COMPOUNDS AND METHODS FOR THE TREATMENT OR PREVENTION OF *FLAVIVIRUS* INFECTIONS

FIELD OF THE INVENTION

The present invention relates to novel compounds and a method for the treatment or prevention of *Flavivirus* infections using novel compounds.

BACKGROUND OF THE INVENTION

Hepatitis is a disease occurring throughout the world. It is generally of viral nature, although there are other causes known. Viral hepatitis is by far the most common form of hepatitis. Nearly 750,000 Americans are affected by hepatitis each year, and out of those, more than 150,000 are infected with the hepatitis C virus ("HCV").

HCV is a positive-stranded RNA virus belonging to the *Flaviviridae* family and has closest relationship to the pestiviruses that include hog cholera virus and bovine viral diarrhea virus (BVDV). HCV is believed to replicate through the production of a complementary negative-strand RNA template. Due to the lack of efficient culture replication system for the virus, HCV particles were isolated from pooled human plasma and shown, by electron microscopy, to have a diameter of about 50-60 nm. The HCV genome is a single-stranded, positive-sense RNA of about 9,600 bp coding for a polyprotein of 3009-3030 amino-acids, which is cleaved co and post-translationally by cellular and two viral proteinases into mature viral proteins (core, E1, E2, p7, NS2, NS3, NS4A, NS4B, NS5A, NS5B). It is believed that the structural proteins, E1 and E2, the major glycoproteins are embedded into a viral lipid envelope and form stable heterodimers. It is also believed that the structural core protein interacts with the viral RNA genome to form the nucleocapsid. The nonstructural proteins designated NS2 to NS5 include proteins with enzymatic functions involved in virus replication and protein processing including a polymerase, protease and helicase.

The main source of contamination with HCV is blood. The magnitude

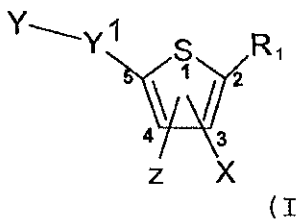
of the HCV infection as a health problem is illustrated by the prevalence among high-risk groups. For example, 60% to 90% of hemophiliacs and more than 80% of intravenous drug abusers in western countries are chronically infected with HCV. For intravenous drug abusers, the prevalence varies from about 28% to 70% depending on the population studied. The proportion of new HCV infections associated with post-transfusion has been markedly reduced lately due to advances in diagnostic tools used to screen blood donors.

The only treatment currently available for HCV infection is interferon-α (IFN-α). However, according to different clinical studies, only 70% of treated patients normalize alanine aminotransferase (ALT) levels in the serum and after discontinuation of IFN, 35% to 45% of these responders relapse. In general, only 20% to 25% of patients have long-term responses to IFN. Clinical studies have shown that combination treatment with IFN and ribavirin (RIBA) results in a superior clinical response than IFN alone. Different genotypes of HCV respond differently to IFN therapy, genotype 1b is more resistant to IFN therapy than type 2 and 3.

There is therefore a great need for the development of anti-viral agents.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides novel compounds represented by formula I:

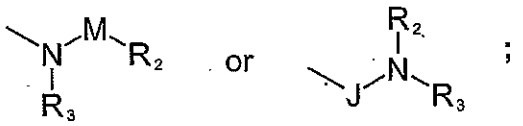


(I)

or pharmaceutically acceptable salts thereof;

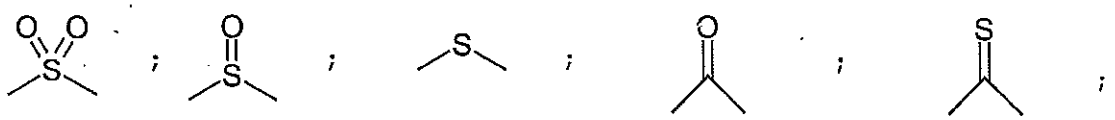
wherein,

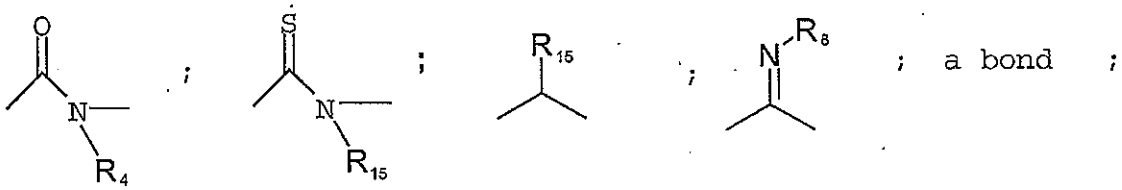
X is chosen from:



wherein,

M is chosen from:





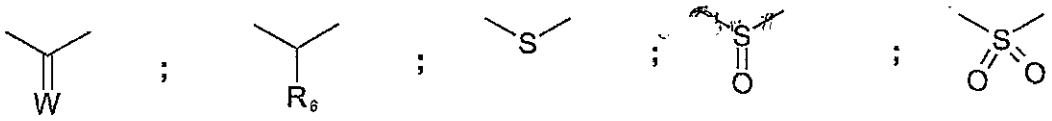
wherein,

R_4 is C_{1-6} alkyl;

R_8 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-12} heteroaralkyl, C_{6-16} aralkyl; and

R_{15} is chosen from H or C_{1-6} alkyl;

J is chosen from:



wherein W is chosen from O, S or NR_7,

wherein R_7 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-12} heteroaralkyl, C_{6-16} aralkyl;

and R_6 is chosen from H, C_{1-12} alkyl, C_{6-14} aryl or C_{6-16} aralkyl;

Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)-SO_2-R_5$, $CONR_9OH$ or halogen, wherein R_9, R_5, R_{10} and R_{11} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;
R_a and R_b are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
R_{16} is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
provided that R_{16} is other than methyl or ethyl;

R_1 is chosen from C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

R_2 is chosen from C_{2-12} alkyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C_{1-6} alkyl;

with the proviso that:

i) when X is 4-Chloro-2,6-dimethyl-benzenesulfonamide and, R_1 is phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #580

ii) when X is Toluene-4-sulfonamide and R_1 is 4-chloro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #563

iii) when X is Toluene-4-sulfonamide and R_1 is 4-fluoro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #564

iv) when X is Toluene-4-sulfonamide and R_1 is 4-methoxy-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #565

v) when X is Benzamide and R_1 is phenyl Y^1 is a bond and Y is COOH then R_3 is other than hydrogen.

The compounds of the present invention are useful in therapy, particularly as antivirals.

In another aspect, there is provided a method of treating viral infections in a subject in need of such treatment comprising administering to the subject a therapeutically effective amount of a compound of formula (I) or composition of the invention.

In still another aspect, there is provided a method of treating viral infections in a subject in need of such treatment comprising administering to the subject a combination comprising at least one compound of formula (I) and at least one further therapeutic agent.

In another aspect, there is provided a pharmaceutical formulation comprising the compound of the invention in combination with a pharmaceutically acceptable carrier or excipient.

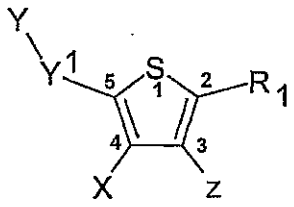
Another aspect of the invention is the use of a compound according to formula (I), for the manufacture of a medicament for the treatment of viral infections.

In another aspect, there is provided a method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of a compound of formula (I).

DETAILED DESCRIPTION OF THE INVENTION

In one embodiment, compounds of the present invention comprise those wherein the following embodiments are present, either independently or in combination.

In one embodiment, the present invention provides novel compounds of formula (Ia):

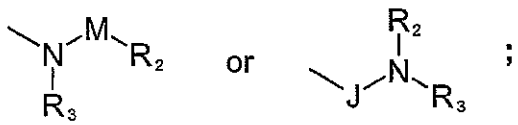


(Ia)

or pharmaceutically acceptable salts thereof;

wherein,

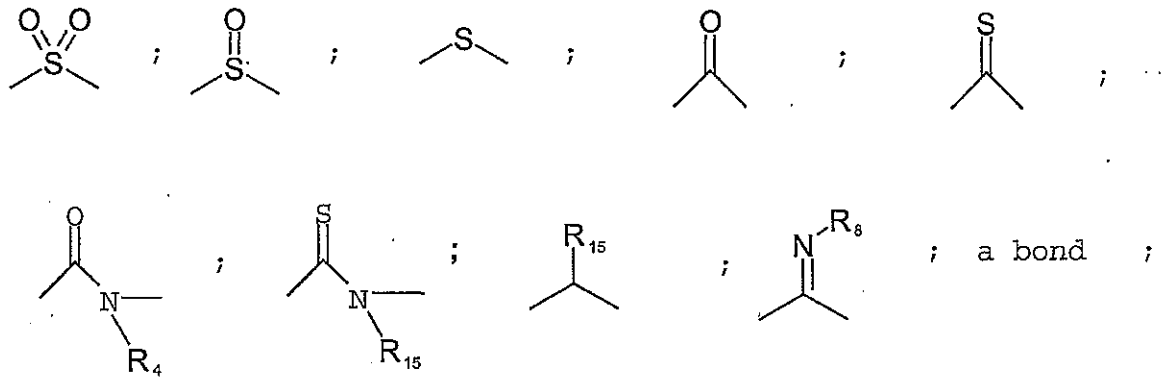
X is chosen from:



;

wherein,

M is chosen from:



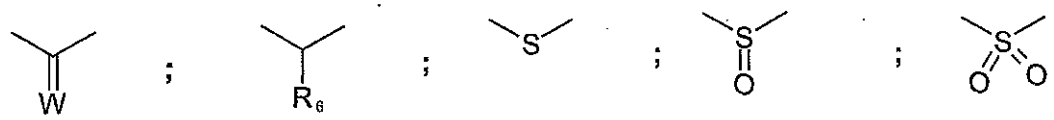
wherein,

R_4 is C_{1-6} alkyl;

R_8 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-12} heteroaralkyl, C_{6-16} aralkyl; and

R_{15} is chosen from H or C_{1-6} alkyl;

J is chosen from:



wherein W is chosen from O, S or NR_7,

wherein R_7 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-12} heteroaralkyl, C_{6-16} aralkyl;

and R_6 is chosen from H, C_{1-12} alkyl, C_{6-14} aryl or C_{6-16} aralkyl;

Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)-SO_2-R_5$, $CONR_9OH$ or halogen, wherein R_9, R_5, R_{10} and R_{11} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
R_{16} is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
provided that R_{16} is other than methyl or ethyl;

R_1 is chosen from C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

R_2 is chosen from C_{2-12} alkyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C_{1-6} alkyl;

with the proviso that:

i) when X is 4-Chloro-2,6-dimethyl-benzenesulfonamide and, R_1 is phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #580

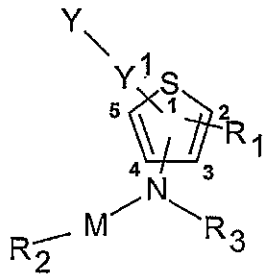
ii) when X is Toluene-4-sulfonamide and R_1 is 4-chloro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #563

iii) when X is Toluene-4-sulfonamide and R_1 is 4-fluoro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #564

iv) when X is Toluene-4-sulfonamide and R_1 is 4-methoxy-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #565

v) when X is Benzamide and R_1 is phenyl Y^1 is a bond and Y is COOH then R_3 is other than hydrogen.

In a further aspect, the present invention provides novel compounds represented by formula II:

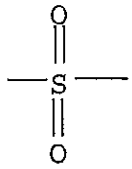
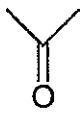
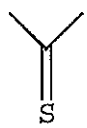


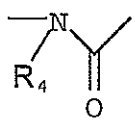
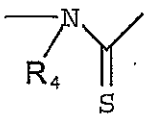
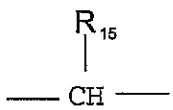
(II)

and pharmaceutically acceptable salts thereof,

wherein,

M is chosen from:

 ;  ;  ;

 ;  ;  ; a bond ;

Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $CO-COOR_5$, $PO_3R_aR_b$, SO_3R_5, tetrazole, $CON(R_9)CH(R_5)-COOR_5$, CON $R_{10}R_{11}$ or $CONR_9OH$, wherein each R_5 R_9, R_{10}, R_{11}, R_{16}, R_a, and R_b are independently chosen from H or C_{1-6} alkyl,;

R_1 is chosen from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aryl, C_{3-10} heterocycle, C_{3-10} heteroaralkyl, C_{6-12} aralkyl, or a halogen;

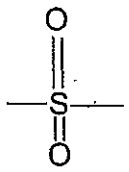
R_2 is chosen from C_{6-12} aryl, C_{3-10} heterocycle, C_{6-12} aralkyl or C_{3-10} heteroaralkyl;

R_3 is chosen from H or C_{1-6} alkyl; C_{6-12} aralkyl or C_{3-10} heteroaralkyl;

R_4 is chosen from H or C_{1-6} alkyl;
R_{15} is chosen from H or C_{1-6} alkyl

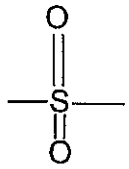
with the proviso that:

i) when M is



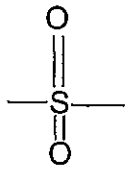
and R_2 is 4-chloro-2,5-dimethyl-phenyl, R_1 is phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #580

ii) when M is



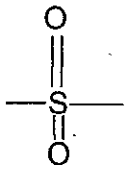
and R_2 is 4-methylphenyl, R_1 is 4-chloro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #563

iii) when M is



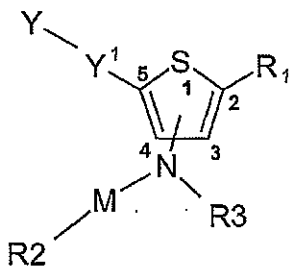
and R_2 is 4-methylphenyl, R_1 is 4-fluoro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #564

iv) when M is



and R_2 is 4-methylphenyl, R_1 is 4-methoxy-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #565

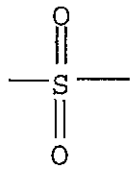
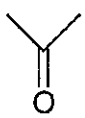
In still a further embodiment, the present invention provides novel compounds of formula (IIa):

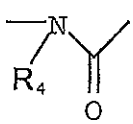
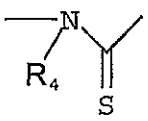
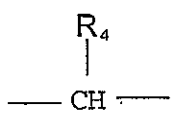


(IIa)

wherein,

M is chosen from:

 ;  ; ;

 ;  ;  ; a bond ;

Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $CO-COOR_5$, $PO_3R_aR_b$, SO_3R_5, tetrazole, $CON(R_9)CH(R_5)-COOR_5$, $CON\ R_{10}R_{11}$ or $CONR_9OH$, wherein each R_5 R_9, R_{10}, R_{11}, R_{16}, R_a, and R_b are independently chosen from H or C_{1-6} alkyl,;

R_1 is chosen from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aryl, C_{3-10} heterocycle, C_{3-10} heteroaralkyl, C_{6-12} aralkyl, or a halogen;

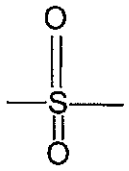
R_2 is chosen from C_{6-12} aryl, C_{3-10} heterocycle, C_{6-12} aralkyl or C_{3-10} heteroaralkyl;

R_3 is chosen from H or C_{1-6} alkyl; C_{6-12} aralkyl or C_{3-10} heteroaralkyl;

R_4 is chosen from H or C_{1-6} alkyl;
R_{15} is chosen from H or C_{1-6} alkyl;

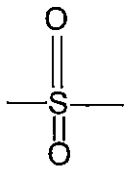
with the proviso that:

i) when M is



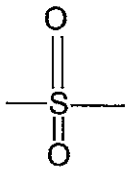
and R_2 is 4-chloro-2,5-dimethyl-phenyl, R_1 is phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #580

ii) when M is



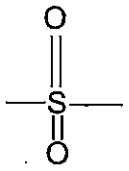
and R_2 is 4-methylphenyl, R_1 is 4-chloro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #563

iii) when M is



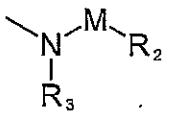
and R_2 is 4-methylphenyl, R_1 is 4-fluoro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #564

iv) when M is

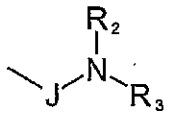


and R_2 is 4-methylphenyl, R_1 is 4-methoxy-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; compound #565.

In one embodiment, X is:



In a further embodiment, X is:



In one embodiment, Z is chosen from H, halogen, C_{1-6} alkyl.

In further embodiments,

Z is H

Z is halogen

Z is fluoride

Z is C_{1-6} alkyl

Z is chosen from methyl, trifluoromethyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, cyclobutyl, pentyl, neopentyl, cyclopentyl, hexyl or cyclohexyl.

In further embodiments;

R_1 is chosen from C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl.

R_1 is chosen from a C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

R_1 is a C_{2-12} alkyl.

R_1 is a C_{6-14} aryl.

R_1 is a C_{3-12} heterocycle.

R_1 is chosen from t-butyl, isobutyl, allyl, ethynyl, 2-phenylethenyl, isobutenyl, benzyl, phenyl, phenethyl,

benzodioxolyl, thienyl, thiophenyl, pyridinyl, isoxazolyl, thiazolyl, pyrazolyl, tetrazolyl, benzofuranyl, indolyl, furanyl, or benzothiophenyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO_2R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;
wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
R_1 is chosen from thienyl, t-butyl, phenyl or pyridinyl.
R_1 is isoxazolyl substituted by at least one methyl.
R_1 is pyridinyl.

In one embodiment, R_1 is chosen from a C_{1-6} alkyl, C_{6-12} aryl or C_{3-10} heterocycle.

In one embodiment, R_1 is chosen from t-butyl, isobutyl, allyl, ethynyl, 2-phenylethenyl, isobutenyl, benzyl, phenyl, phenethyl, benzodioxolyl, thienyl, thiophenyl, pyridinyl, isoxazolyl, thiazolyl, pyrazolyl, tetrazolyl, benzofuranyl, indolyl, furanyl, or benzothiophenyl, any of which can be substituted by at least one substituent chosen from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} heterocycle, halogen, nitro, $CONR_{13}R_{14}$, $NR_{13}R_{14}$, amidino, guanido, Cyano, SO_2-C_{1-6} alkyl, $C(O)OR_{12}$, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, or C_{6-12} aryloxy;
wherein R_{12}, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

In one embodiment, R_1 is chosen from thienyl, t-butyl, phenyl, thiophenyl, pyridinyl, isoxazolyl, any of which can be substituted by at least one substituent chosen from a halogen, C_{1-6} alkyl, C_{1-6} alkyloxy, C_{2-6} alkenyl, C_{2-6} alkynyl, nitro, cyano, SO_2-C_{1-6} alkyl, NO-C_{1-6} alkyl.

In further embodiments;
R_1 is phenyl.
R_1 is phenyl substituted with fluoride.
R_1 is phenyl substituted with at least one fluoride
R_1 is phenyl di-substituted with fluoride.
R_1 is phenyl substituted with chloride.
R_1 is phenyl substituted with at least one chloride
R_1 is phenyl di-substituted with chloride.
R_1 is phenyl substituted with fluoride and chloride.
R_1 is phenyl substituted with nitro..
R_1 is phenyl substituted with at least one nitro.
R_1 is phenyl substituted with methoxy.
R_1 is phenyl substituted with OCF_3.
R_1 is phenyl substituted with CF_3.
R_1 is phenyl substituted with methyl.
R_1 is phenyl substituted with at least one methyl.
R_1 is phenyl substituted with CN.
R_1 is phenyl substituted with SO_2-CH_3.
R_1 is phenyl substituted with NH(CO)-CH_3.

In further embodiments,
R_1 is thiophenyl.
R_1 is thiophenyl substituted by at least one halogen.
R_1 is thiophenyl substituted by at least one chloride.
R_1 is thiophenyl substituted by at least one methyl.
R_1 is thiophenyl substituted by at least one methyl and one chloride.

In further embodiments,
R_1 is thienyl.

R_1 is thienyl substituted by at least one halogen.

R_1 is thienyl substituted by at least one chloride.

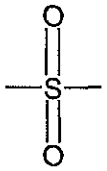
R_1 is thienyl substituted by at least one methyl.

R_1 is thienyl substituted by at least one methyl and one chloride.

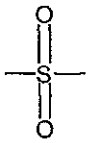
R_1 is isoxazole di-substituted with CH_3.

R_1 is pyridine.

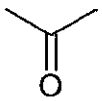
In one embodiment, M is chosen from:

;  ; a bond

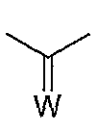
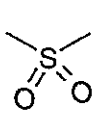
In a further embodiment, M is:



In an alternative embodiment, M is:

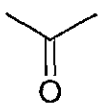


In one embodiment, J is chosen from:

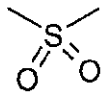
 ; 

wherein, W is as defined above.

In an alternative embodiment, J is:



In a further embodiment, J is:



In one embodiment, Y is chosen from $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CONR_9OH$.

In a further embodiment, any of R_5, Ra, Rb, R_9, R_{10}, R_{11} and R_{16} are each independently chosen from H or C_{1-6} alkyl; provided that R_{16} is other than methyl or ethyl.

In one embodiment, Y is chosen from $COOR_{16}$, $CONR_{10}R_{11}$ or $CON(R_9)CH(R_5)-COOR_5$.

In a further embodiment, any of R_5, R_9, R_{10}, R_{11} and R_{16} are each independently chosen from H or C_{1-6} alkyl; provided that R_{16} is other than methyl or ethyl.

In a further embodiment, Y is chosen from $COOR_{16}$, $CONR_{10}R_{11}$ or $CONR_9CH_2COOR_5$.

In a further embodiment, Y is chosen from $COOR_5$, $CONR_5R_5$ or $CON(R_5)CH(R_5)\_COOR_5$.

In a further embodiment, Y is COOH.

In a further embodiment, Y is $CONH_2$.

In a further embodiment, Y is $CONHCH_2COOH$.

In a further embodiment, Y is $COOCH_3$.

In a further embodiment, Y^1 is chosen from CH_2, C=CH, $CH-CH_2$ or a bond.

In further embodiments;

R_3 is chosen from H, C_{1-12} alkyl, C_{6-18} aralkyl, C_{3-12} heterocycle or C_{3-18} heteroaralkyl.

R_3 is chosen from H, C_{1-12} alkyl, C_{6-18} aralkyl or C_{3-12} heterocycle.

R_3 is C_{1-12} alkyl.

R_3 is C_{6-18} aralkyl.

R_3 is C_{3-12} heterocycle.

R_3 is chosen from H, methyl, ethyl, i-propyl, cyclopropyl, cyclohexyl, allyl, piperidinyl, piperazinyl, pyrrolidinyl, azetidinyl, aziridinyl, pyridinyl, piperidinylmethyl, dioxanyl, dioxolanyl, azepanyl or benzyl; any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;
wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

R_3 is chosen from H or Methyl, isopropyl, piperidinyl, piperidinylmethyl, dioxolanyl or cyclohexyl.

In a further embodiment, R_3 is H or methyl.
In a further embodiment, R_3 is H.
In a further embodiment, R_3 is methyl.
In a further embodiment, R_3 is benzyl, thiophenylmethyl, furanylmethyl.

In additional embodiments;
R_2 is C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle;
R_2 is C_{3-6} heterocycle.
R_2 is chosen from thienyl, furanyl, pyridinyl, oxazolyl, thiazolyl, pyrrolyl, benzofuranyl, indolyl, benzoxazolyl, benzothienyl, benzothiazolyl, piperazinyl, pyrrolidinyl or quinolinyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy,

$C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

R_2 is a heterocycle chosen from thienyl, furanyl, pyridinyl, pyrrolyl, indolyl, piperazinyl or benzothienyl.

R_2 is C_{2-12} alkyl.

R_2 is chosen from cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl cyclohexyl, cycloheptyl, 2-(cyclopentyl)-ethyl, methyl, ethyl, vinyl, propyl, propenyl, isopropyl, butyl, butenyl isobutyl, pentyl, neopentyl or t-butyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, NR13R14, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

R_2 is C_{6-12} aryl.

R_2 is an aryl chosen from indenyl, naphthyl or biphenyl.

R_2 is phenyl substituted by one or more substituent chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

R_2 is phenyl substituted by one or two substituents chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

R_2 is phenyl substituted by one or more substituent chosen from halogen, nitro, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkyloxy, $C(O)C_{1-6}$ alkyl, C_{6-12} aryl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, wherein R_{12}, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

R_2 is phenyl substituted by one or two substituents chosen from halogen, nitro, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkyloxy, $C(O)C_{1-6}$ alkyl, C_{6-12} aryl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, wherein R_{12}, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

R_2 is phenyl substituted by one or two substituents chosen from halogen, C_{1-6} alkyl, $NR_{13}R_{14}$, nitro, $CONR_{13}R_{14}$, $C(O)OC_{1-6}$ alkyl, COOH or C_{1-6} alkyloxy $C(O)OR_{12}$, cyano, azido, wherein R_{12}, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

In one embodiment, R_2 is chosen from C_{6-14} aryl, C_{3-12} heterocycle, C_{6-12} aralkyl or C_{3-10} heteroaralkyl.

In a further embodiment, R_2 is chosen from a C_{6-12} aryl or C_{3-10} heterocycle.

In a further embodiment, R_2 is a C_6 aryl or a C_{3-6} heterocycle.

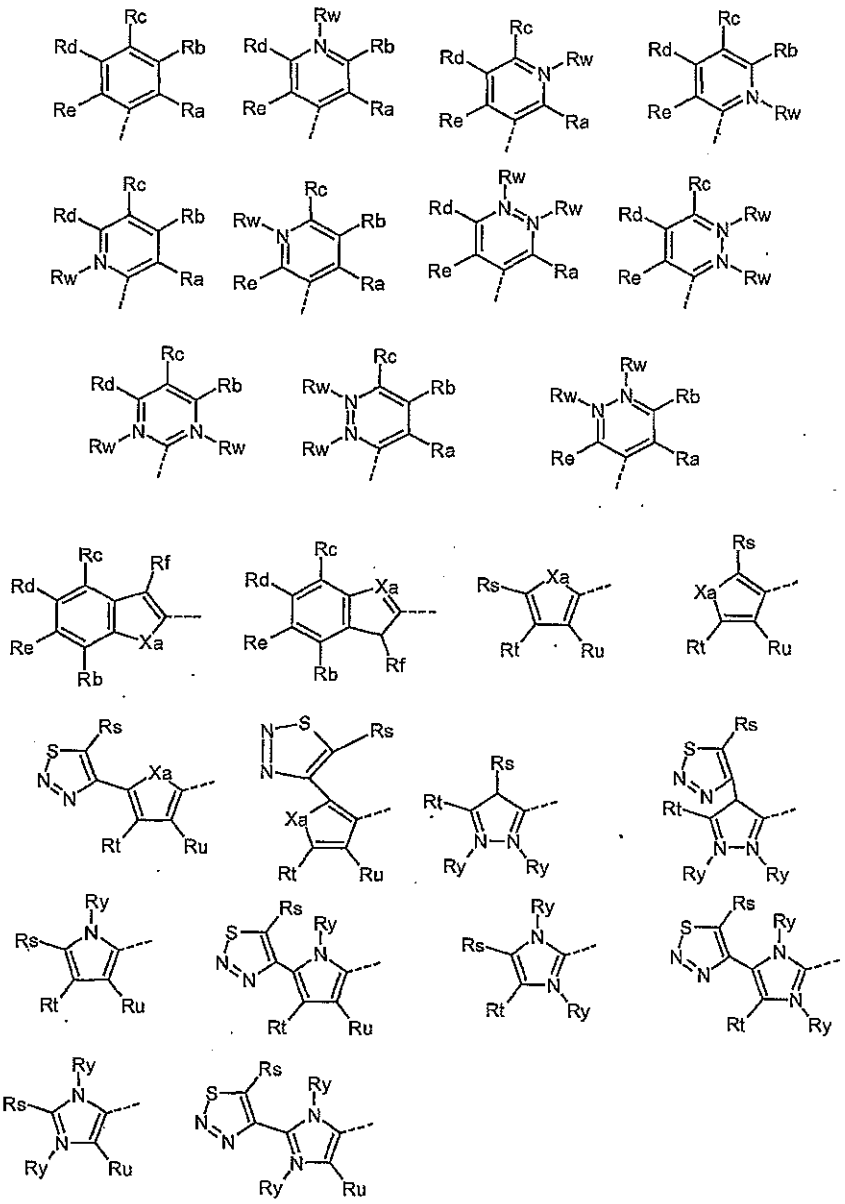
In a further embodiment, R_2 is chosen from phenyl, pyridinyl, thiophenyl, benzofuran, thiazole, pyrazole, substituted with at least one substituent chosen from a halogen, C_{1-6} alkyl, C_{1-6} alkyloxy, CF_3, COOH, $COOC_{1-6}$ alkyl, cyano, NH_2, nitro, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl$)_2$ or a C_{3-8} heterocycle.

R_2 is chosen from thienyl, furanyl, pyridyl, oxazolyl, thiazolyl, pyrrolyl, benzofuranyl, indolyl, benzoxazolyl, benzothienyl, benzothiazolyl or quinolinyl any of which can be substituted by at least one substituent chosen from C_{1-6} alkyl, amino, halogen, nitro, amido, CN, $COOC_{1-6}$ alkyl, or C_{1-6} alkyloxy.

R_2 is methylphenyl.

R_2 is dichlorophenyl.

In a further embodiment, R_2 is chosen from:



wherein:

Rw is H, O or methyl;

Ry is H or methyl;

Rw is H;

Rw is methyl;

Ry is H;

Ry is methyl;

and wherein, Xa is S, N, O or carbon.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, Br, I, F, C_{1-6} alkyl, OC_{1-6} alkyl, CF_3, COOH, $COOC_{1-6}$ alkyl, CN, NH_2, NO_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl$)_2$.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF_3, COOH, $COOCH_3$, CN, NH_2, NO_2, $NH(CH_3)$ or $N(CH_3)_2$.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF_3, COOH, $COOCH_3$, CN, NH_2, or NO_2.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, methyl, O-methyl, CF_3, COOH, $COOCH_3$, CN, NH_2, or NO_2.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, F, methyl, CF_3 or O-methyl.

In one embodiment, Rf is H or methyl.
In another embodiment, Rf is H.
In another embodiment, Rf is methyl.
In a further embodiment, each of Ra, Rb, Rc, Rd and Re is independently chosen from, H or Cl.
In a further embodiment, each of Ra, Rb, Rc, Rd and Re is H.

In one embodiment:
Ra is chosen from Cl, F, methyl or O-methyl;
Rb is H;
Rc is chosen from Cl, F, methyl or O-methyl;
Rd is H;
Re is chosen from Cl, F, methyl or O-methyl.

In one embodiment:

Ra is methyl;

Rb is H;

Rc is Cl;

Rd is H;

Re is methyl.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, C_{1-6} alkyl, OC_{1-6} alkyl, CF_3, COOH, $COOC_{1-6}$ alkyl, CN, NH_2, NO_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl$)_2$.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF_3, COOH, $COOCH_3$, CN, NH_2, NO_2, $NH(CH_3)$ or $N(CH_3)_2$.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF_3, COOH, $COOCH_3$, CN, NH_2, or NO_2.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF_3, COOH, $COOCH_3$, CN, NH_2, or NO_2.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, methyl, O-methyl, CF_3, COOH, $COOCH_3$, CN, NH_2, or NO_2.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, F, methyl, CF_3 or O-methyl.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H or Cl.

In a further embodiment, each of Rs, Rt, Ru, are H.

In one embodiment:

Rs and Ru are Cl and Rt is H.

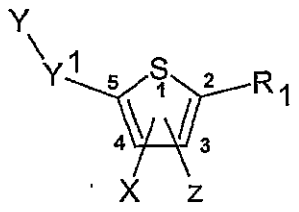
Rs is Cl, Rt and Ru are H.

In one embodiment, the viral infection is chosen from Flavivirus infections.

In one embodiment, the Flavivirus infection is chosen from Hepatitis C virus (HCV), bovine viral diarrhea virus (BVDV), hog cholera virus and yellow fever virus.

In another embodiment, the Flavivirus infection is Hepatitis C viral infection.

In one embodiment, there is provided a method for treating or preventing a Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula (III)

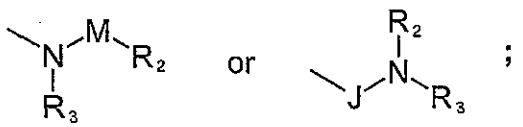


(III)

or pharmaceutically acceptable salts thereof;

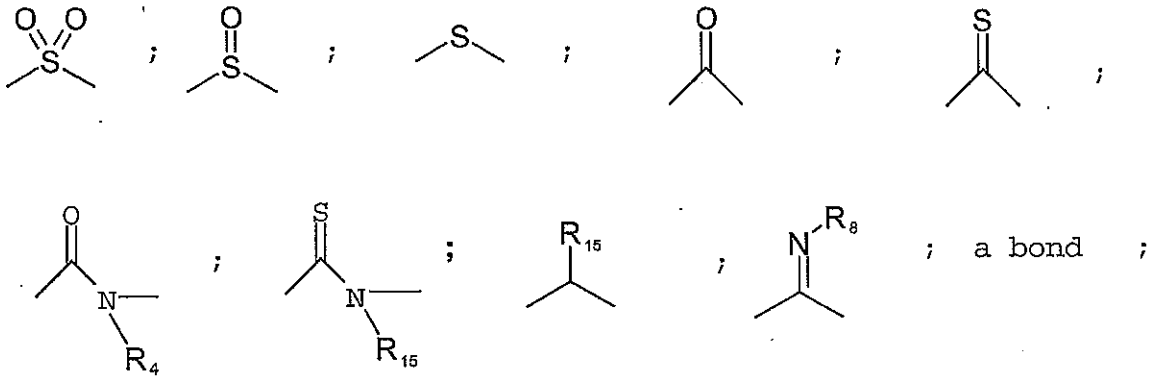
wherein,

X is chosen from:



wherein,

M is chosen from:



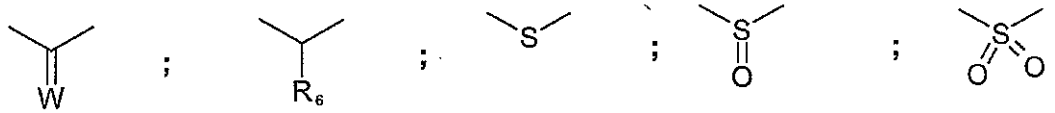
wherein,

R_4 is chosen from H or C_{1-6} alkyl;

R_8 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-12} heteroaralkyl, C_{6-16} aralkyl; and

R_{15} is chosen from H or C_{1-6} alkyl;

J is chosen from:



wherein

W is chosen from O, S or NR_7,

wherein R_7 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-12} aryl, C_{3-12} heterocycle, C_{3-12} heteroaralkyl, C_{6-16} aralkyl;

and R_6 is chosen from H, C_{1-12} alkyl, C_{6-12} aryl or C_{6-16} aralkyl;

Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)-SO_2-R_5$, $CONR_9OH$ or halogen, wherein R_9, R_5, R_{10} and R_{11} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

R_{16} is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl, or halogen;

R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C_{1-6} alkyl.

In one embodiment, there is provided a method for treating or preventing Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula (III), further comprising at least one antiviral agent.

In one embodiment, the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.

In a further embodiment, the antiviral agent is chosen from interferon α and ribavirin.

In a further embodiment, said compound of formula (III) and said antiviral agent are administered sequentially.

In a further embodiment, said compound of formula (III) and said antiviral agent are administered simultaneously.

In one embodiment, there is provided a method for treating or preventing Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula (III) and at least one additional agent chosen from immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

In another embodiment, the additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

In further embodiments;

The compound of formula (III) and the additional agent are administered sequentially.

The compound of formula (III) and the additional agent are administered simultaneously.

In one embodiment, the present invention further provides A pharmaceutical composition comprising at least one compound having the formula III or pharmaceutically acceptable salts thereof;and at least one pharmaceutically acceptable carrier or excipient.

In a further embodiment, the pharmaceutical composition, is further comprising one or more additional agent chosen from antiviral agent, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

In one embodiment, the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.

In one embodiment, the antiviral agent is chosen from interferon α and ribavirin.

In one embodiment, the additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

In one embodiment, the invention further provides the use of a compound having the formula III for the manufacture of a medicament for treating or preventing a viral Flaviridea infection in a host

In one embodiment, there is provided the use of a compound having the formula III or pharmaceutically acceptable salts thereof in therapy

In one embodiment, the invention provides the use of a compound having the formula III for treating or preventing Flaviviridae viral infection in a host.

In one embodiment, the use of a compound having the compound of formula III for treating or preventing Flaviviridae viral infection in a host is further comprising one or more additional agent chosen from antiviral agent, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

In one embodiment, the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.

In one embodiment, the antiviral agent is chosen from interferon α and ribavirin.

In one embodiment, the additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

In one embodiment, the compound of formula III and the additionnal agent are administered sequentially.

In one embodiment, the compound of formula III and the additionnal agent are administered simultaneously.

In one embodiment, there is provided a method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of a compound of formula (III).

In one embodiment, the method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of a compound of formula (III) is further comprising one or more viral polymerase inhibitor.

In further embodiments;

The viral polymerase is a Flaviviridae viral polymerase.

The viral polymerase is a RNA-dependant RNA-polymerase.

The viral polymerase is HCV polymerase.

In one embodiment, the invention provides a method for inhibiting or reducing the activity of viral helicase in a host comprising administering a therapeutically effective amount of a compound having the formula III.

In one embodiment, the invention provides a method for inhibiting or reducing the activity of viral helicase in a host comprising administering a therapeutically effective amount of a compound chosen from:

Compound #14 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid

Compound #19 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid

Compound #223 3-(4-Bromo-2-fluorobenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #224 3-(4-Bromo-2-methylbenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #225 5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-amino)-thiophene-2-carboxylic acid

Compound #581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-2-carboxylic acid

Compound #227 3-[2,5-Bis-(2,2,2-trifluoroethoxy)-benzenesulfonylamino]-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid

Compound #228 3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid

or pharmaceutically acceptable salts thereof.

In further embodiments;

The viral helicase is a flaviviridea helicase.

The viral helicase is HCV helicase.

In a further embodiment, there is provided the use of a compound having the formula III for inhibiting or reducing the activity of viral polymerase in a host.

In still a further embodiment, there is provided the use of a compound having the formula III for inhibiting or reducing the activity of viral polymerase in a host, further comprising one or more viral polymerase inhibitor.

In further embodiments;

The viral polymerase is Flaviviridae viral polymerase.

The viral polymerase is RNA-dependant RNA-polymerase.

The viral polymerase is HCV polymerase.

In one embodiment, the invention provides the use of a compound having the formula III for inhibiting or reducing the activity of viral helicase in a host.

In one embodiment, the invention provides the use of a compound chosen from:

Compound #14 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid

Compound #19 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid

Compound #223 3-(4-Bromo-2-fluorobenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #224 3-(4-Bromo-2-methylbenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #225 5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-

amino)-thiophene-2-carboxylic acid

Compound #581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-2-carboxylic acid

Compound #227 3-[2,5-Bis-(2,2,2-trifluoroethoxy)-benzenesulfonylamino]-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid

Compound #228 3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid

or pharmaceutically acceptable salts thereof for inhibiting or reducing the activity of viral helicase in a host.

In one embodiment, the invention provides the use of a compound having the formula III for inhibiting or reducing the activity of viral helicase in a host further comprising one or more viral helicase inhibitor.

In further embodiments;

The viral helicase is Flaviviridae viral helicase.

The viral helicase is HCV helicase.

In one embodiment, the present invention provides a combination comprising a compound having the formula III and one or more additionnal agent chosen from viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

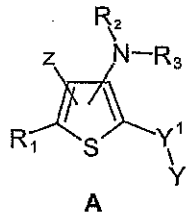
In a further embodiment, the additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine, cyclosporin, interferon α and ribavirin.

In further embodiments;

The compound of formula (III) and the additionnal agent are administered sequentially.

The compound of formula (III) and the additionnal agent are administered simultaneously.

In still a further embodiment, the present invention provides a process for preparing a compound of formula A:

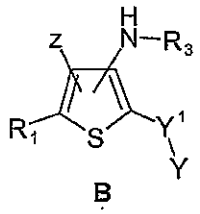


A

said process comprising the steps of adding:

- an enol ether;
- an hydride donating agent; and
- an organic carboxylic acid;

to a compound of formula B:



B

wherein;

Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)-SO_2-R_5$, $CONR_9OH$ or halogen, wherein R_9, R_5, R_{10} and R_{11} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
R_{16} is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;

R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C_{1-6} alkyl.

It will be appreciated by those skilled in the art that the compounds of formula (I) or (Ia) can contain a chiral centre on the general formula (I), The compounds of formula (I) or (Ia) thus exist in the form of two different optical isomers (i.e. (+) or (-) enantiomers). All such enantiomers and mixtures thereof including racemic mixtures are included within the scope of the invention. The single optical isomer or enantiomer can be obtained by method well known in the art, such as chiral HPLC, enzymatic resolution and chiral auxiliary.

In accordance with the present invention, the compounds of formula (I) or (Ia) include:

Compound 1 3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-(3-IODO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 2 3-[(3-BENZOFURAN-2-YL-BENZYL)-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 3 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 4 3-{(2,4-DICHLORO-BENZOYL)-[5-(3-TRIFLUOROMETHYL-PHENYL)-FURAN-2-YLMETHYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 5 3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 6 5-(4-FLUORO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 7 3-(2,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 8 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 9 3-[(2,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 10 5- TERT -BUTYL-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 11 4-(TOLUENE-4-SULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 12 3-[(5-BENZOFURAN-2-YL-THIOPHEN-2-YLMETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 13 5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 14 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-CHLORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 15 5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 16 5-PHENYL-3-(TOLUENE-3-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 17 3-BENZENESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 18 3-(4-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 19 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 20 5-TERT-BUTYL-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 21 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 22 3-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 23 5-PHENYL-3-(THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 24 4-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 25 5-(3,5-BIS-TRIFLUOROMETHYL-PHENYL)-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 26 8-CHLORO-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-4H-1,5-DITHIA-CYCLOPENTA[A]NAPHTHALENE-2-CARBOXYLIC ACID

Compound 27 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 28 3-[3-(2,6-DICHLORO-PYRIDIN-4-YL)-UREIDO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 29 3-(2-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 30 3-(2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 31 5-PHENYL-3-(2-TRIFLUOROMETHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 32 3-(4- TERT -BUTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 33 3-(4-CHLORO-PHENOXYCARBONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 34 3-(3,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 35 5-PHENYL-3-(2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 36 3-(5-BROMO-6-CHLORO-PYRIDINE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 37 3-(5-CHLORO-THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 38 3-(5-CHLORO-3-METHYL-BENZO[B]THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 39 3-(4-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 40 3-(3-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 41 3-(5-CHLORO-1,3-DIMETHYL-1H-PYRAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 42 3-(3-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 43 3-(4-ISOPROPYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 44 3-(2,6-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 45 3-(2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 46 5-PHENYL-3-(5-[1,2,3]THIADIAZOL-4-YL-THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 47 5-PHENYL-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 48 3-(2,4-DICHLORO-BENZYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 49 3-(3-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 50 5-PHENYL-3-(3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 51 3-(2-CARBOXY-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER

Compound 52 5-PHENYL-3-(4-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 53 3-(2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 54 3-(2-CYANO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 55 3-(2,5-DICHLORO-THIOPHENE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 56 4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 57 5'-CHLORO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 58 5-(2,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 59 5-(4-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 60 3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 61 5-QUINOLIN-8-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 62 5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 63 5-(3-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 64 3-(TOLUENE-2-SULFONYLAMINO)-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 65 5-(3-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 66 5-(4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 67 5-(3-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 68 5-(4-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 69 5-(3,5-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 70 5-(3,4-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 71 3-(TOLUENE-2-SULFONYLAMINO)-5-VINYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 72 3-(4-CHLORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 73 3-[(4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 74 5-PHENYL-3-[(THIOPHENE-2-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 75 3-[METHYL-(THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 76 3-(2-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 77 3-(2,4-DIFLUORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 78 3-[(2,4-DIFLUORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 79 3-(TOLUENE-2-SULFONYLAMINO)-5-TRIMETHYLSILANYLETHYNYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 80 5-ETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 81 3-(TOLUENE-2-SULFONYLAMINO)-5-(3-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 82 5-BENZOYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 83 5-(4-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 84 5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 85 5-(3,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 86 5-PYRIDIN-4-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 87 5-PYRIDIN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 88 3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 89 5-(4-METHANESULFONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 90 5-(3-ACETYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 91 5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 92 3-(4-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 93 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 94 3-(3,5-DIMETHYL-ISOXAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 95 3-[(2-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 96 3-(2-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 97 3-[METHYL-(2-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 98 5-PHENYL-3-(5-TRIFLUOROMETHYL-PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 99 5-PHENYLETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 100 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 101 5-(2-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 102 5-(2-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 103 5-(2-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 104 5-(2-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 105 3'-METHYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 106 3-(TOLUENE-2-SULFONYLAMINO)-5-(2-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 107 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 108 5-STYRYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 109 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 110 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 111 3-[[5-(3-CHLORO-4-FLUORO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 112 3-[(4-OXO-1-PHENYL-1,3,8-TRIAZA-SPIRO[4.5]DECANE-8-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 113 3-{[4-(2-OXO-2,3-DIHYDRO-BENZOIMIDAZOL-1-YL)-PIPERIDINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 114 3-{[4-(4-NITRO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 115 5-(2-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 116 5-(4-CHLORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 117 5-(3-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 118 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 119 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 120 5-PHENETHYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 121 5-(3-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 122 5-(4-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 123 5-(3-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 124 5-(4'-BROMO-BIPHENYL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 125 5-(4-HYDROXYMETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 126 5-FURAN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 127 5-BENZOFURAN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 128 5-PYRIDIN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 129 5-(4-NITRO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 130 3-[(BENZOFURAN-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 131 3-[(2,4-DIMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 132 3-[[5-(2-CYANO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 133 5-(4-FLUORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 134 5-[2-(4-CHLORO-PHENYL)-VINYL]-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 135 3-BENZENESULFONYLAMINO-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 136 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 137 5-PHENYL-3-(2-VINYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 138 3-(4-BROMO-2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 139 3-(2-ACETYLAMINO-4-METHYL-THIAZOLE-5-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 140 3-(4-ACETYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 141 3-(4-FLUORO-2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 142 3-(2-METHOXY-4-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 143 3-(3,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 144 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID ETHYL ESTER

Compound 145 3-(4-FLUORO-3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 146 3-(2-AMINO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 147 3-(3-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 148 3-(4-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 149 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 150 5-(3-CYANO-BENZYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 151 5-PHENYL-3-(2,4,6-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 152 3-(4-METHOXY-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 153 5-PHENYL-3-(2,3,4-TRICHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 154 5-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID METHYL ESTER

Compound 155 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-1,5-DIPHENYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER

Compound 156 5-PHENYL-3-{[4-(3-TRIFLUOROMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMIN}-THIOPHENE-2-CARBOXYLIC ACID

Compound 157 3-{[4-(4-FLUORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 158 3-{[4-(2,6-DIMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 159 3-{[4-(2-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 160 3-{[4-(3-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 161 4,4'-BIS-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5,5'-DICARBOXYLIC ACID

Compound 162 3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 163 5-(1-DIMETHYLSULFAMOYL-1H-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 164 5-(3-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 165 5-(4-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 166 5-(4-ACETYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 167 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2,5-DIMETHYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER

Compound 168 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-3-METHYL-1-PHENYL-1H-PYRROLE-2-CARBOXYLIC ACID ETHYL ESTER

Compound 169 3-(3,5-DICHLORO-4-HYDROXY-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 170 5-(1H-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 171 5-(3-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 172 3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 173 3-{[2-(4-FLUORO-PHENYL)-ACETYL]-METHYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 174 3-(4-PENTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 175 3-(METHYL-PHENYLACETYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 176 3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 177 3-(4-METHYL-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 178 5-THIAZOL-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 179 5-PHENYL-3-[3-(3-PHENYL-PROPYL)-UREIDO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 180 3-[(3,4-DIHYDRO-1H-ISOQUINOLINE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 181 3-{[4-(4-METHOXY-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 182 3-{[4-(6-METHYL-PYRIDIN-2-YL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE

Compound 183 3-{[4-(4-CHLORO-BENZYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE

Compound 184 5-(5-METHYL-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 185 3-[ETHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 186 3-[(3-CHLORO-THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 187 3-[(2-BROMO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 188 3-[(4-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 189 3-(2-CHLOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 190 5-(4-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 191 5-(5-CHLORO-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 192 5-(4-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 193 5-(4-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 194 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 195 5-(4-HYDROXYMETHYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 196 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 197 5-(4-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 198 5-(4-METHOXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 199 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 200 5-(4-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 201 3-[CYCLOPENTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 202 5-BENZO[1,3]DIOXOL-5-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 203 3-[(2-HYDROXY-ETHYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 204 3-[(2,4-DICHLORO-BENZOYL)-ISOBUTYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 205 3-[(2-METHOXY-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 206 5-(3-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 207 5-(2-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 208 3-[(2,4-DICHLORO-BENZOYL)-PHENYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 209 3-[4-(TRIFLUOROMETHYL-BENZOYL)METHYLAMINE]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 210 3-[(4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 211 3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 212 5-(3,5-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 213 5-(3-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 214 5-(2,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 215 5-(4-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 216 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 217 5-(2-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 218 3-[(2-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 219 3-[(3,5-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 220 3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 221 3-(5-CARBOXY-4-CHLORO-2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 222 5-PHENYL-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 223 3-(4-BROMO-2-FLUORO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 224 3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 225 5-(4-ISOBUTYL-PHENYL)-3-(3-METHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 226 3-[(4-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 227 3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 228 3-(2-CHLORO-4-CYANO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 229 5'-ACETYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 230 5-BENZO[B]THIOPHEN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 231 5-(4-BUTYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 232 5-(4-ETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 233 3-[BENZYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 234 3-[(4-CHLORO-2-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 235 3-[(2,4-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 236 5-(4-ACETYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 237 5-(4-ACETYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 238 5-(4-ACETYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 239 5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID TERT-BUTYL ESTER

Compound 240 3-[(2,4-DIMETHYL-BENZENESULFONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 241 3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 242 3-ETHANESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 243 3-[ISOPROPYL-(4-TRIFLUOROMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 244 3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 245 3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 246 3-[(6-CHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 247 3-[(4-TERT-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 248 5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 249 5-(4-ETHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 250 3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 251 3-[(BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 252 3-[METHYL-(NAPHTHALENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 253 3-[(3,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 254 3-[(3,5-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 255 3-[(4-BROMO-3-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 256 3-[(3-CHLORO-BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 257 3-[METHYL-(4-METHYL-3-NITRO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 258 5-(4-CARBAMOYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 259 5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 260 5-(1H-INDOL-5-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 261 3-[SEC -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 262 3-[(2,4-DIMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 263 5-(4-AZIDO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 264 3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 265 5-(4-CARBAMOYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 266 5-(2-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 267 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5- O -TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 268 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 269 5-(3-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 270 5-(3,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 271 5-(3-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 272 5-(3-ACETYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 273 5-(3-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 274 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 275 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 276 3-[(3,4-DIMETHOXY-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 277 3-[METHYL-(2,4,6-TRIFLUORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 278 3-[(2,3-DIFLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 279 3-[(3-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 280 3-[(2,3-DIFLUORO-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 281 3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 282 5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 283 5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 284 3-[(2-BROMO-4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 285 3-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 286 3-[METHYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 287 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER

Compound 288 5-(4-CYANO-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 289 3-(4-CHLORO-BENZENESULFONYLAMINO)-5-(4-CYANO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 290 5-(4-CYANO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 291 5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 292 5'-ACETYL-4-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 293 3-[METHYL-(4-METHYL-THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 294 5-(3-CHLORO-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 295 5'-CYANO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 296 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-2-YL-THIOPHENE-2-CARBOXYLIC ACID

Compound 297 3-[(2,4-DICHLORO-THIOBENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 298 5-PHENYL-3-(2,4,6-TRIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 299 3-[(1-CARBOXY-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 300 3-[(4-METHYL-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 301 3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 302 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-3-YL-THIOPHENE-2-CARBOXYLIC ACID

Compound 303 5'-ACETYL-4-[METHYL-(4-METHYL-BENZOYL)-AMINO]-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 304 3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 305 3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 306 3-[(2-BROMO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 307 3-[(4-CHLORO-2-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 308 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-4-METHYL-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 309 3-[(2-BROMO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 310 3-[(4-CHLORO-2-IODO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 311 3-[(4-CYANO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 312 3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[4-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID

Compound 313 3-[(4-CHLORO-2-HYDROXY-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 314 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-METHYL-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 315 5- TERT -BUTYL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 316 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 317 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 318 5-[4-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 319 5-BENZOFURAN-2-YL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 320 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-HYDROXYMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 321 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 322 5-[4-(2-CARBOXY-VINYL)-PHENYL]-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 323 3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[3-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID

Compound 324 3-[ISOPROPYL-(2,4,6-TRIMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 325 5-[3-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 326 3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 327 3-[TERT -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 328 3-[(2-AMINO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 329 3-[(4-CHLORO-2-NITRO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 330 3-[(4-METHYL-BENZOYL)-(3-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 331 3-[(3-FLUORO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 332 5-(4-CARBOXY-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 333 3-[CYCLOPROPYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 334 3-[(3-TERT-BUTYL-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 335 3-[(3-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 336 3-[(2,4-DIFLUORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 337 3-[(4-CHLORO-2,5-DIFLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 338 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(2-METHYL-ALLYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 339 3-{ALLYL-[2-(4-CHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 340 3-[BENZYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 341 3-[(4-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 342 3-[(4-METHYL-BENZOYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 343 3-[(4-METHYL-BENZOYL)-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 344 3-[(3-METHOXY-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 345 3-[(2-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 346 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-ISOBUTYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 347 3-[ALLYL-(2-NAPHTHALEN-2-YL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 348 3-{ALLYL-[2-(2,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 349 3-{ALLYL-[2-(2-CHLORO-4-FLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 350 3-{ALLYL-[2-(3,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 351 3-{ALLYL-[2-(2,4-DIFLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 352 3-{ALLYL-[2-(4-TRIFLUOROMETHYL-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 353 3-{ALLYL-[2-(2,6-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 354 3-[ALLYL-(2-M-TOLYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 355 5-(4-ACETYL-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 356 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 357 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 358 5'-ACETYL-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 359 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 360 4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5'-METHYL-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 361 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 362 3-(CYCLOHEXANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 363 3-{(2,4-DICHLORO-BENZOYL)-[1-(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 364 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER

Compound 365 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER

Compound 366 3-[(4-METHYL-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 367 5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 368 3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 369 5-(4-METHANESULFONYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 370 3-(4-FLUORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 371 3-[(3-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 372 3-(4-CHLORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 373 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 374 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFINYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 375 5-(4-CARBOXY-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 376 5-BENZOFURAN-2-YL-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 377 3-[(2-ACETOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 378 3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 379 3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 380 3-(CYCLOHEPTANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 381 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 382 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-METHYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 383. 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 384 3-[(3-CYCLOPENTYL-PROPIONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 385 3-(BUTYRYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 386 3-(METHYL-PENT-4-ENOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 387 3-[ISOPROPYL-(5-METHYL-3-OXO-3H-ISOINDOL-1-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 388 3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 389 3-(METHYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 390 3-[METHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 391 3-(CYCLOPENTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 392 3-[(3-CYCLOPENTYL-PROPIONYL)-ETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 393 3-(CYCLOBUTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 394 3-(BUT-2-ENOYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 395 3-[ISOPROPYL-(4-METHYL-2-VINYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 396 3-[ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 397 3-(ALLYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 398 3-(ALLYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 399 3-(ALLYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 400 3-[ALLYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 401 3-[ALLYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 402 3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 403 3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 404 3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 405 3-[ISOPROPYL-(3-METHYL-CYCLOPENT-3-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 406 3-[(2-BENZYLOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 407 3-[(2,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 408 3-[ISOPROPYL-(3-METHYL-CYCLOPENTANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 409 3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 410 5-PHENYL-3-[PROPIONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 411 3-[ISOBUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 412 3-[(3-METHYL-BUTYRYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 413 3-[CYCLOPROPANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 414 3-[CYCLOBUTANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 415 3-[BUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 416 3-[(2-CYCLOPENTYL-ACETYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 417 3-[(4-TERT-BUTYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 418 3-[(4-NITRO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 419 3-[(3-METHYL-BUTYRYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 420 3-[CYCLOPROPANECARBONYL-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 421 3-[(2-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 422 3-[(2-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 423 3-[(2-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 424 3-[(ADAMANTANE-1-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 425 3-[(2-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 426 3-[ACETYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 427 3-[(2-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 428 3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 429 3-[(1-ACETYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 430 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-[4-(1 H -TETRAZOL-5-YL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID

Compound 431 3-[(2-CYANO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 432 3-[CYCLOBUTANECARBONYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 433 3-[BUTYRYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 434 3-[ACETYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 435 3-[CYCLOBUTANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 436 3-[CYCLOHEXANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 437 3-[(4-TERT-BUTYL-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 438 3-[(4-TERT-BUTYL-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 439 3-[(4-TERT-BUTYL-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 440 3-[(4-TERT-BUTYL-BENZYL)-BUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 441 3-[(4-TERT-BUTYL-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 442 3-[(4-TERT-BUTYL-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 443 3-[(2-CYCLOPENTYL-ACETYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 444 3-[(2-CHLORO-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 445 3-[(2-CYCLOPENTYL-ACETYL)-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 446 3-[BUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 447 3-[BUTYRYL-(2-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 448 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- M - TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 449 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-THIAZOL-2-YL-THIOPHENE-2-CARBOXYLIC ACID

Compound 450 3-(ACETYL-BENZYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 451 3-(BENZYL-PROPIONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 452 3-[BENZYL-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 453 3-[BENZYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 454 3-(BENZYL-CYCLOPROPANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 455 3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 456 3-[(4-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 457 3-[(4-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 458 3-[(4-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 459 3-[(4-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 460 5-(4-ACETYL-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 461 3-[(4-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 462 3-[BUTYRYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 463. 3-[(4-CHLORO-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 464 3-[ACETYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 465 3-[ISOBUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 466 3-[CYCLOPROPANECARBONYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 467 3-[(4-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 468 3-[ISOBUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 469 3-[CYCLOPROPANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 470 3-[BUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 471 3-[(3-METHOXY-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 472 3-[(3-METHOXY-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 473 3-[CYCLOBUTANECARBONYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 474 3-[(2-CARBAMOYL-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 475 3-[BUTYRYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 476 3-[ACETYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 477 3-[(3-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 478 3-[(3-CHLORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 479 3-[(3-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 480 3-[(3-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 481 3-[(3-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 482 3-[BUTYRYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 483 3-[ACETYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 484 3-[(2,4-DIFLUORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 485 3-[(2,4-DIFLUORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 486 3-[(2,4-DIFLUORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 487 3-[BENZYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 488 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(1H-INDOL-5-YL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 489 3-(BENZYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 490 3-[CYCLOHEXANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 491 3-{ALLYL-[2-(4-METHOXY-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 492 3-(ETHYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 493 3-(BUTYRYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 494 3-[ETHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 495 3-[CYCLOBUTANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 496 3-[BUTYRYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 497 3-(CYCLOPENTANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 498 3-(CYCLOHEXANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 499 3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PYRROLIDINE-1-CARBOXYLIC ACID TERT-BUTYL ESTER

Compound 500 3-[(1,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 501 5-(4-ETHYL-PHENYL)-3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 502 3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5- M -TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 503 3-[(2,4-DICHLORO-BENZOYL)-PYRROLIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 504 4-{5-CARBOXY-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2H-PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 505 3-{[2-(HYDROXYIMINO-METHYL)-4-METHYL-BENZOYL]-ISOPROPYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 506 3-[(1-CARBAMIMIDOYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 507 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-AZEPANE-1-CARBOXYLIC ACID TERT -BUTYL ESTER

Compound 508 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 509 3-[AZEPAN-4-YL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 510 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID LITHIUM SALT

Compound 511 3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER

Compound 512 3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 513 3-[ISOPROPYL-(4-METHYL-2-OXO-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 514 3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH GENERIC INORGANIC NEUTRAL COMPONENT

Compound 515 3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 516 3-[(2-BENZYLOXY-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 517 3-[(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 518 3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-HYDROXYMETHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 519 3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 520 3-[(2-CHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 521 3-[(4,6-DICHLORO-1H-INDOLE-2-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 522 3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-METHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 523 4-(1-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-ETHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 524 4-(5-CARBOXY-4-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2 H -PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 525 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PYRIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 526 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PIPERIDIN-4-YL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID

Compound 527 3-[ISOPROPYL-(4-PROPYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 528 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM; TRIFLUORO-ACETATE

Compound 529 3-[(2,4-DICHLORO-BENZOYL)-(1-PIPERIDIN-4-YL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID

Compound 530 3-[(CYCLOHEX-3-ENECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 531 3-[(4-ETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 532 3-[(4-CHLORO-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 533 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-3-METHYL-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 534 3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 535 3-[(2,4-DICHLORO-BENZOYL)-(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 536 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(1-METHYL-PIPERIDIN-4-YL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 537 3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID

Compound 538 3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 539 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE CARBONYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 540 3-[((1R,2S,4R)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 541 3-{ISOPROPYL-[1-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYL)-5-METHYL-1,2,3,6-TETRAHYDRO-PYRIDINE-2-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 542 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-FLUORO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 543 3-[(2,4-DICHLORO-BENZOYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 544 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE CARBONYL)-AMINO]-METHYL}-PIPERIDINIUM; TRIFLUORO-ACETATE

Compound 545 3-[(2-TERT-BUTOXYCARBONYLAMINO-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 546 2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PROPYL-AMINE TRIFLUOROACETIC ACID SALT

Compound 547 3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 548 3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 549 2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM CHLORIDE

Compound 550 3-(BENZOYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 551 {[5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBONYL]-AMINO}-ACETIC ACID

Compound 552 5-BROMO-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 553 3-[CYCLOHEXYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 554 3-[[1,3]DIOXAN-5-YL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 555 3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 556 3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 557 3-[(2,4-DICHLORO-BENZOYL)-(2-DIETHYLAMINO-THIAZOL-5-YLMETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 558 (5-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-THIAZOL-2-YL)-DIETHYL-AMMONIUM; CHLORIDE

Compound 559 5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 560 3-[((1S,2R,4S)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 561 3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-1-METHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 562 3-[(4S)-ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 566 3-METHYL-(4-METHYLBENZOYL)-AMINO)5-PHENYL THIOPHENE-2-CARBOXYLIC ACID (2-HYDROXY-ETHYL)AMIDE

Compound 567 5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID CYCLOBUTYLAMIDE

Compound 568 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMIDE

Compound 569 5-BROMO-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 570 5-(4-CHLORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANE-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 571 . 5-(4'-CHLORO-BIPHENYL-4-YL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 572 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(TETRAHYDRO-PYRAN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 573 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 574 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 575 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 576 5-(4-CYANO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 577 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 578 3-[(2-METHOXY-1-METHYL-ETHYL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 579 3-[CYCLOHEXYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 581 5-(4-ISOBUTYL-PHENYL)-3-[5-(5-TRIFLUOROMETHYL-ISOXAZOL-3-YL)-THIOPHENE-2-SULFONYLAMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 582 5-(4-ISOBUTYL-PHENYL)-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 583 3-[(2,4-DICHLORO-PHENYL)-ISOPROPYL-CARBAMOYL]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 584 3-(METHYL-P-TOLYL-CARBAMOYL)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 585 3-[(2,4-DICHLORO-PHENYL)-METHYL-CARBAMOYL]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

or pharmaceutically acceptable salts thereof.

Preferably, the compounds of the present invention are provided in the form of a single enantiomer at least 95%, more preferrably at least 97% and most preferably at least 99% free of the corresponding enantiomer.

More preferably the compound of the present invention are in the form of the (+) enantiomer at least 95% free of the corresponding (-)enantiomer.

More preferably the compound of the present invention are in the form of the (+) enantiomer at least 97% free of the corresponding (-) enantiomer.

More preferably the compound of the present invention are in the form of the (+) enantiomer at least 99% free of the corresponding (-) enantiomer.

In a more preferred embodiment, the compound of the present invention are in the form of the (-) enantiomer at least 95% free of the corresponding (+) enantiomer.
Most preferably the compound of the present invention are in the form of the (-) enantiomer at least 97% free of the corresponding (+) enantiomer.

More preferably the compound of the present invention are in the form of the (-) enantiomer at least 99% free of the corresponding (+) enantiomer.

There is also provided a pharmaceutically acceptable salts of the present invention. By the term pharmaceutically acceptable salts of compounds of general formula (I) or (Ia) are meant those derived from pharmaceutically acceptable inorganic and organic acids and bases. Examples of suitable acids include hydrochloric, hydrobromic, sulphuric, nitric, perchloric, fumaric, maleic, phosphoric, glycollic, lactic, salicylic, succinic, toleune-p-sulphonic, tartaric, acetic, trifluoroacetic, citric, methanesulphonic, formic, benzoic, malonic, naphthalene-2-sulphonic and benzenesulphonic acids. Other acids such as oxalic, while not in themselves pharmaceutically acceptable, may be useful as intermediates in obtaining the compounds of the invention and their pharmaceutically acceptable acid addition salts.

Salts derived from appropriate bases include alkali metal (e.g. sodium), alkaline earth metal (e.g. magnesium), ammonium and NR_4+ (where R is C_{1-4} alkyl) salts.

References hereinafter to a compound according to the invention includes compounds of the general formula (I)or (Ia) and their pharmaceutically acceptable salts.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

As used in this application, the term "alkyl" represents a straight chain, branched chain or cyclic hydrocarbon moiety which may optionally be substituted by one or more of: halogen, nitro, nitroso, SO3R12, PO3RcRd, CONR13R14, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-12 aralkyl, C6-12 aryl, C1-6 alkyloxy, C2-6 alkenyloxy, C2-6 alkynyloxy, C6-12 aryloxy, C(O)C1-6 alkyl, C(O)C2-6 alkenyl, C(O)C2-6 alkynyl, C(O)C6-12 aryl, C(O)C6-12 aralkyl, C3-10 heterocycle, hydroxyl, NR13R14, C(O)OR12, cyano, azido, amidino or guanido;

wherein R12, Rc, Rd, R13 and R14 are each independently chosen from H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-14 aryl, C3-12 heterocycle, C3-18 heteroaralkyl, C6-18 aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

or R13 and R14 are taken together with the nitrogen to form a 3 to 10 membered heterocycle. Useful examples of alkyls include isopropyl, ethyl, fluorohexyl or cyclopropyl. The term alkyl is also meant to include alkyls in which one or more hydrogen atoms is replaced by an oxygen, (e.g. a benzoyl) or an halogen, more preferably, the halogen is fluoro (e.g. CF3- or CF3CH2-).

The terms "alkenyl" and "alkynyl" represent an alkyl containing at least one unsaturated group (e.g. allyl, acetylene, ethylene).

The term "aryl" represents a carbocyclic moiety containing at least one benzenoid-type ring which may optionally be substituted by one or more of halogen, nitro, nitroso, SO3R12, PO3RcRd, CONR13R14, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-12 aralkyl, C6-12 aryl, C1-6 alkyloxy, C2-6 alkenyloxy, C2-6 alkynyloxy, C6-12 aryloxy, C(O)C1-6 alkyl, C(O)C2-6 alkenyl, C(O)C2-6 alkynyl, C(O)C6-12 aryl, C(O)C6-12 aralkyl, C3-10 heterocycle, hydroxyl, NR13R14, C(O)OR12, cyano, azido, amidino or guanido;

wherein R12, Rc, Rd, R13 and R14 are each independently chosen from H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-14 aryl, C3-12 heterocycle, C3-18 heteroaralkyl, C6-18 aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R13 and R14 are taken together with the nitrogen to form a 3 to 10 membered heterocycle. Examples of aryl include phenyl and naphthyl.

The term "aralkyl" represents an aryl group attached to the adjacent atom by a C1-6alkyl, C1-6alkenyl, or C1-6alkynyl(e.g., benzyl).

The term "heterocycle" represents a saturated or unsaturated, cyclic moiety wherein said cyclic moeity is interrupted by at least one heteroatom, (e.g. oxygen, sulfur or nitrogen) which may optionally be substituted halogen, nitro, nitroso, SO3R12, PO3RcRd, CONR13R14, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-12 aralkyl, C6-12 aryl, C1-6 alkyloxy, C2-6 alkenyloxy, C2-6 alkynyloxy, C6-12 aryloxy, C(O)C1-6 alkyl, C(O)C2-6 alkenyl, C(O)C2-6 alkynyl, C(O)C6-12 aryl, C(O)C6-12 aralkyl, C3-10 heterocycle, hydroxyl, NR13R14, C(O)OR12, cyano, azido, amidino or guanido;
wherein R12, Rc, Rd, R13 and R14 are each independently chosen from H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-14 aryl, C3-12 heterocycle, C3-18 heteroaralkyl, C6-18 aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

or R13 and R14 are taken together with the nitrogen to form a 3 to 10 membered heterocycle. It is understood that the term heterocyclic ring represents a mono or polycyclic (e.g., bicyclic) ring. Examples of heterocyclic rings include but are not limited to epoxide; furan; benzofuran; isobenzofuran; oxathiolane; dithiolane; dioxolane; pyrrole; pyrrolidine; imidazole; pyridine; pyrimidine; indole; piperidine; morpholine; thiophene and thiomorpholine.

The term "heteroaralkyl" represents an heterocycle group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl.

When there is a sulfur atom present, the sulfur atom can be at different oxidation levels, ie. S, SO, or SO2. All such oxidation levels are within the scope of the present invention.

The term "independently" means that a substituent can be the same or different definition for each item.

As used in this application, the term " hydride donating agent " means a suitable ionic or covalent inorganic compound of hydrogen with another element (e.g. boron, sodium, lithium or aluminum) allowing the process to occur under the reaction conditions without causing adverse effect on the reagents or product. Useful examples of hydride donating agent include but are not limited to sodium borohydride ($NaBH_4$), sodium cyanoborohydride ($NaCNBH_3$), sodium triacetoxyborohydride ($Na(OAc)_3BH$) and borane-pyridine complexe (BH_3-Py). Alternatively, resin or polymer supported hydride donating agent on a may be used.

The term "organic carboxylic acid" include but is not limited to aliphatic acid (e.g. acetic, formic, trifluoroacetic), aromatic acid (e.g. benzoic and salicylic), dicarboxylic acid (e.g. oxalic and phthalic). It will be apparent to one of ordinary skill that resin supported organic carboxylic acid may also be used.

The term ''enol ether'' as used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Enol ethers may be obtained commercially or prepared by well-known methods. Non-limiting examples of preparation include alkylation or silylation of enolates obtained from carbonyl compounds such as aldehydes, ketones, esters.

It will be appreciated that the amount of a compound of the invention required for use in treatment will vary not only with the particular compound selected but also with the route of administration, the nature of the condition for which treatment is required and the age and condition of the patient and will be ultimately at the discretion of the attendant physician or veterinarian. In general however a suitable dose will be in the range of from about 0.1 to about 750 mg/kg of body weight per day, preferably in the range of 0.5 to 60 mg/kg/day, most preferably in the range of 1 to 20 mg/kg/day.

The desired dose may conveniently be presented in a single dose or as divided dose administered at appropriate intervals, for example as two, three, four or more doses per day.

The compound is conveniently administered in unit dosage form; for example containing 10 to 1500 mg, conveniently 20 to 1000 mg, most conveniently 50 to 700 mg of active ingredient per unit dosage form.

Ideally the active ingredient should be administered to achieve peak plasma concentrations of the active compound of from about 1 to about 75μM, preferably about 2 to 50 μM, most preferably about 3 to about 30 μM. This may be achieved, for example, by the intravenous injection of a 0.1 to 5% solution of the active ingredient, optionally in saline, or orally administered as a bolus containing about 1 to about 500 mg of the active ingredient. Desirable blood levels may be maintained by a continuous infusion to provide about 0.01 to about 5.0

mg/kg/hour or by intermittent infusions containing about 0.4 to about 15 mg/kg of the active ingredient.

While it is possible that, for use in therapy, a compound of the invention may be administered as the raw chemical it is preferable to present the active ingredient as a pharmaceutical formulation. The invention thus further provides a pharmaceutical formulation comprising compounds of formula (I) or (Ia) or a pharmaceutically acceptable derivative thereof together with one or more pharmaceutically acceptable carriers therefor and, optionally, other therapeutic and/or prophylactic ingredients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

Pharmaceutical formulations include those suitable for oral, rectal, nasal, topical (including buccal and sub-lingual), transdermal, vaginal or parenteral (including intramuscular, sub-cutaneous and intravenous) administration or in a form suitable for administration by inhalation or insufflation. The formulations may, where appropriate, be conveniently presented in discrete dosage units and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing into association the active compound with liquid carriers or finely divided solid carriers or both and then, if necessary, shaping the product into the desired formulation.

Pharmaceutical formulation suitable for oral administration may conveniently be presented as discrete units such as capsules, cachets or tablets each containing a predetermined amount of the active ingredient; as a powder or granules; as a solution, a suspension or as an emulsion. The active ingredient may also be presented as a bolus, electuary or paste. Tablets and capsules for oral administration may contain conventional excipients such as binding agents, fillers, lubricants, disintegrants, or wetting agents. The tablets may be coated according to methods well known in the art. Oral liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, emulsions, syrups or elixirs, or may be presented as a dry

product for constitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, emulsifying agents, non-aqueous vehicles (which may include edible oils), or preservatives.

The compounds according to the invention may also be formulated for parenteral administration (e.g. by injection, for example bolus injection or continuous infusion) and may be presented in unit dose form in ampoules, pre-filled syringes, small volume infusion or in multi-dose containers with an added preservative. The compositions may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing an/or dispersing agents. Alternatively, the active ingredient may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilisation from solution, for constitution with a suitable vehicle, e.g. sterile, pyrogen-free water, before use.

For topical administration to the epidermis, the compounds according to the invention may be formulated as ointments, creams or lotions, or as a transdermal patch. Such transdermal patches may contain penetration enhancers such as linalool, carvacrol, thymol, citral, menthol and t-anethole. Ointments and creams may, for example, be formulated with an aqueous or oily base with the addition of suitable thickening and/or gelling agents. Lotions may be formulated with an aqueous or oily base and will in general also contain one or more emulsifying agents, stabilizing agents, dispersing agents, suspending agents, thickening agents, or colouring agents.

Formulations suitable for topical administration in the mouth include lozenges comprising active ingredient in a flavoured base, usually sucrose and acacia or tragacanth; pastilles comprising the active ingredient in an inert base such as gelatin and glycerin or sucrose and acacia; and mouthwashes comprising the active ingredient in a suitable liquid carrier.

Pharmaceutical formulations suitable for rectal administration wherein the carrier is a solid are most preferably presented as

unit dose suppositories. Suitable carriers include cocoa butter and other materials commonly used in the art, and the suppositories may be conveniently formed by admixture of the active compound with the softened or melted carrier(s) followed by chilling and shaping in moulds.

Formulations suitable for vaginal administration may be presented as pessaries, tampons, creams, gels, pastes, foams or sprays containing in addition to the active ingredient such carriers as are known in the art to be appropriate.

For intra-nasal administration the compounds of the invention may be used as a liquid spray or dispersible powder or in the form of drops. Drops may be formulated with an aqueous or non-aqueous base also comprising one more dispersing agents, solubilising agents or suspending agents. Liquid sprays are conveniently delivered from pressurized packs.

For administration by inhalation the compounds according to the invention are conveniently delivered from an insufflator, nebulizer or a pressurized pack or other convenient means of delivering an aerosol spray. Pressurized packs may comprise a suitable propellant such as dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount.

Alternatively, for administration by inhalation or insufflation, the compounds according to the invention may take the form of a dry powder composition, for example a powder mix of the compound and a suitable powder base such as lactose or starch. The powder composition may be presented in unit dosage form in, for example, capsules or cartridges or e.g. gelatin or blister packs from which the powder may be administered with the aid of an inhalator or insufflator.

When desired the above described formulations adapted to give sustained release of the active ingredient may be employed.

The compounds of the invention may also be used in combination with other antiviral agents or in combination with any additional agents useful in therapy and may be administered sequentially or simultaneously.

In one aspect of the invention, the compounds of the invention may be employed together with at least one other antiviral agent chosen from protease inhibitors, polymerase inhibitors, and helicase inhibitors.

In another aspect of the invention, the compounds of the invention may be employed together with at least one other antiviral agent chosen from Interferon-α and Ribavirin.

The combinations referred to above may conveniently be presented for use in the form of a pharmaceutical formulation and thus pharmaceutical formulations comprising a combination as defined above together with a pharmaceutically acceptable carrier therefor comprise a further aspect of the invention.

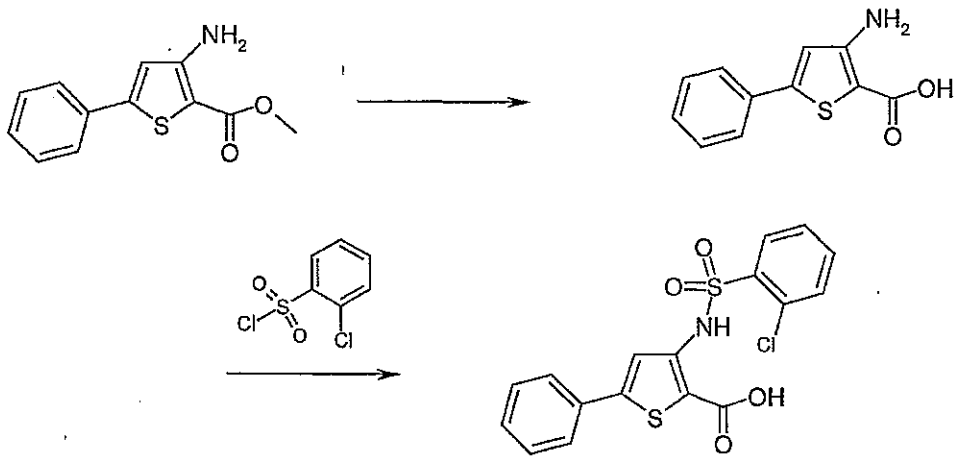
The individual components of such combinations may be administered either sequentially or simultaneously in separate or combined pharmaceutical formulations.

When the compounds of formula (I) or (Ia) or a pharmaceutically acceptable salts thereof is used in combination with a second therapeutic agent active against the same virus the dose of each compound may be either the same as or differ from that when the compound is used alone. Appropriate doses will be readily appreciated by those skilled in the art.

The following general schemes and examples are provided to illustrate various embodiments of the present invention and shall not be considered as limiting in scope.

Example 1

Preparation of 3-(2-Chloro-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid, compound #29



STEP I

3-Amino-5-phenyl-thiophene-2-carboxylic acid.

To a suspension of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (5 g, 21.459 mmol) in a mixture of THF:MeOH:H_2O (3:2:1, 75 mL), 1N aqueous solution of LiOH.H_2O (64 mL, 64.378 mmol) was added. The reaction mixture was stirred at 85°C (external temperature) for 4h. Solvents were removed under reduced pressure and the residue was partitioned between water and ethyl acetate. The water layer was separated and acidified with 1N HCl solution and then ethyl acetate was added to it. The organic phase was separated, dried (Na_2SO_4) and concentrated to obtain 3-Amino-5-phenyl-thiophene-2-carboxylic acid (4.15 g, 88%) as a yellowish solid. ^1H NMR (DMSO-D_6, 400 MHz): 7.59 (d, 2H), 7.40 (m, 3H), 6.92 (s, 1H).

STEP II

3-(2-Chloro-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid

3-Amino-5-phenyl-thiophene-2-carboxylic acid (100mg, 0.457 mmol) was taken in a mixture of dioxane and water (1:1, 25 mL) and then added sodium carbonate (242 mg, 2.285 mmol) and 1-chlorobenzenesulfonyl chloride (289 mg, 1.369 mmol). The reaction mixture was stirred at room temperature for 12 h. Half of the solvent was removed under reduced pressure and then diluted with water and ether in a separatory funnel. The ether layer was separated and the aqueous layer was acidified with 10% $KHSO_4$ solution. Ethyl acetate was added to the aqueous phase to dissolve the white precipitate. The ethyl acetate layer was

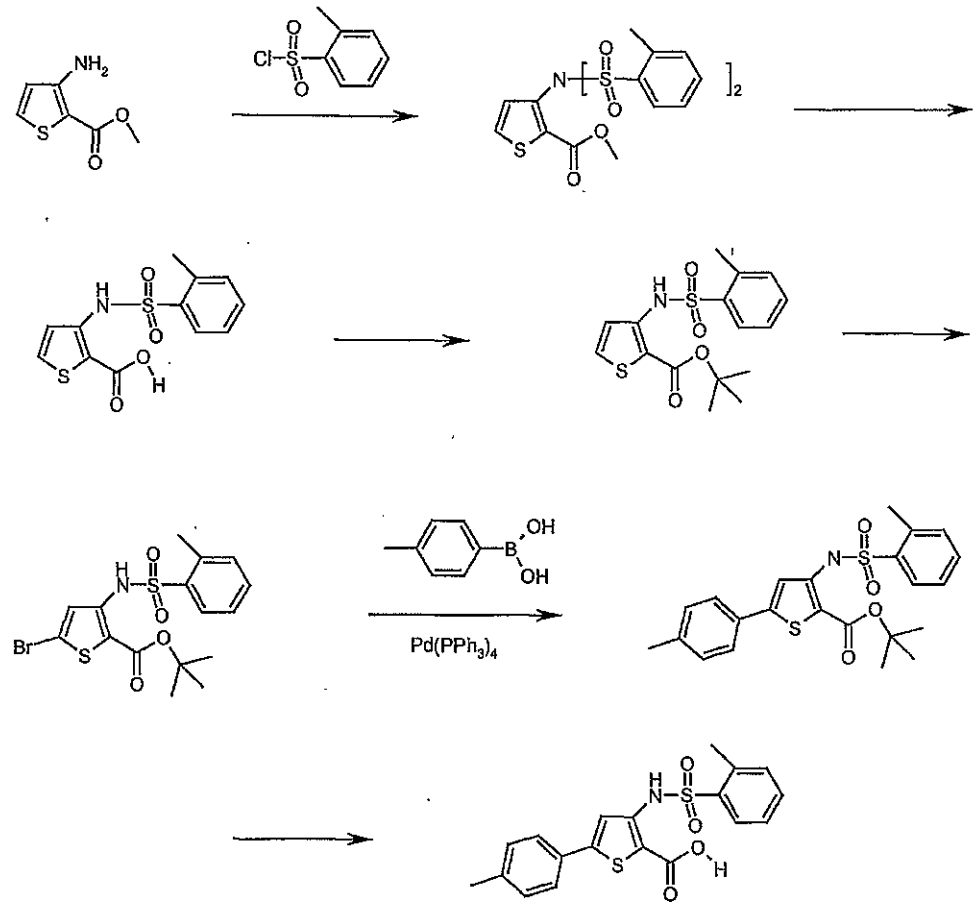
separated, dried (Na_2SO_4) and concentrated to 5 mL. The white solid was filtered and then washed with cold ethyl acetate to obtain 3-(2-Chloro-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid (125 mg, 69%). ^1H NMR (DMSO-D_6, 400 MHz): 10.51 (bs, 1H), 8.30 (d, 1H), 7.72-7.60 (m, 4H), 7.57 (m, 1H), 7.44 (m, 4H).

The following compounds were prepared in a similar manner as described in general scheme 1:

Compound #3, Compound #5, Compound #7, Compound #13, Compound #15, Compound #16, Compound #17, Compound #18, Compound #21, Compound #22, Compound #23, Compound #29, Compound #30, Compound #34, Compound #37, Compound #38, Compound #39, Compound #40, Compound #41, Compound #42, Compound #44, Compound #45, Compound #46, Compound #49, Compound #50, Compound #52, Compound #53, Compound #54, Compound #55, Compound #76, Compound #94

Example 2

3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid , compound #62



STEP I

3-(bis-(Toluene-2-sulfonyl)-amino)-thiophene-2-carboxylic acid methyl ester

To a cold (0°C) stirred sodium hypochlorite (NaOCl, 10.8% commercial bleach, 124 mL, 180.00 mmol) solution was added o-thiocresol (2.23 g, 2.12 mL, 18.0 mmol). To this vigorous stirred solution was added conc. Sulfuric acid (caution! extremely exothermic, 92 g, 50 mL, 938 mmol) dropwise. The resultant yellow reaction mixture was stirred for 2 h at the same temperature, diluted with water (50 mL) and dichloro-methane 50 mL. The organic solution was separated, aqueous solution was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic extracts were washed with water, brine and dried. Evaporation of the solvent under reduced pressure furnished the

2-methylsulfonyl chloride (3.13 g, 91.5% yield), which was used in the next step without purification. ^{1}H NMR ($CDCl_3$,300 MHz) 8.07 (td, J = 7.3, 1.5 Hz, 1H), 7.61 (tt, J = 7.5, 1.1 Hz, 1H), 7.44-7.40 (m, 2H), 2.80 (s, 3H).

To a stirred solution of the methyl 3-amino-thiophene-2-carboxylic acid (1.0 g, 6.36 mmol) and DMAP (776 mg, 6.36 mmol) in CH_2Cl_2 was sequentially added triethyl amine (1.61 g, 15.9 mmol, 2.5 eq) and o-toluenesulfonyl chloride (3.02 g, 15.9 mmol, 2.5 eq), stirred for 24 h. The reaction mixture was diluted with EtOAc (100 mL), washed with 1.2 N HCl (2 x 50 mL), 6 N HCl (40 mL), saturated $NaHCO_3$ solution, brine and dried. Evaporation of the solvent under reduced pressure yielded 3-(bis-(Toluene-2-sulfonyl)-amino)-thiophene-2-carboxylic acid methyl ester (2.78 g, 93.3%) as a solid. The crude product was used in the next step without purification. ^{1}H NMR ($CDCl_3$,300 MHz) 8.198 (dd, J = 8.0, 1.2 Hz, 2H), 7.52 (d, J = 5.3 Hz, 1H), 7.5 (dt, J = 7.5 Hz, 1.1 Hz, 2H), 7.36 (t, J = 7.5 Hz, 3H), 7.28 (d, J = 7.6 Hz, 2H), 7.16 (d, J = 5.3 Hz, 1H), 3.44 (s, 3H), 2.43 (s, 3H).

STEP II

3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid

To a stirred mixture of 3-(bis-(Toluene-2-sulfonyl)-amino)-thiophene-2-carboxylic acid methyl ester (2.5 g, 5.35 mmol) in 1,4-dioxane/MeOH/water (3:1:1; 62.5 mL) was added aq. 1 N NaOH solution (16.05 mL, 16.05 mmol, 3.0 eq) and heated at 85°C for 3.5 h and it was then cooled to rt. To the reaction mixture was added 1.2 N HCl (16.0 mL), extracted with $CHCl_3$ (3 x 30 mL), washed with brine and dried. Evaporation of the solvent gave 3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid (1.5 g, 99%) as a white solid. ^{1}H NMR (DMSO-d_6,300 MHz) 7.94 (dd, J = 7.9 Hz, 1.3 Hz, 1H), 7.76 (d, J = 5.5 Hz, 1H), 7.55 (dt, J = 7.5 Hz, 1.3 Hz, 1H), 7.42-7.37 (m, 2H), 7.1 (d, J = 5.5 Hz, 1H), 2.57 (s, 3H).

STEP III

3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester

To a cold (-40°C) mixture of 3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid (1.5 g, 5.05 mmol) in 1,4-dioxane/$CHCl_3$ (1:2, 12 mL) was bubbled 2-methyl-2-propene gas (15 mL) in a sealed tube. To this was added Conc. H_2SO_4 (0.070 mL, 1.3 mmol) and slowly warmed up to room temperature. The resultant reaction mixture was heated at 70°C for 2.5 days in a sealed tube, cooled to -40°C, stopper was removed. The reaction mixture was slowly brought up to room temperature and stirred until the excess gas is released. The mixture was extracted with EtOAc, washed with aq. $NaHCO_3$ solution, brine and dried. Evaporation of the solvent and purification of the residue on silica gel using EtOAc/hexane (1:10) as an eluent furnished 3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (1.31 g, 73.5% based on 90% conversion). ^1H NMR ($CDCl_3$, 300 MHz) 9.89 (s, 1H), 8.01 (d, J = 7.9 Hz, 1H), 7.43 (dt, J = 7.5 Hz, 1.5 Hz, 1H), 7.3-7.25 (m, 3H), 7.2 (d, J = 5.4 Hz, 1H), 2.69 (s, 3H), 1.56 (s, 9H).

STEP IV

5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester

To a cold (-30°C) stirred solution of diisopropylamine (1.345 g, 1.86 mL, 13.3 mmol, 3.6 eq) in THF (74.0 mL) was added n-BuLi (1.6 M in hexane, 7.63 mL, 12.21 mmol, 3.3 eq) dropwise and stirred for 20 min. To the cold (-78°C) LDA solution was added a solution of 3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (1.31 g, 3.7 mmol, 1.0 eq) in THF (20 mL) dropwise and the solution was stirred for 2h at the same temperature. The resultant red colored solution was then quenched with 1,2-dibromotetrafluoroethane (5.77 g, 2.65 mL, 22.2 mmol, 6.0 eq, passed through K_2CO_3 prior to use) in one portion, stirred for 1 h before being added sat. NH_4Cl solution (15.0 mL). The reaction mixture was warmed up to rt, extracted with EtOAc, washed with brine and dried. Evaporation of the solvent and purification of the residue over silica gel column furnished 5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-

carboxylic acid tert-butyl ester (1.2 g, 75% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) 9.72 (s, 1H), 8.0 (dd, J = 7.8, 1.3 Hz, 1H), 7.47 (dt, J = 7.5, 1.2 Hz, 1H), 7.35-7.30 (m, 2H), 7.24 (s, 1H), 2.68 (s, 3H), 1.53 (s, 9H).

STEP V

3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid tert-butyl ester

To the mixture of 4-methylbenzeneboronic acid (38.0 mg, 0.279 mmol) and 5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (40 mg, 0.0925 mmol) in 5:1 mixture of toluene/MeOH (2.0 mL) was added a solution of $Pd(PPh_3)_4$ (12.0 mg, 0.01 mmol, 10 mol%) in toluene (1.0 mL) followed by aqueous 2M Na_2CO_3 solution (0.1 mL, 0.2 mmol). The resultant reaction mixture was heated at 70°C for 16 h, cooled to room temperature, filtered off through $MgSO_4$ and washed with EtOAc. Evaporation of the solvent and purification of the residue over preparative TLC (1 mm, 60A°) using ethyl acetate/hexane (1:10) as an eluent furnished 3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid tert-butyl ester (36.0 mg, 81% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) 9.94 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.44-7.25 (m, 6H), 7.18 (d, J = 8.1 Hz, 2H), 2.71 (s, 3H), 2.36 (s, 3H), 1.56 (s, 9H).

STEP VI

3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid

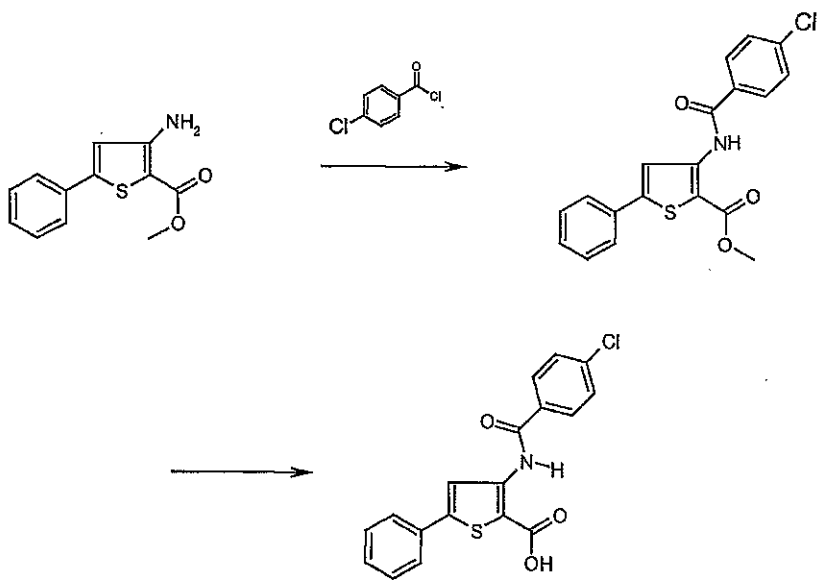
To a stirred solution of 3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid tert-butyl ester (36.0 mg, 0.081 mmol) in CH_2Cl_2 (1.0 mL) was added TFA (0.5 mL), stirred for 1 h at room temperature and diluted with hexane. Evaporation of the solvent under reduced pressure gave essentially the pure product as a solid. The product was purified by triturating with hexane/CH_2Cl_2 furnished 3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid (28.0 mg, 89% yield). ^{1}H NMR (DMSO-d_6, 300 MHz) 10.21 (br s, 1H), 8.06 (d, J = 7.9 Hz, 1H), 7.56-7.36 (m, 6H), 7.24 (d, J = 7.9 Hz, 2H), 2.59 (s, 3H), 2.48 (s, 3H).

The following compounds were prepared in a similar manner as described in general scheme 2:

Compound #6, Compound #8, Compound #11, Compound #14, Compound #24, Compound #56, Compound #57, Compound #58, Compound #59, Compound #60, Compound #62, Compound #63, Compound #64, Compound #65, Compound #66, Compound #67, Compound #68, Compound #69, Compound #70, Compound #71, Compound #552, Compound #79, Compound #80, Compound #81, Compound #83, Compound #84, Compound #85, Compound #86, Compound #87, Compound #88, Compound #89, Compound #90, Compound #91

Example 3

3-(4-Choro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid compound #72



STEP I

3-(4-Chloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester

To mixture of methyl-3-amino-5-phenylthiophene-2-carboxylate (100 mg, 0.428 mmol) in anhydrous pyridine (4.3 ml) was added p-chlorobenzoyl chloride (71 µl, 0.556 mmol). The mixture was stirred for 3 hours at room temperature and concentrated. Purification chromatography (silica gel, hexane to hexane: ethyl acetate; 95:5) gave 145 mg (91% yield) of 3-(4-Chloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester. ^{1}H NMR ($CDCl_3$, 400 MHz) 8.54(s, 1H), 7.99-7.96 (m, 2H), 7.73-7.71 (m, 2H), 7.52-7.50 (m, 2H), 7.46-7.39 (m, 3H), 3.95 (s, 3H).

STEP II

3-(4-Chlorobenzoylamino)-5-phenyl-thiophene-2-carboxylic acid

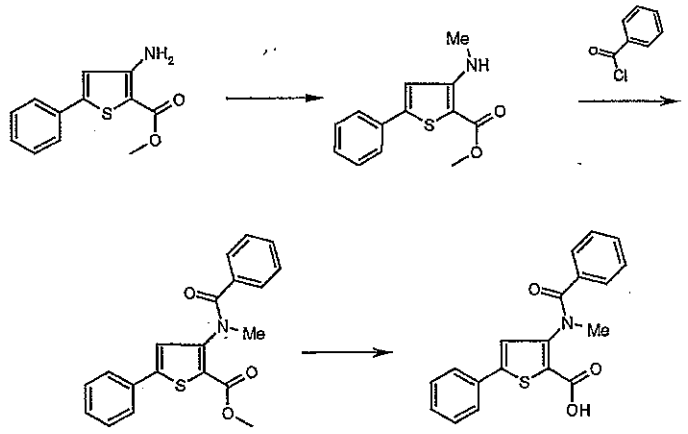
To a mixture of 3-(4-Chloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester (30 mg, 0.081 mmol) in 1 ml of a 3:2:1 solution made with tetrahydrofuran, methanol and water respectively was added lithium hydroxide monohydrated (20 mg, 0.484 mmol). The mixture was stirred 30 minutes at 60°C, cooled to room temperature, diluted with water and washed with ether (2x). The collected aqueous layer was then acidified with $KHSO_4$ 20% to pH 3 and extracted with ethyl acetate (3x). The combined ethyl acetate layers were washed with brine, dried (Na_2SO_4) and concentrated. The resulting crude was taken in ethyl acetate and reexctracted with NaOH 0.5 N (2x). The combined aqueous layers were then back-washed with ethyl acetate and acidified to pH3 with $KHSO_4$ 20% and back-extracted with ethyl acetate (2x). The combined organic layers were washed with brine and dried (Na_2SO_4). ^{1}H NMR (DMSO-d_6, 400 MHz) 8.35 (s, 1H), 8.02-7.99 (m, 2H), 7.71-7.68 (m, 2H), 7.56-7.53 (m, 2H), 7.43-7.39 (m, 2H), 7.35-7.31 (m, 1H).

The following compounds were prepared in a similar manner as described in example 3:

Compound #74, Compound #77, Compound #92, Compound #96 ;

Example 4

3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid; compound #550



STEP I

3-Methylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester

To a mixture of methyl-3-amino-5-phenylthiophene-2-carboxylate (200 mg, 0.855 mmol) in anhydrous N,N-dimethylformamide (4.6 ml) were added 4.2 ml (8.55 mmol) of 2M iodomethane solution in t-buthylmethylether. The mixture was stirred at 60°C for 18 hours, concentrated and purified using biotage technics (silica gel, hexane to hexane:ethyl acetate;95:5 containing few drops of triethylamine) to give 68 mg (32% yield) of 3-methylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.65-7.62 (m, 2H), 7.42-7.36 (m, 3H), 6.86 (broad s, 1H),. 3.83 (s, 3H), 3.04 (d, 3H)

STEP II

3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid methyl ester

This compound was prepared in a similar manner as for Example 3, Step I; 3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid methyl ester was obtained ^{1}H NMR ($CDCl_3$, 400 MHz) 7.60-7.49 (m, 2H), 7.47-7.35 (m, 5H), 7.28-7.20 (m, 3H), 7.11 (broad s, 1H), 3.83 (s, 3H), 3.44 (s, 3H)

STEP III

3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid

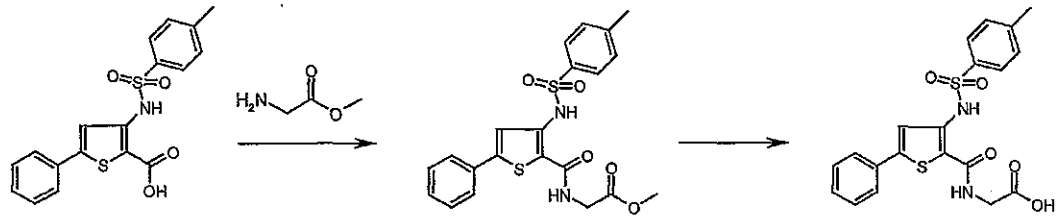
This compound was prepared in a similar manner as in Example 3, step II; 3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid was obtained; ^{1}H NMR (CD_3OD, 400 MHz) 7.64-7.62 (m, 2H), 7.47 (s, 1H), 7.44-7.36 (m, 5H), 7.29-7.20 (m, 3H), 3.42 (s, 3H)

The following compounds were prepared in a similar manner as described in example 4:

Compound #9 ; Compound #73 Compound #75 ; Compound #75 ; Compound #78 ; Compound #93 ; Compound #95.

Example 5

{[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid , compound #551



STEP I

{[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid methyl ester

To a mixture of 5-phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carboxylic acid (prepared according to example 2) (50 mg, 0.134 mmol) in anhydrous dimethylformamide (1.4 ml) were added HATU 152 mg, 0.402 mmol), glycine methyl ester hydrochloride (20 mg, 0.161 mmol) followed by collidine (124µl, 0.938 mmol). The mixture was stirred at room temperature for 1 hour, concentrated and pre-absorbed on SiO_2. Purification chromatography (hexane to hexane: ethyl acetate; 6:4 to dichloromethane: methanol;95:5) gave 47 mg of a mixture of {[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid methyl ester and collidine. ^{1}H NMR ($CDCl_3$, 400 MHz)

7.76-7.73 (m, 2H), 7.61 (s, 1H), 7.57-7.54 (m, 2H), 7.42-7.36 (m, 3H), 7.24-7.22 (m, 2H), 6.19-6.17 (m, 1H), 4.14-4.12 (m, 2H), 3.79 (s, 3H), 2.35 (s, 3H).

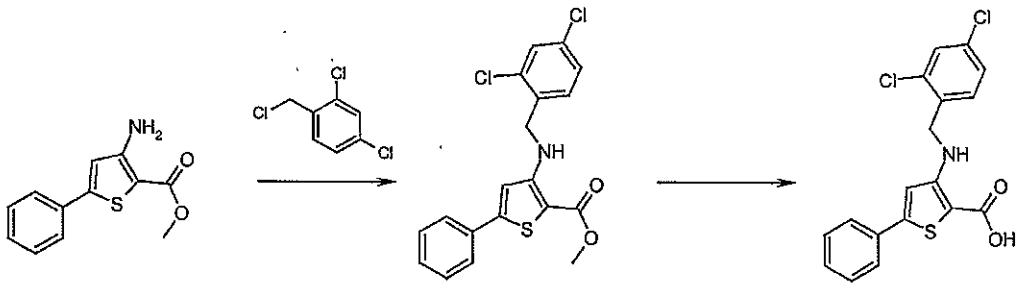
STEP II

{[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid

Following the procedure described for example 3 (STEP II), 28 mg (88% yield) of {[5-phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid were isolated from 33 mg (0.075 mmol) of the {[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid methyl ester. ^{1}H NMR (CD_3OD, 400 MHz): 7.73-7.71 (m, 2H), 7.63-7.61 (m, 2H), 7.54 (s, 1H), 7.45-7.39 (m, 3H), 7.33-7.31 (m, 2H), 4.88 (s, 2H), 2.36 (s,3H).

Example 6

3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid Compound #48



STEP I

3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester

Sodium hydride (60% dispersion in oil, 180 mg, 4,72 mmol) was added to an ice-cold solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1000 mg, 4,29 mmol) in 25 ml of dimethylformamide in an atmosphere of N_2. After 5 min, 2,4-dichloro-1-chloromethyl-benzene (755 mg, 3,86 mmol) was added to the solution and then the reaction mixture was stirred for 30 min at 0°C and 30 min at room temperature. The mixture was partitioned between ether (20 mL) and water (20 mL) and the organic layer was separated. The aqueous phase was washed twice

with ether (2X20 mL) and the combined ether layer was dried ($MgSO_4$) and concentrated. The residue obtained was then purified by precipitation. The crude product was taken in 25 ml of ethyl acetate, a yellow precipitate came out which was filtered to obtain 3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester, 835 mg (55%). ^{1}H-NMR (DMSO,400 MHz): 7,67 ppm (m, 2H, H_{aro}); 7,44-7,35 ppm (m, 6H, H_{aro}); 7,26 ppm (s, 1H, H_{aro}); 4,63 ppm (d, 2H, N-CH_2); 3,75 ppm (s, 3H, O-CH_3)

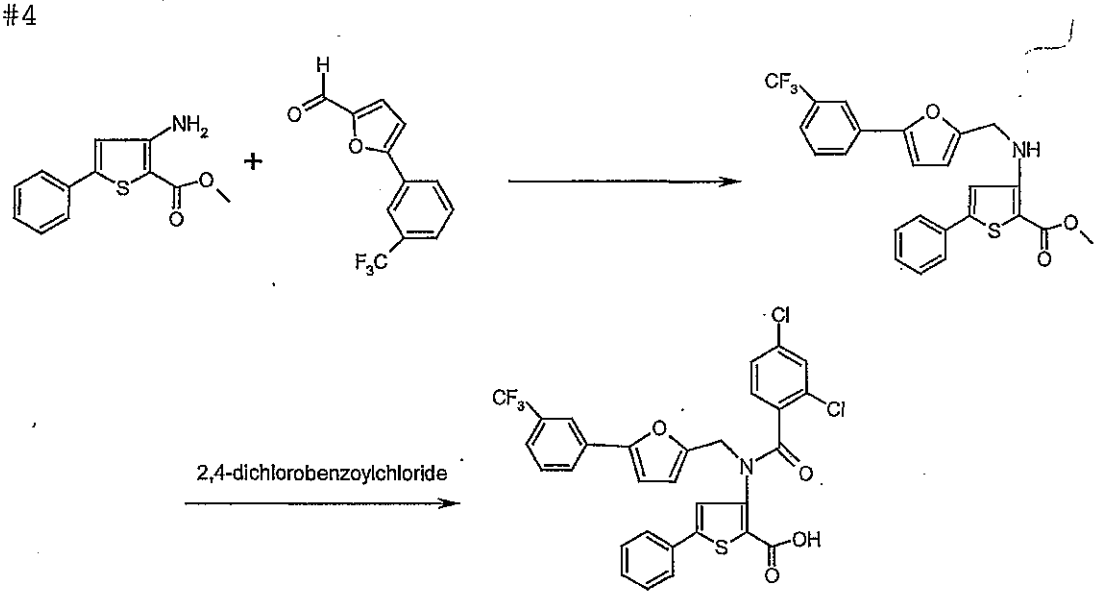
STEP II

3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid

3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester (70 mg, 0,18 mmol) was dissolved in a mixture of THF-MeOH-H_2O (3:2:1) (20 mL) and then 1080 ul of LiOH 1N was added to it. After 16 h of stirring at temperature of 100°C, solvents were removed and then partitioned between 10 ml of H_2O, 2 ml of $KHSO_4$ 5% and 10 ml of EtOAc. The organic layer was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried (MgSO4) and concentrated to obtain 43 mg (63%) of 3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid ^{1}H-NMR (DMSO, 400 MHz):δ 7,65 ppm (m, 3H, H_{aro}); 7,43-7,32 ppm (m, 5H, H_{aro}); 7,23 ppm (s, 1H, H_{aro}); 4,61 ppm (d, 2H, N-CH_2).

Example 7

3-{(2,4-Dichloro-benzoyl)-[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid, Compound #4



STEP I

5-Phenyl-3-{[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl] amino}-thiophene-2-carboxylic acid methylester

To a stirred solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (100 mg, 0.416mmol) in dichloromethane (15 mL) were added 5-(trifluoromethyl-phenyl)-furan-2-carbaldehyde (100 mg, 0.429 mmol) and molecular sieves. The reaction mixture was stirred at room temperature overnight. The solution was filtered over celite and the filtrate was evaporated under reduced pressure. The residue was dissolved in anhydrous methanol (15 mL). and cooled to 0°C in an ice bath. Sodium borohydride (18 mg, 1.1 eq.) was added. The reaction mixture was stirred at this temperature for 2 h. Saturated ammonium chloride (10 mL) was added and stirring was continued for an additional 15 min. at room temperature . Methanol was removed and the resulted mixture was extracted with dichloromethane (3 x 30 mL). The organic solution was washed with water, brine and was dried over sodium sulfate. Solvent was evaporated and the crude product was purified on silica gel using hexane : ethylacetate 9:1 as eluent to provide the desired product in 34% yield (65 mg).

^{1}HNMR(CDCl3, 400MHz): 7.80 (s, 1H), 7.73 (m, 1H), 7.55 (m, 2H), 7.41 (m, 2H), 7.33 (m, 3H), 6.93 (s, 1H), 6.48 (d, 1H), 6.24 (d,

1H), 4.43 (s, 2H), 3.76 (s, 3H).

STEP II

3-{(2,4-Dichloro-benzoyl) -[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid methyl ester

To a stirred solution of 5-Phenyl-3-{[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-thiophene-2-carboxylic acid methylester (65 mg 0.142 mmol) in dichloromethane (3 ml) and saturated $NaHCO_3$ solution (3 ml) was added a solution of 2,4-dichloro-benzoyl chloride (36 mg, 1.2 eq.) in dichloromethane (0.9 ml). The reaction mixture was stirred vigorously at room temperature for overnight. The organic phase was collected and the aqueous phase was extracted twice with methylene chloride (2 x 15 ml). The organic layers were combined, washed with water, brine and dried over anhydrous Na_2SO_4. Solvent was removed and residue was purified on silica gel using Hexane : EtOAc 9:1 as eluant to give the desired product in 78% yield (70 mg). The proton NMR indicated the presence of rotamers.

^{1}HNMR($CDCl_3$, 400MHz): 7.80 (s, 1H), 7.73 (m, 1H), 7.55 (m, 2H), 7.45 (m, 2H), 7.33 (m, 3H), 7.20 (m, 2H), 7.12 (m, 1H), 6.93 (s, 1H), 6.62 (d, 1H), 6.42 (d, 1H), 5.60 (bd, 1H), 4.70 (bd, 1H), 3.76 (s, 3H).

STEP III

3-{(2,4-Dichloro-benzoyl) -[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid

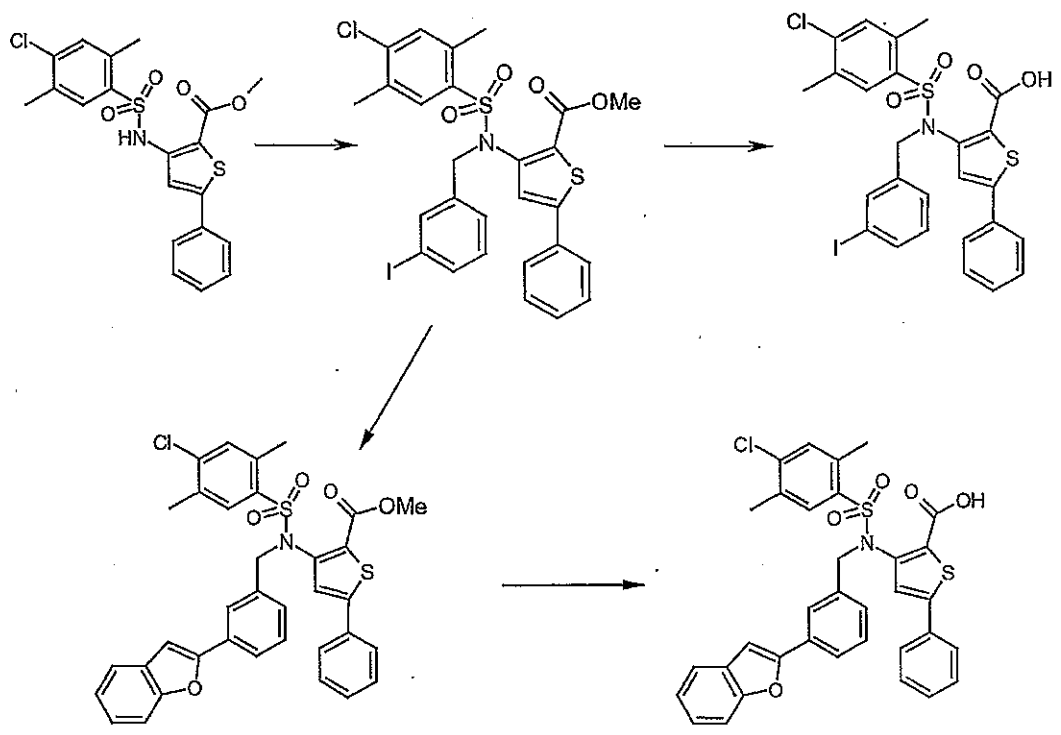
3-{(2,4-Dichloro-benzoyl) -[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid methyl ester (62 mg, 0.098 mmol) was dissolved in THF (5 mL) and water (2 mL). A solution of lithium hydroxide (13 mg, 3eq. in 2 mL of water) was added dropwise. After first few drop, a pink color appeared and disappeared. Mixture was stirred for 5 hrs and acidified with 1N HCl-solution. The product was extracted into ethyl acetate, washed once with water, dried over magnesium sulfate. Solvent was evaporated and the residue was purified on silica gel (Bond-Elute 2 g). The product was elute with a 20 mL gradient of Hexane:EtOAc 9:1. 4:1, 7:3, 3:2, 1:1, 2:3 and EtOAc to give the desired product

in 76% yield (46 mg).

^{1}HNMR(CD_3OD, 400MHz): 7.90 (s, 1H), 7.83 (m, 1H), 7.55 (m, 2H), 7.40-7.20 (m, 8H), 7.10 (s, 1H), 6.82 (d, 1H), 6.42 (d, 1H), 5.60 (bd, 1H), 4.70 (bd, 1H), 3.86 (s, 3H).

Example 8

Preparation of 3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid Compound #1 and 3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethyl-benzenesulfonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid compound #2.



STEP I

To a solution of 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester (100 mg, 0.229 mmol) in anhydrous DMF (6 mL), 3-iodobenzyl bromide (82 mg, 0.276 mmol) and cesium carbonate (88 mg, 0.276 mmol) were added and the reaction mixture was stirred at room temperature under a N_2 atmosphere for 12 h. The reaction mixture was partitioned between water and ether. The ether layer was separated, dried (Na_2SO_4),

concentrated. The residue was purified by silica gel column chromatography using ethyl acetate and hexane (1:3) as eluent to obtain 3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (130 mg, 87%) as a syrup.

STEP II

3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (25 mg, 0.038 mmol) was taken in a mixture of THF:MeOH:H_2O (3:2:1, 3 mL) and then added 1N aqueous solution of LiOH.H_2O (0.24 mL, 0.228 mmol). The reaction mixture was stirred at room temperature for 12 h. Solvents were removed and the residue was partitioned between water and ethyl acetate. The aqueous layer was acidified using 10 % $KHSO_4$ solution. The organic layer was separated, dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography using dichloromethane and methanol (9:1) to obtain 3-[(4-Chloro-2,5-dimethyl-benzene-sulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid (22 mg, 88%) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz): 7.69(m, 3H), 7.57 (m, 3H), 7.42 (m, 3H), 7.33 (d, 1H), 7.16 (s, 1H), 6.04 (dd, 1H), 4.90 (bs, 2H), 2.36 (s, 6H).

Compound #5 was prepared in a similar manner;

3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethyl-benzenesulfonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid compound #2

STEP I

To a degassed solution of 3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (110 mg, 0.169 mmol) and benzofuran-2-boronic acid (55 mg, 0.185 mmol) in a mixture of DME (8 mL) and 2M aqueous Na_2CO_3 (4 mL), $Pd(PPh_3)_4$ (9 mg) was added and the reaction mixture was stirred at reflux conditions for 2h under a N_2 atmosphere. The reaction mixture was diluted with ethyl acetate and water. The organic layer was separated, dried (Na_2SO_4) and concentrated. 3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethyl-benzenesulfonyl)-amino]-5-phenyl-

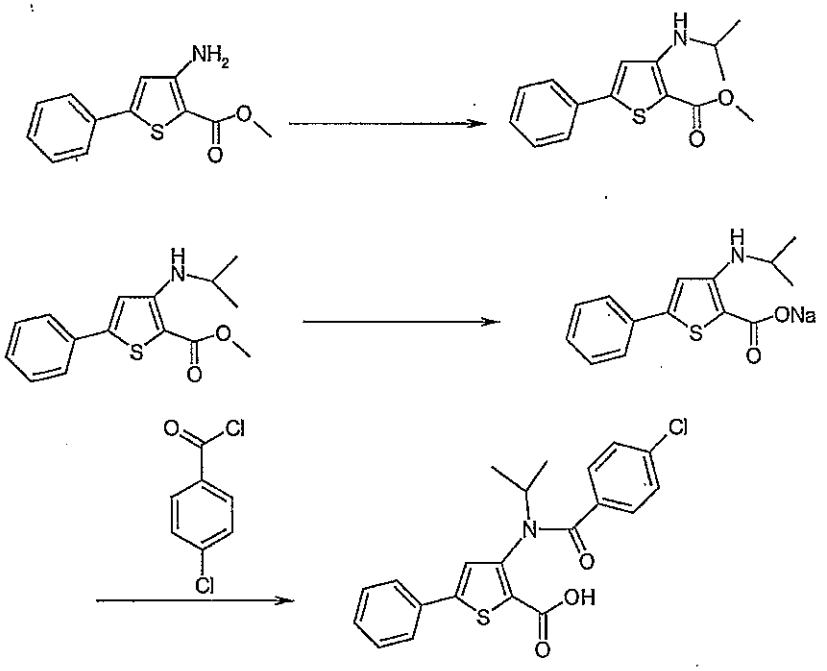
thiophene-2-carboxylic acid methyl ester (107 mg, 100%) was isolated as a thick syrup and used for the next reaction without any further purification.

STEP II

3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethyl-benzenesulfonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (20 mg, 0.031 mmol) was taken in a mixture of THF:MeOH:H_2O (3:2:1, 3 mL) and then added 1N aqueous solution of LiOH.H_20 (0.20 mL, 0.186 mmol). The reaction mixture was stirred at room temperature for 12 h. Solvents were removed and the residue was partitioned between water and ethyl acetate. The aqueous layer was acidified using 10 % $KHSO_4$ solution. The organic layer was separated, dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography using dichloromethane and methanol (9:1) to obtain 3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethyl-benzene-sulfonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid (14 mg, 70%) as a white solid. ^1H NMR (DMSO, 400 MHz): δ7.93(s, 1H), 7.84 (s, 1H), 7.74 (bd, 1H), 7.65-7.22 (m, 14H), 4.95 (s, 2H), 2.33, 2.23 (2s, 6H).

Example 9

3-[(4-Chloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid compound #210 .

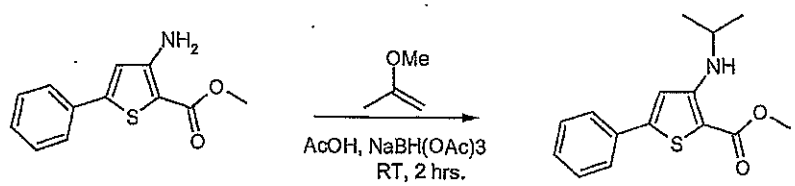


STEP I

Method A

A DMF (15 mL) solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (500 mg, 21.5 mmol) was cooled to 0 ^{0}C and then isopropyl iodide (2.57 mL) and NaH (60%, 775 mg, 32.3 mmol) were added under an atmosphere of N_2. The ice bath was removed and the reaction mixture was stirred at room temperature for 1h. The mixture was partitioned between ether and water, the ether layer was separated, dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography using ethyl acetate and hexane (5:95) as eluent to obtain 3-isopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (189 mg, 32%) as a solid. ^{1}H NMR ($CDCl_3$, 400 MHz): 7.62 (d, 2H), 7.40 (m, 3H), 6.91 (s, 1H), 3.84 (s, 3H), 1.35 (d, 6H).

Method B



To a stirred solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1.82 g, 7.8 mmol) in 1,2-dichloroethane (40 mL) was added sequentially 2-methoxypropene (3.0 mL, 31.2 mmol), AcOH (1.8 mL, 31.2 mmol) and $NaBH(OAc)_3$ (3.31 g, 15.6 mmol) and stirred for 2 hrs. It was then diluted with EtOAc and H_2O. The aqueous solution was adjusted to pH = 7 by adding $NaHCO_3$. The aqueous phase was extracted with EtOAc, the combined extract was washed with brine and dried on MgSO4 and filtered. Purification on bond elute with hexane to 5% EtOAc-hexane furnished 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (2.07 g, 96% yield).

The intermediate compounds 3-Cyclohexylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester, 3-(1-Methyl-piperidin-4-ylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester and 3-(1-Methyl-piperidin-4-ylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester were prepared in a similar manner as described and used as intermediates in the synthesis of compound #543, compound #553 and compound #573

STEP II

To a suspension of 3-isopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1.2 g, 4.364 mmol) in a mixture of H_2O (22 mL) and dioxane (35 mL), 1N aqueous solution of NaOH (13 mL, 13.00 mmol) was added. The reaction mixture was stirred at 100^0C for 3h. The reaction mixture was used for the next reaction without any further purification.

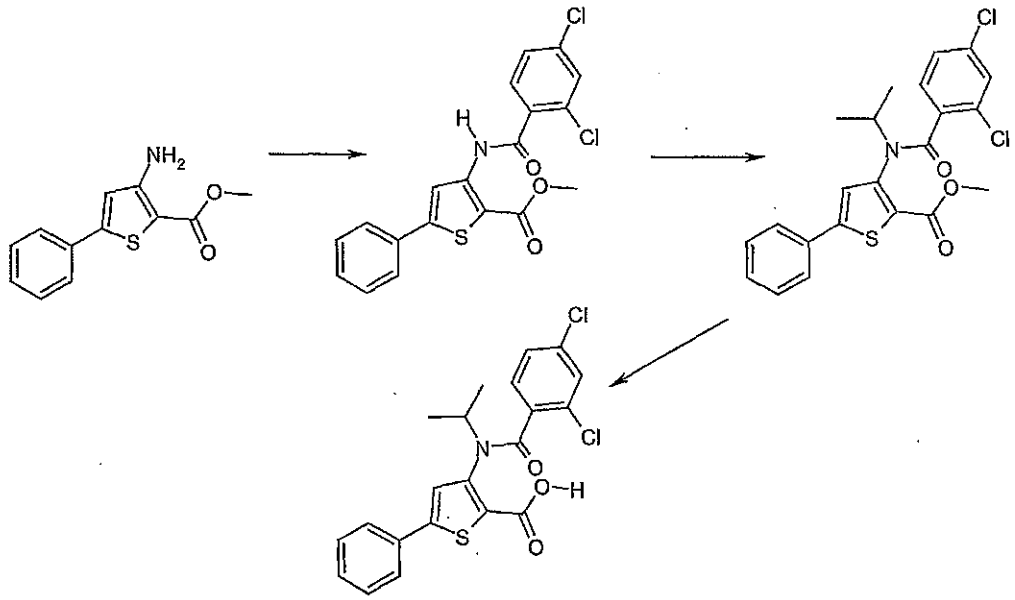
To this reaction mixture of 3-Amino-5-phenyl-thiophene-2-carboxylic acid sodium salt (23 mL, 1.41 mmol), 4-chlorobenzoyl chloride (0.269 mL, 2.11 mmol) was added at 0^0C. The pH of the solution was maintained at 9 by adding 1N NaOH solution and then stirred at room temperature for 5h. The reaction mixture was diluted with ethyl acetate and water. The water layer was acidified by adding 1N HCl solution. The organic layer was separated, dried (Na_2SO_4) and concentrated. The crude product was

purified by recrystallization from ethyl acetate to obtain the pure 3-[(4-Chloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid (45 mg) as a white solid. ^{1}H NMR (DMSO-D_6, 400 MHz): 7.58 (d, 2H), 7.38-7.26 (m, 6H), 7.13 (d, 1H), 4.77 (m, 1H), 1.25 (d, 3H), 1.02 (d, 3H). ESI$^-$ (M-H): 398.

Similarly, the following compounds were made: Compound #218 , Compound #219 , Compound #226 , Compound #234 , Compound #243 , Compound #246 , Compound #250 , Compound #262 , Compound #324 , Compound 326 , Compound #331 .

Example 10

3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid compound #149



Step I

3-(2,4-Dichloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a ice-cold solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester 1 (5 g, 21.5 mmol) and triethylamine (4.56 g, 45.0 mmol) in dichloromethane (100 ml)

was added 2,4-dichlorobenzoyl chloride (3.90 g, 19.4 mmol). The reaction mixture was stirred for 30 min a 0°C and 16 h at room temperature. Then, the reaction mixture was partitioned between 25 ml of H_2O, 50 ml sat. $NaHCO_3$ and 50 ml of CH_2Cl_2. The organic layer was separated and the aqueous phase was washed twice with CH_2Cl_2 (2 X 50 mL). The combined dichloromethane layer was dried ($MgSO_4$), concentrated and the residue was purified by recrystallization in CH_2Cl_2 to obtain 5.832 g (74%) as a white solid of 3-(2,4-Dichloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 8,30 ppm (s, 1H, H_{aro}); 7,74-7,66 ppm (m , 3H, H_{aro}); 7,51 ppm (d, 1H, H_{aro}); 7,46-7,34 ppm (m, 4H, H_{aro}); 3,91 ppm (s, 3H).

Step II

3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

Sodium Hydride (60% dispersion in oil, 190 mg, 5,2 mmol) was added to an ice-cold solution of 3-(2,4-Dichloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester (2) (1.5 g, 3,69 mmol) in 350 ml of *N,N*-dimethylformamide in an atmosphere of N_2. After 5 min, 2-Iodo-propane (941 mg, 5.54 mmol) was added to the solution and then the reaction mixture was stirred for 30 min at 0°C and 64 h at room temperature. The mixture was partitioned between ether (200 mL) and water (350 mL) and the organic layer was separated. The aqueous phase was washed twice with ether (2 X 70 mL) and the combined ether layer was dried ($MgSO_4$), concentrated and the residue was purified by flash chromatography (10% EtOAc/Hexane) to obtain 908 mg (55%) of 3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): Rotamere 95/05 : 7,54 ppm (dd, 2H, H_{aro}); 7,49-7.35 ppm (m, 3H, H_{aro}); 7,29-7,25 ppm (m, 2H, H_{aro}); 7,15 ppm (d, 1H, H_{aro}); 7,05 ppm (d, 1H, H_{aro}) 5,09 ppm (hex, 1H, N-C<u>H</u>(CH_3), major rotamere); 3,99 ppm (hex, N-C<u>H</u>(CH_3), minor rotamere); 3,89 ppm (s, 3H); 1,40 ppm (d,

3H, N-CH($C\underline{H}_3$), major rotamere); 1,28 ppm (d, N-CH($C\underline{H}_3$), minor rotamere); 1,09 ppm (d, 3H, N-CH($C\underline{H}_3$), major rotamere); 1,01 ppm (d, N-CH($C\underline{H}_3$), minor rotamere).

Step III

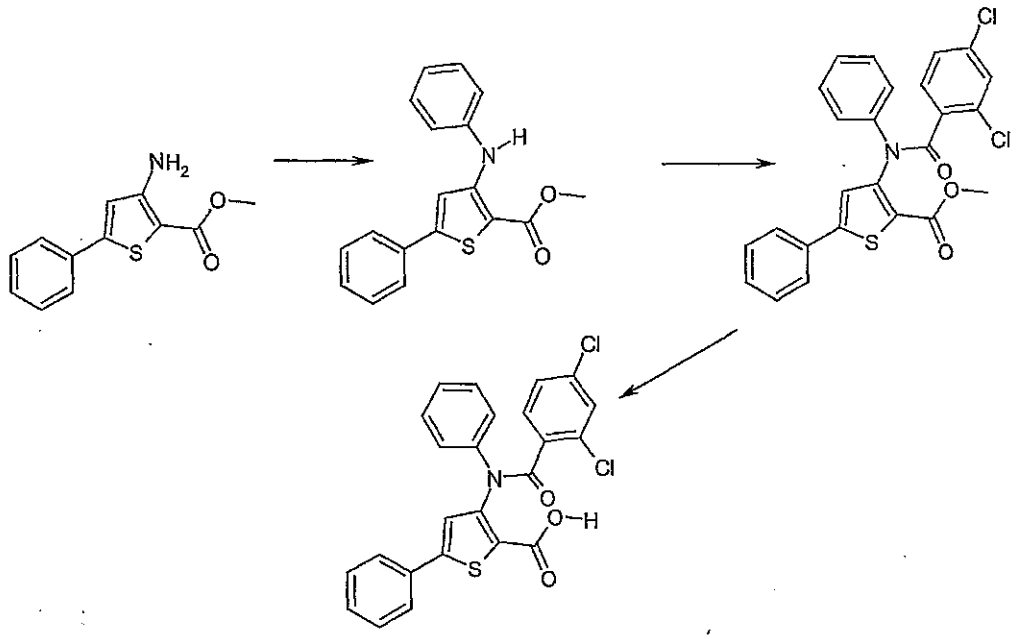
3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid.

3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (3) (345 mg, 0.77 mmol) was dissolved in a mixture of THF-MeOH-H_2O (3:2:1) (30 mL) and then 4,6 ml of LiOH 1N was added to it. After 120 min of stirring at room temperature, solvant was removed and then partitioned between 25 ml of H_2O, 4 ml of $KHSO_4$ 5% and 25 ml of EtOAc. The organic layer was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried ($MgSO_4$), concentrated and the residue was purified by preparative chromatography (10% MeOH/CH_2Cl_2) to obtain 175 mg (53%) as a white solid of 3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid. NMR ^1H (DMSO, 400 MHz): Rotamer 95/05 : 7,82 ppm (m, H_{aro}, minor rotamer); 7,69 ppm (d, 2H, H_{aro}); 7,61 ppm (d, 1H, H_{aro}); 7,51-7,37 ppm (m, 4H, H_{aro}); 7,35-7,28 ppm (m, 2H, H_{aro}); 4,89 ppm (hex, 1H, N-C$\underline{H}$(CH_3), major rotamer); 3,84 ppm (hex, N-C$\underline{H}$(CH_3), minor rotamer); 1,36 ppm (d, 3H, N-CH($C\underline{H}_3$), major rotamer); 1,25 ppm (d, N-CH($C\underline{H}_3$), minor rotamer); 1,03 ppm (d, 3H, N-CH($C\underline{H}_3$), major rotamer); 0,93 ppm (d, N-CH($C\underline{H}_3$), minor rotamere).

The following compounds were prepared in a similar manner: Compound #201 , Compound #204 , Compound #233 , Compound #244 , Compound #261 , Compound #264 , Compound #299 .

Example 11

3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid. Compound #208.



Step I

5-Phenyl-3-phenylamino-thiophene-2-carboxylic acid methyl ester.

To a solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1 g, 4.29 mmol) in dichloromethane (50 ml) was added phenyl boronic acid (1.05 g, 8.6 mmol), pyridine (680 mg, 8.6 mmol) and copper(II) acetate (1.18 g, 6.5 mmol). The reaction mixture was stirred for 16 h at room temperature. Then, the reaction mixture was filtered through celite, concentrated and the residue was purified by flash chromatography (9:1 Hexane/EtOAc) to obtain 435 mg (33%) of 5-Phenyl-3-phenylamino-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 7,38 ppm (dd, 2H, H_{aro}); 7,35-7,26 ppm (m , 5H, H_{aro}); 7,19 ppm (s, 1H, H_{aro}); 7,15 ppm (dd, 2H, H_{aro}); 7,02 ppm (ddt, 1H, H_{aro}); 3,82 ppm (s, 3H).

Step II

3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

Sodium Hydride (60% dispersion in oil, 80 mg, 1,5 mmol) was added to an ice-cold solution 5-Phenyl-3-phenylamino-thiophene-2-carboxylic acid methyl ester (2) (230 mg, 0,74 mmol) in 20 ml of *N,N*-dimethylformamide in an atmosphere of N_2. After 5 min, 2,4-Dichloro-benzoyl chloride (310 mg, 1.48 mmol) was added to the solution and then the reaction mixture was stirred for 30 min at 0°C and 16 h at room temperature. The mixture was partitioned between ether (20 mL) and water (20 mL) and the organic layer was separated. The aqueous phase was washed twice with ether (2 X 10 mL) and the combined ether layer was dried ($MgSO_4$), concentrated and the residue was purified by preparative chromatography (30% EtOAc/Hexane) to obtain 58 mg (16%) of 3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 7,65-7,10 ppm (m, 14H, H_{aro}); 3,77 ppm (s, 3H).

Step III

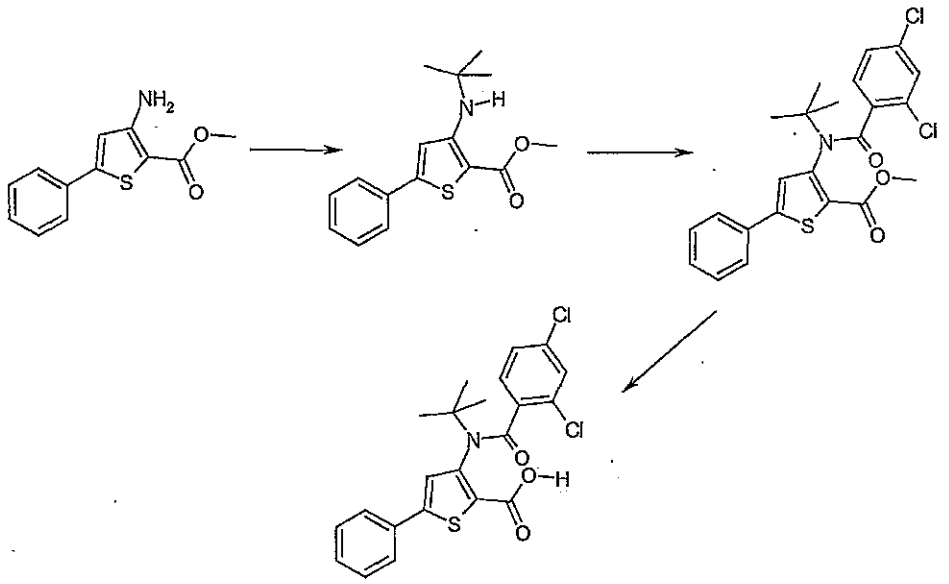
3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid.

3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (55 mg, 0.11 mmol) was dissolved in a mixture of THF-MeOH-H_2O (3:2:1) (15 mL) and then 0.66 ml of LiOH 1N was added to it. After 60 min of stirring at room temperature, solvents were removed and then partitioned between 15 ml of H_2O, 4 ml of $KHSO_4$ 5% and 15 ml of EtOAc. The organic layer was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried ($MgSO_4$), concentrated and the residue was purified by preparative chromatography (10% MeOH/CH_2Cl_2) to obtain 32 mg (60%) of 3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid. NMR ^1H (DMSO, 400 MHz): Rotamer : 7,75 ppm (d, 1H, H_{aro}); 7,68 ppm (2H, H_{aro}); 7,53 ppm (d, H_{aro}, minor rotamer); 7,51-7.23 ppm (m, 11H, H_{aro}, minor rotamer); 7,17 ppm (H_{aro}, minor rotamer).

Compound #525 was prepared in a similar manner.

Example 12

3-[tert-Butyl-(2',4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid compound #327



Step I

3-tert-Butylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester.

Concentrated sulfuric acid (10 drop) was added to a solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (500 mg, 2,15 mmol) in 20 ml of dioxane/ chloroforme (2 :3) in a sealed tube. After cooling the solution at -78 °C, put 20 ml of isobutene gaz. The sealed tube was closed and then the reaction mixture was stirred for 6 days at 60 °C. The solvant was removed and then partitioned between 15 ml of sat. Na_2CO_3 solution and 15 ml of EtOAc. The organic layer was separated, the aqueous phase was washed twice with ethyl acetate and the combined ethyl acetate layer was dried ($MgSO_4$), concentrated and the residue was purified by flash chromatography (5% EtOAc/Hexane) to obtain 385 mg (62%) of 3-tert-Butylamino-5-phenyl-thiophene-2-carboxylic

acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 7,65 ppm (d, 2H, H_{aro}); 7,44-7,38 ppm (m , 3H, H_{aro}); 7,07 ppm (s, 1H, H_{aro}); 3,86 ppm (s, 3H); 1,48 ppm (s, 9H).

Step II

3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a solution of 3-tert-Butylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (100 mg, 0.35 mmol) in dichloroethane (10 ml) in an atmosphere of N_2 was added 2,4-dichloro-benzoyl chloride (79 mg, 0.38 mmol). The reaction mixture was stirred for 16 h at reflux. Then, the solvents were removed and the residue was purified by flash chromatography (9:1 Hexane/EtOAc) to obtain 112 mg (69%) of 3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 7,50 ppm (m, 2H, H_{aro}); 7,44-7,34 ppm (m, 3H, H_{aro}); 7,27 ppm (s, 1H, H_{aro}); 7,18 ppm (dl, 1H, H_{aro}); 7,14 ppm (d, 1H, H_{aro}); 7,00 ppm (dd, 1H, H_{aro}); 3,93 ppm (s, 3H); 1,56 ppm (s, 9H).

Step III

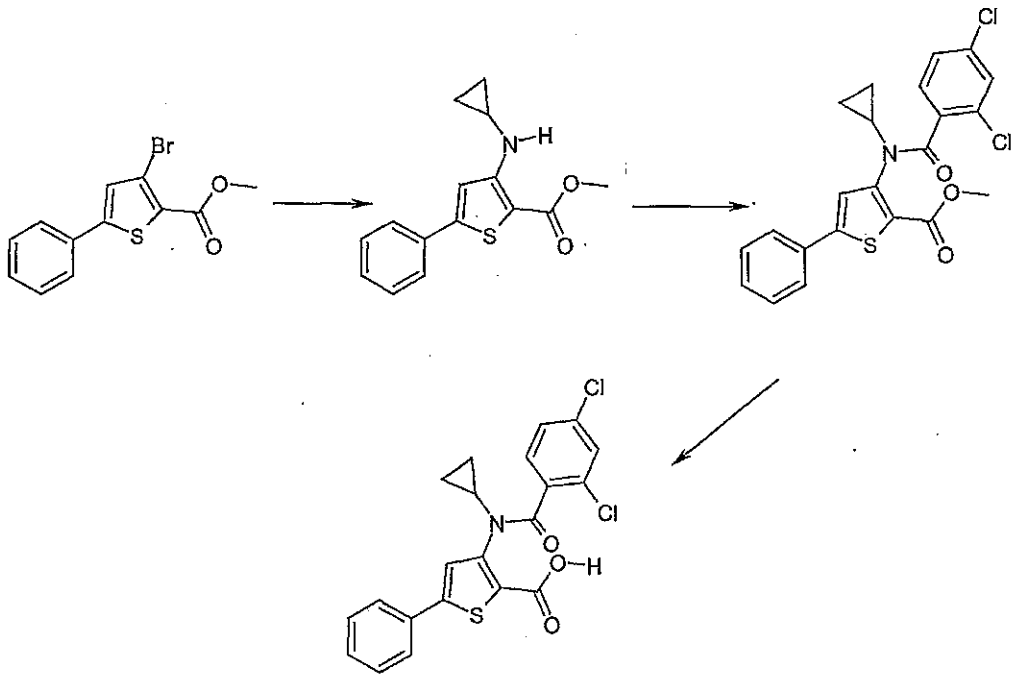
3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid.

3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (112 mg, 0.24 mmol) was dissolved in a mixture of THF-MeOH-H_2O (3:2:1) (15 mL) and then 1.5 ml of LiOH 1N was added to it. After 3 h of stirring at room temperature, solvant was removed and then partitioned between 15 ml of H_2O, 4 ml of $KHSO_4$ 5% and 15 ml of EtOAc. The organic layer was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried ($MgSO_4$), concentrated and the residue was purified by preparative chromatography (10% MeOH/CH_2Cl_2) to obtain 32 mg (29 %) of 3-

[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid. NMR ^{1}H (DMSO, 400 MHz): 7,62 ppm (d, 2H, H_{aro}); 7,44-7,34 ppm (m , 4H, H_{aro}); 7,32-7,12 ppm (m, 3H, H_{aro}); 2,48 ppm (s, 9H).

Example 13

3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid. Compound #333



Step I

3-Cyclopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a solution of 3-Bromo-5-phenyl-thiophene-2-carboxylic acid methyl ester (250 mg, 0.89 mmol) in toluene (25 ml) was added cyclopropylamine (57 mg, 1.0 mmol), cesium carbonate (382 mg, 1.2 mmol), BINAP (50 mg, 0.08 mmol) and tris (dibenzylideneacetone)dipaladium (0) (38 mg, 0.04 mmol). The reaction mixture was stirred for 16 h at 110 °C in a sealed tube. The mixture was partitioned between toluene (20 mL) and water (20 mL) and the organic layer was separated. The aqueous phase was

washed twice with toluene (2 X 10 mL) and the combined toluene layer was dried ($MgSO_4$), concentrated and the residue was purified by preparative chromatography (10% EtOAc/Hexane) to obtain 52 mg (22 %) of 3-Cyclopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 7,67-7,62 ppm (m, 2H, H_{aro}); 7,43-7,32 ppm (m , 3H, H_{aro}); 7,16 ppm (s, 1H, H_{aro}); 3,82 ppm (s, 3H); 2,65 ppm (m, 1H); 0,62 ppm (m, 2H); 0,35 ppm (m, 2H).

Step II

3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a solution of 3-Cyclopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (52 mg, 0.19 mmol) in dichloroethane (10 ml) in an atmosphere of N_2 was added 2,4-dichlorobenzoyl chloride (45 mg, 0.21 mmol). The reaction mixture was stirred for 16 h at reflux. Then, the solvant was removed and the residue was purified by flash chromatography (8:2 Hexane/EtOAc) to obtain 85 mg (99%) of 3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 7,64 ppm (d, 2H, H_{aro}); 7,47 ppm (m , 2H, H_{aro}); 7,44-7,33 ppm (m, 3H, H_{aro}); 7,21-7,12 ppm (m, 2H, H_{aro}); 3,89 ppm (s, 3H); 3,33 ppm (m, minor rotamer); 3,13 ppm (m, 1H, major rotamer) 1,01-0,49 ppm (m, 4H).

Step III

3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid.

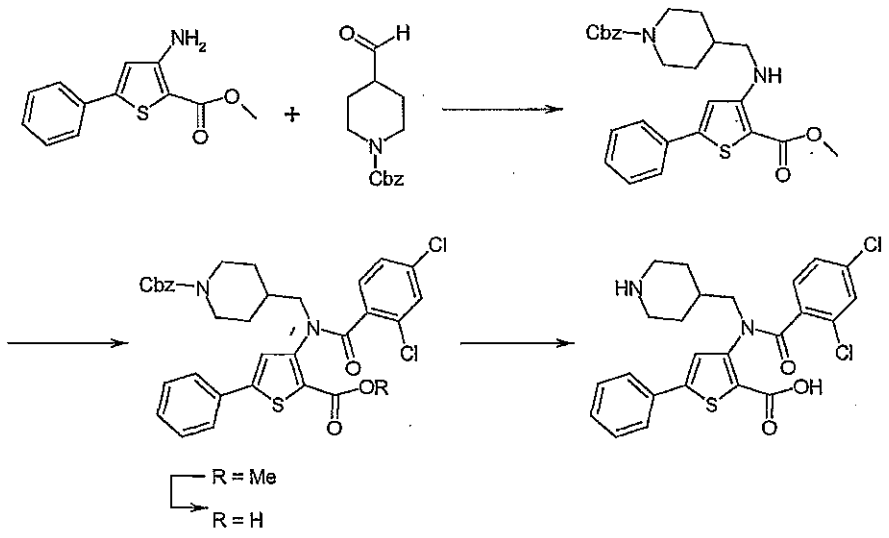
3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (85mg, 0.19mmol) was dissolved in a mixture of THF-MeOH-H_2O (3:2:1) (10 mL) and then 1.2 ml of LiOH 1N was added to it. After 60 min of stirring at room temperature, solvant was removed and then partitioned between 15 ml of H_2O, 4 ml of $KHSO_4$ 5% and 15 ml of EtOAc. The organic layer

was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried ($MgSO_4$), concentrated and the residue was purified by preparative chromatography (10% MeOH/CH_2Cl_2) to obtain 22 mg (27 %) of 3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid. NMR ^1H (DMSO, 400 MHz): rotamer : 7,75 ppm (m, 2H, H_{aro}); 7,68 ppm (m , H_{aro}, minor rotamer) ; 7,62-7,55 ppm (m, 2H, H_{aro}); 7,52 ppm (m, H_{aro}, minor rotamer) ; 7,48-7.27 ppm (m, 5H, H_{aro}); 3,14 ppm (m, minor rotamer); 3,04 ppm (m, 1H, major rotamer); 0,87-0,42 ppm (m, 4H,).

The following compounds were prepared in a similar manner: Compound #403 , Compound #404

Example 14

3-[(2,4-dichloro-benzoyl)-piperidin-4-ylmethylamino]-5-phenyl-thiophene-2-carboxylic acid Compound #519 .



STEP I

A suspension of 3-amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (0.70 g, 3 mmol) and 4-formyl N-Cbz-piperidine (0.74 g, 3 mmol) in THF (1.2 mL) was treated with dibutyltin dichloride (46 mg, 0.15 mol) followed by phenylsilane (0.41 mL, 3.3 mmol). The mixture was stirred for 2 days at room temperature. The solvent was then evaporated and the residue was purified by silica gel column chromatography using

CH_2Cl_2:hexanes:EtOAc as eluent to provide 4-[(2-Methoxycarbonyl-5-phenyl-thiophen-3-ylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester (0.6906 g, 50% yield).

STEP II

4-[(2-Methoxycarbonyl-5-phenyl-thiophen-3-ylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester (133 mg ,0.28 mmol) was dissolved in 1,2-dichloroethane (2.8 mL) and was treated with 2,4-dichlorobenzoyl chloride (60 µL, 0.43 mmol). The solution was heated at reflux for 1 day. The solvent was then evaporated and the residue purified by silica gel column chromatography using hexanes:EtOAc as eluent to provide 4-{[(2,4-Dichloro-benzoyl)-(2-methoxycarbonyl-5-phenyl-thiophen-3-yl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (0.156 g, 85% yield).

STEP III

4-{[(2,4-Dichloro-benzoyl)-(2-methoxycarbonyl-5-phenyl-thiophen-3-yl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (150 mg, 0.24 mmol) was dissolved in a mixture of THF:MeOH:H_2O (3:2:1, 2.4 mL) and treated with $LiOH.H_2O$ (29.6 mg, 0.7 mmol). The solution was heated at 55 ºC for 2 h. The solvents were removed and the residue was acidified using HCl. The product was extracted with EtOAc and the organic layers were washed with brine and dried. The residue was purified by silica gel column chromatography using EtOAc:MeOH:AcOH as eluent to provide 4-{[(2-Carboxy-5-phenyl-thiophen-3-yl)-(2,4-dichloro-benzoyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (124 mg, 85% yield).

STEP IV

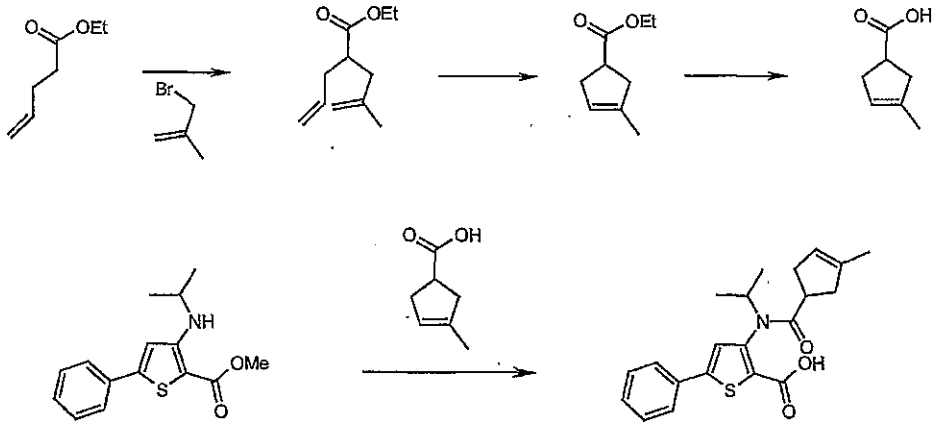
4-{[(2-Carboxy-5-phenyl-thiophen-3-yl)-(2,4-dichloro-benzoyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (124 mg, 0.2 mmol) was dissolved in MeOH (2 mL) and treated with 10% Pd/C (200 mg) under H_2 balloon. The reaction was stirred at room temperature for 18 h and the mixture was filtered on celite. The solution was evaporated to a residue that was purified by

reverse-phase HPLC to provide 3-[(2,4-Dichloro-benzoyl)-piperidin-4-ylmethyl-amino]-5-phenyl-thiophene-2-carboxylic acid (17.3 mg, 18% yield). ^{1}H NMR (CD_3OD, 300 MHz): 7.55 (d, 1 H), 7.50 (m, 2 H), 7.27-7.39 (m, 4 H), 7.25 (s, 1 H), 7.18 (dd, 1 H), 4.12 (m, 1 H), 3.75 (m, 1 H), 3.43 (m, 2 H), 2.96 (q, 2 H), 2.65 (d, 2 H), 2.05 (m, 1 H), 1.62 (m, 2 H).

The following compounds were prepared in a similar manner: Compound #503 , Compound #509 , Compound #519 , Compound #529 , Compound #537 , Compound #538 , Compound #516 , Compound #522 , Compound #535 .

Example 15

3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5 phenyl-thiophene-2-carboxylic acid Compound #405



Step I:

To a cold (-78 °C) stirred solution of LDA (generated from DIPA (1.42 mL, 10.14 mmol), BuLi (5.85 mL, 9.36 mmol) in THF at -78°C for 20 min) in THF (31 mL) was added a solution of Pent-4-enoic acid ethyl ester (1.0 g, 7.8 mmol, 1.2 eq.) in THF (9.0 mL). After stirred for 1 h, neat 3-Bromo-2-methyl-propene (2.03 g, 15.0 mmol, 1.51 mL) was added and slowly warmed up to room temperature for overnight. The reaction mixture was then quenched with saturated NH_4Cl solution, extracted with ether, washed with brine and dried. Evaporation of the solution furnished the 2-Allyl-4-methyl-pent-4-enoic acid ethyl ester

(1.45 g, 100%) as an oil which was used in the next step without purification. ^{1}H NMR (400 MHz, $CDCl_3$), 5.78-5.71 (m, 1H), 5.05 (d, J = 18.6 Hz, 1H), 5.02 (d, J = 9.4 Hz, 1H), 4.76 (brs, 1H), 4.70 (s, 1H), 4.11 (dq, J = 7.2, 1.0 Hz, 2H), 2.66-2.13 (m, 5H), 1.72 (s, 3H), 1.23 (dt, J = 7.2, 1.3 Hz, 3H).

Step II:

To a refluxing stirred solution of the 2-Allyl-4-methyl-pent-4-enoic acid ethyl ester (364 mg, 2.0 mmol) in CH_2Cl_2 (100 mL, 0.02 M solution) was added drop wise a solution of the tricyclohexylphosphine (1,3-Bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene)(benzylidine)ruthenium (IV)dichloride (85 mg, 0.1 mmol) in CH_2Cl_2 (3.0 mL). After 50 min, the reaction mixture was cooled to room temperature, concentrated and purified on silica gel bond elute using EtOAc/hexane (1:20) as an eluent furnished the 3-Methyl-cyclopent-3-enecarboxylic acid ethyl ester (286 mg, 93% yield) as an oil. ^{1}H NMR ($CDCl_3$, 400 MHz), 5.25 (brs, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.2-3.1 (m, 1H), 2.65-2.46 (m, 4H), 1.74 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H).

Step III:

A solution of the 3-Methyl-cyclopent-3-enecarboxylic acid ethyl ester (255 mg, 1.65 mmol) in MeOH (4.0 mL) and 10% aq. NaOH (3.3 mL, 8.25 mmol) was heated at 50°C for 16 h, reaction mixture was cooled to room temperature, solvent was evaporated, diluted with water. The aqueous solution was washed with ether, and acidified with aq. 1 N HCl, extracted with ether. The ethereal solution was washed with brine and dried. Evaporation of the solvent furnished the 3-Methyl-cyclopent-3-enecarboxylic acid (200 mg, 97% yield). 1H NMR ($CDCl_3$, 400 MHz) 5.27 (brs, 1H), 3.26-3.17 (m, 1H), 2.7-2.55 (m, 4H), 1.74 (s, 3H).

Step IV:

The coupling of the 3-Isopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (82 mg, 0.3 mmol) and the 3-Methyl-

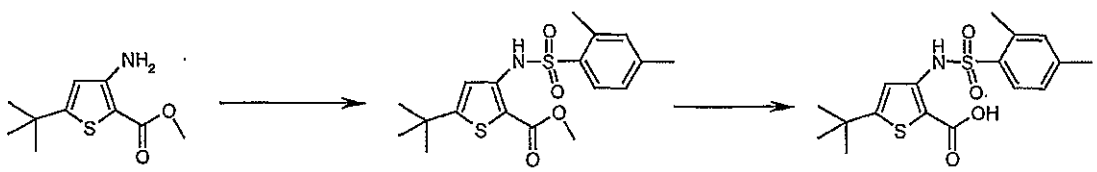
cyclopent-3-enecarboxylic acid (45 mg, 0.357 mmol) using PPh_3 (95.4 mg, 0.363 mmol) and NCS (48.5 mg, 0.363 mmol) furnished the 3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (70 mg, 61% yield) ^1H NMR ($CDCl_3$, 400 MHz 1:1 mixture of rotamers), 7.68-7.64 (m, 4H), 7.5-7.4 (m, 6H), 7.1 (s, 1H), 7.09 (s, 1H), 5.2 (s, 1H), 5.1 (s, 1H), 5.06-4.98 (m, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.08-3.0 (m, 2H), 2.85-2.76 (m, 2H), 2.5-2.42 (m, 2H), 2.3-2.1 (m, 4H), 1.69 (s, 3H), 1.64 (s, 3H), 1.24 (d, J = 6.7 Hz, 3H), 1.23 (d, J = 6.7 Hz, 3H), 1.01 (d, J = 6.9 Hz, 3H), 1.007 (d, J = 6.8 Hz, 3H).

Saponification of 3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (50 mg, 0.13 mmol) using $LiOH.H_2O$ (22 mg) as previously described furnished the 3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid (30 mg, 62.5% yield) as a solid.

^1H NMR (CD_3OD, 400 MHz 1:1 mixture of rotamers) 7.73-7.70 (m, 4H), 7.47-7.35 (m, 6H), 7.29 (s, 1H), 7.27 (s, 1H), 5.16 (s, 1H), 5.08 (s, 1H), 4.9-4.8 (m, 2H), 3.15-3.05 (m, 2H), 2.76-2.65 (m, 2H), 2.42-2.12 (m, 6H), 1.65 (s, 3H), 1.61 (s, 3H), 1.25 (d, J = 6.6 Hz, 3H), 1.24 (d, J = 6.6 Hz, 3H), 1.03 (d, J = 6.9 Hz, 6H).

Example 16

5-tert-Butyl-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid Compound #315 :



STEP I

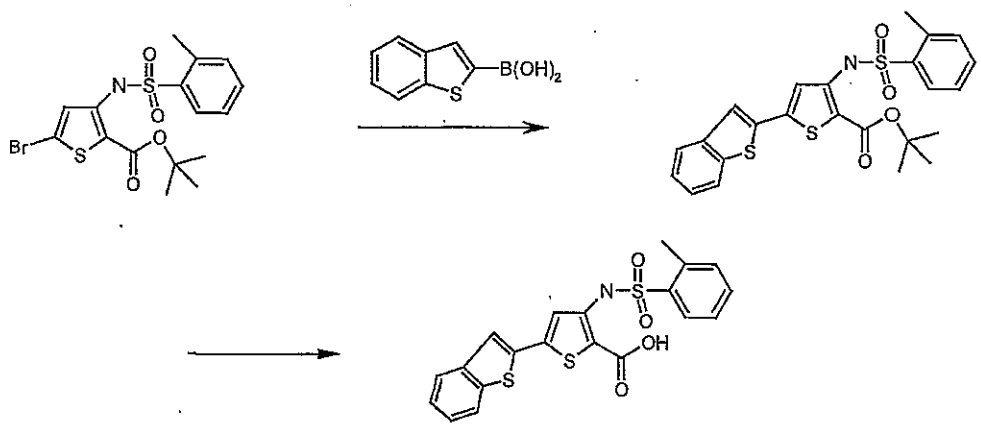
A mixture of 3-Amino-5-tert-butyl-thiophene-2-carboxylic acid methyl ester (106.5 mg, 0.5 mmol) and 2,4-dimethylsulfonyl chloride (156 mg, 0.75 mmol) in pyridine (1.5 mL) was heated at 72 °C for 16 h. The reaction mixture was diluted with EtOAc, washed with aq. 1N HCl, brine and dried. Evaporation of the solvent and purification of the residue on silica gel bond elute using EtOAc (1:20 to 1:10) as an eluent furnished the 5-tert-Butyl-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid methyl ester (188 mg, 99% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) 9.73 (s, 1H), 7.89 (d, J = 8.6 Hz, 1H), 7.04-7.08 (m, 2H), 7.03 (s, 1H), 3.82 (s, 3H), 2.62 (s, 3H), 2.33 (s, 3H), 1.28 (s, 9H).

STEP II

Hydrolysis of the 5-tert-Butyl-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid methyl ester (55 mg, 0.14 mmol) using $LiOH.H_2O$ (22 mg) as previously described provided the 5-tert-Butyl-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid (36 mg, 70% yield) as a solid. ^{1}H NMR (CD_3OD, 400 MHz) 7.85 (d, J = 8.6 Hz, 1H), 7.14-7.10 (m, 2H), 7.0 (s, 1H), 2.56 (s, 3H), 2.31 (s, 3H), 1.27 (s, 9H).

Example 17

5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid Compound #230



STEP I

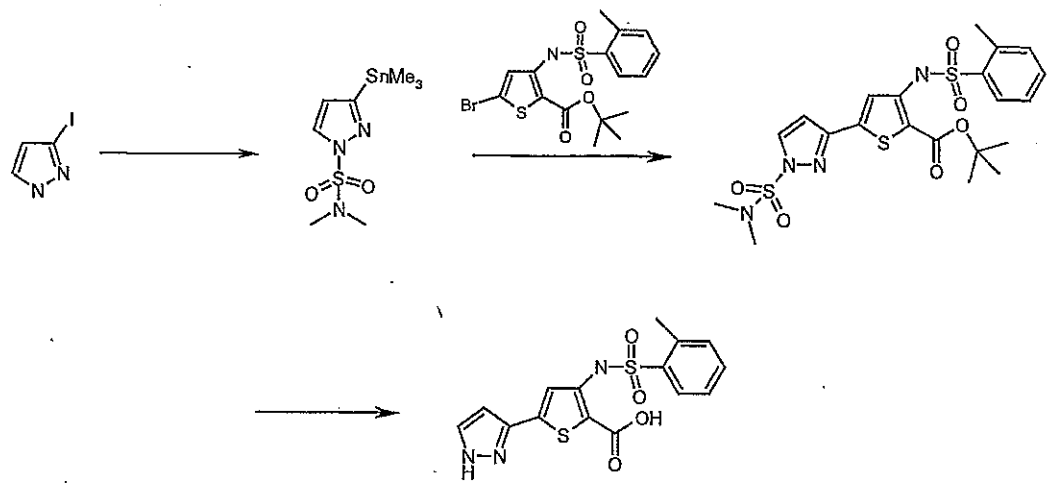
Suzuki coupling of 5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (43 mg, 0.1 mmol) and bezothiophene-2-boronic acid (53.4 mg, 0.3 mmol) was carried out using $Pd(PPh_3)_4$ and Na_2CO_3 (as described in example 2) resulted in 5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (27 mg, 55% yield). ^1H NMR ($CDCl_3$, 400 MHz) 9.92 (s, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.79-7.71 (m, 2H), 7.45-7.24 (m, 7H), 2.7 (s, 3H), 1.56 (s, 9H).

STEP II

5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester was hydrolyzed to the acid using TFA as described for example 2 providing 5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid (24 mg, 99% yield). ^1H NMR (DMSO-D_6, 400 MHz) 10.19 (s, 1H), 8.0 (d, J = 7.7 Hz, 1H), 7.79-7.74 (m, 1H), 7.86 (s, 1H), 7.84-7.81 (m, 1H), 7.54 (t, J = 7.7 Hz, 1H), 7.53-7.36 (m, 4H), 7.32 (s, 1H), 2.58 (s, 3H).

Example 18

5-(1H-Pyrazol-3-yl)-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid Compound #170



Step I

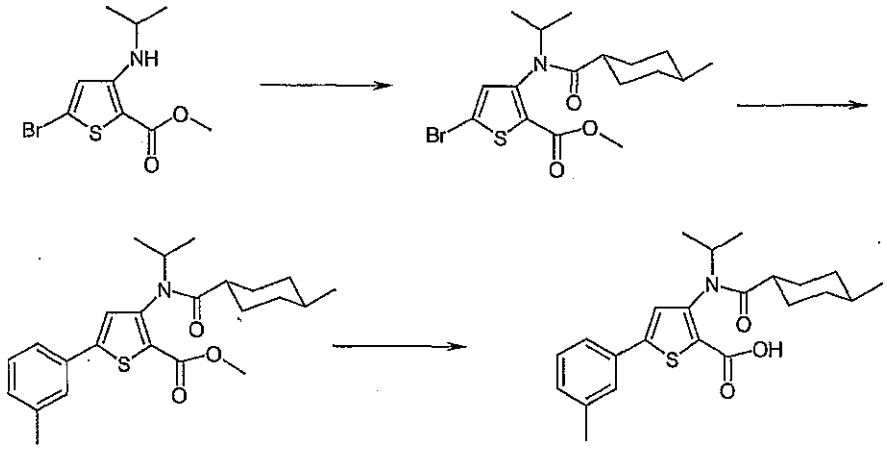
To a stirred solution of 5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (43mg, 0.1mmol) in toluene (3.0 mL) was sequentially added a solution of Pd(PPh3)4 (12 mg, 0.01 mmol) in toluene (1.0 mL) and 3-Trimethylstannanyl-pyrazole-1-sulfonic acid dimethylamide (prepared according to *J. Med. Chem* (1998), **41**, p-2019) (75 mg, 0.2 mmol, 2.0 eq), and heated the resulting overnight at 80°C. It was then cooled to room temperature, the solvent was evaporated and the crude was purified on preparative TLC using EtOAc/hexane (1:5). 5-(1-Dimethylsulfamoyl-1H-pyrazol-3-yl)-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (35 mg, 66.5% yield) was isolated. ^{1}H NMR ($CDCl_3$, 400 MHz) 9.93 (s, 1H), 8.11 (d, J = 0.7 Hz, 1H), 8.02 (dd, J = 6.7, 1.32 Hz, 1H), 7.84 (d, J = 0.7 Hz, 1H), 7.45 (dt, J = 7.5, 1.3 Hz, 1H), 7.31 (t, J = 8.2 Hz, 2H), 7.26 (d, J = 1.0 Hz, 1H), 2.98 (s, 6H), 2.7 (s, 3H), 1.55 (s, 9H).

Step II

A reaction mixture of 5-(1-Dimethylsulfamoyl-1H-pyrazol-3-yl)-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (10 mg, 0.019 mmol) and 4N HCl (0.3 mL) solution in dioxane in MeOH (0.3 mL) was stirred at room temperature 26 h. Reaction mixture was then diluted with water and extracted with EtOAc, concentrated and purified on preparative TLC using MeOH/CH_2Cl_2/AcOH (5:95:1) furnished the 5-(1H-Pyrazol-3-yl)-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid (4.5 mg, 65.2% yield). ^{1}H NMR (CD_3OD, 400 MHz) 7.99 (d, J = 7.9 Hz, 1H), 7.81 (s, 1H), 7.43 (t, J = 7.5, 1.3 Hz, 1H), 7.42-7.26 (m, 2H), 7.19 (s, 1H), 2.69 (s, 3H).

Example 19

3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5-m-tolyl-thiophene-2-carboxylic acid Compound #448



STEP I

Trans-4-methyl-cyclohexanecarbonyl chloride was prepared by heating to reflux trans-4-methyl-cyclohexanecarboxylic acid (5g, 0.035 mmol) in thionylchloride (5.0 ml) for 2h followed by purification of the corresponding acyl chloride under reduced pressure in a Kugel-Rhorr apparatus collecting the fraction distilling at 95 °C yielding 5.1 g of the desired material which was used in the next step without further purification. This acyl chloride (1.5 ml, aprox. 10 mmol) was dissolved along with 5-Bromo-3-isopropylamino-thiophene-2-carboxylic acid methyl ester (2 g, 7.12 mmol) in anhydrous dichloroethane (2 mL) and heated at 80 °C (closed vial) for 12h. The solvents were evaporated, the resulting crude material was dissolved in methanol and left 30 min. at room temperature, concentrated and purified via flash chromatography on silica gel using a 5% EtOAc 95% hexanes mixture of eluents, in this manner 600 mg (21%) of 5-Bromo-3-[isopropyl-(4-methyl-cyclohexanecarbonyl)-amino]-thiophene-2-carboxylic acid methyl ester the was isolated. ^{1}H NMR($CDCl_3$, 300 MHz): 6.78 (s, 1H), 4.93 (m, 1H), 3.69 (s, 3H), 2.00-1.20 (m, 8H), 1.14 (d, 3H), 0.93 (d, 3H), 0.81 (d, 3H), 0.72-0.70 (m, 2H).

STEP II

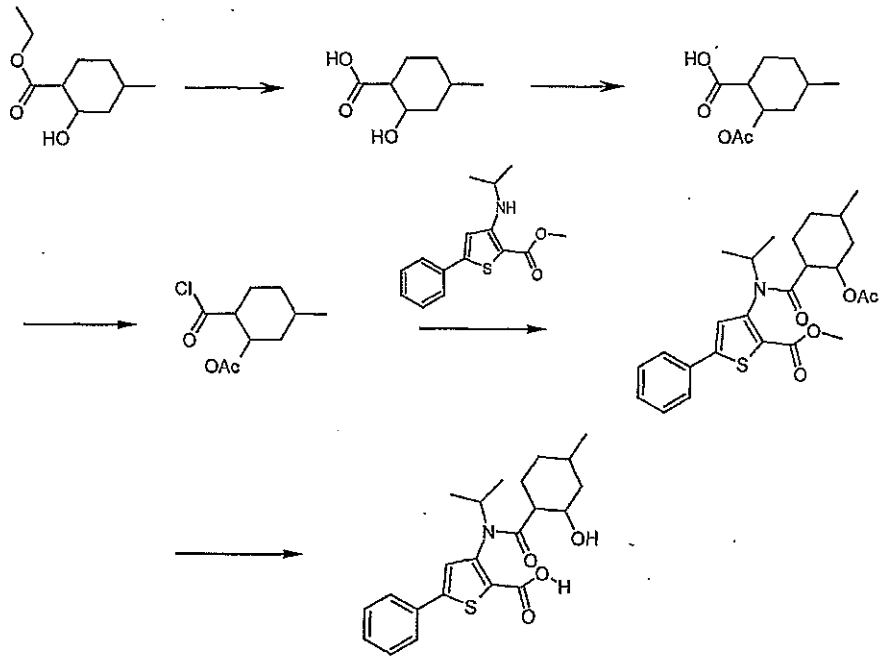
To a degassed solution of 5-Bromo-3-[isopropyl-(4-methyl-cyclohexanecarbonyl)-amino]-thiophene-2-carboxylic acid methyl ester (100 mg, 0.249 mmol) and 3-methyl boronic acid (38 mg, 0.279 mmol) in a mixture of DME (6 mL) and 2M aqueous Na_2CO_3 (3 mL), $Pd(PPh_3)_4$ (12 mg) was added and the reaction mixture was stirred at reflux conditions for 12h under a N_2 atmosphere. The reaction mixture was diluted with ethyl acetate and water. The organic layer was separated, dried (Na_2SO_4), concentrated. The residue was purified by column chromatography using ethyl acetate and hexane (1:3) as eluent. 35 mg (34%) of 3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5-m-tolyl-thiophene-2-carboxylic acid methyl ester was isolated. ^1H NMR ($CDCl_3$, 400 MHz): 7.45 (bs, 2H), 7.36 (t, 1H), 7.23 (m, 1H), 7.01 (s, 1H), 4.99 (m, 1H), 3.83 (s, 3H), 2.41 (s, 3H), 2.01-0.61 (m, 20H).

Step III

3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5-m-tolyl-thiophene-2-carboxylic acid methyl ester (30 mg, 0.073 mmol) was taken in a mixture of THF:MeOH:H_2O (3:2:1, 3 mL) and then added 1N aqueous solution of $LiOH.H_2O$ (0.44 mL, 0.438 mmol). The reaction mixture was stirred at room temperature for 12 h. Solvents were removed and the residue was partitioned between water and ethyl acetate. The aqueous layer was acidified using 10 % $KHSO_4$ solution. The organic layer was separated, dried (Na_2SO_4) and concentrated. The residue was purified by preparative TLC using chloroform:methanol:acetic acid (9:1:0.1) to obtain 3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5-m-tolyl-thiophene-2-carboxylic acid (15 mg, 52%) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz): (s, 2H), 7.38 (t, 1H), 7.24 (m, 1H), 7.08 (s, 1H), 5.01 (s, 1H), 2.42 (s, 3H), 2.10-0.62 (m, 20H). ESI^- (M-H): 398.

Example 20

(1R,2S,4R)-3-[Isopropyl-(2-hydroxy-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid Compound #402



(1R,2S,4R)-2-Hydroxy-4-methyl-cyclohexanecarboxylic acid methyl ester was prepared as described in J. Org. Chem, (1993), 58, pp.6255-6265. NMR ^1H ($CDCl_3$, 400 MHz): 4,26 ppm (s, 1H); 4,19-4,13 ppm (m , 2H); 3,16 ppm (s, 1H); 2,35-2,29 ppm (m, 1H); 1,92-1,74 ppm (m, 5H); 1,31-1,24 ppm (m, 3H); 1,08-1,01 ppm (m, 1H); 0,96-0,92 ppm (m, 1H); 0,88 ppm (d, 3H).

STEP I

To a solution of (1R,2S,4R)-2-Hydroxy-4-methyl-cyclohexanecarboxylic acid methyl ester (450 mg, 2.42 mmol) in methanol (12 ml) was added a 2.5 M solution of sodium hydroxide (9.7 ml, 24.2 mmol). The reaction mixture was stirred for 4 h at 50 °C. Then, the solvents were removed and the residue was partitioned between 20 ml of H_2O acidified to pH 4 and 20 ml of EtOAc. The organic layer was separated and the aqueous phase was washed with ethyl acetate (2 X 20 ml). The combined ethyl acetate layers were dried (Na_2SO_4) and concentrated to obtain 313 mg (82 %) of (1R,2S,4R)-2-Hydroxy-4-methyl-cyclohexanecarboxylic

acid. NMR ^1H ($CDCl_3$, 400 MHz): 4,34 ppm (s, 1H); 2,43-2,39 ppm (m, 1H); 1,96-1,76 ppm (m, 5H); 1,14-1,08 ppm (m, 1H); 1,02-0,93 ppm (m, 1H); 0,90 ppm (d, 3H).

Step II

To a solution of (1R,2S,4R)-2-Hydroxy-4-methyl-cyclohexanecarboxylic acid (162 mg, 1.02 mmol) in dichloromethane (5 ml) was added pyridine (495 ul, 6.12 mmol) followed by acetic anhydride (385 ul, 4.08 mmol). The reaction mixture was stirred for 20 h at room temperature. Then, the solvents were removed and 10 ml of 3N HCl solution was added. This mixture was stirred for 30 minutes and then a saturated solution of $NaHCO_3$ was slowly added until pH = 9-10. This solution was then extracted with ethyl acetate (2 X 5 ml). The aqueous phase was then acidified with a 10% HCl solution and extracted with ethyl acetate (3X5 ml). The following ethyl acetate layers were combined, dried (Na_2SO_4) and concentrated to obtain 109 mg (53 %) of (1R,2S,4R)-2-Acetoxy-4-methyl-cyclohexanecarboxylic acid. NMR ^1H ($CDCl_3$, 400 MHz): 5,45 ppm (s, 1H); 2,46-2,42 ppm (m, 1H); 2,02 ppm (s, 3H); 2,02-1,96 ppm (m, 1H); 1,91-1,76 ppm (m, 3H); 1,70-1,61 ppm (m, 1H); 1,16-1,08 ppm (m, 1H); 0,99-0,88 ppm (m, 1H); 0,87 ppm (d, 3H).

Step III

To a solution of (1R,2S,4R)-2-Acetoxy-4-methyl-cyclohexanecarboxylic acid (109 mg, 0.54 mmol) in dichloromethane (2.7 ml) was added oxalyl chloride (545 µl, 1.09 mmol) followed by 1 drop of dimethylformamide. The reaction mixture was stirred for 4 h at room temperature. The solvents were then removed to obtain 119 mg (99%) of (1R,2S,4R)-2-Acetoxy-4-methyl-cyclohexanecarboxylic acid chloride.

Step IV

To a solution of 3-Isopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (136 mg, 0.50 mmol) in 1,2-dichloroethane (1.0

ml) was added (1R,2S,4R)-2-Acetoxy-4-methyl-cyclohexanecarboxylic acid chloride (119 mg, 0.54 mmol) dissolved in 1,2-dichloroethane (0.6 ml) followed by PPh_3 (136 mg, 0.52 mmol). The resulting solution was stirred for 20 h at 90 °C and then cooled to room temperature. It was then diluted with ethyl acetate (10 ml) and a solution of saturated $NaHCO_3$ (10 ml). The aqueous phase was separated and washed with ethyl acetate (2x10 ml) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residue was purified by flash chromatography (0% to 25% EtOAc/Hexane) to obtain 110 mg (45%) of (1R,2S,4R)-3-[Isopropyl-(2-Acetoxy-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ^1H ($CDCl_3$, 400 MHz): 1.5:1.0 mixture of rotamers 7,73-7,70 ppm (m, 2H, H_{aro}); 7,69-7,63 ppm (m, 1H, H_{aro}); 7,51-7,41 ppm (m, 4H, H_{aro}); 7,13 ppm (s, 0.6H, H_{aro}, major rotamer); 5,79 ppm (s, 0.4H, minor rotamer); 5,21 ppm (s, 0.6H, major rotamer); 4,95-4,88 ppm (m, 1H); 3,88 ppm (s, 1.8H, major rotamer); 3,87 ppm (s, 1.2H, minor rotamer); 2,40-2,36 ppm (m, 0.6H, major rotamer); 2.11 ppm (s, 3H); 1,78-0,77 ppm (m, 16H).

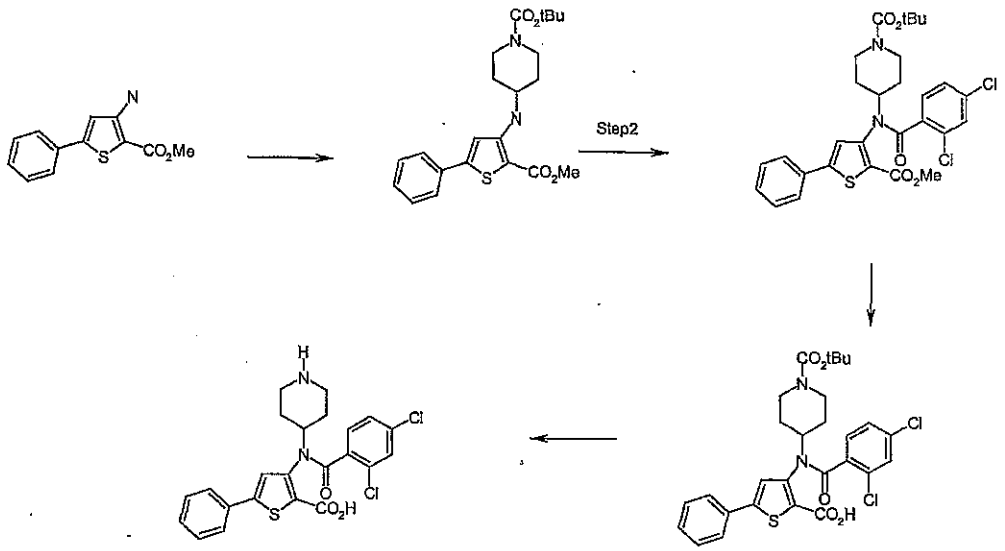
Step V

(1R,2S,4R)-3-[Isopropyl-(2-Acetoxy-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (36 mg, 0.17 mmol) was dissolved in a mixture of dioxane:H_2O (4:1) (700 µl) and then 470 µl of LiOH 1N was added to it. After 3 h at 50 °C the reaction mixture was cooled to room temperature and the solvents were removed. The residue was then partitioned between 10 ml of H_2O acidified to pH 4 and 10 ml of EtOAc. The organic layer was separated and the aqueous phase was washed with ethyl acetate (2 X 10 ml). The combined ethyl acetate layers were dried (Na_2SO_4), concentrated and the residue was purified by preparative chromatography to obtain 9 mg (29 %) of (1R,2S,4R)-3-[Isopropyl-(2-hydroxy-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid. NMR ^1H ($CDCl_3$, 400 MHz): 3:2 mixture of rotamers 7,76-

7,73 ppm (m, 2H, H_{aro}); 7,50-7,38 ppm (m, 3H, H_{aro}); 7,36 ppm (s, 1H, H_{aro}); 4,93-4,87 ppm (m, 1H); 4,25 ppm (s, 0.70H, major rotamer); 3,97 ppm (s, 0.3H, minor rotamer); 2,35-2,28 ppm (m, 1H); 1,99-1,53 ppm (m, 5H); 1,28 ppm (d, 0,6H, minor rotamer); 1,25 ppm (d, 1,4H, major rotamer); 1,06-1,03 ppm (m, 3H), 0,96-0,72 ppm (m, 1H); 0,79 ppm (d, 3H); 0,67-0,56 ppm (m, 1H).

Example 21

3-[(2,4-Dichloro-benzoyl)-piperidin-4-yl-amino]-5-phenyl-thiophene-2-carboxylic acid hydrochloride salt compound #368



Step I

A suspension of 3-amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (745 mg, 3.2 mmol) in dry THF (1.3 ml), at 21 °C, under nitrogen, was treated with tert-butyl 4-oxo-1-piperidine carboxylate (673 mg, 3.2 mmol), followed by dibutyltin dichloride (19 mg, 0.064 mmol, 0.02 eq.). After 5 min the reaction was treated with phenyl silane (435 µL, 380 mg, 3.52 mmol, 1.1 eq). The mixture was left to stir for 74h when a clear solution resulted. The reaction was stripped off solvent to leave a thick bright yellow gum (1.59 g). The crude material was purified by column chromatography using (CH_2Cl_2 :Hexane :EtOAc) = 15 : 5 :1 as eluent to provide 4-(2-Methoxycarbonyl-5-phenyl-

thiophen-3-ylamino)-piperidine-1-carboxylic acid tert-butyl ester as a yellow foam (713 mg, 54%). ^{1}H NMR ($CDCl_3$, 400 MHz) 7.63-7.60 (m, 2H), 7.74-7.36 (m, 3H), 6.90-6.84 (bs, 1H), 6.84 (s, 1H), 3.97- 4.01 (m, 2H), 3.80 (s, 3H), 3.48 (bs, 1H), 3.06-2.99 (m, 2H), 2.03-1.99 (m, 2H), 1.51-1.48 (m, 2H), 1.47 (bs, 9H)

Step II

4-(2-Methoxycarbonyl-5-phenyl-thiophen-3-ylamino)-piperidine-1-carboxylic acid tert-butyl ester (200 mg, 0.48 mmol) was treated with 2,4 dichlorobenzoylchloride (202 µL, 302 mg, 1.44 mmol, 3 eq) under previously described conditions (e.g. Example 14) to provide, after column chromatography using (CH_2Cl_2 : Hexane : EtOAc = 15 :5 :1) as eluent , 4-[(2,4-Dichloro-benzoyl)-(2-methoxycarbonyl-5-phenyl-thiophen-3-yl)-amino]-piperidine-1-carboxylic acid tert-butyl ester as a pale yellow foam (165 mg, 58%), ^{1}H NMR ($CDCl_3$, 400 MHz) 7.54-7.51 (m, 2H), 7.45-7.39 (m, 3H), 7.27-7.25 (m , 2H), 7.17(d, J = 1.96Hz, 1H), 7.06 (dd, J = 1.92Hz, J = 8.34Hz, 1H), 4.86-4.92 (m, 1H), 4.11-4.21 (m, 2H), 3.89 (s, 3H), 2.82-2.89 (m, 2H), 2.17-2.20 (m, 1H), 1.89-1.92 (m, 1H), 1.49-1.61 (m, 1H), 1.40 (bs, 9H), 1.19-1.25 (m, 1H)

Step III

A suspension of 4-[(2,4-Dichloro-benzoyl)-(2-methoxycarbonyl-5-phenyl-thiophen-3-yl)-amino]-piperidine-1-carboxylic acid tert-butyl ester (160 mg, 0.27 mmol) above in dioxane: water (4 :1, 3 ml) was treated with lithium hydroxide (2M aqueous solution, 41 µL, 341 mg, 0.814 mmol, 3 eq) and the reaction allowed to stir overnight for 18h. The reaction was stripped-off solvent and the residue partitioned between EtOAc : water (4 : 1). The aqueous phase was separated and extracted several times, with EtOAc , following acidification to pH 5.5 with 0.1N HCl. The combined organic extract was evaporated to a solid. The solid was taken into EtOAc and the above acid wash repeated to give, after drying and evaporation, 4-[(2-Carboxy-5-phenyl-thiophen-3-yl)-(2,4-

dichloro-benzoyl)-amino]-piperidine-1-carboxylic acid tert-butyl ester as a colourless solid (128 mg, 91%), ^{1}H NMR (Acetone, 400 MHz) 7.75-7.70 (m, 1H), 7.64 (s, 1H), 7.52-7.40 (m, 3H), 7.52 (d, J = 1.98 Hz, 1H), 7.21 (dd, J = 1.96 Hz, J = 8.19 Hz, 1H), 4.80-4.71 (m, 1H), 4.26-4.01 (m, 2H), 2.71- 2.30 (bs, 3H), 2.25-2.17 (m, 1H), 1.82-1.69 (m, 1H), 1.40 (bs, 9H), 1.33-1.24 (m, 1H).

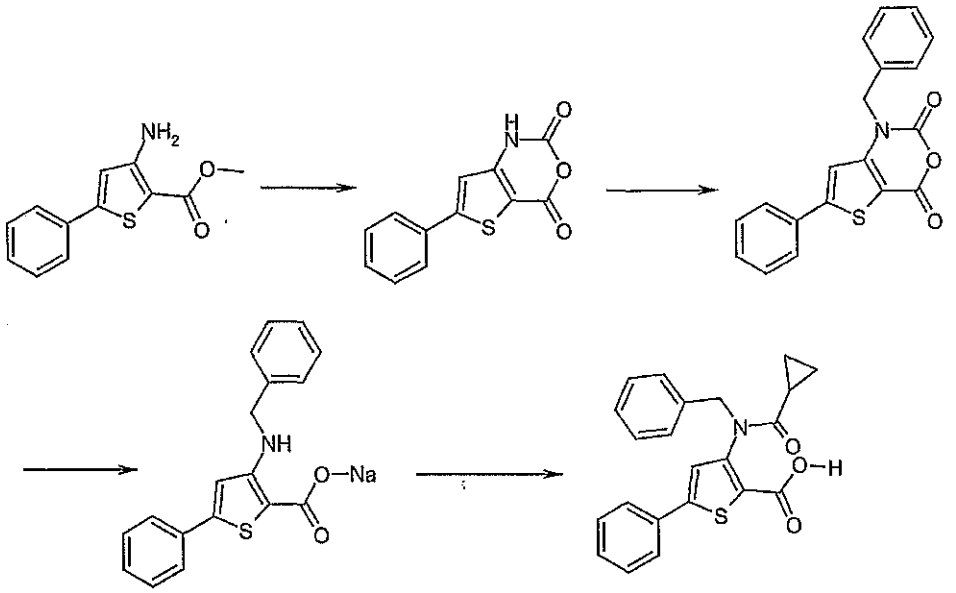
Step IV

A solution of 4-[(2-Carboxy-5-phenyl-thiophen-3-yl)-(2,4-dichloro-benzoyl)-amino]-piperidine-1-carboxylic acid tert-butyl ester (240 mg, 0.42 mmol) in dioxane (4 ml) at 21 °C under nitrogen was treated with anhydrous 4M HCl (3 ml, 12.6 mmol, 30 eq). After 4h the reaction was stripped off solvent and the residue triturated with ether to give 3-[(2,4-Dichloro-benzoyl)-piperidin-4-yl-amino]-5-phenyl-thiophene-2-carboxylic acid as a pale yellow powder (214 mg, 100 %) ^{1}H NMR (Acetone, 400 MHz) 7.76-7.73 (m, 2H), 7.64 (s, 1H), 7.45-7,38 (m, 3H), 7.30 (bs, 1H), 7.28-7.24 (m, 1H), 4.93-4.84 (m, 1H), 3.56-3.49 (m, 2H), 3.25-3.14 (m, 2H), 3.05-2.55 (bs, 1H), 2.50-2.37 (m, 2H), 2.13-1.83 (m, 1H).

Similarly prepared were Compound #366 , Compound #553 , Compound #543

Example 22

3-(Benzyl-cyclopropanecarbonyl-amino)-5-phenyl-thiophene-2-carboxylic acid. Compound #454



Step I

A solvent mixture of THF/MeOH/H_2O (3:2:1) was added to 3.04 g of methyl(3-amino-5-phenyl)thiophene-2-carboxylate (13 mmol) and 1.64 g of lithium hydroxide monohydrate (39 mmol). The mixture was refluxed for 8 hours and concentrated *in vacuo*. The crude material was taken in 100 ml of water, washed with ethyl acetate (2 x 100 ml) and transferred into a multineck flask. A 20% phosgene solution in toluene (11 ml, 39 mmol) was added dropwise at 0°C. A precipitate was then collected by filtration and sequentially washed by trituration with a saturated solution of bicarbonate, water, acetone and diethyl ether. 2.52 g (79%) of 6-phenyl-1H-thieno[3,2-d][1,3]oxazine-2,4-dione were isolated as a white solid. NMR ^1H (DMSO D_6, 400 MHz): 7.79-7.76 ppm (m, 2H, H_{aro}); 7.52-7.47 ppm (m, 3H, H_{aro}); 7.25 ppm (s, 1H, H_{azole}); 0.4 ppm (s, 1H, N*H*).

Step II

A solution of 6-phenyl-1H-thieno[3,2-d][1,3]oxazine-2,4-dione (1 g, 4.1 mmol) and anhydrous sodium carbonate (477 mg, 4.5 mmol) diluted in 15 ml of anhydrous dimethylacetamide was stirred for one hour under nitrogen before adding benzyl bromide (785 mg, 4.5 mmol). The mixture was stirred overnight at room temperature. 912 mg (66.3%) of 1-benzyl-6-phenyl-1H-thieno[3,2-

d][1,3]oxazine-2,4-dione were obtained as a pale yellow solid after filtration and washing the precipitate with acetone and pentane. NMR ^{1}H (DMSO D_6, 400 MHz): 7.8-7.76 ppm (m, 3H, H_{aro}); 7.51-7.45 ppm (m, 3H, H_{aro}); 7.43-7.41 ppm (m, 2H, H_{aro}); 7.35-7.3 ppm (m, 2H, H_{aro}); 7.28-7.24 ppm (m, 1H, H_{aro}); 5.22 ppm (s, 1H, NC*H*$_2$).

Step III

To a solution of 1-benzyl-6-phenyl-1H-thieno[3,2-d][1,3]oxazine-2,4-dione (880 mg, 2.62 mmol) were successively added 32 ml of dioxane and 7.87 ml of NaOH 1N aqueous solution. The mixture was vigourously stirred for 2 h and then the solvents were concentrated *in vacuo*. Dichloromethane was added to the crude material and sodium 3-benzylamino-5-phenyl-thiophene-2-carboxylate (1.07 g, 100%) precipitated as a pale yellow solid. NMR ^{1}H (DMSO D_6, 400 MHz): 7.76 ppm (t, 1H, J = 6.4 Hz, N*H*); 7.53-7.51 ppm (m, 2H, H_{aro}); 7.33-7.26 ppm (m, 6H, H_{aro}); 7.23-7.16 ppm (m, 2H, H_{aro}); 7.07 ppm (s, 1H, H_{azole}); 4.36 ppm (d, 2H, J = 6.4 Hz, NHC*H*$_2$).

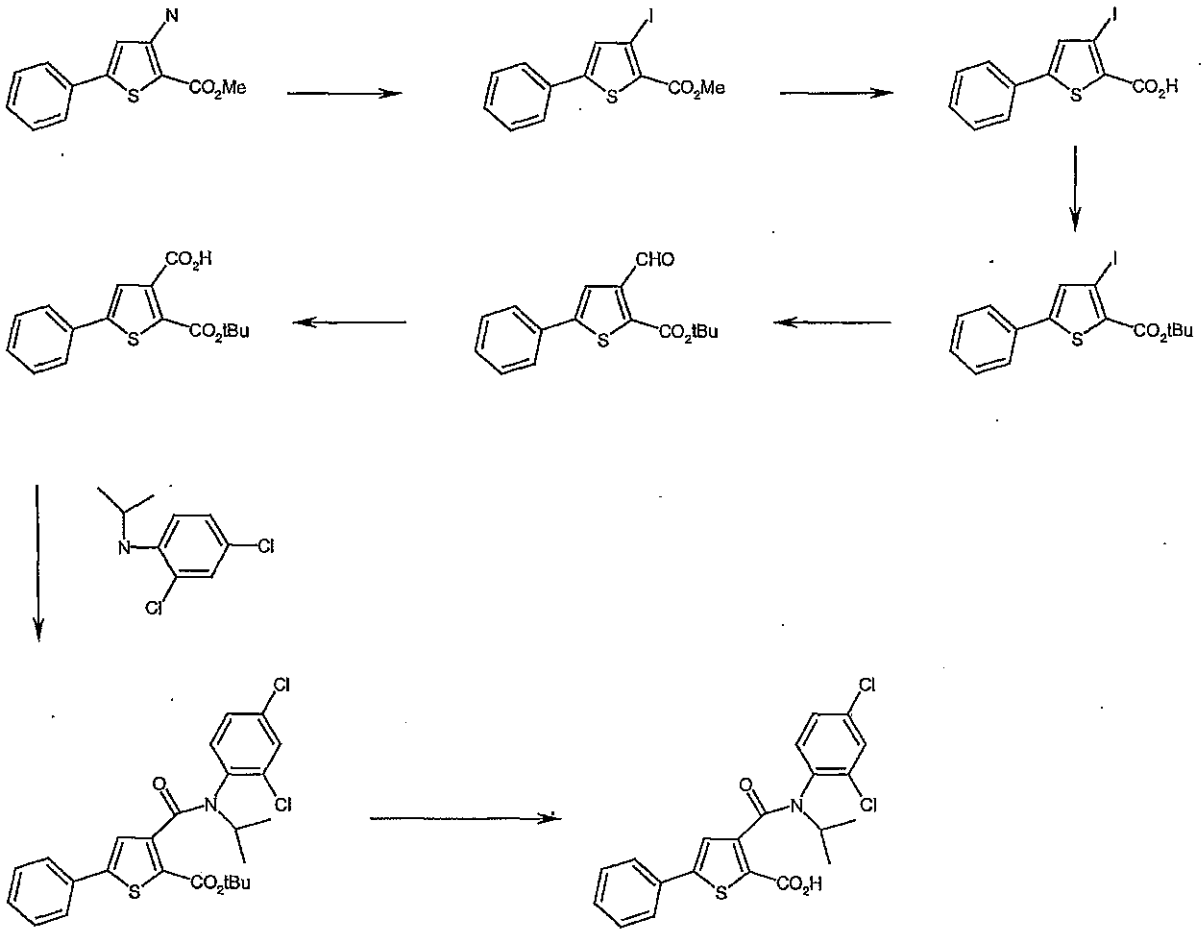
Step IV

To a solution of sodium 3-benzylamino-5-phenyl-thiophene-2-carboxylate (41.1 mg, 0.1 mmol) was added 32 mg (0.3 mmol) of cyclopropanecarbonyl chloride, 1.5 ml of dioxane and 0.5 ml of water. The mixture was stirred overnight at room temperature and concentrated *in vacuo*. A 4N hydrogen chloride solution in dioxane (1 ml) was added and the mixture was stirred for one hour at room temperature. The mixture was again concentrated and the crude material was purified by reverse phase HPLC giving access to 11.9 mg (31.5%) of 3-(benzyl-cyclopropanecarbonyl-amino)-5-phenyl-thiophene-2-carboxylic acid as a pale yellow solid. NMR ^{1}H (DMSO D_6, 400 MHz): 7.56-7.54 ppm (m, 2H, H_{aro}); 7.39-7.13 ppm (m, 10H, H_{aro}, H_{azole} and COO*H*); 5.27 ppm (d, 1H, J = 15.2 Hz); 4.48 ppm (d, 1H, J = 15.2 Hz); 1.49 ppm (m, 1H); 0.77 ppm (m, 2H); 0.61 ppm (m, 2H).

The following compounds were prepared in a similar manner:
Compound #172 , Compound #173 , Compound #175 , Compound #186 ,
Compound #187 , Compound #188 , Compound #241 , Compound #247 ,
Compound #251 , Compound #252 , Compound #253 , Compound #254 ,
Compound #255 , Compound #256 , Compound #257 , Compound #276 ,
Compound #277 , Compound #278 , Compound #279 , Compound #280 ,
Compound #281 , Compound #330 , Compound #334 , Compound #335 ,
Compound #336 , Compound #339 , Compound #340 , Compound #341 ,
Compound #342 , Compound #343 , Compound #344 , Compound #345 ,
Compound #347 , Compound #349 , Compound #350 , Compound #351 ,
Compound #352 , Compound #353 BCH-23932, Compound #354 ,
Compound #384 , Compound #385 , Compound #386 , Compound #388 ,
Compound #389 , Compound #390 , Compound #391 , Compound #392 ,
Compound #393 , Compound #394 , Compound #397 , Compound #398 ,
Compound #399 , Compound #400 , Compound #401 .

Example 23

3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid



Step I

3-Iodo-5-phenyl-thiophene-2-carboxylic acid methyl ester

A suspension of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (10 g, 43 mmol) in anhydrous benzene (200 ml), at 21 °C, under N_2, was treated with t-butyl nitrite (21.8 g, 86 mmol) and the dark mixture cooled to 0 °C and treated dropwise, over 15 min, with iodine (21.8 ml, 184 mmol) . After 30 min at 0 °C, the solution was allowed to warm-up to ambient temperature and stirred for 2h. The reaction mixture was then poured into water (300 ml) and stirred vigorously for 15 min. The organic phase was separated and washed several times with 20% sodium thiosulfate (4x100 ml). The resulting emulsion was filtered through celite. The celite pad was washed with EtOAc and the combined filtrate and washings were washed with more sodium

thiosulfate (100 ml) to give an orange solution which was washed wth brine and dried. Evaporation of the solvent afforded an oil (7.4 g). The crude oil was purified by biotage flash chromatography using Hexane/CH_2Cl_2/EtOAc (20/2/1) as eluent to give 4.42g (29%) of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid methyl ester as a pale yellow oil. NMR ^1H ($CDCl_3$, 400 MHz,) : 7.62-7.57 (m, 2H); 7.58 (s, 1H); 7.50-7.36 (m, 3H); 3.91 (s, 3H)

Step II

3-Iodo-5-phenyl-thiophene-2-carboxylic acid

A solution of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid methyl ester (4.4 g, 12.78 mmol) in dioxane/water 4/1 (50 ml), at 21 °C, under N_2, was treated with lithium hydroxyde (2N, 19.3 ml, 38 mmol) and the solution left to stir for 21.5 h. The reaction mixture was evaporated to dryness and the residue partitioned between EtOAc (75 ml) and water (25 ml) and acidified with 2N HCl to pH 5.5. The aqueous phase was separated and extracted with EtOAc (3x50 ml). The combined organic extract were washed with brine, dried and evaporated to give 4.12 g (97%) of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid as a pale yellow solid. NMR ^1H (CD_3OD, 400 MHz) : 7.69-7.67 (m, 2H); 7.55 (s, 1H); 7.46-7.39 (m, 3H).

Step III

3-Iodo-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester

A suspension of magnesium sulfate (4.61 g, 38.32 mmol) in dichloromethane (37 ml) at 21 °C, under N_2, was treated with conc H_2SO_4 (510 µl, 9.58 mmol). After 15 min solid 3-Iodo-5-phenyl-thiophene-2-carboxylic acid (3.7 g, 9.58 mmol) was added followed by t-butanol (4.55 ml, 47.9 mmol) and the flask was stoppered and left over-night for 19.5 h. The reaction mixture was treated with saturated bicarbonate aqueous solution, and filtered. The solid was washed with CH_2Cl_2 and the filtrate dried

and concentrated to an oil. The crude material was purified by flash chromatography using Hexane/CH_2Cl_2 (3:1) as eluent to give 1,63 g (44%) of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester as a colorless solid. NMR ^1H ($CDCl_3$, 400 MHz) 7.61-7.59 (m, 2H); 7.43-7.35 (m, 3H), 7.25 (s, 1H), 1.60 (bs, 9H).

Step IV

3-Formyl-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester

A solution of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester (1.41 g, 3.65 mmol) in dry THF (37 ml) at -78° C, under nitrogen, was treated dropwise, over 5 min with n-butyl lithium (4.8 ml, 7.66 mmol). The reaction gradually darkened to a red-brown color. After 15 min at -78 °C dimethylformamide (1.7 ml, 21.9 mmol) was added dropwise over 7 min. The dark solution was allowed to stirr for 2 h then quenched with saturated NH_4Cl solution (10 ml) and allowed to reach 21°C. The aqueous phase was separated and extracted with EtOAc (3x50 ml). The combined organic extracts were evaporated and the residue taken into EtOAc and washed with water, brine, dried and concentrated to give 1.14 g of a brownn oil. The crude material was purified by flash chromatography using Hexane/CH2Cl2 (1/1) as eluent to provide 303 mg (28%) of 3-Formyl-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester as a colorless solid. NMR ^1H : ($CDCl_3$, 400 MHz) : 10.62 (s, 1H); 7.78 (s, 1H); 7.64-7.62 (m, 2H); 7.48-7.38 (m, 3H); 1.62 (bs, 9H).

Step V

5-Phenyl-thiophene-2,3-dicarboxylic acid 2-tert-butyl ester

A solution of 3-Formyl-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester (300 mg, 1.04 mmol) in dry THF (20 ml), at 0 °C, under nitrogen, was treated with methyl sulfide (10% w/w in THF, 3.8 ml, 5.2 mmol) followed by sodium dihydrogenphosphate (30%

aqueous solution , 9.56 ml, 2.05 mmol). After 0.5 h, the solution was treated with sodium chlorite (30% w/w aqueous solution, 1.9 ml, 2.08 mmol) added over 1 min via a syringe. The pale yellow solution was stirred for 1.5 h at 0 °C, then diluted with water (20 ml) and extracted with EtOAc (4x 40 ml). The aqueous phase was separated, extracted with more EtOAc (40 ml) and the combined extracts were washed with brine dried and concentrated to give 316 mg (100 %) of 5-Phenyl-thiophene-2,3-dicarboxylic acid 2-tert-butyl ester as a pale brown solid. NMR ^1H (CD_3CO; 400 MHz): 7.87 (s, 1H); 7.83-7.81 (m, 2H); 7.17-7.53 (m, 3H); 1.65 (bs, 9H).

Step VI

3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester

A solution of 5-Phenyl-thiophene-2,3-dicarboxylic acid 2-tert-butyl ester (40 mg, 0.13 mmol) in CH_2Cl_2 (1.3 ml), under nitrogen, at 0°C, was treated with diisopropylethylamine (27 □L, 0.16 mmol) followed by dimethylformamide (10 □L, 0.13 mmol) and oxalyl chloride (170 L, 0.34 mmol). Slight effervescence was observed. The reaction was kept at 0 °C for 30 min before being treated with (2,4-Dichloro-phenyl)-isopropyl-amine (described previously) (79 mg, 0.39 mmol). The reaction was allowed to reach 21 °C and then placed in a bath at 90 °C for 15 h. Solvent was removed to leave a pale brown gum (144 mg). The crude material was purified on bond-elute using Hexane/CH_2Cl_2/EtOAc (12.5/2/1) as eluent to give 39 mg, (62%) of 3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester as a pale brown solid. NMR ^1H ($CDCl_3$; 400 MHz) 7.50-7.48 (m, 2H); 7.38-7.25 (m, 6H); 7.10-7.03 (m, 1H); 5.05 (quint, J = 6.88 Hz, 1H); 1.57 (bs, 9H); 1.40 (d, J = 6.88 Hz, 3H); 1.12 (d, J = 6.88 Hz, 3H)

Step VII

3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid

A solution of 3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester (37 mg, 0.08 mmol) in CH_2Cl_2 (0.2 ml) at room temperature, under nitrogen was treated with trifluoroacetic acid (0.8 ml). After 1 h the reaction was concentrated the residue was taken into EtOAc and washed sequentially with 2N HCl (2x15 ml), water, brine dried and evaporated to a foam (33 mg). The foam was redissolved in EtOAc and above acidic wash was repeated to yield 27 mg (84 %) of 3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid compound as pale brown foam. NMR ^1H : (CD_3OD; 400 MHz) 7.57-7.55 (m, 2H); 7.49-7.36 (m, 6H), 7.30-7.27 (m, 1H); 4.89 (quint, J = 6.73 Hz, 1H); 1.42 (d, J = 6.73 Hz, 3H); 1.12 (d, J = 6.73 Hz, 3H).

Example 24 The following compound was obtained from Discovery Technology:
3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid amide Compound #580

Example 25 The following compounds were obtained from Maybridge:
5-(4-Chloro-phenyl)-3-(toluene-4-sulfonylamino)-thiophene-2-carboxylic acid amide, Compound #563
5-(4-Fluoro-phenyl)-3-(toluene-4-sulfonylamino)-thiophene-2-carboxylic acid amide, Compound #564, GK 01137
5-(4-Methoxy-phenyl)-3-(toluene-4-sulfonylamino)-thiophene-2-carboxylic acid amide, Compound #565, GK 01175

Example 26 Evaluation of compounds in The HCV RNA-Dependent RNA Polymerase Assay

The following references are all incorporated by reference:
1. Behrens, S., Tomei, L., De Francesco, R. (1996) *EMBO* 15, 12-22

2. Harlow, E, and Lane, D. (1988) *Antibodies: A Laboratory Manual*. Cold Spring Harbord Laboratory. Cold Spring Harbord. NY.

3. Lohmann, V., Körner, F., Herian, U., and Bartenschlager, R. (1997) *J. Virol*. 71, 8416-8428

4. Tomei, L., Failla, C., Santolini, E., De Francesco, R., and La Monica, N. (1993) *J Virol* 67, 4017-4026

Compounds were evaluated using an *in vitro* polymerase assay containing purified recombinant HCV RNA-dependent RNA polymerase (NS5B protein). HCV NS5B was expressed in insect cells using a recombinant baculovirus as vector. The experimental procedures used for the cloning, expression and purification of the HCV NS5B protein are described below. Follows, are details of the RNA-dependent RNA polymerase assays used to test the compounds.

Expression of the HCV NS5B protein in insect cells:

The cDNA encoding the entire NS5B protein of HCV-Bk strain, genotype 1b, was amplified by PCR using the primers NS5Nhe5' (5'-GCTAGCGCTAGCTCAATGTCCTACACATGG-3') and XhoNS53' (5'-CTCGAGCTCGAGCGTCCATCGGTTGGGGAG-3') and the plasmid pCD 3.8-9.4 as template (Tomei et al, 1993). NS5Nhe5' and XhoNS53' contain two *Nhe*I and *Xho*I sites (underlined sequences), respectively, at their 5' end. The amplified DNA fragment was cloned in the bacterial expression plasmid pET-21b (Novagen) between the restriction sites *Nhe*I and *Xho*I, to generate the plasmid pET/NS5B. This plasmid was later used as template to PCR-amplify the NS5B coding region, using the primers NS5B-H9 (5'-ATACATATGGCTAGCATGTCAATGTCCTACACATGG-3') and NS5B-R4 (5'-GGATCCGGATCCCGTTCATCGGTTGGGGAG-3'). NS5B-H9 spans a region of 15 nucleotides in the plasmid pET-21b followed by the translation initiation codon (ATG) and 8 nucleotides corresponding to the 5' end of the NS5B coding region (nt. 7590-7607 in the HCV sequence with the accession number M58335). NS5B-R4 contains two *Bam*HI sites (underlined) followed by 18 nucleotides corresponding to the region around the stop codon in the HCV genome (nt. 9365-9347). The amplified sequence, of 1.8 kb, was digested with *Nhe*I and *Bam*HI and ligated to a predigested pBlueBacII plasmid (Invitrogen). The resulting recombinant plasmid was designated pBac/NS5B. Sf9 cells were

co-transfected with 3 µg of pBac/NS5B, together with 1 µg of linearized baculovirus DNA (Invitrogen), as described in the manufacturer's protocol. Following two rounds of plaque purification, an NS5B-recombinant baculovirus, BacNS5B, was isolated. The presence of the recombinant NS5B protein was determined by western blot analysis (Harlow and Lane, 1988) of BacNS5B-infected Sf9 cells, using a rabbit polyclonal antiserum (anti-NS5B) raised against a His-tagged version of the NS5B protein expressed in *E. coli*. Infections of Sf9 cells with this plaque purified virus were performed in one-liter spinner flasks at a cell density of 1.2 x 10^6 cells/ml and a multiplicity of infection of 5.

Preparation of a soluble recombinant NS5B protein

Sf9 cells were infected as described above. Sixty hours post-infection, cells were harvested then washed twice with phosphate buffer saline (PBS). Total proteins were solubilized as described in Lohmann *et al.* (1997) with some modifications. In brief, proteins were extracted in three steps, S1, S2, S3, using lysis buffers (LB) I, LB II and LB III (Lohmann et al, 1997). The composition of LBII was modified to contain 0.1 % triton X-100 and 150 mM NaCl to reduce the amount of solubilized NS5B protein at this step. In addition, sonication of cell extracts was avoided throughout the protocol to preserve the integrity of the protein structure.

Purification of recombinant NS5B using fast protein liquid chromatography (FPLC):

Soluble NS5B protein in the S3 fraction was diluted to lower the NaCl concentration to 300 mM, then it incubated batchwise with DEAE sepharose beads (Amersham-Pharmacia) for 2 hrs at 4°C, as described by Behrens et al. (1996). Unbound material was cleared by centrifugation for 15 min at 4°C, at 25 000 rpm using a SW41 rotor (Beckman). The supernatant was further diluted to lower the NaCl concentration to 200 mM and subsequently loaded, with a flow rate of 1 ml/min, on a 5 ml HiTrap® heparin column (Amersham-Pharmacia) connected to an FPLC® system (Amersham-Pharmacia). Bound proteins were eluted in 1 ml fractions, using a continuous NaCl gradient of 0.2 to 1 M, over a 25 ml volume.

NS5B-containing fractions were identified by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), followed by western blotting using the anti-NS5B antiserum at a dilution of 1:2000. Positive fractions were pooled and the elution buffer was exchanged against a 50 mM $NaPO_4$ pH 7.0, 20 % glycerol, 0.5 % triton X-100 and 10 mM DTT, using a PD-10 column (Amersham-Pharmacia). The sample was then loaded onto a 1 ml HiTrap® SP column (Amersham-Pharmacia), with a flow rate of 0.1 ml/min. Bound proteins were eluted using a continuous 0 to 1 M NaCl gradient over a 15 ml volume. Eluted fractions were analyzed by SDS-PAGE and western blotting. Alternatively, proteins were visualized, following SDS-PAGE, by silver staining using the Silver Stain Plus kit (BioRad) as described by the manufacturer. Positive fractions were tested for RdRp activity (see below) and the most active ones were pooled, and stored as a 40 % glycerol solution at -70°C.

<u>In vitro HCV RdRp Flashplate scintillation proximity assay (STREP-FLASH ASSAY) used to evaluate analogues:</u>

This assay consists on measuring the incorporation of [^{3}H] radiolabelled UTP in a polyrA/ biotinylated-oligo dT template-primer, captured on the surface of streptavidin-coated scintillant-embeded microtiter Flashplates™ (NEN Life Science Products inc, MA, USA, SMP 103A). In brief, a 400 ng/µl polyrA solution (Amersham Pharmacia Biotech) was mixed volume-to-volume with 5' biotin-oligo dT_{15} at 20 pmol/µl. The template and primers were denatured at 95 C for 5 minutes then incubated at 37 C for 10 minutes. Annealed template-primers were subsequently diluted in a Tris-HCl containing buffer and allowed to bind to streptavidin-coated flashplates overnight. Unbound material was discarded, compounds were added in a 10 µl solution followed by a 10 µl of a solution containing 50 mM $MgCl_2$, 100 mM Tris-HCl pH 7.5, 250 mM NaCl and 5 mM DTT. The enzymatic reaction was initiated upon addition of a 30 µl solution containing the enzyme and substrate to obtain the following concentrations: 25 µM UTP, 1 µCi [^{3}H] UTP and 100 nM recombinant HCV NS5B. RdRp reactions were allowed to proceed for 2 hrs at room temperature after which wells were washed three times with a 250µL of 0.15 M NaCl solution, air dried at 37 C, and counted

using a liquid scintillation counter (Wallac Microbeta Trilex, Perkin-Elmer, MA, USA). Results are shown in Table 1.

In vitro HCV RdRp filtration assay used to evaluate analogues

RdRp assays were conducted using the homopolymeric template/primer polyA/oligo dT. All RdRp reactions were performed in a total volume of 50 µl, and in a basic buffer consisting of 20 mM Tris-HCl pH 7.5, 1mM DTT, 50 mM NaCl, 5 mM $MgCl_2$, 0.5 µCi [γ^{32}P]-UTP (3000 Ci/mmol), 15 µM cold UTP and 20 U RNasin (Promega). Standard HCV RdRp reactions contained 200 ng of purified NS5B protein. PolyA RNAs (Amersham-Pharmacia) was resuspended at 400 ng/µl. The primer oligodT_{15} (Canadian life technologies) was diluted to a concentration of 20 pmol/µl (7.6 ng/ml). Templates and primers were mixed volume to volume, denatured at 95°C for 5 min and annealed at 37°C for 10 min. Following a two hour incubation at 22°C, reactions were stopped by the addition of 100 µg of sonicated salmon sperm DNA (Life Technologies) and 1 ml of 10 % trichloroacetic acid-0.5 % tetrasodium pyrophosphate (TCA-PPi). Nucleic acids were precipitated at 4°C for 30 min after which samples were filtered on GF/C glass microfiber filters (Millipore). Membranes were subsequently washed with 25 ml of a 1% TCA-0.1 % PPi solution, then air dried. Incorporated radioactivity was quantified using a liquid scintillation counter (1450-Microbeta, Wallac). Results are shown in Table 1.

Example 27 Evaluation of Analogues for measurement of ATPase activity of HCV NS3 helicase

Malachite Green Assay:

The measurement of ATPase activity was performed by measuring the amount of free inorganic phosphate released during the conversion of ATP to ADP by the HCV NS3 ATPase activity. The assay is as follows: In a 96-well microtiter-plate, compounds were dissolved at various concentrations in a final volume of 25 µL of ATPase buffer containing 400 µM ATP. The enzymatic

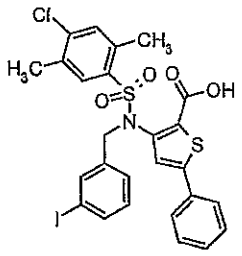
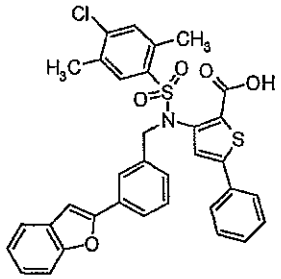
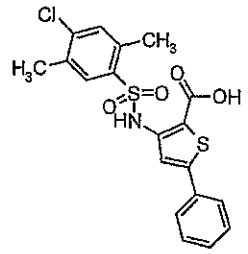
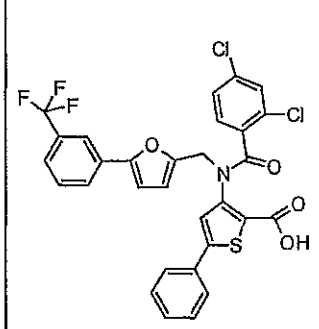
reaction was initiated by the addition of 25 µl of ATPase buffer containing 6 nM of HCV NS3 enzyme without ATP to the wells followed by an incubation of 30 min. at 37 C. Essentially, the final concentration of the ATPase buffer components are as follows: 44 mM MOPS pH 7.0, 8.8 mM NaCl, 2.2 mM $MgCl_2$, 125 µg/ml poly A, 1% DMSO, 200 µM ATP, and 3 nM HCV NS3 enzyme. The reaction was stopped by the addition of 100 µl of Biomol Green™ reagent (BIOMOL® Research Laboratories Inc., Plymouth Meeting, PA). In order to allow the development of the green color, the plate was incubated for 15 min. at room temperature. Then the plate was read on a micro-plate reader at 620 nm. The 50% inhibitory concentration (IC_{50}) for anti-ATPase activity was defined as the concentration of compound that resulted in a 50 % reduction of the signal compared to the signal observed in control sample without compound. The signal recorded was also corrected from the background signal obtained with control samples with compound only. The IC_{50} was determined from dose-response curves using six to eight concentrations per compound. Curves were fitted to data points using a non-linear regression analysis, and IC_{50}s were interpolated from the resulting curves using GraphPad Prism software, version 2.0 (GraphPad Software Inc, San Diego, CA).

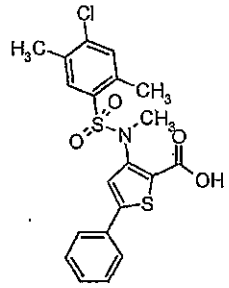
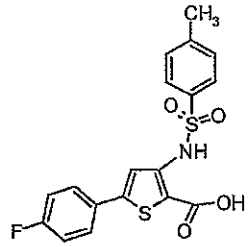
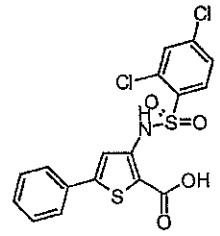
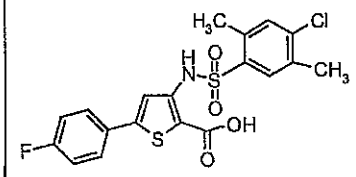
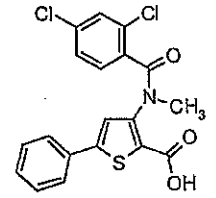
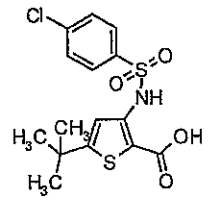
HPLC Assay:

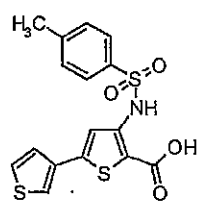
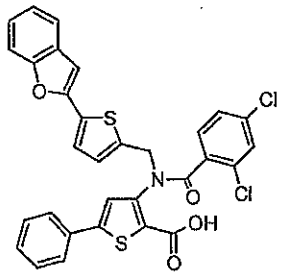
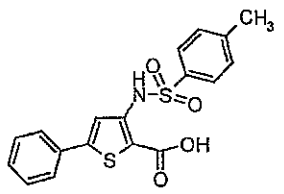
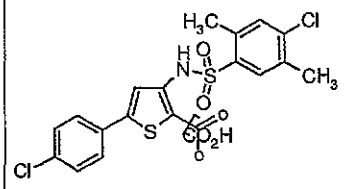
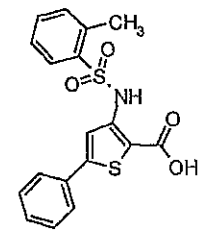
The measurement of HCV NS3 ATPase activity was performed by measuring the amount of ADP produced during the conversion of ATP to ADP by the HCV NS3 enzyme using paired-ion HPLC on a reverse phase column. The assay is as follows: The same protocol as mentioned above was used except that the final concentration of HCV NS3 enzyme was reduced to 1 nM in a 50 µl reaction mixture and that the ATPase reaction was stopped by the addition of 12.5 µl of 0.5 M EDTA. A modular liquid chromatography system (TSP Spectrasystem®, ThermoQuest Corporation, San Diego, USA) using a ChromQuest™ software (ThermoQuest Corporation, San Diego, USA) controlled the autosampling of 25 µl from each reaction. The mobile phase was

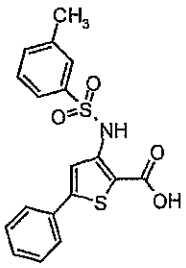
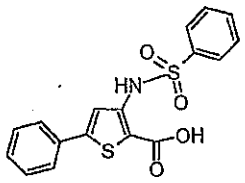
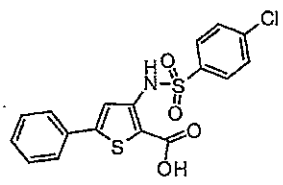
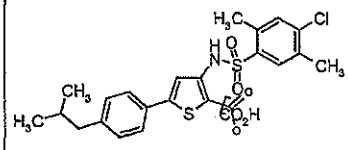
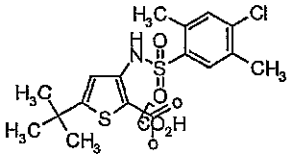
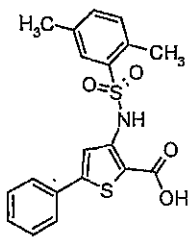
an isocratic solution of 0.15 M triethylamine, 6% methanol, and phosphoric acid to pH 5.5. ADP and ATP peaks were resolved using the Aqua 5 μ, C18, 125 Å, (150 X 4.6 mm) reverse phase column. The extent of ATP conversion to ADP was evaluated by measuring the area under the ADP peak produced which was detected at 259 nm. The amount of ADP was corrected for the presence of ADP contaminant in the original ATP solution. The 50% inhibitory concentration (IC_{50}) for anti-ATPase activity was defined as the concentration of compound that resulted in a 50 % reduction of the ADP peak area compared to the ADP peak area observed in control sample without compound. The IC_{50} was determined from dose-response curves using six to eight concentrations per compound. Curves were fitted to data points using a non-linear regression analysis, and IC_{50}s were interpolated from the resulting curves using GraphPad Prism software, version 2.0 (GraphPad Software Inc, San Diego, CA).

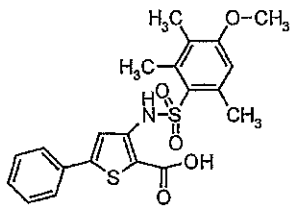
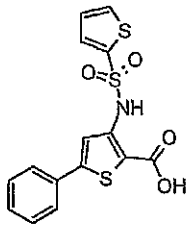
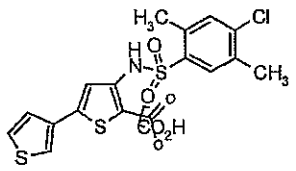
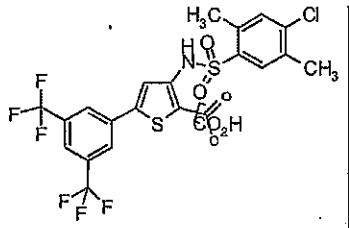
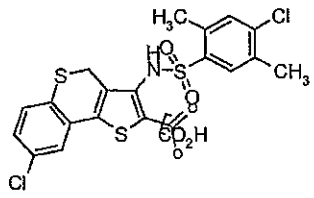
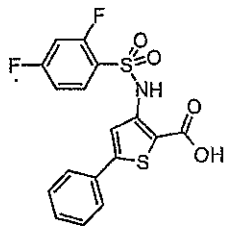
EXAMPLE 27 List of compounds and related polymerase activity *

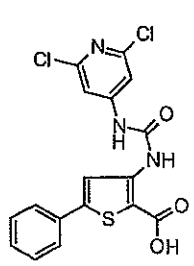
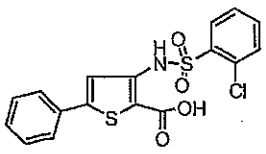
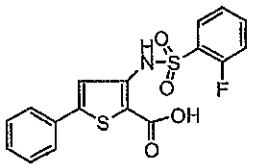
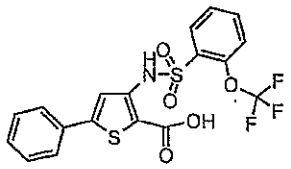
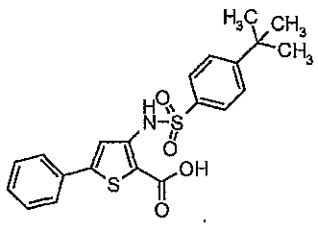
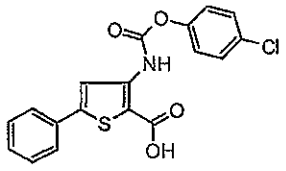
	MOLSTRUCTURE	COMPOUND NAME	IC50
1		3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-(3-IODO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
2		3-[(3-BENZOFURAN-2-YL-BENZYL)-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
3		3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
4		3-{(2,4-DICHLORO-BENZOYL)-[5-(3-TRIFLUOROMETHYL-PHENYL)-FURAN-2-YLMETHYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

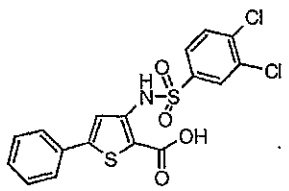
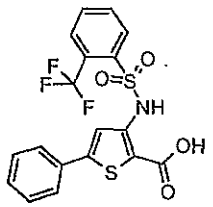
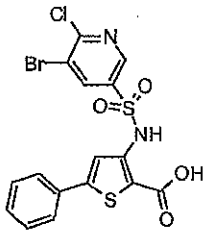
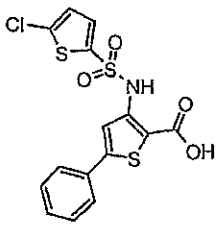
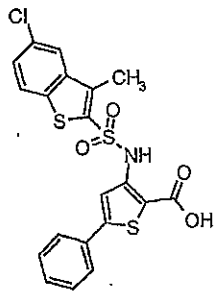
	MOLSTRUCTURE	COMPOUND NAME	IC50
5		3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
6		5-(4-FLUORO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
7		3-(2,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
8		3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
9		3-[(2,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
10		5-#TERT!-BUTYL-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

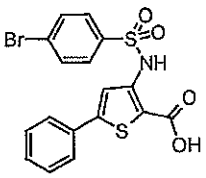
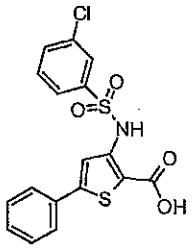
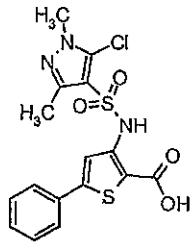
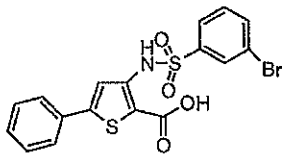
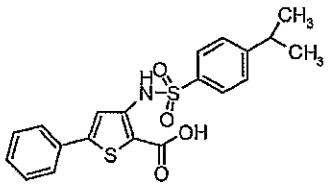
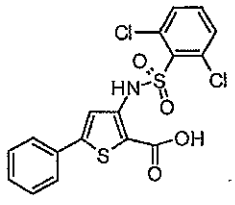
	MOLSTRUCTURE	COMPOUND NAME	IC50
11		4-(TOLUENE-4-SULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID	++
12		3-[(5-BENZOFURAN-2-YL-THIOPHEN-2-YLMETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
13		5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
14		3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-CHLORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
15		5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+

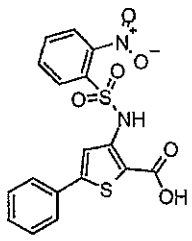
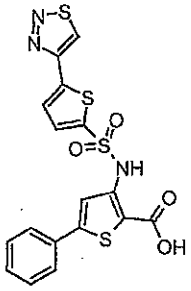
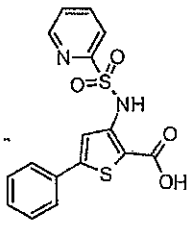
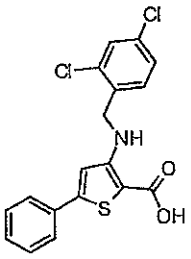
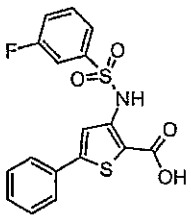
	MOLSTRUCTURE	COMPOUND NAME	IC50
16		5-PHENYL-3-(TOLUENE-3-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
17		3-BENZENESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
18		3-(4-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
19		3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	++
20		5-TERT-BUTYL-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
21		3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

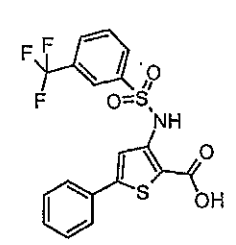
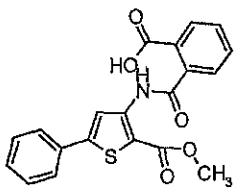
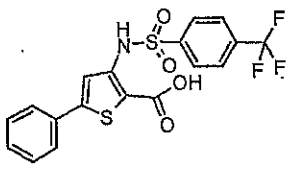
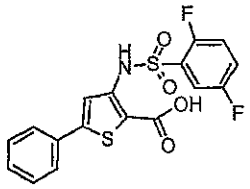
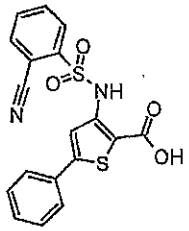
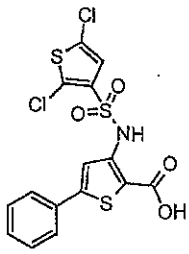
	MOLSTRUCTURE	COMPOUND NAME	IC50
22		3-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
23		5-PHENYL-3-(THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
24		4-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
25		5-(3,5-BIS-TRIFLUOROMETHYL-PHENYL)-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+
26		8-CHLORO-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-4#H!-1,5-DITHIA-CYCLOPENTA[#A!]NAPHTHALENE-2-CARBOXYLIC ACID	++
27		3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

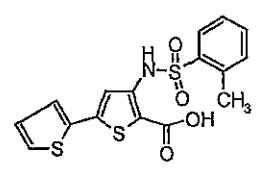
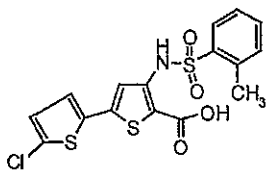
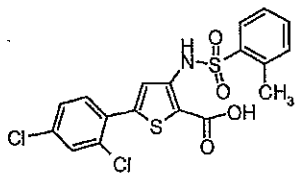
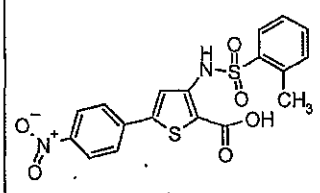
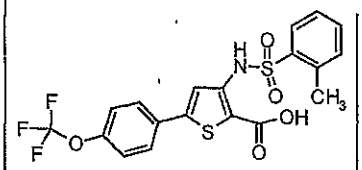
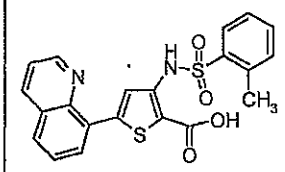
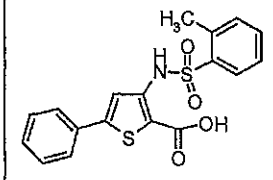
	MOLSTRUCTURE	COMPOUND NAME	IC50
28		3-[3-(2,6-DICHLORO-PYRIDIN-4-YL)-UREIDO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
29		3-(2-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
30		3-(2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
31		5-PHENYL-3-(2-TRIFLUOROMETHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+
32		3-(4-#TERT!-BUTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
33		3-(4-CHLORO-PHENOXYCARBONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

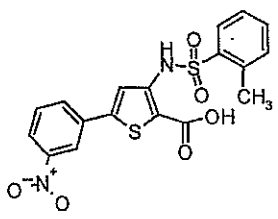
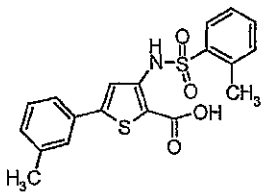
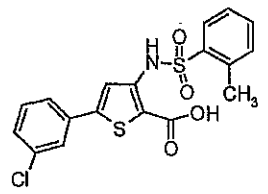
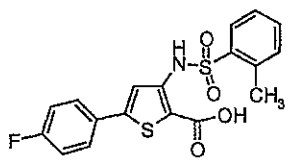
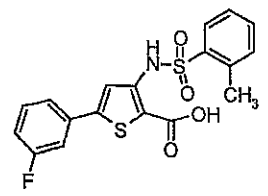
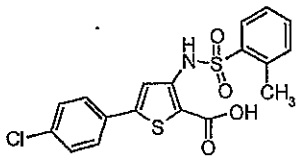
	MOLSTRUCTURE	COMPOUND NAME	IC50
34		3-(3,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
35		5-PHENYL-3-(2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+
36		3-(5-BROMO-6-CHLORO-PYRIDINE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
37		3-(5-CHLORO-THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
38		3-(5-CHLORO-3-METHYL-BENZO[#B!]THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

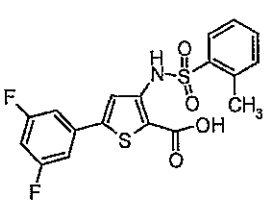
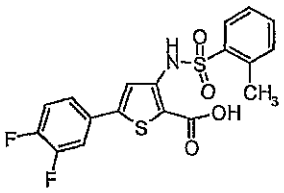
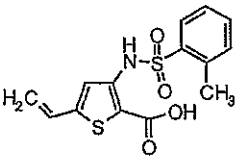
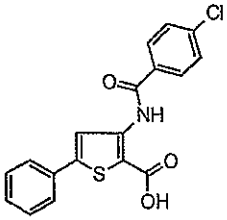
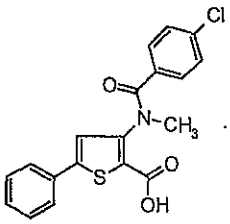
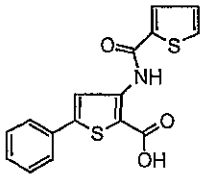
	MOLSTRUCTURE	COMPOUND NAME	IC50
39		3-(4-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
40		3-(3-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
41		3-(5-CHLORO-1,3-DIMETHYL-1#H!-PYRAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
42		3-(3-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
43		3-(4-ISOPROPYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
44		3-(2,6-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

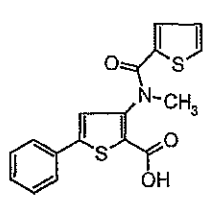
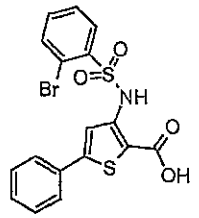
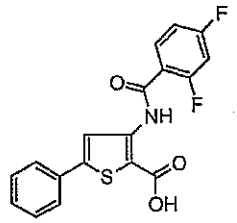
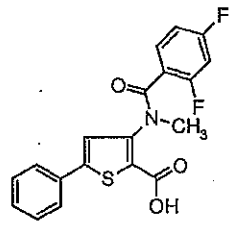
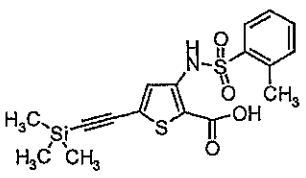
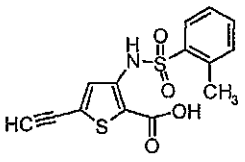
	MOLSTRUCTURE	COMPOUND NAME	IC50
45		3-(2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
46		5-PHENYL-3-(5-[1,2,3]THIADIAZOL-4-YL-THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
47		5-PHENYL-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+
48		3-(2,4-DICHLORO-BENZYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
49		3-(3-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

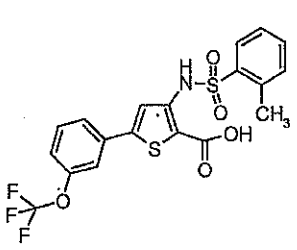
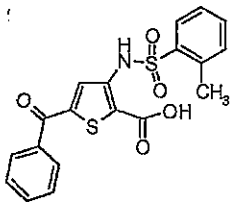
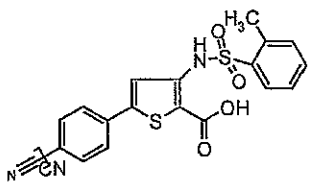
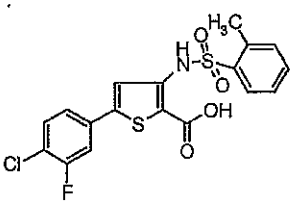
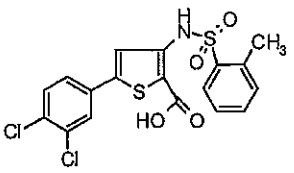
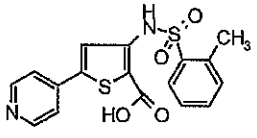
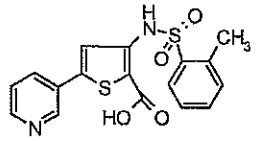
	MOLSTRUCTURE	COMPOUND NAME	IC50
50		5-PHENYL-3-(3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
51		3-(2-CARBOXY-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER	++
52		5-PHENYL-3-(4-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
53		3-(2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
54		3-(2-CYANO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
55		3-(2,5-DICHLORO-THIOPHENE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

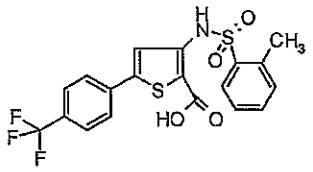
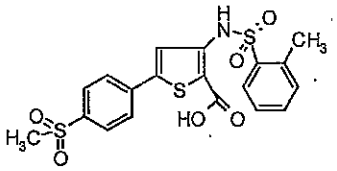
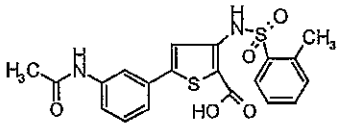
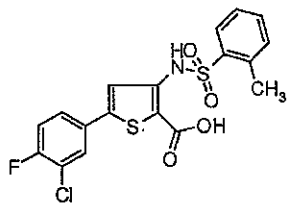
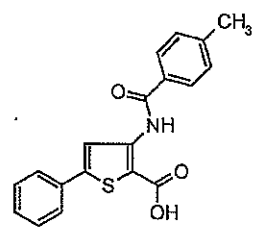
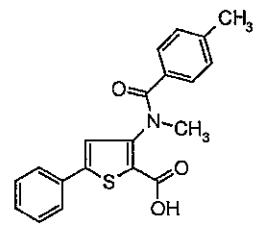
	MOLSTRUCTURE	COMPOUND NAME	IC50
56		4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
57		5'-CHLORO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
58		5-(2,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
59		5-(4-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
60		3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
61		5-QUINOLIN-8-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+
62		5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

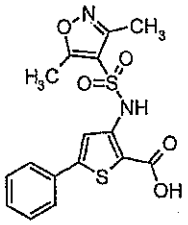
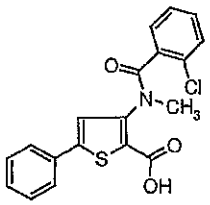
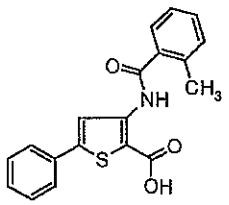
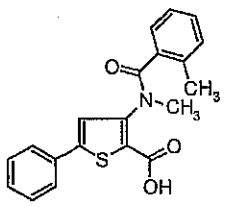
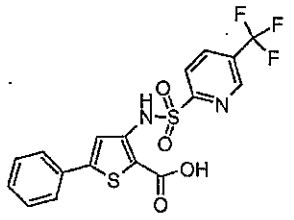
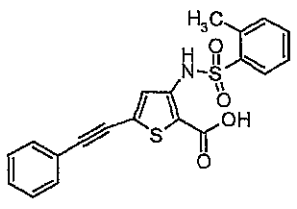
	MOLSTRUCTURE	COMPOUND NAME	IC50
63		5-(3-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
64		3-(TOLUENE-2-SULFONYLAMINO)-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
65		5-(3-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
66		5-(4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
67		5-(3-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
68		5-(4-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

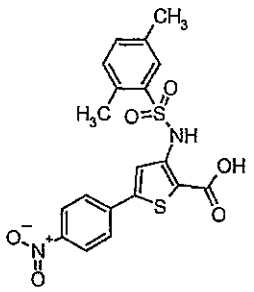
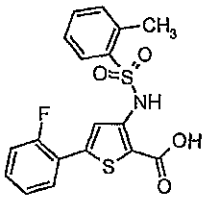
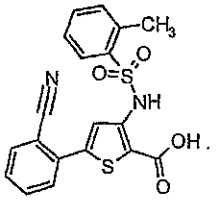
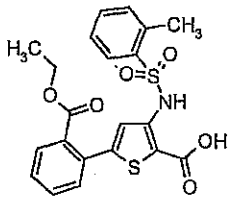
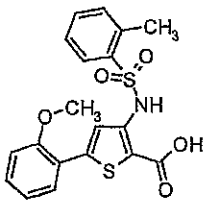
	MOLSTRUCTURE	COMPOUND NAME	IC50
69		5-(3,5-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
70		5-(3,4-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
71		3-(TOLUENE-2-SULFONYLAMINO)-5-VINYL-THIOPHENE-2-CARBOXYLIC ACID	++
72		3-(4-CHLORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
73		3-[(4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
74		5-PHENYL-3-[(THIOPHENE-2-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++

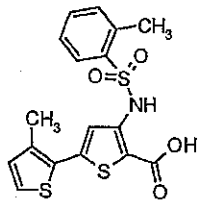
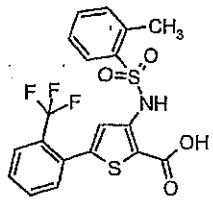
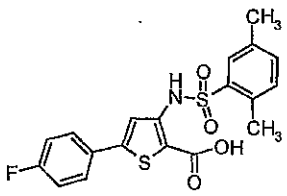
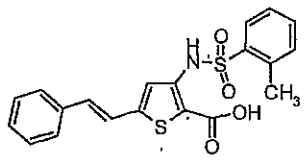
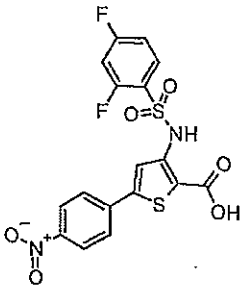
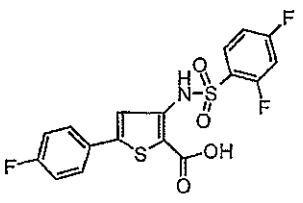
	MOLSTRUCTURE	COMPOUND NAME	IC50
75		3-[METHYL-(THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
76		3-(2-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
77		3-(2,4-DIFLUORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
78		3-[(2,4-DIFLUORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
79		3-(TOLUENE-2-SULFONYLAMINO)-5-TRIMETHYLSILANYLETHYNYL-THIOPHENE-2-CARBOXYLIC ACID	+++
80		5-ETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++

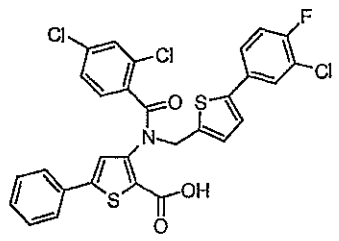
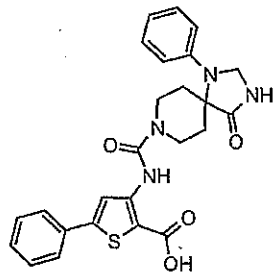
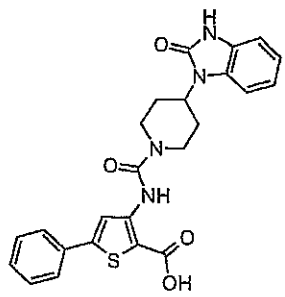
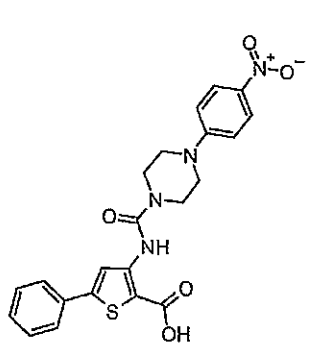
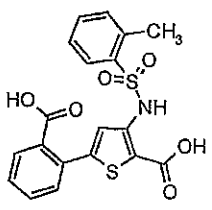
	MOLSTRUCTURE	COMPOUND NAME	IC50
81		3-(TOLUENE-2-SULFONYLAMINO)-5-(3-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	++
82		5-BENZOYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
83		5-(4-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
84		5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
85		5-(3,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
86		5-PYRIDIN-4-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
87		5-PYRIDIN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

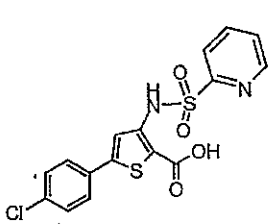
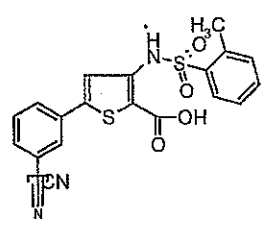
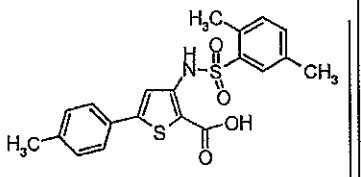
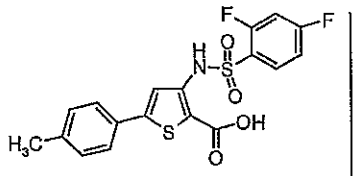
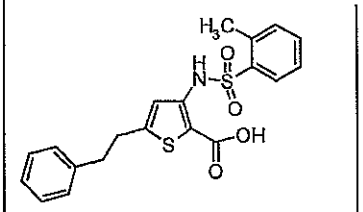
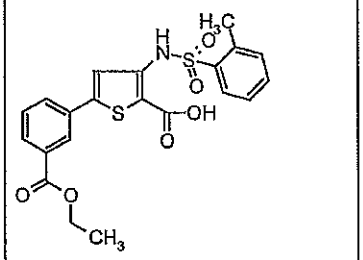
	MOLSTRUCTURE	COMPOUND NAME	IC50
88		3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
89		5-(4-METHANESULFONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
90		5-(3-ACETYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
91		5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
92		3-(4-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
93		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

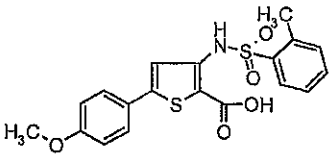
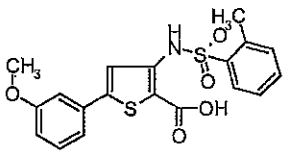
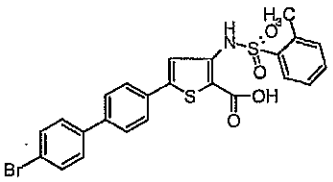
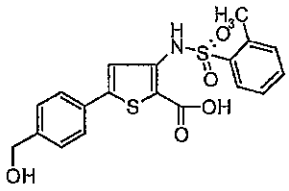
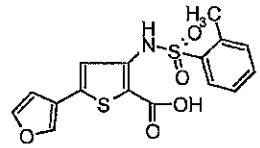
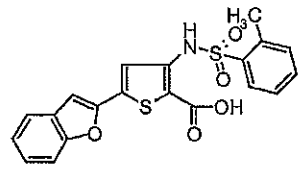
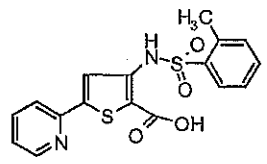
	MOLSTRUCTURE	COMPOUND NAME	IC50
94		3-(3,5-DIMETHYL-ISOXAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
95		3-[(2-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
96		3-(2-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
97		3-[METHYL-(2-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
98		5-PHENYL-3-(5-TRIFLUOROMETHYL-PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
99		5-PHENYLETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

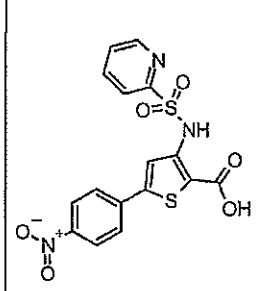
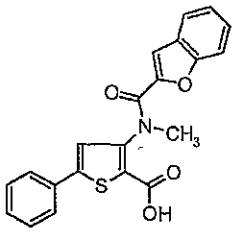
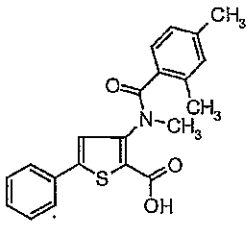
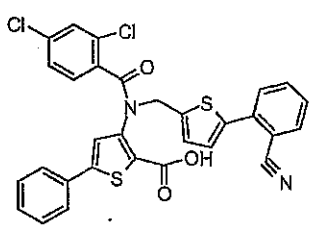
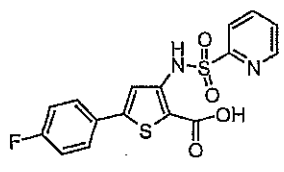
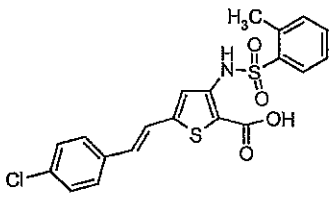
	MOLSTRUCTURE	COMPOUND NAME	IC50
100		3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
101		5-(2-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
102		5-(2-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
103		5-(2-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
104		5-(2-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++

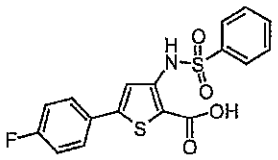
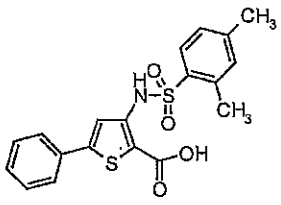
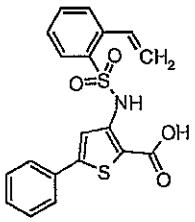
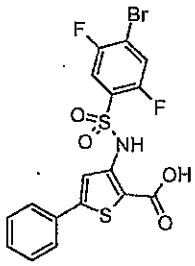
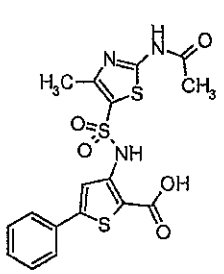
	MOLSTRUCTURE	COMPOUND NAME	IC50
105		3'-METHYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	++
106		3-(TOLUENE-2-SULFONYLAMINO)-5-(2-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	++
107		3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
108		5-STYRYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
109		3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
110		3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++

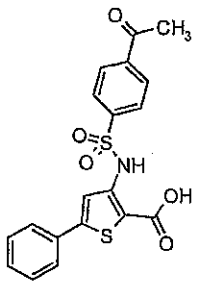
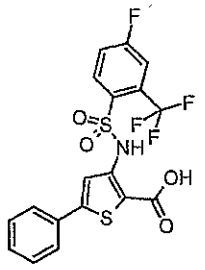
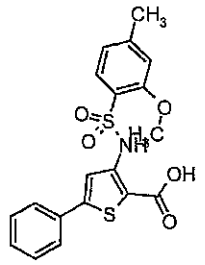
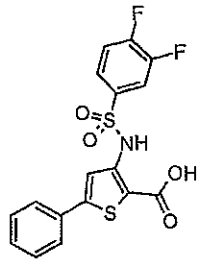
	MOLSTRUCTURE	COMPOUND NAME	IC50
111		3-[[5-(3-CHLORO-4-FLUORO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
112		3-[(4-OXO-1-PHENYL-1,3,8-TRIAZA-SPIRO[4.5]DECANE-8-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
113		3-{[4-(2-OXO-2,3-DIHYDRO-BENZOIMIDAZOL-1-YL)-PIPERIDINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
114		3-{[4-(4-NITRO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
115		5-(2-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++

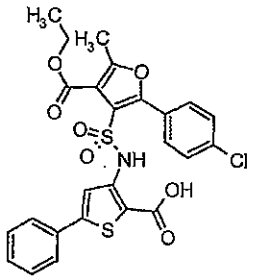
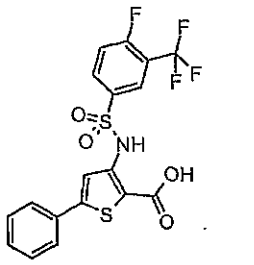
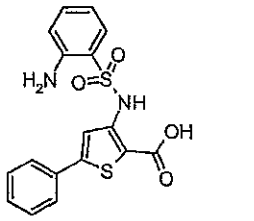
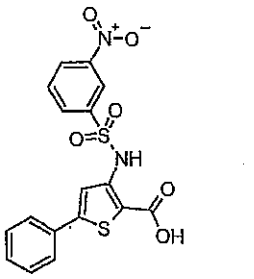
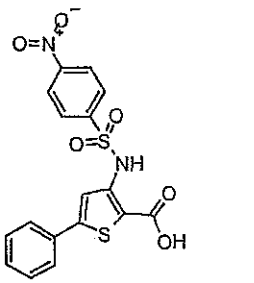
	MOLSTRUCTURE	COMPOUND NAME	IC50
116		5-(4-CHLORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
117		5-(3-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
118		3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
119		3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
120		5-PHENETHYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
121		5-(3-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++

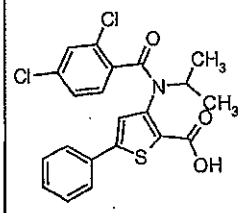
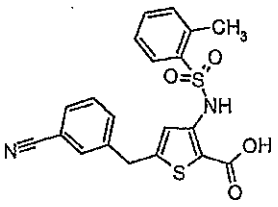
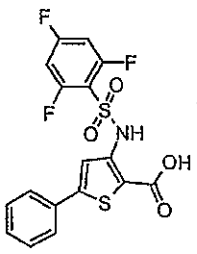
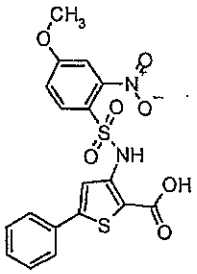
	MOLSTRUCTURE	COMPOUND NAME	IC50
122		5-(4-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
123		5-(3-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
124		5-(4'-BROMO-BIPHENYL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
125		5-(4-HYDROXYMETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
126		5-FURAN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
127		5-BENZOFURAN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
128		5-PYRIDIN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

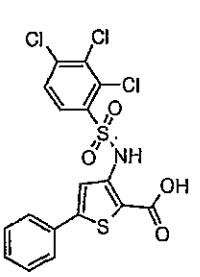
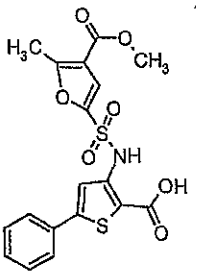
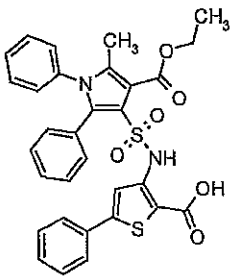
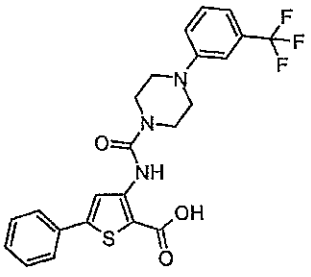
	MOLSTRUCTURE	COMPOUND NAME	IC50
129		5-(4-NITRO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
130		3-[(BENZOFURAN-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
131		3-[(2,4-DIMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
132		3-[[5-(2-CYANO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
133		5-(4-FLUORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
134		5-[2-(4-CHLORO-PHENYL)-VINYL]-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++

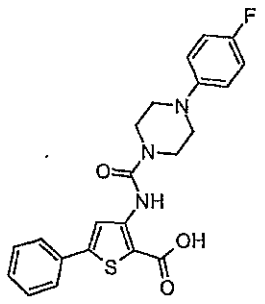
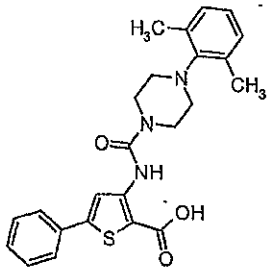
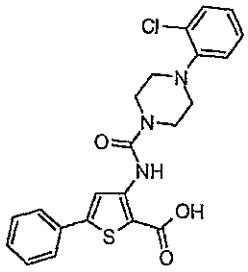
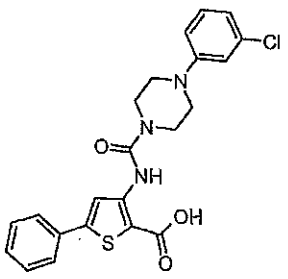
	MOLSTRUCTURE	COMPOUND NAME	IC50
135		3-BENZENESULFONYLAMINO-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
136		3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
137		5-PHENYL-3-(2-VINYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
138		3-(4-BROMO-2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
139		3-(2-ACETYLAMINO-4-METHYL-THIAZOLE-5-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

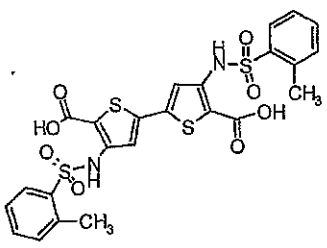
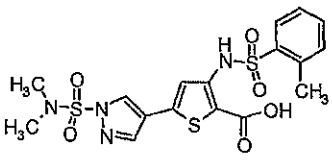
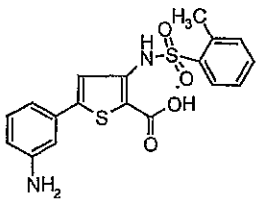
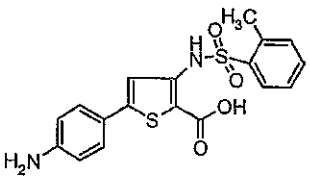
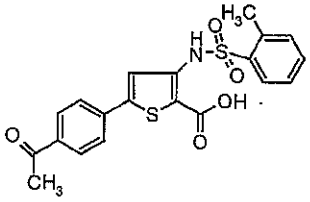
	MOLSTRUCTURE	COMPOUND NAME	IC50
140		3-(4-ACETYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
141		3-(4-FLUORO-2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
142		3-(2-METHOXY-4-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
143		3-(3,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

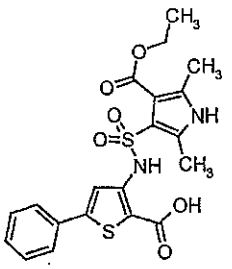
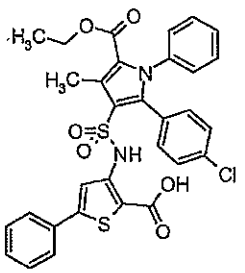
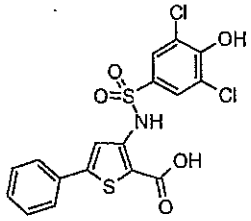
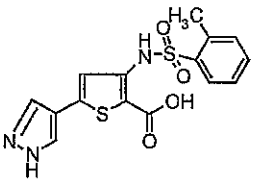
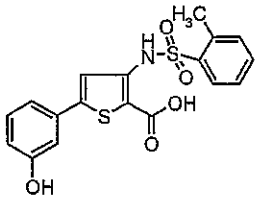
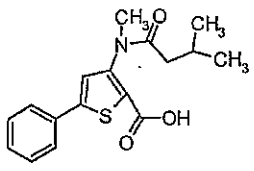
	MOLSTRUCTURE	COMPOUND NAME	IC50
144		4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID ETHYL ESTER	++
145		3-(4-FLUORO-3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
146		3-(2-AMINO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
147		3-(3-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
148		3-(4-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

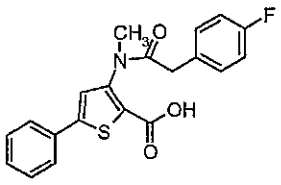
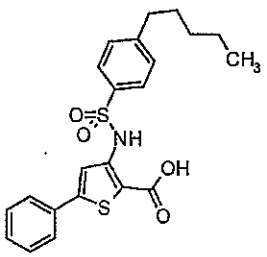
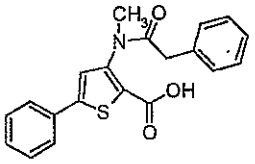
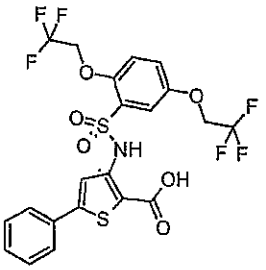
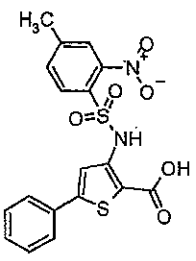
	MOLSTRUCTURE	COMPOUND NAME	IC50
149		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
150		5-(3-CYANO-BENZYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+
151		5-PHENYL-3-(2,4,6-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
152		3-(4-METHOXY-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

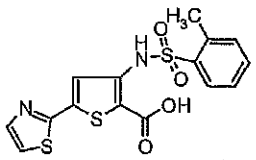
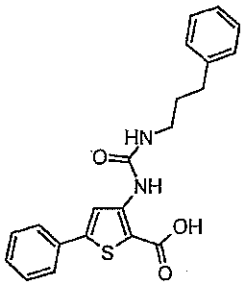
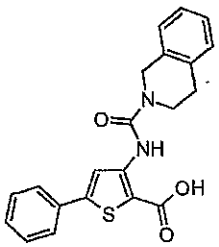
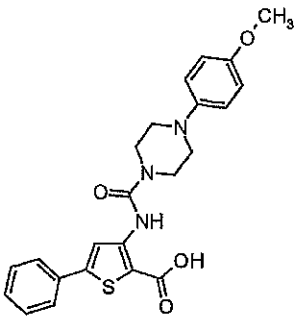
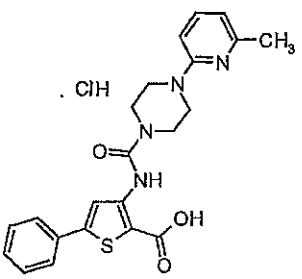
	MOLSTRUCTURE	COMPOUND NAME	IC50
153		5-PHENYL-3-(2,3,4-TRICHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
154		5-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID METHYL ESTER	+++
155		4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-1,5-DIPHENYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER	+++
156		5-PHENYL-3-{[4-(3-TRIFLUOROMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMIN}-THIOPHENE-2-CARBOXYLIC ACID	++

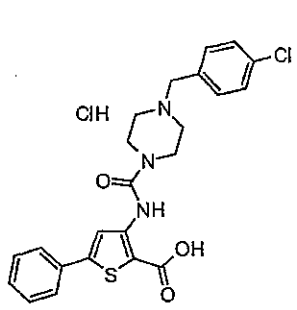
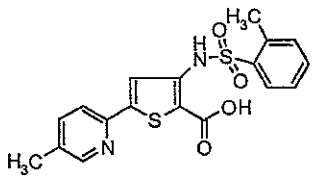
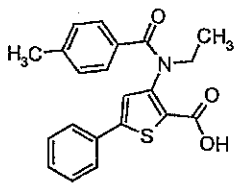
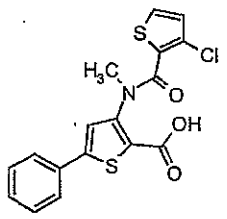
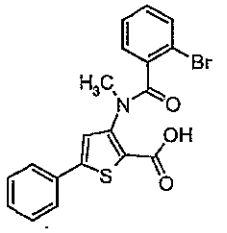
	MOLSTRUCTURE	COMPOUND NAME	IC50
157		3-{[4-(4-FLUORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
158		3-{[4-(2,6-DIMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
159		3-{[4-(2-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
160		3-{[4-(3-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

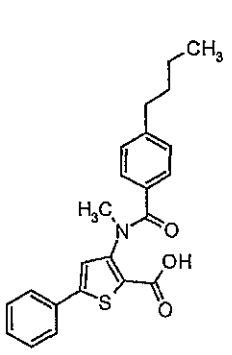
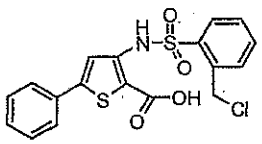
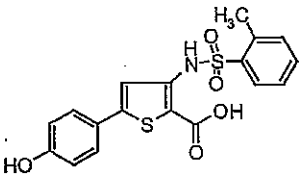
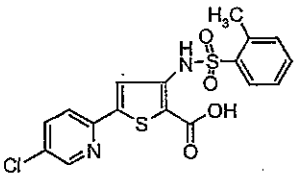
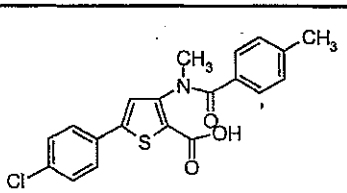
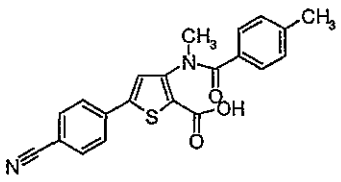
	MOLSTRUCTURE	COMPOUND NAME	IC50
161		4,4'-BIS-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5,5'-DICARBOXYLIC ACID	+++
162		3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
163		5-(1-DIMETHYLSULFAMOYL-1#H!-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
164		5-(3-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
165		5-(4-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
166		5-(4-ACETYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

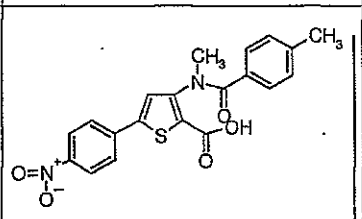
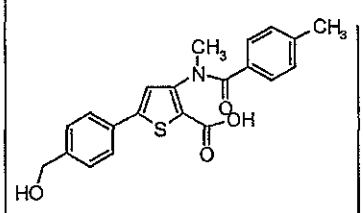
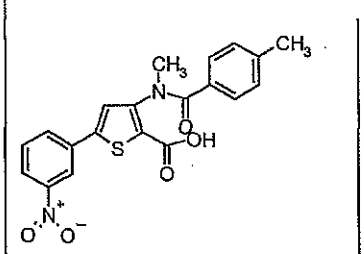
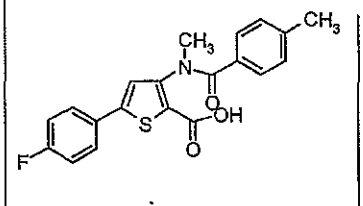
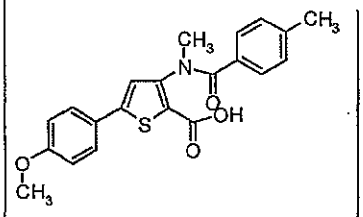
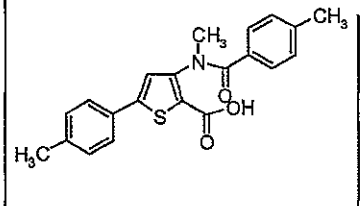
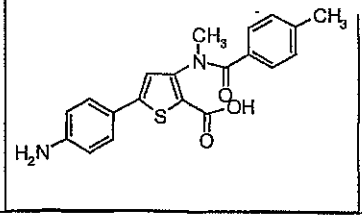
	MOLSTRUCTURE	COMPOUND NAME	IC50
167		4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2,5-DIMETHYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER	++
168		4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-3-METHYL-1-PHENYL-1H-PYRROLE-2-CARBOXYLIC ACID ETHYL ESTER	++
169		3-(3,5-DICHLORO-4-HYDROXY-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
170		5-(1#H!-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
171		5-(3-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
172		3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

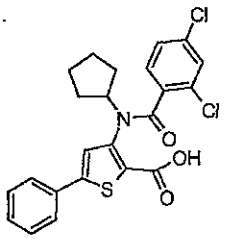
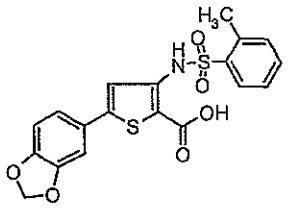
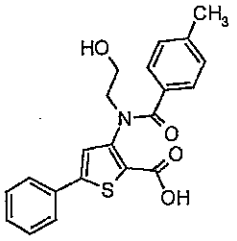
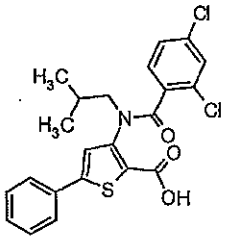
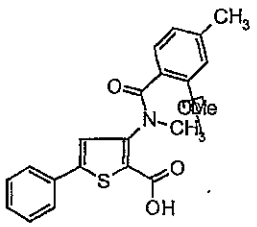
	MOLSTRUCTURE	COMPOUND NAME	IC50
173		3-{[2-(4-FLUORO-PHENYL)-ACETYL]-METHYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
174		3-(4-PENTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
175		3-(METHYL-PHENYLACETYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
176		3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
177		3-(4-METHYL-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

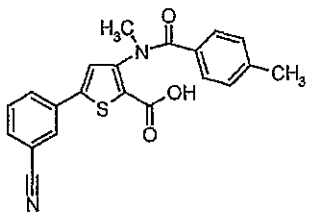
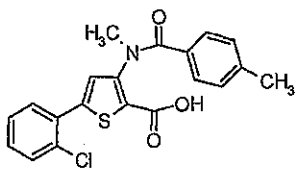
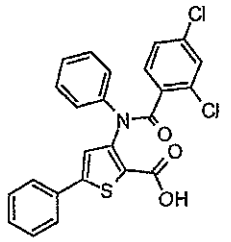
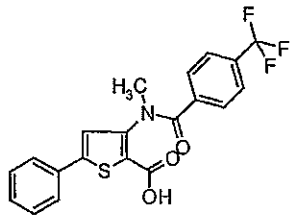
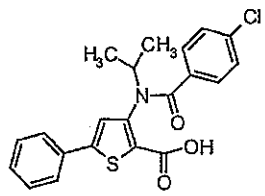
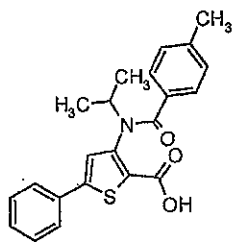
	MOLSTRUCTURE	COMPOUND NAME	IC50
178		5-THIAZOL-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
179		5-PHENYL-3-[3-(3-PHENYL-PROPYL)-UREIDO]-THIOPHENE-2-CARBOXYLIC ACID	++
180		3-[(3,4-DIHYDRO-1H-ISOQUINOLINE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
181		3-{[4-(4-METHOXY-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
182		3-{[4-(6-METHYL-PYRIDIN-2-YL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE	++

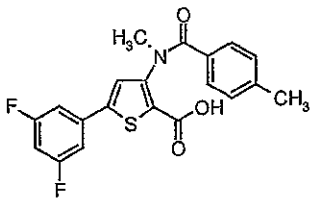
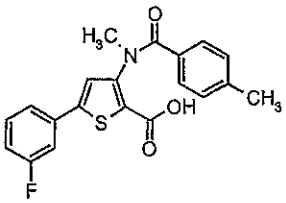
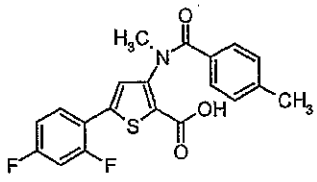
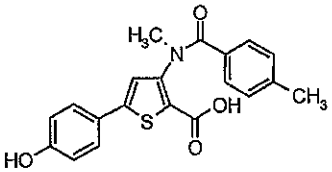
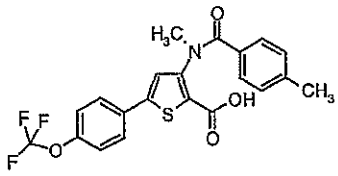
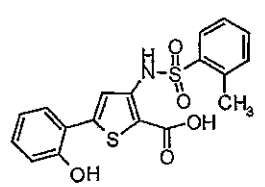
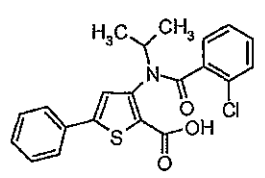
	MOLSTRUCTURE	COMPOUND NAME	IC50
183		3-{[4-(4-CHLORO-BENZYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE	++
184		5-(5-METHYL-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
185		3-[ETHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
186		3-[(3-CHLORO-THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
187		3-[(2-BROMO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

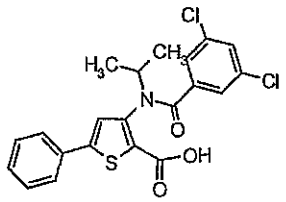
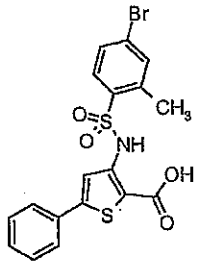
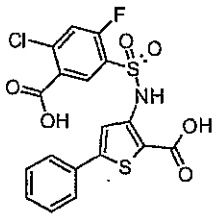
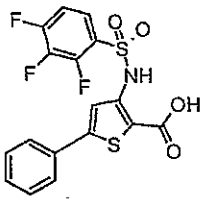
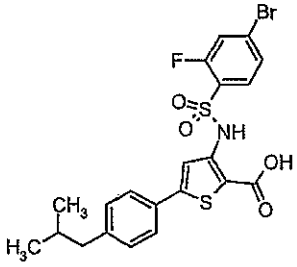
	MOLSTRUCTURE	COMPOUND NAME	IC50
188		3-[(4-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
189		3-(2-CHLOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
190		5-(4-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
191		5-(5-CHLORO-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
192		5-(4-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++
193		5-(4-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++

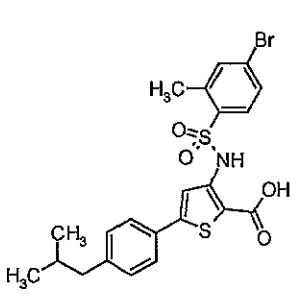
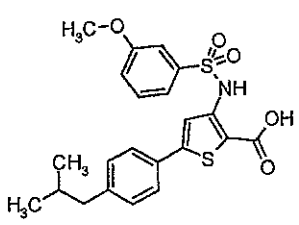
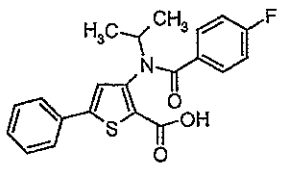
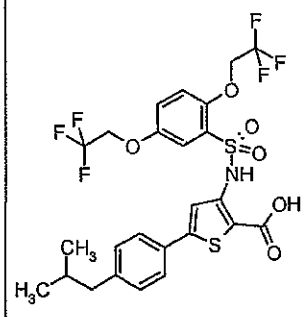
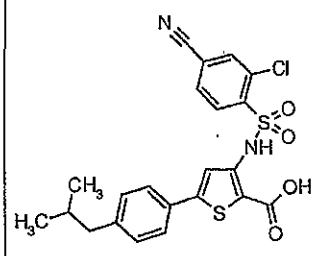
	MOLSTRUCTURE	COMPOUND NAME	IC50
194		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	++
195		5-(4-HYDROXYMETHYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++
196		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
197		5-(4-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
198		5-(4-METHOXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++
199		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-#P!-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	++
200		5-(4-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++

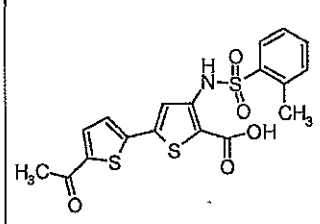
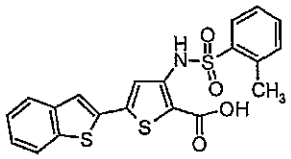
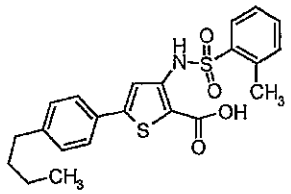
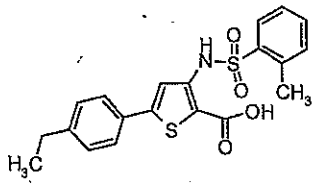
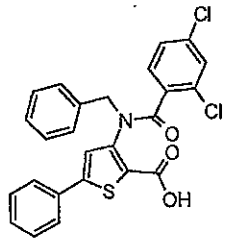
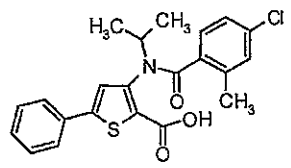
	MOLSTRUCTURE	COMPOUND NAME	IC50
201		3-[CYCLOPENTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
202		5-BENZO[1,3]DIOXOL-5-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
203		3-[(2-HYDROXY-ETHYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
204		3-[(2,4-DICHLORO-BENZOYL)-ISOBUTYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
205		3-[(2-METHOXY-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

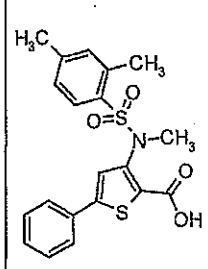
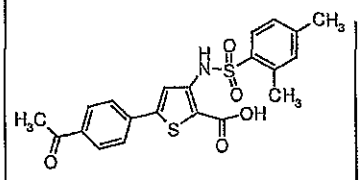
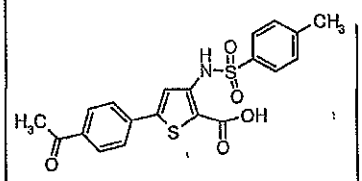
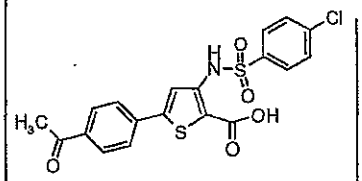
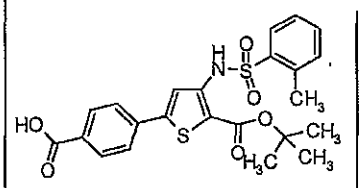
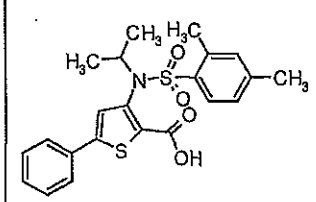
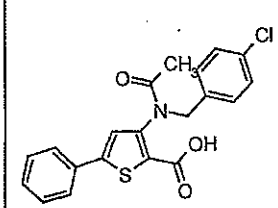
	MOLSTRUCTURE	COMPOUND NAME	IC50
206		5-(3-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
207		5-(2-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++
208		3-[(2,4-DICHLORO-BENZOYL)-PHENYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
209		3-[4-(TRIFLUOROMETHYL-BENZOYL)METHYLAMINE]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
210		3-[(4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
211		3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

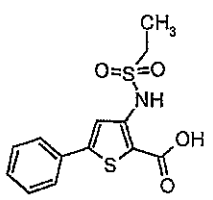
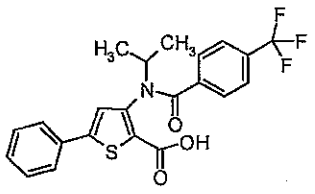
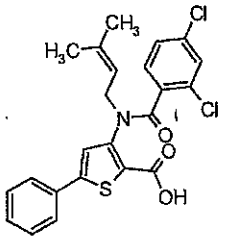
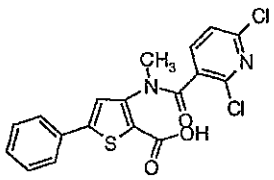
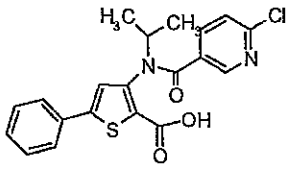
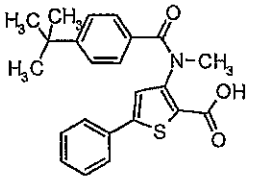
	MOLSTRUCTURE	COMPOUND NAME	IC50
212		5-(3,5-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
213		5-(3-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
214		5-(2,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++
215		5-(4-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
216		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	++
217		5-(2-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
218		3-[(2-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

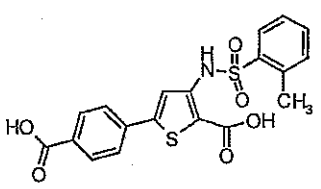
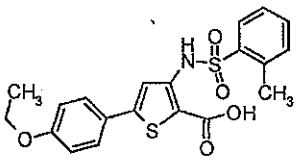
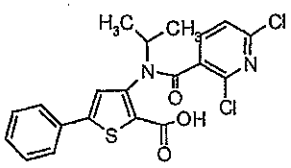
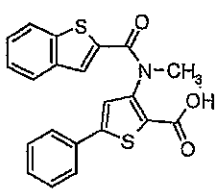
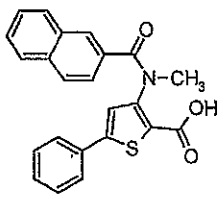
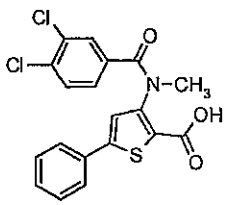
	MOLSTRUCTURE	COMPOUND NAME	IC50
219		3-[(3,5-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
220		3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
221		3-(5-CARBOXY-4-CHLORO-2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
222		5-PHENYL-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
223		3-(4-BROMO-2-FLUORO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	++

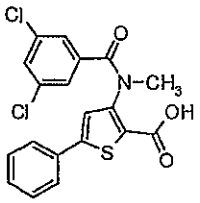
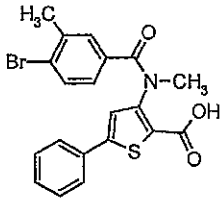
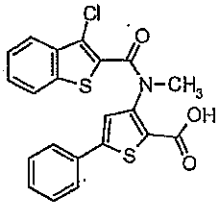
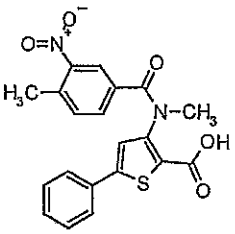
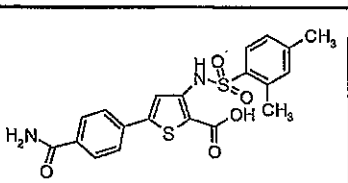
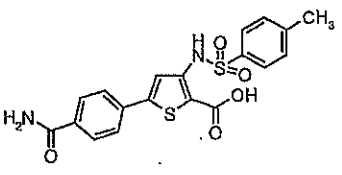
	MOLSTRUCTURE	COMPOUND NAME	IC50
224		3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+
225		5-(4-ISOBUTYL-PHENYL)-3-(3-METHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+
226		3-[(4-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
227		3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+
228		3-(2-CHLORO-4-CYANO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+

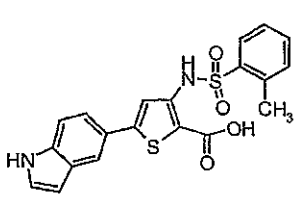
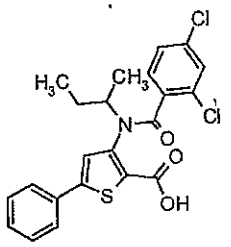
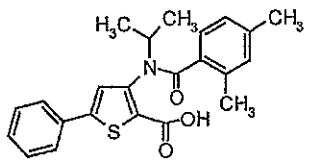
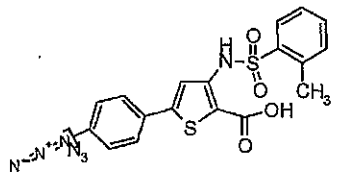
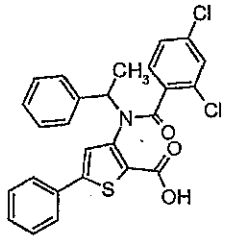
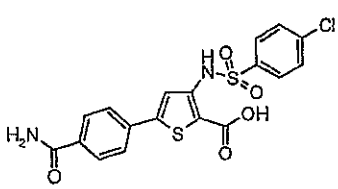
	MOLSTRUCTURE	COMPOUND NAME	IC50
229		5'-ACETYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
230		5-BENZO[B]THIOPHEN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
231		5-(4-BUTYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
232		5-(4-ETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
233		3-[BENZYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
234		3-[(4-CHLORO-2-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

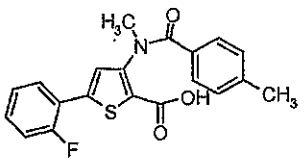
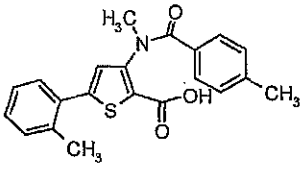
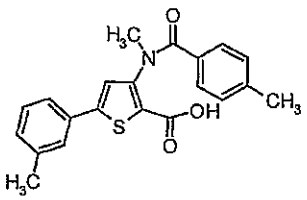
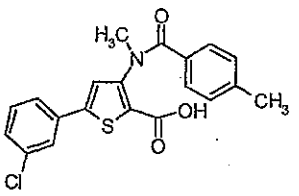
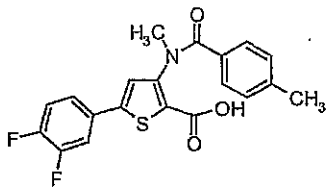
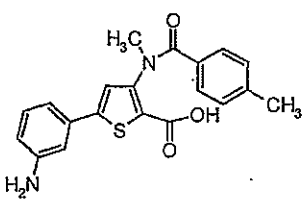
	MOLSTRUCTURE	COMPOUND NAME	IC50
235		3-[(2,4-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
236		5-(4-ACETYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
237		5-(4-ACETYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
238		5-(4-ACETYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
239		5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID #TERT!-BUTYL ESTER	++
240		3-[(2,4-DIMETHYL-BENZENESULFONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
241		3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

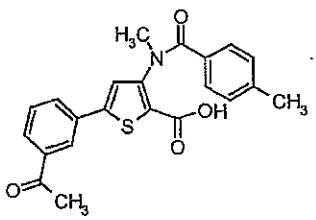
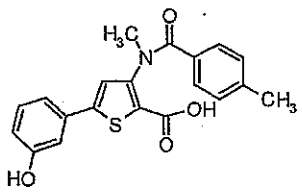
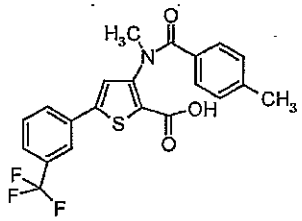
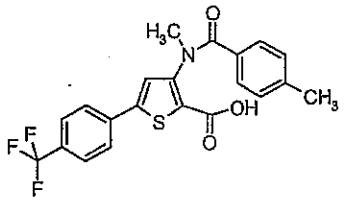
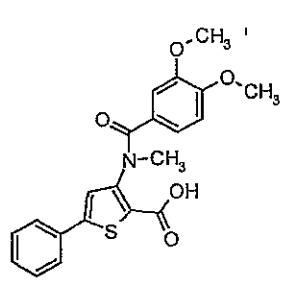
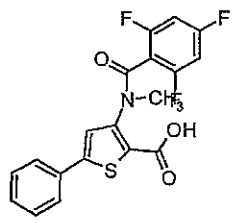
	MOLSTRUCTURE	COMPOUND NAME	IC50
242		3-ETHANESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
243		3-[ISOPROPYL-(4-TRIFLUOROMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
244		3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
245		3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
246		3-[(6-CHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
247		3-[(4-TERT-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

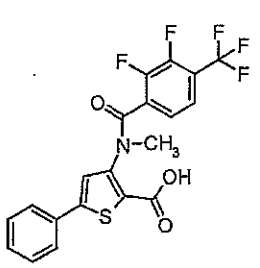
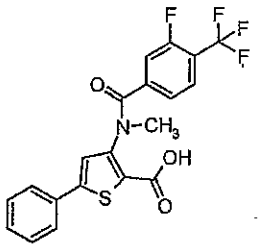
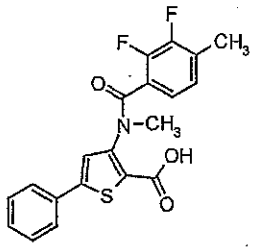
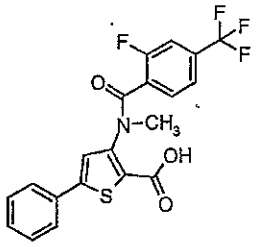
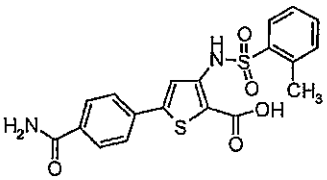
	MOLSTRUCTURE	COMPOUND NAME	IC50
248		5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
249		5-(4-ETHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
250		3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
251		3-[(BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
252		3-[METHYL-(NAPHTHALENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
253		3-[(3,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

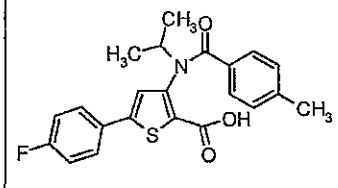
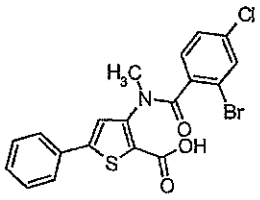
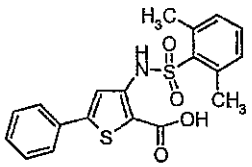
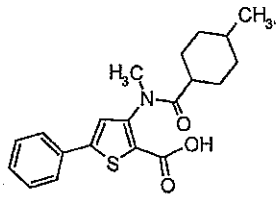
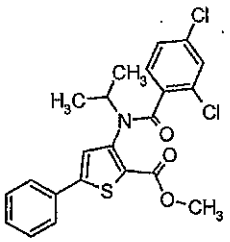
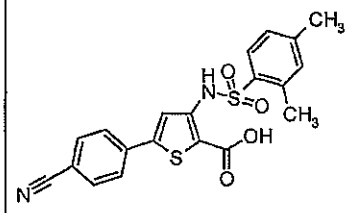
	MOLSTRUCTURE	COMPOUND NAME	IC50
254		3-[(3,5-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
255		3-[(4-BROMO-3-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
256		3-[(3-CHLORO-BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
257		3-[METHYL-(4-METHYL-3-NITRO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
258		5-(4-CARBAMOYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
259		5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

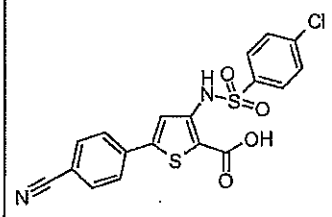
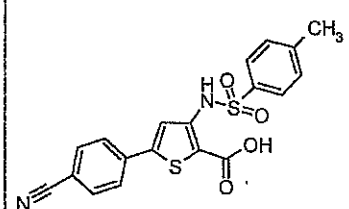
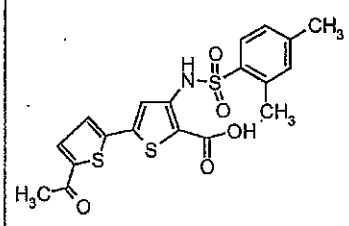
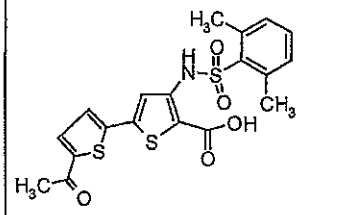
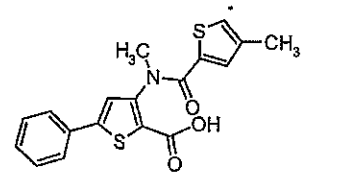
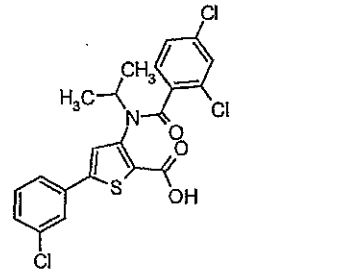
	MOLSTRUCTURE	COMPOUND NAME	IC50
260		5-(1H-INDOL-5-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
261		3-[#SEC!-BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
262		3-[(2,4-DIMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
263		5-(4-AZIDO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
264		3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
265		5-(4-CARBAMOYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

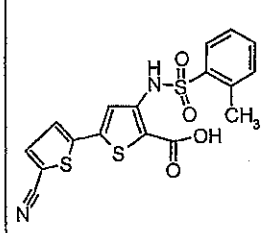
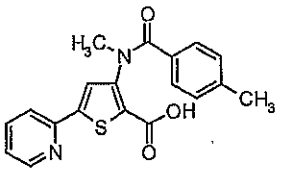
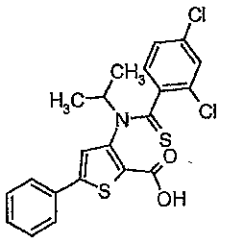
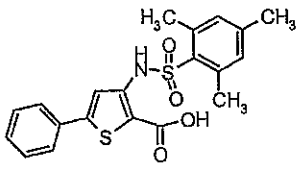
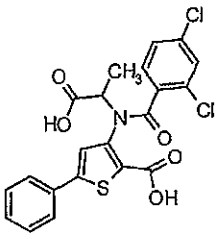
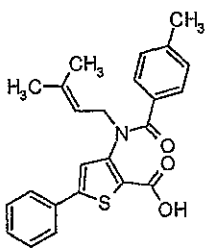
	MOLSTRUCTURE	COMPOUND NAME	IC50
266		5-(2-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
267		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-#O!-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
268		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
269		5-(3-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
270		5-(3,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
271		5-(3-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++

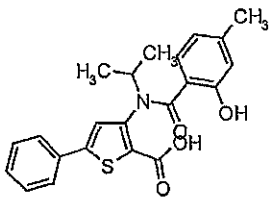
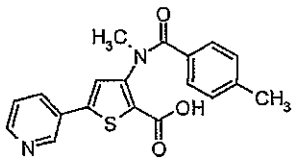
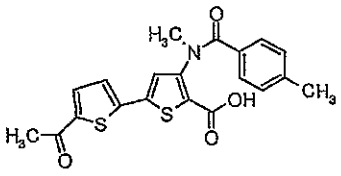
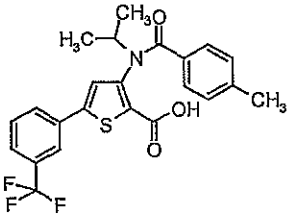
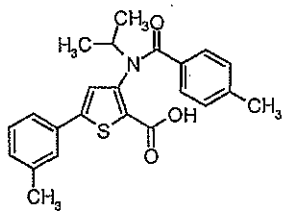
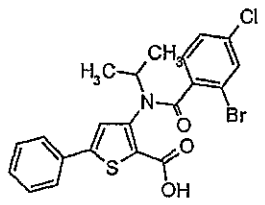
	MOLSTRUCTURE	COMPOUND NAME	IC50
272		5-(3-ACETYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++
273		5-(3-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
274		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
275		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
276		3-[(3,4-DIMETHOXY-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
277		3-[METHYL-(2,4,6-TRIFLUORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

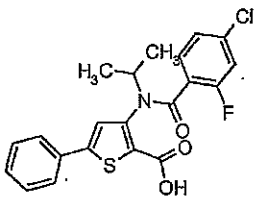
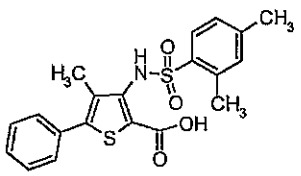
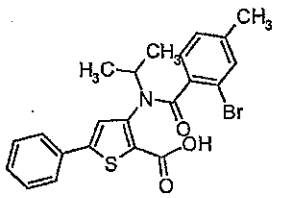
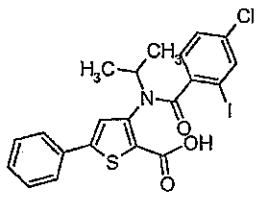
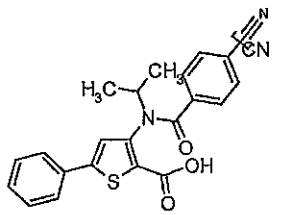
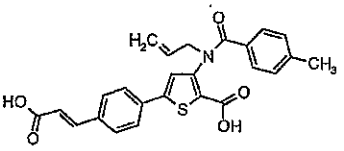
	MOLSTRUCTURE	COMPOUND NAME	IC50
278		3-[(2,3-DIFLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
279		3-[(3-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
280		3-[(2,3-DIFLUORO-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
281		3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
282		5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++

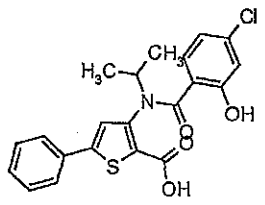
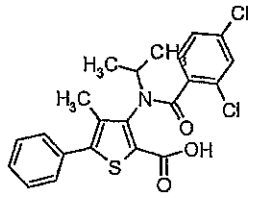
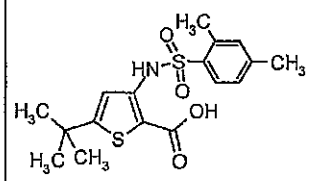
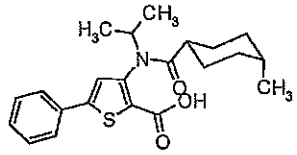
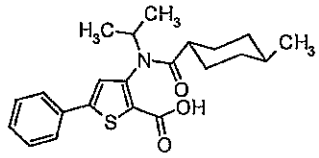
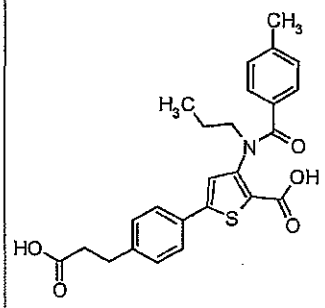
	MOLSTRUCTURE	COMPOUND NAME	IC50
283		5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
284		3-[(2-BROMO-4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
285		3-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
286		3-[METHYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
287		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER	++
288		5-(4-CYANO-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++

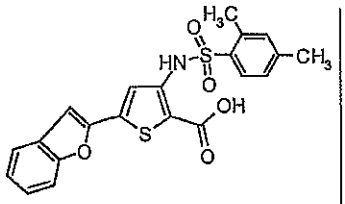
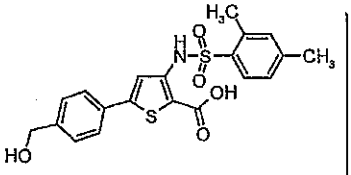
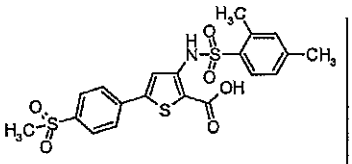
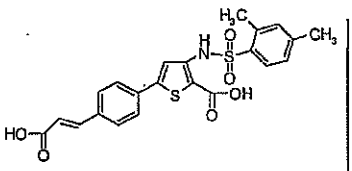
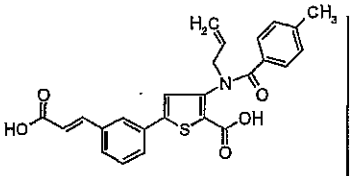
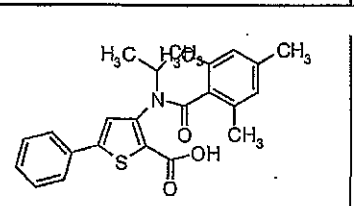
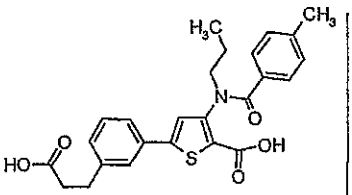
	MOLSTRUCTURE	COMPOUND NAME	IC50
289		3-(4-CHLORO-BENZENESULFONYLAMINO)-5-(4-CYANO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
290		5-(4-CYANO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
291		5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
292		5'-ACETYL-4-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
293		3-[METHYL-(4-METHYL-THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
294		5-(3-CHLORO-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++

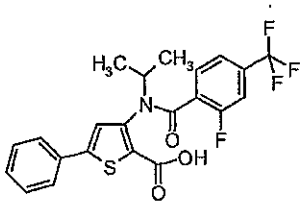
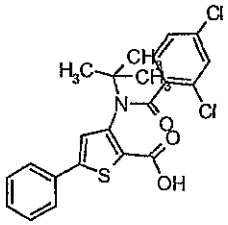
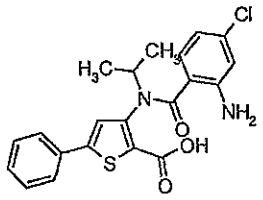
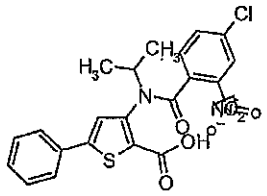
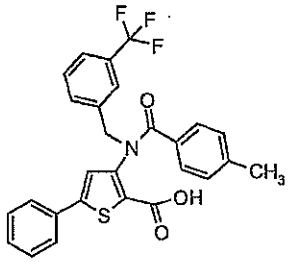
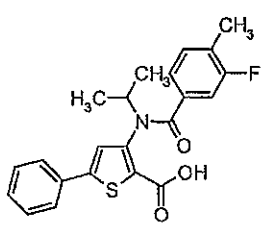
	MOLSTRUCTURE	COMPOUND NAME	IC50
295		5'-CYANO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
296		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-2-YL-THIOPHENE-2-CARBOXYLIC ACID	++
297		3-[(2,4-DICHLORO-THIOBENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
298		5-PHENYL-3-(2,4,6-TRIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
299		3-[(1-CARBOXY-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
300		3-[(4-METHYL-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

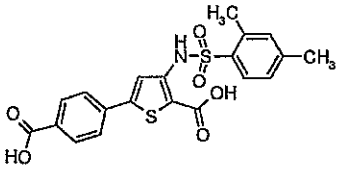
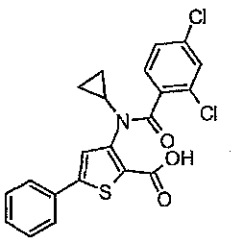
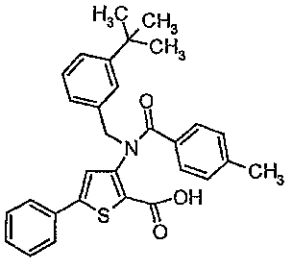
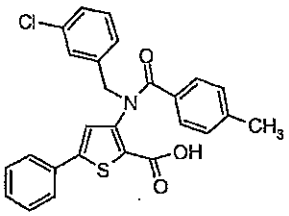
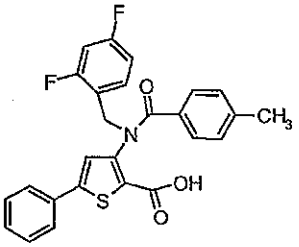
	MOLSTRUCTURE	COMPOUND NAME	IC50
301		3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
302		3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-3-YL-THIOPHENE-2-CARBOXYLIC ACID	++
303		5'-ACETYL-4-[METHYL-(4-METHYL-BENZOYL)-AMINO]-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
304		3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
305		3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
306		3-[(2-BROMO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

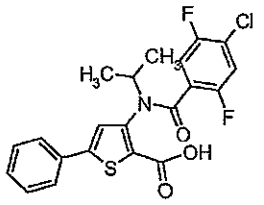
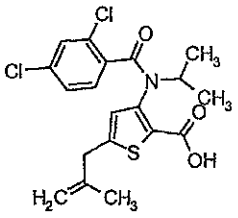
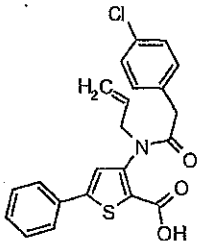
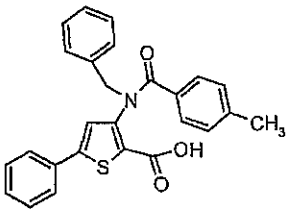
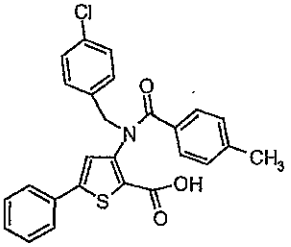
	MOLSTRUCTURE	COMPOUND NAME	IC50
307		3-[(4-CHLORO-2-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
308		3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-4-METHYL-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
309		3-[(2-BROMO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
310		3-[(4-CHLORO-2-IODO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
311		3-[(4-CYANO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
312		3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[4-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID.	+++

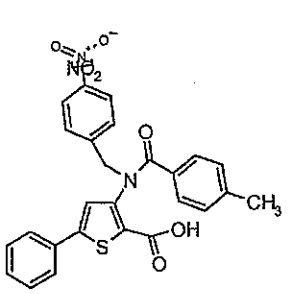
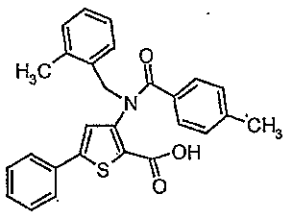
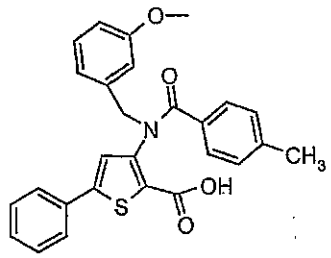
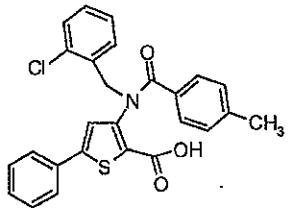
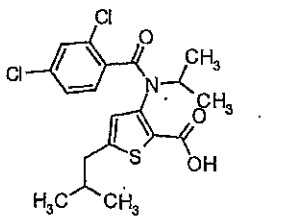
	MOLSTRUCTURE	COMPOUND NAME	IC50
313		3-[(4-CHLORO-2-HYDROXY-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
314		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-METHYL-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
315		5-#TERT!-BUTYL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++
316		3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
317		3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
318		5-[4-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++

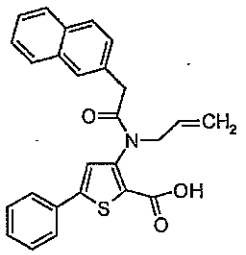
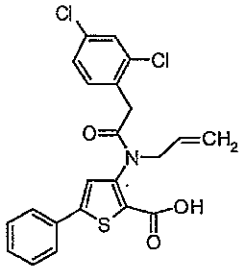
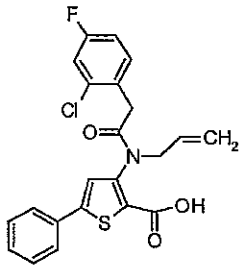
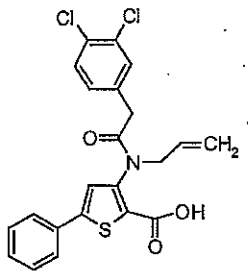
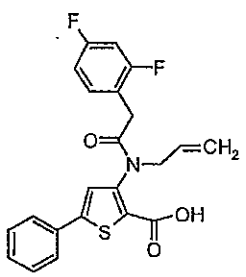
	MOLSTRUCTURE	COMPOUND NAME	IC50
319		5-BENZOFURAN-2-YL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
320		3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-HYDROXYMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
321		3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
322		5-[4-(2-CARBOXY-VINYL)-PHENYL]-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
323		3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[3-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID	++
324		3-[ISOPROPYL-(2,4,6-TRIMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
325		5-[3-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID.	++

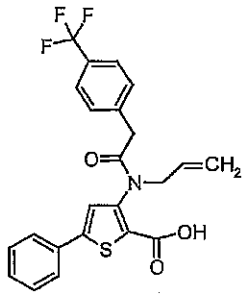
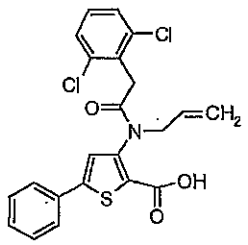
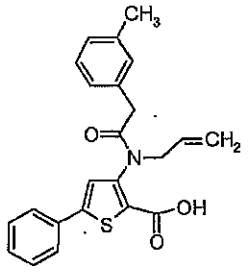
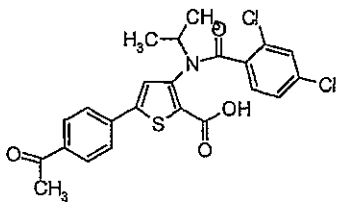
	MOLSTRUCTURE	COMPOUND NAME	IC50
326		3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
327		3-[#TERT!-BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
328		3-[(2-AMINO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
329		3-[(4-CHLORO-2-NITRO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
330		3-[(4-METHYL-BENZOYL)-(3-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
331		3-[(3-FLUORO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

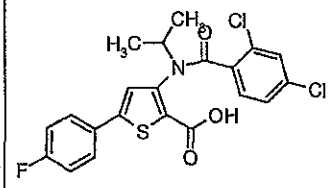
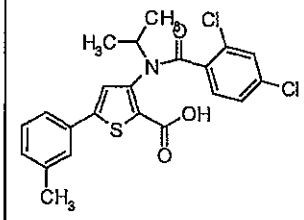
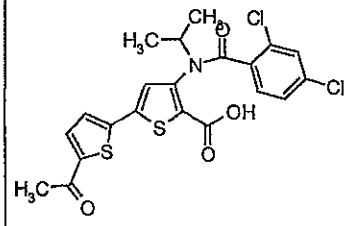
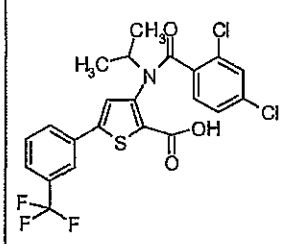
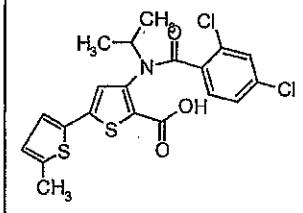
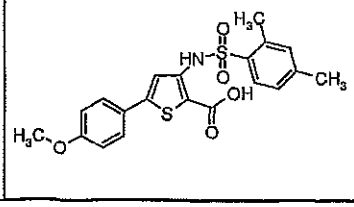
	MOLSTRUCTURE	COMPOUND NAME	IC50
332		5-(4-CARBOXY-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	+++
333		3-[CYCLOPROPYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
334		3-[(3-TERT-BUTYL-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
335		3-[(3-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
336		3-[(2,4-DIFLUORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

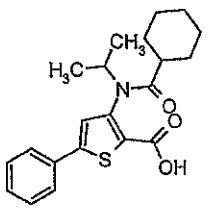
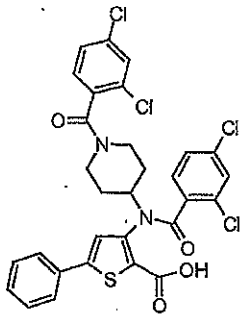
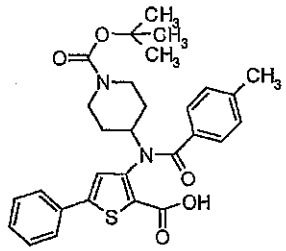
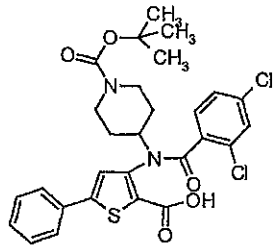
	MOLSTRUCTURE	COMPOUND NAME	IC50
337		3-[(4-CHLORO-2,5-DIFLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
338		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(2-METHYL-ALLYL)-THIOPHEN E-2-CARBOXYLIC ACID	+++
339		3-{ALLYL-[2-(4-CHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
340		3-[BENZYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
341		3-[(4-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

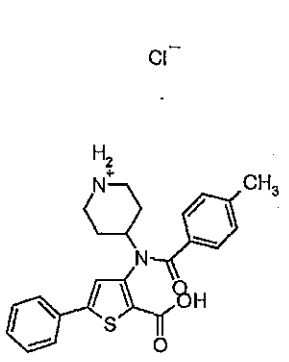
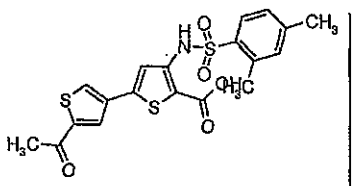
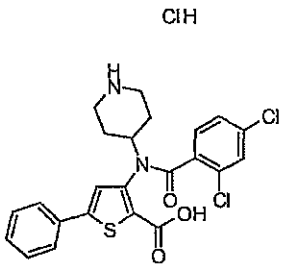
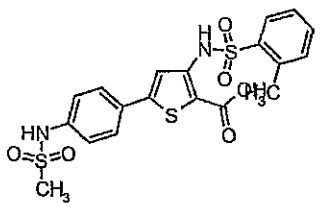
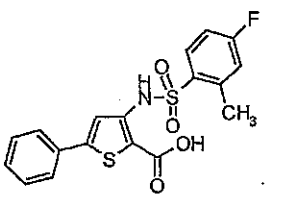
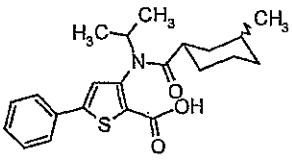
	MOLSTRUCTURE	COMPOUND NAME	IC50
342		3-[(4-METHYL-BENZOYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
343		3-[(4-METHYL-BENZOYL)-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
344		3-[(3-METHOXY-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
345		3-[(2-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
346		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-ISOBUTYL-THIOPHENE-2-CARBOXYLIC ACID	+++

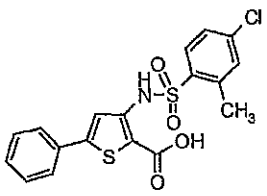
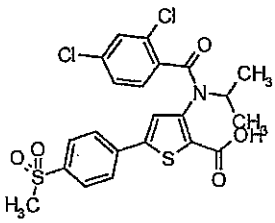
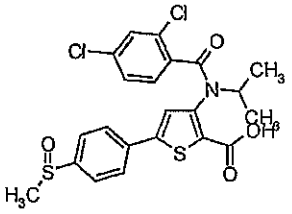
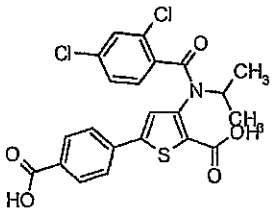
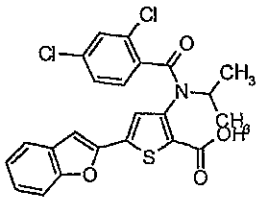
	MOLSTRUCTURE	COMPOUND NAME	IC50
347		3-[ALLYL-(2-NAPHTHALEN-2-YL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
348		3-{ALLYL-[2-(2,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
349		3-{ALLYL-[2-(2-CHLORO-4-FLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
350		3-{ALLYL-[2-(3,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
351		3-{ALLYL-[2-(2,4-DIFLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

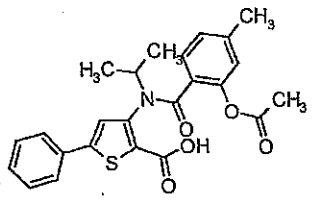
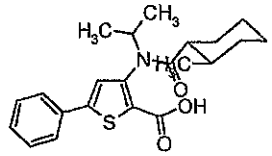
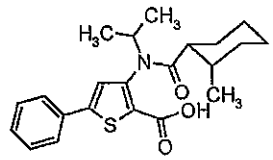
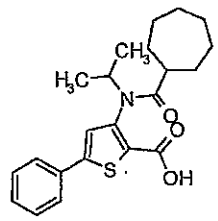
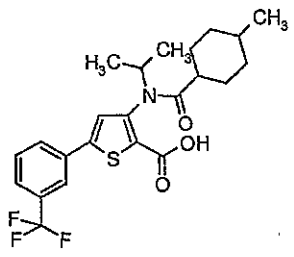
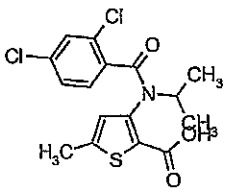
	MOLSTRUCTURE	COMPOUND NAME	IC50
352		3-{ALLYL-[2-(4-TRIFLUOROMETHYL-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
353		3-{ALLYL-[2-(2,6-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
354		3-[ALLYL-(2-M-TOLYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
355		5-(4-ACETYL-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++

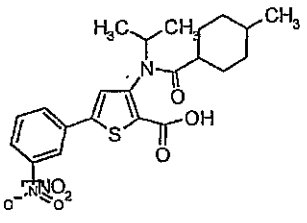
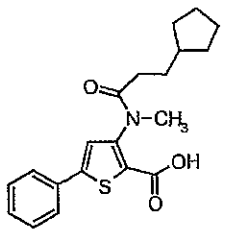
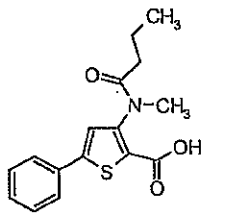
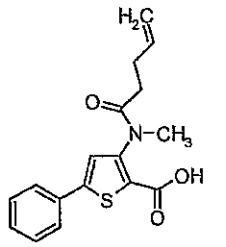
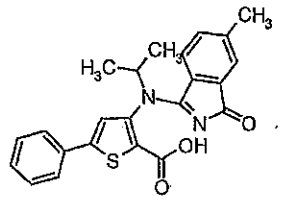
	MOLSTRUCTURE	COMPOUND NAME	IC50
356		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
357		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
358		5'-ACETYL-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
359		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
360		4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5'-METHYL-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
361		3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++

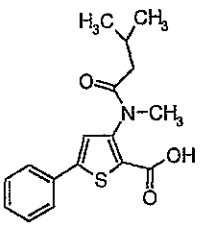
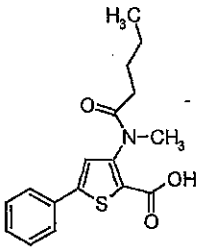
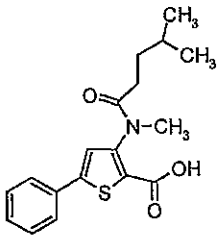
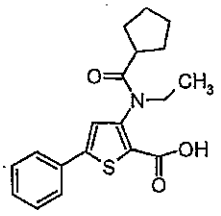
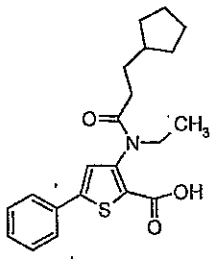
	MOLSTRUCTURE	COMPOUND NAME	IC50
362		3-(CYCLOHEXANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
363		3-{(2,4-DICHLORO-BENZOYL)-[1-(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
364		4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID #TERT!-BUTYL ESTER	+++
365		4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID #TERT!-BUTYL ESTER	+++

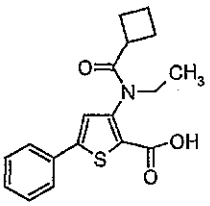
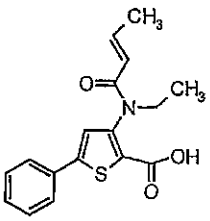
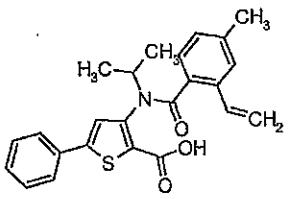
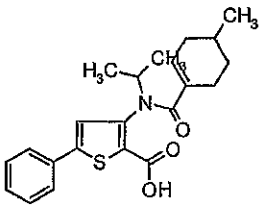
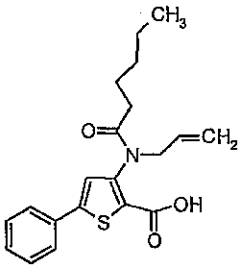
	MOLSTRUCTURE	COMPOUND NAME	IC50
366		3-[(4-METHYL-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
367		5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
368		3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
369		5-(4-METHANESULFONYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHEN E-2-CARBOXYLIC ACID	++
370		3-(4-FLUORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
371		3-[(3-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+

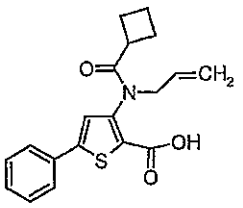
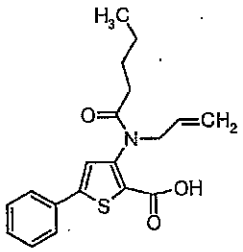
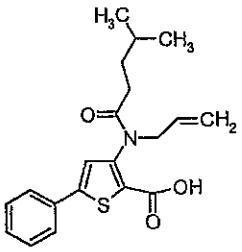
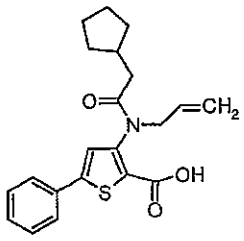
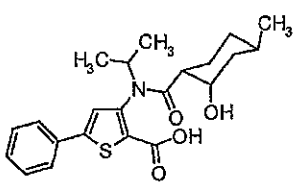
	MOLSTRUCTURE	COMPOUND NAME	IC50
372		3-(4-CHLORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
373		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
374		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFINYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
375		5-(4-CARBOXY-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
376		5-BENZOFURAN-2-YL-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++

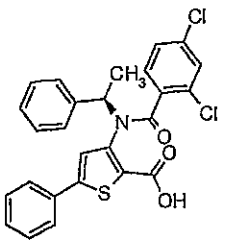
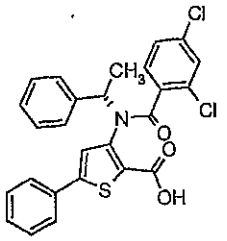
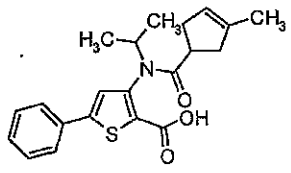
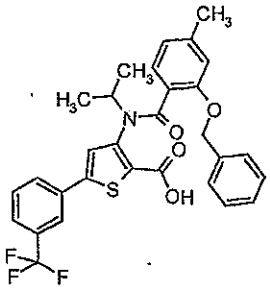
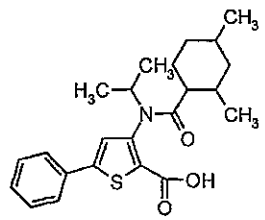
	MOLSTRUCTURE	COMPOUND NAME	IC50
377		3-[(2-ACETOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
378		3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
379		3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
380		3-(CYCLOHEPTANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
381		3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
382		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-METHYL-THIOPHENE-2-CARBOXYLIC ACID	+++

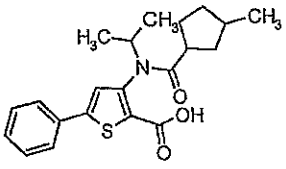
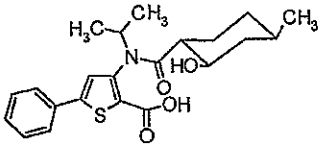
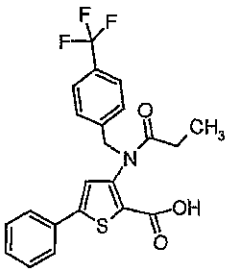
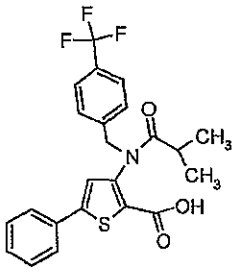
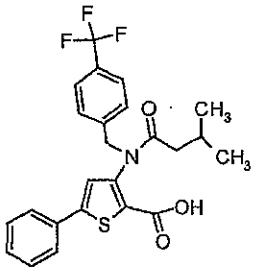
	MOLSTRUCTURE	COMPOUND NAME	IC50
383		3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
384		3-[(3-CYCLOPENTYL-PROPIONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
385		3-(BUTYRYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
386		3-(METHYL-PENT-4-ENOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
387		3-[ISOPROPYL-(5-METHYL-3-OXO-3H-ISOINDOL-1-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

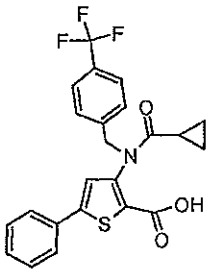
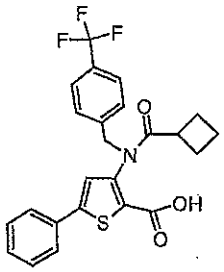
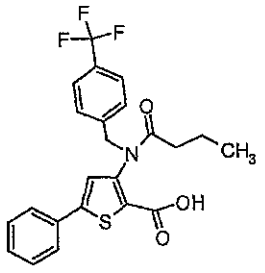
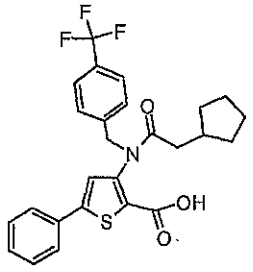
	MOLSTRUCTURE	COMPOUND NAME	IC50
388		3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
389		3-(METHYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
390		3-[METHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
391		3-(CYCLOPENTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
392		3-[(3-CYCLOPENTYL-PROPIONYL)-ETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

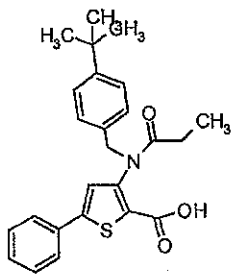
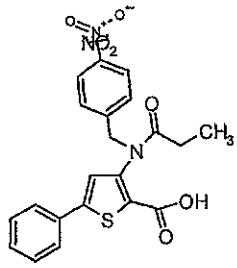
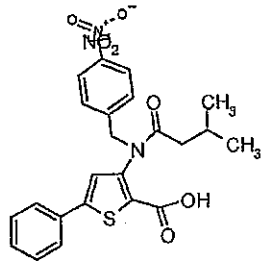
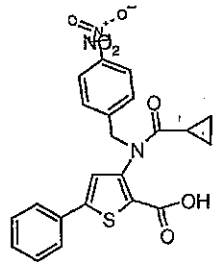
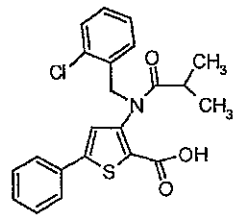
	MOLSTRUCTURE	COMPOUND NAME	IC50
393		3-(CYCLOBUTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
394		3-(BUT-2-ENOYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
395		3-[ISOPROPYL-(4-METHYL-2-VINYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
396		3-[ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
397		3-(ALLYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

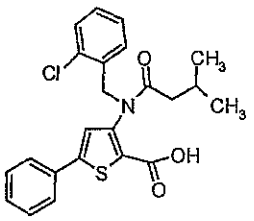
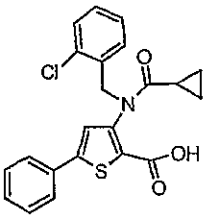
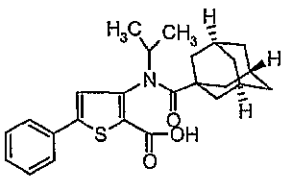
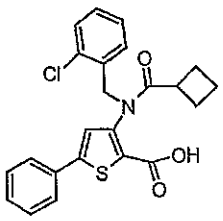
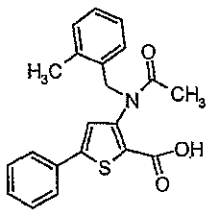
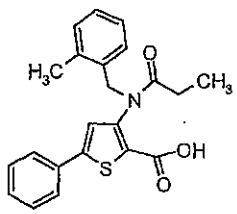
	MOLSTRUCTURE	COMPOUND NAME	IC50
398		3-(ALLYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
399		3-(ALLYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
400		3-[ALLYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
401		3-[ALLYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
402		3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

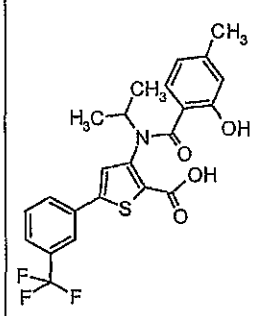
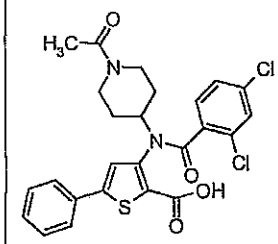
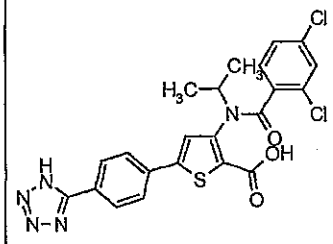
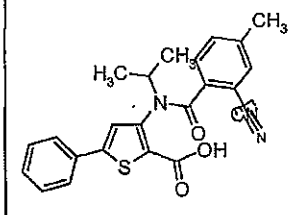
	MOLSTRUCTURE	COMPOUND NAME	IC50
403		3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
404		3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
405		3-[ISOPROPYL-(3-METHYL-CYCLOPENT-3-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
406		3-[(2-BENZYLOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
407		3-[(2,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

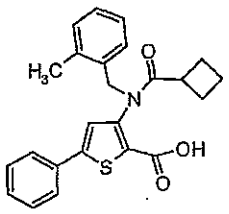
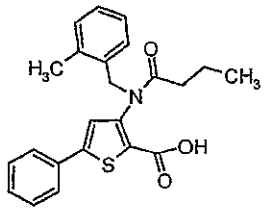
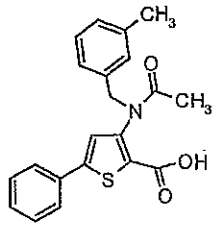
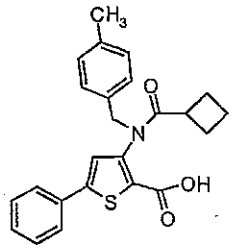
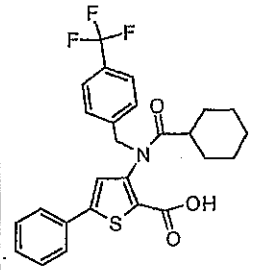
	MOLSTRUCTURE	COMPOUND NAME	IC50
408		3-[ISOPROPYL-(3-METHYL-CYCLOPENTANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
409		3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
410		5-PHENYL-3-[PROPIONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	++
411		3-[ISOBUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
412		3-[(3-METHYL-BUTYRYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

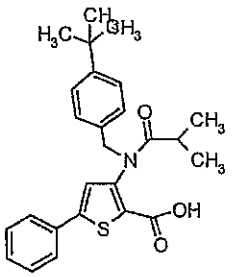
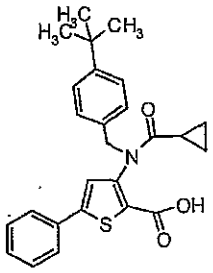
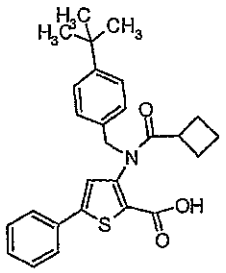
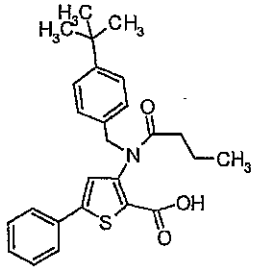
	MOLSTRUCTURE	COMPOUND NAME	IC50
413		3-[CYCLOPROPANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
414		3-[CYCLOBUTANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
415		3-[BUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
416		3-[(2-CYCLOPENTYL-ACETYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

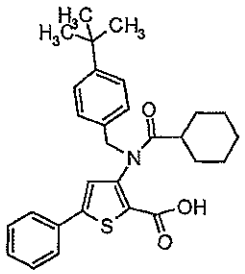
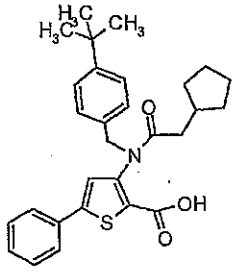
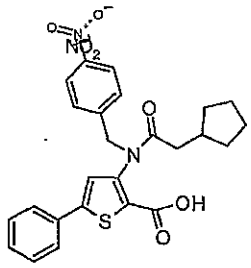
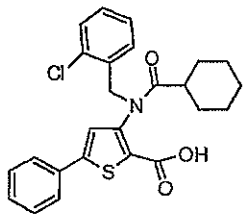
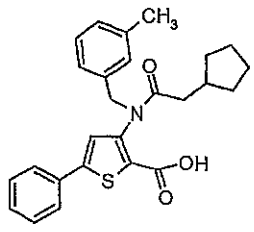
	MOLSTRUCTURE	COMPOUND NAME	IC50
417		3-[(4-TERT-BUTYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
418		3-[(4-NITRO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
419		3-[(3-METHYL-BUTYRYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
420		3-[CYCLOPROPANECARBONYL-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
421		3-[(2-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

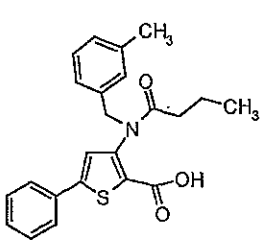
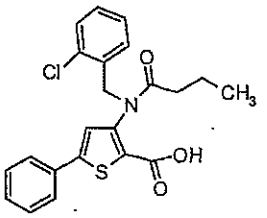
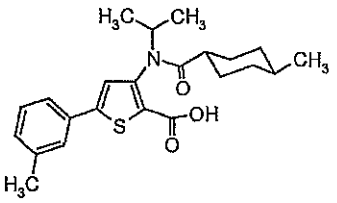
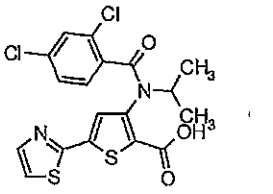
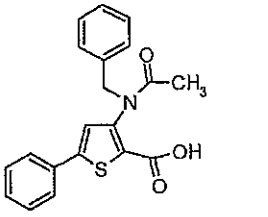
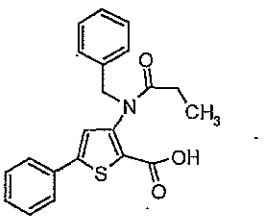
	MOLSTRUCTURE	COMPOUND NAME	IC50
422		3-[(2-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
423		3-[(2-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
424		3-[(ADAMANTANE-1-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
425		3-[(2-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
426		3-[ACETYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
427		3-[(2-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

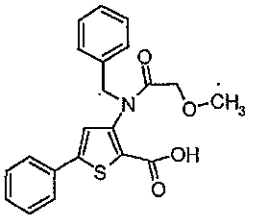
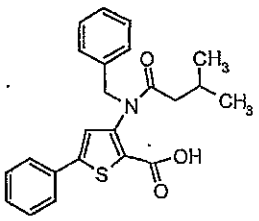
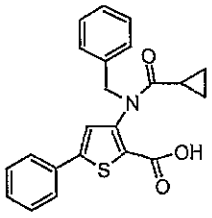
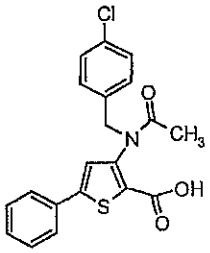
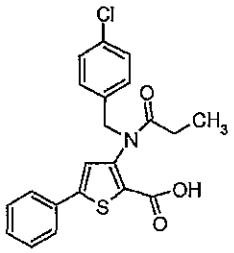
	MOLSTRUCTURE	COMPOUND NAME	IC50
428		3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	++
429		3-[(1-ACETYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
430		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-[4-(1#H!-TETRAZOL-5-YL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID	+++
431		3-[(2-CYANO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

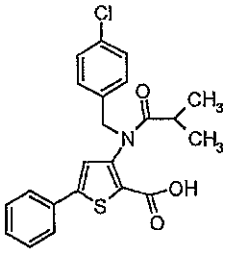
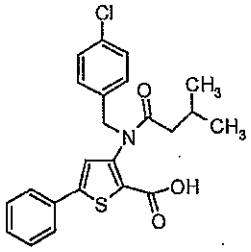
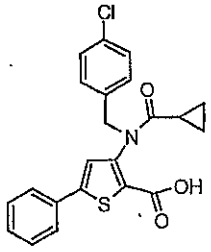
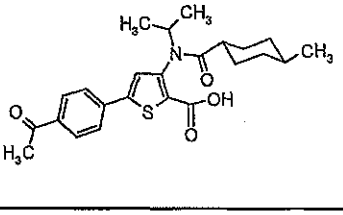
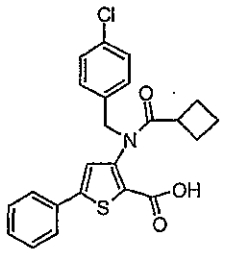
	MOLSTRUCTURE	COMPOUND NAME	IC50
432		3-[CYCLOBUTANECARBONYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
433		3-[BUTYRYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
434		3-[ACETYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
435		3-[CYCLOBUTANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
436		3-[CYCLOHEXANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

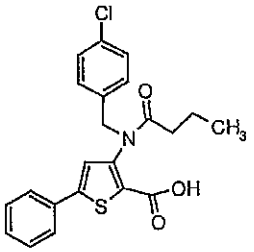
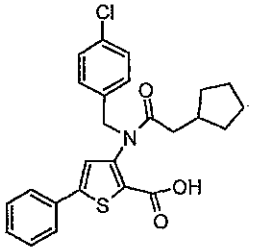
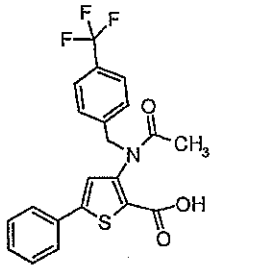
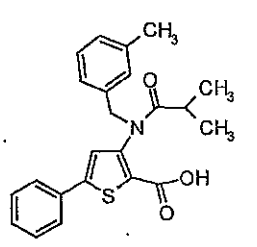
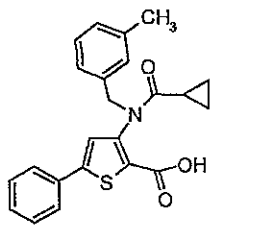
	MOLSTRUCTURE	COMPOUND NAME	IC50
437		3-[(4-TERT-BUTYL-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
438		3-[(4-TERT-BUTYL-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
439		3-[(4-TERT-BUTYL-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
440		3-[(4-TERT-BUTYL-BENZYL)-BUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

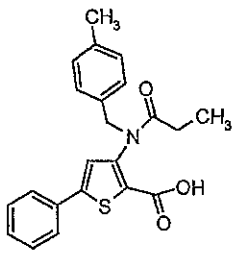
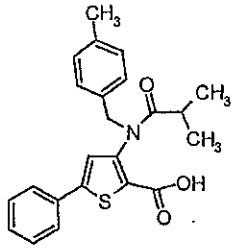
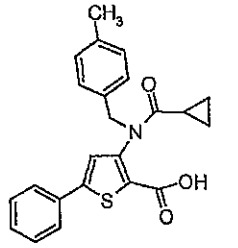
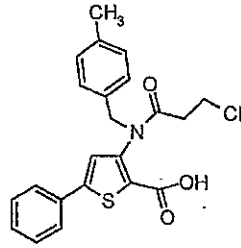
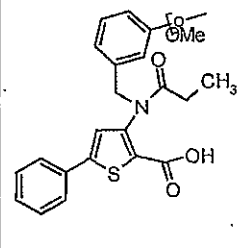
	MOLSTRUCTURE	COMPOUND NAME	IC50
441		3-[(4-TERT-BUTYL-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
442		3-[(4-TERT-BUTYL-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
443		3-[(2-CYCLOPENTYL-ACETYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
444		3-[(2-CHLORO-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
445		3-[(2-CYCLOPENTYL-ACETYL)-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

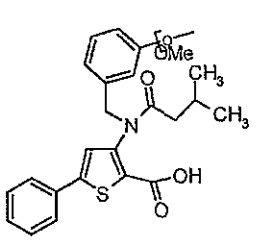
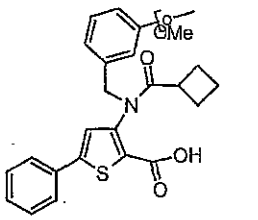
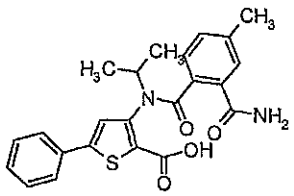
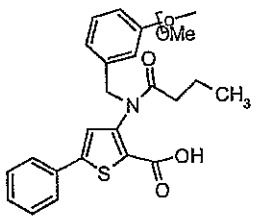
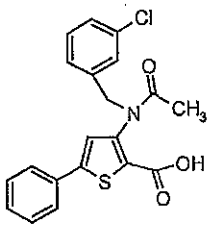
	MOLSTRUCTURE	COMPOUND NAME	IC50
446		3-[BUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
447		3-[BUTYRYL-(2-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
448		3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-#M!-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
449		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-THIAZOL-2-YL-THIOPHENE-2-CARBOXYLIC ACID	+++
450		3-(ACETYL-BENZYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
451		3-(BENZYL-PROPIONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

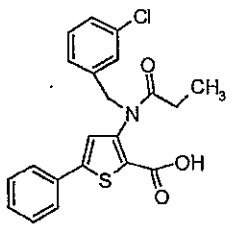
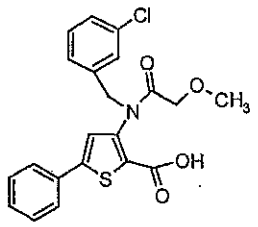
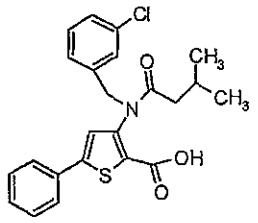
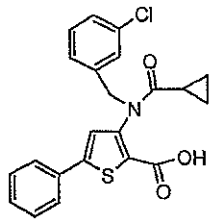
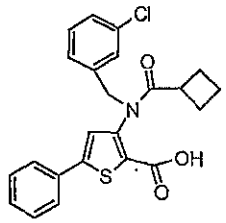
	MOLSTRUCTURE	COMPOUND NAME	IC50
452		3-[BENZYL-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
453		3-[BENZYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
454		3-(BENZYL-CYCLOPROPANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
455		3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
456		3-[(4-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

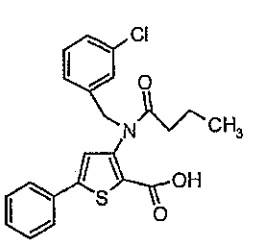
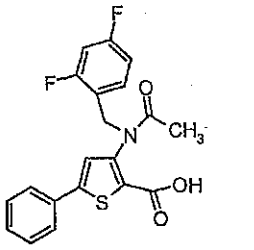
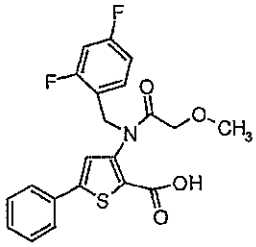
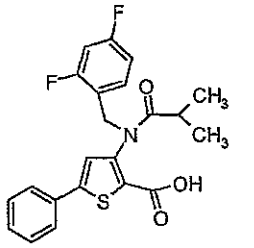
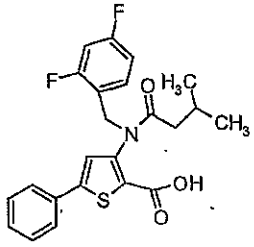
	MOLSTRUCTURE	COMPOUND NAME	IC50
457		3-[(4-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
458		3-[(4-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
459		3-[(4-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
460		5-(4-ACETYL-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
461		3-[(4-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

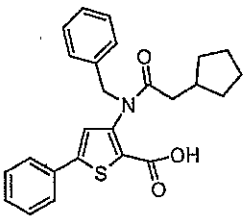
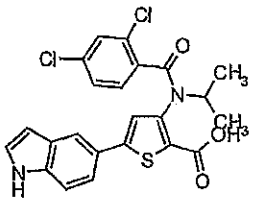
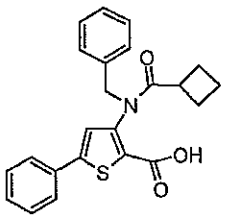
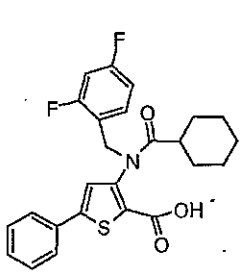
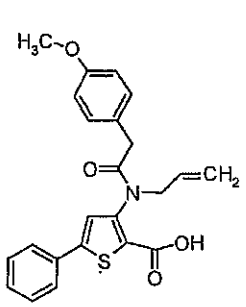
	MOLSTRUCTURE	COMPOUND NAME	IC50
462		3-[BUTYRYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
463		3-[(4-CHLORO-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
464		3-[ACETYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
465		3-[ISOBUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
466		3-[CYCLOPROPANECARBONYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

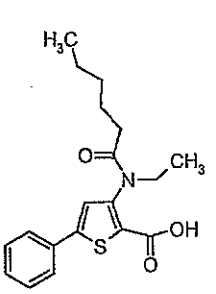
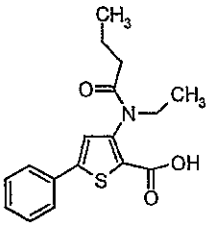
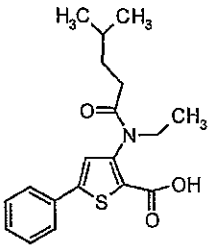
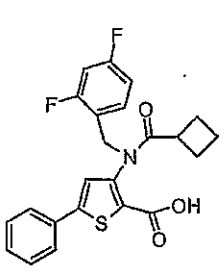
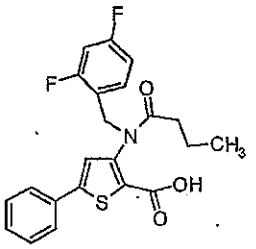
	MOLSTRUCTURE	COMPOUND NAME	IC50
467		3-[(4-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
468		3-[ISOBUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
469		3-[CYCLOPROPANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
470		3-[BUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
471		3-[(3-METHOXY-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+

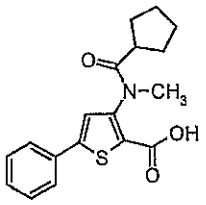
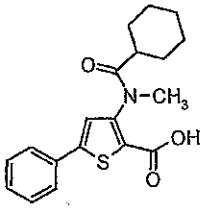
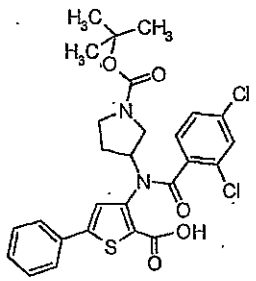
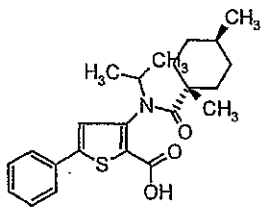
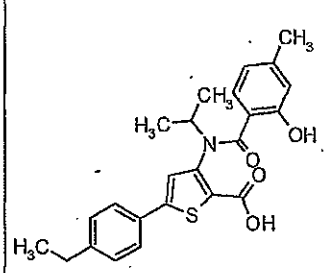
	MOLSTRUCTURE	COMPOUND NAME	IC50
472		3-[(3-METHOXY-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
473		3-[CYCLOBUTANECARBONYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
474		3-[(2-CARBAMOYL-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
475		3-[BUTYRYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
476		3-[ACETYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+

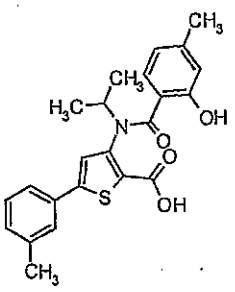
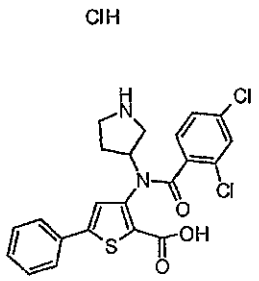
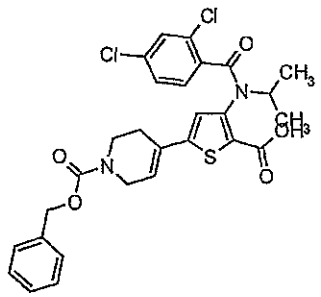
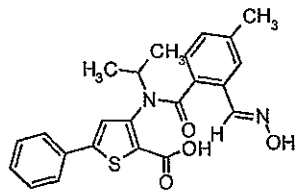
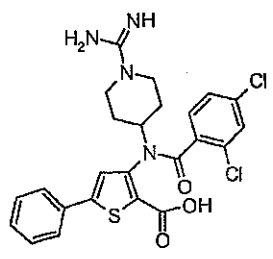
	MOLSTRUCTURE	COMPOUND NAME	IC50
477		3-[(3-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
478		3-[(3-CHLORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
479		3-[(3-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
480		3-[(3-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
481		3-[(3-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

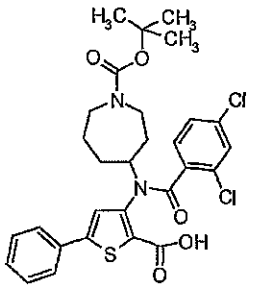
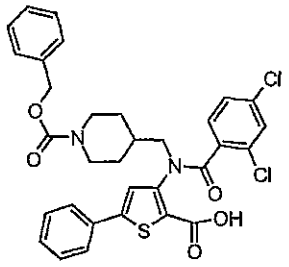
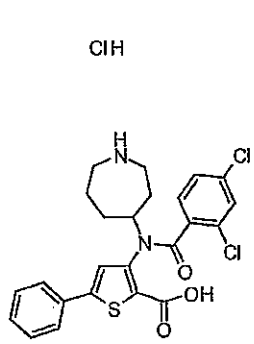
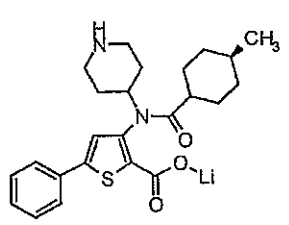
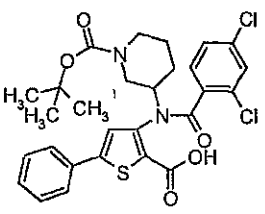
	MOLSTRUCTURE	COMPOUND NAME	IC50
482		3-[BUTYRYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
483		3-[ACETYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
484		3-[(2,4-DIFLUORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
485		3-[(2,4-DIFLUORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
486		3-[(2,4-DIFLUORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

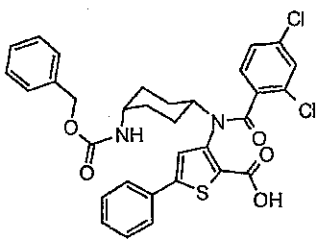
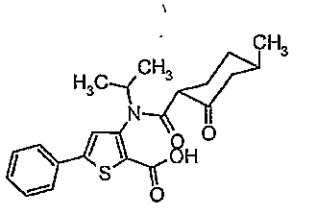
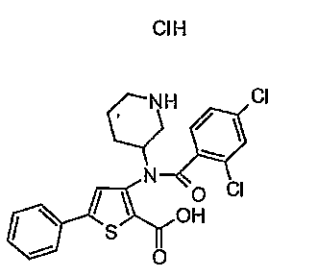
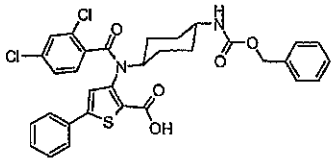
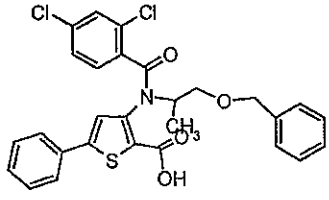
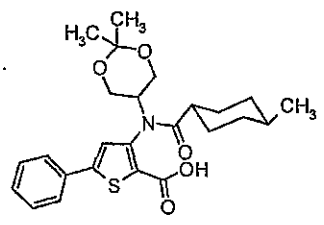
	MOLSTRUCTURE	COMPOUND NAME	IC50
487		3-[BENZYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
488		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(1H-INDOL-5-YL)-THIOPHENE-2-CARBOXYLIC ACID	+++
489		3-(BENZYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
490		3-[CYCLOHEXANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
491		3-{ALLYL-[2-(4-METHOXY-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+

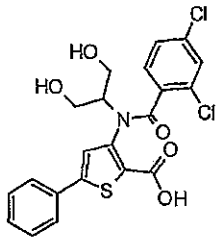
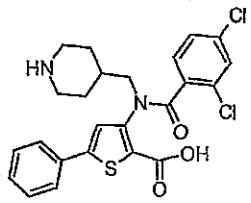
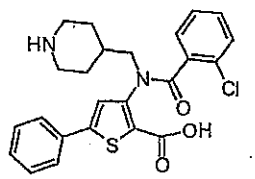
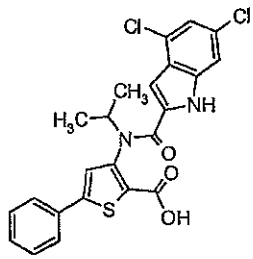
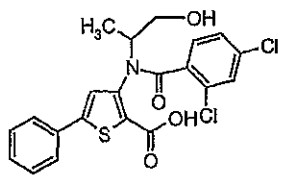
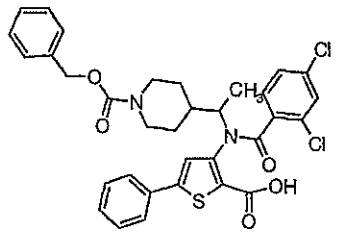
	MOLSTRUCTURE	COMPOUND NAME	IC50
492		3-(ETHYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
493		3-(BUTYRYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
494		3-[ETHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
495		3-[CYCLOBUTANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
496		3-[BUTYRYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

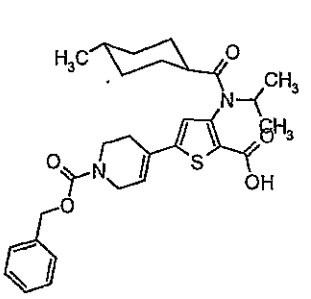
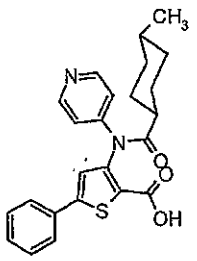
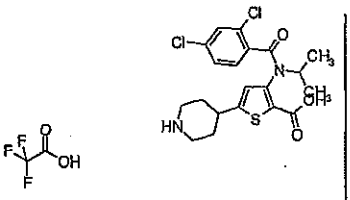
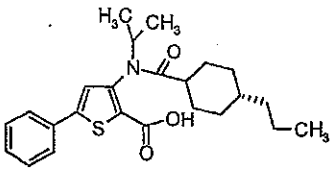
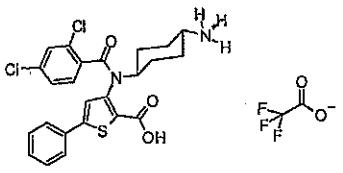
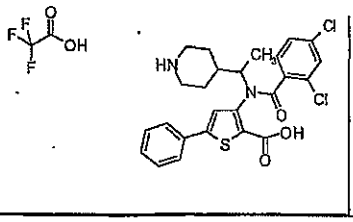
	MOLSTRUCTURE	COMPOUND NAME	IC50
497		3-(CYCLOPENTANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
498		3-(CYCLOHEXANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
499		3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PYRROLIDINE-1-CARBOXYLIC ACID #TERT!-BUTYL ESTER	+++
500		3-[(1,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
501		5-(4-ETHYL-PHENYL)-3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++

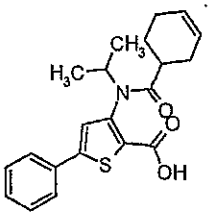
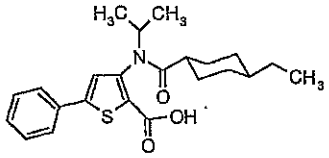
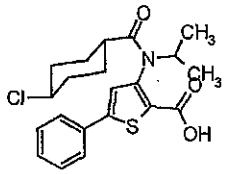
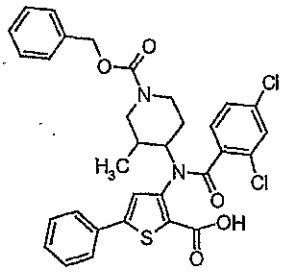
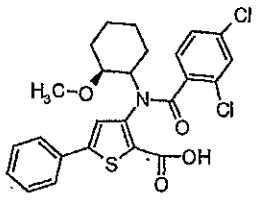
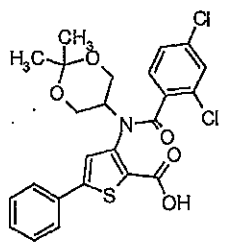
	MOLSTRUCTURE	COMPOUND NAME	IC50
502		3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-#M!-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	+++
503		3-[(2,4-DICHLORO-BENZOYL)-PYRROLIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
504		4-{5-CARBOXY-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2#H!-PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
505		3-{[2-(HYDROXYIMINO-METHYL)-4-METHYL-BENZOYL]-ISOPROPYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
506		3-[(1-CARBAMIMIDOYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

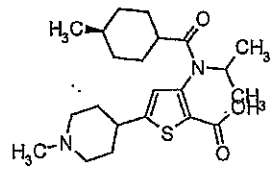
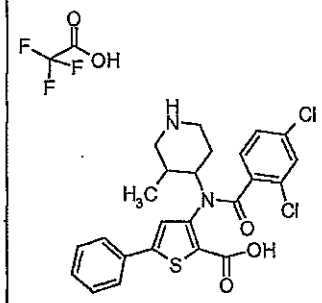
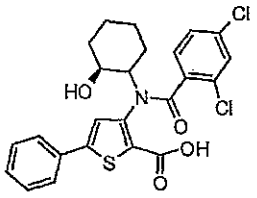
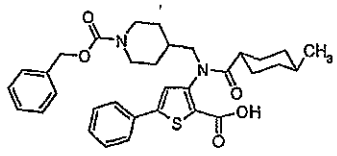
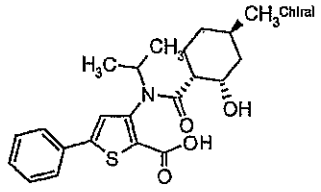
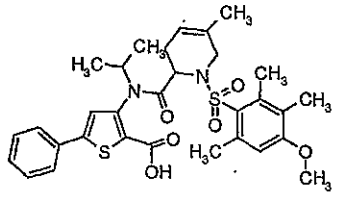
	MOLSTRUCTURE	COMPOUND NAME	IC50
507		4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-AZEPANE-1-CARBOXYLIC ACID TERT!-BUTYL ESTER	+++
508		4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
509		3-[AZEPAN-4-YL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
510		3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID LITHIUM SALT	++
511		3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID #TERT!-BUTYL ESTER	+++

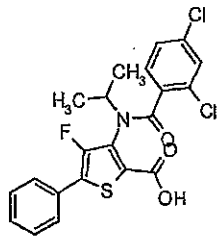
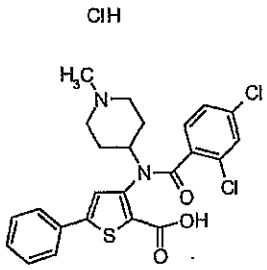
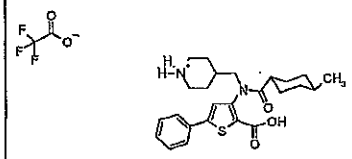
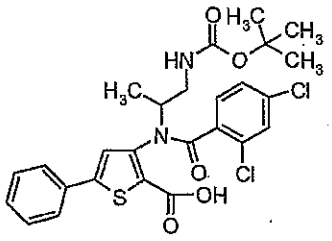
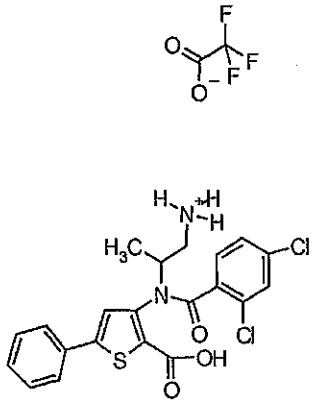
	MOLSTRUCTURE	COMPOUND NAME	IC50
512		3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
513		3-[ISOPROPYL-(4-METHYL-2-OXO-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
514		3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH GENERIC INORGANIC NEUTRAL COMPONENT	+++
515		3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
516		3-[(2-BENZYLOXY-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
517		3-[(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

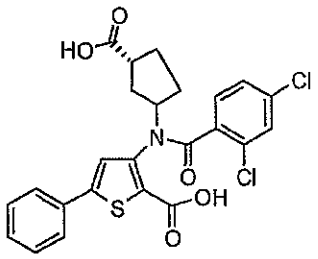
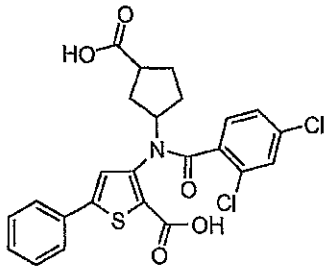
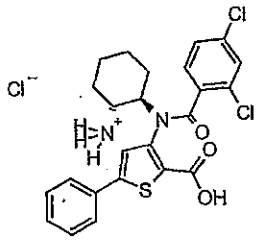
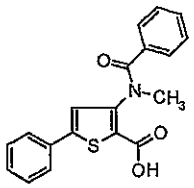
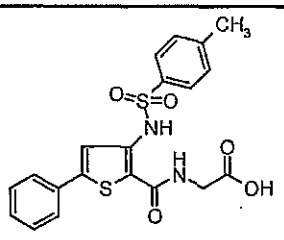
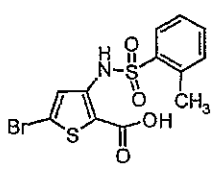
	MOLSTRUCTURE	COMPOUND NAME	IC50
518		3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-HYDROXYMETHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
519		3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
520		3-[(2-CHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
521		3-[(4,6-DICHLORO-1#H!-INDOLE-2-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
522		3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-METHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
523		4-{1-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-ETHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	++

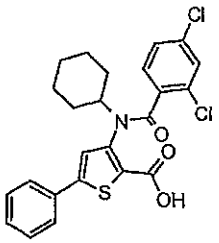
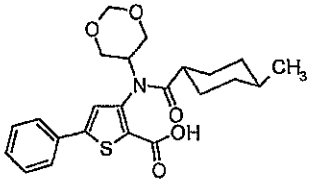
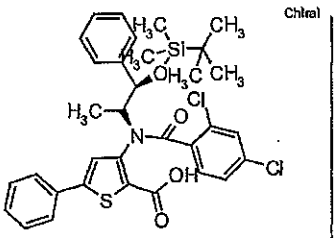
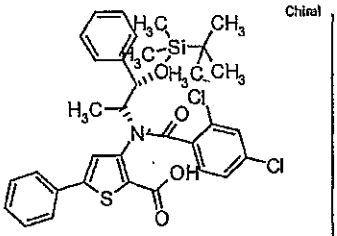
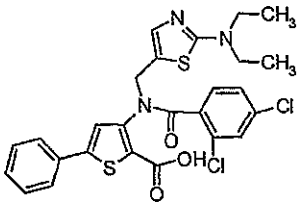
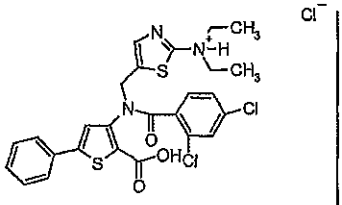
	MOLSTRUCTURE	COMPOUND NAME	IC50
524		4-{5-CARBOXY-4-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2#H!-PYRIDINE-1-CARBOXYLIC ACID , BENZYL ESTER	+++
525		3-[(4-METHYL-CYCLOHEXANECARBONYL)-PYRIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
526		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PIPERIDIN-4-YL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID	+
527		3-[ISOPROPYL-(4-PROPYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
528		4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM; TRIFLUORO-ACETATE	+++
529		3-[(2,4-DICHLORO-BENZOYL)-(1-PIPERIDIN-4-YL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID	+++

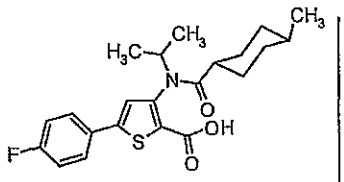
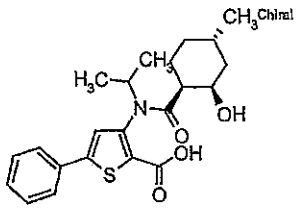
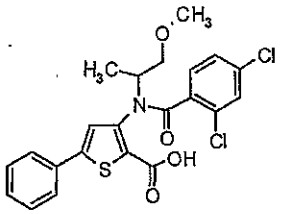
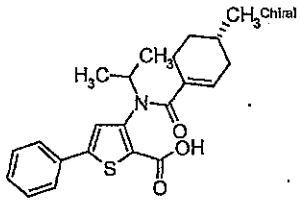
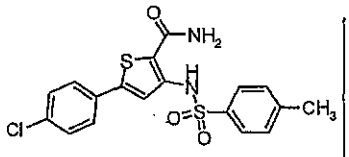
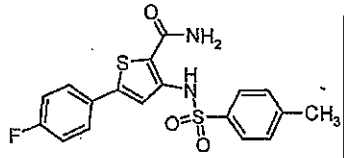
	MOLSTRUCTURE	COMPOUND NAME	IC50
530		3-[(CYCLOHEX-3-ENECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
531		3-[(4-ETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
532		3-[(4-CHLORO-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
533		4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-3-METHYL-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
534		3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
535		3-[(2,4-DICHLORO-BENZOYL)-(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

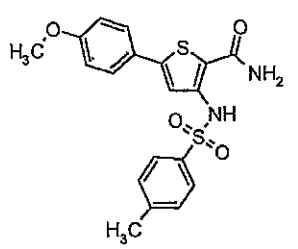
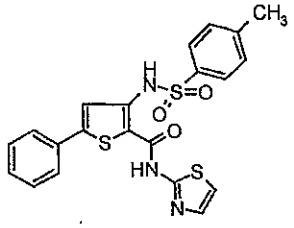
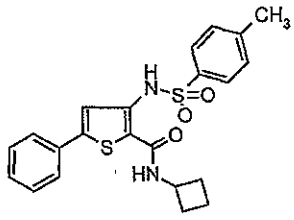
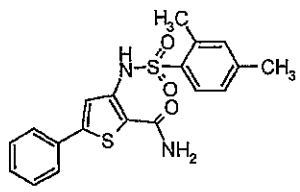
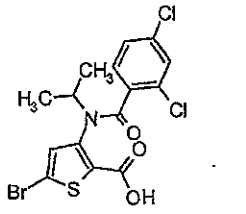
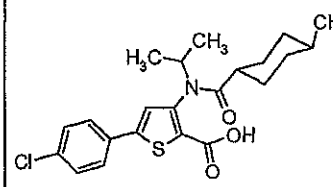
	MOLSTRUCTURE	COMPOUND NAME	IC50
536		3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(1-METHYL-PIPERIDIN-4-YL)-THIOPHENE-2-CARBOXYLIC ACID	+++
537		3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID	+++
538		3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
539		4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
540		3-[((1R,2S,4R)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
541		3-{ISOPROPYL-[1-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYL)-5-METHYL-1,2,3,6-TETRAHYDRO-PYRIDINE-2-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

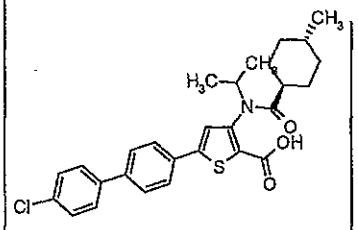
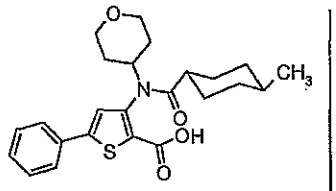
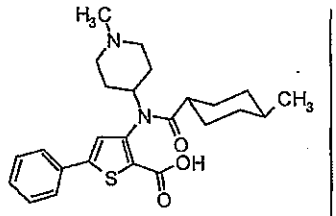
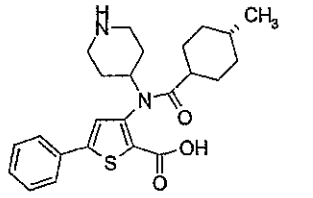
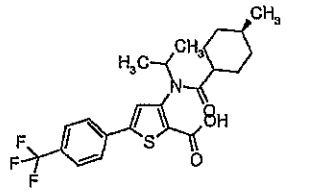
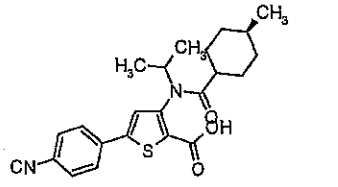
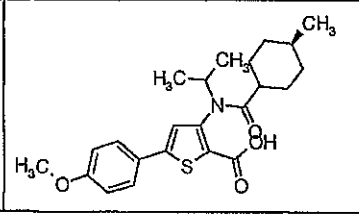
	MOLSTRUCTURE	COMPOUND NAME	IC50
542		3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-FLUORO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
543		3-[(2,4-DICHLORO-BENZOYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
544		4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-METHYL}-PIPERIDINIUM; TRIFLUORO-ACETATE	+++
545		3-[(2-TERT-BUTOXYCARBONYLAMINO-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
546		2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PROPYL-AMINE TRIFLUOROACETIC ACID SALT	+++

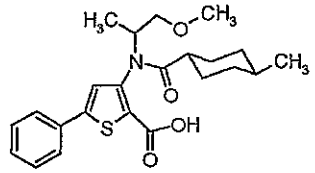
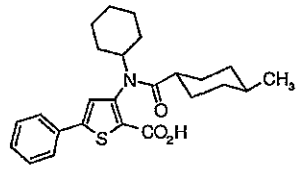
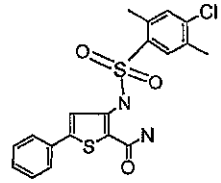
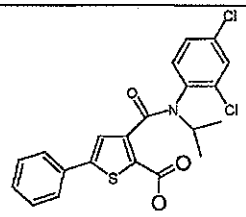
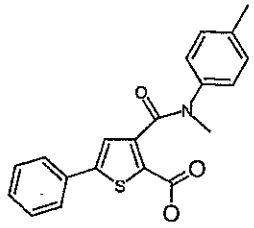
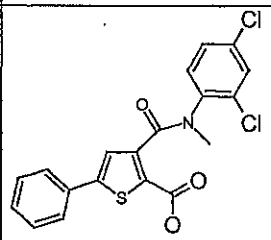
	MOLSTRUCTURE	COMPOUND NAME	IC50
547		3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
548		3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
549		2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM; CHLORIDE	+++
550		3-(BENZOYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
551		{[5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBONYL]-AMINO}-ACETIC ACID	++
552		5-BROMO-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
553		3-[CYCLOHEXYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
554		3-[[1,3]DIOXAN-5-YL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
555		3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
556		3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
557		3-[(2,4-DICHLORO-BENZOYL)-(2-DIETHYLAMINO-THIAZOL-5-YLMETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
558		(5-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-THIAZOL-2-YL)-DIETHYL-AMMONIUM; CHLORIDE	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
559		5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
560		3-[((1S,2R,4S)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
561		3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-1-METHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
562		3-[(4S)-ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
563		5-(4-CHLORO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID AMIDE	++
564		5-(4-FLUORO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID AMIDE	++

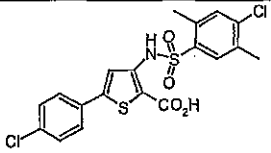
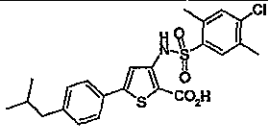
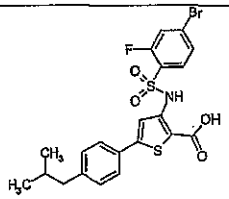
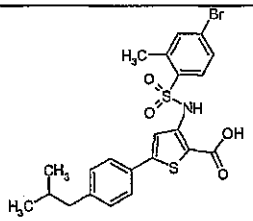
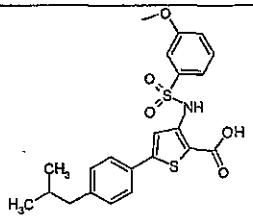
	MOLSTRUCTURE	COMPOUND NAME	IC50
565		5-(4-METHOXY-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID AMIDE	++
566		3-METHYL-(4-METHYLBENZOYL)-AMINO)5-PHENYL THIOPHENE-2-CARBOXYLIC ACID (2-HYDROXY-ETHYL)AMIDE	++
567		5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID CYCLOBUTYLAMIDE	++
568		3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMIDE	++
569		5-BROMO-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
570		5-(4-CHLORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++

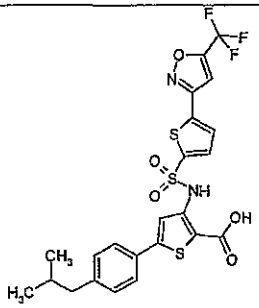
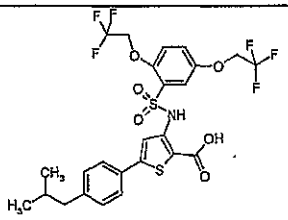
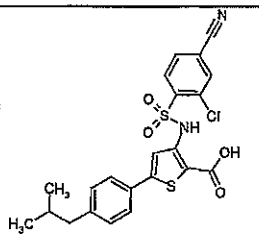
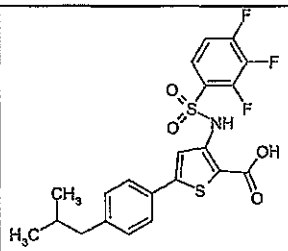
	MOLSTRUCTURE	COMPOUND NAME	IC50
571		5-(4'-CHLORO-BIPHENYL-4-YL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
572		3-[(4-METHYL-CYCLOHEXANECARBONYL)-(TETRAHYDRO-PYRAN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
573		3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
574		3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
575		'3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
576		5-(4-CYANO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
577		'3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
578		3-[(2-METHOXY-1-METHYL-ETHYL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
579		3-[CYCLOHEXYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
580		3-(4-CHLORO-2,5 DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE--2-CARBOXYLIC ACID AMIDE	+++
583		3-[(2,4-DICHLORO-PHENYL)-ISOPROPYL-CARBAMOYL]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
584		3-(METHYL-P-TOLYL-CARBAMOYL)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
585		3-[(2,4-DICHLORO-PHENYL)-METHYL-CARBAMOYL]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

*: +++ IC_{50} <5μM
++ IC_{50} 5μM-20μM
+ IC_{50} >20μM

EXAMPLE 28 List of compounds having anti-helicase activity *

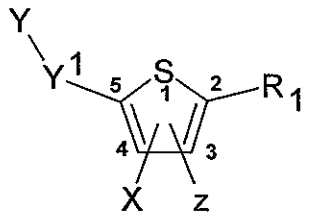
Compound #	Compound name	Structure	Anti-ATPase (Malachite Green assay) EC_{50}	Anti-ATPase (HPLC method) EC_{50}
Compound #14	3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid		+	ND
Compound #19	3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid		+++	++
Compound #223	3-(4-Bromo-2-fluorobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid		ND	+++
Compound #224	3-(4-Bromo-2-methylbenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid		ND	++
Compound #225	5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-amino)-thiophene-2-carboxylic acid		ND	+

Compound #581	5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-2-carboxylic acid		ND	++
Compound #227	3-[2,5-Bis-(2,2,2-trifluoroethoxy)-benzenesulfonylamino]-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid		ND	+
Compound #228	3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid		ND	+
Compound #582	5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid		ND	+

*: +++ IC_{50} <5μM
++ IC_{50} 5μM-20μM
+ IC_{50} >20μM

Claims:

1. A compound having the formula I:

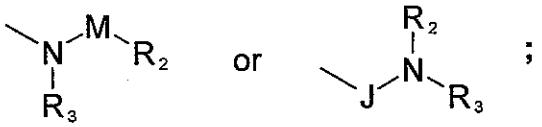


(I)

or a pharmaceutically acceptable salt thereof;

wherein,

X is:



M is:

;

J is:

;

W is O or S;

Y^1 is a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)\text{-}SO_2\text{-}R_5$, $CONR_9OH$ or halogen;

R_9, R_5, R_{10} and R_{11} are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl, or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl, or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

R_{16} is H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl, provided that R_{16} is other than methyl or ethyl;

R_1 is C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

R_2 is C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R_3 is C_{1-12} alkyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl; and

Z is H, halogen, or C_{1-6} alkyl;

wherein

in each case above alkyl is straight chain, branched chain or cyclic and is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkenyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkynyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aryl is a carbocyclic moiety containing at least one benzenoid-type ring which are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aralkyl is an aryl group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl group.

in each case above heterocycle groups are saturated or unsaturated,

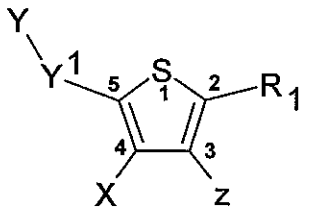
monocyclic or polycyclic moieties containing at least one heteroatom selected from oxygen, sulfur or nitrogen, and are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above heteroaralkyl groups are heterocycle groups attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

sulfur atoms are in each case above present in the form of S, SO, or SO_2; and

R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-10} heterocycle, C_{3-10} heteroaralkyl, and C_{6-18} aralkyl, or Rc and Rd are taken together with the oxygens form a 5 to 10 membered heterocycle, or R_{13} and R_{14} are taken together with the nitrogen form a 3 to 10 membered heterocycle.

2. A compound having the formula Ia:

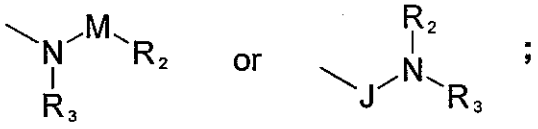


(Ia)

or a pharmaceutically acceptable salt thereof;

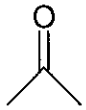
wherein,

X is:



;

M is:


;

J is:

;

W is O or S;

Y^1 is a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)\text{-}SO_2\text{-}R_5$, $CONR_9OH$ or halogen;

R_9, R_5, R_{10} and R_{11} are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl, or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl, or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

R_{16} is H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18}

heteroaralkyl or C_{6-18} aralkyl; provided that R_{16} is other than methyl or ethyl;

R_1 is C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C $_{6-18}$ aralkyl;

R_2 is C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, or C $_{6-18}$ aralkyl;

R_3 is C $_{1-12}$ alkyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C $_{6-18}$ aralkyl;

Z is H, halogen, or C_{1-6} alkyl;
wherein

in each case above alkyl is straight chain, branched chain or cyclic and is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkenyl is unsubstituted or substituted by one or more

halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkynyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aryl is a carbocyclic moiety containing at least one benzenoid-type ring which are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aralkyl is an aryl group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl group.

in each case above C_{3-10} heterocycle groups are saturated or unsaturated, monocyclic or polycyclic moieties containing at least one heteroatom selected from oxygen, sulfur or nitrogen, and are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above C_{3-10} heteroaralkyl groups are heterocycle groups attached

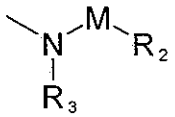
to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

sulfur atoms are in each case above present in the form of S, SO, or SO_2,

R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-10} heterocycle, C_{3-10} heteroaralkyl, and C_{6-18} aralkyl, or Rc and Rd are taken together with the oxygens form a 5 to 10 membered heterocycle, or R_{13} and R_{14} are taken together with the nitrogen form a 3 to 10 membered heterocycle.

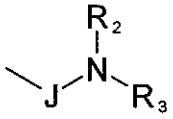
3. A compound as defined in claims 1 or 2, wherein

X is:



4. A compound as defined in claims 1 or 2, wherein

X is:



5. The compound as defined in claims 1 or 2, wherein Z is H.

6. The compound as defined in claims 1 or 2, wherein Y^1 is a bond.

7. The compound as defined in anyone of claims 1 or 2, wherein R_1 is C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, or C_{6-18} aralkyl.

8. The compound as defined in anyone of claims 1 or 2, wherein R_1 is C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

9. The compound as defined in anyone of claims 1 or 2, wherein R_1 is a C_{2-12} alkyl.

10. The compound as defined in anyone of claims 1 or 2, wherein R_1 is a C_{6-14} aryl.

11. The compound as defined in anyone of claims 1 or 2, wherein R_1 is a C_{3-12} heterocycle.

12. The compound as defined in anyone of claims 1 or 2, wherein R_1 is

t-butyl, isobutyl, allyl, ethynyl, 2-phenylethenyl, isobutenyl, benzyl, phenyl, phenethyl, benzodioxolyl, thienyl, thiophenyl, pyridinyl, isoxazolyl, thiazolyl, pyrazolyl, tetrazolyl, benzofuranyl, indolyl, furanyl, or benzothiophenyl, which in each case is unsubstituted or substituted one or more times by halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, COOH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido; and

R_{12}, Rc, Rd, R_{13} and R_{14} are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl, [[;]] or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle, or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

13. The compound as defined in claim 12, wherein R_1 is thienyl, t-butyl, phenyl or pyridinyl.

14. The compound as defined in claim 12, wherein R_1 is phenyl.

15. The compound as defined in anyone of claims 1 or 2, wherein R_1 is phenyl substituted by at least one fluoride.

16. The compound as defined in anyone of claims 1 or 2, wherein R_1 is phenyl substituted by at least one chloride.

17. The compound as defined in anyone of claims 1 or 2, wherein R_1 is phenyl substituted by at least one nitro.

18. The compound as defined in anyone of claims 1 or 2, wherein R_1 is phenyl substituted by at least one methyl.

19. The compound as defined in anyone of claims 1 or 2, wherein R_1 is

phenyl substituted by at least one methoxy.

20. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl.

21. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl substituted by at least one halogen.

22. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl substituted by at least one chloride.

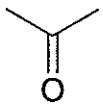
23. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl substituted by at least one methyl.

24. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl substituted by at least one methyl and one chloride.

25. The compound as defined in anyone of claims 1 or 2, wherein R_1 is isoxazolyl substituted by at least one methyl.

26. The compound as defined in anyone of claims 1 or 2, wherein R_1 is pyridinyl.

27. The compound as defined in anyone of claims 1 or 2, wherein J is:



28. The compound as defined in anyone of claims 1 or 2, wherein Y is $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, or $CONR_9OH$.

29. The compound as defined in claim 28, wherein R_5, R_a, R_b, R_9, R_{10}, R_{11}

and R_{16} are each independently H or C_{1-6} alkyl, provided that R_{16} is other than methyl or ethyl.

30. The compound as defined in anyone of claims 1 or 2, wherein Y is $COOR_{16}$, $CONR_{10}R_{11}$ or $CON(R_9)CH(R_5)$-$COOR_5$.

31. The compound as defined in claim 33, wherein R_5, R_9, R_{10}, R_{11} and R_{16} are each independently H or C_{1-6} alkyl, provided that R_{16} is other than methyl or ethyl.

32. The compound as defined in anyone of claims 1 or 2, wherein Y is COOH.

33. The compound as defined in anyone of claims 1 or 2, wherein Y is $CONHCH_2COOH$.

34. The compound as defined in anyone of claims 1 or 2, wherein Y is $COOCH_3$.

35. The compound as defined in anyone of claims 1 or 2, wherein Y is $COONH_2$.

36. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_{1-12} alkyl, C_{6-18} aralkyl, C_{3-12} heterocycle or C_{3-18} heteroaralkyl.

37. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_{1-12} alkyl, C_{6-18} aralkyl or C_{3-12} heterocycle.

38. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_{1-12} alkyl.

39. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_{6-18} aralkyl.

40. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_3-

$_{12}$ heterocycle.

41. The compound as defined in anyone of claims 1 or 2, wherein R_3 is methyl, ethyl, i-propyl, cyclopropyl, cyclohexyl, piperidinyl, piperazinyl, pyrrolidinyl, azetidinyl, aziridinyl, pyridinyl, piperidinylmethyl, dioxanyl, azepanyl or benzyl, which in each case is unsubstituted or substituted by one or more substituents chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino and guanido;
wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

42. The compound as defined in claim 41, wherein R_3 is chosen from H or methyl, isopropyl, piperidinyl, piperidinylmethyl or cyclohexyl.

43. The compound as defined in anyone of claims 1 or 2, wherein R_3 is H.

44. The compound as defined in anyone of claims 1 or 2, wherein R_3 is methyl.

45. The compound as defined in anyone of claims 1 or 2, wherein R_2 is C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

46. The compound as defined in anyone of claims 1 or 2, wherein R_2 is C_{3-6} heterocycle.

47. The compound as defined in anyone of claims 1 or 2, wherein R_2 is thienyl, furanyl, pyridinyl, oxazolyl, thiazolyl, pyrrolyl, benzofuranyl, indolyl,

benzoxazolyl, benzothienyl, benzothiazolyl, piperazinyl, pyrrolidinyl or quinolinyl, which in each case is unsubstituted or substituted by one or more substituents chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino and guanido;
wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

48. The compound as defined in claim 47, wherein R_2 is a heterocycle chosen from thienyl, furanyl, pyridinyl, pyrrolyl, indolyl, piperazinyl or benzothienyl.

49. The compound as defined in anyone of claims 1 or 2, wherein R_2 is C_{2-12} alkyl.

50. The compound as defined in anyone of claims 2 to 4, wherein R_2 is cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl cyclohexyl, cycloheptyl, 2-(cyclopentyl)-ethyl, methyl, ethyl, vinyl, propyl, propenyl, isopropyl, butyl, butenyl isobutyl, pentyl, neopentyl or t-butyl, which in each case is unsubstituted or substituted by one or more substituents chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino and guanido;
wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

51. The compound as defined in anyone of claims 1 or 2, wherein R_2 is C_{6-12} aryl.

52. The compound as defined in anyone of claims 1 or 2, wherein R_2 is indenyl, naphthyl or biphenyl.

53. The compound as defined in anyone of claims 2 to 4, wherein R_2 is phenyl substituted by one or more substituents chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino and guanido;
wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

54. The compound as defined in anyone of claims 1 or 2, wherein R_2 is phenyl substituted by one or two substituents chosen from halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino and guanido;
wherein R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

55. The compound as defined in anyone of claims 1 or 2, wherein R_2 is phenyl substituted by one or more substituent chosen from halogen, nitro, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkyloxy, $C(O)C_{1-6}$ alkyl, C_{6-12} aryl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, and azido,

wherein R_{12}, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, and C_{6-18} aralkyl,

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

56. The compound as defined in anyone of claims 1 or 2, wherein R_2 is phenyl substituted by one or two substituents chosen from halogen, nitro, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkyloxy, $C(O)C_{1-6}$ alkyl, C_{6-12} aryl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(O)OR_{12}$, cyano, and azido,

wherein R_{12}, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, and C_{6-18} aralkyl,

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

57. The compound as defined in anyone of claims 1 or 2, wherein R_2 is phenyl substituted by one or two substituents chosen from halogen, C_{1-6} alkyl, $NR_{13}R_{14}$, nitro, $CONR_{13}R_{14}$, $C(O)OC_{1-6}$ alkyl, COOH or C_{1-6} alkyloxy $C(O)OR_{12}$, cyano, and azido,

wherein R_{12}, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, and C_{6-18} aralkyl,
or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

58. The compound as defined in anyone of claims 1 or 2, wherein R_2 is methylphenyl.

59. The compound as defined in anyone of claims 1 or 2, wherein R_2 is dichlorophenyl.

60. The compound as defined in anyone of claims 1 or 2, wherein R_2 is chlorophenyl.

61. A compound chosen from:

Compound 1 3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-(3-IODO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 2 3-[(3-BENZOFURAN-2-YL-BENZYL)-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 3 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 4 3-{(2,4-DICHLORO-BENZOYL)-[5-(3-TRIFLUOROMETHYL-PHENYL)-FURAN-2-YLMETHYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 5 3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 6 5-(4-FLUORO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 7 3-(2,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 8 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 9 3-[(2,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 10 5- TERT -BUTYL-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 11 4-(TOLUENE-4-SULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 12 3-[(5-BENZOFURAN-2-YL-THIOPHEN-2-YLMETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 13 5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 14 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-CHLORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 15 5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 16 5-PHENYL-3-(TOLUENE-3-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 17 3-BENZENESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 18 3-(4-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 19 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 20 5-TERT-BUTYL-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 21 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 22 3-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 23 5-PHENYL-3-(THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 24 4-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 25 5-(3,5-BIS-TRIFLUOROMETHYL-PHENYL)-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 26 8-CHLORO-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-4H-1,5-DITHIA-CYCLOPENTA[A]NAPHTHALENE-2-CARBOXYLIC ACID

Compound 27 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 28 3-[3-(2,6-DICHLORO-PYRIDIN-4-YL)-UREIDO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 29 3-(2-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 30 3-(2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 31 5-PHENYL-3-(2-TRIFLUOROMETHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 32 3-(4- TERT -BUTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 33 3-(4-CHLORO-PHENOXYCARBONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 34 3-(3,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 35 5-PHENYL-3-(2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 36 3-(5-BROMO-6-CHLORO-PYRIDINE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 37 3-(5-CHLORO-THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 38 3-(5-CHLORO-3-METHYL-BENZO[B]THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 39 3-(4-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 40 3-(3-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 41 3-(5-CHLORO-1,3-DIMETHYL-1H-PYRAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 42 3-(3-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 43 3-(4-ISOPROPYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 44 3-(2,6-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 45 3-(2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 46 5-PHENYL-3-(5-[1,2,3]THIADIAZOL-4-YL-THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 47 5-PHENYL-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 48 3-(2,4-DICHLORO-BENZYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 49 3-(3-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 50 5-PHENYL-3-(3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 51 3-(2-CARBOXY-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER

Compound 52 5-PHENYL-3-(4-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 53 3-(2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 54 3-(2-CYANO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 55 3-(2,5-DICHLORO-THIOPHENE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 56 4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 57 5'-CHLORO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 58 5-(2,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 59 5-(4-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 60 3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 61 5-QUINOLIN-8-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 62 5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 63 5-(3-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 64 3-(TOLUENE-2-SULFONYLAMINO)-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 65 5-(3-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 66 5-(4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 67 5-(3-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 68 5-(4-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 69 5-(3,5-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 70 5-(3,4-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 71 3-(TOLUENE-2-SULFONYLAMINO)-5-VINYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 72 3-(4-CHLORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 73 3-[(4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 74 5-PHENYL-3-[(THIOPHENE-2-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 75 3-[METHYL-(THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 76 3-(2-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 77 3-(2,4-DIFLUORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 78 3-[(2,4-DIFLUORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 79 3-(TOLUENE-2-SULFONYLAMINO)-5-TRIMETHYLSILANYLETHYNYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 80 5-ETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 81 3-(TOLUENE-2-SULFONYLAMINO)-5-(3-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 82 5-BENZOYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 83 5-(4-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 84 5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 85 5-(3,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 86 5-PYRIDIN-4-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 87 5-PYRIDIN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 88 3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 89 5-(4-METHANESULFONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 90 5-(3-ACETYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 91 5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 92 3-(4-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 93 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 94 3-(3,5-DIMETHYL-ISOXAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 95 3-[(2-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 96 3-(2-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 97 3-[METHYL-(2-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 98 5-PHENYL-3-(5-TRIFLUOROMETHYL-PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 99 5-PHENYLETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 100 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 101 5-(2-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 102 5-(2-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 103 5-(2-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 104 5-(2-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 105 3'-METHYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 106 3-(TOLUENE-2-SULFONYLAMINO)-5-(2-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 107 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 108 5-STYRYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 109 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 110 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 111 3-[[5-(3-CHLORO-4-FLUORO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 112 3-[(4-OXO-1-PHENYL-1,3,8-TRIAZA-SPIRO[4.5]DECANE-8-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 113 3-{[4-(2-OXO-2,3-DIHYDRO-BENZOIMIDAZOL-1-YL)-PIPERIDINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-

CARBOXYLIC ACID

Compound 114 3-{[4-(4-NITRO-PHENYL)-PIPERAZINE-1-CARBONYL]-

AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 115 5-(2-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 116 5-(4-CHLORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 117 5-(3-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 118 3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 119 3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 120 5-PHENETHYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 121 5-(3-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 122 5-(4-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 123 5-(3-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 124 5-(4'-BROMO-BIPHENYL-4-YL)-3-(TOLUENE-2-

SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 125 5-(4-HYDROXYMETHYL-PHENYL)-3-(TOLUENE-2-

SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 126 5-FURAN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 127 5-BENZOFURAN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 128 5-PYRIDIN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 129 5-(4-NITRO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 130 3-[(BENZOFURAN-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 131 3-[(2,4-DIMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 132 3-[[5-(2-CYANO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 133 5-(4-FLUORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 134 5-[2-(4-CHLORO-PHENYL)-VINYL]-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 135 3-BENZENESULFONYLAMINO-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 136 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 137 5-PHENYL-3-(2-VINYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 138 3-(4-BROMO-2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 139 3-(2-ACETYLAMINO-4-METHYL-THIAZOLE-5-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 140 3-(4-ACETYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 141 3-(4-FLUORO-2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 142 3-(2-METHOXY-4-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 143 3-(3,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 144 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID ETHYL ESTER

Compound 145 3-(4-FLUORO-3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 146 3-(2-AMINO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 147 3-(3-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 148 3-(4-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 149 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 150 5-(3-CYANO-BENZYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 151 5-PHENYL-3-(2,4,6-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 152 3-(4-METHOXY-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 153 5-PHENYL-3-(2,3,4-TRICHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 154 5-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID METHYL ESTER

Compound 155 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-

YLSULFAMOYL)-2-METHYL-1,5-DIPHENYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER

Compound 156 5-PHENYL-3-{[4-(3-TRIFLUOROMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMIN}-THIOPHENE-2-CARBOXYLIC ACID

Compound 157 3-{[4-(4-FLUORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 158 3-{[4-(2,6-DIMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 159 3-{[4-(2-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 160 3-{[4-(3-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 161 4,4'-BIS-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5,5'-DICARBOXYLIC ACID

Compound 162 3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 163 5-(1-DIMETHYLSULFAMOYL-1H-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 164 5-(3-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 165 5-(4-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 166 5-(4-ACETYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 167 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-

YLSULFAMOYL)-2,5-DIMETHYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER

Compound 168 4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-3-METHYL-1-PHENYL-1H-PYRROLE-2-CARBOXYLIC ACID ETHYL ESTER

Compound 169 3-(3,5-DICHLORO-4-HYDROXY-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 170 5-(1H-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 171 5-(3-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 172 3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 173 3-{[2-(4-FLUORO-PHENYL)-ACETYL]-METHYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 174 3-(4-PENTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 175 3-(METHYL-PHENYLACETYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 176 3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 177 3-(4-METHYL-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 178 5-THIAZOL-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 179 5-PHENYL-3-[3-(3-PHENYL-PROPYL)-UREIDO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 180 3-[(3,4-DIHYDRO-1H-ISOQUINOLINE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 181 3-{[4-(4-METHOXY-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 182 3-{[4-(6-METHYL-PYRIDIN-2-YL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE

Compound 183 3-{[4-(4-CHLORO-BENZYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE

Compound 184 5-(5-METHYL-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 185 3-[ETHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 186 3-[(3-CHLORO-THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 187 3-[(2-BROMO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 188 3-[(4-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 189 3-(2-CHLOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 190 5-(4-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 191 5-(5-CHLORO-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 192 5-(4-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 193 5-(4-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 194 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 195 5-(4-HYDROXYMETHYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 196 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 197 5-(4-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 198 5-(4-METHOXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 199 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 200 5-(4-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 201 3-[CYCLOPENTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 202 5-BENZO[1,3]DIOXOL-5-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 203 3-[(2-HYDROXY-ETHYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 204 3-[(2,4-DICHLORO-BENZOYL)-ISOBUTYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 205 3-[(2-METHOXY-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 206 5-(3-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 207 5-(2-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 208 3-[(2,4-DICHLORO-BENZOYL)-PHENYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 209 3-[4-(TRIFLUOROMETHYL-BENZOYL)METHYLAMINE]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 210 3-[(4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-

PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 211 3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 212 5-(3,5-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 213 5-(3-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 214 5-(2,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 215 5-(4-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 216 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 217 5-(2-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 218 3-[(2-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 219 3-[(3,5-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 220 3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 221 3-(5-CARBOXY-4-CHLORO-2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC

ACID

Compound 222 5-PHENYL-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 223 3-(4-BROMO-2-FLUORO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 224 3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 225 5-(4-ISOBUTYL-PHENYL)-3-(3-METHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 226 3-[(4-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 227 3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 228 3-(2-CHLORO-4-CYANO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 229 5'-ACETYL-4-(TOLUENE-2-SULFONYLAMINO)-

[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 230 5-BENZO[B]THIOPHEN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 231 5-(4-BUTYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 232 5-(4-ETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 233 3-[BENZYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 234 3-[(4-CHLORO-2-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 235 3-[(2,4-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 236 5-(4-ACETYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 237 5-(4-ACETYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 238 5-(4-ACETYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 239 5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID TERT-BUTYL ESTER

Compound 240 3-[(2,4-DIMETHYL-BENZENESULFONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 241 3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 242 3-ETHANESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 243 3-[ISOPROPYL-(4-TRIFLUOROMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 244 3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 245 3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 246 3-[(6-CHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 247 3-[(4-TERT-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 248 5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 249 5-(4-ETHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 250 3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 251 3-[(BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 252 3-[METHYL-(NAPHTHALENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 253 3-[(3,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 254 3-[(3,5-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 255 3-[(4-BROMO-3-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 256 3-[(3-CHLORO-BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 257 3-[METHYL-(4-METHYL-3-NITRO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 258 5-(4-CARBAMOYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 259 5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 260 5-(1H-INDOL-5-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 261 3-[SEC -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 262 3-[(2,4-DIMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 263 5-(4-AZIDO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 264 3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 265 5-(4-CARBAMOYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 266 5-(2-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 267 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5- O - TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 268 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 269 5-(3-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 270 5-(3,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 271 5-(3-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 272 5-(3-ACETYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 273 5-(3-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 274 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 275 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 276 3-[(3,4-DIMETHOXY-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 277 3-[METHYL-(2,4,6-TRIFLUORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 278 3-[(2,3-DIFLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 279 3-[(3-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 280 3-[(2,3-DIFLUORO-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 281 3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 282 5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 283 5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 284 3-[(2-BROMO-4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 285 3-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 286 3-[METHYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 287 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-

PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER

Compound 288 5-(4-CYANO-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 289 3-(4-CHLORO-BENZENESULFONYLAMINO)-5-(4-CYANO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 290 5-(4-CYANO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 291 5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 292 5'-ACETYL-4-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 293 3-[METHYL-(4-METHYL-THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 294 5-(3-CHLORO-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 295 5'-CYANO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 296 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-2-YL-THIOPHENE-2-CARBOXYLIC ACID

Compound 297 3-[(2,4-DICHLORO-THIOBENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 298 5-PHENYL-3-(2,4,6-TRIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 299 3-[(1-CARBOXY-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 300 3-[(4-METHYL-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 301 3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 302 3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-3-YL-THIOPHENE-2-CARBOXYLIC ACID

Compound 303 5'-ACETYL-4-[METHYL-(4-METHYL-BENZOYL)-AMINO]-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 304 3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 305 3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 306 3-[(2-BROMO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 307 3-[(4-CHLORO-2-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 308 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-4-METHYL-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 309 3-[(2-BROMO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 310 3-[(4-CHLORO-2-IODO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 311 3-[(4-CYANO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 312 3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[4-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID

Compound 313 3-[(4-CHLORO-2-HYDROXY-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 314 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-METHYL-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 315 5- TERT -BUTYL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 316 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 317 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 318 5-[4-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 319 5-BENZOFURAN-2-YL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 320 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-HYDROXYMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 321 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 322 5-[4-(2-CARBOXY-VINYL)-PHENYL]-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 323 3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[3-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID

Compound 324 3-[ISOPROPYL-(2,4,6-TRIMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 325 5-[3-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 326 3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 327 3-[TERT -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 328 3-[(2-AMINO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 329 3-[(4-CHLORO-2-NITRO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 330 3-[(4-METHYL-BENZOYL)-(3-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 331 3-[(3-FLUORO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 332 5-(4-CARBOXY-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 333 3-[CYCLOPROPYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 334 3-[(3-TERT-BUTYL-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 335 3-[(3-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 336 3-[(2,4-DIFLUORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 337 3-[(4-CHLORO-2,5-DIFLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 338 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(2-METHYL-ALLYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 339 3-{ALLYL-[2-(4-CHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 340 3-[BENZYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 341 3-[(4-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 342 3-[(4-METHYL-BENZOYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 343 3-[(4-METHYL-BENZOYL)-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 344 3-[(3-METHOXY-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 345 3-[(2-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 346 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-ISOBUTYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 347 3-[ALLYL-(2-NAPHTHALEN-2-YL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 348 3-{ALLYL-[2-(2,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 349 3-{ALLYL-[2-(2-CHLORO-4-FLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 350 3-{ALLYL-[2-(3,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 351 3-{ALLYL-[2-(2,4-DIFLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 352 3-{ALLYL-[2-(4-TRIFLUOROMETHYL-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 353 3-{ALLYL-[2-(2,6-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 354 3-[ALLYL-(2-M-TOLYL-ACETYL)-AMINO]-5-PHENYL-

THIOPHENE-2-CARBOXYLIC ACID

Compound 355 5-(4-ACETYL-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 356 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 357 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 358 5'-ACETYL-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 359 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 360 4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5'-METHYL-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 361 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 362 3-(CYCLOHEXANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 363 3-{(2,4-DICHLORO-BENZOYL)-[1-(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 364 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT-BUTYL ESTER

Compound 365 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER

Compound 366 3-[(4-METHYL-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 367 5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound 368 3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 369 5-(4-METHANESULFONYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 370 3-(4-FLUORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 371 3-[(3-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 372 3-(4-CHLORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 373 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 374 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFINYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 375 5-(4-CARBOXY-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 376 5-BENZOFURAN-2-YL-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 377 3-[(2-ACETOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 378 3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 379 3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 380 3-(CYCLOHEPTANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 381 3-[ISOPROPYL-(4-METHYL-

CYCLOHEXANECARBONYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 382 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-METHYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 383 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 384 3-[(3-CYCLOPENTYL-PROPIONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 385 3-(BUTYRYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 386 3-(METHYL-PENT-4-ENOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 387 3-[ISOPROPYL-(5-METHYL-3-OXO-3H-ISOINDOL-1-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 388 3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 389 3-(METHYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 390 3-[METHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 391 3-(CYCLOPENTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 392 3-[(3-CYCLOPENTYL-PROPIONYL)-ETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 393 3-(CYCLOBUTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 394 3-(BUT-2-ENOYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 395 3-[ISOPROPYL-(4-METHYL-2-VINYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 396 3-[ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 397 3-(ALLYL-HEXANOYL-AMINO)-5-PHENYL-

THIOPHENE-2-CARBOXYLIC ACID

Compound 398 3-(ALLYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 399 3-(ALLYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 400 3-[ALLYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 401 3-[ALLYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 402 3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 403 3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 404 3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 405 3-[ISOPROPYL-(3-METHYL-CYCLOPENT-3-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 406 3-[(2-BENZYLOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 407 3-[(2,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 408 3-[ISOPROPYL-(3-METHYL-CYCLOPENTANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 409 3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 410 5-PHENYL-3-[PROPIONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 411 3-[ISOBUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 412 3-[(3-METHYL-BUTYRYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 413 3-[CYCLOPROPANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 414 3-[CYCLOBUTANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 415 3-[BUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 416 3-[(2-CYCLOPENTYL-ACETYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 417 3-[(4-TERT-BUTYL-BENZYL)-PROPIONYL-AMINO]-5-

PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 418 3-[(4-NITRO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 419 3-[(3-METHYL-BUTYRYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 420 3-[CYCLOPROPANECARBONYL-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 421 3-[(2-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 422 3-[(2-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 423 3-[(2-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 424 3-[(ADAMANTANE-1-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 425 3-[(2-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 426 3-[ACETYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 427 3-[(2-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 428 3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC

ACID

Compound 429 3-[(1-ACETYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 430 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-[4-(1 H -TETRAZOL-5-YL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID

Compound 431 3-[(2-CYANO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 432 3-[CYCLOBUTANECARBONYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 433 3-[BUTYRYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 434 3-[ACETYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 435 3-[CYCLOBUTANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 436 3-[CYCLOHEXANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 437 3-[(4-TERT-BUTYL-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 438 3-[(4-TERT-BUTYL-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 439 3-[(4-TERT-BUTYL-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 440 3-[(4-TERT-BUTYL-BENZYL)-BUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 441 3-[(4-TERT-BUTYL-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 442 3-[(4-TERT-BUTYL-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 443 3-[(2-CYCLOPENTYL-ACETYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 444 3-[(2-CHLORO-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 445 3-[(2-CYCLOPENTYL-ACETYL)-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 446 3-[BUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 447 3-[BUTYRYL-(2-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 448 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- M -TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 449 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-

THIAZOL-2-YL-THIOPHENE-2-CARBOXYLIC ACID

Compound 450 3-(ACETYL-BENZYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 451 3-(BENZYL-PROPIONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 452 3-[BENZYL-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 453 3-[BENZYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 454 3-(BENZYL-CYCLOPROPANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 455 3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 456 3-[(4-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 457 3-[(4-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 458 3-[(4-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 459 3-[(4-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 460 5-(4-ACETYL-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 461 3-[(4-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 462 3-[BUTYRYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 463 3-[(4-CHLORO-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 464 3-[ACETYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 465 3-[ISOBUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 466 3-[CYCLOPROPANECARBONYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 467 3-[(4-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 468 3-[ISOBUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 469 3-[CYCLOPROPANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 470 3-[BUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 471 3-[(3-METHOXY-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 472 3-[(3-METHOXY-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 473 3-[CYCLOBUTANECARBONYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 474 3-[(2-CARBAMOYL-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 475 3-[BUTYRYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 476 3-[ACETYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 477 3-[(3-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 478 3-[(3-CHLORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 479 3-[(3-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 480 3-[(3-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 481 3-[(3-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 482 3-[BUTYRYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 483 3-[ACETYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-

PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 484 3-[(2,4-DIFLUORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 485 3-[(2,4-DIFLUORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 486 3-[(2,4-DIFLUORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 487 3-[BENZYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 488 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(1H-INDOL-5-YL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 489 3-(BENZYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 490 3-[CYCLOHEXANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 491 3-{ALLYL-[2-(4-METHOXY-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 492 3-(ETHYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 493 3-(BUTYRYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 494 3-[ETHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 495 3-[CYCLOBUTANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 496 3-[BUTYRYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 497 3-(CYCLOPENTANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 498 3-(CYCLOHEXANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 499 3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PYRROLIDINE-1-CARBOXYLIC ACID TERT-BUTYL ESTER

Compound 500 3-[(1,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 501 5-(4-ETHYL-PHENYL)-3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 502 3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5- M -TOLYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 503 3-[(2,4-DICHLORO-BENZOYL)-PYRROLIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 504 4-{5-CARBOXY-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2H-PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 505 3-{[2-(HYDROXYIMINO-METHYL)-4-METHYL-

BENZOYL]-ISOPROPYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 506 3-[(1-CARBAMIMIDOYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 507 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-AZEPANE-1-CARBOXYLIC ACID TERT - BUTYL ESTER

Compound 508 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-

DICHLORO-BENZOYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 509 3-[AZEPAN-4-YL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 510 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID LITHIUM SALT

Compound 511 3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT - BUTYL ESTER

Compound 512 3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 513 3-[ISOPROPYL-(4-METHYL-2-OXO-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 514 3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH GENERIC INORGANIC NEUTRAL COMPONENT

Compound 515 3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 516 3-[(2-BENZYLOXY-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 517 3-[(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 518 3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-HYDROXYMETHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 519 3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 520 3-[(2-CHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 521 3-[(4,6-DICHLORO-1H-INDOLE-2-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 522 3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-METHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 523 4-{1-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-ETHYL}-PIPERIDINE-1-CARBOXYLIC

ACID BENZYL ESTER

Compound 524 4-{5-CARBOXY-4-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2 H -PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 525 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PYRIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 526 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PIPERIDIN-4-YL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH

TRIFLUORO-ACETIC ACID

Compound 527 3-[ISOPROPYL-(4-PROPYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 528 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM; TRIFLUORO-ACETATE

Compound 529 3-[(2,4-DICHLORO-BENZOYL)-(1-PIPERIDIN-4-YL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID

Compound 530 3-[(CYCLOHEX-3-ENECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 531 3-[(4-ETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 532 3-[(4-CHLORO-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 533 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-3-METHYL-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 534 3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 535 3-[(2,4-DICHLORO-BENZOYL)-(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 536 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(1-METHYL-PIPERIDIN-4-YL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 537 3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID

Compound 538 3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 539 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE CARBONYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER

Compound 540 3-[((1R,2S,4R)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 541 3-{ISOPROPYL-[1-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYL)-5-METHYL-1,2,3,6-TETRAHYDRO-PYRIDINE-2-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 542 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-FLUORO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 543 3-[(2,4-DICHLORO-BENZOYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 544 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE CARBONYL)-AMINO]-METHYL}-PIPERIDINIUM; TRIFLUORO-ACETATE

Compound 545 3-[(2-TERT-BUTOXYCARBONYLAMINO-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 546 2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PROPYL-AMINE TRIFLUOROACETIC ACID SALT

Compound 547 3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 548 3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 549 2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM CHLORIDE

Compound 550 3-(BENZOYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 551 {[5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBONYL]-AMINO}-ACETIC ACID

Compound 552 5-BROMO-3-(TOLUENE-2-SULFONYLAMINO)-

THIOPHENE-2-CARBOXYLIC ACID

Compound 553 3-[CYCLOHEXYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 554 3-[[1,3]DIOXAN-5-YL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 555 3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 556 3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 557 3-[(2,4-DICHLORO-BENZOYL)-(2-DIETHYLAMINO-THIAZOL-5-YLMETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 558 (5-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-THIAZOL-2-YL)-DIETHYL-AMMONIUM; CHLORIDE

Compound 559 5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 560 3-[((1S,2R,4S)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 561 3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-1-METHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 562 3-[(4S)-ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 566 3-METHYL-(4-METHYLBENZOYL)-AMINO)5-PHENYL THIOPHENE-2-CARBOXYLIC ACID (2-HYDROXY-ETHYL)AMIDE

Compound 567 5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID CYCLOBUTYLAMIDE

Compound 568 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMIDE

Compound 569 5-BROMO-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 570 5-(4-CHLORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANE-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 571 5-(4'-CHLORO-BIPHENYL-4-YL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 572 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(TETRAHYDRO-PYRAN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 573 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 574 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 575 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 576 5-(4-CYANO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound 577 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 578 3-[(2-METHOXY-1-METHYL-ETHYL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 579 3-[CYCLOHEXYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-2-carboxylic acid

Compound 582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid

Compound 583 3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid

Compound 584 3-(Methyl-p-tolyl-carbamoyl)-5-phenyl-thiophene-2-carboxylic acid

Compound 585 3-[(2,4-Dichloro-phenyl)-methyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid

or pharmaceutically acceptable salts thereof.

62. Use of a compound according to anyone of claims 1 to 61 for the manufacture of a medicament for treating or preventing a Flaviviridae viral infection in a host.

63. The use according to claim 62, wherein said medicament further comprises at least one other antiviral agent.

64. The use according to claim 63, wherein the at least one other antiviral agent is a viral serine protease inhibitor, a viral polymerase inhibitor, or a viral helicase inhibitor.

65. The use according to claim 63, wherein the at least one other antiviral agent is interferon α and ribavirin.

66. The use according to anyone of claims 63 to 65, wherein said compound and said at least one other antiviral agent are to be administered sequentially.

67. The use according to anyone of claims 62 to 65, wherein said compound and said at least one other antiviral agent are to be administered simultaneously.

68. The use according to claim 60, wherein said medicament further comprises at least one additional agent chosen from immunomudulating agents, antioxidant agents, antibacterial agents, and antisense agents.

69. The use of claim 68, wherein said additional agent is silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

70. The use according to anyone of claims 68 or 69, wherein said

compound and said additional agent are to be administered sequentially.

71. The use according to anyone of claims 68 to 69, wherein said compound and said additional agent are to be administered simultaneously.

72. The use as defined in anyone of claims 62 to 70, wherein said Flaviviridea viral infection is hepatitis C viral infection (HCV).

73. A pharmaceutical composition comprising at least one compound according to any one of claims 1 to 61 and at least one pharmaceutically acceptable carrier or excipient.

74. A pharmaceutical composition as defined in claim 73, further comprising one or more additional agents chosen from antiviral agents, immunomudulating agents, antioxidant agents, antibacterial agents, and antisense agents.

75. The pharmaceutical composition as defined in claim 74, wherein said one or more additional agents is an antiviral agent ~~is~~ chosen from ~~a~~ viral serine protease inhibitors, viral polymerase inhibitors and viral helicase inhibitors.

76. The pharmaceutical composition as defined in claim 74, wherein said one or more additional agents is an antiviral agent ~~is~~ chosen from interferon α and ribavirin.

77. The pharmaceutical composition as defined in claim 74, wherein said additional agent is silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

78. The composition as defined in anyone of claims 73-77 wherein said Flaviviridae viral infection is hepatitis C viral infection (HCV).

79. The use of a compound according to any one of claims 1 to 61 for the

manufacture of a medicament for inhibiting or reducing the activity of viral polymerase in a host.

80. The use of a compound as defined in claim 79, wherein said medicament further comprises one or more additional agents chosen from antiviral agents, immunomudulating agents, antioxidant agents, antibacterial agents, and antisense agents.

81. The use as defined in claim 80, wherein the said one or more additional agents is an antiviral agent is chosen from viral serine protease inhibitors, viral polymerase inhibitors and viral helicase inhibitors.

82. The use as defined in claim 80, wherein the said one or more additional agents is an antiviral agent is chosen from interferon α and ribavirin.

83. The use of as defined in claim 80, wherein said additional agent is silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

84. The use as defined in anyone claims 80 to 83, wherein said compound and said additional agent are administered sequentially.

85. The use as defined in anyone of claims 80 to 83, wherein said compound and said additional agent are administered simultaneously.

86. The use as defined in claim 79, wherein said medicament further comprises one or more viral polymerase inhibitors.

87. The method as defined in anyone of claims 79 or 86, wherein said viral polymerase is a Flaviviridae viral polymerase.

88. The method as defined in anyone of claims 79 or 86, wherein said viral polymerase is a RNA-dependant RNA-polymerase.

89. The method as defined in anyone of claims 79 or 86, wherein said viral polymerase is HCV polymerase.

90. The use of a compound according to any one of claims 1 to 61 for the manufacture of a medicament for inhibiting or reducing the activity of viral helicase in a host.

91. The use as defined in claim 90, wherein said compound is chosen from:

Compound #14 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid,

Compound #19 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid,

Compound #223 3-(4-Bromo-2-fluorobenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid,

Compound #224 3-(4-Bromo-2-methylbenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid,

Compound #225 5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-amino)-thiophene-2-carboxylic acid,

Compound #581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-2-carboxylic acid,

Compound #227 3-[2,5-Bis-(2,2,2-trifluoroethoxy)-benzenesulfonylamino]-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid,

Compound #228 3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid,

Compound #582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid, and

pharmaceutically acceptable salts thereof.

92. The use as defined in anyone of claims 90 or 91, wherein said viral helicase is a flaviviridea helicase.

93. The use as defined in anyone of claims 90 or 91, wherein said viral helicase is HCV helicase.

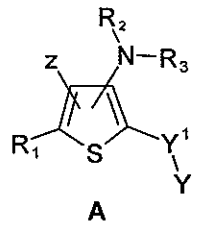
94. A combination comprising a compound according to any one of claims 1 to 61 and one or more additional agents chosen from viral serine protease inhibitors, viral polymerase inhibitors, viral helicase inhibitors, immunomudulating agents, antioxidant agents, antibacterial agents, and antisense agents.

95. The combination as defined in claim 94, wherein said additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine, cyclosporin, interferon α and ribavirin.

96. The combination as defined in anyone of claims 94 or 95, wherein said compound and said additional agent are administered sequentially.

97. The combination as defined in anyone of claims 94 or 95, wherein said compound and said additional agent are administered simultaneously.

98. A process for preparing a compound of formula A:

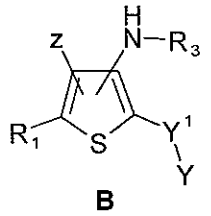


A

said process comprising the steps of adding:

an enol ether;
an hydride donating agent; and
an organic carboxylic acid;

to a compound of formula B:



B

wherein,

Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)\text{-}SO_2\text{-}R_5$, $CONR_9OH$ or halogen, wherein R_9, R_5, R_{10} and R_{11} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl; or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
R_{16} is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;

R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl; and

Z is chosen from H, halogen, C_{1-6} alkyl,

wherein

in each case above alkyl is straight chain, branched chain or cyclic and is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkenyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkynyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aryl is a carbocyclic moiety containing at least one benzenoid-type ring which are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aralkyl is an aryl group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl group.

in each case above heterocycle groups are saturated or unsaturated,

monocyclic or polycyclic moieties containing at least one heteroatom selected from oxygen, sulfur or nitrogen, and are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

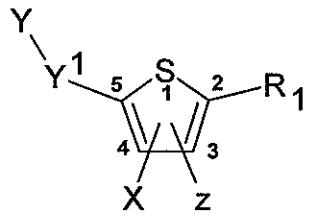
in each case above heteroaralkyl groups are heterocycle groups attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

sulfur atoms are in each case above present in the form of S, SO, or SO_2; and

R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-10} heterocycle, C_{3-10} heteroaralkyl, and C_{6-18}

aralkyl, or Rc and Rd are taken together with the oxygens form a 5 to 10 membered heterocycle, or R_{13} and R_{14} are taken together with the nitrogen form a 3 to 10 membered heterocycle.

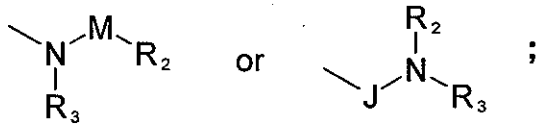
99. A compound having the formula I:



(I)

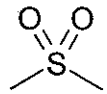
or a pharmaceutically acceptable salt thereof;

wherein,
X is:



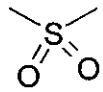
;

M is:



;

J is:



;

Y^1 is a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)\text{-}SO_2\text{-}R_5$, $CONR_9OH$ or halogen;

R_9, R_5, R_{10} and R_{11} are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl, or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl, or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

R_{16} is H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl, provided that R_{16} is other than methyl or ethyl;

R_1 is C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

R_2 is C_{2-12} alkyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R_3 is H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C $_{6-18}$ aralkyl; and

Z is H, halogen, or C_{1-6} alkyl;

wherein

in each case above alkyl is straight chain, branched chain or cyclic and is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkenyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkynyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aryl is a carbocyclic moiety containing at least one benzenoid-type ring which are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl,

C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aralkyl is an aryl group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl group.

in each case above heterocycle groups are saturated or unsaturated, monocyclic or polycyclic moieties containing at least one heteroatom selected from oxygen, sulfur or nitrogen, and are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above heteroaralkyl groups are heterocycle groups attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

sulfur atoms are in each case above present in the form of S, SO, or SO_2; and

R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-10} heterocycle, C_{3-10} heteroaralkyl, and C_{6-18} aralkyl, or Rc and Rd are taken together with the oxygens form a 5 to 10 membered heterocycle, or R_{13} and R_{14} are taken together with the nitrogen form a 3 to 10 membered heterocycle,

with the proviso that:

i) when X is 4-Chloro-2,6-dimethyl-benzenesulfonamide and, R_1 is phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$;

ii) when X is Toluene-4-sulfonamide and R_1 is 4-chloro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$;

iii) when X is Toluene-4-sulfonamide and R_1 is 4-fluoro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$; and

iv) when X is Toluene-4-sulfonamide and R_1 is 4-methoxy-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than $CONH_2$.

100. The compound as defined in claim 99, wherein R_1 is a C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

101. The compound as defined in claim 99, wherein Y^1 is a bond.

102. The compound as defined in claim 99, wherein Y^1 is COOH.

103. The compound as defined in claim 99, wherein R_3 is H, C_{1-12} alkyl, C_{6-18} aralkyl or C_{3-12} heterocycle.

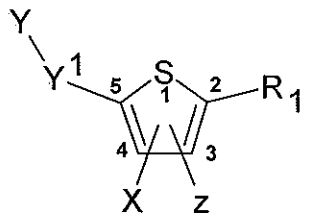
104. The compound as defined in claim 99, wherein R_2 is C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

105. A pharmaceutical composition comprising at least one compound according to claim 99 and a pharmaceutically acceptable carrier or excipient.

106. Use of a compound according to claim 99 for the manufacture of a medicament for treating or preventing a Flaviridea infection in a host and/or for inhibiting or reducing the activity of viral polymerase in a host and/or for inhibiting or reducing the activity of viral helicase in a host.

107. A combination comprising least one compound according to claim 99 and one or more additional agents chosen from viral serine protease inhibitors, viral polymerase inhibitors, viral helicase inhibitors, immunomudulating agents, antioxidant agents, antibacterial agents and antisense agents.

108. A compound having the formula I:

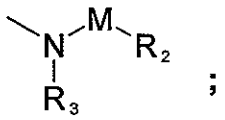


(I)

or a pharmaceutically acceptable salt thereof;

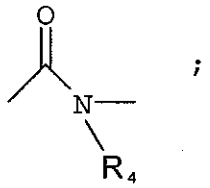
wherein,

X is:



;

M is:



;

R_4 is C $_{1-6}$ alkyl;

Y^1 is a bond, C_{1-6} alkyl, C $_{2-6}$ alkenyl or C $_{2-6}$ alkynyl;

Y is $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)\text{-}SO_2\text{-}R_5$, $CONR_9OH$ or halogen;

R_9, R_5, R_{10} and R_{11} are each independently H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl, or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

R_a and R_b are each independently H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl, or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

R_{16} is H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl, provided that R_{16} is other than methyl or ethyl;

R_1 is C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C $_{6-18}$ aralkyl;

R_2 is C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, or C $_{6-18}$ aralkyl;

R_3 is H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C $_{6-18}$ aralkyl; and

Z is H, halogen, or C_{1-6} alkyl;

wherein

in each case above alkyl is straight chain, branched chain or cyclic and is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkenyl is unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above alkynyl is unsubstituted or substituted by one or more

halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aryl is a carbocyclic moiety containing at least one benzenoid-type ring which are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above aralkyl is an aryl group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl group.

in each case above C_{3-10} heterocycle groups are saturated or unsaturated, monocyclic or polycyclic moieties containing at least one heteroatom selected from oxygen, sulfur or nitrogen, and are unsubstituted or substituted by one or more halogen, nitro, nitroso, SO_3R_{12}, PO_3RcRd, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(O)C_{1-6}$ alkyl, $C(O)C_{2-6}$ alkenyl, $C(O)C_{2-6}$ alkynyl, $C(O)C_{6-12}$ aryl, $C(O)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, N $R_{13}R_{14}$, $C(O)OR_{12}$, cyano, azido, amidino or guanido;

in each case above C_{3-10} heteroaralkyl groups are heterocycle groups attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

sulfur atoms are in each case above present in the form of S, SO, or SO_2; and

R_{12}, Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-10} heterocycle, C_{3-10} heteroaralkyl, and C_{6-18} aralkyl, or Rc and Rd are taken together with the oxygens form a 5 to 10 membered heterocycle, or R_{13} and R_{14} are taken together with the nitrogen form a 3 to 10

membered heterocycle.

109. The compound as defined in claim 108, wherein R_1 is a C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

110. The compound as defined in claim 108, wherein Y^1 is a bond.

111. The compound as defined in claim 108, wherein Y^1 is COOH.

112. The compound as defined in claim 108, wherein R_3 is H, C_{1-12} alkyl, C_{6-18} aralkyl or C_{3-12} heterocycle.

113. The compound as defined in claim 108, wherein R_2 is C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

114. A pharmaceutical composition comprising at least one compound according to claim 108 and a pharmaceutically acceptable carrier or excipient.

115. Use of a compound according to claim 108 for the manufacture of a medicament for treating or preventing a Flaviridea infection in a host and/or for inhibiting or reducing the activity of viral polymerase in a host and/or for inhibiting or reducing the activity of viral helicase in a host.

116. A combination comprising least one compound according to claim 108 and one or more additional agents chosen from viral serine protease inhibitors, viral polymerase inhibitors, viral helicase inhibitors, immunomudulating agents, antioxidant agents, antibacterial agents and antisense agents.