H), 9.72 (br s, 2H), 11.18 (s, 1H) ppm; MS (ISP loop): m/z 478 (M+H).

Table 1: Amide Analogs Derived From C-6 Carboxylic Acid.

Example #	Name	m/z [M+H]
787	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid ethylamide	492
788	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide	492
789	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid benzylamide	554
790	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid (2-hydroxy-ethyl)-amide	508
791	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid bis-(2-hydroxy-ethyl)-amide	552

792	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-(morpholine-4-carbonyl)-piperazin-2-one	534
793	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylcarbamoylmethyl-amide	535

The following compounds are prepared using the procedures described above.

Example #	Name	m/z [M+H]
794	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid	458
795	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid methyl ester	472
796	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid amide	457
797	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid ethylamide	458
798	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-(4-methyl-piperazine-1-carbonyl)-piperazin-2-one	540

EXAMPLE 799. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester.

A solution containing (±)-1-(3-amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester (42 mg, 0.08 mmol), EXAMPLE 99, 1,3,5-triazine (40 mg, 0.48 mmol), and glacial HOAc (30 mg, 0.48 mmol) in absolute EtOH (1 mL) is maintained at reflux for 16 hours. The reaction mixture is concentrated and then dissolved in water/CH_3CN and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 17 mg (32%) of the title compound as a white solid.

^{1}H NMR (300 MHz, d_6-DMSO) δ 3.47 (m, 1H), 3.67 (s, 3H), 3.71 (d, J = 16.1 Hz, 1H), 4.00 (d, J = 16.5 Hz, 1H), 4.05 (m, 1H), 4.52 (m, 1H), 4.72 (ABq, Δ_{AB} = 248 Hz, J_{AB} = 16.5 Hz, 2H), 7.57 (m, 2H), 8.05 (d, J = 8.6 Hz, 1H), 8.20 (s, 1H), 8.23 (d, J = 8.5 Hz, 1H), 8.35 (d, J = 1.9 Hz, 1H), 8.49 (s, 1H), 8.72 (s, 1H), 9.57 (br s, 2H) ppm; MS (ion spray): m/z 546 (M+H).

EXAMPLE 800. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid.

Water (1 mL) is added to a solution containing (±)-1-(4-amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester (20 mg, 0.03 mmol), EXAMPLE 799, in a 1:1 mixture of THF/MeOH (2 mL). At ambient temperature, LiOH monohydrate (15 mg, 0.35 mmol) is then added. After 16 h, the reaction mixture is diluted with water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 12 mg (63%) of the title compound as a white solid. ^{1}H NMR (300 MHz, d_6-DMSO) δ 3.69 (d, J = 16.0 Hz, 1H), 3.97 (d, J = 16.0 Hz, 1H), 4.08 (d, J = 11.7 Hz, 1H), 4.18 (d, J =16.2 Hz, 1H), 4.31 (d, J = 2.7 Hz, 1H), 5.20 (d, J =16.2 Hz, 1H), 7.47 (d, J = 8.7 Hz, 1H), 7.52 (s, 1H), 7.58 (dd, J = 8.6, 1.9 Hz, 1H), 8.06 (d, J = 8.7 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 8.19 (s, 1H), 8.34 (d, J = 1.9 Hz, 1H), 8.54 (s, 1H), 8.77 (br s, 1H) ppm; MS (ion spray): m/z 532 (M+H).

EXAMPLE 801. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid amide

To a mixture containing (±)-1-(4-amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid (45 mg, 0.08 mmol), EXAMPLE 800, N-methylmorpholine (18 mg, 0.18 mmol), and HATU (35 mg, 0.09 mmol) in anhydrous DMF (1 mL) is added NH_3 (7N in MeOH, 2 drops, approx. 0.5 mmol). The heterogeneous mixture is stirred 16 h at ambient temprature and then concentrated to dryness. The residue is dissolved in water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 25 mg (46%) of the title compound as a white solid. ^{1}H NMR (300 MHz, d_6-DMSO) δ 3.63 (d, J = 16.0 Hz, 1H), 4.01 (m, 4H), 5.17 (d, J = 16.6 Hz, 1H), 7.58 (m, 3H), 8.08 (d, J = 8.6 Hz, 1H), 8.17 (s, 1H), 8.26 (d, J = 8.6 Hz, 1H), 8.34 (d, J = 1.9 Hz, 1H), 8.74 (s, 1H), 9.63 (br s, 2H) ppm; MS (ISP loop): m/z 531 (M+H).

The following compounds are prepared using the procedures described above.

Example #	Name	m/z [M+H]
802	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethyl ester	560
803	(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid	531
804	(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-	544

	benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide	
805	(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide	558
806	(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide	558
807	(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one	600

EXAMPLE 808. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester.

A. (±)-1-[3-(Benzhydrylidene-amino)-4-cyano-benzyl]-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester.

To a solution containing (±)-1-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-6-oxo-piperazine-2-carboxylic acid methyl ester (1.17 g, 2.6 mmol), EXAMPLE 784, Part B, 5-chlorothiophen-2-yloxyacetic acid (0.5 g, 2.6 mmol), EXAMPLE 24,and N-methylmorpholine (0.58 g, 5.72 mmol) in anhydrous DMF (10 mL) is added HATU (1.09 g, 2.86 mmol) at ambient temperature. After 1.5 h, the reaction mixture is diluted with CH_2Cl_2 (100 mL) and aqueous $NaHCO_3$ (100 mL) and the layers are separated. The aqueous phase is washed four times with CH_2Cl_2 (100 mL) and the combined organic phase is washed once with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude amide is purified by flash silica gel chromatography (hexane/EtOAc, 4:1 to 1:2) to afford 1.5 g of the title compound which is used directly in the next reaction. ^1H NMR (300 MHz, $CDCl_3$, ~2:1 mixture of rotomers) major rotomer: δ 3.55 (d, J = 15.2 Hz, 1H), 3.60 (m, 1H), 3.69 (m, 5H), 4.37 (d, J = 17.7 Hz, 1H), 4.62 (m, 2H), 4.79 (d, J = 13.3 Hz, 1H), 5.35 (d, J = 15.2 Hz, 1H), 6.05 (d, J = 3.9 Hz, 1H), 6.52 (m. 2H), 6.84 (d, J = 8.1 Hz, 1H), 7.18-7.49 (m, 11H), 7.76 (m, 1H) ppm; MS (ISP loop): m/z 627 (M+H).

B. (±)-1-(3-Amino-4-cyano-benzyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester.

Concentrated HCl (12M, 0.5 mL) is added at 0 °C to a solution containing (±)-1-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester (1.5 g, 2.39 mmol) in 4:1 MeOH/THF (25 mL). After 1.5 h, the reaction

mixture is concentrated to dryness and then partitioned between a 1:1 mixture of EtOAc/aqueous $NaHCO_3$ (200 mL) and the layers are separated. The aqueous phase is extracted with EtOAc and then the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is chromatographed on silica gel (hexane/EtOAc, 4:1 to 1:2) to provide 934 mg (84%, two steps) of the title compound. ^1H NMR (300 MHz, $CDCl_3$, ~2:1 mixture of rotomers) selected peaks: δ 3.16 (app. dd, J 14.0, 3.8 Hz, 1H), 3.68 (s, 3H), 3.96 (app. dd, J = 3.8, 2.0 Hz, 1H), 4.17 (d, J = 17.7 Hz, 1H), 4.45 (br s, 2H), 4.62 (m, 2H), 4.87 (d, J = 14.1 Hz, 1H), 5.21 (d, J = 15.1 Hz, 1H), 6.07 (m, 1H), 6.51 (d, J = 3.8 Hz, 1H), 6.57 (d, J = 7.9 Hz, 1H), 6.62 (br s, 1H), 7.35 (d, J = 7.9 Hz, 1H) ppm; MS (ISP loop): m/z 463 (M+H).

C. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester.

A solution containing (±)-1-(3-amino-4-cyano-benzyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester (110 mg, 0.25 mmol), 1,3,5-triazine (207 mg, 2.55 mmol), and glacial HOAc (157 mg, 2.55 mmol) in absolute EtOH (5 mL) is maintained at reflux for 16 hours. The reaction mixture is concentrated to dryness and then purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 50 mg (32%) of the title compound as a white solid. ^1H NMR (300 MHz, d_6-DMSO) δ 3.34-3.89 (m, 2H), 3.60 (s, 3H), 4.14-4.54 (m, 3H), 4.64 (br d, J = 14.4 Hz, 1H), 4.78-5.11 (m, 3H), 6.19 (d, J = 4.1 Hz, 1H), 6.73 (d, J = 4.1 Hz, 1H), 7.64 (s, 1H), 7.65 (d, J = 9.0 Hz, 1H), 8.34 (d, J = 9.0 Hz, 1H), 8.79 (s, 1H), 9.71 (br s, 2H) ppm; MS (ion spray): m/z 490 (M+H).

EXAMPLE 809. (±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methylamide.

Water (1 mL) is added to a solution containing (±)-1-(4-amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester (20 mg, 0.03 mmol), EXAMPLE 808, in a 1:1 mixture of THF/MeOH (2 mL). At ambient temperature, LiOH monohydrate (3 mg, 0.07 mmol) is then added. After 16 h, the reaction mixture is diluted with water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 25 mg (>100 %) of the associated acid as a white solid after lyophilization which is used directly in the next reaction. To a mixture containing (+/-)-1-(4-amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid (12 mg, 0.02 mmol), N-methylmorpholine (19 mg, 0.19 mmol), and HATU (22 mg, 0.05 mmol) in anhydrous DMF (1 mL) is added $MeNH_2$ hydrochloride (5 mg, 0.19 mmol). The reaction mixture is stirred 1 h at ambient temperature and then concentrated to dryness. The residue is dissolved in water

and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 7 mg (58%) of the title compound as a white solid. ^{1}H NMR (300 MHz, d_6-DMSO) mixture of rotamers: δ 2.51 (m, 3H), 4.07-4.54 (m, 6H), 4.87 (m, 2H), 5.10 (m, 1H), 6.18 (m, 1H), 6.74 (m, 1H), 7.62 (m, 2H), 8.06 (br s, 1H), 8.32 (br d, J = 8.8 Hz, 1H), 8.78 (s, 1H), 9.61 (br s, 2H) ppm; MS (ISP loop): 489 (M+H).

The following compound is prepared using the procedures described above.

Example #	Name	m/z [M+H]
810	(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid ethylamide	503

EXAMPLE 811. (+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid.

Water (0.5 mL) is added to a solution containing (±)-1-(3-amino-4-cyano-benzyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester (35 mg, 0.08 mmol), EXAMPLE 808, Part B, in a 1:1 mixture of THF/MeOH (1 mL). At ambient temperature, LiOH monohydrate (4 mg, 0.10 mmol) is then added. After 16 h, an additional portion of LiOH monohydrate (4 mg, 0.10 mmol) is added and the reaction mixture is stirred for another 2 h then diluted with water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 40 mg (95%) of the associated acid as a white solid after lyophilization which is used directly in the next reaction. MS (ISP loop): m/z 449 (M+H).

A solution containing (+/-)-1-(3-amino-4-cyano-benzyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid (20 mg, 0.03 mmol), 1,3,5-triazine (28 mg, 0.34 mmol), and glacial HOAc (20 mg, 0.34 mmol) in absolute EtOH (6 mL) is maintained at reflux for 16 hours. The reaction mixture is concentrated to dryness and then purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 60% B over 30 min] to provide 15 mg (75%) of the title compound as a white solid. ^{1}H NMR (300 MHz, d_6-DMSO) δ 3.75-4.38 (m, 5H), 4.67 (d, J = 14.8 Hz, 1H), 4.79 (d, J = 15.3 Hz, 1H), 4.95 (m, 1H), 5.09 (br d, J = 16.0 Hz, 1H), 6.18 (m, 1H), 6.71 (m, 1H), 7.64 (m, 2H), 8.31 (d, J = 8.5 Hz, 1H), 8.75 (s, 1H), 9.64 (br s, 2H) ppm; MS (ISP loop): m/z 476 (M+H).

EXAMPLE 812. 4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. 2-(2-Oxo-4-prop-2-ynyl-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

A solution containing 2-(2-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (4.3 g, 13.0 mmol), EXAMPLE 69, in CH_3CN (250 mL) is cooled to 0°C. Potassium carbonate (1.98 g, 14.3 mmol) is added to the reaction mixture followed by propargyl bromide (1.55g, 13.0 mmol). The mixture is slowly warmed to ambient temperature and maintained until complete consumption of starting material is observed by TLC (approx. 8 h). The mixture is concentrated to dryness and then partitioned between aqueous $NaHCO_3$ (200 mL) and CH_2Cl_2 (200 mL) and the layers are separated. The aqueous phase is extracted twice with CH_2Cl_2 (100 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 5% MeOH/CH_2Cl_2) to provide 3.38 g (70%) of the title compound as a pale yellow solid. ^1H NMR (300 MHz, $CDCl_3$) δ 1.69 (s, 9H), 2.34 (t, J = 2.4 Hz, 1H), 2.89 (m, 2H), 3.42 (s, 2H), 3.45 (d, J = 2.4 Hz, 2H), 3.52 (m, 2H), 4.95 (d, J = 1.4 Hz, 2H), 6.42 (br s, 1H), 7.88 (dd, J = 5.8, 0.8 Hz, 1H), 8.41 (d, J = 5.8 Hz, 1H), 8.78 (d, J = 0.8 Hz, 1H) ppm; MS (EI): m/z 368 (M+).

B. 4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

To a solution containing 2-(2-oxo-4-prop-2-ynyl-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (1.3 g, 3.53 mmol) in CH_2Cl_2 (100 mL) is added TFA (20 mL) at 0 °C. After 6 h, the reaction mixture is concentrated to dryness and then partitioned between aqueous $NaHCO_3$ (500 mL) and CH_2Cl_2 (200 mL) and the layers are separated. The aqueous phase is extracted four times with CH_2Cl_2 (100 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 10% MeOH/CH_2Cl_2) to provide 616 mg (65%) of the title compound as a pale yellow solid. ^1H NMR (300 MHz, $CDCl_3$) δ 2.27 (app t, J = 2.4 Hz, 1H), 2.76 (m, 2H), 3.33 (s, 2H), 3.83 (d, J = 2.4 Hz, 2H), 3.45 (m, 2H), 4.57 (s, 2H), 6.47 (s, 1H), 7.23 (d, J = 5.7 Hz, 1H), 8.28 (d, J = 5.7 Hz, 1H), 8.85 (d, J = 0.9 Hz, 1H), 9.34 (br s, 1H) ppm; MS (EI): m/z 268 (M+).

EXAMPLE 813. 1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. 2-{4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-prop-2-ynyl]-2-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

A solution containing 2-(2-oxo-4-prop-2-ynyl-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (100 mg, 0.27 mmol), EXAMPLE 812, (3-iodo-pyridin-4-yl)-carbamic acid tert-butyl ester (87 mg, 0.27 mmol), EXAMPLE 69, Part B, Et_3N (110 mg, 1.08 mmol),

$(Ph_3P)_4PdCl_2$ (10 mg, 0.013 mmol), and CuI (1 mg, 0.008 mmol) in anhydrous DMF (5 mL) is stirred at ambient temperature. After 5 h, the reaction mixture is diluted with EtOAc (50 mL) and water (50 mL) and the layers are separated. The aqueous layer is extracted twice with EtOAc (25 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue is purified by flash silica gel chromatography (CH_2Cl_2 to 10% MeOH CH_2Cl_2) to provide 77 mg (51%) of SC41 as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$, ~2:1mixture of rotamers) major rotamer: δ 1.53 (s, 9H), 1.69 (s, 9H), 2.98 (m, 2H), 3.49 (s, 2H), 3.56 (m, 2H), 3.78 (s, 2H), 4.98 (s, 2H), 6.43 (s, 1H), 7.89 (m, 1H), 8.09 (m, 2H), 8.34 (m, 1H), 8.41 (m, 1H), 8.75 (m, 1H) ppm; MS (ISP loop): m/z 561 (M+H).

B. 2-[4-(1-tert-Butoxycarbonyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester.

1,8-Diazabicyclo[5.4.0]undec-7-ene (42 mg, 0.27 mmol) is added to a suspension containing 2-{4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-prop-2-ynyl]-2-oxo-piperazin-1-ylmethyl}-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (SC41, 77 mg, 0.14 mmol) in anhydrous CH_3CN (10 mL) and the mixture is warmed to 50 °C. After 4 h, the reaction mixture is concentrated to dryness and the residue is partitioned between CH_2Cl_2 (50 mL) and water (50 mL) and the layers are separated. The aqueous layer is extracted twice with CH_2Cl_2 (25 mL) and the combined organic phase is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to provide 85 mg of SC42 as a crude solid which is used directly without further purification. ^1H NMR (300 MHz, $CDCl_3$) δ 1.68 (s, 9H), 1.70 (s, 9H), 2.91 (m, 2H), 3.41 (s, 2H), 3.49 (m, 2H), 4.26 (s, 2H), 4.95 (d, J = 1.1 Hz, 2H), 6.39 (d, J = 0.7 Hz, 1H), 6.68 (d, J = 0.7 Hz, 1H), 7.86 (m, 1H), 8.41 (m, 1H), 8.76 (br s, 1H), 8.82 (br s, 1H) ppm; MS (EI): m/z 561 (M+H).

C. 1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

To a solution containing 2-[4-(1-tert-Butoxycarbonyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester (85 mg, 0.14mmol) in CH_2Cl_2 (5 mL) is added TFA (1 mL) at 0 °C and the solution is allowed to slowly warm to ambient temperature. After 16 h, the reaction mixture is concentrated to dryness, diluted with water and purified by reverse-phase HPLC [Buffer A: water w/ 0.1% TFA; Buffer B: CH3CN w/ 0.1% TFA; Gradient: 0% B to 45% B over 30 min] to provide 35 mg (36%, two steps) of SC43 as a pale yellow, lyophilized solid. ^1H NMR (300 MHz, d_6-DMSO) δ 2.80 (m, 2H), 3.25 (s, 2H), 3.37 (m, 2H), 3.93 (s, 2H), 4.76 (s, 2H), 6.88 (s, 1H), 6.94 (s, 1H), 7.85 (d, J = 6.6 Hz, 1H), 7.89 (d, J = 6.6 Hz, 1H), 8.37 (d, J = 6.7 Hz, 1H), 8.38 (d, J = 6.7 Hz, 1H), 9.17 (s, 1H), 9.19 (s, 1H), 12.80 (s, 1H), 12.96 (s, 1H), 14.91 (br s, 2H) ppm; MS (ion spray): m/z 361 (M+H). $C_{23}H_{25}ClN_4OS$ MS m/z: 441,443.

EXAMPLE 814. 2-Amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile.

A. {1-[3-benzhydrylidene-amino)-4-cyano-benzyl]-2-oxo-piperidin-4-yl}-acetic acid ethyl ester:

Sodium hydride (140 mg, 3.51 mmol) is added to a cooled solution of (2-oxo-piperidin-4-yl)-acetic acid ethyl ester (500 mg, 2.70 mmol) in 10 mL of THF. After stirring for forty five minutes, 2-(benzhydrylidene-amino)-4-bromomethyl-benzonitrile (1.43 g, 3.82 mmol), EXAMPLE 13, is added, and the reaction is left to stir overnight. THF is removed, and the residue is taken up in 250 mL of ethyl acetate. Excess sodium hydride is quenched with 5 mL of water, and normal aqueous work-up followed. The crude product is chromatographed on silica gel (50% EtOAc/Hexane) to give{1-[3-benzhydrylidene-amino)-4-cyano-benzyl]-2-oxo-piperidin-4-yl}-acetic acid ethyl ester (732 mg, 57%)as a light yellow solid. $C_{30}H_{29}N_3O_3$ MS m/z: 480, 482. Anal cald. for $C_{30}H_{29}N_3O_3$: C,75.13; H, 6.09; N, 8.76. Found C, 73.01; H, 6.02; N, 8.46.

B. {1-[3-benzhydrylidene-amino)-4-cyano-benzyl]-2-oxo-piperidin-4-yl}-acetic acid

To a solution of {1-[3-benzhydrylidene-amino)-4-cyano-benzyl]-2-oxo-piperidin-4-yl}-acetic acid ethyl ester (732 mg, 1.53 mmol) in 5 mL of THF is added 1N sodium hydroxide (1.53 ml, 1.53 mmol). After stirring for four hours, the THF is removed and EtOAc (500 mL) is added. The reaction mixture is acidified to a pH of 6 and normal aqueous work-up followed. The desired carboxylic acid (571 mg, 83% yield) is isolated as a white solid.

C. N-(2-amino-5-chloro-phenyl)-2-{1-[3-(benzhydrylidene-amino)-4-cyano-benyl]-2-oxo-piperidin-4-yl}-acetamide

To a slurry of the {1-[3-(benzhydrylidene-amino)-4-cyano-benzyl]-2-oxo-piperidin-4-yl}-acetic acid (190 mg, 0.422 mmol) in THF (5 mL) and methylene chloride (3 mL) is added triethylamine (0.09 ml, 0.633 mmol). The solution is cooled to 0 °C , and 1M isopropyl chloroformate in toluene (0.422 mL, 0.422 mmol) is added. The homogenous mixture is allowed to warm to room temperature, and 4-chloro-1,2-phenylene-diamine (150 mg, 1.06 mmol) is added. The reaction is stirred at room temperature overnight. The volatile solvents are removed, and the resulting residue is chromatographed (SiO_2, 5%MeOH/EtOAc) to give N-(2-amino-5-chloro-phenyl)-2-{1-[3-(benzhydrylidene-amino)-4-cyano-benyl]-2-oxo-piperidin-4-yl}-acetamide (200 mg, 82% yield). $C_{34}H_{30}ClN_5O_2$ MS m/z: 576, 578.

D. 2-(Benzhydrylidene-amino)-4-[4-(6-cloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl}-benzonitrile

The acetamide (200 mg, 0.35 mmol) is dissolved in 2 mL of acetic acid and refluxed for three hours. The acetic acid is removed, and the residue taken up in ethyl acetate and washed with saturated sodium bicarbonate. Concentration of the solvent afforded 2-(benzhydrylidene-amino)-4-[4-(6-cloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl}-benzonitrile (200 mg, 100% yield) which is used without further purification. $C_{34}H_{28}ClN_5O_5$ MS m/z:+ 558, 560.

E. 2-Amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile hydrochloric acid salt

The above benzonitrile (220 mg, 0.36 mmol) is dissolved in 5 ml of methanol. Hydrochloric acid is bubbled into the ice-cooled methanol solution followed by three drops of water. After stirring at room temperature for one hour, the MeOH is removed. The resulting white solid is titurated with EtOAc. After drying under high vacuum, 2-amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile hydrochloric acid salt (145.6 mg, 87% yield) is obtained as a white solid. $C_{21}H_{20}ClN_5O$: MS m/z: 394,396.

EXAMPLE 815. 4-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzamidine

Hydrochloric acid is bubbled into an ice cooled solution of 4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile (127 mg, 0.336 mmol) in 10 mL of methanol. The solution also contained 3Å molecular sieves. The reaction is stored at -30 for forty-eight hours. The methanol is condensed on the rotovap. Fresh methanol (15 mL) is added followed by a stream of ammonia gas. The reaction is heated to reflux for two and half hours. The reaction mixture is filtered at room temperature. Methanol is removed from the mother liquor. The resulting residue is purified by reverse phase HPLC (0-50 % ACN/H_2O). The product is isolated as a white solid with a melting point of 105-110 °C . $C_{21}H_{22}ClN_5O$ MS m/z: 396,398. Anal. cald. for $C_{21}H_{22}ClN_5O \cdot 2C_2HF_3O_2$: C, 48.13; H, 3.88; N,11.22. Found: C, 45.05; H, 3.52; N, 9.89.

EXAMPLE 816. 1-(4-Amino-quinazolin-7-ylmethly)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperidin-2-one.

To a solution of 2-Amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile hydrochloric acid salt (143 mg, 0.308 mmol), EXAMPLE 814, Part E, in 2 mL of ethanol is added triethylamine (0.05 mL, 0.366 mmol), glacial acetic acid (0.02mL, 0.366 mmol) and triazine (15 mg, 0.183 mmol). The resulting mixture is refluxed overnight. The volatile solvents are removed on the rotovap, and the residue is purified by reverse phase HPLC (0 - 50% Acetonitrile/H_2O). The desired product (110 mg, 55% yield) is isolated as a white powder with a melting point of 128-132

°C . $C_{22}H_{21}ClN_6O$ MS m/z: 421, 423. Anal. calcd. for $C_{22}H_{21}ClN_6O$: C, 48.12; H, 3.57; N, 12.95. Found: C, 45.79; H, 3.68; N, 11.94. H NMR (CD_3OD) δ: 8.67 (s, 1H); 8.31 (d, 1H, J = 4.0 Hz); 7.83-7.55 (m, 5H); 4.93-4.73 (m, 2H); 3.48-3.42 (m, 2H); 3.31-3.21 (m, 2H); 2.71-2.58 (m, 2H); 2.43-2.33 (m, 1H); 2.07- 2.01 (m, 1H); 1.82 - 1.69 (m, 1H).

EXAMPLE 817. 4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-1-(2,4-diamino-quinazolin-7-ylmethyl)-piperidin-2-one

2-Amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile hydrochloric acid salt (70 mg, 0.15 mmol), EXAMPLE 814, Part E, pyridine (1.0 mL) and freshly made chloroformamide hydrochloride (150 mg, 1.33 mmol) are placed in a sealed tube and heated to 200 °C . The resulting mixture is heated for twenty four hours. The crude reaction mixture is directly purified by reverse phase HPLC (0-50% ACN/H_2O). The product (53 mg, 45% yield) is isolated as a tanish solid. $C_{22}H_{22}ClN_7O$ MS m/z: 436,438. Anal. calcd. for $C_{22}H_{22}ClN_7O$: C, 43.23; H, 3.24; N, 12.60. Found: C, 43.16; H, 3.44; N, 13.40.

EXAMPLE 818. 1-(4-Amino-2-methyl-quinazolin-7-ylmethly)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperidin-2-one.

A stream of hydrogen chloride gas is bubbled intermittently through an ice-cold mixture of 2-amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile hydrochloric acid salt (57 mg, 0.123 mmol), EXAMPLE 814, Part E, and acetonitrile (0.03 mL, 0.93 mmol) in 1.5 mL of dioxane for six hours. The dioxane is removed; the residue is purified by reverse phase HPLC (0-40 % ACN/H_2O). The desired product (9.5 mg, 12% yield) is isolated as a clear wax. $C_{23}H_{23}ClN_6O$ MS m/z : 435, 437.

The following compounds are prepared using the methods described above.

Example #	Name	m/z [M+H]
819	(3S, 5R)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine	441, 443
820	(3S,5S)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine	441, 443
821	4-{4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl}-benzamidine	431, 433
822	(3R,5S)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine	441, 443

EXAMPLE 823. 2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]acetamide.

A. 4-tert-Butoxycarbonylmethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester.

To a solution of 3-oxopiperazine-1-carboxylic acid benzyl ester (4.68g, 20mmol) in 20 mL of DMF at) 0°C is added sodium hydride (60%, 880 mg, 22 mmol). The suspension is stirred at ambient temperature for one t-butyl bromoacetate (4.68 g, 24 mmol) is added. The resulting mixture is stirred at ambient temperature overnight. After dilution with ethyl acetate (200 mL), the mixture is washed with brine (3 x 50 mL). The crude residue obtained from concentration of the organic phase is chromatographied on silica gel (30% ethyl acetate/Hexane) to give 5.57 g (80%) of 4-tert-butoxycarbonylmethyl-3-oxopiperazine-1-carboxylic acid benzyl ester as a white solid.

B. (2-Oxo-piperazin-1-yl)acetic acid tert-butyl ester.

4-tert-Butoxycarbonylmethyl-3-oxopiperazine-1-carboxylic acid benzyl ester (2.0g, 5.75 mmol) is dissolved in 20 mL of methanol and 2 mL of acetic acid. Palladium (5%) on carbon (100 mg) is added, and the reaction mixture is stirred in an atmosphere of hydrogen overnight. The mixture is filtered and concentrated. Ethyl acetate is added, and the mixture is neutralized to pH 7 using 1N NaOH. The organic layer is concentrated to give (2-oxo-piperazin-1-yl)acetic acid tert-butyl ester (1.22g).

C. [4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazine-1-yl]acetic acid tert-butyl ester.

To a solution of (2-oxo-piperazin-1-yl)acetic acid tert-butyl ester (1.22 g, 5.7 mmol) in 10 ml of methylene chloride is added triethylamine (1.2 mL, 8.55 mmol) and 6-chlorobenzothiophenesulfonyl chloride (1.52 g, 5.7 mmol). The reaction mixture is stirred overnight at ambient temperature. Flash column chromatography (50 % ethyl acetate / hexane) affords 2.3 g (92%) of [4-(6-chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazine-1-yl]acetic acid tert-butyl ester.

D. [4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazine-1-yl]-acetic acid.

[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazine-1-yl]acetic acid tert-butyl ester (500 mg, 1.13 mmol) is dissolved in 1 mL of trifluoroacetic acid and 3 mL of CH_2Cl_2. The solvents are azeotropically removed with toluene. [4-(6-chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazine-1-yl]acetic acid (438 mg) is isolated as a white solid.\

E. 2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]acetamide.

To a slurry of [4-(6-chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazine-1-yl]acetic acid (47 mg, 0.12 mmol) in 2 mL of tetrahydrofuran is added Et_3N (0.025 mL, 0.18 mmol). The mixture is cooled to 0°C, and 1M solution of isopropyl chloroformate in toluene (0.12 mL, 0.12mmol) is added. The mixture is stirred for fifteen minutes and histamine (13.3 mg, 0.12 mmol) is added. The mixture is stirred overnight at room temperature. Reverse phase HPLC ($AcCN/H_2O$/TFA) affords 2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]acetamide trifluoroacetic acid salt (17 mg, 25%) as a solid. mp 77-82°C; MS m/z 482 (M+H).

The followin compounds are prepared from the appropriate starting materials using the method of EXAMPLE 823.

Example #	Name	m/z [M+H]
824	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-4-yl-acetamide	465, 467
825	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-3-ylmethyl-acetamide	479, 481
826	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-piperidin-4-yl-acetamide	471, 473
827	N-(1-Carbamimidoyl-piperidin-4-yl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide	513, 515
828	5-(2-{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetylamino}-ethyl)-imidazole-1-carboxylic acid ethyl ester	554, 556
829	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyrimidin-4-yl-acetamide	466, 468
830	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-phenyl-acetamide	464, 466
831	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(9H-purin-6-yl)-acetamide	506, 508
832	N-(4-Amino-2-methyl-pyrimidin-5-ylmethyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide	509, 511
833	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-acetamide	496, 498
834	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-	496, 498

	N-[2-(1-methyl-1H-imidazol-4-yl)-ethyl]-acetamide	
835	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-4-yl-ethyl)-acetamide	493, 495
836	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(3-methyl-3H-imidazol-4-yl)-ethyl]-acetamide	496, 498
837	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-2-yl-ethyl)-acetamide	493, 495
838	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-3-yl-ethyl)-acetamide	493, 495
839	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-imidazol-1-yl-ethyl)-acetamide	482, 484
840	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(1-methyl-1H-pyrrol-2-yl)-ethyl]-acetamide	495, 497
841	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(5-methyl-1H-imidazol-4-yl)-ethyl]-acetamide	496, 498
842	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(4-dimethylamino-[1,3,5]triazin-2-yl)-acetamide	510, 512
843	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-pyridin-4-yl-acetamide	479, 481
844	N-[2-(2-Amino-pyridin-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide	508, 510
845	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(4-methyl-thiazol-5-yl)-ethyl]-acetamide	513, 515
846	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-thiazol-4-yl-ethyl)-acetamide	499, 501
847	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-guanidino-propyl)-acetamide trifluoroacetic acid salt	487, 489
848	N-(3-Amino-propyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide	445, 447
849	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-mercapto-1H-imidazol-4-yl)-ethyl]-acetamide	514, 516
850	N-[2-(2-Amino-thiazol-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide	514, 516

851	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-(2-pyridin-4-yl-ethyl)-acetamide	507, 509
852	2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-methylsulfanyl-1H-imidazol-4-yl)-ethyl]-acetamide	528, 530

EXAMPLE 853. 4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[3-(3H-imidazol-4-yl)-propyl]-piperazin-2-one.

A. 3-Oxo-4-[3-(3-trityl-3H-imidazol-4-yl)-allyl-piperazine-1-carboxylic acid benzyl ester.

3-Oxo-piperazin-1-carboxylic acid benzyl ester (702 mg, 3.0 mmol) is dissolved in dimethylformamide (10 mL) and cooled to 0°C . Sodium hydride (60%, 148 mg, 3.7 mmol) is added, followed by the addition of 5-(3-chloro-propenyl)-1-trityl-1H-imidazole (473 mg, 1.2 mmol). The resulting mixture is left to stir at room temperature overnight. Most of the dimethylformamide is removed on the high vacuum. The reaction mixture is diluted with ethyl acetate (250 mL) and quenched with water. The two layers are separated and ethyl acetate (2x 100 mL) is used to extract and dried over magnesium sulfate. The residue after filtration and concentration is chromatographed on silica gel (50% EtOAc/hexane) to give 3-oxo-4-[3-(3-trityl-3H-imidazol-4-yl)-allyl-piperazine-1-carboxylic acid benzyl ester (360 mg) as the desired product.

B. 4-[3-(3-tert-Butoxycarbonyl-3H-imidazol-4-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid benzyl ester.

3-Oxo-4-[3-(3-trityl-3H-imidazol-4-yl)-allyl-piperazine-1-carboxylic acid benzyl ester (360 mg, 0.62 mmol) is stirred vigorously in a 30% solution of trifluoroacetic acid and methylene chloride (10 mL). After stirring for three hours, the trityl group is removed. The volatile solvents are removed in vacuo, and the crude product is taken-up in methylene chloride (10 mL). Pyridine (0.5 ml) and Di-tert-butyl dicarbonate (176 mg, 0.81 mmol) is added to the solution, and the resulting mixture is left to stir overnight. The reaction mixture is condensed and purified by flash column (SiO_2, 20% EtOAc/Hexane) to give 4-[3-(3-tert-butoxycarbonyl-3H-imidazol-4-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid benzyl ester (100 mg).

C. 5-{3-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-propyl}-imidazol-1-carboxylic acid tert-butyl ester.

Palladium on carbon (10 %, 15 mg) is added to a solution of 4-[3-(3-tert-butoxycarbonyl-3H-imidazol-4-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid benzyl ester (50 mg, 0.114 mmol) in 5 mL of methanol. The reaction mixture is left to stir in an atmosphere of hydrogen overnight. The palladium is

filtered off, and the volatile solvents are removed on the rotovap. The crude product (50 mg, 0.114 mmol) is redissolved in methylene chloride (5 mL). Triethylamine (0.06 ml, 0.43 mmol) 6-chloro-benzo[b]thiophene-2-sulfonyl chloride (39 mg, 0.15 mmol) is added, and the resulting mixture is stirred overnight. The crude product is directly purified by flash column (SiO_2, 30% EtOAc/Hexane) to afford 5-{3-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-propyl}-imidazol-1-carboxylic acid tert-butyl ester (30 mg).

D. 4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[3-(3H-imidazol-4-yl)-propyl]-piperazin-2-one:

5-{3-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-propyl}-imidazol-1-carboxylic acid tert-butyl ester (30 mg, 0.055 mmol) is stirred vigorously in a 30 % solution of trifluoroacetic acid and methylene chloride (2 mL). The reaction is complete after stirring for three hours. The volatile solvents are removed on the rotovap, and the gummy solid is titurated with ether several times to afford 4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-1-[3-(3H-imidazol-4-yl)-propyl]-piperazin-2-one trifluoroacetic acid salt (30 mg) as a yellow solid. $C_{18}H_{19}ClN_4O_3S_2$ (m/z)+: 439, 441. Anal cald. for $C_{18}H_{19}ClN_4O_3S_2 \cdot C_2HF_3O_2$: C, 43.44; H, 3.65; N, 10.13. Found C, 42.03; H, 3.55; N, 8.26.

The following compounds are prepared using the methods described above.

Example #	Name	m/z [M+H]
854	4-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-piperidine-1-carboxamidine	470, 472 Cl pattern
855	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-piperazin-1-yl-propyl)-piperazin-2-one	457, 459 Cl pattern
856	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-pyridin-4-yl-propyl)-piperazin-2-one	450, 452 Cl pattern
857	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-piperidin-4-yl-butyl)-piperazin-2-one	470, 472 Cl pattern
858	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(2-piperidin-4-yl-ethyl)-piperazin-2-one	442
859	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-piperidin-4-yl-propyl)-piperazin-2-one	456

EXAMPLE 860. 4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one.

A. 3-Methoxymethyl-4-[4-(6-methoxy-pyridin-3-yl)-benzyl]-3-oxo-piperazine-1-carboxylic acid benzyl ester.

The title compound is prepared by the method in EXAMPLE 66, Part A, substituting 5-(4-bromomethyl-phenyl)-2-methoxy-pyridine for 4-bromomethyl tolynitrile and 2-methoxymethyl-3oxopiperazin-1-carboxylic acid benzyl ester for 3-oxopiperazin-1-carboxylic acid benzyl ester. MS (ISP) m/z 476, (M+H).

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one

The title compound is prepared by deprotecting 3-methoxymethyl-4-[4-(6-methoxy-pyridin-3-yl)-benzyl]-3-oxo-piperazine-1-carboxylic acid benzyl ester as described in EXAMPLE 75, Part C. The crude amine is then coupled as described in EXAMPLE 123 with 3-(5-chloro-thiophen-2-yl)-(E)-acrylic acid, EXAMPLE 25. MS (ISP) m/z 516, 518, (M+H), Cl pattern.

The following compounds are prepared according to the method of Example 860.

Example #	Name	m/z [M+H]
861	4'-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-biphenyl-2-carbonitrile	522, 524 Cl pattern
862	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-chloro-3-hydroxy-benzyl)-piperazin-2-one	471, 473 Cl pattern
863	1-Benzyl-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one	421,423 Cl pattern
864	4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-chloro-benzyl)-piperazin-2-one	455, 457 Cl pattern
865	4-[(4-Chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one	516, 518 Cl pattern
866	4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one	502, 504 Cl pattern
867	4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one	516, 518 Cl pattern
868	4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one	502, 504 Cl pattern
869	4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-[4-(6-methoxy-	482

	pyridin-3-yl)-benzyl]-3-(S)-methyl-piperazin-2-one	
870	4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methyl-1-[4-(6-oxo-1,6-dihydro-pyridin-3-yl)-benzyl]-piperazin-2-one	468
871	1-Biphenyl-4-ylmethyl-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one	
872	4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one	498, 500 Cl pattern
873	4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one	512, 514 Cl pattern

EXAMPLE 874. 1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one.

A. 2-Amino-4-(2-oxo-piperazin-1-ylmethyl)-benzonitrile.

To a solution of 4-(3-Amino-4-cyano-benzyl)-3-oxo-piperazine-1-carboxylic acid benzyl ester hydrochloride (4.0 g, 10.0mmol) in CH_3OH (45 ml) and CH_2Cl_2 (10 ml) is added 10% Pd on carbon (0.6 g). The mixture is stirred under an atmosphere of H_2 for 2 hours then is filtered through a pad of celite. The filtrate is concentrated and the residue purified by column chromatography eluting with 10% 7M NH_3 in CH_3OH / CH_2Cl_2 to yield the title compound (1.62 g, 7.0 mmol). ^{1}H NMR (DMSO,300MHz) δ 7.34 (d, 1H), 6.64 (s, 1H), 6.46 (d, 1H), 6.04 (bs, 2H), 4.40 (s, 2H), 3.28 (s, 2H), 3.14 (m, 2H), 2.87 (m, 2H), 2.77 (bs, 1H). MS (ion spray): m/z 231 $(M+H)^+$.

B. 2-Amino-4-[4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzonitrile.

To a cooled solution (0° C) of 2-Amino-4-(2-oxo-piperazin-1-ylmethyl)-benzonitrile (0.345 g, 1.5 mmol) in DMF (2 ml) is added finely powdered anhydrous K_2CO_3 (0.311 g, 2.25 mmol) and allowed to stir for 20 minutes. To this mixture is added a solution of 2-bromomethyl-benzo[b]thiophene (0.392 g, 1.5 mmol) in DMF (3 ml), the cold bath removed and allowed to stir for 2 hours. The reaction mixture is concentrated under high vacuum and the residue purified by column chromatography eluting with 55% EtOAc/ 5% CH_3OH/ hexane to yield the title compound (0.477 g, 1.16 mmol) as a white solid. ^{1}H NMR (DMSO,300MHz) δ 8.06 (d, 1H), 7.78 (d, 1H), 7.37 (m, 3H), 6.64 (s, 1H), 6.44 (d, 1H), 6.09 (bs, 2H), 4.42 (s, 2H), 3.88 (s, 2H), 3.21 (m, 4H), 2.72 (m, 2H). MS (ion spray): m/z 411, 413 $(M+H)^+$, Cl pattern.

C. 1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one.

To a cooled solution (0° C) of 2-Amino-4-[4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzonitrile (0.365 g, 0.89 mmol) in concentrated HCl (2.1 ml) is added dropwise a solution of sodium nitrite (0.068 g, 0.98 mmol) in H_2O (0.2 ml). The reaction mixture is added to a cooled solution (0° C) of tin (II) chloride dihydrate (1.61 g, 7.12 mmol) in concentrated HCl (0.62 ml) and H_2O (3 ml). The precipitate is collected by vacuum filtration and dried under high vacuum. The crude solid is purified by column chromatography eluting with 10% 7M NH_3 in CH_3OH / CH_2Cl_2 to yield the title compound (0.144 g, 0.34 mmol) as a yellow solid. ^{1}H NMR (DMSO,300MHz) δ 11.35 (bs, 1H), 8.05 (d, 1H), 7.78 (d, 1H), 7.64 (d, 1H), 7.37 (m, 2H), 7.08 (s, 1H), 6.78 (d, 1H), 5.75 (s, 1H), 5.40 (bs, 1H), 4.58 (s, 2H), 3.88 (s, 2H), 3.20 (m, 4H), 2.70 (bt, 2H). MS (ion spray): m/z 426 $(M+H)^+$. Anal. cald. for $C_{21}H_{20}N_5OSCl;(H_2O)_{0.25}$: C, 58.6; H, 4.8; N, 16.3. Found C, 58.6; H, 4.7; N, 15.9. M.P.= 246-248°C.

EXAMPLE 875. 1-(3-Amino-1H-indazol-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)]-piperazin-2-one.

A. 2-Amino-4-{4-[3-(5-chloro-thiophen-2-yl)-allyl]-2-oxo-piperazin-1-ylmethyl}-benzonitrile.

Using essentially the same procedure as in EXAMPLE 874, Part B using 2-(3-bromo-propenyl)-5-chloro-thiophene is obtained the title compound. MS (EI): m/z 386, 388 (M^+), Cl pattern.

B. 1-(3-Amino-1H-indazol-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)]-piperazin-2-one.

Using essentially the same procedure as in EXAMPLE 874, Part C there is obtained the title compound. ^{1}H NMR (DMSO, 300MHz) δ 11.32 (bs, 1H), 7.62 (d, 1H), 7.06 (s, 1H), 7.02 (d, 1H), 6.96 (d, 1H), 6.78 (d, 1H), 6.67 (d, 1H), 5.96 (m, 1H), 5.32 (bs, 2H), 4.57 (s, 2H), 3.19 (bt, 2H), 3.12 (m, 4H), 2.64 (bt, 2H). MS (EI): m/z 401, 403 (M^+), Cl pattern. Anal. cald. for $C_{19}H_{20}ClN_5OS$: C, 56.8; H, 5.0; N, 17.4. Found C, 56.6; H, 4.8; N, 17.2. M.P.= 167-169°C

EXAMPLE 876. 1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one.

A. 2-Amino-4-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperzin-1-ylmethyl]-benzonitrile.

Using essentially the same procedure as in EXAMPLE 874, Part B except using 6-chloro-benzo[b]thiophene-2-sulfonyl chloride, EXAMPLE 1, is obtained the title compound. MS (ion spray): m/z 461, 463 $(M+H)^+$, Cl pattern.

B. 1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one.

Using essentially the same procedure as in EXAMPLE 874, Part C there is obtained the title compound. ^{1}H NMR (DMSO, 300MHz) δ 11.29 (s, 1H), 8.35 (s, 1H), 8.18 (s, 1H), 8.08 (d, 1H), 7.58

(m, 2H), 7.05 (s, 1H), 6.70 (d, 1H), 5.30 (bs, 2H), 4.56 (s, 2H), 3.84 (s, 2H), 3.40 (m, 2H), 3.30 (m, 2H). MS (ion spray): m/z 476, 478 $(M+H)^+$, Cl pattern. Anal. cald. for $C_{20}H_{18}ClN_5O_3S_2$: C, 50.5; H, 3.8; N, 14.7. Found C, 50.3; H, 3.6; N, 14.5. M.P.=274-276°C.

The following compounds are prepared using the procedures described above.

Example #	Name	m/z
877	4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-(S)-methyl-3,6-dioxo-piperazin-1-ylmethyl]-benzamidine	441, 443 Cl pattern
878	4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-(R)-methyl-3,6-dioxo-piperazin-1-ylmethyl]-benzamidine	441, 443 Cl pattern
879	3-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2,5-dioxo-piperazin-1-ylmethyl]-benzamidine	427, 429 Cl pattern
880	4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2,5-dioxo-piperazin-1-ylmethyl]-benzamidine	427, 429 Cl pattern

Inhibition of Factor Xa

The compounds described herein inhibit blood coagulation by virtue of their ability to inhibit the penultimate enzyme in the coagulation cascade, controlling the activity of Factor Xa. Both the activity of free Factor Xa and Factor Xa assembled in the prothrombinase complex (Factor Xa, Factor Va, calcium and phospholipid) are inhibited by compounds of formula 1. The inhibition of the Factor Xa activity is obtained by direct complex formation between the inhibitor and the enzyme and is therefore independent of the plasma co-factor antithrombin III. Effective inhibition of the Factor Xa activity is achieved by administering the compounds either by oral administration, continuous intravenous infusion, bolus intravenous administration or any other parenteral route such that it achieves the desired effect of preventing the activity of Factor Xa induced formation of thrombin from prothrombin.

Anticoagulant therapy is indicated for the treatment and prophylaxis of a variety of thrombotic conditions of both the venous and arterial vasculature. In the arterial system, abnormal thrombus formation is primarily associated with arteries of the coronary, cerebral and peripheral vasculature. The diseases associated with thrombotic occlusion of these vessels principally include acute myocardial infarction (AMI), unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy and percutaneous transluminal coronary angioplasty (PTCA), transient ischemic attacks, stroke, intermittent claudication and bypass grafting of the coronary (CABG) or peripheral arteries. Chronic anticoagulant therapy may also be beneficial in preventing the vessel luminal narrowing (restenosis) that

often occurs following PTCA and CABG, and in the maintenance of vascular access patency in long-term hemodialysis patients. With respect to the venous vasculature, pathologic thrombus formation frequently occurs in the veins of the lower extremities following abdominal, knee and hip surgery (deep vein thrombosis, DVT). DVT further predisposes the patient to a higher risk of pulmonary thromboembolism. A systemic, disseminated intravascular coagulopathy (DIC) commonly occurs in both vascular systems during septic shock, certain viral infections and cancer. This condition is characterized by a rapid consumption of coagulation factors and their plasma inhibitors resulting in the formation of life-threatening thrombin throughout the microvasculature of several organ systems. The indications discussed above include some, but not all, of the possible clinical situations where anticoagulant therapy is warranted. Those experienced in this field are well aware of the circumstances requiring either acute or chronic prophylactic anticoagulant therapy.

Accumulated experimental evidence has also reflected that prothrombin activation is only one of the biological activities of Factor Xa. EPR-1 (effector cell protease receptor-1, recognizing Factor Xa), is believed to mediate several of the vascular wall interactions by Factor Xa. It has been shown to be expressed on human umbilical vein endothelial cells, rat smooth muscle cells and platelets(CR McKenzie, et al., Arterioscler Thromb Vasc Biol 16 1285-91 (1996); also F Bono, et al., J Cell Physiol 172 36-43 (1997), AC Nicholson, et al., J Biol Chem 271 28407-13 (1996),J.M. Herbert, et al., J Clin Invest 101 993-1000 (1998)). This protease-receptor interaction could mediate not only prothrombinase-catalyzed thrombin generation, but also diverse cellular functions such as cell proliferation, release of PDGF and DNA syntheses. The mitogenic effect of Factor Xa has been reported to be dependent on Factor Xa enzymatic activity (F Bono, et al., J Cell Physiol 172 36-43 (1997), J.M. Herbert, et al., J Clin Invest 101 993-1000 (1998)). TAP for example inhibited the mitogenesis of human and rat cultured vascular smooth muscle cells (F Bono, et al., J Cell Physiol 172 36-43 (1997)). In a study of the rabbit carotid artery air-drying injury model, increased EPR-1 expression is detected after vascular injury. Animals treated with the specific Factor Xa inhibitor, DX-9065a, exhibited less neointimal proliferation. The important regulatory role of Factor Xa in the coagulation process coupled with its mitogenic effects points to Factor Xa's involvement in the formation of thrombin at the luminal surface of the vessel wall and contribution to the atherothrombotic process and abnormal proliferation of vascular cells resulting in restenosis or angiogenesis.

These compounds may be used alone or in combination with other diagnostic, anticoagulant, antiplatelet or fibrinolytic agents. For example adjunctive administration of inhibitors of the activity of Factor Xa with standard heparin, low molecular weight heparin, direct thrombin inhibitors (i.e. hirudin), aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and/or tissue plasminogen activator may result in greater antithrombotic or thrombolytic efficacy or efficiency. The compounds described herein may be administered to treat thrombotic complications in a variety of animals such as primates

including humans. Inhibition of factor Xa is useful not only in the anticoagulant therapy of individuals having thrombotic conditions but is useful whenever inhibition of blood coagulation is required such as to prevent coagulation of stored whole blood and to prevent coagulation in other biological samples for testing or storage. Thus, any inhibitor of Factor Xa activity can be added to or contacted with any medium containing or suspected of containing Factor Xa and in which it is desired that blood coagulation be inhibited.

In addition to their use in anticoagulant therapy, Factor Xa inhibitors may find utility in the treatment or prevention of other diseases in which the generation of thrombin has been implicated as playing a physiologic role. For example, thrombin has been proposed to contribute to the morbidity and mortality of such chronic and degenerative diseases as arthritis, cancer, atherosclerosis and Alzheimer's disease by virtue of its ability to regulate many different cell types through specific cleavage and activation of a cell surface thrombin receptor, mitogenic effects, diverse cellular functions such as cell proliferation, for example, abnormal proliferation of vascular cells resulting in restenosis or angiogenesis, release of PDGF and DNA syntheses. Inhibition of Factor Xa will effectively block thrombin generation and therefore neutralize any physiologic effects of thrombin on various cell types.

According to a further feature of the invention there is provided a method for the treatment of a human or animal patient suffering from, or subject to, a physiological condition which can be ameliorated by the administration of an inhibitor of the Factor Xa activity, for example conditions as hereinbefore described, which comprises the administration to the patient of a therapeutically effective amount of compound of formula I or a composition containing a compound of formula I. "Effective amount" is meant to describe an amount of compound of the present invention effective in inhibiting the activity of Factor Xa and thus producing the desired therapeutic effect.

The present invention also includes within its scope pharmaceutical formulations which comprise at least one of the compounds of formula I in association with a pharmaceutically acceptable carrier or coating.

In practice compounds of the present invention may generally be administered parenterally, intravenously, subcutaneously intramuscularly, colonically, nasally, intraperitoneally, rectally or orally.

The products according to the invention may be presented in forms permitting administration by the most suitable route and the invention also relates to pharmaceutical compositions containing at least one product according to the invention which are suitable for use in human or veterinary medicine. These compositions may be prepared according to the customary methods, using one or more pharmaceutically acceptable adjuvants or excipients. The adjuvants comprise, inter alia, diluents, sterile aqueous media and the various non-toxic organic solvents. The compositions may be presented in the form of tablets, pills, granules, powders, aqueous solutions or suspensions, injectable solutions, elixirs or syrups, and can

contain one or more agents chosen from the group comprising sweeteners, flavorings, colorings, or stabilizers in order to obtain pharmaceutically acceptable preparations.

The choice of vehicle and the content of active substance in the vehicle are generally determined in accordance with the solubility and chemical properties of the product, the particular mode of administration and the provisions to be observed in pharmaceutical practice. For example, excipients such as lactose, sodium citrate, calcium carbonate, dicalcium phosphate and disintegrating agents such as starch, alginic acids and certain complex silicates combined with lubricants such as magnesium stearate, sodium lauryl sulfate and talc may be used for preparing tablets. To prepare a capsule, it is advantageous to use lactose and high molecular weight polyethylene glycols. When aqueous suspensions are used they can contain emulsifying agents or agents which facilitate suspension. Diluents such as sucrose, ethanol, polyethylene glycol, propylene glycol, glycerol and chloroform or mixtures thereof may also be used.

For parenteral administration, emulsions, suspensions or solutions of the products according to the invention in vegetable oil, for example sesame oil, groundnut oil or olive oil, or aqueous-organic solutions such as water and propylene glycol, injectable organic esters such as ethyl oleate, as well as sterile aqueous solutions of the pharmaceutically acceptable salts, are used. The solutions of the salts of the products according to the invention are especially useful for administration by intramuscular or subcutaneous injection. The aqueous solutions, also comprising solutions of the salts in pure distilled water, may be used for intravenous administration with the proviso that their pH is suitably adjusted, that they are judiciously buffered and rendered isotonic with a sufficient quantity of glucose or sodium chloride and that they are sterilized by heating, irradiation or microfiltration.

Suitable compositions containing the compounds of the invention may be prepared by conventional means. For example, compounds of the invention may be dissolved or suspended in a suitable carrier for use in a nebulizer or a suspension or solution aerosol, or may be absorbed or adsorbed onto a suitable solid carrier for use in a dry powder inhaler.

Solid compositions for rectal administration include suppositories formulated in accordance with known methods and containing at least one compound of formula I.

Actual dosage levels of active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active compound(s) that is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration. The selected dosage level will depend upon the activity of the particular compound, the route of administration, the severity of the condition being treated, and the condition and prior medical history of the patient being treated. However, it is within the skill of the art to start doses of the compound at levels lower than required for to achieve the desired therapeutic effect and to gradually increase the dosage until the desired effect is achieved. In the adult, the doses are generally from about 0.01 to about 100, preferably about 0.01 to about 10, mg/kg body weight per day by inhalation, from about 0.01 to about 100,

preferably 0.1 to 70, more especially 0.5 to 10, mg/kg body weight per day by oral administration, and from about 0.01 to about 50, preferably 0.01 to 10, mg/kg body weight per day by intravenous administration. In each particular case, the doses will be determined in accordance with the factors distinctive to the subject to be treated, such as age, weight, general state of health and other characteristics which can influence the efficacy of the medicinal product.

The products according to the invention may be administered as frequently as necessary in order to obtain the desired therapeutic effect. Some patients may respond rapidly to a higher or lower dose and may find much weaker maintenance doses adequate. For other patients, it may be necessary to have long-term treatments at the rate of 1 to 4 doses per day, in accordance with the physiological requirements of each particular patient. Generally, the active product may be administered orally 1 to 4 times per day. It goes without saying that, for other patients, it will be necessary to prescribe not more than one or two doses per day.

Compounds within the scope of the present invention exhibit marked pharmacological activities according to tests described in the literature which tests results are believed to correlate to pharmacological activity in humans and other mammals. The following pharmacological test results are typical characteristics of compounds of the present invention.

Enzyme Assays:

The ability of the compounds in the present invention to act as inhibitors of factor Xa, thrombin, trypsin, tissue-plasminogen activator (t-PA), urokinase-plasminogen activator (u-PA), plasmin and activated protein C is evaluated by determining the concentration of inhibitor which resulted in a 50% loss in enzyme activity (IC50) using purified enzymes.

All enzyme assays are carried out at room temperature in 96-well microtiter plates using a final enzyme concentration of 1 nM. The concentrations of factor Xa and thrombin are determined by active site titration and the concentrations of all other enzymes are based on the protein concentration supplied by the manufacturer. Compounds according to the invention are dissolved in DMSO, diluted with their respective buffers and assayed at a maximal final DMSO concentration of 1.25%. Compound dilutions are added to wells containing buffer and enzyme and pre-equilibrated for between 5 and 30 minutes. The enzyme reactions are initiated by the addition of substrate and the color developed from the hydrolysis of the peptide-p-nitroanilide substrates is monitored continuously for 5 minutes at 405 nm on a Vmax microplate reader (Molecular Devices). Under these conditions, less than 10% of the substrate is utilized in all assays. The initial velocities measured are used to calculate the amount of inhibitor which resulted in a 50% reduction of the control velocity (IC50). The apparent Ki values are then determined according to the Cheng-Prusoff equation (IC50 = Ki [1+[S]/Km]) assuming competitive inhibition kinetics.

An additional in vitro assay may be used to evaluate the potency of compounds according to the invention in normal human plasma. The activated partial thromboplastin time is a plasma-based clotting assay that relies on the in situ generation of factor Xa, its assembly into the prothrombinase complex and the subsequent generation of thrombin and fibrin which ultimately yields the formation of a clot as the assay endpoint. This assay is currently used clinically to monitor the ex vivo effects of the commonly used anticoagulant drug heparin as well as direct acting antithrombin agents undergoing clinical evaluation. Therefore, activity in this in vitro assay is considered as a surrogate marker for in vivo anticoagulant activity.

Human Plasma Based Clotting Assay:

Activated partial thromboplastin clotting times are determined in duplicate on a MLA Electra 800 instrument. A volume of 100 ml of citrated normal human pooled plasma (George King Biomedical) is added to a cuvette containing 100 ml of a compound according to the invention in Tris/NaCl buffer (pH 7.5) and placed in the instrument. Following a 3 minute warming period the instrument automatically adds 100 ml of activated cephaloplastin reagent (Actin, Dade) followed by 100 ml of 0.035 M $CaCl_2$ to initiate the clotting reaction. Clot formation is determined spectrophotometrically and measured in seconds. Compound potency is quantitated as the concentration required to double a control clotting time measured with human plasma in the absence of the compound according to the invention.

A compound according to the invention may also be evaluated for their in vivo antithrombotic efficacy in two well established animal experimental models of acute vascular thrombosis. A rabbit model of jugular vein thrombosis and a rat model of carotid artery thrombosis are used to demonstrate the antithrombotic activity of these compounds in distinct animal model paradigms of human venous thrombosis and arterial thrombosis, respectively.

Experimental Plazma Protein Binding Assay

Compounds are dissolved into DMSO to prepare a 10 mM stock. Serial dilutions of compounds are made in a buffer containing 0.05M Tris, 0.15M NaCl, 0.1% PEG-8000, PH 7.5. Human FXa and the substrate, Spectrozyme FXa, are prepared in the aforementioned buffer containing human Albumin and fibrinogen at 3.45 mg/ml and 2.3 mg/ml, respectively. The FXa assay is carried out at room temperature in the 96-well microtiter plates with a final enzyme concentration and substrate concentration of 1nM and 200 μM, respectively. Compound dilutions are added to the wells containing buffer and FXa and preincubated for 30 minutes. The enzyme reactions are initiated by the addition of substrate, Spectrozyme FXa, and the color

developed from the release of p-nitroanilide from each chromogenic substrate is monitored continuously for 5 minutes at 405 nm on a Thermomax microtiter plate reader(Molecular Devices, Sunnyvale, CA.). In the final reaction mixture, the concentration of albumin and fibeinogen is 3mg/ml and 2 mg/ml, respectively.Under the experimental conditions, less than 10% of the substrate is consumed in all assays. The initial velocities measured are used to determine the amount of inhibitor required to diminish 50% of the control velocity and defined as IC_{50} of the inhibitor. Assuming the kinetic mechanisms are competitive inhibition, the apparent Ki values are then calculated according to the Cheng-Prusoff equation , $Ki = IC_{50}/(1 + [S]/Km)$

Experimental In Vivo Rabbit Venous Thrombosis Model:

This is a well characterized model of fibrin rich venous thrombosis that is validated in the literature and shown to be sensitive to several anticoagulant drugs including heparin (Antithrombotic Effect of Recombinant Truncated Tissue Factor Pathway Inhibitor (TFPI 1-161) in Experimental Venous Thrombosis-a Comparison with Low Molecular Weight Heparin, J. Holst, B. Lindblad, D. Bergqvist, O. Nordfang, P.B. Ostergaard, J.G.L. Petersen, G. Nielsen and U. Hedner. Thrombosis and Haemostasis, 71, 214-219 (1994). The purpose of utilizing this model is to evaluate the ability of compounds to prevent the formation of venous thrombi (clots) in vivo generated at a site of injury and partial stasis in the jugular vein.

Male and female New Zealand white rabbits weighing 1.5-2 kg are anesthetized with 35 mg/kg of ketamine and 5 mg/kg xylazine in a volume of 1 ml/kg (i.m.). The right jugular vein is cannulated for infusion of anesthetic (ketamine/xylazine 17/2.5 mg/kg/hr at a rate of approximately 0.5 ml/hr) and administration of test substances. The right carotid artery is cannulated for recording arterial blood pressure and collecting blood samples. Body temperature is maintained at 39°C with a GAYMAR T-PUMP. The left external jugular vein is isolated and all side branches along an exposed 2-3 cm of vessel are tied off. The internal jugular vein is cannulated, just above the bifurcation of the common jugular, and the tip of the cannula is advanced just proximal to the common jugular vein. A 1 cm segment of the vein is isolated with non-traumatic vascular clamps and a relative stenosis is formed by tying a ligature around the vein with an 18G needle just below the distal most clamp. This creates a region of reduced flow and partial stasis at the injury site. The isolated segment is gently rinsed with saline 2-3 times via the cannula in the internal jugular. Thereafter the isolated segment is filled with 0.5 ml of 0.5% polyoxyethylene ether (W-1) for 5 minutes. W-1 is a detergent which disrupts the endothelial cell lining of the segment, thus providing a thrombogenic surface for initiating clot formation. After 5 minutes the W-1 is withdrawn from the segment, and the segment is again gently rinsed with saline 2-3 times. The

vascular clamps are then removed, restoring blood flow through this portion of the vessel. Clot formation is allowed to form and grow for 30 minutes after which the vein is cut just below the stenotic ligature and inspected for blood flow (the absence of blood flow is recorded as complete occlusion). The entire isolated segment of vein is then ligated and the formed clot is removed and weighed (wet weight). The effect of test agents on final clot weights is used as the primary end point. Animals are maintained for an additional thirty minutes to obtain a final pharmacodynamic measure of anticoagulation. Drug administration is initiated 15 minutes prior to vascular injury with W-1 and continued through the period of clot formation and maturation. Three blood samples (3 ml ea.) are obtained for evaluation of hemostatic parameters: one just prior to administration of W-1; a second 30 minutes after removal of the vascular clamps and a third at the termination of the experiment. Antithrombotic efficacy is expressed as a reduction in the final clot weight in preparations treated with a compound according to the invention relative to vehicle treated control animals.

Experimental In Vivo Rat Arterial Thrombosis Model:

The antithrombotic efficacy of factor Xa inhibitors against platelet-rich arterial thrombosis may be evaluated using a well characterized rat carotid artery $FeCl_2$-induced thrombosis model (Superior Activity of a Thromboxane Receptor Antagonist as Compared with Aspirin in Rat Models of Arterial and Venous Thrombosis, W.A. Schumacher, C.L. Heran, T.E. Steinbacher, S. Youssef and M.L. Ogletree. Journal of Cardiovascular Pharmacology, 22, 526-533 (1993); Rat Model of Arterial Thrombosis Induced by Ferric Chloride, K.D. Kurtz, B.W. Main, and G.E. Sandusky. Thrombosis Research, 60, 269-280 (1990); The Effect of Thrombin Inhibition in a Rat Arterial Thrombosis Model, R.J. Broersma, L.W. Kutcher and E.F. Heminger. Thrombosis Research 64, 405-412 (1991). This model is widely used to evaluate the antithrombotic potential of a variety of agents including heparin and the direct acting thrombin inhibitors.

Sprague Dawley rats weighing 375-450 g are anesthetized with sodium pentobarbital (50 mg/kg i.p.). Upon reaching an acceptable level of anesthesia, the ventral surface of the neck is shaved and prepared for aseptic surgery. Electrocardiogram electrodes are connected and lead II is monitored throughout the experiment. The right femoral vein and artery are cannulated with PE-50 tubing for administration of a compound according to the invention and for obtaining blood samples and monitoring blood pressure, respectively. A midline incision is made in the ventral surface of the neck. The trachea is exposed and intubated with PE-240 tubing to ensure airway patency. The right carotid artery is isolated and two 4-0 silk sutures are placed around the vessel to facilitate instrumentation. An electromagnetic flow probe (0.95-1.0 mm lumen) is placed around the vessel to measure blood flow. Distal to the probe a 4x4 mm strip of parafilm is placed under the vessel to isolate it from the surrounding muscle bed. After baseline flow measurements are made, a 2x5 mm strip of filter paper

previously saturated in 35% $FeCl_2$ is placed on top of the vessel downstream from the probe for ten minutes and then removed. The $FeCl_2$ is thought to diffuse into the underlying segment of artery and cause deendothelialization resulting in acute thrombus formation. Following application of the $FeCl_2$-soaked filter paper, blood pressure, carotid artery blood flow and heart rate are monitored for an observation period of 60 minutes. Following occlusion of the vessel (defined as the attainment of zero blood flow), or 60 minutes after filter paper application if patency is maintained, the artery is ligated proximal and distal to the area of injury and the vessel is excised. The thrombus is removed and weighed immediately and recorded as the primary end point of the study.

Following surgical instrumentation a control blood sample (B1) is drawn. All blood samples are collected from the arterial catheter and mixed with sodium citrate to prevent clotting. After each blood sample, the catheter is flushed with 0.5 ml of 0.9% saline. A compound according to the invention is administered intravenously (i.v.) starting 5 minutes prior to $FeCl_2$ application. The time between $FeCl_2$ application and the time at which carotid blood flow reached zero is recorded as time to occlusion (TTO). For vessels that did not occlude within 60 minutes, TTO is assigned a value of 60 minutes. Five minutes after application of $FeCl_2$, a second blood sample is drawn (B2). After 10 minutes of $FeCl_2$ exposure, the filter paper is removed from the vessel and the animal is monitored for the remainder of the experiment. Upon reaching zero blood flow blood a third blood sample is drawn (B3) and the clot is removed and weighed. Template bleeding time measurements are performed on the forelimb toe pads at the same time that blood samples are obtained. Coagulation profiles consisting of activated partial thromboplastin time (APTT) and prothrombin time (PT) are performed on all blood samples. In some instances a compound according to the invention may be administered orally. Rats are restrained manually using standard techniques and compounds are administered by intragastric gavage using a 18 gauge curved dosing needle (volume of 5 ml/kg). Fifteen minutes after intragastric dosing, the animal is anesthetized and instrumented as described previously. Experiments are then performed according to the protocol described above.

Experimental Canine intravenous and intragastric dosing experiments.

Beagle dogs (9-13 kg) of either sex are used to evaluate the pharmacodynamic effect of compounds of this invention after intravenous and intragastric dosing. Blood samples for these experiments are obtained via venipuncture of the cephalic vein. After discarding the first 0.5 ml of blood drawn, the control sample of 4.5 ml of blood is drawn into chilled plastic syringes containing 0.5 ml of trisodium citrate. After drug administration, 0.9 ml of blood is obtained at each time point (after discarding the first 0.5 ml of blood) by drawing the sample directly into chilled plastic syringes containing 0.1 ml trisodium citrate.

For the intravenous experiments, compounds are administered in the cephalic vein in the forelimb contralateral to that used for blood sampling. Compounds are dissolved in saline (0.5 ml/kg body weight) and administered as an i.v. bolus. Post-dosing blood samples are obtained at specific time points after dosing.

For the intragastric experiments, Compounds (in 0.5% methyl cellulose and 1 % polysorbate-80, 1 ml/kg dosing volume) are administered via an intragastric feeding tube. A pre-dosing control blood sample is obtained as above and post-dosing samples are obtained at specific time points after dosing.

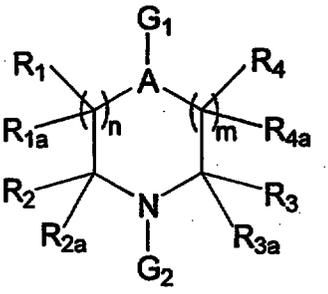
Coagulation times. Platelet-poor plasma is used for determination of activated partial thromboplastin time (APTT) and prothrombin time (PT), which are measured using a Microsample Coagulation Analyzer (MCA210, Bio Data Corp, Horsham, PA) and Dade® reagents (Thromboplastin-C Plus and Actin® FS Activated PTT reagent, Baxter Diagnostics, Inc., Deerfield, IL).

Ex vivo inhibition of Factor Xa. Factor-Xa inhibitory activity is analyzed by chromogenic methods using reagents (bovine factor Xa and spectrozyme Xa) supplied by American Diagnostica (Greenwich, CT). The rate of change of optical density (Vmax, 405 nm) is measured using a SPECTRAmax microtiter plate spectrophotometer and Softmax Pro software (Molecular Devices Corp., Sunnyvale, CA). Inhibition of Xa activity is determined as follows: percent inhibition of Xa activity = 1-(Vmax of sample with inhibitor/Vmax of the pre-drug control sample) X 100.

One skilled in the art will readily appreciate that the present invention is well adapted to carry out the objects of the invention and obtain the ends and advantages mentioned, as well as those inherent therein. The compounds, compositions and methods described herein are presented as representative of the preferred embodiments, or intended to be exemplary and not intended as limitations on the scope of the present invention.

We Claim

1. A compound of formula



or a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof

wherein

G_1 and G_2 are L_1-Cy_1 or L_2-Cy_2, provided that when R_1 and R_{1a} or R_4 and R_{4a} taken together form O or S, then G_1 is L_2-Cy_2 and G_2 is L_1-Cy_1, or when R_2 and R_{2a} or R_3 and R_{3a} taken together form O or S, then G_1 is L_1-Cy_1 and G_2 is L_2-Cy_2;

Cy_1 and Cy_2 are independently selected from optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclenyl, optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkenyl, optionally substituted fused arylheterocyclyl, optionally substituted fused arylheterocyclenyl, optionally substituted fused heteroarylcycloalkyl, optionally substituted fused heteroarylcycloalkenyl, optionally substituted fused heteroarylheterocyclyl and optionally substituted fused heteroarylheterocyclenyl;

L_1 is O, NR_5, $-S(O)_p-$, $-S(O)_pNR_5-$, $-C(X)Y-$ or $-L_3-Q-L_4-Q'-L_5-$,

L_3 and L_5 are independently absent, optionally substituted alkylene, optionally substituted alkenylene or optionally substituted alkynylene;

L_4 is optionally substituted alkylene, optionally substituted alkenylene, or optionally substituted alkynylene;

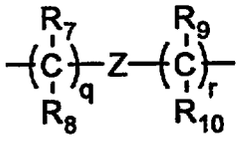
Q and Q' are independently absent, O, S, NR_5, $-S(O)_p-$, $-S(O)_pNR_5-$ or -C(X)Y-;

A is CH or N;

R_1, R_{1a}, R_2, R_{2a}, R_3, R_{3a}, R_4 and R_{4a} are independently selected from hydrogen, carboxy, alkoxycarbonyl, Y^1Y^2NCO, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl and optionally substituted heteroaralkyl, or R_1 and R_{1a}, R_2 and R_{2a}, R_3 and R_{3a}, or R_4 and R_{4a} taken together form O or S;

m and n are independently 0, 1 or 2, provided that m and n are not both 0 and further provided that when R_1 and R_{1a} taken together form O or S, n is 1 and when R_4 and R_{4a} taken together form O or S, m is 1;

L_2 is absent or a group of formula



R_5 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted heteroaralkyl, $R_6O(CH_2)_v-$, $R_6O_2C(CH_2)_x-$, $Y^1Y^2NC(O)(CH_2)_x-$, or $Y^1Y^2N(CH_2)_v-$;

R_6 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl or optionally substituted heteroaralkyl;

Y^1 and Y^2 are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a monocyclic heterocyclyl;

R_7, R_8, R_9 and R_{10} are independently selected from hydrogen, hydroxy, alkoxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl and optionally substituted heteroaralkyl, provided that only one of R_7 and R_8 or one of R_9 and R_{10} is hydroxy

or alkoxy, and further provided when R_7, R_8, R_9 and R_{10} is hydroxy or alkoxy, then the hydroxy or alkoxy is not α substituted to a N, O or S in Z;

X is O or S;

Y is absent or is selected from O, S and NR_5;

Z is absent or is selected from optionally substituted lower alkenylene, optionally substituted lower alkynylene, O, $S(O)_p$, NR_5, $-NR_5C(O)-$ and $-C(O)NR_5-$;

x is 1, 2, 3 or 4;

v is 2, 3 or 4;

p is 1 or 2; and

q and r are independently 0, 1, 2 or 3, provided that q and r are not both 0;

2. A compound according to claim 1 wherein Cy_2 contains at least one nitrogen atom and when Cy_2 is optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted fused phenylcycloalkyl or optionally substituted fused phenylcycloalkenyl, then said nitrogen atom is a basic nitrogen atom.

3. A compound according to claim 1 wherein Z is absent or is selected from O, $S(O)_p$ and NR_5;

4. A compound according to claim 3 wherein m is 1; and n is 1.

5. A compound according to claim 4 wherein A is N.

6. A compound according to claim 5 wherein R_3 and R_{3a} taken together are O; and R_1, R_{1a}, R_2, R_{2a}, R_4 and R_{4a} are hydrogen.

7. A compound according to claim 5 wherein R_3 and R_{3a} taken together are O; R_1, R_{1a}, R_2, R_{2a} and R_4 are hydrogen; and R_{4a} is optionally substituted alkyl.

8. A compound according to claim 5 wherein R_3 and R_{3a} taken together are O; R_1, R_{1a}, R_2 and R_4 are hydrogen; and R_{2a} and R_{4a} are optionally substituted alkyl.

9. A compound according to claim 5 wherein R_3 and R_{3a} taken together are O; R_1, R_2, R_{2a} and R_4 are hydrogen; and R_{1a} and R_{4a} are optionally substituted alkyl.

10. A compound according to claim 5 wherein R_3 and R_{3a} taken together are O; R_1, R_2, R_{2a}, R_4 and R_{4a} are hydrogen; and R_{1a} is carboxy, alkoxycarbonyl, Y^1Y^2NCO or optionally substituted alkyl.

11. A compound according to claim 5 wherein R_3 and R_{3a} taken together are O; and R_1, R_{1a}, R_2, R_4 and R_{4a} are hydrogen; and R_{2a} is carboxy, alkoxycarbonyl, Y^1Y^2NCO or optionally substituted alkyl.

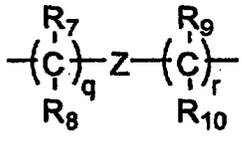
12. A compound according to claim 5 wherein L_1 is $-S(O)_p-$, -C(X)Y- or -L3-Q-L4-Q'-L5-.

13. A compound according to claim 5 wherein Cy_1 is optionally substituted aryl or optionally substituted heteroaryl.

14. A compound according to claim 5 wherein L_2 is alkylene of one to three carbon atoms.

15. A compound according to claim 14 wherein L_2 is $-CH_2-$.

16. A compound according to claim 5 wherein L_2 is a group of formula



wherein Z is NR_5; q is 2; r is 0; R_5 is hydrogen or optionally substituted alkyl; and R_7 and R_8 are hydrogen.

17. A compound according to claim 16 wherein R_5 is hydrogen.

18. A compound according to claim 5 wherein Cy_2 is optionally substituted aryl or optionally substituted heteroaryl.

19. A compound according to claim 5 wherein L_1 is $-S(O)_2-$.

20. A compound according to claim 5 wherein L_1 is -C(X)Y-; X is O; and Y is NH.

21. A compound according to claim 5 wherein L_1 is -L3-Q-L4-Q'-L5-; Q is $-S(O)_2-$ or -C(O)-; and L_4 is optionally substituted alkenylene.

22. A compound according to claim 5 wherein L_1 is -L3-Q-L4-Q'-L5-; and L_4 is optionally substituted alkylene.

23. A compound according to claim 5 wherein L_1 is -L3-Q-L4-Q'-L5-; Q is -C(O)-; Q' is O; and L_4 is optionally substituted alkylene.

24. A compound according to claim 5 wherein L_1 is -L3-Q-L4-Q'-L5-; L_3 is optionally substituted alkylene; and L_4 is optionally substituted alkenylene.

25. A compound according to claim 5 wherein Cy_1 is optionally substituted phenyl, optionally substituted thienyl, optionally substituted benzothienyl, optionally substituted isoquinolinyl, optionally substituted indolyl, optionally substituted thienopyridyl, optionally substituted furanyl, optionally substituted pyridyl, or optionally substituted benzimidazolyl.

26. A compound according to claim 5 wherein Cy_2 is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted imidazolyl, optionally substituted quinolinyl, optionally substituted isoquinolinyl, optionally substituted quinazolinyl, optionally substituted cinnolinyl, optionally substituted azaindolyl, or optionally substituted thienopyridyl.

27. A compound according to claim 1 wherein Z is $-NR_5C(O)-$ and $-C(O)NR_5-$.

28. A compound according to claim 27 wherein m is 1; and n is 1.

29. A compound according to claim 28 wherein A is N.

30. A compound according to claim 29 wherein R_3 and R_{3a} taken together are O; and R_1, R_{1a}, R_2, R_{2a}, R_4 and R_{4a} are hydrogen.

31. A compound according to claim 29 wherein R_3 and R_{3a} taken together are O; R_1, R_{1a}, R_2, R_{2a} and R_4 are hydrogen; and R_{4a} is optionally substituted alkyl.

32. A compound according to claim 29 wherein R_3 and R_{3a} taken together are O; R_1, R_{1a}, R_2 and R_4 are hydrogen; and R_{2a} and R_{4a} are optionally substituted alkyl.

33. A compound according to claim 29 wherein R_3 and R_{3a} taken together are O; R_1, R_2, R_{2a} and R_4 are hydrogen; and R_{1a} and R_{4a} are optionally substituted alkyl.

34. A compound according to claim 29 wherein R_3 and R_{3a} taken together are O; R_1, R_2, R_{2a}, R_4 and R_{4a} are hydrogen; and R_{1a} is carboxy, alkoxycarbonyl or optionally substituted alkyl.

35. A compound according to claim 29 wherein R_3 and R_{3a} taken together are O; and R_1, R_{1a}, R_2, R_4 and R_{4a} are hydrogen; and R_{2a} is carboxy, alkoxycarbonyl or optionally substituted alkyl.

36. A compound according to claim 29 wherein L_1 is $-S(O)_p-$, -C(X)Y- or-L3-Q-L4-Q'-L5-.

37. A compound according to claim 29 wherein Cy_1 is optionally substituted aryl or optionally substituted heteroaryl.

38. A compound according to claim 29 wherein R_5, R_7, R_8, R_9 and R_{10} are hydrogen.

39. A compound according to claim 29 wherein Cy_2 is optionally substituted aryl or optionally substituted heteroaryl.

40. A compound according to claim 29 wherein L_1 is $-S(O)_2-$.

41. A compound according to claim 29 wherein L_1 is -C(X)Y-; X is O; and Y is NH.

42. A compound according to claim 29 wherein L_1 is -L3-Q-L4-Q'-L5-; Q is $-S(O)_2-$ or -C(O)-; and L_4 is optionally substituted alkenylene.

43. A compound according to claim 29 wherein L_1 is-L3-Q-L4-Q'-L5-; and L_4 is optionally substituted alkylene.

44. A compound according to claim 29 wherein L_1 is-L3-Q-L4-Q'-L5-; Q is -C(O)-; Q' is O; and L_4 is optionally substituted alkylene.

45. A compound according to claim 29 wherein L_1 is-L3-Q-L4-Q'-L5-; L_3 is optionally substituted alkylene; and L_4 is optionally substituted alkenylene.

46. A compound according to claim 29 wherein Cy_1 is optionally substituted phenyl, optionally substituted thienyl, optionally substituted benzothienyl, optionally substituted isoquinolinyl, optionally substituted indolyl, optionally substituted thienopyridyl, optionally substituted furanyl, optionally substituted pyridyl, or optionally substituted benzimidazolyl.

47. A compound according to claim 29 wherein Cy_2 is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted imidazolyl, optionally substituted quinolinyl, optionally substituted isoquinolinyl, optionally substituted quinazolinyl, optionally substituted cinnolinyl, optionally substituted azaindolyl, or optionally substituted thienopyridyl.

48. A pharmaceutical composition comprising a pharmaceutically acceptable amount of the compound according to claim 1 and a pharmaceutically acceptable carrier.

49. A method for treating a patient suffering from a physiological condition capable of being modulated by inhibiting activity of Factor Xa comprising administering to said patient a pharmaceutically effective amount of the compound according to claim 1.

50. A compound selected from

4-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxo-piperazine-1-ylmethyl]benzamidine,

4-[4-(4-Methoxy-benzenesulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(5-Chloro-thieno[3,2-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[2-Oxo-4-(thieno[2,3-c]pyridine-2-sulfonyl)-piperazin-1-ylmethyl]-benzamidine,

4-[4-(7-Chloro-thieno[2,3-c]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(4-Chloro-thieno[3,2-c]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[2-Oxo-4-(toluene-4-sulfonyl)-piperazin-1-ylmethyl]-benzamidine,

4-[4-(Benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-Amino-3-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[2-Oxo-4-(toluene-4-sulfonyl)-piperazin-1-ylmethyl]-benzamidine,

3-[4-(6-Fluoro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(4-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(5-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(6-Methoxy-naphthalene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

3-{4-[5-(5-Nitro-pyridine-2-sulfonyl)-thiophene-2-sulfonyl]-2-oxo-piperazin- 1-ylmethyl}-benzamidine,

3-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]- benzamidine,

3-{4-[2-(3-Chloro-phenyl)-ethenesulfonyl]-2-oxo-piperazin-1-ylmethyl}- benzamidine,

3-[2-Oxo-4-(4-phenylazo-benzenesulfonyl)-piperazin-1-ylmethyl]-benzamidine,

3-[4-(Benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]- benzamidine,

4-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-{4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-2-oxopiperazin-1-ylmethyl}benzamidine,

3-{4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-2-oxopiperazin-1-ylmethyl}benzamidine,

3-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

1-(2-Aminoquinolin-6-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)piperazin-2-one,

6-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]-1H-quinolin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[2,3-c]pyridin-3-ylmethyl-piperazin-2-one,

1-(2-Amino-quinoxalin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[2,3-c]pyridin-2-ylmethyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-thieno[3,2-c]pyridin-2-ylmethyl-piperazin-2-one,

1-(2-Amino-quinolin-6-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-hydroxy-isoquinolin-6-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-chloro-isoquinolin-6-ylmethyl)-piperazin-2-one,

7-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-2H-isoquinolin-1-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-chloro-isoquinolin-7-ylmethyl)-piperazin-2-one,

1-(7-Amino-thieno[2,3-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(2-chloro-quinolin-6-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-quinolin-6-ylmethyl-piperazin-2-one,

7-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-1H-quinolin-2-one,

1-(2-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1,2,3,4-tetrahydro-isoquinolin-6-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-isoquinolin-6-ylmethyl-piperazin-2-one,

1-(2-Amino-quinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(decahydro-isoquinolin-6-ylmethyl)-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(decahydro-isoquinolin-7-ylmethyl)-piperazin-2-one,

1-(1-Amino-isoquinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-c]pyridin-3-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

(+/-)-[1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-4-thieno[3,2-c]pyridin-2-ylmethyl-piperazin-2-yl]-acetic acid,

(+/-)-[1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-4-thieno[2,3-c]pyridin-2-ylmethyl-piperazin-2-yl]-acetic acid,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

(3S)-1-(7-Chloro-isoquinolin-3-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-methoxymethyl-piperazin-2-one,

(3S)-1-(7-Chloro-isoquinolin-3-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3-methoxymethyl-piperazin-2-one,

(S)-4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-3-ethyl-1-(4-hydroxy-quinolin-7-ylmethyl)-piperazin-2-one,

1-(2-Amino-quinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

1-(2-Aminoquinolin-6-ylmethyl)-4-(4-methoxybenzyl)piperazin-2-one,

1-(2-Aminoquinolin-6-ylmethyl)-4-6-chlorobenzo[b]thiophen-2-ylmethyl)piperazin-2-one,

1-(2-Aminoquinolin-6-ylmethyl)-4-(5-methoxy-1H-benzoimidazol-2-ylmethyl)piperazin-2-one,

1-(2-Aminoquinolin-6-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)piperazin-2-one,

1-(2-Aminoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(2-Aminoquinolin-6-ylmethyl)-4-[3-(3,5-dibromo-4-methoxy-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]piperazin-2-one,

3-[4-(2-Aminoquinolin-6-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-fluoro-1H-quinolin-2-one,

1-(2-Aminoquinolin-6-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one,

3-(4-Biphenyl-3-ylmethyl-3-oxo-piperazin-1-ylmethyl)-benzamidine,

4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-piperazin-2-one,

1,4-Bis-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-benzamidine,

4-(4-Cyclohexylmethyl-2-oxo-piperazin-1-ylmethyl)-benzamidine,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-3-(S)-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-1-[4-(6-oxo-1,6-dihydro-pyridin-3-yl)-benzyl]-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-3-methoxymethyl-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-chloro-quinolin-7-ylmethyl)-3-methyl-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-sulfonyl)piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid 3-chloro-benzylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid 4-chloro-benzylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-isoxazol-3-yl-thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid [2-(3-chloro-phenyl)-ethyl]-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-sulfonic acid [2-(4-chloro-phenyl)-ethyl]-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-(3-Amino-benzenesulfonyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-methyl-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-methyl-piperazin-2-one,

(+/-)-[4-(4-Amino-quinazolin-7-ylmethyl)-1-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-oxo-piperazin-2-yl]-acetic acid,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-hydroxy-quinazolin-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-hydroxy-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(5-oxy-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1-methyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(3-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorothieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Bromobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

2-[3-Oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazine-1-sulfonyl]-benzo[b]thiophene-6-carbonitrile,

4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-[2-(4-Chlorophenyl)ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl} acetic acid,

4-(5-Pyridin-4-ylthiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl} acetic acid ethyl ester,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-[1-(2-methoxyethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]piperazin-2-one,

4-(6-Chlorothieno[3,2-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[2,3-c]pyridin-1-yl} acetic acid methyl ester,

2-[3-Oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazine-1-sulfonyl]benzo[b]thiophene-5-carbonitrile,

4-(5-Aminomethylbenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

2-{2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-ylmethyl]pyrrolo[3,2-c]pyridin-1-yl}acetamide,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-[1-(2-hydroxyethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]piperazin-2-one,

4-(6-Chloro-1H-benzoimidazole-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(1H-Benzoimidazole-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Aminomethyl-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethanesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(2-Benzo[b]thiophen-2-yl-ethenesulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[2-(5-Chloro-4-methoxy-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-furo[3,2-c]pyridin-2-ylmethyl-piperazin-2-one,

4-(6-Fluoro-benzo[b]thiophene-2-sulfonyl)-1-furo[3,2-c]pyridin-2-ylmethyl-piperazin-2-one,

4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)piperazin-2-one,

4-(6-Chlorothieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)piperazin-2-one,

{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-pyrrolo[2,3-c]pyridin-1-yl}-acetic acid methyl ester,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-b]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)piperazin-2-one,

(±)-4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-1-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-5-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(-)-1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(+)-1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(±)-4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid amide,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[2-(4-Chloro-phenyl)-ethenesulfonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-ylmethyl)piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzothioazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzooxazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzothioazol-2-ylmethyl)-piperazin-2-one,

3-[4-(4-Aminoquinazoline-7-ylmethyl)-3-oxopiperazin-1-ylmethyl]-7-chloro-1H-quinolin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-(E)-enyl]-piperazin-2-one ditrifluoroacetate,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-2-methyl-(E)-allyl]-piperazin-2-one ditrifluoroacetate,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-furan-2-yl)-(E)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-methoxy-pyridin-3-yl)-(E)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-allyl]-4-oxy-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-prop-2-ynyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-prop-2-ynyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-2-yl-prop-2-ynyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yloxy)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1-methyl-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-4-methyl-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzofuran-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,7-dichloro-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-p-tolyl-prop-2-ynyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-m-tolyl-prop-2-ynyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2-chloro-phenyl)-prop-2-ynyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-4-yl-prop-2-ynyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4,5-dibromo-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-biphenyl-3-yl-prop-2-ynyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2,5-dichloro-thiophen-3-yl)-prop-2-ynyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-propyl]-piperazin-2-one,

1,4-Bis-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-nitro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-pyridin-3-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(5-methyl-thiophen-2-yl)-penta-2,4-dienyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophen-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-methyl-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-methoxy-thiophen-2-yl)-allyl]-piperazin-2-one,

4-(1-Amino-7-chloro-isoquinolin-3-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-N-(5-chloro-thiophen-2-yl)-acetamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenyl)-2-(S)-hydroxy-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenylsulfanyl)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-methylene-1,1-dioxo-2,3-dihydro-1H-11 6-benzo[b]thiophen-3-yl)-piperazin-2-one ,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-nitro-phenyl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophen-6-ylmethyl)-piperazin-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-N-(4-chloro-phenyl)-acetamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(4-chloro-phenyl)-pyrrolidin-3-yl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-propyl]-piperazin-2-one,

2-[4-(4-Aminoquinazoline-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-3-(4-chlorophenyl)-acrylic acid,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-1-hydroxy-isoquinolin-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-isoquinolin-3-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(3-chloro-phenyl)-pyrrolidin-3-yl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1,7-dichloro-isoquinolin-3-ylmethyl)-piperazin-2-one,

4-(2-Amino-7-chloro-quinolin-3-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophene-2-ylmethyl)piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(4-chloro-phenylsulfanyl)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(6-chloro-benzo[b]thiophen-2-yl)-ethyl]-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-[2-(4-chloro-phenoxy)-ethyl]-piperazine-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-4H-benzo[1,4]thiazin-3-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,7-dichloro-quinolin-3-ylmethyl)-piperazin-2-one,

2-[[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-(4-chloro-phenyl)-methyl]-acrylic acid ethyl ester,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-3-(4-chloro-phenyl)-acrylic acid ethyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-allyl]-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-fluoro-1H-quinolin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-1H-quinoxalin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1-methyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-3H-quinazolin-4-one,.

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-thiophen-2-yl-propyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-quinolin-3-ylmethyl)-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-5,7-dichloro-1H-quinolin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6,7-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-5-chloro-1H-quinolin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-[2,3']bithiophenyl-5'-ylmethyl)-piperazin-2-one,

4-(6-Amino-benzo[b]thiophen-2-ylmethyl)-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-quinolin-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-bromo-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-nitro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(3-chloro-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-3-methoxy-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-6-chloro-1H-quinolin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-trifluoromethyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3,3'-dimethyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3,5-dibromo-4-methoxy-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3'-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-bromo-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-oxazol-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,6-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4,5-dichloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzooxazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-5-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-5-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-3-methyl-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thieno[3,2-b]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5,6-dichloro-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-benzooxazol-2-yl-benzyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(4-chloro-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-methyl-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2,2']bithiophenyl-5-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-fluoro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-(6-fluoro-benzo[b]thiophene-2-ylmethyl)piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(1-methyl-5-trifluoro-methyl-1H-pyrazol-3-yl)-thiophen-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3,4-dimethyl-thieno[2,3-b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-3-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-3-methyl-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(2-methyl-5-trifluoromethyl-2H-pyrazol-3-yl)thiophen-2-ylmethyl] piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(3-nitro-phenyl)-furan-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thieno[3,2-b]pyridin-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[5-(4-methoxy-phenyl)-thiophen-2-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-hydroxy-2-pyridin-2-yl-pyrimidin-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-fluoro-phenoxy)-benzyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(4-chloro-phenyl)-thiazol-4-ylmethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-bromo-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-benzo[b]thiophen-2-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3,5-bis-trifluoromethyl-benzyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-biphenyl-4-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-naphthalen-2-ylmethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Aminoquinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(4-chloro-thiophene-2-carbonyl)-piperazin-2-one,

4-[3-(3-Amino-4-chloro-phenyl)-(E)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

5-Chloro-thiophene-2-carboxylic acid {2-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-2-oxo-ethyl}-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indole-2-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-(E)-acryloyl]-piperazin-2-one,

5-Chloro-thiophene-2-carboxylic acid {2-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-1-methyl-2-oxo-ethyl}-amide,

5-Chloro-thiophene-2-carboxylic acid {3-[4-(4-amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-3-oxo-propyl}-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-2-methyl-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-(E)-acryloyl]-piperazin-2-one,

N-[2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-yl]-1-(5-chloro-thiophen-2-ylmethyl)-2-oxo-ethyl]-benzamide,

N-[1-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-2-(5-chloro-thiophen-2-yl)-vinyl]-benzamide,

N-[1-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-2-(5-chloro-thiophen-2-yl)-vinyl]-acetamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-(E)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yl)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-piperazin-2-one,

2-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carbonyl]-6-chloro-4H-benzo[1,4]thiazin-3-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-benzo[b]thiophen-2-yl)-acetyl]-piperazin-2-one,

4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid 4-chloro-benzylamide,

4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid (5-chloro-thiophen-2-ylmethyl)amide,

4-(4-Aminoquinazolin-7-ylmethyl)-3-oxopiperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (3-amino-4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (4-methoxy-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid (3,4-dichloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid 5-chloro-thiophen-2-ylmethyl ester,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-carboxylic acid 6-chloro-benzooxazol -2-ylmethyl ester,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazine-1-carboxylic acid 1-(3-chloro-phenyl)-pyrrolidin-3-yl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)- 4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(6-chloro-benzo[b]thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-benzoimidazol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-benzo[b]thiophen-2-ylmethyl)-3-(R)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(R)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enoyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-allyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridin-2-ylmethyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-(S)-3-ethyl-piperazin-2-one,

2-(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetamide,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,3-dichloro-benzo[b]thiophene-6-carbonyl)-(S)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophene-6-carbonyl)-(S)-3-ethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid ethyl ,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-thiophen-2-yloxy)-acetyl]-(S)-3-ethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-ethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid methyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indole-6-carbonyl)-(3S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[1-(4-chloro-phenyl)-1H-pyrrole-2-carbonyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenylsulfanyl)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-but-2-enoyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indole-2-carbonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-propionyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-ethyl-4-[3-(4-methoxy-phenyl)-propionyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-5-methoxy-phenoxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yloxy)-ethyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(R)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(4-Amino-phenyl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-3H-imidazol-4-yl-acryloyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

(1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-thiophene-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-bromo-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(3-chloro-phenyl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)--methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-5-methoxy-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-fluoro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-fluoro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(3-chloro-phenoxy)-propionyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-4-[(4-trifluoromethylsulfanyl-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-ylsulfanyl)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

2-(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2-chloro-benzo[b]thiophene-6-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(2,3-dichloro-benzo[b]thiophene-6-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid methyl ester,

(2-{2-[4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazin-1-yl]-2-oxo-ethoxy}-5-chloro-thiophen-3-yl)-acetic acid ethyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,3-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-fluoro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-2-methyl-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,4-dichloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinoline-3-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

(1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(R)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-ethoxymethyl-4-[(3-fluoro-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(6-chloro-pyridin-3-ylamino)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[(4-chloro-phenoxy)-acetyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-(6-chloro-naphthalen-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-benzyl-4-[3-(5-chloro-thiophen-2-yl)-propyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3-(S)-isopropyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3,3-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-(2-methoxy-ethyl)-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-(2-methoxy-ethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-(2-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-(2-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-6-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-(S)-methoxymethyl-6-(R)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

(1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(4-chloro-thiophen-2-yloxy)-acetyl]-(S)-3-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-(S)-3-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-4-fluoro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3,5-dichloro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(2,5-dichloro-phenyl)-acryloyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-2-methyl-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(2,5-dichloro-phenoxy)-acetyl]-3(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(3-chloro-phenoxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-propionyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methoxymethyl-6-methyl-piperazin-2-one,

(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-carbonyl)-3(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-6-methyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2(S)-(2-methoxy-ethyl)-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-butyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-3-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(S)-2-propyl-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (3-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(2S)-propyl-piperazine-1-carboxylic acid (4-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(S)-2-propyl-piperazine-1-carboxylic acid (5-chloro-2-methoxy-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-2-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-trifluoromethoxy-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-fluoro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (2,4-dichloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (2,4-difluoro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (3-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-(2S)-propyl-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (6-chloro-pyridin-3-yl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-5-(R,S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-ethyl-3-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-methyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(2S)-ethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

4-(4-Amino-quinazolin-7-ylmethyl)-(S)-2-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-4-methoxy-thiophen-2-yl)-amide,

(3S, 5RS)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

(3S,5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-sulfonyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

(3S, 5S)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-bromo-phenyl)-amide,

(3S, 5S)-4-(4-Amino-quinazolin-7-ylmethyl)-2,6-dimethyl-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

1-(4-Aminoquinolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophen-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3-methyl-piperazin-2-one,

(3S,5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(3S,5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

(S,R)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

(S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(5-chlorothiophen-2-yl)-allyl]-3-methylpiperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-methyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-methyl-piperazin-2-one,

(3S,5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

(3S,5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-naphthalen-2-ylmethyl)-3-ethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-(S)-3-((R)-1-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-(S)-3-((R)-1-methoxy-ethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-methoxymethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-methyl-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-1-[4-(2-hydroxy-ethylamino)-quinolin-7-ylmethyl]-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-ethylamino-quinolin-7-ylmethyl)-3-methyl-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-1-(4-ethylamino-quinolin-7-ylmethyl)-3-methoxymethyl-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-3-methyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

(S)-4-(5-Chloro-1H-indol-2-ylmethyl)-3-methoxymethyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-methyl-4-oxy-piperazin-2-one,

(S)-1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)acryloyl]-3-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-(S)-3-ethyl-1-(4-hydroxyamino-quinolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methoxymethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-ethyl-piperazin-2-one,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-(S)-3-(1-(R)-methoxy-ethyl)-piperazin-2-one,

1-(4-Aminoquinolin-7-ylmethyl)-4-[3-(4-bromothiophen-2-yl)-acryloyl]-3-(S)-(1-(R)-methoxyethyl)-piperazin-2-one trifluoroacetate,

1-(4-Aminoquinolin-7-ylmethyl)-4-[(5-chlorothiophen-2-yloxy-acetyl]-3-(S)-(1-(R)-methoxyethyl)-piperazin-2-one trifluoroacetate,

(S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-ethyl-piperazin-2-one,

1-(4-Aminocinnolin-7-ylmethyl)-4-[2-(5-chlorothiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(methyl-pyridin-4-yl-amino)-ethyl]-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(3-methyl-pyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-[2-(Pyridin-4-ylamino)-ethyl]-4-(thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-sulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-[2-(Pyridin-4-ylamino)-ethyl]-4-(thieno[3,2-b]pyridine-2-sulfonyl)-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(methylpyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-(2-Benzo[b]thiophen-2-yl-ethenesulfonyl)-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(3-methyl-pyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(2-pyrrolo[3,2-c]pyridin-1-yl-ethyl)-piperazin-2-one,

1-[2-(2-Amino-3-chloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-[2-(2-Amino-5-chloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(2,3,5,6-tetrachloro-pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-[2-(2-Amino-3,5,6-trichloro-pyridin-4-ylamino)-ethyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[2-(pyridazin-4-yl-amino)-ethyl]-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propenyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propenyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-allyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-allyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propyl]-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-[3-(4-Amino-pyridin-3-yl)-propyl]-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

4-[2-(5-Chlorothiophen-2-yl)-ethenesulfonyl]-1-(2-pyrrolo[3,2-c]pyridin-1-ylethyl)-piperazin-2-one,

4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

. 1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-naphthalen-2-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(7-Chloro-isoquinolin-3-ylmethyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester,

1-(5-Chloro-1H-indol-2-ylmethyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-(±)-carboxylic acid methyl ester,

1-[(5-Chloro-thiophen-2-yloxy)-acetyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-(6-Chloro-benzo[b]thiophene-2-carbonyl)-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-(1H-Pyrrolo[3,2-c]pyridin-2-ylmethyl)-4-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(3-Phenyl-prop-2-ynyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-prop-2-ynyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(4-Chloro-phenyl)-(E)-acryloyl]-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(S)-2-Methoxymethyl-3-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

(S)-4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)piperazin-2-one,

4-[3-(6-Chloro-benzo[b]thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[1-(3,5-Dichloro-phenyl)-2,5-dimethyl-1H-pyrrole-3-carbonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indole-2-carbonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[4-(6-Methoxy-pyridin-3-yl)-benzoyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(4-Pyridin-3-yl-benzoyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(4-Bromo-thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-propionyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[(5-Chloro-3-methyl-benzo[b]thiophen-2-yl)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[2-(4-Chloro-phenyl)-2-methyl-propionyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(3,4-Dichloro-phenyl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[(4-Chloro-phenyl)-acetyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(4-Chloro-phenyl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methyl ester,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid benzylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid (2-hydroxy-ethyl)-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid bis-(2-hydroxy-ethyl)-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylcarbamoylmethyl-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-(4-methyl-piperazine-1-carbonyl)-piperazin-2-one,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethyl ester,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(±)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid ethylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid,

4-Prop-2-ynyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one.

A. 2-(2-Oxo-4-prop-2-ynyl-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester,

1,4-Bis-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

2-Amino-4-[4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzonitrile,

4-[4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-2-oxo-piperidin-1-ylmethyl]-benzamidine,

1-(4-Amino-quinazolin-7-ylmethly)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperidin-2-one,

4-(6-Chloro-1H-benzoimidazol-2-ylmethyl)-1-(2,4-diamino-quinazolin-7-ylmethyl)-piperidin-2-one,

1-(4-Amino-2-methyl-quinazolin-7-ylmethly)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperidin-2-one,

(3S, 5R)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine,

(3S,5S)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-{4-[3-(5-Chloro-thiophen-2-yl)-acryloyl]-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl}-benzamidine,

(3R,5S)-4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-3,5-dimethyl-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[3-(3H-imidazol-4-yl)-propyl]-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-piperidine-1-carboxamidine,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-piperazin-1-yl-propyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-pyridin-4-yl-propyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-piperidin-4-yl-butyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(2-piperidin-4-yl-ethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(3-piperidin-4-yl-propyl)-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

4'-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-biphenyl-2-carbonitrile,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-chloro-3-hydroxy-benzyl)-piperazin-2-one,

1-Benzyl-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(4-chloro-benzyl)-piperazin-2-one,

4-[(4-Chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-3-(S)-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methyl-1-[4-(6-oxo-1,6-dihydro-pyridin-3-yl)-benzyl]-piperazin-2-one,

1-Biphenyl-4-ylmethyl-4-[3-(5-chloro-thiophen-2-yl)-(E)-acryloyl]-3(S)-ethyl-6-methyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[3-(5-Chloro-thiophen-2-yl)-(E)-acryloyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)]-piperazin-2-one,

1-(3-Amino-1H-indazol-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-(S)-methyl-3,6-dioxo-piperazin-1-ylmethyl]-benzamidine,

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2-(R)-methyl-3,6-dioxo-piperazin-1-ylmethyl]-benzamidine,

3-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2,5-dioxo-piperazin-1-ylmethyl]-benzamidine, and

4-[4-(6-Chloro-benzo[b]thiophen-2-ylmethyl)-2,5-dioxo-piperazin-1-ylmethyl]-benzamidine, or a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

51. A compound selected from

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(1-Amino-isoquinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-3-(S)-methoxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophen-2-ylmethyl)-piperazin-2-one,

(S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-4-oxy-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-[2-(pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (4-chloro-phenyl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-furan-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-4-oxy-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-((S)-1-(R)-methoxy-ethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(R)-carboxylic acid ethyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one,

3-[4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-piperazin-1-ylmethyl]-7-chloro-1H-quinolin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-3-(S)-butyl-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-piperazin-2-one,

4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-propyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(3-chloro-1H-indol-6-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

(3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5'-chloro-[2,2']bithiophenyl-5-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-propyl-piperazin-2-one,

4-[(5-Chloro-thiophen-2-yloxy)-acetyl]-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethoxymethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3,5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-6-dimethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(7-chloro-isoquinolin-3-ylmethyl)-3-(S)-methyl-piperazin-2-one,

(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-ethyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-piperidine-1-carboxamidine,

4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-[(5-Chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-1-[4-(6-methoxy-pyridin-3-yl)-benzyl]-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-3-oxo-2-(S)-propyl-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-3-yl)-acryloyl]-3-(S)-propyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-1H-benzoimidazole-2-sulfonyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-[1-(2-hydroxy-ethyl)-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl]-piperazin-2-one,

4-(6-Bromo-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1-methyl-1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one,

(3S, 5R)-1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3, 5-dimethyl-piperazin-2-one,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(R)-carboxylic acid methyl ester,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(S)-carboxylic acid methyl ester,

1-(4-Amino-quinolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-ethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-(R)-hydroxymethyl-3-(S)-methoxymethyl-piperazin-2-one,

1-(1-Amino-isoquinolin-6-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-3-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

4-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)- propyl-piperazin-2-one,

4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid amide

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

(+/-)-1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-bromo-thiophen-2-yl)-amide,

4-[4-(6-Chloro-thieno[2,3-b]pyridine-2-sulfonyl)-2-oxo-piperazin-1-ylmethyl]-benzamidine,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-chloro-thiophen-2-yl)-acryloyl]-3-(S)- propyl-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-ethyl-piperazin-2-one,

4-(4-Amino-quinazolin-7-ylmethyl)-2-(S)-methoxymethyl-3-oxo-piperazine-1-carboxylic acid (5-chloro-thiophen-2-yl)-amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(4-bromo-thiophen-2-yl)-acryloyl]-3-(S)- propyl-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)- propyl-piperazin-2-one,

1-(4-Amino-cinnolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-(morpholine-4-carbonyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(S)-carboxylic acid ethyl ester,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3, 5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-thieno[2,3-b]pyridine-2-sulfonyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-piperazin-2-one,

(3S, 5S)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-3, 5-dimethyl-piperazin-2-one,

1-(4-Amino-quinazolin-7-ylmethyl)-4-[2-(5-chloro-thiophen-2-yl)-ethenesulfonyl]-piperazin-2-one,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid,

1-(4-Amino-quinolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-3-(S)-methyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

4-(5-Chloro-1H-indol-2-ylmethyl)-3-(S)-methoxymethyl-1-(4-methylamino-quinolin-7-ylmethyl)-piperazin-2-one,

1-(4-Amino-quinolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid dimethylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-(S)-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid amide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(1H-5 3-chloro-1-aza-inden-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid methylamide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid ethylamide,

1-(4-Amino-quinazolin-7-ylmethyl)-4-(5-chloro-1H-indol-2-ylmethyl)-6-oxo-piperazine-2-carboxylic acid (2-hydroxy-ethyl)-amide,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid methyl ester,

(+/-)-1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-6-oxo-piperazine-2-carboxylic acid,

4-(5'-Chloro-[2,2']bithiophenyl-5-ylmethyl)-6-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one,

1-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-5-oxo-4-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazine-2-carboxylic acid methyl ester,

or a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

52. A compound which is

2-[4-(6-Chlorobenzo[b]thiophene-2-sulfonyl)-2-oxopiperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-4-yl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyridin-3-ylmethyl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-piperidin-4-yl-acetamide,

N-(1-Carbamimidoyl-piperidin-4-yl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

5-(2-{2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetylamino}-ethyl)-imidazole-1-carboxylic acid ethyl ester,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-pyrimidin-4-yl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-phenyl-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(9H-purin-6-yl)-acetamide,

N-(4-Amino-2-methyl-pyrimidin-5-ylmethyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(1-methyl-1H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-4-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(3-methyl-3H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-2-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-pyridin-3-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-imidazol-1-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(1-methyl-1H-pyrrol-2-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(5-methyl-1H-imidazol-4-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(4-dimethylamino-[1,3,5]triazin-2-yl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-pyridin-4-yl-acetamide,

N-[2-(2-Amino-pyridin-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(4-methyl-thiazol-5-yl)-ethyl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(2-thiazol-4-yl-ethyl)-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-(3-guanidino-propyl)-acetamide trifluoroacetic acid salt,

N-(3-Amino-propyl)-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-mercapto-1H-imidazol-4-yl)-ethyl]-acetamide,

N-[2-(2-Amino-thiazol-4-yl)-ethyl]-2-[4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-acetamide,

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-methyl-N-(2-pyridin-4-yl-ethyl)-acetamide, or

2-[4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-2-oxo-piperazin-1-yl]-N-[2-(2-methylsulfanyl-1H-imidazol-4-yl)-ethyl]-acetamide,

or a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

53. A compound which is 1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-piperazin-2-one, or

a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

54. A compound which is 1-(4-Amino-quinazolin-7-ylmethyl)-4-[(5-chloro-thiophen-2-yloxy)-acetyl]-3-(S)-methoxymethyl-6-methyl-piperazin-2-one, or

a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

55. A compound which is 4-(6-Chloro-benzo[b]thiophene-2-sulfonyl)-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one, or

a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

56. A compound which is 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one, or

a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

57. A compound which is 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-acryloyl]-3-(S)-methoxymethyl-piperazin-2-one, or

a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

58. A compound which is 1-(4-Amino-quinazolin-7-ylmethyl)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-piperazin-2-one, or
a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

59. A compound which is 4-[2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-6-(R)-hydroxymethyl-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-piperazin-2-one, or
a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

60. A compound which is 4-[3-(6-Amino-pyridin-3-yl)-acryloyl]-1-(4-amino-quinazolin-7-ylmethyl)-3-(S)-propyl-piperazin-2-one, or
a pharmaceutically acceptable salt thereof, pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

61. A pharmaceutical composition comprising a pharmaceutically acceptable amount of the compound according to claim 1 and a pharmaceutically acceptable carrier.

62. A method of inhibiting Factor Xa comprising contacting a Factor Xa inhibitory amount of a compound according to claim 1 with a composition containing Factor Xa.

63. A method of inhibiting the formation of thrombin comprising contacting Factor Xa inhibitory amount of a compound according to claim 1 with a composition containing Factor Xa.

64. A method for treating a patient suffering from a physiological condition capable of being modulated by inhibiting activity of Factor Xa comprising administering to said patient a pharmaceutically effective amount of the compound according to claim 1.

65. The method according to claim 63 wherein the physiological condition is venous vasculature, arterial vasculature, abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy, percutaneous transluminal coronary angioplasty, transient ischemic attacks, stroke, intermittent claudication or bypass grafting of the coronary or peripheral arteries, vessel luminal narrowing, restenosis post coronary or venous angioplasty, maintenance of vascular access patency in long-term hemodialysis patients, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip

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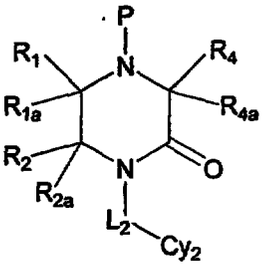
surgery, a risk of pulmonary thromboembolism, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.

66. The method according to claim 63 wherein the physiological condition is abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy, transient ischemic attacks, intermittent claudication or bypass grafting of the coronary or peripheral arteries, restenosis post coronary or venous angioplasty, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery or a risk of pulmonary thromboembolism.

67. The method according to claim 63 wherein the physiological condition is stroke, vessel luminal narrowing, maintenance of vascular access patency in long-term hemodialysis patients, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.

68. A compound of formula

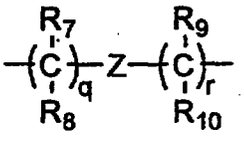


wherein

P is H or a nitrogen protecting group;

R_1, R_{1a}, R_2, R_{2a}, R_3, R_{3a}, R_4 and R_{4a} are independently selected from hydrogen, carboxy, alkoxycarbonyl, Y^1Y^2NCO, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl and optionally substituted heteroaralkyl;

L_2 is a group of formula



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Cy_2 is selected from optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclenyl, optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkenyl, optionally substituted fused arylheterocyclyl, optionally substituted fused arylheterocyclenyl, optionally substituted fused heteroarylcycloalkyl, optionally substituted fused heteroarylcycloalkenyl, optionally substituted fused heteroarylheterocyclyl and optionally substituted fused heteroarylheterocyclenyl;

R_5 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted heteroaralkyl, $R_6O(CH_2)_v$-, $R_6O_2C(CH_2)_x$-, $Y^1Y^2NC(O)(CH_2)_x$-, or $Y^1Y^2N(CH_2)_v$-;

R_6 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl or optionally substituted heteroaralkyl;

Y^1 and Y^2 are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a monocyclic heterocyclyl;

R_7, R_8, R_9 and R_{10} are independently selected from hydrogen, hydroxy, alkoxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl and optionally substituted heteroaralkyl, provided that only one of R_7 and R_8 or one of R_9 and R_{10} is hydroxy or alkoxy, and further provided when R_7, R_8, R_9 and R_{10} is hydroxy or alkoxy, then the hydroxy or alkoxy is not α substituted to a N, O or S in Z;

Z is absent or is selected from optionally substituted lower alkenylene, optionally substituted lower alkynylene, O, $S(O)_p$, NR_5, $-NR_5C(O)-$ and $-C(O)NR_5-$;

x is 1, 2, 3 or 4;

v is 2, 3 or 4; and

q and r are independently 0, 1, 2 or 3, provided that q and r are not both 0.

69. A compound according to claim 68 wherein Cy_2 contains at least one nitrogen atom and when Cy_2 is optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted fused phenylcycloalkyl or optionally substituted fused phenylcycloalkenyl, then said nitrogen atom is a basic nitrogen atom.

70. A compound according to claim 67 wherein Z is absent.

71. A compound according to claim 68 wherein R_1, R_{1a}, R_2, R_{2a}, R_4 and R_{4a} are hydrogen.

72. A compound according to claim 67 which is

(2S, 6RS)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester,

(3S,5RS)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5S)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(3S, 5R)-1-(4-chloro-quinolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

(2S, 6R)-4-(4-chloro-quinolin-7-ylmethyl)-2,6-dimethyl-3-oxo-piperazine-1-carboxylic acid benzyl ester,

(3S, 5S)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one,

(3S, 5R)-1-(4-chloro-quinolin-7-ylmethly)-4-[3-(5-chloro-thiophen-2-yl)-allyl]-3,5-dimethyl-piperazine-2-one,

4-(2-Oxopiperazin-1-ylmethyl)benzamidine,

1-(2-Aminoquinolin-6-ylmethyl)piperazin-2-one,

1-(1-Aminoisoquinolin-6-ylmethyl)piperazin-2-one,

2-(2-Oxopiperazin-1-ylmethyl)pyrrolo[3,2-c]pyridin-1-carboxylic acid tert-butyl ester,

2-(5-(±)-Methoxycarbonyl-2-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester,

2-(2-(±)-Methoxycarbonyl-6-oxo-piperazin-1-ylmethyl)-pyrrolo[3,2-c]pyridine-1-carboxylic acid tert-butyl ester,

1-(4-Aminoquinazoline-7-ylmethyl)piperazine-2-one,

1-(4-Amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-piperazin-2-one,

4-[3-(2-Oxo-piperazin-1-yl)-propyl]-piperidine-1-carboxylic acid tert-butyl ester,

1-(4-Amino-quinazoline-7-ylmethyl)-3-methoxymethyl-piperazine-2-one,

1-(4-Aminoquinazoline-7-ylmethyl)-3-butyl-piperazine-2-one,

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1-(4-Aminoquinazoline-7-ylmethyl)-3-ethyl-piperazine-2-one,

1-(4-Aminoquinazoline-7-ylmethyl)-3-propyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-ethoxymethyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-methyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-benzyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-(1-methoxyethyl)-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3,3-dimethyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-isopropyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-isobutyl-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-(2-methoxyethyl) l-piperazine-2-one,

1-(4-Amino-quinazoline-7-ylmethyl)-3-methoxymethyl-6-methyl-piperazine-2-one,

(3S,5RS)-1-(4-amino-quinazolin-7-ylmethyl)-3,5-dimethyl-piperazin-2-one,

1-(4-Chloroquinolin-7-ylmethyl)-piperazin-2-one,

1-(4-Chlorocinnolin-7-ylmethyl)-piperazin-2-one,

1-(4-Chloroquinolin-7-ylmethyl)-3-(S)-methylpiperazin-2-one,

1-[2-(Pyridin-4-ylamino)-ethyl]-piperazin-2-one,

1-[2-{(Methyl)-(pyridin-4-yl)-amino}-ethyl]-piperazin-2-one trifluroacetate,

1-[2-(3-Methylpyridin-4-yl-amino)-ethyl]-piperazin-2-one,

1-[2-(Pyridazin-4-ylamino)-ethyl]-piperazin-2-one,

4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propenyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester,

4-[3-(4-tert-butoxycarbonylamino-pyridin-3-yl)-allyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester

4-[3-(4-tert-Butoxycarbonylamino-pyridin-3-yl)-propyl]-3-oxo-piperazine-1-carboxylic acid tert-butyl ester.

4-(Benzyloxycarbonyl)-1-(2-pyrrolo[3,2-c]pyridin-1-ylethyl)-piperazin-2-one,

(±)-1-(3-Amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid methyl ester, or

(±)-1-(3-Amino-4-cyano-benzyl)-4-(6-chloro-benzo[b]thiophene-2-sulfonyl)-6-oxo-piperazine-2-carboxylic acid.