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(54) Title: ALPHA-METHYL-BENZYL-CONTAINING THIOUREA INHIBITORS OF HERPES VIRUSES CONTAINING A PHENYLENYLAMINE GROUP

(57) Abstract

Compounds having formula (I) wherein R₁ – R₅ are independently selected from hydrogen, alkyl of 1 to 6 carbon atoms, alkyloxy of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 carbon members, aryl, heteroaryl, halogen, CN, NO₂, CO₂R₆, OR₆, OR₆, SR₆, OR₆, SO₂R₆, CONR₆, N(R₆), or W-Y-(CH₂)n-Z provided that at least one of R₁-R₅ is not hydrogen; or R₁ and R₅, or R₁ and R₄, or R₂ and R₃, or R₂ and R₄, taken together to form a 3 to 7 membered heterocycloalkyl or 3 to 7 membered heteroaryl; and R₆ are independently hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 members, aryl or heteroaryl, or R₂ and R₅, taken together may form a 3 to 7 membered heterocycloalkyl; W is O, NR₆, or is absent; Y is –(CO)₆ or –(CO₂)₆, or is absent; Z is alkyl of 1 to 4 carbon atoms, –CN, –CO₂R₆, COR₆, –CONR₆, OR₆, –OR₆, –SR₆, –SOR₆, –SO₂R₆, SR₆N(R₇R₈) –N(R₇R₈) or phenyl; G is aryl or fused bicyclic heteroaryl; X is a bond, –NH, alkyl of 1 to 6 carbon atoms, alkyloxy of 1 to 6 carbon atoms, alkylamino of 1 to 6 carbon atoms, or (CH₂)₆; J is alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, phenyl or benzyl; and n is an integer from 1 to 6; useful in the treatment of diseases associated with herpes viruses including human cytomegalovirus, herpes simplex viruses, Epstein–Barr virus, varicella–zoster virus, human herpesviruses–6 and–7, and Kaposi herpesvirus.
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ALPHA-METHYL BENZYL-CONTAINING THIOUREA INHIBITORS
OF HERPES VIRUSES CONTAINING A PHENYLENEDIAMINE GROUP

Background of the Invention

[Frenkel, N., and Roffman, E. 1996. Human Herpesvirus 7, p. 2609-2622. In B. N. Fields, D. M. Knipe, and P. M. Howley (ed.), Fields Virology, 3rd ed. Lippincott-Raven Publishers, Philadelphia, PA)]; and Kaposi’s sarcoma (HHV-8 [Neipel, F., Albrecht, J.C., and Fleckenstein, B. 1997. Cell-homologous genes in the Kaposi’s sarcoma-associated rhadinovirus human herpesvirus 8: determinants of its pathogenicity? J. Virol. 71:4187-92, 1997]). HCMV is considered in more detail below. Following the primary infection, herpesviruses establish latency within the infected individual and remain there for the remainder of his/her life. Periodic reactivation of latent virus is clinically relevant. In the case of HSV, reactivated virus can be transmitted to infants during birth, causing either skin or eye infection, central nervous system infection, or disseminated infection (i.e. multiple organs or systems). Shingles is the clinical manifestation of VZV reactivation. Treatment of HSV and VZV is generally with antiviral drugs such as acyclovir (Glaxo Wellcome), ganciclovir (Roche) and foscarnet (Asta) which target viral encoded DNA polymerase.

HCMV is a ubiquitous opportunistic pathogen infecting 50-90% of the adult population (Britt, W. J., and Alford, C. A. 1996. Cytomegalovirus, p. 2493-2523. In B. N. Fields, D. M. Knipe, and P. M. Howley (ed.), Fields Virology, 3rd ed. Lippincott-Raven Publishers, Philadelphia, Pa.). Primary infection with HCMV is usually asymptomatic, although heterophile negative mononucleosis has been observed. The virus is horizontally transmitted by sexual contact, breast milk, and saliva. Intrauterine transmission of HCMV from the pregnant mother to the fetus occurs and is often the cause of serious clinical consequences. HCMV remains in a latent state within the infected person for the remainder of his/her life. Cell-mediated immunity plays a central role in controlling reactivation from latency. Impaired cellular immunity leads to reactivation of latent HCMV in seropositive persons.

HCMV disease is associated with deficient or immature cellular immunity. There are 3 major categories of persons with HCMV disease (reviewed by Britt and Alford, 1996). (1) In immunocompromised (AIDS) patients, HCMV is one of the two most common pathogens causing clinical disease (the other is Pneumocystis). The most common manifestation of HCMV in AIDS is retinitis, although infection of
other organs including the adrenal glands, lungs, GI tract, and central nervous system are also reported frequently. 90% of AIDs patients have active HCMV infection; 25-40% (~85,000 patients in the United States) have life- or sight-threatening HCMV disease. HCMV is the cause of death in 10% of persons with AIDs. (2) Due to immune system suppression to reduce the risk of graft rejection, HCMV reactivation or reinfection is common amongst kidney, liver, heart, and allogeneic bone marrow transplant patients. Pneumonia is the most common HCMV disease in these patients, occurring in up to 70% of these transplant patients. (3) Congenital infection due to HCMV occurs in 1% of all births, about 40K per year. Up to 25% of these infants are symptomatic for HCMV disease between ages 0-3 years. HCMV disease is progressive, causing mental retardation and neurological abnormalities, in children. Recent studies suggest that treatment with anti-HCMV drugs may reduce morbidity in these children.

Several antiviral drugs are currently being marketed (Bron, D., R. Snoeck, and L. Lagneaux. 1996. New insights into the pathogenesis and treatment of cytomegalovirus. Exp. Opin. Invest. Drugs 5:337-344; Crumpacker, C. 1996. Ganciclovir. New Eng. J. Med. 335:721-729; Sachs, S., and F. Alrabiah. 1996. Novel herpes treatments: a review. Exp. Opin. Invest. Drugs 5:169-183). These include: ganciclovir (Roche), a nucleoside analog with hemopoietic cell toxicity; foscarnet (Astra), a pyrophosphate analog with nephrotoxicity; and cidofovir, Gilead), a nucleoside phosphonate with acute nephrotoxicity. Each of these drugs target the viral-encoded DNA polymerase, are typically administered intravenously due to their low bioavailability, and, as noted above, are the source of significant toxicity. Ganciclovir-resistant mutants which arise clinically are often cross-resistant with cidofovir. Hence, there is a need for safer (i.e. less toxic), orally bioavailable antiviral drugs which are directed against novel viral targets.

Phenyl thioureas are disclosed for use in a variety of pharmaceutical applications. Armistead, et al., WO 97/40028, teaches phenyl ureas and thioureas as inhibitors of the inosine monophosphate dehydrogenase (IMPDH) enzyme which is taught to play a role in viral replication diseases such herpes.

Widdowson, et al., WO 96/25157, teaches phenyl urea and thiourea compounds of the below formula for treating diseases mediated by the chemokine, interleukin-8.
Morin, Jr., et al., U.S. Patent No. 5,593,993 teaches certain phenyl thiourea compounds for treatment of AIDs and the inhibition of the replication of HIV and related viruses.

Therefore, it is an object of this invention to provide compounds, and pharmaceutically acceptable salts thereof, to inhibit and/or treat diseases associated with herpes viruses including human cytomegalovirus, herpes simplex viruses, Epstein-Barr virus, varicella-zoster virus, human herpesviruses-6 and -7, and Kaposi herpesvirus.

**Description of the Invention**

In accordance with the present invention are provided compounds having the formula:

![Chemical Structure](image)

wherein

- $R_1$-$R_5$ are independently selected from hydrogen, alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 carbon members, aryl, heteroaryl, halogen, -CN, -NO$_2$, -CO$_2$R, -COR, -OR, -SR, -SOR, -SO$_2$R, -CONR, -NR, -N(R,R)$_2$, -N(R,R) or W-Y-(CH)Z-Z provided that at least one of $R_1$-$R_5$ is not hydrogen; or $R_1$ and $R_2$ or $R_3$ and $R_4$, taken
together form a 3 to 7 membered heterocycloalkyl or 3 to 7 membered
heteroaryl;
\( R_9 \) and \( R_9 \) are independently hydrogen, alkyl of 1 to 6 carbon atoms,
perhaloalkyl of 1 to 6 carbon atoms, or aryl;

5 \( R_9 \) is hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon
atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10
members, aryl or heteroaryl, or

\( R_9 \) and \( R_{9'} \), taken together may form a 3 to 7 membered heterocycloalkyl;
\( W \) is O, NR\(_{9'} \), or is absent;

10 \( Y \) is -(CO)\( \)- or -(CO\(_2\))\( \)-, or is absent;
\( Z \) is alkyl of 1 to 4 carbon atoms, -CN, -CO\(_2\)R\(_{9''} \), COR\(_{9'} \), -CONR\(_{9'} \)R\(_{9''} \), -OCOR\(_{9'} \),
-NR\(_{9'}\)COR\(_{9''} \), -OCNOR\(_{9''} \), -OR\(_{9'} \), -SR\(_{9'} \), -SOR\(_{9'} \), -SO\(_{2}\)R\(_{9'} \), SR6N(R7R8),
-N(R(R\(_9\),R\(_9\)) or phenyl;

G is aryl optionally substituted with one or more substituents selected from
alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl
of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl
of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 carbon members,
aryl, heteroaryl, halogen, -CN, -NO\(_2\), -CO\(_2\)R\(_9\), -COR\(_{9'} \), -OR\(_{9'} \), -SR\(_{9'} \),
-SOR\(_{9'} \), -SO\(_{2}\)R\(_{9'} \), -CONR\(_{9'} \), -NR\(_{9'}\)N(R\(_{9'}\),R\(_9\)), -N(R(R\(_9\),R\(_9\)) or W-Y-(CH\(_2\))\( _n \)-Z;
or

G is a fused bicyclic heteroaryl;

X is a bond, -NH, alkyl of 1 to 6 carbon atoms, alkenyl of 1 to 6 carbon
atoms, alkoxy of 1 to 6 carbon atoms, thioalkyl of 1 to 6 carbon
atoms, alkylamino of 1 to 6 carbon atoms, or (CH\(_2\))\( J \)

25 \( J \) is alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, phenyl or
benzyl; and

\( n \) is an integer from 1 to 6;
or a pharmaceutically acceptable salt.

30 In some preferred embodiments of the present invention, \( R_9 \) are
independently, alkyl of 1 to 6 carbon atoms, halogen, perhaloalkyl of 1 to 6 carbon
atoms, OR\(_{9'} \) or N(R(R\(_9\))_. Preferably, 1 to 3 of \( R_9 \) is not hydrogen. In still more
preferred embodiments of the invention \( R_9 \) is halogen, cyano or trifluoromethyl.
In some embodiments of the present invention G is substituted. In preferred embodiments of the invention G is 2-fluorophenyl. In other preferred embodiments of the present invention G is benzofuran, isoquinoline or quinoline.

In some embodiments of the present invention X is a bond, C1-C4 alkyl or CH(J) where J is C1-C6 alkyl. Preferably, when X is C1-C4 alkyl, said alkyl is straight chain alkyl. When X is CH(J), J is preferably methyl.

Preferred compounds of the present invention are the following compounds which include pharmaceutical salts thereof.

N-{4-[3-(1-Benzofuran-2-yl-ethyl)-thioureido]-phenyl}-2-trifluoromethyl-benzamide,

N-(4-Fluoro-phenyl)-4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl-amide,

Isoquinoline-1-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-amide,

Isoquinoline-1-carboxylic acid {4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl}-amide,

Isoquinoline-1-carboxylic acid {4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl}-amide,

Isoquinoline-1-carboxylic acid (4-{3-[1-(4-cyano-phenyl)-ethyl]-thioureido}-phenyl)-amide,

Benzofuran-2-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-amide,

Benzofuran-2-carboxylic acid {4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl}-amide,

Benzofuran-2-carboxylic acid (4-{3-[1-(4-bromo-phenyl)-ethyl]-thioureido}-phenyl)-amide,

Benzofuran-2-carboxylic acid (4-{3-[1-(4-cyano-phenyl)-ethyl]-thioureido}-phenyl)-amide,

Isoquinoline-3-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-amide,

Isoquinoline-3-carboxylic acid {4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl}-amide,
Isoquinoline-3-carboxylic acid (4-[3-[1-(4-cyano-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Isoquinoline-3-carboxylic acid (4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Quinoline-3-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Quinoline-4-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Quinoline-6-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Quinoline-8-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide,
N-(4-[3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido]-phenyl)-2-trifluoromethyl-benzamide,
2-Cyano-N-(4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-benzamide,
N-(4-[3-[3-Chloro-4-isobutoxy-phenyl]-thioureido]-phenyl)-2-fluoro-benzamide,
2-Fluoro-N-{4-[3-(3-fluoro-4-methoxy-phenyl)-thioureido]-phenyl}-benzamide,
N-(4-[3-[3-Chloro-4-(2-methoxy-ethoxy)-phenyl]-thioureido]-phenyl)-2-fluoro-benzamide,
2-Fluoro-N-{4-[3-(3-fluoro-4-methyl-phenyl)-thioureido]-phenyl}-benzamide,
2-Fluoro-N-{4-[3-(4-methoxy-3-trifluoromethyl-phenyl)-thioureido]-phenyl}-benzamide,
N-{4-[3-(2-Amino-5-trifluoromethyl-phenyl)-thioureido]-phenyl}-2-fluoro-benzamide,
N-(4-[3-[1-(3-Chloro-4-methoxy-phenyl)-ethyl]-thioureido]-phenyl)-2-fluoro-benzamide,
N-{4-[3-(5-Chloro-2-hydroxy-phenyl)-thioureido]-phenyl}-2-fluoro-benzamide,
N-{4-[3-(1-Benzofuran-2-yl-ethyl)-thioureido]-phenyl}-2-fluoro-benzamide,
2-Fluoro-N-{4-[3-(4-methyl-3-trifluoromethyl-phenyl)-thioureido]-phenyl}-benzamide,
(S)-N-{4-[3-{1-(4-Bromo-phenyl)-ethyl}-thioureido]-phenyl}-2-fluoro-benzamide,
5 N-(4-{3-{[(1R)-1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl}-2-fluoro-benzamide,
2-Fluoro-N-{4-[3-{2-methoxy-4-(2,2,2-trifluoro-ethoxy)-phenyl]-thioureido}{
phenyl}-benzamide,
N-{4-[3-{2-Amino-5-fluoro-phenyl}-thioureido]-phenyl}-2-fluoro-benzamide,
10 N-(4-{3-[1-(4-Dimethylsulfamoyl-phenyl)-ethyl]-thioureido}-phenyl}-2-fluoro-benzamide,
2-Fluoro-N-{4-{3-{1-[4-(piperidine-1-sulfonyle-phenyl)-ethyl]-thioureido}\{
phenyl}-benzamide,
N-(4-{3-[2,4-Bis-(2,2,2-trifluoro-ethoxy)-phenyl]-thioureido}-phenyl}-2-fluoro-benzamide,
2-Fluoro-N-{4-[3-{[(1S)-1-p-tolyl-ethyl]-thioureido}-phenyl}-benzamide,
2-Fluoro-N-{4-[3-{[(1R)-1-p-tolyl-ethyl]-thioureido}-phenyl}-benzamide,
2-Fluoro-N-{4-[3-{[(1S)-1-phenyl-ethyl]-thioureido}-phenyl}-benzamide,
N-(4-{3-{[(1R)-1-(4-Chloro-phenyl)-ethyl]-thioureido}{-phenyl)-2-fluoro-
benzamide,
N-(4-{3-{[(1S)-1-(4-Chloro-phenyl)-ethyl]-thioureido}-phenyl}-2-fluoro-
benzamide,
2-Fluoro-N-{4-{3-{[(1R)-1-phenyl-ethyl]-thioureido}-phenyl}-benzamide,
2-Fluoro-N-{4-{3-[1-(4-Cyanophenyl)-ethyl]-thioureido}{-phenyl}-2-methoxy-
benzamide,
N-{4-{3-[1-Benzofuran-2-yl-ethyl]-thioureido]-phenyl}-2-methoxy-
benzamide,
N-(4-{3-[1-(4-Bromophenyl)-ethyl]-thioureido}-phenyl}-2-methoxy-
benzamide,
30 3-Cyano-N-{4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}{-phenyl}-benzamide,
N-(4-{3-[1-(4-Fluorophenyl)-ethyl]-thioureido}{-phenyl}-4-trifluoromethyl-
benzamide,
4-Cyano-N-{4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}{-phenyl}-benzamide,
N-(4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-2-fluoro-benzamide,
N-(4-{3-[1S)-1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-4-fluoro-benzamide,
N-(4-{3-[1S)-1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-2-methoxy-benzamide,
N-(4-{3-[1R)-1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-2-methoxy-benzamide,
2-fluoro-N-{4-{[(1-[2-fluoro-4-(trifluoromethyl)phenyl]ethyl)amino}
carbothioyl]amino}phenyl)benzamide,
Isoquinoline-1-carboxylic acid (4-{3-[1S)-1-(4-bromo-phenyl)-ethyl]-
thioureido}-phenyl)-amide,
Isoquinoline-3-carboxylic acid (4-{3-[1S)-1-(4-bromo-phenyl)-ethyl]-
thioureido}-phenyl)-amide,
Isoquinoline-1-carboxylic acid (4-{3-[1S)-1-(4-chloro-phenyl)-ethyl]-
thioureido}-phenyl)-amide,
Isoquinoline-1-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-amide, and
N-{4-{[(1S)-1-(4-cyanophenyl)ethyl]amino}carbothioyl]amino}phenyl}-1-
nophenyl)ethyl]amino}carbothioyl]amino]phenyl}-1-isoquinolinecarboxamide,
and pharmaceutical salts thereof.

Unless otherwise defined, the terms used herein have the following meanings.
Alkyl as used herein refers to straight or branched chain lower alkyl of 1 to 6
carbon atoms. Exemplary alkyl groups include methyl, ethyl, propyl, isopropyl,
butyl, isobutyl, t-butyl, pentyl and hexyl.
Alkenyl as used herein refers to straight or branched chain lower alkyl of 2 to
6 carbon atoms containing at least one carbon-carbon double bond. Alkenyl includes
vinyl groups.
Alkynyl as used herein refers to straight or branched chain lower alkyl of 2 to
6 carbon atoms containing at least one carbon-carbon triple bond.
Alkyl, alkenyl and alkynyl groups of the present invention may be substituted
or unsubstituted.
Cycloalkyl refers to a saturated mono or bicyclic ring system of 3 to 10 carbon atoms. Exemplary cycloalkyl groups include cyclopentyl, cyclohexyl and cycloheptyl. Cycloalkyl groups of the present invention may be substituted or unsubstituted.

Heterocycloalkyl refers to a saturated mono or bicyclic ring system of 3 to 10 members having 1 to 3 heteroatoms selected from N, S and O, including, but not limited to aziridinyl, azetidinyl, imidazolidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyrazolidinyl, piperidinyl, and pyrrolidinyl. Heterocycloalkyl groups of the present invention may be substituted or unsubstituted.

Aryl, as used herein refers to an aromatic mono or bicyclic ring of 5 to 10 carbon atoms. Exemplary aryl groups include phenyl, naphthyl, and biphenyl. Aryl groups of the present invention may be substituted or unsubstituted.

Heteroaryl as used herein refers to an aromatic mono or bicyclic ring of 5 to 10 members having 1 to 3 heteroatoms selected from N, S or O including, but not limited to thiazolyl, thiazadiazolyl, oxazolyl, furyl, indolyl, benzothiazolyl, benzotriazolyl, benzodioxyl, indazolyl, and benzofuryl. Preferred heteroaryls include quinolyl, isoquinolyl, napthalenyl, benzofuranyl, benzothienyl, indolyl, pyridyl, pyrazinyl, thienyl, furyl, pyrrolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, pyrazolyl, triazolyl, thiazadiazolyl, and imidazolyl. Heteroaryl groups of the present invention may be substituted or unsubstituted.

Perhaloalkyl refers to an alkyl group of 1 to 6 carbon atoms in which three or more hydrogens are substituted with halogen.

Phenyl as used herein refers to a 6 membered aromatic ring.

Halogen, as used herein refers to chlorine, bromine, iodine and fluorine.

Unless otherwise limited, substituents are unsubstituted and may include alkyl of 1 to 6 carbon atoms, cycloalkyl of 1 to 6 carbon atoms, heterocycloalkyl of 1 to 6 members, perhaloalkyl of 1 to 6 carbon atoms, amino, azido, hydroxy, alkylamino, dialkylamino, aryl or heteroaryl.

Carbon number refers to the number of carbons in the carbon backbone and does not include carbon atoms occurring in substituents such as an alkyl or alkoxy substituents.
Where terms are used in combination, the definition for each individual part of the combination applies unless defined otherwise. For instance, alkylcycloalkyl is an alkyl-cycloalkyl group in which alkyl and cycloalkyl are as previously described.

Pharmaceutically acceptable salts are the acid addition salts which can be formed from a compound of the above general formula and a pharmaceutically acceptable acid such as phosphoric, sulfuric, hydrochloric, hydrobromic, citric, maleic, succinic, fumaric, acetic, lactic, nitric, sulfonic, p-toluene sulfonic, methane sulfonic acid, and the like.

The compounds of this invention contain a chiral center, providing for various stereoisomeric forms of the compounds such as racemic mixtures as well as the individual optical isomers. In some preferred embodiments of the present invention the compounds of the present invention are substantially pure optical isomers. By substantially pure is meant the composition contains greater than 75% of the desired isomer and may include no more than 25% of the undesired isomer. In more preferred embodiments the pure optical isomer is greater than 90% of the desired isomer. In some preferred embodiments, when the target is VZV, the (S) isomer is preferred. The individual isomers can be prepared directly or by asymmetric or stereospecific synthesis or by conventional separation of optical isomers from the racemic mixture.

Compounds of the present invention may be prepared by those skilled in the art of organic synthesis employing methods described below which utilize readily available reagents and starting materials unless otherwise described. Compounds of the present invention are thus prepared in accordance with the following schemes.

The novel compounds of the present invention are prepared according to the following reaction schemes.

Referring to Methods 31 (2 and 3, top) and 34 (4 and 5, bottom), reacting appropriately substituted amines 2, wherein the substituents \( R_1 - R_5 \), and \( X \) are described as above, with appropriately substituted isothiocyanates 3, wherein the substituent \( G \) is described above, either neat or in an appropriate solvent such as tetrahydrofuran, acetonitrile, ethyl acetate, dichloromethane, or N,N-dimethylformamide affords the desired thioureas 1. Similarly, reaction of appropriately substituted isothiocyanates 4, wherein the substituents \( R_1 - R_5 \), and \( X \) are described as above with appropriately substituted anilines 5, wherein the substituent
G is described above, in a convenient solvent such as those listed above affords the desired thioureas 1.

Methods 31 and 34

Alternatively, appropriately substituted thioureas 1 can be prepared as described by Methods 32 and 33 by reacting anilines 2 and 5, wherein R₁-R₅, and G are described as above, in the presence of either one molar equivalent of 1,1'-thiocarbonyldiimidazole or 1,1'-carbonyldiimidazole in an appropriate solvent such as dichloromethane and tetrahydrofuran or mixtures thereof or one molar equivalent of 1,1'-thiocarbonyl-di-(1,2,4)-triazole or 1,1'-carbonyl-di-(1,2,4)-triazole in an appropriate solvent such as dichloromethane and tetrahydrofuran or mixtures thereof at room temperature.

Methods 32, 33
In certain instances, subsequent chemical modification of the final thioureas 1 was required. These methods, Methods 35-39, are summarized below.

Thioureas 1 wherein at least one substituent of R₁-R₅ is 1-hydroxyethoxy or carboxy-methoxy, G is defined as above and X is defined above, may be prepared
from the corresponding alkyl esters by alkaline hydrolysis with aqueous sodium or potassium hydroxide in a suitable solvent such as methanol, tetrahydrofuran or mixtures thereof at room temperature in accordance with Methods 35 and 36.

Thioureas 1 wherein at least one substituent of $R_1$-$R_3$ is 1-acyloxyethoxy or methansulfonyloxyethoxy, G is defined as above and X equals a bond, may be prepared from the corresponding 1-hydroxyethoxy derivative by acylation with appropriate acylating agents such as benzoic acid chloride or methanesulfonic acid chloride in the presence of a suitable tertiary amine base such as triethylamine or diisopropylethylamine in a suitable solvent such as dichloromethane or the like at room temperature in accordance with Methods 37 and 38.

Thioureas 1 wherein at least one substituent of $R_1$-$R_3$ is 1-aminoethoxy, G is defined as above and X equals a bond, may be prepared from the corresponding 1-methanesulfonyloxy-ethoxy derivative by reaction with an appropriate secondary amine such as dimethylamine in a suitable solvent mixture such as tetrahydrofuran and water or the like at room temperature in accordance with Method 39.

Thioureas 1 wherein at least one substituent of $R_1$-$R_3$ is 1-aminoalkyl, G is defined as above and X equals a bond, may be prepared from the corresponding 1-azidoalkyl derivative by reaction with stannous chloride in a suitable solvent such as methanol, ethanol or the like at room temperature in accordance with Method 40.

The intermediate isothiocyanates 3 and 4 shown above in Methods 31 and 34 are prepared in accordance with Method 41 (below) essentially according to the procedures of Staab, H.A. and Walther, G. *Justus Liebigs Ann. Chem.* 657, 104 (1962)) by reacting appropriately substituted amines 5 or 2, respectively, wherein $R_1$-$R_4$ and G are described above and X is defined above, with one molar equivalent of 1,1′-thiocarbonyldiimidazole in an appropriate solvent such as dichloromethane and tetrahydrofuran or mixtures thereof.
Method 41

The intermediates 2 and 5 may be prepared according to the following protocols:

According to Methods 1A-1G, amines 2, wherein R₁-R₅ are defined above and X is defined above and amines 5 may be prepared by reduction of the appropriately substituted nitrobenzenes according to a variety of procedures known to those skilled in the art and described in R. J. Lindsay, Comprehensive Organic Chemistry (ed. Sutherland), Volume 2, Chapter 6.3.1, Aromatic Amines, 1979. Such procedures include the reduction of nitrobenzenes to form anilines upon exposure to:

a) iron powder and a strong acid, such as hydrochloric acid (Methods 1A) either neat or in alcohol solvent such as methanol or ethanol, at temperatures ranging from room temperature to the refluxing temperature of the solvent, or;

b) iron powder and glacial acetic acid (Method 1B), either neat or in alcohol solvent such as methanol or ethanol, at temperatures ranging from room temperature to the refluxing temperature of the solvent, or;

c) iron powder and aqueous ammonium chloride (Method 1C), either neat or in alcohol solvent such as methanol or ethanol, at temperatures ranging from room temperature to the refluxing temperature of the solvent, or;
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d) tin and a strong mineral acid, such as hydrochloric acid (Method 1D), either neat or in alcohol solvent such as methanol or ethanol, at temperatures ranging from room temperature to the refluxing temperature of the solvent, or;

e) when \( R_1 - R_s \) are selected from Cl, Br, I, -(OSO₂)₂-CF₃, or -(OSO₂)-1-(4-methylphenyl), by catalytic reduction such as with hydrogen and palladium on carbon (Method 1E) in an appropriate solvent such as methanol, ethanol, or ethyl acetate, under one or more atmospheres of pressure or;

f) when \( R_1 - R_s \) and \( R₅ - R₁₂ \) are selected from Cl, Br, I, -(OSO₂)₂-CF₃, or -(OSO₂)-1-(4-methylphenyl), by catalytic reduction such as with cyclohexene and palladium on carbon (Method 1F) in an appropriate solvent such as methanol or ethanol, at temperatures ranging from room temperature to the refluxing temperature of the solvent, or;

g) aqueous sodium hydrosulfite in alcohol solvent at temperatures ranging from room temperature to the refluxing temperature of the solvent (Method 1G).

Alternatively, according to Methods 3A-3C, amines 2, wherein \( R₁ - R₅ \) are defined above and \( X \) is defined above and anilines 5, above may be prepared by the cleavage of the aniline nitrogen-carbon bond of amide and carbamate derivatives of these anilines according to a variety of procedures known to those skilled in the art and described in Greene, Protective Groups in Organic Synthesis, volume 2, Chapter 7, 1991, and references therein. Such procedures include:

a) the exposure of appropriately substituted arylamino-tert-butyl-carbamates to a strong acid such as trifluoroacetic acid (Method 3A) either neat or in an appropriate solvent such as dichloromethane at temperatures between 0°C and room temperature, or;

b) the exposure of appropriately substituted arylamino-(2-trimethylsilylethyl)-carbamates to a fluoride ion source such as tetrabutylammonium fluoride or potassium fluoride (Method 3B) in aqueous acetonitrile or tetrahydrofuran or mixtures thereof at temperatures ranging from room temperature to the reflux temperature of the solvent, or;

c) the exposure of appropriately substituted arylamino-trifluoroacetamides to a strong base such as sodium or potassium hydroxide or sodium or potassium carbonate in an alcohol solvent such as methanol or ethanol (Method 3C) at temperatures ranging from room temperature to the reflux temperature of the solvent.
Alternatively, according to Method 11, amines 2, wherein R₁-R₄ are defined above, and X equals a bond and at least one substituent of R₁-R₅ is defined as vinyl, may be prepared by the palladium catalyzed coupling of a vinyl trialkyltin reagent, such as tributylvinyltin, with an appropriately substituted bromo- or iodo-aniline, for example 3-chloro-4-iodo-aniline, employing a palladium catalyst, such as tris(dibenzylideneacetone)-bipalladium, and a ligand, such as triphenylarsine, in a suitable solvent such as tetrahydrofuran or N-methylpyrrolidinone, at temperatures ranging from room temperature to the reflux temperature of the solvent, essentially according to the procedures of V. Farina and G.P. Roth in Advances in Metal-


Alternatively, according to Method 42, amines 2, wherein R₂-R₅ are defined above and X is defined above and at least one substituent of R₂ or R₄ is defined as dialkylamino, may be prepared by the palladium catalyzed amination of an appropriately substituted 3- or 5-bromo- or iodo-aniline, for example 3-amino-5-
bromobenzotri fluoride, by secondary amines under conditions which employ a palladium catalyst, such as bis(dibenzy lideneacetone)palladium, and a ligand, such as tri-o-tolylphosphine, and at least two molar equivalents of a strong base, such as lithium bis-(trimethylsilyl)amide in a sealed tube, in a suitable solvent such as tetrahydrofuran or toluene, at temperatures ranging from room temperature to 100°C, essentially according to the procedures of J.F. Hartwig and J. Louie Tetrahedron Letters 36 (21), 3609 (1995).

Alternatively, according to Method 43, amines 2, wherein R₁-R₄ are defined above and X equals a bond and at least one substituent of R₂ or R₄ is defined as alkyl, may be prepared by the palladium catalyzed alkylation of an appropriately substituted 3- or 5-bromo- or iodo-aniline, for example 3-amino-5-bromobenzotri fluoride by alkenes under conditions which employ a palladium catalyst such as [1,1'-
bis(diphenylphosphino)ferrocene]palladium(II) chloride-dichloromethane complex and in the presence of 9-borabicyclo[3.3.1]nonane and a suitable base such as aqueous sodium hydroxide in a suitable solvent such as tetrahydrofuran or the like at temperatures ranging from room temperature to the reflux temperature of the solvent.

The acyl and carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C may be prepared by the derivatization of the corresponding amines as described in Methods 2A-2G according to a variety of procedures known to those
skilled in the art and described in Greene, *Protective Groups in Organic Synthesis* volume 2, Chapter 7, 1991, and references therein. Such procedures include:

a) the reaction of an appropriately substituted amine with di-tert-butyl-dicarbonate (Method 2A) in the presence or absence of one or more molar equivalents of a tertiary amine such as triethylamine or N,N-diisopropylethylamine in a suitable solvent such as acetone, tetrahydrofuran, dimethylformamide, dichloromethane, and the like, at temperatures ranging from room temperature to the reflux temperature of the solvent to produce the corresponding arylamino-tert-butyl-carbamate, or;

b) the reaction of an appropriately substituted aniline with 1-[2-(trimethylsilyl)ethoxycarbonyl-oxyl]benzotriazole (Method 2B) in the presence of a tertiary amine such as triethylamine or diisopropylethylamine in a suitable solvent such as dimethylformamide at room temperature to produce the corresponding arylamino-(2-trimethylsilylethyl)-carbamate, or;

c) the reaction of an appropriately substituted aniline with a carboxylic acid chloride or acid anhydride (Method 2C) either neat or in an appropriate solvent such as tetrahydrofuran, dimethylformamide, dichloromethane, pyridine and the like, in the presence of one or more molar equivalents of a tertiary amine base such as triethylamine or N,N-diisopropylethyl-amine to produce the corresponding arylaminoamide, or;

d) the reaction of an appropriately substituted nitro aniline with a carboxylic acid chloride (Method 2D) in the absence of one or more molar equivalents of a tertiary amine base such as triethylamine or N,N-diisopropylethylamine either neat or in an appropriate solvent such as tetrahydrofuran, 1,4-dioxane and the like at temperatures ranging from room temperature to the reflux temperature of the solvent to produce the corresponding nitro arylaminoamide, or;

e) the reaction of an appropriately substituted aniline with a carboxylic acid (Method 2E) in the presence of a coupling agent such as benzotriazole-1-yloxy-tris-(dimethylamino)-phosphonium hexafluorophosphate, 2-(1H-benzotriazole-1-yloxy)-1,1,3,3-tetramethyluronium hexafluorophosphate, dicyclohexyl carbodiimide and the like and in the presence of a tertiary amine such as triethylamine or diisopropylethylamine in a suitable solvent such as
diichloromethane, dimethylformamide and the like, at room temperature to produce the corresponding arylaminoamide, or;

f) the reaction of an appropriately protected aniline such as an arylamino-tert-butyl-carbamate or the like in which at least one substituent of R₁-R₁₀ is defined as -W-Y-(CH₂)ₙ-Z wherein W, Y, and Z are defined as above, with a carboxylic acid anhydride (Method 2F) in the presence of a suitable base such as pyridine in an appropriate such as dichloromethane, dimethylformamide or the like at temperatures ranging from 0°C to room temperature to produce the corresponding carboxylic acid ester, or;

g) the reaction of an appropriately substituted aniline in which at least one substituent of R₁-R₁₀ is defined as hydroxyl with di-tert-butyl-dicarbonate (Method 2G) in the absence of one or more molar equivalents of a tertiary amine such as triethylamine or N,N-diisopropylethylamine in a suitable solvent such as acetone, tetrahydrofuran, dimethylformamide, dichloromethane, and the like, at temperatures ranging from room temperature to the reflux temperature of the solvent to produce the corresponding arylamino-tert-butyl-carbamate.

Nitrobenzene intermediates that are ultimately converted to amines 2 and 5 by methods shown above in Methods 1A-1G may be prepared in accordance with Methods 4A, 4C, 4E-4F.

Referring to Methods 4A, 4C, and 4E-4H, the nitrobenzene intermediates which are ultimately converted into amines 2, R₂ and R₄ are defined above and R₁, R₃, and/or R₅ are defined as alkoxy, thioalkoxy, alkylsulfenyl, alkylsulfanyl, and dialkylamino may be prepared by the nucleophilic displacement of appropriately substituted 2-, 4-, and/or 6-fluoro-, chloro-, bromo-, iodo-, trifluoromethylsulfonyl-, or (4-methylphenyl)sulfonyl-substituted nitrobenzenes by methods which include the following:

a) reaction of alcohols with appropriately substituted 2- or 4- halo- or sulfonate esters of nitrobenzenes or benzonitriles (Method 4A) either neat or in an appropriate solvent such as tetrahydrofuran, dioxane, acetonitrile, N,N-dimethylformamide or dimethylsulfoxide in the presence or absence of one or more molar equivalents of a base such as sodium carbonate, potassium carbonate, sodium hydroxide, potassium hydroxide, sodium hydride, potassium hydride, or the like, at
temperatures ranging from room temperature to the reflux temperature of the solvent;
b) reactions of preformed sodium, lithium, or potassium phenoxides with
appropriately substituted 2- or 4- halo- or sulfonate esters of nitrobenzenes or
benzonitriles (Method 4H) either neat or in an appropriate solvent such as
tetrahydrofuran, dioxane, acetonitrile, N,N-dimethylformamide or
dimethylsulfoxide, at temperatures ranging from room temperature to the reflux
temperature of the solvent, or;
c) reaction of ammonia, primary or secondary amines with appropriately substituted
2- or 4-halo- or sulfonate esters of nitrobenzenes or benzonitriles (Methods 4C,F)
either neat or in an appropriate solvent such as tetrahydrofuran, dioxane,
acetonitrile, N,N-dimethyl-formamide or dimethylsulfoxide, at temperatures
ranging from room temperature to the reflux temperature of the solvent;
d) reaction of preformed sodium, lithium, or potassium salts of amines with
appropriately substituted 2- or 4- halo- or sulfonate esters of nitrobenzenes or
benzonitriles (Method 4G) in an appropriate solvent such as tetrahydrofuran at
temperatures ranging from 0°C to the reflux temperature of the solvent, or;
e) reaction of sodium sulfide with appropriately substituted 2- or 4- halo- or sulfonate
esters of nitrobenzenes or benzonitriles either neat or in an appropriate solvent
such as tetrahydro-furan, dioxane, acetonitrile, N,N-dimethylformamide or
dimethylsulfoxide, at temperatures ranging from room temperature to the reflux
temperature of the solvent, followed by the addition of an alkyl halide directly to
the reaction mixture (Method 4E).

Alternatively, referring to Methods 5C and 6, the nitrobenzene intermediates
which are ultimately converted into amines 2, wherein at least one substituent R₁-R₂
is defined as alkoxy may be prepared from the corresponding substituted hydroxy-
nitrobenzenes by methods which include the following:
a) reaction of the hydroxy-nitrobenzene with an alkyl halide or dialkyl sulfonate ester
(Method 5C) in the presence of a base, such as potassium carbonate, sodium
carbonate, potassium hydroxide, sodium hydroxide, potassium hydride, or sodium
hydride, in an appropriate solvent such as acetone, N,N-dimethylformamide,
tetrahydrofuran or dimethylsulfoxide at temperatures ranging from room
temperature to the reflux temperature of the solvent, or;
b) reaction of the hydroxy-nitrobenzene with an alkyl alcohol, triphenylphosphine, and a dialkylazodicarboxylate reagent (Method 6), such as diethylazodicarboxylate, in an anhydrous aprotic solvent such as diethyl ether or tetrahydrofuran at temperatures ranging from 0°C to the reflux temperature of the solvent, essentially according to methods described in Mitsunobu, O, Synthesis 1981, 1 and references therein.

In addition, referring to Method 5A and 5E, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein at least one substituent R₁-R₂ is defined as alkoxy may be prepared the corresponding substituted hydroxy arylamino-tert-butyl-carbamate by reaction with alkyl halides, trifluormethane-sulfonates, 4-methylbenzenesulfonates, dialkylsulfonate, ethylene carbonate and the like in the presence of a suitable base such as potassium carbonate in an appropriate solvent such as acetone, toluene, or N,N-dimethylformamide at temperatures ranging from room temperature to the reflux temperature of the solvent.

Alternatively, referring to Methods 7A-G, the nitrobenzene intermediates which are ultimately converted into amines 2, R₁ and/or R₂ is alkoxy, and R₂ and/or R₃ is a halogen, and X equals a bond, may be prepared by standard halogenation reactions which include the following:

a) reaction of a 2- or 4- hydroxy-nitrobenzene with aqueous sodium hypochlorite (Methods 7A and 7B), at room temperature or;
b) reaction of a 2-hydroxy-4-methoxy or 2,4-dimethoxynitrobenzene (Method 7C and 7D) with bromine in suitable solvent such as chloroform, dichloromethane, glacial acetic acid or the like in the presence or the absence of silver trifluoroacetate at room temperature, or;
c) reaction of a 2,4-dimethoxynitrobenzene (Method 7E) with benzytrimethylammonium dichloroiodate in the presence of anhydrous zinc chloride in a suitable solvent such as glacial acetic acid, at room temperature or;
d) reaction of a 2-hydroxy-4-methoxynitrobenzene (Method 7F) with benzytrimethyl-ammonium dichloroiodate in the presence of sodium bicarbonate
in a suitable solvent mixture such as dichloromethane and methanol, at room
temperature or;
e) reaction of a 2,4-dimethoxynitrobenzene (Method 7G) with 3,5-dichloro-1-
fluoropyridine triflate in a suitable solvent such as tetrachloroethane, at a
temperature ranging from room temperature to the reflux temperature of the
solvent.

Referring to Method 8, the nitrobenzene intermediates which are ultimately
converted into amines 2, wherein R₁ = -CF₃, and R₂-R₅ and R₆-R₆ are defined as
above and X equals a bond may be prepared from the corresponding substituted 4-
iodo-nitrobenzenes by reaction with trimethyl(trifluoromethyl)silane in the presence
of cuprous iodide and potassium fluoride in a suitable solvent such as N,N-
dimethylformamide or the like at a temperature ranging from room temperature to
the reflux temperature of the solvent in a sealed reaction vessel.

Referring to Methods 19A and 19B, the nitrobenzene intermediates which are
ultimately converted into amines 2, wherein R₁ = -HNOCH₂NR₂R₃ or
-HNOCH₂SR₄, and R₂-R₅ and R₆ are defined as above and X equals a bond may be
prepared from the corresponding substituted 4-(N-chloroacetyl)-nitroaniline by
reaction with either a suitable secondary amine such as dimethylamine, morpholine
or the like in a suitable solvent such as tetrahydrofuran and/or water mixtures at
temperatures ranging from room temperature to the reflux temperature of the solvent
or by reaction with an appropriate thiol in the presence of a suitable base such as
sodium or potassium carbonate or the like in a suitable solvent such as
tetrahydrofuran, 1,4-dioxane or the like at temperatures ranging from room
temperature to the reflux temperature of the solvent.

Referring to Method 25, the nitrobenzene intermediates which are ultimately
converted into amines 2, wherein at least one substituent of R₁-R₅ is defined as triflate
and X equals a bond may be prepared from the corresponding phenol by reaction
with trifluoromethane-sulfonic anhydride in the presence of a tertiary amines such as
triethylamine or diisopropyl-ethylamine or the like in a suitable solvent such as
dichloromethane at temperatures ranging from 0°C to room temperature.

Referring to Methods 9, 9B, and 10, the carbamoyl amine derivatives utilized
as starting materials in Methods 3A-3C which are ultimately converted into amines 2,
wherein at least one substituent R₁-R₅ is defined as either alkylsulfenyl or
alkylsulfanyl, may be prepared by reaction of the appropriate 4-alkylthio acyl-aryl amino or carbamoyl arylamino derivative with an appropriate oxidizing agent such as dimethyloxirane or sodium periodate in a suitable solvent mixture such as acetone and dichloromethane or water at room temperature.

Referring to Method 12, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein R₄ is defined as 1-hydroxyethyl and R₅-R₇ and R₉ are defined as above and X equals a bond may be prepared by reacting the corresponding 4-vinyl carbamoyl aniline with sodium borohydride in the presence of mercuric acetate in a suitable solvent such as tetrahydrofuran, 1,4-dioxane or the like and water at room temperature.

Referring to Method 13, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein R₄ is defined as 2-hydroxyethyl and R₅-R₇ and R₉ are defined as above and X is a bond, may be prepared by reacting the corresponding 4-vinyl carbamoyl aniline with sodium borohydride in the presence of glacial acetic acid in a suitable solvent such as tetrahydrofuran, 1,4-dioxane or the like at temperatures ranging from 0°C to room temperature.

Referring to Method 14, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein R₄ is defined as 1-azidoethyl and R₅-R₇ and R₉ are defined as above and X is defined above, may be prepared by reacting the corresponding 4-(1-hydroxyethyl) carbamoyl aniline with hydrazoic acid in the presence of a dialkylazodicarboxylate such as diethylazodicarboxylate and triphenylphosphine in a suitable solvent mixture such as tetrahydrofuran and dichloromethane at temperatures ranging from 0°C to room temperature.

Referring to Method 15, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein R₄ is defined as 3-dimethylaminoprop-1-ynyl and R₅-R₇ and R₉ are defined as above and X is defined above, may be prepared by reacting the corresponding 4-iodocarbamoyl aniline with 1-dimethylamino-2-propyne in a suitable tertiary amine solvent such as triethylamine or diisopropylethylamine in the presence of bis(triphenylphosphine)palladium(II) chloride and cuprous iodide at temperatures ranging from room temperature to the reflux temperature of the solvent.
Referring to Method 16, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein R₄ is defined as 3-dimethylaminoacryloyl and R₁-R₃ are defined as above and X equals a bond, may be prepared by reacting the corresponding 4-(3-dimethylaminoprop-1-ynyl)carbamoyl aniline with a suitable peracid such as 3-chloroper oxybenzoic acid in a suitable solvent mixture such as dichloromethane and methanol at temperatures ranging from 0°C to room temperature.

Referring to Methods 17 and 18, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein R₄ is defined as either 4-isoxazol-5-yl or 4-(1H-pyrazol-3-yl) and R₁-R₃ and R₆ are defined as above and X equals a bond, may be prepared by reacting the corresponding 4-(3-dimethylamino-acryloyl)carbamoyl aniline with either hydroxylamine hydrochloride or hydrazine hydrate in a suitable solvent such as 1,4-dioxane or ethanol and the like at room temperature.

Referring to Method 20, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein R₄ = -HNCO₂Z, and R₁-R₃, R₆, and Z are defined as above and X equals a bond, may be prepared by reacting the corresponding 4-aminocarbamoyl aniline with 1,1-carbonyl-di-(1,2,4)-triazole and an appropriately substituted alcohol in a suitable solvent mixture such as tetrahydrofuran and dichloromethane and the like at temperatures ranging from room temperature to the reflux temperature of the solvent.

Referring to Methods 26 and 30, the carbamoyl amine derivatives utilized as starting materials in Methods 3A-3C which are ultimately converted into amines 2, wherein at least one substituent of R₁-R₃ is defined as dialkylamino and X is defined above may be prepared by reaction of appropriately substituted aldehydes in the presence of either sodium cyanoboro-hydride or hydrogen gas and 10 % palladium on carbon in a suitable solvent such as water, methanol, tetrahydrofuran mixtures or toluene or the like at room temperature.

Referring to Methods 27 and 28, amines 2 wherein at least one substituent of R₁-R₃ is defined as hydroxy and X is defined above can be prepared by reaction of the corresponding ester such as acetate with an appropriate base such as sodium bicarbonate or sodium hydroxide in a suitable solvent mixture such as methanol-
water mixtures at temperatures ranging from room temperature to the reflux
temperature of the solvent.

Referring to Method 29, amines 2 wherein at least one substituent of R₇-R₉ is
defined as 2-hydroxybenzamido and X is defined above can be prepared by reaction
of the corresponding N-(4-aminophenyl)phthalimide with lithium borohydride in an
appropriate solvent such as tetrahydrofuran, diethyl ether, or the like at room
temperature.

The intermediate amines 2 wherein R₇-R₉ are defined as above and X equals
either -CH₂⁻ or -(CH₃)₂⁻ can be prepared by the following procedures:

a) reduction of an appropriately substituted benzo- or phenylacetonitrile with
borane-dimethylsulfide complex in a suitable solvent such as ethylene
glycol dimethyl ether, tetrahydrofuran or the like at temperatures ranging
from room temperature to the reflux temperature of the solvent. (Method
44);

b) reduction under one or more atmospheres of hydrogen in the presence of a
suitable catalyst such as 5 % or 10 % palladium on carbon and an acid such as
4-methyl-benzenesulfonic acid, hydrochloric acid or the like in a suitable
solvent such as ethylene glycol monomethyl ether, ethyl acetate, ethanol or
the like at room temperature. (Method 50);

c) reduction with lithium aluminum hydride in a suitable solvent such as
tetrahydrofuran or diethyl ether at temperatures ranging from 0°C to room
 temperature. (Method 51);

The unsaturated nitro precursors which are utilized as starting materials in
Method 51 and are ultimately converted to amines 2 wherein R₇-R₉ are defined as
above and X equals -(CH₂)₂⁻ can be prepared by reaction of an appropriately
substituted benzaldehyde with nitro-methane in the presence of ammonium acetate in
a suitable solvent such as acetic acid at temperatures ranging from room temperature
to the reflux temperature of the solvent. (Method 53); The benzaldehydes, utilized as
starting materials in Method 53, can be prepared by diisobutylaluminum hydride
reduction of an appropriately substituted benzonitrile. (Method 52) The substituted
benzonitriles, utilized as starting materials in Method 52, can be prepared from the
corresponding aryl bromide by reaction with copper cyanide in a suitable solvent
such as N,N-dimethylformamide at temperatures ranging from room temperature to the reflux temperature of the solvent. (Method 59)

For amines 2, wherein \( R_1-R_2 \) is defined as above and \( X \) equals either \( \text{O(\( \text{CH}_2 \))}_2\text{NH}_2 \) or \( \text{S(\( \text{CH}_2 \))}_2\text{NH}_2 \), the requisite nitrile precursors may be prepared by reaction of an appropriately substituted phenol or thiophenol with bromoacetanilide in the presence of a suitable base such as potassium carbonate in an appropriate solvent such as acetone at room temperature according to Method 49.

Alternatively, for amines 2, wherein \( R_1-R_2 \) are defined as above and \( X \) equals \(-\text{(\( \text{CH}_2 \))}_2\text{-}\), the nitrile precursors can be prepared essentially according to the procedure of Wilk, B. Synthetic Comm. 23, 2481 (1993), by reaction of an appropriately substituted phenethanol with acetone cyanohydrin and triphenylphosphine in the presence of a suitable azodicarboxylate such as diethyl azodicarboxylate in an appropriate solvent such as diethyl ether or tetrahydro-furan or the like at temperatures ranging from 0°C to room temperature. (Method 54)

Alternatively, intermediate amines 2 wherein \( R_1-R_2 \) are defined as above and \( X \) equals \(-\text{(\( \text{CH}(\text{CH}_3) \))}_2\text{-}\) can be prepared by acid or base catalyzed hydrolysis of the corresponding formamide using an appropriate acid catalyst such as 6N hydrochloric acid or a suitable base catalyst such as 5N sodium or potassium hydroxide in an appropriate solvent mixture such as water and methanol or water and ethanol at temperatures ranging from room temperature to the reflux temperature of the solvent. (Method 46)

The formamide precursors utilized as starting materials in Method 46 and which are ultimately converted into amines 2, are prepared according to Method 45 by treatment of an appropriately substituted acetophenone with ammonium formate, formic acid and formamide at temperatures ranging from room temperature to the reflux temperature of the solvent.

Alternatively, amines 2 wherein \( R_1-R_2 \) are defined as above and \( X \) equals \(-\text{(\( \text{CH}(\text{CH}_3) \))}_2\text{-}\) can be prepared by reduction of an appropriately substituted O-methyl oxime in the presence of sodium borohydride and zirconium tetrachloride in a suitable solvent such as tetrahydrofuran or diethyl ether at room temperature Method 48 essentially according to the procedure of Itsuno, S., Sakurai, Y., Ito, K. Synthesis 1988, 995. The requisite O-methyl oximes can be prepared from the corresponding
acetophenone by reaction with methoxylamine hydrochloride and pyridine in a suitable solvent such as ethanol or methanol at temperatures ranging from room temperature to the reflux temperature of the solvent. (Method 47)

Amines 2 for which R₁, R₂, are defined as above and X equals -CH(J)- where J is defined as above, can be prepared by reduction of the appropriately substituted ketone by the methods described above (Methods 45, 47, and 48). These requisite ketones, when not commercially available, can be prepared by reaction of a suitably substituted benzaldehyde with an appropriate organometallic reagent such as phenyllithium, isopropylmagnesium bromide or ethylmagnesium bromide or the like in a suitable solvent such as diethyl ether or tetrahydrofuran at temperatures ranging from -78 °C to 0°C. (Method 57) The resulting alcohols can be oxidized to the corresponding ketone with an appropriate oxidizing agent such as chromium trioxide in aqueous sulfuric acid and acetone or pyridinium chlorochromate or pyridium dichromate in an appropriate solvent such as dichloromethane or the like at room temperature. (Method 58)

The intermediate anilines 5 may be prepared as previously described Method 3A. Thus treating phenyl carbamic acid tert-butyl ester 6, wherein G is described as above, with neat trifluoroacetic acid at room temperature followed by neutralization with aqueous sodium hydroxide affords the desired anilines 5. The requisite carbamic acid esters 6, wherein G is described as above, are prepared as shown in Method 2C by reaction of substituted acid chlorides, 8, where G is described as above, and 4-aminophenylcarbamic acid tert-butyl esters 7 in the presence of triethylamine in an appropriate solvent such as dichloromethane, dimethylsulfoxide, or dimethylformamide or mixtures thereof. Carboxylic acid chlorides 8 are either commercially available or prepared from the corresponding carboxylic acid by reaction with oxalyl chloride in a suitable solvent such as dichloromethane at room temperature.
Alternatively, carbamic acid esters 6, wherein G is described as above, are prepared as shown in Method 2E by reaction of substituted carboxylic acids 8a, wherein G is described as above, and an appropriately substituted 4-aminophenyl carbamic acid tert-butyl esters 7 in the presence of a suitable coupling agent such as benzotriazole-1-yloxy-tris-(dimethylamino)phosphonium hexafluorophosphate, 2-(1H-benzotriazole-1-yloxy)-1,1,3,3-tetramethyluronium hexafluorophosphate, dicyclohexyl carbodiimide or the like and in the presence of a tertiary amine base such as triethylamine or diisopropylethylamine in a suitable solvent such as dichloromethane, dimethylformamide and the like, at room temperature to produce the corresponding arylaminoamide.

Carboxylic acids 8a are either commercially available or are prepared according to literature methods. For example, when G is a substituted thiadiazole, the acid is available from the corresponding carboxylic acid ester by reaction with an appropriate base such as sodium or potassium hydroxide in a suitable solvent mixture such as methanol or ethanol and water at room temperature.

When the carboxylic acid ester precursors which are ultimately converted to acids 8 are not commercially available, they may be prepared by methods known in the literature. For example, 5-substituted-1,2,3-thiadiazole-4 carboxylic acid esters may be prepared essentially according to the procedure of Caron, *M J. Org. Chem.* 51, 4075 (1986) and Taber, D. F., Ruckle, R. E. *J. Amer. Chem. Soc.* 108, 7686 (1986). Thus, according to Method 21, treatment of a beta-keto carboxylic acid ester with 4-methylbenzenesulfonyl azide or methanesulfonyl azide or the like in the presence of a tertiary amine base such triethylamine or diisopropylethylamine in a suitable solvent such as acetonitrile affords the corresponding diazo-beta-keto
carboxylic acid ester. Treatment of this compound with 2,4-bis(4-methoxyphenyl)-
1,3-dithia-2,4-diphosphetane-2,4-disulfide in a suitable solvent such as benzene or
toluene or the like at temperatures ranging from room temperature to the reflux
temperature of the solvent gives the desired 5-substituted-1,2,3-thiadiazole-4-
carboxylic acid ester.

Alternatively, 4-substituted-1,2,3-thiadiazole-5-carboxylic acid esters may be
prepared essentially according to the procedure of Shafiee, A., Lalezari, I., Yazdani,
S., Shahbazian, F. M., Partovi, T. J. Pharmaceutical Sci. 65, 304 (1976). Thus,
according to Method 22 and 23, reaction of an appropriately substituted beta-keto
carboxylic acid ester in a suitable alcoholic solvent such as methanol or ethanol with
an aqueous solution semicarbazide hydrochloride at temperatures ranging from room
temperature to the reflux temperature of the solvent in the presence of a suitable base
such as pyridine gives corresponding semicarbazide derivative. Treatment of this
compound with neat thionyl chloride at 0°C followed by treatment with an excess
aqueous solution of sodium bicarbonate affords the corresponding 4-substituted-
1,2,3-thiadiazole-5-carboxylic acid esters.

4-carboalkoxythiazoles are prepared essentially according to the procedure of
Schöllkopf, U., Porsch, P., Lau, H. Liebigs Ann. Chem. 1444 (1979). Thus,
according to Method 55 and 56, reaction of ethyl isocynoacetate with N,N-
dimethylformamide dimethyl acetal in a suitable alcoholic solvent such as ethanol at
room temperature gives the corresponding 3-dimethylamino-2-isocyno-acrylic acid
ethyl ester. A solution of this compound in a suitable solvent such as tetrahydrofuran
is treated with gaseous hydrogen sulfide in the presence of a suitable tertiary amine
base such as triethylamine or diiso-propylethylamine or the like at room temperature
to give the corresponding 4-carboethoxy-thiazole.

Additional appropriately substituted thiazoles may be prepared essentially
according to the procedure of Bredenkamp, M. W., Holzafel, C. W., van Zyl, W. J.
Synthetic Comm. 20, 2235 (1990). Appropriate unsaturated oxazoles are prepared
especially according to the procedure of Henneke, K. H., Schöllkopf, U., Neudecker,
T. Liebigs Ann. Chem. 1979 (1979). Substituted oxazoles may be prepared
essentially according to the procedures of Galeotti, N., Montagne, C., Poncet, J.,
Jouin, P. Tetrahedron Lett. 33, 2807, (1992) and Shin, C., Okumura, K., Ito, A.,
The following specific examples are illustrative, but are not meant to be limiting of the present invention.

**EXAMPLE 1 (METHOD 1A)**

**4-Methoxy-3-trifluoromethyl- phenylamine**

A suspension of 4-methoxy-3-trifluoromethyl-nitrobenzene (2.2 g) and iron powder (1.68 g) in ethanol (35 mL) and water (15 mL) is treated with a solution of concentrated hydrochloric acid (0.42 mL) in ethanol (6 mL) and water (3 mL) and the mixture is heated to reflux for approximately 1 hour. The mixture is then cooled, filtered, and concentrated under reduced pressure. The resulting oil is dissolved in ethyl acetate and extracted three times with 5% aqueous hydrochloric acid. The pooled acidic extracts are then cooled in an ice bath and basified with solid potassium carbonate, then extracted with ethyl acetate. These organic extracts are washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, concentrated under reduced pressure, then passed through a short column of silica gel (ethyl acetate is used as the eluant) to provide the desired compound as an amber oil.

Using the above procedure and appropriate starting materials the following compounds were prepared:

2,6-Dichloro-benzene-1,4-diamine
3-Chloro-4-methylsulfanyl-phenylamine
2,6-Dibromo-benzene-1,4-diamine
3-Chloro-4-trifluoromethyl-phenylamine
3-Chloro-4-ethylsulfanyl-phenylamine
4-Methoxy-3-trifluoromethyl-phenylamine
3,5-Dichloro-4-methoxy-2-methyl-phenylamine
5-Chloro-2-ethoxy-4-methoxy-phenylamine
5-Chloro-4-ethoxy-2-methoxy-phenylamine
5-Iodo-2,4-dimethoxy-phenylamine
3,5-Diiodo-2,4-dimethoxy-phenylamine
3,5-Dibromo-2,4-dimethoxy-phenylamine
5-Chloro-2-methoxy-4-methyl-phenylamine
2-Chloro-N(1),N(1)-dimethyl-benzene-1,4-diamine
3-Chloro-4-piperidin-1-yl-phenylamine
3-Chloro-4-pyrrolidin-1-yl-phenylamine
N(1)-Benzyl-2-chloro-benzene-1,4-diamine
3-Chloro-4-(4-methyl-piperazin-1-yl)-phenylamine
2-Chloro-N(1)-methyl-N(1)-(1-methyl-piperidin-4-yl)-benzene-1,4-diamine
2-Chloro-N(1)-methyl-N(1)-(1-methyl-pyrrolidin-3-yl)-benzene-1,4-diamine
2-Chloro-N(1)-methyl-N(1)-phenyl-benzene-1,4-diamine
N(1)-(1-Benzyl-pyrrolidin-3-yl)-2-chloro-N(1)-methyl-benzene-1,4-diamine
2-Chloro-N(1)-cyclopentyl-N(1)-methyl-benzene-1,4-diamine
2-[(4-Amino-2-chloro-phenyl)-(2-hydroxy-ethyl)-amino]-ethanol
2-Chloro-N(1)-hexyl-N(1)-methyl-benzene-1,4-diamine
2-Chloro-N(1)-isobutyl-N(1)-methyl-benzene-1,4-diamine
2-[(4-Amino-2-chloro-phenyl)-methyl-amino]-ethanol
2-Chloro-N(1)-(3-dimethylamino-propyl)-N(1)-methyl-benzene-1,4-diamine
2-Chloro-N(1)-(2-dimethylamino-ethyl)-N(1)-methyl-benzene-1,4-diamine
2-Chloro-N(1)-(2-dimethylamino-ethyl)-benzene-1,4-diamine
N(1)-(1-Benzyl-piperidin-4-yl)-2-chloro-benzene-1,4-diamine
2-Chloro-N(1)-(2-methoxy-ethyl)-N(1)-methyl-benzene-1,4-diamine
2-Chloro-N(1)-(3-dimethylamino-propyl)-benzene-1,4-diamine
N(1)-(1-Benzyl-pyrrolidin-3-yl)-2-chloro-benzene-1,4-diamine
3-Chloro-4-(1-methyl-piperidin-4-yloxy)-phenylamine
3-Chloro-4-(2-dimethylamino-ethoxy)-phenylamine
3-Chloro-4-(3-dimethylamino-propoxy)-phenylamine
3-Chloro-4-(1-methyl-pyrrolidin-3-yloxy)-phenylamine
3-Chloro-4-cyclohexyloxy-phenylamine
EXAMPLE 2 (METHOD 1B)
4-Bromo-2,4-dimethoxy-phenylamine

A suspension of 4-bromo-2,4-dimethoxy-nitrobenzene (0.48 g) and iron powder (0.42 g) in acetic acid (10 mL) and ethanol (10 mL) is heated to 120 °C for approximately 5 hours. The mixture is then cooled, filtered, and concentrated under reduced pressure. Water is added and the mixture is cooled in an ice bath and neutralized with solid potassium carbonate and then extracted with dichloromethane. These organic extracts are washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, concentrated under reduced pressure, then chromatographed over silica gel (20% ethyl acetate in hexanes is used as the eluant) to provide the desired compound as an amber oil.

EXAMPLE 3 (METHOD 1C)
(4-Amino-2,6-dichloro-phenoxy)-acetic acid tert-butyl ester

A solution of (4-nitro-2,6-dichloro-phenoxy)-acetic acid tert-butyl ester (1 g) in ethanol (17 mL) and water (8.6 mL) is treated with iron powder (0.861 g) and ammonium chloride (86 mg) and the mixture is heated to reflux for approximately 1 hour. The mixture is then filtered and concentrated under reduced pressure. The resulting oil is partitioned between water and ethyl acetate, and the organic phase is then washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to provide the desired compound as a pale yellow solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

4-Chloro-benzene-1,2-diamine
N-(4-Amino-2-chloro-phenyl)-acetamide
(4-Amino-2,6-dichloro-phenoxy)-acetonitrile
(4-Amino-2,6-dichloro-phenoxy)-acetic acid tert-butyl ester
(2-Amino-4-chloro-5-methoxy-phenoxy)-acetonitrile
(4-Amino-2-chloro-5-methoxy-phenoxy)-acetic acid methyl ester
(4-Amino-2-chloro-5-methoxy-phenoxy)-acetic acid tert-butyl ester
(2-Amino-4-chloro-5-methoxy-phenoxy)-acetic acid tert-butyl ester
N(1)-Benzyl-4-chloro-5-methoxy-benzene-1,2-diamine
N-(4-Amino-2-chloro-phenyl)-2-fluoro-benzamide
N-(4-Amino-5-chloro-2-hydroxy-phenyl)-acetamide
N-(4-Amino-5-chloro-2-hydroxy-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-2-chloro-phenyl)-amide
(4-Amino-2-chloro-phenyl)-carbamic acid ethyl ester
N-(4-Amino-5-chloro-2-methyl-phenyl)-acetamide
N-(4-Amino-5-chloro-2-methyl-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-5-chloro-2-methyl-phenyl)amide
N-(4-Amino-3-chloro-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-3-chloro-phenyl)-amide
N-(4-Amino-2-chloro-phenyl)-2-dimethylamino-acetamide
N-(4-Amino-2-chloro-phenyl)-2-piperidin-1-yl-acetamide
N-(4-Amino-2-chloro-phenyl)-2-morpholin-4-yl-acetamide
N-(4-Amino-2-chloro-phenyl)-methanesulfonamide
N-(4-Amino-2-chloro-phenyl)-benzamide
N-(4-Amino-2-chloro-phenyl)-2-diethylamino-acetamide
N-(4-Amino-2-chloro-phenyl)-2-pyrrolidin-1-yl-acetamide
N-(4-Amino-2-chloro-phenyl)-2-azepan-1-yl-acetamide
N-(4-Amino-2-chloro-phenyl)-2-(2-methyl-piperidin-1-yl)-acetamide
N-(4-Amino-2-chloro-phenyl)-2-(3-methyl-piperidin-1-yl)-acetamide
3-Chloro-benzene-1,2-diamine
4-Chloro-N,N-dimethyl-benzene-1,2-diamine
EXAMPLE 4 (METHOD 1D)
3,5-Dichloro-4-phenoxy-phenylamine

To a slurry of 3,5-dichloro-4-phenoxy-nitrobenzene (6.1 g) and tin powder (12 g) is added dropwise concentrated hydrochloric acid (60 mL). Ethanol (60 mL) is added and the mixture is heated to reflux for approximately 1 hour. The mixture is then cooled in an ice bath and basified by addition of solid sodium hydroxide. The resulting suspension is filtered through a pad of diatomaceous earth and extracted three times with ethyl acetate. The combined organic extracts are then washed with saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide the desired product as a yellow solid. Recrystallization from ethyl acetate-hexanes provided the product as a pale yellow solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

1-Fluran-2-yl-ethylamine
3-Chloro-4-isopropoxy-phenylamine
2-Butoxy-5-chloro-4-methoxy-phenylamine
3,5-Dichloro-2-methoxy-4-methyl-phenylamine
2-Benzylolx-5-chloro-4-methoxy-phenylamine
4-Benzylolx-5-chloro-2-methoxy-phenylamine
5-Flurolo-2,4-dimethoxy-phenylamine
(4-Amino-2,6-dichloro-phenoxy)-acetic acid ethyl ester
3,5-Dichloro-4-phenoxy-phenylamine
2-(4-Amino-2-chloro-5-methoxy-phenoxy)-acetamide
(4-Amino-2-chloro-5-methoxy-phenoxy)-acetonitrile
2-(2-Amino-4-chloro-5-methoxy-phenoxy)-ethanol
2-(4-Amino-2-chloro-5-methoxy-phenoxy)-ethanol
4-(4-Amino-2-chloro-5-methoxy-phenoxy)-butyronitrile
4-Amino-2-chloro-5-methoxy-phenol
2-Amino-4-chloro-5-methoxy-phenol
5-Chloro-4-methoxy-2-morpholin-4-yl-phenylamine
4-Chloro-5-methoxy-N(1),N(1)-dimethyl-benzene-1,2-diamine
5-Chloro-4-methoxy-2-piperidin-1-yl-phenylamine
5-Chloro-4-methoxy-2-pyrrolidin-1-yl-phenylamine
2-Chloro-N(1)-cyclohexyl-N(1)-methyl-benzene-1,4-diamine
N(2)-Benzyl-4-methoxy-benzene-1,2-diamine
2-(4-Amino-2-chloro-phenoxy)-ethanol
2-Chloro-N(1)-cyclohexyl-N(1)-ethyl-benzene-1,4-diamine
4-Butoxy-3-chloro-phenylamine
(4-Amino-2-chloro-phenoxy)-acetonitrile
2-Chloro-N(1)-cyclohexyl-benzene-1,4-diamine
2-Chloro-N(1),N(1)-dipropyl-benzene-1,4-diamine
3-Chloro-4-(2,2,2-trifluoro-ethoxy)-phenylamine
3-Chloro-4-(octahydro-quinolin-1-yl)-phenylamine
N(1)-Allyl-2-chloro-N(1)-cyclohexyl-benzene-1,4-diamine
N-(4-Amino-2-methoxy-5-methyl-phenyl)-2-fluoro-benamide
Furan-2-carboxylic acid (4-amino-2-methoxy-5-methyl-phenyl)amide
N-(4-Amino-naphthalen-1-yl)-2-fluoro-benamide
3-Chloro-N,N-dimethyl-benzene-1,2-diamine
3-Chloro-4-propoxy-phenylamine
3-Iodo-4-methoxy-phenylamine
3-Chloro-2,4-dimethoxy-aniline
3-Bromo-4-methoxy-phenylamine
3-Chloro-4-ethoxy-phenylamine

EXAMPLE 5 (Method 1E)
(4-Amino-phenyl)-carbamic acid isobutyl ester

To a solution of N-(4-Nitro-phenyl)-isobutyryl amide (2.0 g) in 100 mL ethylene
glycol monomethyl ether (100 mL) is added 10% palladium on carbon (275 mg).
The mixture is hydrogenated for 2 hours at room temperature under 30 psi of
hydrogen on a Parr hydrogenation apparatus. The catalyst is then removed by
filtration through diatomaceous earth and the filtrate is evaporated to dryness under reduced pressure by azeotroping three times with heptane. Trituration of the residue with heptane provides the desired product as a white solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

- 2-Methyl-3H-benzoimidazol-5-ylamine
- N-(4-Amino-phenyl)-formamide
- 1H-Benzimidazol-5-ylamine
- (4-Amino-phenyl)-carbamic acid isobutyl ester
- N-(4-Amino-phenyl)-isobutyramide
- N-(5-Amino-pyridin-2-yl)-2-methyl-benzamide
- Furan-2-carboxylic acid (5-amino-pyridin-2-yl)-amide
- N-(5-Amino-pyridin-2-yl)-2-fluoro-benzamide
- [6-(2,2,2-Trifluoro-acetamino)-pyridin-3-yl]-carbamic acid tert-butyl ester
- N-(5-Amino-pyridin-2-yl)-2,2,2-trifluoro-acetamide
- (4-Amino-benzyl)-carbamic acid tert-butyl ester
- 2-(3,5-Bis-trifluoromethyl-phenyl)-ethylamine
- 1-tert-Butyl-1H-imidazol-2-ylamine
- 3-(3-Dimethylamino-propyl)-5-trifluoromethyl-phenylamine

**EXAMPLE 6 (METHOD 1F)**

N-(4-Amino-2-methylphenyl)-2-fluorobenzamide

A mixture of 2-fluoro-N-(2-methyl-4-nitrophenyl)benzamide (4.55 g), cyclohexene (30 mL), ethanol (70 mL), water (30 mL) and 10% palladium on charcoal (3 g) is heated at reflux for 30 minutes. The mixture is filtered through diatomaceous earth and concentrated under reduced pressure. The resulting oil is dissolved in 50 mL of ethyl acetate and cooled at 4°C for 12 hours. Filtration provides the product as a tan solid.
Using the above procedure and appropriate starting materials the following compounds were prepared:

N-(4-Amino-2-methyl-phenyl)-acetamide
2-Methyl-benzooxazol-6-ylamine
N-(4-Amino-3-methoxy-phenyl)-acetamide
2-Acetylamino-5-amino-benzoic acid
N-(4-Amino-phenyl)-acetamide
[4-(3-Amino-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Amino-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
N-(4-Amino-2-cyano-phenyl)-acetamide
N-(4-Amino-2,5-dimethoxy-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-2,5-dimethoxy-phenyl)-amide
N-(4-Amino-2-cyano-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-2-methoxy-phenyl)-amide
N-(4-Amino-2-methoxy-phenyl)-2-fluoro-benzamide
N-(4-Amino-2-methoxy-5-methyl-phenyl)-acetamide
N-(4-Amino-2-benzoyl-phenyl)-acetamide
N-(4-Amino-2-benzoyl-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-2-benzoyl-phenyl)-amide
N-(4-Amino-3-methyl-phenyl)-acetamide
N-(4-Amino-3-methyl-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-3-methyl-phenyl)-amide
5-Amino-2-[(2-fluorobenzoyl)amino]-N-phenylbenzamide
Furan-2-carboxylic acid (4-amino-2-phenylcarbamoyl-phenyl)amide
N-(4-Amino-naphthalen-1-yl)-acetamide
Furan-2-carboxylic acid (4-amino-naphthalen-1-yl)-amide
N-(4-Amino-2-trifluoromethyl-phenyl)-acetamide
Furan-2-carboxylic acid (4-amino-2-cyano-phenyl)-amide
Furan-2-carboxylic acid (4-amino-2-trifluoromethyl-phenyl)-amide
N-(4-Amino-2-methyl-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-2-methyl-phenyl)-amide
5-Amino-2-(2-fluoro-benzoylamino)-benzoic acid
5-Amino-2-[(furan-2-carbonyl)-amino]-benzoic acid
N-(4-Amino-2-cyano-phenyl)-2,2,2-trifluoro-acetamide
N-(4-Amino-3-methyl-phenyl)-2,6-difluoro-benzamide
N-(4-Amino-3-trifluoromethyl-phenyl)-acetamide
N-(4-Amino-3-trifluoromethyl-phenyl)-2-fluoro-benzamide
N-(4-Amino-2-trifluoromethyl-phenyl)-2,2,2-trifluoro-acetamide
N-(4-Amino-2-methoxy-phenyl)-2,2,2-trifluoro-acetamide
N-(4-Amino-2-trifluoromethyl-phenyl)-2-fluoro-N-(2-fluoro-benzoyl)-benzamide
N-(4-Amino-2-trifluoromethyl-phenyl)-2-fluoro-benzamide

EXAMPLE 7 (METHOD 1G)
N-(4-Amino-2-chlorophenyl)-2-thiomorpholino-4-yl-acetamide

A solution of N-(2-chloro-4-nitrophenyl)-2-thiomorpholino-4-yl-acetamide (3.02 g) in ethanol (200 mL) is added to a solution of sodium thiosulfate (12 g) in water (60 mL). The mixture is heated at reflux for 12 hours, cooled and poured into water. The mixture is then extracted with ethyl acetate. The ethyl acetate solution is washed twice with saturated aqueous sodium chloride, dried over anhydrous potassium carbonate, filtered through a pad of diatomaceous earth and concentrated under reduced pressure to give an oil. Toluene is added and the solution chilled to give the desired product as a light orange crystalline solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

N-(4-Amino-2-chloro-phenyl)-2-thiomorpholin-4-yl-acetamide
N-(4-Amino-2-chloro-phenyl)-2-dipropylamino-acetamide
EXAMPLE 8 (METHOD 2A)
(3-Chloro-4-iodo-phenyl)-carbamic acid tert-butyl ester

To a solution of 3-chloro-4-iodo-aniline (10 g) in tetrahydrofuran (40 mL) containing
diisopropylethylamine (6.9 mL) is added di-tert-butyl-dicarbonate (8.6 g) and the
mixture is heated to reflux. After approximately 15 hours additional portions of
diisopropylethylamine (6.9 mL) and di-tert-butyl-dicarbonate (21 g) is added and
heating is continued for approximately 24 hours. The solution is then cooled,
concentrated under reduced pressure, diluted with ethyl acetate, and washed
successively three times with 5% aqueous hydrochloric acid then once with saturated
aqueous sodium chloride. The solution is dried over anhydrous sodium sulfate then
concentrated under reduced pressure to provide the desired crude product as a brown
oil. Crystallization is induced by addition of hexanes, and the collected solid material
is recrystallized from hexanes to give the desired product as a white solid.

Using the above procedure and appropriate starting materials the following
compounds were prepared:

N'-(4-Nitro-benzoyl)-hydrazinecarboxylic acid tert-butyl ester
(3-Chloro-4-iodo-phenyl)-carbamic acid tert-butyl ester
(4-Bromo-3-chloro-phenyl)-carbamic acid tert-butyl ester
(3-Chloro-4-vinyl-phenyl)-carbamic acid tert-butyl ester
(3-Chloro-4-methylsulfonyl-phenyl)-carbamic acid tert-butyl ester
(4-Amino-3-chloro-phenyl)-carbamic acid tert-butyl ester
(4-Chloro-2-nitro-phenyl)-carbamic acid tert-butyl ester
(3-tert-Butoxycarbonylamino-5-chloro-phenyl)-carbamic acid tert-butyl ester
(4-Nitro-benzyl)-carbamic acid tert-butyl ester
(3-Bromo-5-trifluoromethyl-phenyl)-carbamic acid tert-butyl ester
(2-Amino-3-chloro-5-trifluoromethyl-phenyl)-carbamic acid tert-butyl ester
EXAMPLE 9 (METHOD 2B)

(3-Chloro-4-vinyl-phenyl)-carbamic acid 2-trimethylsilyl-ethyl ester

To a solution of 3-chloro-4-vinyl-phenylamine (3.4 g) in N,N-dimethylformamide (44 mL) containing diisopropylethylamine (5.8 mL) is added 1-[2-(trimethylsilyl)-ethoxycarbonyl-oxy]benzotriazole (7.1 g) and the mixture is stirred at room temperature under an atmosphere of argon for three days. The solution is then diluted with water and extracted three times with diethyl ether. The combined organic extracts are washed successively with water, saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The resulting residue is chromatographed over silica gel (10% ethyl acetate in hexanes is used as the eluant) to provide the desired product as a yellow oil.

EXAMPLE 10 (METHOD 2C)

[4-(2-Fluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester

To a solution of mono-N-(t-butoxycarbonyl)-1,4-phenylenediamine (1.58 g) and triethylamine (1.50 mL) in 25 mL of dichloromethane is added o-fluorobenzoyl chloride (1.20 g). A solid formed immediately forms and is filtered and washed with fresh solvent to yield a white solid, 1.90 g.

Using the above procedure and appropriate starting materials the following compounds were prepared:

N-(3-Methoxy-4-nitro-phenyl)-acetamide
N-(4-Amino-phenyl)-isobutyrlamide
2,2,2-Trifluoro-N-(2-methoxy-4-nitro-phenyl)-acetamide
[4-(2-Methyl-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
Acetic acid 2-(4-tert-butoxycarbonylamino-phenylcarbamoyl)-phenyl ester
[4-(4-Fluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(3-Fluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Fluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Methoxy-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(3-Methoxy-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(4-Methoxy-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2,2-Dimethyl-propionylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Bromo-acetylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2,2,2-Trifluoro-acetylamino)-phenyl]-carbamic acid tert-butyl ester
(4-Benzoylamino-phenyl)-carbamic acid tert-butyl ester
(4-Methanesulfonlamino-phenyl)-carbamic acid tert-butyl ester
(4-Phenylacetylaminol-phenyl)-carbamic acid tert-butyl ester
[4-[(Thiophene-2-carbonyl)-amino]-phenyl]-carbamic acid tert-butyl ester
[4-(3-Nitro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(3-Acetylaminobenzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(3-Methanesulfonamino-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Trifluoromethyl-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2,6-Difluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Chloro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Bromo-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Nitro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-[(Benz[b]thiophene-2-carbonyl)-amino]-phenyl]-carbamic acid tert-butyl ester
[4-[(Pyridine-4-carbonyl)-amino]-phenyl]-carbamic acid tert-butyl ester
[4-[(Naphthalene-2-carbonyl)-amino]-phenyl]-carbamic acid tert-butyl ester
[4-[(Naphthalene-1-carbonyl)-amino]-phenyl]-carbamic acid tert-butyl ester
[4-[(3-Bromo-thiophene-2-carbonyl)-amino]-phenyl]-carbamic acid tert-butyl ester
[4-[(Biphenyl-2-carbonyl)-amino]-phenyl]-carbamic acid tert-butyl ester
N-(4-tert-Butoxy carbonylamino-phenyl)-phthalamic acid
[4-(2,3-Difluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2,5-Difluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2,4-Difluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Acetylamino-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2-Methanesulfonamino-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2,3,4-Trifluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(2,3,4,5,6-Pentafluoro-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
N-(4-tert-Butyloxycarbonylamino-phenyl)-isophthalamic acid methyl ester
2-Methylsulfanyl-N-[4-(2,2,2-trifluoro-acetylamino)-phenyl]-benzamide
[4-(3-Benzoyloxy-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-(3-Butoxy-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
[4-{(5-Difluoromethyl-furan-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
(4-{(Thiophene-3-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
(4-{(5-Methyl-furan-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
(4-{(5-Bromo-furan-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
(4-Hexanoylamino-phenyl)-carbamic acid tert-butyl ester
[4-(2-Thiophen-2-yl-acetylaminio)-phenyl]-carbamic acid tert-butyl ester
(4-{[Pyridine-3-carbonyl]-amino]-phenyl}-carbamic acid tert-butyl ester
(4-{[4-Bromo-furan-2-carbonyl]-amino]-phenyl}-carbamic acid tert-butyl ester
(4-{[Furan-3-carbonyl]-amino]-phenyl}-carbamic acid tert-butyl ester
(4-Phenoxy-carbonylamino-phenyl)-carbamic acid tert-butyl ester
(4-{[Benzo[1,3]dioxole-4-carbonyl]-amino]-phenyl}-carbamic acid tert-butyl ester
[4-(3-Trifluoromethoxy-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
N-(2,5-Dimethoxy-4-nitro-phenyl)-2-fluoro-benzamide
[4-{(Furan-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
[4-(2-Phenoxy-acetylaminio)-phenyl]-carbamic acid tert-butyl ester
[4-{(5-Nitro-furan-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
[4-{(5-Chloro-furan-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
[4-{[3-Methyl-furan-2-carbonyl]-amino]-phenyl}-carbamic acid tert-butyl ester
[4-(2-Methoxy-acetylaminio)-phenyl]-carbamic acid tert-butyl ester
[4-{[4-Furan-3-yl-[1,2,3]thiadiazole-5-carbonyl]-amino]-phenyl}-carbamic acid tert-butyl ester
(4-{[5-tet-Butyl-furan-2-carbonyl]-amino]-phenyl}-carbamic acid tert-butyl ester
N-[3-Cyano-4-(2,2,2-trifluoro-acetylamino)-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid [3-cyano-4-(2,2,2-trifluoro-acetylamino)-phenyl]amide
N-(4-Acetylamino-2-cyano-phenyl)-2,2,2-trifluoro-acetamide
2,2,2-Trifluoro-N-(4-nitro-2-trifluoromethyl-phenyl)-acetamide
N-(4-Acetylamino-2-trifluoromethyl-phenyl)-2,2,2-trifluoro-acetamide
2-Fluoro-N-[4-(2,2,2-trifluoro-acetylamino)-3-trifluoromethyl-phenyl]benzamide
Furan-2-carboxylic acid [4-(2,2,2-trifluoro-acetylamino)-3-trifluoromethyl-phenyl]amide
2-Fluoro-N-(2-methyl-benzooxazol-6-yl)-benzamide
4-(2-Fluoro-benzoylamino)-2-hydroxy-benzoic acid phenyl ester
{4-[(Isoxazole-5-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
N-(4-Acetylamino-2-methoxy-phenyl)-2,2,2-trifluoro-acetamide
2-Fluoro-N-[3-methoxy-4-(2,2,2-trifluoro-acetylamino)-phenyl]benzamide
2-Fluoro-N-(2-fluoro-benzoyl)-N-(4-nitro-2-trifluoromethyl-phenyl)benzamide
{4-[(1H-Pyrazole-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(1H-Imidazole-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(5-Methyl-[1,2,3]thiadiazole-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(5-Furan-3-yl-[1,2,3]thiadiazole-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
2,2,2-Trifluoro-N-(5-nitro-pyridin-2-yl)-acetamide
{4-[(1-Methyl-1H-pyrazole-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
4-(2-Fluoro-benzoylamino)-2-hydroxy-benzoic acid methyl ester
N-(5-Chloro-2,4-dimethoxy-phenyl)-oxalamic acid
Isoxazole-5-carboxylic acid (4-amino-phenyl)-amide
2-Fluoro-N-(4-nitro-benzyl)-benzamide
Furan-2-carboxylic acid 4-nitro-benzylamide
N-[3-Chloro-5-(2,2,2-trifluoro-acetylamino)-phenyl]-2,2,2-trifluoro-acetamide
N-(3-Amino-5-chloro-phenyl)-2,2,2-trifluoro-acetamide
[4-(2-Fluoro-benzoylamino)-benzyl]-carbamic acid tert-butyl ester
[4-(2,6-Difluoro-benzoylamino)-benzyl]-carbamic acid tert-butyl ester
2,6-Difluoro-N-(4-nitro-benzyl)-benzamide
{4-[(Furan-2-carbonyl)-amino]-benzyl}-carbamic acid tert-butyl ester
N-(3-Amino-5-chloro-phenyl)-acetamide
[4-(3-Chloro-benzyolamino)-phenyl]-carbamic acid tert-butyl ester
[4-(4-Chloro-benzyolamino)-phenyl]-carbamic acid tert-butyl ester
[4-(4-Dimethylamino-benzyolamino)-phenyl]-carbamic acid tert-butyl ester
(4-Benzenesulfonylamino-phenyl)-carbamic acid tert-butyl ester
[4-(3-Trifluoromethyl-benzyolamino)-phenyl]-carbamic acid tert-butyl ester
2,2,2-Trifluoro-N-(5-nitro-pyrimidin-2-yl)-acetamide

EXAMPLE 11 (METHOD 2D)
2-Chloro-N-(2-chloro-4-nitrophenyl)acetamide

5 A solution of 2-chloro-4-nitroaniline (19.0 g) and chloroacetyl chloride (30 mL) in tetrahydrofuran (150 mL) is heated at reflux for 1 hour. The solution is cooled and concentrated under reduced pressure, giving a wet yellow solid. Ether (250 mL) is added and the yellow solid is collected.

10 Using the above procedure and appropriate starting materials the following compounds were prepared:

N-(4-Nitro-3-trifluoromethyl-phenyl)-acetamide
(2-Chloro-4-nitro-phenyl)-carbamic acid ethyl ester
2-Acetylamino-5-nitro-benzoic acid
Furan-2-carboxylic acid (5-chloro-2-hydroxy-4-nitro-phenyl)-amide
Furan-2-carboxylic acid (2-methyl-4-nitro-phenyl)-amide
Furan-2-carboxylic acid (2-methoxy-4-nitro-phenyl)-amide
N-(2-Chloro-4-nitro-phenyl)-benzamide
2-Methoxy-N-(4-nitro-phenyl)-acetamide
N-(4-Nitro-phenyl)-acrylamide
N-(4-Nitro-phenyl)-isobutyrilamide
[4)-(acylloylamino)-phenyl]carbamic acid tert-butyl ester
(4-Nitro-phenyl)-carbamic acid isobutyl ester
[1,2,3]Thiadiazole-4-carboxylic acid (5-nitro-pyridin-2-yl)-amide
Furan-2-carboxylic acid (5-nitro-pyridin-2-yl)-amide
2-Fluoro-N-(5-nitro-pyridin-2-yl)-benzamide
N-(2-Chloro-4-nitro-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (2,5-dimethoxy-4-nitro-phenyl)-amide
N-(2-Cyano-4-nitro-phenyl)-2-fluoro-benzamide
2-Fluoro-N-(2-methoxy-4-nitro-phenyl)-benzamide
2-Methyl-N-(5-nitro-pyridin-2-yl)-benzamide
Furan-2-carboxylic acid (2-methoxy-5-methyl-4-nitro-phenyl)-amide
2-Fluoro-N-(2-methoxy-5-methyl-4-nitro-phenyl)-benzamide
N-(2-Benzoyl-4-nitro-phenyl)-acetamide
N-(2-Benzoyl-4-nitro-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (2-benzoyl-4-nitro-phenyl)-amide
N-(3-Methyl-4-nitro-phenyl)-acetamide
2-Fluoro-N-(3-methyl-4-nitro-phenyl)-benzamide
Furan-2-carboxylic acid (3-methyl-4-nitro-phenyl)-amide
2-Acetylamino-5-nitro-N-phenyl-benzamide
2-[(2-Fluorobenzoyl)amino]-5-nitro-N-phenyl-benzamide
Furan-2-carboxylic acid (4-nitro-2-phenylcarbamoyl-phenyl)-amide
2-Fluoro-N-(4-nitro-naphthalen-1-yl)-benzamide
Furan-2-carboxylic acid (4-nitro-naphthalen-1-yl)-amide
N-(5-Chloro-2-hydroxy-4-nitro-phenyl)-acetamide
N-(5-Chloro-2-hydroxy-4-nitro-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (2-chloro-4-nitro-phenyl)-amide
N-(4-Nitro-2-trifluoromethyl-phenyl)-acetamide
Furan-2-carboxylic acid (2-cyano-4-nitro-phenyl)-amide
2-Fluoro-N-(4-nitro-2-trifluoromethyl-phenyl)-benzamide
Furan-2-carboxylic acid (4-nitro-2-trifluoromethyl-phenyl)-amide
2-Fluoro-N-(2-methyl-4-nitro-phenyl)-benzamide
N-(5-Chloro-2-methyl-4-nitro-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (5-chloro-2-methyl-4-nitro-phenyl)-amide
2-(2-Fluoro-benzoylamino)-5-nitro-benzoic acid
2-[(Furan-2-carbonyl)-amino]-5-nitro-benzoic acid
N-(3-Chloro-4-nitro-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (3-chloro-4-nitro-phenyl)-amide
2,6-Difluoro-N-(3-methyl-4-nitro-phenyl)-benzamide
2-Fluoro-N-(4-nitro-3-trifluoromethyl-phenyl)-benzamide
Furan-2-carboxylic acid (4-nitro-3-trifluoromethyl-phenyl)-amide
2-Chloro-N-(2-chloro-4-nitro-phenyl)-acetamide
N-(2-Chloro-4-nitrophenyl)methanesulfonamide
Furan-2-carboxylic acid [3-methoxy-4-(2,2,2-trifluoro-acetylamino)-phenyl]-amide
N-(2-Chloro-4-nitro-phenyl)-2,2,2-trifluoro-acetamide

EXAMPLE 12

\{4-[(4-Phenyl-[1,2,3]thiadazole-5-carbonyl)-amino]-phenyl\}-
carbamic acid tert-butyl

A solution of 1-(N-tert-butoxycarbonyl)-1,4-phenylenediamine (0.8 g) and 4-phenyl-
[1,2,3]thiadiazole-5-carboxylic acid (0.7 g) in dichloromethane (10 mL) is treated
with triethylamine (1.3 mL) and benzotriazole-1-yl-oxo-tris(dimethylamino)-
phosphonium hexa-fluorophosphate (1.6 g). After stirring at room temperature, the
reaction is diluted with water and extracted with dichloromethane. The organic layer
is washed with 0.5 N hydrochloric acid, saturated sodium bicarbonate, and water then
dried over magnesium sulfate, filtered, and concentrated under reduced pressure to
give the desired product.

Using the above procedure and appropriate starting materials the following
compounds were prepared:

\{4-[(1H-Pyrrole-2-carbonyl)-amino]-phenyl\}-carbamic acid tert-butyl ester
\{4-[(Pyrazine-2-carbonyl)-amino]-phenyl\}-carbamic acid tert-butyl ester
\{4-[(5-Methyl-thiophene-2-carbonyl)-amino]-phenyl\}-carbamic acid tert-butyl ester
\{4-[(1-Methyl-1H-pyrrole-2-carbonyl)-amino]-phenyl\}-carbamic acid tert-butyl ester
\{4-[(Quinoline-8-carbonyl)-amino]-phenyl\}-carbamic acid tert-butyl ester
\{4-[(Benzofuran-2-carbonyl)-amino]-phenyl\}-carbamic acid tert-butyl ester
\{4-[(Isoquinoline-1-carbonyl)-amino]-phenyl\}-carbamic acid tert-butyl ester
{4-[(Quinoline-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(Pyridine-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(Isoquinoline-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(1,2,3)Thiadiazole-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(1H-[1,2,3]Triazole-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-(2-Methylsulfanyl-benzoylamino)-phenyl}-carbamic acid tert-butyl ester
{4-[(Quinoline-4-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(4-Methyl-[1,2,3]thiadiazole-5-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(4-Phenyl-[1,2,3]thiadiazole-5-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
{4-[(1H-Indole-2-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester
[1,2,3]Thiadiazole-4-carboxylic acid 4-nitro-benzyllamide
{4-[(1,2,3)Thiadiazole-4-carbonyl)-amino]-benzyl}-carbamic acid tert-butyl ester
Acetic acid 4-(4-tert-butoxycarbonylamino-phenylcarbamoyle)-(phenyl ester
{4-[(Quinoline-6-carbonyl)-amino]-phenyl}-carbamic acid tert-butyl ester

EXAMPLE 13 (METHOD 2F)
Acetic acid 2-(4-tert-butoxycarbonylamino-2,6-dichloro-phenoxy)-ethyl ester

A solution of [3,5-dichloro-4-(2-hydroxy-ethoxy)-phenyl]-carbamic acid tert-butyl ester (0.85 g) in pyridine (14 mL) is treated with acetic anhydride (1.24 mL) and the mixture is stirred at room temperature for 15 hours. The solvent is removed under reduced pressure and the residue dissolved in ethyl acetate. This solution is then washed twice with 5% aqueous hydrochloric acid, once with saturated aqueous sodium bicarbonate, and then with saturated aqueous sodium chloride. The solution is dried over anhydrous magnesium sulfate and the solvent is removed under reduced pressure to provide the desired product as a colorless oil.
Using the above procedure and appropriate starting materials the following compounds were prepared:

 Phenylsulfanyl-acetonitrile
 Acetic acid 2-(4-tert-butoxycarbonylamino-2,6-dichloro-phenoxy)-ethyl ester

**EXAMPLE 14 (METHOD 2G)**

**(3,5-Dichloro-4-hydroxy-phenyl)-carbamic acid tert-butyl ester**

To a solution of 2,6-dichloro-4-amino phenol (9.5 g) in tetrahydrofuran (130 mL) is added di-tert-butyl-dicarbonate (11.7 g) and the mixture is heated to reflux for approximately 15 hours. The solution is then cooled, concentrated under reduced pressure, diluted with ethyl acetate, and washed successively three times with 5% aqueous hydrochloric acid then once with saturated aqueous sodium chloride. The solution is dried over anhydrous sodium sulfate then concentrated under reduced pressure to provide the desired crude product. This material is then triturated with cold dichloromethane to provide the product as a white solid.

Using the above procedure and appropriate starting materials the following compound was prepared:

**(3-Amino-5-chloro-phenyl)-carbamic acid tert-butyl ester**

**EXAMPLE 15 (METHOD 3A)**

**3,5-Dichloro-4-ethoxy-phenylamine**

Trifluoroacetic acid (5 mL) is added to solid (3,5-dichloro-4-ethoxy-phenyl)-carbamic acid tert-butyl ester (0.97 g) and the mixture is stirred for approximately 45 minutes at room temperature. Water is then added, and the mixture is cooled in an ice bath and basified with solid potassium carbonate. The solution is extracted three times with ethyl acetate and the combined organic phases are washed with saturated aqueous sodium chloride then dried over anhydrous sodium sulfate. Concentration
under reduced pressure and recrystallization from hexanes provides the desired product as a pale yellow crystalline solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

5-Bromo-pyridin-3-ylamine
3-Chloro-4-methanesulfonyl-phenylamine
N-(4-Amino-phenyl)-2-methyl-benzamide
Acetic acid 2-(4-amino-phenylcarbamoyl)-phenyl ester
N-(4-Amino-phenyl)-4-fluoro-benzamide
N-(4-Amino-phenyl)-3-fluoro-benzamide
N-(4-Amino-phenyl)-2-fluoro-benzamide
N-(4-Amino-phenyl)-2-methoxy-benzamide
N-(4-Amino-phenyl)-3-methoxy-benzamide
N-(4-Amino-phenyl)-4-methoxy-benzamide
N-(4-Amino-phenyl)-2-phenyl-acetamide
N-(4-Amino-phenyl)-2,2-dimethyl-propionamide
N-(4-Amino-phenyl)-2,2,2-trifluoro-acetamide
Thiophene-2-carboxylic acid (4-amino-phenyl)-amide
1H-Pyrrole-2-carboxylic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-3-nitro-benzamide
3-Acetylamino-N-(4-amino-phenyl)-benzamide
N-(4-Amino-phenyl)-3-dimethylamino-benzamide
N-(4-Amino-phenyl)-3-methanesulfonylamino-benzamide
N-(4-Amino-phenyl)-2-trifluoromethyl-benzamide
N-(4-Amino-phenyl)-2,6-difluoro-benzamide
N-(4-Amino-phenyl)-2-chloro-benzamide
N-(4-Amino-phenyl)-2-bromo-benzamide
N-(4-Amino-phenyl)-2-nitro-benzamide
Pyrazine-2-carboxylic acid (4-amino-phenyl)-amide
5-Methyl-thiophene-2-carboxylic acid (4-amino-phenyl)-amide
Quinoline-8-carboxylic acid (4-amino-phenyl)-amide
1-Methyl-1H-pyrrole-2-carboxylic acid (4-amino-phenyl)-amide
Benzo[b]thiophene-2-carboxylic acid (4-amino-phenyl)-amide
Benzofuran-2-carboxylic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-isonicotinamide
Naphthalene-2-carboxylic acid (4-amino-phenyl)-amide
Naphthalene-1-carboxylic acid (4-amino-phenyl)-amide
Isoquinoline-1-carboxylic acid (4-amino-phenyl)-amide
Quinoline-2-carboxylic acid (4-amino-phenyl)-amide
3,5-Dichloro-4-ethoxy-phenylamine
4-Butoxy-3,5-dichloro-phenylamine
Isoquinoline-4-carboxylic acid (4-amino-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-amino-phenyl)-amide
1H-[1,2,3]Triazole-4-carboxylic acid (4-amino-phenyl)-amide
3-Bromo-thiophene-2-carboxylic acid (4-amino-phenyl)-amide
4-Benzyloxy-3,5-dichloro-phenylamine
2-(4-Amino-2,6-dichloro-phenoxy)-acetamide
(4-Amino-2,6-dichloro-phenoxy)acetic acid methyl ester
[3-(4-Amino-phenylcarbamoyl)-phenyl]-carbamic acid ethyl ester
2-Amino-N-(4-amino-phenyl)-benzamide
Biphenyl-2-carboxylic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-2,3-difluoro-benzamide
N-(4-Amino-phenyl)-2,5-difluoro-benzamide
N-(4-Amino-phenyl)-2,4-difluoro-benzamide
2-Acetylamino-N-(4-amino-phenyl)-benzamide
N-(4-Amino-phenyl)-2-methanesulfonylamino-benzamide
N-(4-Amino-phenyl)-2,3,4-trifluoro-benzamide
N-(4-Amino-phenyl)-2,3,4,5,6-pentafluoro-benzamide
N-(4-Amino-phenyl)-2-methylsulfonyl-benzamide
Acetic acid 2-(4-amino-2,6-dichloro-phenoxy)-ethyl ester
N-(4-Amino-phenyl)-isophthalamic acid methyl ester
N-(4-Amino-phenyl)-3-benzyloxy-benzamide
N-(4-Amino-phenyl)-3-butoxy-benzamide
[3-(4-Amino-phenylcarbamoyl)-phenoxy]-acetic acid ethyl ester
Pyridine-2-carboxylic acid (4-amoio-phenyl)-amide
Quinoline-4-carboxylic acid (4-amino-phenyl)-amide
5-Methyl-furan-2-carboxylic acid (4-amino-phenyl)-amide
5-Difluoromethyl-furan-2-carboxylic acid (4-amino-phenyl)-amide
1H-Indole-2-carboxylic acid (4-amino-phenyl)-amide
4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid (4-amino-phenyl)-amide
Thiophene-3-carboxylic acid (4-amino-phenyl)-amide
5-Chloro-furan-2-carboxylic acid (4-amino-phenyl)-amide
5-Nitro-furan-2-carboxylic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-2-thiophen-2-yl-acetamide
3-Methyl-furan-2-carboxylic acid (4-amino-phenyl)-amide
5-Bromo-furan-2-carboxylic acid (4-amino-phenyl)-amide
4-Bromo-furan-2-carboxylic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-nicotinamide
N-(4-Aminophenyl)-3-furancarboxamide
4-Phenyl-[1,2,3]thiadiazole-5-carboxylic acid (4-amino-phenyl)-amide
Acetic acid 3-(4-amino-phenylcarbamoyl)-phenyl ester
Benzo[1,3]dioxole-4-carboxylic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-3-(2-dimethylamino-ethoxy)-benzamide
N-(4-Amino-phenyl)-3-trifluoromethoxy-benzamide
N-(4-Amino-phenyl)-3-(2-morpholin-4-yl-ethoxy)-benzamide
(4-Amino-phenyl)-carbamic acid hexyl ester
Furan-2-carboxylic acid (4-amino-phenyl)-amide
(4-Amino-phenyl)-carbamic acid phenyl ester
Hexanoic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-acrylamide
N-(4-Amino-phenyl)-2-methoxy-acetamide
4-Furan-3-yl-[1,2,3]thiadiazole-5-carboxylic acid (4-amino-phenyl)-amide
5-tert-Butyl-furan-2-carboxylic acid (4-amino-phenyl)-amide
3-Chloro-4-methanesulfinyl-phenylamine
5-Methyl-[1,2,3]thiadiazole-4-carboxylic acid (4-amino-phenyl)-amide
2-(4-Amino-2-chloro-phenyl)-ethanol
(4-Amino-2-chloro-phenyl)-carbamic acid 2-piperidin-1-yl-ethyl ester
5-Chloro-N,N-dimethyl-benzene-1,3-diamine
3-(2-Methyl-butyl)-5-trifluoromethyl-phenylamine
3-Isobutyl-5-trifluoromethyl-phenylamine
Furan-2-carboxylic acid (4-aminomethyl-phenyl)-amide
N-(4-Aminomethyl-phenyl)-2-fluoro-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid (4-aminomethyl-phenyl)-amide
N-(4-Aminomethyl-phenyl)-2,6-difluoro-benzamide
Oxazole-4-carboxylic acid (4-amino-phenyl)-amide
N-(4-Amino-phenyl)-3-chloro-benzamide
N-(4-Amino-phenyl)-4-chloro-benzamide
Acetic acid 4-(4-amino-phenylcarbamoyl)-phenyl ester
N-(4-Amino-phenyl)-4-dimethylamino-benzamide
1-(4-Amino-phenyl)-3-(3,5-bis-trifluoromethyl-phenyl)-thiourea
N-(4-Amino-phenyl)-2-iodo-benzamide
N-(4-Amino-phenyl)-3-trifluoromethyl-benzamide

EXAMPLE 16 (METHOD 3B)
1-(4-Amino-2-chloro-phenyl)-ethanol

A 1M solution of tetrabutylammonium fluoride in tetrahydrofuran (5.7 mL) is added to [3-chloro-4-(1-hydroxy-ethyl)-phenyl]-carbamic acid 2-trimethylsilyl-ethyl ester (0.5 g) and the mixture is stirred at room temperature for approximately 3.5 hours. The solution is then concentrated under reduced pressure, dissolved in a 1:1 mixture of ethyl acetate and hexanes, washed successively with water then saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure followed by chromatography over silica gel (40% ethyl acetate in hexanes is used as the eluant) provides the product as an amber oil.
EXAMPLE 17 (METHOD 3C)

N-(4-Amino-3-cyanophenyl)-2-fluoro-benzamide

Potassium carbonate (5.0 g) is added to a solution of N-[3-cyano-4-(2,2,2-
trifluoroacetyl-amino)-phenyl]-2-fluoro-benzamide (2.5 g) in methanol (270 mL) and
water (16 mL) and the mixture is refluxed overnight. After removing the solvent
under reduced pressure, the residue is suspended in water and extracted with
dichloromethane. The organic extracts are pooled, washed with water and then
saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered
and concentrated under reduced pressure to provide the desired compound as a white
solid.

Using the above procedure and appropriate starting materials the following
compounds were prepared:

N-(4-Amino-phenyl)-2-methanesulfinyl-benzamide
N-(4-Amino-3-cyano-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-3-cyano-phenyl)-amide
N-(4-Amino-3-cyano-phenyl)-acetamide
Furan-2-carboxylic acid (4-amino-3-trifluoromethyl-phenyl)-amide
N-(4-Amino-3-methoxy-phenyl)-acetamide
N-(4-Amino-3-methoxy-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-amino-3-methoxy-phenyl)-amide

EXAMPLE 17 (METHOD 4A)

2-Chloro-1-cyclohexyloxy-4-nitro-benzene

Cylohexanol (2.9 g) in dimethylsulfoxide (20 mL) is added slowly to a flask
containing potassium hydride (0.90 g, pre-washed three times with hexanes) under an
atmosphere of argon and the solution is stirred for about 1 hour at room temperature.
A solution of 3-chloro-4-fluoro-nitrobenzene (1 g) in dimethylsulfoxide (10 mL) is
added and the resulting dark red colored solution is then heated for three hours to
approximately 100 degrees. The reaction mixture is then cooled, diluted with diethyl ether (300 mL), and washed successively with saturated aqueous ammonium chloride, three times with water, then with saturated aqueous sodium chloride. The organic layer is then dried over anhydrous magnesium sulfate, the solvent is removed under reduced pressure, and the resulting oil is chromatographed over silica gel (5% ethyl acetate in hexanes is used as the eluant) to provide the desired product as an orange solid.

EXAMPLE 18 (METHOD 4C)

(2-Chloro-4-nitro-phenyl)-methyl-(1-methyl-pyrrolidin-3-yl)-amine

3-Chloro-4-fluoronitrobenzene (1.0 g) and N,N’-dimethyl-3-aminopyrrolidine (1.72 g) are combined and stirred for approximately 24 hours. The mixture is then diluted with ethyl acetate, washed twice with water and once with saturated sodium chloride, and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure the residue is chromatographed over silica gel (pure ethyl acetate followed by pure methanol is used as the eluants) to provide the desired product as a yellow oil.

Using the above procedure and appropriate starting materials the following compounds were prepared:

(2-Chloro-4-nitro-phenyl)-dipropyl-amine
1-(2-Chloro-4-nitro-phenyl)-piperidine
1-(2-Chloro-4-nitro-phenyl)-pyrrolidine
(2-Chloro-4-nitro-phenyl)-cyclohexyl-methyl-amine
Benzyl-(2-chloro-4-nitro-phenyl)-amine
(2-Chloro-4-nitro-phenyl)-methyl-(1-methyl-piperidin-4-yl)-amine
(2-Chloro-4-nitro-phenyl)-cyclohexyl-ethyl-amine
(2-Chloro-4-nitro-phenyl)-cyclohexyl-amine
(2-Chloro-4-nitro-phenyl)-methyl-(1-methyl-pyrrolidin-3-yl)-amine
(1-Benzyl-pyrrolidin-3-yl)-(2-chloro-4-nitro-phenyl)-methyl-amine
(2-Chloro-4-nitro-phenyl)-cyclopentyl-methyl-amine
1-(2-Chloro-4-nitro-phenyl)-decahydro-quinoline
Allyl-(2-chloro-4-nitro-phenyl)-cyclohexyl-amine
2-[(2-Chloro-4-nitro-phenyl)-(2-hydroxy-ethyl)-amino]-ethanol
(2-Chloro-4-nitro-phenyl)-isobutyl-methyl-amine
(2-Chloro-4-nitro-phenyl)-hexyl-methyl-amine
2-[(2-Chloro-4-nitro-phenyl)-methyl-amino]-ethanol
N-(2-Chloro-4-nitro-phenyl)-N,N',N'-trimethyl-ethane-1,2-diamine
N-(2-Chloro-4-nitro-phenyl)-N,N',N'-trimethyl-propane-1,3-diamine
(1-Benzyl-piperidin-4-yl)-(2-chloro-4-nitro-phenyl)-amine
N-(2-Chloro-4-nitro-phenyl)-N,N'-dimethyl-ethane-1,2-diamine
N-(2-Chloro-4-nitro-phenyl)-N,N'-dimethyl-propane-1,3-diamine
(2-Chloro-4-nitro-phenyl)-(2-methoxy-ethyl)-methyl-amine
(1-Benzyl-pyrroloidin-3-yl)-(2-chloro-4-nitro-phenyl)-amine
4-Piperidin-1-yl-3-trifluoromethyl-benzonitrile
4-Dimethylamino-3-trifluoromethyl-benzonitrile
4-(4-Methyl-piperazin-1-yl)-3-trifluoromethyl-benzonitrile

EXAMPLE 19 (METHOD 4E)
Butyl-(2-chloro-4-nitro-phenyl)thioether

A solution of 3-chloro-4-fluoro-nitrobenzene (5.0 g) and sodium sulfide (2.5 g) in
N,N-dimethylformamide (30 mL) is stirred at room temperature for 1 hour and then
treated with 1-iodobutane (12.6 g). The solvent is then removed under reduced
pressure and the resulting residue is treated with ethyl acetate and hexanes to
precipitate the inorganic salts. The solids are removed by filtration and the filtrate is
reduced under reduced pressure. The resulting residue is then passed through
hydrous magnesium silicate using dichloromethane as the eluent to provide the
desired compound as a yellow solid.

Using the above procedure and appropriate starting materials the following
compounds were prepared:
1-Butylsulfanyl-2-chloro-4-nitro-benzene
2-Chloro-1-cyclohexylsulfanyl-4-nitro-benzene
2-Chloro-1-ethylsulfanyl-4-nitro-benzene

EXAMPLE 20 (METHOD 4F)

(4-Chloro-5-methoxy-2-nitro-phenyl)-dimethyl-amine

5 To a solution of trifluoro-methanesulfonic acid 4-chloro-5-methoxy-2-nitro-phenyl ester (1.0 g) in tetrahydrofuran (2.0 mL) is added dimethylamine (4.0 mL of a 40% aqueous solution) and the mixture is stirred at room temperature for approximately 15 hours. The solution is then concentrated under reduced pressure and the residue is dissolved in ethyl acetate and then washed with water. The aqueous layer is extracted once with ethyl acetate and the combined organic layers are washed with saturated aqueous sodium chloride and dried over anhydrous sodium sulfate. The solvent is removed by evaporation under reduced pressure and the residue is triturated with hexanes to provide the desired product as a colorless solid.

15 Using the above procedure and appropriate starting materials the following compounds were prepared:

(4-Chloro-2-nitro-phenyl)-dimethyl-amine
4-(4-Chloro-5-methoxy-2-nitro-phenyl)-morpholine
(4-Chloro-5-methoxy-2-nitro-phenyl)-dimethyl-amine
1-(4-Chloro-5-methoxy-2-nitro-phenyl)-piperidine
1-(4-Chloro-5-methoxy-2-nitro-phenyl)-pyrroolidine
Benzyl-(4-chloro-5-methoxy-2-nitro-phenyl)-amine
(2-Chloro-6-nitro-phenyl)-dimethyl-amine
EXAMPLE 21 (METHOD 4G)
(2-Chloro-4-nitro-phenyl)-methyl-phenyl-amine

$n$-Butyl lithium (12.3 mL of a 2.5 M solution in hexanes) is added dropwise to a solution of N-methyl aniline (3.0 g) in tetrahydrofuran (75 mL) at 0°C. The mixture is allowed to warm slowly to room temperature and is then re-cooled to 0°C and added by cannula to a solution of 3-chloro-4-fluoronitrobenzene (4.9 g) in tetrahydrofuran (35 mL) that is kept at -78 °C. Following the addition, the reaction mixture is permitted to warm to room temperature over the course of 1 hour, and is then concentrated under reduced pressure, quenched by addition of saturated aqueous ammonium chloride, and extracted three times with ethyl acetate. The pooled organic layers are washed three times with 5% aqueous hydrochloric acid, once with water, once with saturated aqueous sodium bicarbonate, once with saturated aqueous sodium chloride, and then dried over anhydrous magnesium sulfate. Following removal of the solvent under reduced pressure the residue is chromatographed over silica gel (5% diethyl ether in hexanes is used as the eluant) to provide the desired product as a clear colorless oil.

EXAMPLE 22 (METHOD 4H)
2,6-Dichloro-4-nitrophenol

3,4,5-Trichloronitrobenzene (14.86 g) is added to a solution of potassium phenoxide (8.66 g) in diethylene glycol (66 mL) and the mixture is heated to 160°C for approximately 15 hours. The resulting dark brown solution is cooled to room temperature, poured onto 100 mL cold water, and extracted twice with diethyl ether. The pooled organic extracts are washed with water, 10% aqueous sodium hydroxide, and then dried over anhydrous magnesium sulfate. Following removal of the solvent under reduced pressure the resulting oil is distilled in a Kugelrohr apparatus to provide a yellow oil that solidifies on standing. Recrystallization from ethanol-water provides the desired product as a pale yellow solid.
EXAMPLE 23 (METHOD 5A)

(3,5-Dichloro-4-ethoxy-phenyl)-carbamic acid tert-butyl ester

To a solution of (3,5-dichloro-4-hydroxy-phenyl)-carbamic acid tert-butyl ester (1.0 g) and potassium carbonate (1.0 g) in acetone (18 mL) is added ethyl iodide (0.36 mL) and the mixture is stirred for approximately 15 hours at room temperature. The solution is then filtered, concentrated under reduced pressure, and partitioned between ethyl acetate and water. The separated aqueous layer is further extracted twice with ethyl acetate, and the pooled organic extracts are washed successively with 10% aqueous sodium hydroxide, with water, and then dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave the desired product as a tan solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

(3,5-Dichloro-4-ethoxy-phenyl)-carbamic acid tert-butyl ester
(4-Butoxy-3,5-dichloro-phenyl)-carbamic acid tert-butyl ester
(4-Benzyl oxy-3,5-dichloro-phenyl)-carbamic acid tert-butyl ester
(4-Car bamoylmethoxy-3,5-dichloro-phenyl)-carbamic acid tert-butyl ester
[3,5-Dichloro-4-(2-nitrilo-ethoxy)-phenyl]-carbamic acid tert-butyl ester
(4-tert-Butoxycarbonylamino-2,6-dichloro-phenoxy)-acetic acid methyl ester
3-Butoxy-benzoic acid methyl ester
3-tert-Butoxycarbonylmethoxy-benzoic acid methyl ester
3-Car bamoylmethoxy-benzoic acid methyl ester
[4-(3-Car bamoylmethoxy-benzo ylamino)-phenyl]-carbamic acid tert-butyl ester
{4-[3-(2-Chloro-ethoxy)-benzo ylamino]-phenyl}-carbamic acid tert-butyl ester
EXAMPLE 24 (METHOD 5C)
(2,6-Dichloro-4-nitro-phenoxy)-acetic acid tert-butyl ester

To a solution of 2,6-dichloro-4-nitrophenol (2.5 g) and potassium carbonate (3.3 g) in dimethyl-formamide (50 mL) is added tert-butyl-bromoacetate (10 mL) and the mixture is stirred at room temperature for two days. The solution is then poured into 500 mL water, extracted three times with hexanes, and the pooled organic extracts are washed with saturated aqueous ammonium chloride and then dried over anhydrous magnesium sulfate. Evaporation of the solvent under reduced pressure followed by trituration of the resulting oil with hexanes provides the desired product as a white solid.

Using the above procedure and starting materials the following compounds were prepared:

3-Dimethylamino-1-(4-nitro-phenyl)-propenone
2-Chloro-1-isopropoxy-4-nitro-benzene
1,3-Dichloro-2-methoxy-4-methyl-5-nitro-benzene
1-Chloro-4-ethoxy-2-methoxy-5-nitro-benzene
1-Butoxy-4-chloro-5-methoxy-2-nitro-benzene
1-Chloro-2-methoxy-5-nitro-4-(phenylmethoxy)benzene (CA name)
1-Chloro-4-methoxy-5-nitro-2-(phenylmethoxy)benzene (CA name)
(2,6-Dichloro-4-nitro-phenoxy)-acetic acid tert-butyl ester
(2,6-Dichloro-4-nitro-phenoxy)-acetonitrile
1-Chloro-4-methoxy-2-methyl-5-nitro-benzene
2-(4-Chloro-5-methoxy-2-nitro-phenoxy)-acetamide
2-(2-Chloro-5-methoxy-4-nitro-phenoxy)-acetamide
(4-Chloro-5-methoxy-2-nitro-phenoxy)-acetonitrile
(2-Chloro-5-methoxy-4-nitro-phenoxy)-acetonitrile
4-(2-Chloro-5-methoxy-4-nitro-phenoxy)-butyronitrile
2-(4-Chloro-5-methoxy-2-nitro-phenoxy)-ethanol
2-(2-Chloro-5-methoxy-4-nitro-phenoxy)-ethanol
(2-Chloro-5-methoxy-4-nitro-phenoxy)-acetic acid tert-butyl ester
(2-Chloro-5-methoxy-4-nitro-phenoxy)-acetic acid methyl ester
(4-Chloro-5-methoxy-2-nitro-phenoxy)-acetic acid methyl ester
(4-Chloro-5-methoxy-2-nitro-phenoxy)-acetic acid tert-butyl ester
(2-Chloro-4-nitro-phenoxy)-acetonitrile
1-Butoxy-2-chloro-4-nitro-benzene
2-Chloro-4-nitro-1-(2,2,2-trifluoro-ethoxy)-benzene
2-Chloro-4-nitro-1-propoxy-benzene
2-Chloro-1-ethoxy-4-nitro-benzene
1,3-Diiodo-2,4-dimethoxy-5-nitro-benzene
1,3-Dibromo-2,4-dimethoxy-5-nitro-benzene
3-Chloro-2,4-dimethoxy-nitrobenzene

EXAMPLE 25 (METHOD 5E)
[3,5-Dichloro-4-(2-hydroxy-ethoxy)-phenyl]-carbamic acid
tert-butyl ester

To a solution of (3,5-dichloro-4-hydroxy-phenyl)-carbamic acid tert-butyl ester (1.0 g) and potassium carbonate (0.55 g) in toluene (20 mL) is added ethylene carbonate (1.6 g) and the mixture is heated to reflux for 3 hours. To the cooled reaction mixture is added 2.5 M aqueous sodium hydroxide (50 mL), and the separated organic layer is then washed successively with water, then saturated aqueous sodium chloride, and then dried over anhydrous sodium sulfate. The solvent is then removed by evaporation under reduced pressure and the resulting residue is chromatographed over silica gel (30% ethyl acetate in hexanes is used as the eluant) to provide the desired product as a white foam.

EXAMPLE 26 (METHOD 6)
3-(2-Chloro-4-nitro-phenoxy)-1-methyl-pyrrolidine

To a solution of 2-chloro-4-nitrophenol (2.0 g) in tetrahydrofuran (60 mL) is added 1-methyl-3-pyrrolidinol (2.3 g), triphenyl phosphine (6.0 g), and diethylazodi-
carboxylate (3.6 mL) and the mixture is stirred at room temperature under an atmosphere of argon for 1.5 hours. The solution is then concentrated under reduced pressure, diluted with ethyl acetate, washed successively with 10% aqueous sodium hydroxide, water, saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. The solvent is removed by evaporation under reduced pressure and the residue is chromatographed over silica gel (ethyl acetate then 10% methanol in dichloromethane is used as the eluant). Pooled product fractions are then recrystallized from hexanes to provide the desired product as a yellow solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

- 4-(2-Chloro-4-nitro-phenoxy)-1-methyl-piperidine
- 3-(2-Chloro-4-nitro-phenoxy)-1-methyl-pyrrolidine
- [2-(2-Chloro-4-nitro-phenoxy)-ethyl]-dimethyl-amine
- [3-(2-Chloro-4-nitro-phenoxy)-propyl]-dimethyl-amine

**EXAMPLE 27 (METHOD 7A)**

2-Chloro-3-methoxy-6-nitro-phenol

and

2,4-Dichloro-3-methoxy-6-nitro-phenol

To a flask containing 3-methoxy-6-nitro-phenol (0.5 g) is added aqueous sodium hypochlorite (5.25% aqueous solution, 21 mL) and the mixture is stirred at room temperature for approximately 24 hours. The mixture is then cooled in an ice-bath, acidified by addition of concentrated hydrochloric acid, then extracted twice with ethyl acetate. These organic extracts are dried over anhydrous magnesium sulfate, the solvent is removed by evaporation under reduced pressure, and the residue is chromatographed over silica gel (15% acetone in hexanes is used as the eluant) to provide both the mono- and di-chlorinated products as yellow solids.
Using the above procedure and appropriate starting materials the following compounds were prepared:

3-Chloro-2-hydroxy-4-methoxy-nitrobenzene  
3,5-Dichloro-2-hydroxy-4-methoxy-nitrobenzene

5

EXAMPLE 28 (METHOD 7B)
2,4-Dichloro-3-methyl-6-nitro-phenol

To a solution of 3-methyl-4-nitro-phenol (5.0 g) in water (150 mL) is added aqueous sodium hypochlorite (5.25% aqueous solution, 230 mL) and the mixture is stirred at room temperature for approximately 15 hours. Additional aqueous sodium hypochlorite (5.25% aqueous solution, 230 mL) is added and the mixture is permitted to stir at room temperature for 2.5 days. The mixture is then cooled in an ice-bath, acidified by addition of concentrated hydrochloric acid, then extracted twice with ethyl acetate. These organic extracts are dried over anhydrous magnesium sulfate, the solvent is removed by evaporation under reduced pressure, and the residue is chromatographed over silica gel (ethyl acetate is used as the eluant) to provide the desired product as a yellow solid. An analytically pure sample is obtained by a single recrystallization from chloroform.

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EXAMPLE 29 (METHOD 7C)
1-Bromo-2,4-dimethoxy-5-nitro-benzene

To a solution of 2,4-dimethoxy-nitrobenzene (0.50 g) in chloroform (3 mL) is added dropwise a solution of bromine (0.23 g) in chloroform (1 mL) and the mixture is allowed to stir at room temperature for approximately 15 hours. Additional bromine (0.15 g) in chloroform (1 mL) is added and the reaction is stirred for an additional 4 hours. The mixture is then poured onto 5% aqueous sodium bisulfite and then extracted with chloroform. Pooled organic extracts are then washed successively with 5% aqueous sodium bisulfite then saturated sodium chloride, and then dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure and
recrystallization of the residue from toluene provides the desired product as a yellow solid.

**EXAMPLE 30 (METHOD 7D)**

*2,4-Dibromo-3-methoxy-6-nitro-phenol*

To a solution of 5-methoxy-2-nitro-phenol (0.25 g) and silver trifluoroacetate (0.49 g) in glacial acetic acid (3 mL) is added dropwise a solution of bromine (1.42 g) in glacial acetic acid (3 mL) and the mixture is stirred at room temperature for approximately 24 hours. The solution is then partitioned between ethyl acetate and water, and the organic layer is washed successively three times with 5% aqueous sodium bisulfite, three times with saturated aqueous sodium bicarbonate, and once with saturated aqueous sodium chloride. The organic layer is then dried over anhydrous magnesium sulfate and the solvent is removed under reduced pressure. The residue is chromatographed over silica gel (20% ethyl acetate in hexanes is used as the eluant) then recrystallized from chloroform to provide the desired dibrominated product as an orange solid.

**EXAMPLE 31 (METHOD 7E)**

*1-Iodo-2,4-dimethoxy-5-nitro-benzene*

To a solution of 2,4-dimethoxy-nitrobenzene (1.0 g) in glacial acetic acid (30 mL) is added benzyltrimethylammonium dichloroiodate (1.90 g) and anhydrous zinc chloride (1.0 g) and the mixture is stirred at room temperature under an atmosphere of argon. Additional benzyltrimethylammonium dichloroiodate (0.4 g) is added after 5 hours and again after 24 hours. Additional zinc chloride (0.5 g) and glacial acetic acid (15 mL) is added after 24 hours. The mixture is permitted to stir at room temperature for 3 days and is then filtered, diluted with 5% aqueous sodium bisulfite, and extracted three times with ethyl acetate. These pooled organic extracts are washed successively with 5% aqueous sodium bisulfite, saturated aqueous sodium chloride, then dried over anhydrous magnesium sulfate. After removal of the solvent
under reduced pressure the residue is trititated with hexanes to provide the desired product as a pale yellow solid.

**EXAMPLE 32 (METHOD 7F)**

2,4-Diiodo-3-methoxy-6-nitro-phenol

To a solution of 5-methoxy-2-nitro-phenol (0.25 g) in dichloromethane (15 mL) and methanol (6 mL) is added benzyltrimethylammonium dichloroiodate (1.08 g) and sodium bicarbonate (0.85 g) and the mixture is allowed to stir at room temperature for 24 hours. The solution is then filtered, the filtrate is concentrated under reduced pressure, the residue is dissolved in ethyl acetate and then washed successively with 5% aqueous sodium bicarbonate, 5% aqueous sodium bisulfite, and saturated aqueous sodium chloride. After drying over anhydrous magnesium sulfate the solvent is removed by evaporation under reduced pressure and the residue is recrystallized from toluene to provide the desired product as yellow needles.

**EXAMPLE 33 (METHOD 7G)**

1-Fluoro-2,4-dimethoxy-5-nitro-benzene

To a solution of 2,4-dimethoxy-nitrobenzene (1.0 g) in tetrachloroethane (10 mL) is added 3,5-dichloro-1-fluoro-pyridinium triflate (85%, 5.07 g) and the mixture is heated to 120 °C for 5 hours. Additional 3,5-dichloro-1-fluoro-pyridinium triflate (85%, 0.25 g) is added and heating is continued for 1 hour. The solution is then cooled to room temperature and passed over a column of silica gel (hexanes followed by 30% ethyl acetate in hexanes is used as the eluant). Product containing fractions are combined, evaporated under reduced pressure, and the residue is crystallized from hexanes to provide the desired product as a tan solid.
EXAMPLE 34 (METHOD 8)

3-Chloro-4-trifluoromethyl-nitrobenzene

A solution of 3-chloro-4-iodo-nitrobenzene (2.26 g), trimethyl(trifluoromethyl)siulane (5.68 g), copper(I) iodide (2.28 g), and potassium fluoride (0.56 g) in N,N-dimethylformamide (8 mL) is heated in a sealed tube to 80 °C for 40 hours. The solution is then cooled, diluted with diethyl ether, filtered through diatomaceous earth, and the filtrate is washed successively with water, saturated aqueous sodium chloride, and then dried over anhydrous sodium sulfate. The solvent is removed under reduced pressure and the residue is chromatographed over silica gel (1% diethyl ether in hexanes followed by 10% ethyl acetate in hexanes is used as the eluant) to provided the desired product as a colorless oil.

EXAMPLE 35 (METHOD 9)

(3-Chloro-4-methanesulfinyl-phenyl)-carbamic acid tert-butyl ester

To a solution of (3-chloro-4-thiomethyl-phenyl)-carbamic acid tert-butyl ester (0.89 g) in dichloromethane (15 mL) at 0 °C is added a solution of dimethyldioxirane (~0.11 M in acetone, 34 mL) and the mixture is stirred at 0 °C for 1 hour. The solvent is removed under reduced pressure and the residue is dissolved in dichloromethane, washed with saturated aqueous sodium chloride, and then dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure gave the desired product as an orange foam.

EXAMPLE 36 (METHOD 9B)

[4-(2-Methylsulfinyl-benzoylamino)-phenyl]-carbamic acid tert-butyl ester

To a solution of 2-methylsulfanyl-N-[4-(2,2,2-trifluoro-acetylamino)-phenyl]-benzamide (234 mg) is added a saturated solution of sodium periodate (5 mL) and the mixture is stirred for 12 hours. The purple mixture is poured into water, extracted
with ethyl acetate, dried over anhydrous potassium carbonate and evaporated to yield a red solid, 101 mg.

Using the above procedure and appropriate starting materials the following compounds were prepared:

[4-(2-Methanesulfinyl-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
2-Methanesulfinyl-N-[4-(2,2,2-trifluoro-acetylamino)-phenyl]-benzamide

EXAMPLE 37 (METHOD 10)
(3-Chloro-4-methanesulfonyl-phenyl)-carbamic acid tert-butyl ester

To a solution of (3-chloro-4-thiomethyl-phenyl)-carbamic acid tert-butyl ester (0.90 g) in dichloromethane (30 mL) at 0 °C is added a solution of dimethyldioxirane (~0.11 M in acetone, 80 mL) and the mixture is stirred at 0 °C for 1 hour. The solvent is removed under reduced pressure and the residue is dissolved in dichloromethane, washed with saturated aqueous sodium chloride, and then dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure gives the desired product as an orange foam.

EXAMPLE 38 (METHOD 11)
3-Chloro-4-vinyl-phenylamine

To a deoxygenated solution of 3-chloro-4-iodo-aniline (6.95 g), triphenyl arsine (0.67 g), and tris(dibenzylideneacetone)palladium(0) (0.50 g) in tetrahydrofuran (120 mL) at 50 °C is added tributylvinyltin (10 g) and the mixture is stirred for approximately 15 hours at 50 °C under an atmosphere of argon. The reaction is then cooled, filtered through diatomaceous earth, and the filtrate is evaporated to dryness under reduced pressure. The residue is dissolved in hexanes and then extracted three times with 5% aqueous hydrochloric acid. These aqueous acidic extracts are then basified with solid potassium carbonate and extracted three times with ethyl acetate. These pooled organic extracts are then washed with saturated aqueous sodium chloride, dried over
anhydrous magnesium sulfate, and the solvent is removed under reduced pressure. The resulting residue is chromatographed over silica gel (hexanes and then 10% ethyl acetate in hexanes is used as the eluant) to provide the desired product as an amber oil.

**EXAMPLE 39 (METHOD 12)**

**[3-Chloro-4-(1-hydroxy-ethyl)-phenyl]-carbamic acid 2-trimethylsilanyi-ethyl ester**

(3-Chloro-4-vinyl-phenyl)-carbamic acid 2-trimethylsilanyi-ethyl ester (2.6 g) is added to a solution of mercuric acetate (3.48 g) in water (7 mL) and tetrahydrofuran (5.25 mL) and the mixture is stirred for approximately 15 hours. 3N Aqueous sodium hydroxide (8.7 mL) and a 0.5 M solution of sodium borohydride in 3N aqueous sodium hydroxide (8.7 mL) are then added and stirring is continued for 6 hours. The solution is then saturated with sodium chloride and extracted with ethyl acetate. These organic extracts are then washed with saturated aqueous sodium chloride and dried over anhydrous sodium sulfate. Following removal of the solvent under reduced pressure the residue is chromatographed over silica gel (20% ethyl acetate in hexanes is used as the eluant) to provide the desired product as a white solid.

**EXAMPLE 40 (METHOD 13)**

**[3-Chloro-4-(2-hydroxy-ethyl)-phenyl]-carbamic acid tert-butyl ester**

To a stirring suspension of sodium borohydride (0.45 g) in tetrahydrofuran (13 mL) at 0 °C is added glacial acetic acid (0.75 mL) and the mixture is stirred at 0°C for 1 hour. The solution is then warmed to room temperature and (3-chloro-4-vinyl-phenyl)-carbamic acid 2-trimethylsilanyi-ethyl ester (1.0 g) is added. The reaction is stirred at room temperature for approximately 15 hours and then heated to reflux for approximately 20 hours. The mixture is then cooled and solutions of 5 N aqueous sodium hydroxide (0.80 mL) and 30% aqueous hydrogen peroxide (0.56 mL) are added. After stirring for an additional 15 hours the layers are separated, the aqueous
layer is extracted three times with diethyl ether, and these organic extracts are dried over anhydrous magnesium sulfate. Following removal of the solvent under reduced pressure the residue is chromatographed over silica gel (40% ethyl acetate in hexanes is used as the eluant) to provide the desired product as an amber oil.

EXAMPLE 41 (METHOD 14)

[4-(1-Azido-ethyl)-3-chloro-phenyl]-carbamic acid 2-trimethylsilyl-ethyl ester

To a solution of [3-chloro-4-(1-hydroxy-ethyl)-phenyl]-carbamic acid 2-trimethylsilyl-ethyl ester (1.25 g) in tetrahydrofuran (20 mL) at 0 °C under an atmosphere of argon is added triphenyl-phosphine (2.6 g), hydrazoic acid (approximately 2.5 molar equivalents in dichloromethane, prepared by the method of Fieser and Fieser, Reagents for Organic Synthesis, Vol. 1, pg. 446; Wiley, New York) and diethyl azodicarboxylate (1.72 g). After approximately 10 minutes the solvent is removed under reduced pressure and the residue is chromatographed over silica gel (5% ethyl acetate in hexanes is used as the eluant) to provide the desired product as a colorless oil.

EXAMPLE 42 (METHOD 15)

[3-Chloro-4-(3-dimethylamino-prop-1-ynyl)-phenyl]-carbamic acid tert-butyl ester

To a deoxygenated solution of (3-chloro-4-iodo-phenyl)-carbamic acid tert-butyl ester (10.0 g) in triethylamine (120 ml) is added 1-dimethylamino-2-propyne (2.82 g), bis(triphenyl-phosphine)palladium(II) chloride (0.4 g), and cuprous iodide (0.054 g). The mixture is stirred at room temperature under an atmosphere of argon for approximately 6 hours and is then heated briefly (ca. 10 minutes) to 60°C. The reaction mixture is then cooled, filtered through diatomaceous earth, and the solvent is removed by evaporation under reduced pressure. The residue is dissolved in ethyl acetate, washed three times with water, once with saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. The solvent is removed by evaporation under reduced pressure, and the residue is chromatographed over silica gel (80%
ethyl acetate in hexanes is used as the eluant) to give the purified product as an amber oil that solidified on standing.

Using the above procedure and appropriate starting materials the following compounds were prepared:

[3-Chloro-4-(3-dimethylamino-prop-1-ynyl)-phenyl]-carbamic acid tert-butyl ester
[3-(4-Methoxy-phenyl)-prop-2-ynyl]-dimethyl-amine
4-(3-Dimethylamino-prop-1-ynyl)-benzonitrile
Dimethyl-[3-(4-nitro-phenyl)-prop-2-ynyl]-amine

EXAMPLE 43 (METHOD 16)

[3-Chloro-4-(3-dimethylamino-acryloyl)-phenyl]-carbamic acid tert-butyl ester

To an ice cold solution of [3-chloro-4-(3-dimethylamino-prop-1-ynyl)-phenyl]-carbamic acid tert-butyl ester (4.0 g) in dichloromethane (30 ml) is added in small portions 3-chloroperoxybenzoic acid (2.34 g). After the reaction is stirred at 0°C for 20 minutes, the mixture is passed over twenty weight equivalents of basic alumina (Brockmann Grade I, 150 mesh) and the N-oxide is eluted using a solution of 5% methanol in dichloromethane. All fractions containing the desired amine N-oxide were combined and evaporated to near dryness under reduced pressure. The residue is treated successively three times with small portions of methanol (ca. 50 ml) followed by evaporation to near dryness under reduced pressure, and the volume of the solution is adjusted to 250 mL by addition of methanol. The methanolic solution of the N-oxide is then heated to reflux for approximately 15 hours, then cooled, and the solvent is evaporated to dryness under reduced pressure. The residue is purified by chromatography over silica gel (80% ethyl acetate in hexanes is used as the eluant) to give the desired product as a pale yellow solid.
EXAMPLE 44 (METHOD 17)
(3-Chloro-4-isoaxazol-5-yl-phenyl)-carbamic acid tert-butyl ester

A solution of [3-chloro-4-(3-dimethylamino-acryloyl)-phenyl]-carbamic acid tert-butyl ester (270 mg) in dioxane (3 ml) is treated with hydroxylamine hydrochloride (122 mg) and the mixture is stirred at room temperature for 10 days. The mixture is diluted with ethyl acetate, washed successively with water, 5% aqueous sodium bicarbonate, saturated aqueous sodium chloride, and then dried over anhydrous magnesium sulfate. The solvent is removed by evaporation under reduced pressure and the resulting residue is chromatographed over silica gel (33% ethyl acetate in hexanes is used as the eluant) to provide the desired product as a colorless solid.

EXAMPLE 45 (METHOD 18)
[3-Chloro-4-(1H-pyrazol-3-yl)-phenyl]-carbamic acid tert-butyl ester

A solution of [3-chloro-4-(3-dimethylamino-acryloyl)-phenyl]-carbamic acid tert-butyl ester (250 mg) in ethanol (1.25 ml) is treated with hydrazine hydrate (0.25 ml) and the mixture is stirred at room temperature for 3 hours. The mixture is then diluted with 30 mL of diethyl ether, washed three times with water, once with saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. The solvent is removed by evaporation under reduced pressure and the resulting residue is chromatographed over silica gel (67% ethyl acetate in hexanes is used as the eluant) to provide the desired product as an oil.

EXAMPLE 46 (METHOD 19A)
N-(2-Chloro-4-nitrophenyl)-2-thiomorpholin-4-yl-acetamide

To a solution N-(chloroacetyl)-2-chloro-4-nitroaniline (3.80 g) in tetrahydrofuran (50 mL) is added thiomorpholine (10 mL) and the solution allowed to stand for 1 hour. This reaction mixture is poured into water a pale yellow solid is collected and then recrystallized from hot 2-propanol to give a pale yellow crystalline solid.
Using the above procedure and appropriate starting materials the following compounds were prepared:

(4-{2-[Bis-(2-hydroxy-ethyl)-amino]-acetylaminol-phenyl}-carbamic acid tert-butyl ester
[4-(2-Dimethylamino-acetylaminol-phenyl]-carbamic acid tert-butyl ester
{4-[3-(2-Dimethylamino-ethoxy)-benzoylaminol-phenyl]-carbamic acid tert-butyl ester
{4-[3-(2-Morpholin-4-yl-ethoxy)-benzoylaminol-phenyl]-carbamic acid tert-butyl ester
N-(2-Chloro-4-nitro-phenyl)-2-dimethylamino-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-piperidin-1-yl-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-morpholin-4-yl-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-dipropylamino-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-thiomorpholin-4-yl-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-diethylamino-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-pyrrolidin-1-yl-acetamide
2-Azepan-1-yl-N-(2-chloro-4-nitro-phenyl)-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-(2-methyl-piperidin-1-yl)-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-(3-methyl-piperidin-1-yl)-acetamide
N-(2-Chloro-4-nitro-phenyl)-2-(4-methyl-piperidin-1-yl)-acetamide

EXAMPLE 47 (METHOD 19B)

N-(2-Chloro-4-nitrophenyl)-2-(2-dimethylaminoethylsulfanyl)acetamide

To a solution of N-(chloroacetyl)-2-chloro-4-nitroaniline (3.01 g) in N,N-dimethylformamide (100 mL) is added powdered sodium carbonate (6.0 g) and 2-dimethylaminoethanethiol hydrochloride (6.0 g). The mixture is stirred for 1 hour at 25° C, poured into water and extracted into ethyl acetate. The ethyl acetate solution is dried over anhydrous potassium carbonate and concentrated under reduced pressure to give an oil. The oil is crystallized from toluene-hexanes (3:1) to yield a pale yellow crystalline solid.
EXAMPLE 48 (METHOD 20)
(4-tert-butoxycarbonylamino-2-chloro-phenyl)-carbamic acid 2-piperidin-1-yl-ethyl ester

To a suspension of 1,1-carbonyl-di-(1,2,4)-triazole (4.0 g) in dichloromethane (40 mL) is added a solution of (4-amino-3-chloro-phenyl) carbamic acid tert-butyl ester (5.0 g) in dichloromethane (45 mL) dropwise over 20 minutes. The reaction is stirred at room temperature for 30 minutes at which point a precipitate forms. To this mixture is added piperidineethanol (6.6 mL) and tetra-hydrofuran (20 mL) is added to maintain homogeneity. After heating at reflux overnight the reaction is cooled and then poured into water, the organic layer separated and then washed with saturated aqueous sodium chloride. The solution is dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to a crude oil that is purified by chromatography over silica gel (5% methanol in dichloromethane is used as the eluant) to give the desired product as a white foam.

EXAMPLE 49 (METHOD 21)
5-Phenyl-[1,2,3]thiadiazole-4-carboxylic acid methyl ester

A solution of ethyl benzoyleacetate (1.1 g) in acetonitrile (10 mL) is treated with 4-methylbenzenesulfonyl azide (1.3 g) and triethylamine (1.6 g). After stirring overnight at room temperature, the reaction is concentrated under reduced pressure and the resulting crude product is dissolved in ethyl acetate and washed with 1N sodium hydroxide. The organic layer is then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to yield a yellow oil. This oil is taken into dichloromethane and filtered through a pad of hydrous magnesium silicate, eluting with dichloromethane to give the partially purified diazoketone as a colorless oil. A sample of the diazoketone from above (1.2 g) is dissolved in toluene (25 mL) and treated with 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (2.8 g) and the reaction is heated to reflux. After 3 hours, the reaction is cooled to room temperature, loaded onto a pad of silica gel and eluted with
dichloromethane. After removing the solvent under reduced pressure, the resulting oil is purified by chromatography over silica gel (30% diethyl ether in petroleum ether is used as the eluant) and then recrystallized from hexanes to give the desired product as pale yellow needles.

Using the above procedure and appropriate starting materials the following compound was prepared:

5-Phenyl-[1,2,3]thiadiazole-4-carboxylic acid ethyl ester
5-Methyl-[1,2,3]thiadiazole-4-carboxylic acid methyl ester

EXEMPLARY 50

Ethyl benzoylacetate semicarbazide

Ethyl benzoylacetate (5.0 g) is dissolved in methanol (10 mL) and added rapidly to a hot solution of semicarbazide hydrochloride (29 g) in water (130 mL). To this is added pyridine (4.1 g) and after heating to reflux for 5 minutes, the reaction mixture is cooled to -20 °C overnight. The resulting solid semicarbazone is collected by filtration, washed with water and then diethyl ether to give the desired product as white crystals.

Using the above procedure and appropriate starting materials the following compound was prepared:

Ethyl (Z)-3-[(aminocarbonyl)hydrazono]-4,4,4-trifluorobutanoate
3-[(Z)-2-(Aminocarbonyl)hydrazono]-3-phenylpropanoic acid ethyl ester
3-[(E)-2-(Aminocarbonyl)hydrazono]-3-(3-furyl)propanoic acid ethyl ester
EXAMPLE 51

5-Phenyl-[1,2,3]thiadiazole-5-carboxylic acid ethyl ester

A solution of ethyl benzoylacetate semicarbazone (2.5 g) in neat thionyl chloride (5 mL) is stirred at 0 °C for 1 hour. Dichloromethane is then added (25 mL), the excess thionyl chloride is destroyed slowly with saturated aqueous sodium bicarbonate. The precipitate which forms on quenching is removed by filtration and the filtrate is extracted with dichloromethane. Pooled organic extracts are dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Chromatography over silica gel (50% hexanes in dichloromethane is used as the eluant) affords the desired product as a colorless oil.

Using the above procedure and appropriate starting materials the following compounds were prepared:

4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid methyl ester
4-Phenyl-[1,2,3]thiadiazole-5-carboxylic acid ethyl ester
4-Furan-3-yl-[1,2,3]thiadiazole-5-carboxylic acid ethyl ester

EXAMPLE 52

4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid

4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid methyl ester (1.7 g) is dissolved in methanol (15 mL) and treated with 1N sodium hydroxide (16 mL). After stirring at room temperature for 1 hour, the reaction is treated with concentrated hydrochloric acid (1.5 mL) and concentrated under reduced pressure. The resulting turbid aqueous layer is extracted twice with diethyl ether and the pooled organic layers are dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to give the desired compound as a white powder.

Using the above procedure and appropriate starting materials the following compounds were prepared:
3-Ethoxycarbonylmethoxy-benzoic acid
5-Furan-3-yl-[1,2,3]thiadiazole-4-carboxylic acid
Thiazole-4-carboxylic acid
4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid
5-Methyl-[1,2,3]thiadiazole-4-carboxylic acid

EXAMPLE 53 (METHOD 25)

Trifluoro-methanesulfonic acid 4-chloro-5-methoxy-2-nitro-phenyl ester

To a solution of 4-chloro-5-methoxy-2-nitro-phenol (6.5 g) in dichloromethane (150 mL) at 0 °C under an atmosphere of argon is added triethylamine (10 g) and then a solution of trifluoro-methanesulfonic anhydride (13.5 g) in dichloromethane (30 mL). The solution is stirred at 0 °C for 10 minutes, and is then diluted with dichloromethane and washed successively with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride. After drying over anhydrous sodium sulfate the solvent is removed by evaporation under reduced pressure and the residue is dissolved in a solution of 20% dichloromethane in hexanes and passed through a short column of hydrous magnesium silicate (20% dichloromethane in hexanes is used as the eluant). Product containing fractions are pooled and the solvents removed by evaporation under reduced pressure to give the desired product as a yellow oil.

Using the above procedure and appropriate starting materials the following compounds were prepared:

Trifluoro-methanesulfonic acid 4-chloro-5-methoxy-2-nitro-phenyl ester
Trifluoro-methanesulfonic acid 4-chloro-2-nitro-phenyl ester
Trifluoro-methanesulfonic acid 2-chloro-6-nitro-phenyl ester
EXAMPLE 54 (METHOD 26)

[4-(3-Dimethylamino-benzoylamino)-phenyl]-carbamic acid t-butyl ester

A solution of [4-(3-amino-benzoylamino)-phenyl]-carbamic acid t-butyl ester (505 mg), sodium cyanoborohydride (250 mg), acetic acid (3 drops) and 40 % aqueous formaldehyde (4 mL) in 1:2 tetrahydrofuran-methanol (15 mL) is stirred for 15 minutes, and then poured into saturated aqueous sodium bicarbonate and extracted into ethyl acetate. The ethyl acetate solution is dried over anhydrous potassium carbonate and concentrated under reduced pressure to give a solid which is recrystallized from acetonitrile to provide a pale pink crystalline solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

[4-(3-Dimethylamino-benzoylamino)-phenyl]-carbamic acid tert-butyl ester
(3-Bromo-5-trifluoromethyl-phenyl)-dimethyl-amine
N-(3-Chloro-5-dimethylamino-phenyl)-acetamide

EXAMPLE 55 (METHOD 27)

N-(4-Aminophenyl)-2-hydroxybenzamide

To a solution of 2-(4-aminophenylcarbamoyl) phenyl acetate (580 mg) in methanol (10 mL) is added saturated sodium bicarbonate (2 mL) and water (3 mL). The mixture is heated at 80°C for 30 minutes, then poured into half-saturated aqueous sodium chloride and extracted with ethyl acetate. The ethyl acetate solution is dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oil which is then triturated with diethyl ether to provide the desired product as a white solid.
EXAMPLE 56 (METHOD 28)
[4-(3-(Hydroxybenzoylamino)phenyl)carbamic acid t-butyl ester]

To a solution of 3-(4-aminophenylcarbamoyl) phenyl acetate (4.34 g) in methanol (75 mL) is added 0.1 N aqueous sodium hydroxide (25 mL) and tetrahydrofuran (25 mL). This solution is heated at 40° C for 30 minutes, then cooled, poured into 1 M hydrochloric acid and extracted with ethyl acetate. The ethyl acetate solution is dried over anhydrous sodium sulfate and concentrated under reduced pressure to give a white solid, which is further purified by trituration with diethyl ether.

EXAMPLE 57 (METHOD 29)
N-(4-Aminophenyl)-2-hydroxymethylbenzamide

To a solution of N-(4-aminophenyl)phthalimide (332 mg) in tetrahydrofuran (4 mL) is added lithium borohydride (1.0 g) and the mixture is stirred for 1 hour at 25° C. The mixture is poured into water and extracted into ethyl acetate. The ethyl acetate solution is dried over anhydrous sodium sulfate and concentrated under reduced pressure to give a white foam, which when triturated with diethyl ether provides the desired product as a white powder.

EXAMPLE 58 (METHOD 30)
(3-Chloro-5-dimethylamino-phenyl)-carbamic acid tert-butyl ester

To a solution of (3-amino-5-chloro-phenyl)-carbamic acid tert-butyl ester (0.32 g) in toluene (10 mL) is added aqueous formaldehyde (37%, 1.5 mL) then 10% palladium on carbon (0.50 g) and the mixture is stirred under an atmosphere of hydrogen for approximately 15 hours. The solution is then filtered through diatomaceous earth and the filtrate is concentrated under reduced pressure. The residue is chromatographed over silica gel (50% dichloromethane in hexanes is used as the eluant) to provide the desired product as a white solid.
EXAMPLE 59 (METHOD 35)
N-(4-{3-[3,5-Dichloro-4-(2-hydroxy-ethoxy)-phenyl]-thioureido}-phenyl)-acetamide

To a solution of acetic acid 2-{4-[3-(4-acetylamino-phenyl)-thioureido]-2,6-dichlorophenoxy}-ethyl ester (0.16 g) in a 1:1 mixture of tetrahydrofuran and methanol (2.5 mL) is added 1N aqueous sodium hydroxide (1 mL) and the mixture is stirred for approximately 2 hours at room temperature. The solution is then poured into 2 M aqueous hydrochloric acid (3 mL), extracted into ethyl acetate, and the extracts are dried over anhydrous sodium sulfate. The solvent is removed by evaporation under reduced pressure and the residue is triturated with diethyl ether to provide the desired product as a white solid.

EXAMPLE 60 (METHOD 36)

{4-[3-(4-Acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy}-acetic acid

To a solution of {4-[3-(4-acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy}-acetic acid ethyl ester (0.29 g) in a 1:1 mixture of tetrahydrofuran and methanol (4 mL) is added 1N aqueous sodium hydroxide (2 mL) and the mixture is stirred for approximately 2 hours at room temperature. The solution is then poured into 2 M aqueous hydrochloric acid (5 mL), extracted into ethyl acetate, and the extracts are dried over anhydrous sodium sulfate. The solvent is removed by evaporation under reduced pressure and the residue is triturated with diethyl ether to provide the desired product as a white solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

{4-[3-(4-Acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy}-acetic acid
{2-[3-(4-Acetylamino-phenyl)-thioureido]-4-chloro-5-methoxy-phenoxy}-acetic acid
{4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-5-methoxy-phenoxy}-acetic acid
EXAMPLE 61 (METHOD 37)

Benzoic acid 2-{4-[3-(4-acetylamino-phenyl)-thioureido]-2,6-dichlorophenoxy}-ethyl ester

To an ice cooled solution of N-(4-{3-[3,5-dichloro-4-(2-hydroxy-ethoxy)-phenyl]-thioureido})-phenyl)-acetamide (0.20 g) in pyridine (2 mL) and tetrahydrofuran (0.5 mL) is added benzoyl chloride (0.08 g) and the mixture is stirred at 0 °C for 1.5 hours. The mixture is then diluted with ethyl acetate, washed successively two times with 2% aqueous hydrochloric acid, once with saturated aqueous sodium chloride, then dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure the residue is chromatographed over silica gel (5% methanol in dichloromethane is used as the eluant) and product containing fractions are combined, evaporated under reduced pressure, and the residue is recrystallized from acetone-hexanes to provide the desired product as a white powder.

EXAMPLE 62 (METHOD 38)

Methanesulfonic acid 2-{4-[3-(4-acetylamino-phenyl)-thioureido]-2,6-dichlorophenoxy}-ethyl ester

To an ice cooled solution of N-(4-{3-[3,5-dichloro-4-(2-hydroxy-ethoxy)-phenyl]-thioureido})-phenyl)-acetamide (0.20 g) in pyridine (2 mL) and tetrahydrofuran (0.5 mL) is added methanesulfonyl chloride (0.11 g) and the solution is stirred at 0 °C for 45 minutes. The reaction mixture is then diluted with ethyl acetate, washed successively twice with 2% aqueous hydrochloric acid, once with saturated aqueous sodium chloride, and then dried over anhydrous magnesium sulfate. After removing the solvents by evaporation under reduced pressure the resulting residue is recrystallized from acetone-hexanes to give the desired product as a white powder.
EXAMPLE 63 (METHOD 39)
N-(4-[3-[5-Dichloro-4-(2-dimethylamino-ethoxy)-phenyl]-thioureido]-phenyl)-acetamide

To a solution of methanesulfonic acid 2-{4-[3-(4-acetylamino-phenyl)-thioureido]-2,6-dichlorophenoxy}-ethyl ester (0.33 g) in tetrahydrofuran (6 mL) is added aqueous dimethyl-amine (8.8 M, 0.5 mL) and the mixture is stirred at room temperature for 5 days. The reaction mixture is then diluted with ethyl acetate, then washed with saturated aqueous sodium chloride and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure the residue is chromatographed over silica gel (pure methanol is used as the eluant). Pooled product containing fractions are evaporated under reduced pressure and the residue is recrystallized from acetonitrile to provide the desired product as a white powder.

Using the above procedure and appropriate starting materials the following compounds were prepared:

N-(4-[3-[3,5-Dichloro-4-(2-dimethylamino-ethoxy)-phenyl]-thioureido]-phenyl)-acetamide

Benzoic acid 2-{4-[3-(4-acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy}-ethyl ester

EXAMPLE 64 (METHOD 40)

Furan-2-carboxylic acid (4-[3-[4-(1-amino-ethyl)-3-chloro-phenyl]-thioureido]-phenyl)-amide

To a solution of tin(II) chloride dihydrate (0.25 g) in methanol (2.5 mL) is added furan-2-carboxylic acid (4-[3-[4-(1-azido-ethyl)-3-chloro-phenyl]-thioureido]-phenyl)-amide (0.22 g) and the solution is stirred for approximately 15 hours at room temperature. The solution is then diluted with ethyl acetate, washed successively with saturated aqueous sodium bicarbonate then saturated aqueous sodium chloride, then dried over anhydrous sodium sulfate. After removal of the solvent by
evaporation under reduced pressure the residue is chromatographed over silica gel (8% methanol in dichloromethane containing 1% triethylamine is used as the eluant) to provide the desired product as a yellow solid.

EXAMPLE 65 (METHOD 41)

[1,2,3]Thiadiazole-4-carboxylic acid (4-isothiocyanato-phenyl)-amide

To a ice cooled solution of 1,1'-thiocarbonyldiimidazole (7.28 g) in tetrahydrofuran (50 mL) is added [1,2,3]-thiadiazole-4-carboxylic acid (4-amino-phenyl) amide (9.0 g) in tetrahydrofuran (100 mL). After approximately one hour the solvent is removed by evaporation and the residue is dissolved in ethyl acetate. Diethyl ether is added to precipitate the crude product, which is then collected by filtration, dissolved in dichloromethane, and passed through a plug of hydrous magnesium silicate. After removal of solvents, the residue is recrystallized from ethyl acetate-hexanes to provide the desired product as a slightly yellow solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

2-Fluoro-N-(4-isothiocyanato-phenyl)-benzamide
Furan-2-carboxylic acid (4-isothiocyanato-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-isothiocyanato-phenyl)-amide
Thiazole-4-carboxylic acid (4-isothiocyanato-phenyl)-amide

EXAMPLE 66 (METHOD 42)

N,N-Dimethyl-5-trifluoromethyl-benzene-1,3-diamine

To a solution of 3-amino-5-bromo-benzotrifluoride (1.0 g) in degassed (argon) tetrahydrofuran (2 mL) is added bis-(tri-o-tolylphosphino)palladium (0.15 g), a solution of dimethylamine in tetra-hydrofuran (2M, 4.2 mL), and a solution of lithium bis(trimethylsilyl)amide in tetrahydrofuran (1M, 10.4 mL). The reaction mixture is heated in a sealed vessel to 100°C for approximately 2.5 hours to complete
the reaction. The mixture is then cooled to room temperature, quenched by addition of water, and diluted with ethyl acetate. The product is extracted three times into 5% aqueous hydrochloric acid, and pooled acidic extracts are then basified with cooling by addition of 5N aqueous sodium hydroxide. This basic solution is then extracted with ethyl acetate, and these pooled organic extracts are washed with saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and evaporated to dryness under reduced pressure. The resulting residue is chromatographed over silica gel (20-30% ethyl acetate in hexanes is used as the eluant) to provide the desired product as a slightly tinted solid.

Using the above procedure and appropriate starting materials the following compounds were prepared:

3-(4-Methyl-piperazin-1-yl)-5-trifluoromethyl-phenylamine
3-Morpholin-4-yl-5-trifluoromethyl-phenylamine
3-Piperidin-1-yl-5-trifluoromethyl-phenylamine
3-Pyrrolidin-1-yl-5-trifluoromethyl-phenylamine
N,N-Dimethyl-5-trifluoromethyl-benzene-1,3-diamine
N-Isobutyl-N-methyl-5-trifluoromethyl-benzene-1,3-diamine
N-Butyl-N-methyl-5-trifluoromethyl-benzene-1,3-diamine

EXAMPLE 67 (METHOD 43)

(3-Isobutyl-5-trifluoromethyl-phenyl)-carbamic acid tert-butyl ester

To a sealed tube containing tetrahydrofuran (5 mL) that is capped with a rubber septum and cooled in a dry ice-acetone bath is bubbled isobutylene for about 5 minutes. A solution of 9-borabicyclo[3.3.1]nonane in tetrahydrofuran (0.5 M, 11 mL) is added, the vessel is sealed with a teflon cap, slowly warmed to room temperature and kept at room temperature for approximately 2.5 hours. The mixture is then re-cooled in a dry ice-acetone bath, the teflon cap is replaced by a rubber septum, and argon is bubbled through the mixture with venting to removed the excess isobutylene. A solution of (3-bromo-5-trifluoromethyl-phenyl)-carbamic acid tert-
butyl ester (1.7 g) in tetrahydrofuran (12 mL) is added, followed by [1,1'-
bis(diphenylphosphino)-ferrocene]palladium(II) chloride-dichloromethane complex (0.12 g), and then 3N aqueous sodium hydroxide. The vessel is again sealed with the
teflon cap and is then heated to 65°C for approximately 15 hours. The mixture is
then cooled to room temperature, diluted with hexanes, washed with water, saturated
aqueous sodium chloride, dried over anhydrous magnesium sulfate, and evaporated
under reduced pressure. The resulting oil is chromatographed over silica gel (5%
ethyl acetate in hexanes is used as the eluant) to provide the desired product as a
white powder.

Using the above procedure and appropriate starting materials the following
compounds were prepared:

[3-(2-Methyl-butyl)-5-trifluoromethyl-phenyl]-carbamic acid tert-butyl ester
(3-Isobutyl-5-trifluoromethyl-phenyl)-carbamic acid tert-butyl ester

**EXAMPLE 68 (METHOD 44)**

2-(3,5-Dichloro-phenylsulfanyl)-ethylamine

To a solution of (3,5-dichlorophenylthio)acetonitrile (1.2g) in 3.0 mL of ethylene
glycol dimethyl ether is added 0.61 mL of 10M borane dimethyl sulfide complex and
the mixture heated at reflux for 0.5 hours. The reaction is cooled in an ice bath and
2.0 mL of water and 2.0 mL of concentrated hydrochloric acid is added. This mixture
is heated at reflux for 0.5 hr. The clear solution is then cooled and basified with 5N
sodium hydroxide and extracted with ether. The ether extract is dried over potassium
carbonate, filtered and concentrated to give 1.0g of a colorless oil.

Using the above procedure and appropriate starting materials the following
compounds were prepared:
2-(3-Bromo-phenylsulfanyl)-ethylamine
2-(4-Bromo-phenoxy)-ethylamine
2-(4-Iodo-phenoxy)-ethylamine
2-(3,4-Dichloro-phenoxy)-ethylamine
2-(3-Chloro-phenylsulfanyl)-ethylamine
2-(3,4-Dichloro-phenylsulfanyl)-ethylamine
3-(4-Bromo-phenyl)-propylamine
2-(2-Fluoro-phenoxy)-ethylamine
2-(2-Chloro-phenoxy)-ethylamine
2-(3-Bromo-phenoxy)-ethylamine
2-(3-Fluoro-phenoxy)-ethylamine
2-(3-Iodo-phenoxy)-ethylamine
2-(3,5-Dichloro-phenylsulfanyl)-ethylamine
2-Phenylsulfanyl-ethylamine
1-(2-Chloro-phenyl)-ethylamine

EXAMPLE 69 (METHOD 45)
N-(1-Naphthalen-2-yl-ethyl)-formamide

A mixture of 2-acetylnaphthylene (3.0 g), ammonium formate (11.0 g), formic acid (3.3 mL), and formamide (3.5 mL) is heated at 190°C for 3 hours. The mixture is cooled, poured into water and extracted with ether. The ether extract is dried with anhydrous potassium carbonate, filtered and concentrated to give a yellow oil, which is crystallized from toluene-hexanes to give a white solid, 1.97 g.

Using the above procedure and appropriate starting materials the following compounds were prepared:

N-[1-(4-Fluoro-phenyl)-2-methyl-propyl]-formamide
N-(1-Naphthalen-2-yl-ethyl)-formamide
EXAMPLE 70 (METHOD 46)

1-(2-Naphthyl)ethylamine

A mixture of N-(1-naphthalen-2-yl-ethyl)-formamide (1.12 g), ethanol (10 mL) and 5 N sodium hydroxide (10 mL) is heated at reflux for 1 hour. The solution is cooled, poured into water and extracted with ether. The ether solution is dried with anhydrous potassium carbonate, filtered and concentrated to give the product (0.95 g) as a pale yellow oil.

Using the above procedure and appropriate starting materials the following compounds were prepared:

1-(3-Trifluoromethyl-phenyl)-ethylamine
1-(4-Fluoro-phenyl)-2-methyl-propylamine
[3-(1-Amino-ethyl)-phenyl]-dimethyl-amine
3-(1-Amino-ethyl)-benzonitrile

EXAMPLE 71 (METHOD 47)

1-(3-Trifluoromethyl-phenyl)-ethanone O-methyl-oxime

Methoxylamine hydrochloride (2.33 g) is added to a solution of 3’-(trifluoromethyl)-acetophenone (1.5 g) in ethanol (20 mL) and pyridine (2 mL). The solution is heated at reflux for 45 minutes. The reaction mixture is then cooled, concentrated under reduced pressure and partitioned between water and ethyl acetate. The aqueous layer is extracted with ethyl acetate. The combined organic layers are washed with saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give the desired product as a colorless oil (1.61 g).

Using the above procedure and appropriate starting materials the following compounds were prepared:
3,5-Bis-trifluoromethyl-benzaldehyde oxime
1-(4-Fluoro-phenyl)-propan-1-one O-methyl-oxime
1-(2-Chloro-phenyl)-ethanone O-methyl-oxime
1-(3-Bromo-phenyl)-ethanone O-methyl-oxime
1-(3-Chloro-phenyl)-ethanone O-methyl-oxime
1-p-Tolyl-ethanone O-methyl-oxime
1-(4-Fluoro-phenyl)-pentan-1-one O-methyl-oxime
1-(4-Fluoro-phenyl)-2-phenyl-ethanone O-methyl-oxime
1-o-Tolyl-ethanone O-methyl-oxime
1-m-Tolyl-ethanone O-methyl-oxime
1-(2-Fluoro-phenyl)-ethanone O-methyl-oxime
3-(1-Methoxyimino-ethyl)-benzonitrile
4-(1-Methoxyimino-ethyl)-benzonitrile
1-(4-Methoxy-phenyl)-ethanone O-methyl-oxime
1-(2-Methoxy-phenyl)-ethanone O-methyl-oxime
1-(4-Dimethylamino-phenyl)-ethanone O-methyl-oxime
1-(2-Trifluoromethyl-phenyl)-ethanone O-methyl-oxime
1-(3-Methoxy-phenyl)-ethanone O-methyl-oxime
1-(3-Trifluoromethyl-phenyl)-ethanone O-methyl-oxime
1-(4-Trifluoromethyl-phenyl)-ethanone O-methyl-oxime
1-Furan-2-yl-ethanone O-methyl-oxime
1-Pyridin-4-yl-ethanone O-methyl-oxime
1-(1-Methyl-1H-pyrrol-2-yl)-ethanone O-methyl-oxime
1-Thiophen-3-yl-ethanone O-methyl-oxime
(4-Fluoro-phenyl)-phenyl-methanone O-methyl-oxime
1-(4-methoxyphenyl)ethanone O-methylxime
1-(3-Chloro-4-methoxy-phenyl)-ethanone O-methyl-oxime
4-(1-Methoxyimino-ethyl)-benzenesulfonamide
4-(1-Methoxyimino-ethyl)-N,N-dimethyl-benzenesulfonamide
1-[4-(Piperidine-1-sulfonyl)-phenyl]-ethanone O-methyl-oxime
4-(1-Methoxyimino-ethyl)-N,N-dipropyl-benzenesulfonamide
2-Fluoro-N-[4-(1-methoxyimino-ethyl)-phenyl]-benzamidine
1-(3,5-Bis-trifluoromethyl-phenyl)-ethanone O-methyl-oxime
1-[4-(1H-Imidazol-1-yl)phenyl]-1-ethanone, O-methylloxime
1-[4-(Trifluoromethyl)phenyl]-1-ethanone, O-methylloxime
1-[1,1'-Biphenyl]-4-yl-1-ethanone, O-methylloxime
1-(4-Methylphenyl)-1-ethanone, O-methylloxime
1-[4-fluoro-3-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-[3,5-bis(trifluoromethyl)phenyl]ethanone O-benzylloxime
1-[4-chloro-3-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-[3-fluoro-5-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-[2-fluoro-4-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-[2-fluoro-5-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-(2,4-dichlorophenyl)ethanone O-methylloxime
1-(2,4-dimethylphenyl)ethanone O-methylloxime
1-[2,4-bis(trifluoromethyl)phenyl]ethanone O-methylloxime
1-(3-bromophenyl)ethanone O-methylloxime
1-(3-methylphenyl)ethanone O-methylloxime
1-[4-(4-morpholiny1)phenyl]ethanone O-methylloxime
1-(2-chloro-4-fluorophenyl)ethanone O-methylloxime
1-(4-bromo-2-fluorophenyl)ethanone O-methylloxime
1-(3,4-difluorophenyl)ethanone O-methylloxime
1-[3-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-[2-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-(2,4-difluorophenyl)ethanone O-methylloxime
1-[3-fluoro-4-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-(3,4-dichlorophenyl)ethanone O-methylloxime
1-[4-fluoro-2-(trifluoromethyl)phenyl]ethanone O-methylloxime
1-(3-chloro-4-fluorophenyl)ethanone O-methylloxime
1-(4-chloro-3-fluorophenyl)ethanone O-methylloxime
1-(2,5-difluorophenyl)ethanone O-methylloxime
1-(2-bromo-4-fluorophenyl)ethanone O-methylloxime
1-(3,4-dibromophenyl)ethanone O-methylloxime
1-(2-bromophenyl)ethanone O-methylloxime
EXAMPLE 72 (METHOD 48)
1-(2-Trifluoromethyl-phenyl)-ethylamine

Sodium borohydride (1.17 g) is added slowly to a flask containing zirconium tetrachloride (1.8 g) in tetrahydrofuran (27 mL). A solution of 1-(2-trifluoromethyl-phenyl)-ethanone O-methyl-oxime (1.34 g) in tetrahydrofuran (7.7 mL) is added and the resulting solution is stirred at 25 °C for 12 hours. The reaction mixture is then cooled to 0 °C and water (16 mL) is slowly added. Excess ammonium hydroxide is added and the solution is extracted twice with ethyl acetate. The organic portion is washed twice with 1N hydrochloric acid. The aqueous (acid) layer is basified with sodium hydroxide and extracted twice with ethyl acetate. The organic layer is then washed with saturated aqueous sodium chloride and dried over anhydrous magnesium sulfate. The solvent is removed under reduced pressure to provide the desired product as a yellow oil (0.20 g).

Using the above procedure and appropriate starting materials the following compounds were prepared:

1-(3-Methoxy-phenyl)-ethylamine
1-(4-Fluoro-phenyl)-propylamine
1-Naphthalen-2-yl-ethylamine
4-(1-Amino-ethyl)-benzonitrile
1-(4-Trifluoromethyl-phenyl)-ethylamine
1-(4-Methoxy-phenyl)-ethylamine
1-Prop-2-ynyl-pyrrolidone
1-(2-Methoxy-phenyl)-ethylamine
1-m-Toly1-ethylamine
1-(2-Bromo-phenyl)-ethylamine
1-o-Toly1-ethylamine
C-(4-Fluoro-phenyl)-C-phenyl-methylamine
1-(4-Fluoro-phenyl)-pentylamine
1-(4-Fluoro-phenyl)-2-phenyl-ethylamine
1-(2-Trifluoromethyl-phenyl)-ethylamine
1-(3-Bromo-phenyl)-ethylamine
1-(3-Chloro-phenyl)-ethylamine
[4-(1-Amino-ethyl)-phenyl]-dimethyl-amine
1-(1-Methyl-1H-pyrrol-2-yl)-ethylamine

**EXAMPLE 73 (METHOD 49)**

**(2-Fluoro-5-trifluoromethyl-phenoxy)-acetonitrile**

A solution of 2-fluoro-5-trifluoromethylphenol (25 g) in reagent grade acetone (0.55 L) is treated with solid potassium carbonate (7.7 g) followed by the rapid addition of neat bromoacetonitrile (10 mL). The heterogenous mixture is stirred vigorously for approximately 20 hours whereupon it is poured into water and extracted into diethyl ether. The combined ether extracts are washed with saturated sodium chloride and dried over anhydrous potassium carbonate. Filtration and concentration under reduced pressure gives a pale orange solid which is then chromatographed on silica gel, eluting with dichloromethane, to give the desired product as white solid (28.3 g).

Using the above procedure and appropriate starting materials the following compounds were prepared:

(3-Bromo-phenylsulfanyl)-acetonitrile
(3-Chloro-phenylsulfanyl)-acetonitrile
(4-Iodo-phenoxy)-acetonitrile
(3-Trifluoromethyl-phenylsulfanyl)-acetonitrile
(3,5-Dichloro-phenylsulfanyl)-acetonitrile
(3,4-Dichloro-phenylsulfanyl)-acetonitrile
(3,4-Dichloro-phenoxy)-acetonitrile
(2-Fluoro-phenoxy)-acetonitrile
(3-Fluoro-phenoxy)-acetonitrile
(2-Chloro-phenoxy)-acetonitrile
(3-Bromo-phenoxy)-acetonitrile
(2-Fluoro-5-trifluoromethyl-phenoxy)-acetonitrile
(3-Iodo-phenoxy)-acetonitrile
(4-Bromo-phenoxy)-acetonitrile

**EXAMPLE 74 (METHOD 50)**

3-Fluoro-5-trifluoromethylphenethylamine tosylate

A solution of 2.5 g of 3-fluoro-5-trifluoromethylphenyleacetonitrile and 2.34 g (12.3 mmol) of p-toluenesulfonic acid in 75 ml of ethylene glycol monomethyl ether is hydrogenated for 3 hours at room temperature at 40 psi, using 200 mg 10% palladium on carbon catalyst. The catalyst is filtered off and the solvent evaporated to half the volume. Upon standing, the p-toluenesulfonic acid salt of the desired 3-fluoro-5-trifluoromethylphenethylamine crystallizes. The white crystals, 4.26g (91%) are collected by filtration.

Using the above procedure and appropriate starting materials the following compounds were prepared:

2-(3,5-Difluoro-phenyl)-ethylamine
2-(4-Trifluoromethyl-phenyl)-ethylamine
2-(3,4-Difluoro-phenyl)-ethylamine
2-(2-Fluoro-phenyl)-ethylamine
2-(3-Fluoro-5-trifluoromethyl-phenyl)-ethylamine
2-(2-Fluoro-3-trifluoromethyl-phenyl)-ethylamine
2-(2,4-Bis-trifluoromethyl-phenyl)-ethylamine
2-(4-Fluoro-3-trifluoromethyl-phenyl)-ethylamine
EXAMPLE 75 (METHOD 51)

(4-Aminomethyl-2-trifluoromethyl-phenyl)-dimethyl-amine

A solution of 4-dimethylamino-3-trifluoromethylbenzonitrile (0.35 g) in tetrahydrofuran (2 mL) is slowly added to a suspension of lithium aluminum hydride (0.1 g) in tetrahydrofuran (2 mL) at 0 °C and stirred under an atmosphere of argon for 2 hours. While at 0 °C water (0.1 mL) is slowly added followed by 5% sodium hydroxide (0.1 mL) and water (0.3 mL). The resulting gray solid is filtered and washed with tetrahydrofuran. The filtrates are collected and concentrated under reduced pressure and the resulting oil is chromatographed over silica gel (15% methanol in methylene chloride is used as the eluant) to provide the desired product as a pale orange oil (0.164 g).

Using the above procedure and appropriate starting materials the following compounds were prepared:

4-Piperidin-1-yl-3-trifluoromethyl-benzylamine
(4-Aminomethyl-2-trifluoromethyl-phenyl)-dimethyl-amine
4-(4-Methyl-piperazin-1-yl)-3-trifluoromethyl-benzylamine
(3-Aminomethyl-5-trifluoromethyl-phenyl)-dimethyl-amine
[3-(2-Amino-ethyl)-5-trifluoromethyl-phenyl]-dimethyl-amine
[4-(2-Amino-ethyl)-2-methyl-phenyl]-dimethyl-amine

EXAMPLE 76 (METHOD 52)

3-Dimethylamino-5-trifluoromethyl-benzaldehyde

Diisobutylaluminum hydride (10 mL of a 1M solution in methylene chloride) is added dropwise to a solution of 3-dimethylamino-5-trifluoromethylbenzonitrile (1.06 g) in methylene chloride (25 mL) at 0 °C and the mixture stirred for 2 hours. While still at 0 °C a saturated aqueous solution of sodium potassium tartrate (8 mL) is slowly added and the solution is stirred for 1.5 hours. The reaction mixture is then extracted with ethyl acetate, dried over anhydrous magnesium sulfate and
concentrated under reduced pressure to provide the desired product as a yellow solid (0.97 g).

Using the above procedure and appropriate starting materials the following compounds were prepared:

3-Dimethylamino-5-trifluoromethyl-benzaldehyde
4-Dimethylamino-3-methyl-benzaldehyde

**EXAMPLE 77 (METHOD 53)**

**Dimethyl-[3-(2-nitro-vinyl)-5-trifluoromethyl-phenyl]-amine**

Nitromethane (0.473 g) is added to a solution of 3-dimethylamino-5-trifluoromethyl-benzaldehyde (0.885 g) and ammonium acetate (0.339 g) in acetic acid (3.4 mL) and the solution is heated at 110 °C for 6 hours. The reaction mixture is cooled to 0 °C and a solid forms which is filtered and washed with 1:1 water-acetic acid. This solid is recrystallized from ethanol to provide the desired product as a red solid (0.39 g).

Using the above procedure and appropriate starting materials the following compounds were prepared:

Dimethyl-[3-(2-nitro-vinyl)-5-trifluoromethyl-phenyl]-amine
Dimethyl-[2-methyl-4-(2-nitro-vinyl)-phenyl]-amine

**EXAMPLE 78 (METHOD 54)**

**3-(4-Bromo-phenyl)-propionitrile**

Diethylazodicarboxylate (5.2 g) is added dropwise to a solution of 4-bromo-phenethylalcohol (2.01 g), and triphenylphosphine (7.9 g) in diethyl ether (16 mL) at 0 °C. The reaction mixture is stirred for 10 minutes and a solution of acetone cyanohydrin (2.6 g) in diethyl ether (10 mL) is added. The clear orange solution is stirred for 5 minutes at 0 °C and then at 25 °C for 12 hours. The reaction mixture is
then filtered, and washed with diethyl ether. The filtrate is concentrated under reduced pressure and chromatographed over silica gel (10% ethyl acetate-hexanes is used as the eluant) to provide the desired product as a pale yellow oil (2.04 g).

**EXAMPLE 79 (METHOD 55)**

3-Dimethylamino-2-isocyano-acrylic acid ethyl ester

To a solution of ethyl isocyanooacetate (5.0 g) in ethanol (100 mL) is added N,N-dimethyl-formamide dimethyl acetal (6.5 g) dropwise with stirring over 10 minutes. The reaction is stirred for 24 hours and the ethanol is evaporated. The resulting oil is passed through magnesium silicate using 50% ethyl acetate-hexanes as the eluant. The solvents are removed and the resulting oil is crystallized from ethyl acetate-hexanes to yield light yellow needles, 3.0 g.

**EXAMPLE 80 (METHOD 56)**

4-Carboethoxythiazole

A solution of 3-dimethylamino-2-isocyano-acrylic acid ethyl ester (1.0 g) and triethylamine (3.0 g) in tetrahydrofuran (30 mL) is treated with gaseous hydrogen sulfide until all starting material is consumed. The mixture is concentrated to an oil and purified by column chromatography using silica and 25% ethyl acetate-hexanes as the eluant. The purified material (0.61 g) is isolated as an oil.

**EXAMPLE 81 (METHOD 34)**

N-{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-ureido]-phenyl}-2-fluoro-benzamide

A suspension of N-(4-amino-phenyl)-2-fluoro-benzamide (0.43 g) in acetonitrile (4 mL) is treated with 5-chloro-2,4-dimethoxyphenylisocyanate (0.40 g). The mixture becomes a solution and is allowed to stand for 12 hours. A white solid forms and is collected by filtration (0.79 g). [M+H] 444.
Using the above procedure and appropriate starting materials the following compounds were prepared:

<table>
<thead>
<tr>
<th>EX NO.</th>
<th>M+H</th>
<th>COMPOUND NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>81</td>
<td>445</td>
<td>N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-ureido]-phenyl]-2-fluoro-benzamide</td>
</tr>
<tr>
<td>82</td>
<td>441</td>
<td>N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-ureido]-phenyl]-2-methyl-benzamide</td>
</tr>
<tr>
<td>83</td>
<td>435</td>
<td>[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(5-chloro-2,4-dimethoxy-phenyl)-ureido]-phenyl)-amide</td>
</tr>
<tr>
<td>84</td>
<td>443</td>
<td>[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(4-chloro-3-trifluoromethyl-phenyl)-ureido]-phenyl)-amide</td>
</tr>
<tr>
<td>85</td>
<td>453</td>
<td>N-[4-[3-(4-Chloro-3-trifluoromethyl-phenyl)-ureido]-phenyl]-2-fluoro-benzamide</td>
</tr>
<tr>
<td>86</td>
<td>409</td>
<td>[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3,5-dichloro-phenyl)-ureido]-phenyl)-amide</td>
</tr>
<tr>
<td>87</td>
<td>486</td>
<td>N-[4-[3-(3,5-Bis-trifluoromethyl-phenyl)-ureido]-phenyl]-2-fluoro-benzamide</td>
</tr>
<tr>
<td>88</td>
<td>458</td>
<td>Furan-2-carboxylic acid (4-[3-(3,5-bis-trifluoromethyl-phenyl)-ureido]-phenyl)-amide</td>
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<tr>
<td>89</td>
<td>476</td>
<td>[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3,5-bis-trifluoromethyl-phenyl)-ureido]-phenyl)-amide</td>
</tr>
<tr>
<td>90</td>
<td>423</td>
<td>[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3,4-dichloro-benzyl)-ureido]-phenyl)-amide</td>
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</table>

EXAMPLE 91 (METHOD 31)

N-(5-[(1S)-1-[3,5-bis(trifluoromethyl)phenyl]ethyl]amino)carbothioyl]-amino]-2-pyridinyl)-1,3-thiazole-4-carboxamide

A mixture of N-(5-isothiocyanato-2-pyridinyl)-1,3-thiazole-4-carboxamide (0.36 g) and (S)-alpha-methyl-3,5-bis(trifluoromethyl)-benzenemethanamine (0.36 g) is heated with acetonitrile (10 mL) until all solids are dissolved. The solution is allowed to stand for 12 hours. A white solid forms and is collected by filtration (0.40 g). [M+H] 520.

Using the above procedure and appropriate starting materials the following compounds were prepared:
<table>
<thead>
<tr>
<th>EX. NO.</th>
<th>M+H</th>
<th>COMPOUND NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>92</td>
<td>506</td>
<td>[3-Chloro-5-{3-[4-[[1,2,3]thiadiazole-4-carboxyl]-amino]-phenyl]-thiourea]-phenyl]-carbamic acid tert-butyl ester</td>
</tr>
<tr>
<td>93</td>
<td>409</td>
<td>1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(4-morpholin-4-yl-phenyl)-thiourea</td>
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<tr>
<td>94</td>
<td>370</td>
<td>1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(4-methylsulfanyl-phenyl)-thiourea</td>
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<tr>
<td>95</td>
<td>338</td>
<td>1-(5-Chloro-2,4-dimethoxy-phenyl)-3-p-tolyl-thiourea</td>
</tr>
<tr>
<td>96</td>
<td>414</td>
<td>{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenylsulfanyl}-acetic acid</td>
</tr>
<tr>
<td>97</td>
<td>384</td>
<td>1-(5-Chloro-2,4-dimethoxy-phenyl)-3-[4-(2-hydroxy-ethoxy)-phenyl]-thiourea</td>
</tr>
<tr>
<td>98</td>
<td>340</td>
<td>1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(4-hydroxy-phenyl)-thiourea</td>
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<tr>
<td>99</td>
<td>395</td>
<td>N-{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl}-N-methyl-acetamide</td>
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<td>N-{3-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
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<td>{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl}-carbamic acid ethyl ester</td>
</tr>
<tr>
<td>102</td>
<td>319</td>
<td>1-(2,4-Dimethoxy-phenyl)-3-(4-methoxy-phenyl)-thiourea</td>
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<tr>
<td>103</td>
<td>346</td>
<td>N-{4-[3-(2,4-Dimethoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
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<tr>
<td>104</td>
<td>316</td>
<td>N-{4-[3-(4-Methoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
</tr>
<tr>
<td>105</td>
<td>316</td>
<td>N-{4-[3-(2-Methoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
</tr>
<tr>
<td>106</td>
<td>351</td>
<td>N-{4-[3-(3-Chloro-4-methoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
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<tr>
<td>107</td>
<td>351</td>
<td>N-{4-[3-(5-Chloro-2-methoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
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<td>108</td>
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<td>N-{4-[3-(3,5-Dichloro-4-hydroxy-phenyl)-thiourea]-phenyl}-acetamide</td>
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<td>109</td>
<td>385</td>
<td>N-{4-[3-(3,5-Dichloro-4-methoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
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<td>110</td>
<td>381</td>
<td>N-{4-[3-(4-Chloro-2,5-dimethoxy-phenyl)-thiourea]-phenyl}-acetamide</td>
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<td>111</td>
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<td>N-{4-[3-(2-Chloro-5-trifluoromethyl-phenyl)-thiourea]-phenyl}-acetamide</td>
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<td>112</td>
<td>389</td>
<td>N-{4-[3-(4-Chloro-3-trifluoromethyl-phenyl)-thiourea]-phenyl}-acetamide</td>
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<td>113</td>
<td>422</td>
<td>Benzoic acid 4-{3-(4-acetamido-phenyl)-thiourea}-3-hydroxy-phenylester</td>
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<td>114</td>
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<td>N-{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl}-2-methylbenzamide</td>
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<td>501</td>
<td>Acetic acid 2-{4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl-carbamoyl}-phenyl ester</td>
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<tr>
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<td>461</td>
<td>N-{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl}-4-fluorobenzamide</td>
</tr>
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<tr>
<td>117</td>
<td>461</td>
<td>N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-3-fluoro-benzamide</td>
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<td>118</td>
<td>461</td>
<td>N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-2-fluoro-benzamide</td>
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<td>120</td>
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<td>N-[4-[3-(3-Nitro-phenyl)-thiourea]-phenyl]-acetamide</td>
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<td>125</td>
<td>339</td>
<td>1-(3-Chloro-4-methoxy-phenyl)-3-(3-nitro-phenyl)-thiourea</td>
</tr>
<tr>
<td>126</td>
<td>337</td>
<td>N-[4-[3-(5-Chloro-2-hydroxy-phenyl)-thiourea]-phenyl]-acetamide</td>
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<tr>
<td>127</td>
<td>439</td>
<td>4-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-carbamic acid tert-butyl ester</td>
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<tr>
<td>128</td>
<td>351</td>
<td>N-[4-[3-(3-Chloro-4-hydroxy-5-methyl-phenyl)-thiourea]-phenyl]-acetamide</td>
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<td>129</td>
<td>385</td>
<td>N-[4-[3-(3,5-Dichloro-4-hydroxy-2-methyl-phenyl)-thiourea]-phenyl]-acetamide</td>
</tr>
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<td>130</td>
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<td>N-[4-[3-(2,4-Dihydroxy-phenyl)-thiourea]-phenyl]-acetamide</td>
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<td>414</td>
<td>N-[4-[3-(2,4-Dimethoxy-5-trifluoromethyl-phenyl)-thiourea]-phenyl]-acetamide</td>
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<td>132</td>
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<td>N-[4-[3-(2-Hydroxy-4-methoxy-phenyl)-thiourea]-phenyl]-acetamide</td>
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<td>133</td>
<td>465</td>
<td>N-[4-[3-(3,5-Dichloro-4-methoxy-phenyl)-thiourea]-phenyl]-4-fluoro-benzamide</td>
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<td>3-Acetylamino-N-[4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-benzamide</td>
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<td>135</td>
<td>488</td>
<td>N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-3-nitro-benzamide</td>
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<td>N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-3-dimethylamino-benzamide</td>
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<td>N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-2-trifluoromethyl-benzamide</td>
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139 459  N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-2-hydroxy-
benzamide
140 479  N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-2,6-difluoro-
benzamide
141 477  2-Chloro-N-(4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-
benzamide
142 522  2-Bromo-N-(4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-
benzamide
143 488  N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-2-nitro-
benzamide
144 445  Pyrazine-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-
phenyl}-amide
145 463  5-Methyl-thiophene-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
146 494  Quinoline-8-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
147 446  1-Methyl-1H-pyrrole-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-
phenyl)-thioureido]-phenyl}-amide
148 369  1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(2-nitro-phenyl)-thiourea
149 369  1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(4-nitro-phenyl)-thiourea
150 425  N-(4-[3-(5-Bromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-acetamide
151 376  N-(4-[3-(3,4,5-Trimethoxy-phenyl)-thioureido]-phenyl)-acetamide
152 399  N-(4-[3-(3,5-Dichloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl)-
acetamide
153 499  Benzo[b]thiophene-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
154 483  Benzofuran-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
155 444  N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-isonicotinamide
156 493  Naphthalene-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
157 493  Naphthalene-1-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
158 494  Isoquinoline-1-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
159 494  Quinoline-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide
N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-nicotinamide

5-Nitro-furan-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-amide
carbamic acid phenyl ester

{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-

5-Chloro-furan-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-amide

{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-carbamic acid
isobutyl ester

{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-carbamic acid
methyl ester

Furan-3-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-
phenyl}-amide

3-Methyl-furan-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide

5-Bromo-furan-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide

4-Bromo-furan-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide

Furan-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-
phenyl}-amide

{4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-carbamic acid
hexyl ester

Isoquinoline-4-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide

[1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide

1H-[1,2,3]Triazole-4-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide

3-Bromo-thiophene-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-
thioureido]-phenyl}-amide

N-[4-(3-(3,5-Dichloro-4-ethoxy-phenyl)-thioureido]-phenyl)-acetamide

N-[4-(3-(4-Butoxy-3,5-dichloro-phenyl)-thioureido]-phenyl)-acetamide

N-[4-(3-(4-Benzylxy-3,5-dichloro-phenyl)-thioureido]-phenyl)-acetamide

N-[4-(3-(3-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-acetamide

(3-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenylcarbamoyl]-
phenyl)-carbamic acid ethyl ester

2-Amino-N-[4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-
benzamide

182  519 Biphenyl-2-carboxylic acid (4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-amide
183  469 1-(5-Chloro-2,4-dimethoxy-phenyl)-3-[4-(1,3-dioxo-1,3-dihydro-isindol-2-yi)-phenyl]-thiourea
184  487 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-phthalamic acid
185  473 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2-hydroxy-methyl-benzamide
186  479 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2,3-difluoro-benzamide
187  479 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2,5-difluoro-benzamide
188  479 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2,4-difluoro-benzamide
189  500 2-Acetylamino-N-[4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-benzamide
190  441 1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(6-oxo-5,6-dihydro-phenanthridin-2-yi)-thiourea
191  536 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2-methanesulfonylamino-benzamide
192  497 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2,3,4-trifluoro-benzamide
193  533 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2,3,4,5,6-pentafluoro-benzamide
194  489 N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2-methyl-sulfanyl-benzamide
195  431 5-Methyl-furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-urcido]-phenyl]-amide
196  467 5-Difluoromethyl-furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-urcido]-phenyl]-amide
197  472 N-[4-[3-(5-Iodo-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-acetamide
198  364 N-[4-[3-(5-Fluoro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-acetamide
199  365 N-[4-[3-(5-Chloro-2,4-methoxy-4-methyl-phenyl)-thioureido]-phenyl]-acetamide
200  459 [1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureido]-phenyl]-amide
201  455 [1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3,5-dichloro-4-methoxy-phenyl)-
thioureido]-phenyl)-amide

N-[4-[3-(3-Chloro-4-diethylamino-phenyl)-thioureido]-phenyl]-acetamide

N-[4-[3-Chloro-4-(cyclohexyl-methyl-amino)-phenyl]-thioureido]-phenyl)-acetamide

1-Hydroxy-naphthalene-2-carboxylic acid {4-[3-(4-acetylamino-phenyl)thioureido]-2-chloro-phenyl}-amide

N-[4-[3-Chloro-4-morpholin-4-yl-phenyl]-thioureido]-phenyl]-acetamide

1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(3-chloro-4-morpholin-4-yl-phenyl)-thiourea

1-(5-Chloro-2,4-dimethoxy-phenyl)-3-(5-chloro-2-methyl-phenyl)-thiourea

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-isophthalamic acid methyl ester

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-isophthalamic acid

3-Benzyloxy-N-[4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-benzamide

N-[4-[3-[5-Chloro-2-methoxy-4-(4-nitrolo-butoxy)-phenyl]-thioureido]-phenyl]-acetamide

N-[4-[3-[5-Chloro-2-methoxy-4-(2-nitrolo-ethoxy)-phenyl]-thioureido]-phenyl]-acetamide

N-[4-[3-[5-Chloro-4-methoxy-2-(2-nitrolo-ethoxy)-phenyl]-thioureido]-phenyl]-acetamide

N-[4-[3-[5-Chloro-2-(2-hydroxy-ethoxy)-4-methoxy-phenyl]-thioureido]-phenyl]-acetamide

N-[4-[3-[5-Chloro-4-(2-hydroxy-ethoxy)-2-methoxy-phenyl]-thioureido]-phenyl]-acetamide

{4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-5-methoxy-phenoxy}-acetic acid tert-butyl ester

{4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-5-methoxy-phenoxy}-acetic acid methyl ester

{2-[3-(4-Acetylamino-phenyl)-thioureido]-4-chloro-5-methoxy-phenoxy}-acetic acid tert-butyl ester

3-Butoxy-N-[4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-benzamide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2-methanesulfinyl-benzamide

(3-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenylcarbamoyl]-phenoxy)-acetic acid ethyl ester
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<td>(3-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenylcarbamoyl]-phenoxy)-acetic acid</td>
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<td>N-[4-[3-(5-Chloro-4-hydroxy-2-methoxy-phenyl)-thioureido]-phenyl]-acetamide</td>
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<td>Pyridine-2-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-amide</td>
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<td>Quinoline-4-carboxylic acid {4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl}-amide</td>
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<td>N-[4-[3-(5-Chloro-4-methoxy-2-morpholin-4-y1-phenyl)-thioureido]-phenyl]-acetamide</td>
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<td>N-[4-[3-(3-Chloro-4-methyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide</td>
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<td>N-[4-[3-(3-Chloro-4-methyl-phenyl)-thioureido]-phenyl]-3-methoxy-benzamide</td>
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<td>Furan-2-carboxylic acid {4-[3-(3-chloro-4-methyl-phenyl)-thioureido]-phenyl}-amide</td>
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<td>N-[4-[3-(4-Benzylamino-3-chloro-phenyl)-thioureido]-phenyl]-acetamide</td>
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<td>N-[4-[3-(3-Chloro-4-pyrrolidin-1-yl-phenyl)-thioureido]-phenyl]-acetamide</td>
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| 243 | 419 | N-[4-[3-(3-Chloro-4-(4-methyl-piperazin-1-yl)-phenyl]-thioureido]-phenyl]-
acetamide

N-[4-[3-(4-Chloro-3-trifluoromethyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

N-[4-[3-(2-Benzylamino-4-methoxy-phenyl)-thioureido]-phenyl]-acetamide

Furan-2-carboxylic acid (4-[(3-[3-chloro-4-(cyclohexyl-methyl-amino)-phenyl]-thioureido)-phenyl]-amide

N-[4-[3-Chloro-4-(cyclohexyl-methyl-amino)-phenyl]-thioureido]-phenyl)-2-methyl-benzamide

N-[4-[3-Chloro-4-(cyclohexyl-methyl-amino)-phenyl]-thioureido]-phenyl)-2,6-difluoro-benzamide

Pyridine-2-carboxylic acid (4-[(3-[3-chloro-4-(cyclohexyl-methyl-amino)-phenyl]-thioureido)-phenyl]-amide

N-[4-[3-Chloro-4-(cyclohexyl-methyl-amino)-phenyl]-thioureido]-phenyl)-3-methoxy-benzamide

N-[4-[3-Chloro-4-(2-nitro-ethoxy)-phenyl]-thioureido]-phenyl]-acetamide

N-[4-[3-(4-sec-Butoxy-3-chloro-phenyl)-thioureido]-phenyl]-acetamide

Acetic acid 3-[4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-carbamoyl-phenyl ester

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-3-hydroxy-benzamide

Benzol[1,3]dioxole-4-carboxylic acid (4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-amide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-3-trifluoromethoxy-benzamide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-3-(2-dimethylamino-ethoxy)-benzamide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-3-(2-morpholin-4-yl-ethoxy)-benzamide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-cyano-phenyl]-acetamide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2,5-dimethoxy-phenyl]-2-fluoro-benzamide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2,5-dimethoxy-phenyl]-acetamide

2-(4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenoxy)-5-chlorobenzenesulfonic acid

2-(4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenoxy)-4,5-dichlorobenzenesulfonic acid
4-Phenyl-[1,2,3]thiadiazole-5-carboxylic acid-[4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-amide
N-[4-{3-(3-Chloro-4-(2-hydroxy-ethoxy)-phenyl)-thioureido]-phenyl]-acetamide
N-[4-{3-(4-Butoxy-3-chloro-phenyl)-thioureido]-phenyl]-acetamide
N-[4-{3-[3-Chloro-4-(cyclohexyl-ethyl-amino)-phenyl]-thioureido}-phenyl]-acetamide
N-[4-{3-(3-Chloro-4-ethoxy-phenyl)-thioureido]-phenyl]-acetamide
N-[4-{3-(4-Benzylx-3-chloro-phenyl)-thioureido]-phenyl]-acetamide
{(4-{(3-Methyl-furan-2-carbonyl)-amino}-phenyl)-carbamic acid tert-butyl ester}
N-[4-{3-(2-Benzylamino-5-chloro-4-methoxy-phenyl)-thioureido]-phenyl]-acetamide
N-[4-{3-(3-Chloro-4-dipropylamino-phenyl)-thioureido]-phenyl]-acetamide
N-[4-{3-[4-(Allyl-cyclohexyl-amino)-3-chloro-phenyl]-thioureido}-phenyl]-acetamide
N-[4-{3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-methoxy-phenyl]-acetamide
N-[2-Chloro-4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-acetamide
Furan-2-carboxylic acid-[4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2,5-dimethoxy-phenyl]-amide
N-[4-{3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-cyano-phenyl]-2-fluoro-benzamide
N-[2-Chloro-4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide
5-Methyl-[1,2,3]thiadiazole-4-carboxylic acid-[4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-amide
5-Furan-3-y1-[1,2,3]thiadiazole-4-carboxylic acid-[4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido}-phenyl]-amide
5-Phenyl-[1,2,3]thiadiazole-4-carboxylic acid-[4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido}-phenyl]-amide
N-[4-{3-[3-Chloro-4-(octahydro-quinolin-1-yl)-phenyl]-thioureido}-phenyl]-acetamide
N-[5]-[(5-Chloro-2,4-dimethoxyphenyl)amino]thioxomethyl]amino]-2-pyridyln]-2-methylbenzamide
Furan-2-carboxylic acid-[5-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido}-pyridin-2-yl]-amide
285  425  N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-2-methoxy-5-methyl-phenyl]-acetamide
286  505  N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-2-methoxy-5-methyl-phenyl]-2-fluoro-benzamide
287  477  Furan-2-carboxylic acid [4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-2-methoxy-5-methyl-phenyl]-amide
288  517  4-Furan-3-yl-[1,2,3]thiadiazole-5-carboxylic acid [4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-amide
289  462  N-[5-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-pyridin-2-yl]-2-fluoro-benzamide
290  384  N-[4-[3-(4-Methoxy-3-trifluoromethyl-phenyl)-thiourea]-phenyl]-acetamide
291  394  N-[4-[3-{3-Chloro-4-[2-hydroxy-ethyl]-methyl-amino}-phenyl]-thiourea]-phenyl]-acetamide
292  485  N-[2-Benzoyl-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-acetamide
293  565  N-[2-Benzoyl-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-2-fluoro-benzamide
294  537  Furan-2-carboxylic acid [2-benzoyl-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-phenyl]-amide
295  475  N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-3-methyl-phenyl]-2-fluoro-benzamide
296  447  Furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-3-methyl-phenyl]-amide
297  395  N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-3-methyl-phenyl]-acetamide
298  435  N-[4-[3-(3-Chloro-4-{(3-dimethylamino-propyl)-methyl-amino}-phenyl]-thiourea]-phenyl]-acetamide
299  418  N-[4-[3-(3-Chloro-4-cyclohexylamino-phenyl)-thiourea]-phenyl]-acetamide
300  421  N-[4-[3-{3-Chloro-4-[2-dimethylamino-ethyl]-methyl-amino}-phenyl]-thiourea]-phenyl]-acetamide
301  580  5-[[[[5-Chloro-2,4-dimethoxyphenyl)amino][thioxomethyl]amino]-2-[(2-fluorobenzoyl)amino]-N-phenyl-benzamide
302  552  Furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-2-phenylcarbamoyl-phenyl]-amide
303  491  N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thiourea]-2-methoxy-phenyl]-2-fluoro-benzamide
304  463  Furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thiourea]-2-methoxy-phenyl]-amide
N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-trifluoromethyl-phenyl)-acetamide

Furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-cyano-phenyl]-amide

Furan-2-carboxylic acid [2-chloro-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-amide

Furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-trifluoromethyl-phenyl]-amide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-methyl-phenyl]-acetamide

N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-methyl-phenyl]-2-fluoro-benzamide

Furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-methyl-phenyl]-amide

N-[4-[3-(4-Acetilamino-phenyl)-thioureido]-2-chloro-phenyl]-acetamide

[4-[3-(4-Acetilamino-phenyl)-thioureido]-2-chloro-phenyl]-carbamic acid ethyl ester

N-[5-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-2-yl]-acetamide

N-(4-[3-[4-(1-Benzyl-piperidin-4-ylamino)-3-chloro-phenyl]-thioureido]-phenyl)-acetamide

N-(4-[3-[3-Chloro-4-(2-dimethylamino-ethylamino)-phenyl]-thioureido]-phenyl)-acetamide

N-[4-[3-[3-Chloro-4-[(2-methoxy-ethyl)-methyl-amino]-phenyl]-thioureido]-phenyl]-acetamide

N-(4-[3-[3-Chloro-4-(3-dimethylamino-propylamino)-phenyl]-thioureido]-phenyl)-acetamide

N-(4-[3-[4-(1-Benzyl-pyrrrolidin-3-ylamino)-3-chloro-phenyl]-thioureido]-phenyl)-acetamide

Furan-2-carboxylic acid [5-chloro-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-hydroxy-phenyl]-amide

N-[5-Chloro-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-hydroxy-phenyl]-acetamide

(5H,11H-1-Benzoc[5]pyrrrolo[1,2-a][1,4]diazepin-10-yl)-(2-chloro-4-imidazol-1-yl-phenyl)-methanone

[1,2,3]Thiadiazole-5-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-amide

Furan-2-carboxylic acid [4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-naphthalen-1-yl]-amide
N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-naphthalen-1-yl)-2-fluoro-benzamide

N-(5-Chloro-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-methyl-phenyl)-acacetamide

N-(5-Chloro-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-methyl-phenyl)-2-fluoro-benzamide

Furan-2-carboxylic acid {5-chloro-4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-2-methyl-phenyl}-amide

N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-naphthalen-1-yl)-acetamide

Furan-2-carboxylic acid {4-[3-(3-chloro-4-dimethylamino-phenyl)-thioureido]-phenyl}-amide

Furan-2-carboxylic acid {4-[3-(4-[(1-benzyl-pyrrolidin-3-yl)-methyl-amino]-3-chloro-phenyl)-thioureido]-phenyl}-amide

N-(4-[3-Chloro-4-(methyl-(1-methyl-pyrrolidin-3-yl)-amino]-phenyl)-thioureido)-phenyl]-2-fluoro-benzamide

N-(4-[3-(5-Chloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl)-2,6-difluoro-benzamide

N-(4-[3-Chloro-4-(1-methyl-pyrrolidin-3-yloxy)-phenyl]-thioureido)-phenyl)-acetamide

N-(4-[3-Chloro-4-(1-methyl-piperidin-4-yloxy)-phenyl]-thioureido)-phenyl)-acetamide

N-(4-[3-Chloro-4-(3-dimethylamino-propoxy)-phenyl]-thioureido)-phenyl)-acetamide

2-Acetylamino-5-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-benzoic acid

5-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-(2-fluoro-benzoylamino)-benzoic acid

5-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-[(furan-2-carbonyl)-amino]-benzoic acid

N-(4-[3-(3-Chloro-4-[methyl-(1-methyl-piperidin-4-yl)-amino]-phenyl)-thioureido]-phenyl)-2,6-difluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid{4-[3-chloro-4-[methyl-(1-methyl-pyrrolidin-3-yl)-amino]-phenyl}-thioureido]-phenyl]-amide

N-(4-[3-(3-Chloro-4-methylsulfanyl-phenyl)-thioureido]-phenyl)-2-methyl-benzamide

N-(4-[3-Chloro-4-(2-dimethylamino-ethoxy)-phenyl]-thioureido)-phenyl)-acetamide
Furan-2-carboxylic acid [4-(3-{3-chloro-4-{methyl-(1-methyl-piperidin-4-yl)amino}-phenyl}-thioureido)-phenyl]-amide
N-[4-{3-(3-Chloro-4-cyclohexylxy-phenyl)-thioureido}-phenyl]-acetamide
N-[4-{3-(3-Chloro-4-dimethylamino-phenyl)-thioureido}-phenyl]-2-methyl-benzamide
N-[4-{3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido}-3-methyl-phenyl]-2,6-difluoro-benzamide
N-[4-{3-(3-Chloro-4-dimethylamino-phenyl)-thioureido}-phenyl]-2,6-difluoro-benzamide
N-[4-{3-(3-Chloro-4-{methyl-(1-methyl-pyrrolidin-3-yl)-amino}-phenyl}-thioureido)-phenyl]-2,6-difluoro-benzamide
Pyridine-2-carboxylic acid {4-[3-(3-chloro-4-dimethylamino-phenyl)-thioureido]-phenyl}-amide
Pyridine-2-carboxylic acid {4-[3-(3-chloro-4-methylsulfonyl-phenyl)-thioureido]-phenyl}-amide
Pyridine-2-carboxylic acid {4-[3-(5-chloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl}-amide
Furan-2-carboxylic acid {4-[3-(5-chloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl}-amide
Pyridine-2-carboxylic acid [4-{3-(3-chloro-4-{methyl-(1-methyl-pyrrolidin-3-yl)-amino}-phenyl}-thioureido)-phenyl]-amide
N-[3-Chloro-4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid [3-chloro-4-{3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido}-phenyl]-amide
N-[4-{3-(3-Chloro-4-cyclohexylsulfanyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-{3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-3-trifluoromethyl-phenyl]-acetamide
N-[4-{3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-3-trifluoromethyl-phenyl]-2-fluoro-benzamide
N-[4-{3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl]-2-dimethylamino-acetamide
Furan-2-carboxylic acid (4-{3-[3-chloro-4-{(2-dimethylamino-acetylamino)-phenyl}-thioureido]-phenyl})-amide
N-[4-{3-(3-Chloro-2-(2-dimethylamino-acetylamino)-phenyl]-thioureido)-phenyl]-2-fluoro-benzamide
N-[4-{3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl}-2-piperidin-
364 541 1-yl-acetamide
N-(4-[3-Chloro-4-(2-piperidin-1-yl-acetylamino)-phenyl]-thioureido)-phenyl)-2-fluoro-benzamide

365 513 Furan-2-carboxylic acid (4-[3-Chloro-4-(2-piperidin-1-yl-acetylamino)-phenyl]-thioureido)-phenyl)-amide

366 463 N-(4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl)-2-morpholin-4-yl-acetamide

367 543 N-(4-[3-Chloro-4-(2-morpholin-4-yl-acetylamino)-phenyl]-thioureido)-phenyl)-2-fluoro-benzamide

368 515 Furan-2-carboxylic acid (4-[3-Chloro-4-(2-morpholin-4-yl-acetylamino)-phenyl]-thioureido)-phenyl)-amide

369 414 N-(4-[3-Chloro-4-methanesulfonylamino-phenyl]-thioureido)-phenyl)-acetamide

370 494 N-(4-[3-Chloro-4-methanesulfonylamino-phenyl]-thioureido)-phenyl)-2-fluoro-benzamide

371 466 Furan-2-carboxylic acid (4-[3-Chloro-4-methanesulfonylamino-phenyl]-thioureido)-phenyl)-amide

372 481 N-(4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl)-2-(2-dimethylamino-ethylsulfanyl)-acetamide

373 561 N-(4-[3-Chloro-4-[2-(2-dimethylamino-ethylsulfanyl)-acetylamino]-phenyl]-thioureido)-phenyl)-2-fluoro-benzamide

374 585 N-(4-[3-[4-[1-Benzyl-pyrrolidin-3-yl]-methyl-amino]-3-chloro-phenyl]-thioureido)-phenyl)-2-methyl-benzamide

375 523 N-(4-[3-Chloro-4-[methyl-(1-methyl-piperidin-4-yl)-amino]-phenyl]-thioureido)-phenyl)-2-methyl-benzamide

376 510 Pyridine-2-carboxylic acid [4-[3-Chloro-4-[methyl-(1-methyl-piperidin-4-yl)-amino]-phenyl]-thioureido]-phenyl)-amide

377 347 N-(4-[3-Chloro-4-vinyl-phenyl]-thioureido)-phenyl)-acetamide

378 441 Furan-2-carboxylic acid (4-[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureido]-phenyl)-amide

379 452 Pyridine-2-carboxylic acid (4-[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureido]-phenyl)-amide

380 487 N-(4-[3-Chloro-3-trifluoromethyl-phenyl]-thioureido)-phenyl)-2,6-difluoro-benzamide

381 486 N-(4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-3-cyano-phenyl)-2-fluoro-benzamide

382 458 Furan-2-carboxylic acid (4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-3-cyano-phenyl)-amide
N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-3-cyano-phenyl]-acetamide
N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-2-methyl-isothioureido]-phenyl]-acetamide
N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-2-methyl-isothioureido]-phenyl]-acetamide
N-[4-[3-(3-Chloro-4-ethylsulfanyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-(4-Butylsulfanyl-3-chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-3-methoxy-phenyl]-acetamide
N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-3-methoxy-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid \{4-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-3-methoxy-phenyl\}-amide
[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-[3-chloro-4-(2-piperidin-1-yl-acetyl-amino)-phenyl]-thioureido]-phenyl\}-amide
N-[4-[3-(3-Chloro-4-methanesulfinyl-phenyl)-thioureido]-phenyl]-2,6-difluoro-benzamide
N-[4-[3-(3-Chloro-4-methanesulfanyl-phenyl)-thioureido]-phenyl]-2,6-difluoro-benzamide
N-[4-[3-(5-Chloro-2-methoxy-4-methyl-phenyl)-thioureido]-2-methyl-phenyl]-2-fluoro-benzamide
N-[4-[3-(5-Chloro-4-methyl-phenyl)-thioureido]-2-methyl-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid \{4-(3-[3-chloro-4-[2-(2-dimethylamino-ethylsulfanyl)-acetylaminol]-phenyl]-thioureido)-phenyl\}-amide
N-[4-[3-(4-Acetylamino-3-chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
[2-Chloro-4-(3-[4-[(furan-2-carbonyl-amino)-phenyl]-thioureido])-phenyl]-carbamic acid ethyl ester
(2-Chloro-4-[3-[4-(2-fluoro-benzoylamino)-phenyl]-thioureido]-phenyl)-carbamic acid ethyl ester
N-[4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl]-benzamide
N-[4-[[4-(Benzoylamino)-3-chloro-phenyl]-amino]-thioxomethyl-amino]-phenyl]-2-fluoro-benzamide
N-[4-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-2-trifluoromethyl-
phenyl)-2-fluoro-benzamide
403  492 Furan-2-carboxylic acid (4-[3-(4-benzoylamino-3-chloro-phenyl)-thioureido]-phenyl)-amide
404  416 N-[4-[3-(4-Amino-3-chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
405  479 N-[4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl]-2-thiomorpholin-4-yl-acetamide
406  531 Furan-2-carboxylic acid (4-{3-[3-chloro-4-(2-thiomorpholin-4-yl-acetylamino)-phenyl]-thioureido}-phenyl)-amide
407  559 N-[4-[3-Chloro-4-(2-thiomorpholin-4-yl-acetylamino)-phenyl]-thioureido]-phenyl)-2-fluoro-benzamide
408  461 N-[4-[3-Chloro-4-methylsulfanyl-phenyl]-thioureido]-2-methyl-phenyl)-2-fluoro-benzamide
409  430 Furan-2-carboxylic acid (4-[3-(4-acetylamino-3-chloro-phenyl)-thioureido]-phenyl)-amide
410  477 N-[4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl]-2-dipropylamino-acetamide
411  529 Furan-2-carboxylic acid (4-{3-[3-chloro-4-(2-dipropylamino-acetylamino)-phenyl]-thioureido}-phenyl)-amide
412  449 N-[4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl]-2-diethylamino-acetamide
413  501 Furan-2-carboxylic acid (4-{3-[3-chloro-4-(2-diethylamino-acetylamino)-phenyl]-thioureido}-phenyl)-amide
414  529 N-[4-[3-Chloro-4-(2-diethylamino-acetylamino)-phenyl]-thioureido]-phenyl)-2-fluoro-benzamide
415  447 N-[4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl]-2-pyrrolidin-1-yl-acetamide
416  499 Furan-2-carboxylic acid (4-{3-[3-chloro-4-(2-pyrrolidin-1-yl-acetylamino)-phenyl]-thioureido}-phenyl)-amide
417  527 N-[4-[3-Chloro-4-(2-pyrrolidin-1-yl-acetylamino)-phenyl]-thioureido]-phenyl)-2-fluoro-benzamide
418  475 N-[4-[3-(5-Chloro-2-methoxy-4-methyl-phenyl)-thioureido]-3-methoxy-phenyl]-2-fluoro-benzamide
419  445 N-[4-[3-(3-Chloro-4-methyl-phenyl)-thioureido]-3-methoxy-phenyl]-2-fluoro-benzamide
420  477 N-[4-[3-(3-Chloro-4-methylsulfanyl-phenyl)-thioureido]-3-methoxy-phenyl]-2-fluoro-benzamide
421  388 Furan-2-carboxylic acid (4-[3-(4-amino-3-chloro-phenyl)-thioureido]-phenyl)-amide
Furan-2-carboxylic acid (4-[[3-[4-(2-azepan-1-yl-acetylamino)-3-chloro-phenyl]-thioureido]-phenyl]-amide
N-[[4-[[3-[4-(2-azepan-1-yl-acetylamino)-3-chloro-phenyl]-thioureido]-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid [4-[[3-chloro-4-[2-(2-methyl-piperidin-1-yl)-acetyl-amino]-phenyl]-thioureido]-phenyl]-amide
N-[4-[[3-Chloro-4-[2-(2-methyl-piperidin-1-yl)-acetylamino]-phenyl]-thioureido]-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid [4-[[3-pyridin-2-yl-thioureido]-phenyl]-amide
Furan-2-carboxylic acid [4-[[3-pyridin-4-yl-thioureido]-phenyl]-amide
2-Fluoro-N-[4-[[3-pyridin-3-yl-thioureido]-phenyl]-benzamide
Furan-2-carboxylic acid [4-[[3-pyridin-3-yl-thioureido]-phenyl]-amide
Furan-2-carboxylic acid [4-[[3-amino-phenyl]-thioureido]-phenyl]-amide
Furan-2-carboxylic acid [4-[[3-trifluoromethyl-phenyl]-thioureido]-phenyl]-amide
2-Fluoro-N-[4-[[3-m-tolyl-thioureido]-phenyl]-benzamide
2-Fluoro-N-[4-[[3-trifluoromethyl-phenyl]-thioureido]-phenyl]-benzamide
N-[4-[[3-(Amino-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid [4-[[3-(amino-5-chloro-phenyl)-thioureido]-phenyl]-amide
Furan-2-carboxylic acid [4-[[3-m-tolyl-thioureido]-phenyl]-amide
N-[4-[[3-(2-Amino-5-chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
(2-Chloro-4-[[3-[4-(2-fluoro-benzoylamino)-phenyl]-thioureido]-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester
[2-Chloro-4-[[3-[4-[[furan-2-carbonyl]-amino]-phenyl]-thioureido]-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester
Furan-2-carboxylic acid [4-[[3-(2-amino-5-chloro-phenyl)-thioureido]-phenyl]-amide
Furan-2-carboxylic acid [4-[[3-(3-cyano-phenyl)-thioureido]-phenyl]-amide
N-[4-[[3-(Amino-5-chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
2-Fluoro-N-[4-[[3-pyridin-2-yl-thioureido]-phenyl]-benzamide
2-Fluoro-N-[4-[[3-pyridin-4-yl-thioureido]-phenyl]-benzamide
Furan-2-carboxylic acid [4-[[3-(6-chloro-pyridin-3-yl)-thioureido]-phenyl]-amide
Furan-2-carboxylic acid [4-{3-(2-amino-3-chloro-phenyl)-thioureido}-phenyl]-amide
Furan-2-carboxylic acid [4-{3-(3-hydrazinocarbonyl-phenyl)-thioureido}-phenyl]-amide
2-Fluoro-N-[4-{3-(1-hydroxy-ethyl)-phenyl]-thioureido]-phenyl]-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid [4-{3-(3-hydrazinocarbonyl-phenyl)-thioureido}-phenyl]-amide
[1,2,3]Thiadiazole-4-carboxylic acid [4-{3-(3-isopropyl-phenyl)-thioureido}-phenyl]-amide
Furan-2-carboxylic acid [4-{3-(3-isopropyl-phenyl)-thioureido}-phenyl]-amide
2-Fluoro-N-[4-{3-(3-isopropyl-phenyl)-thioureido}-phenyl]-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid [4-{3-(3-cyano-phenyl)-thioureido}-phenyl]-amide
N-[4-{3-(3-Dimethylamino-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid [4-{3-(3-dimethylamino-phenyl)-thioureido}-phenyl]-amide
[1,2,3]Thiadiazole-4-carboxylic acid [4-(3-m-tolyl-thioureido)-phenyl]-amide
[1,2,3]Thiadiazole-4-carboxylic acid [4-{3-(3-trifluoromethyl-phenyl)-thioureido}-phenyl]-amide
N-[3-Chloro-4-{3-(5-chloro-2-methoxy-4-methyl-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide
N-[3-Chloro-4-{3-(3-chloro-4-methyl-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide
N-[3-Chloro-4-{3-(3-chloro-4-methylsulfanyl-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide
N-[4-{3-(3-Cyano-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide
Furan-2-carboxylic acid [4-{3-(3-acetylamino-phenyl)-thioureido}-phenyl]-amide
2-Fluoro-N-[4-{3-(3-hydrazinocarbonyl-phenyl)-thioureido}-phenyl]-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid [4-{3-(3-(1-hydroxy-ethyl)-phenyl)-thioureido}-phenyl]-amide
N-[4-{3-(2-Amino-3-chloro-phenyl)-thioureido}-phenyl]-2,6-difluoro-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid [4-{3-(3-amino-5-chloro-phenyl)-thioureido}-phenyl]-amide
Furan-2-carboxylic acid (4-[(3,5-dimethoxy-phenyl)-thioureido]-phenyl)-amide

Thiadiazole-4-carboxylic acid (4-[(3,5-dimethoxy-phenyl)-thioureido]-phenyl)-amide

5-(3-[(4-(Furan-2-carbonyl)-amino]-phenyl)-thioureido)-isophthalic acid dimethyl ester

Isoxazole-5-carboxylic acid (4-[(3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[(3-(6-chloro-pyridin-3-yl)-thioureido]-phenyl)-amide

Furan-2-carboxylic acid (4-[(3-(1-hydroxy-ethyl)-phenyl)-thioureido]-phenyl)-amide

Furan-2-carboxylic acid (4-[(3-methoxy-phenyl)-thioureido]-phenyl)-amide

Furan-2-carboxylic acid (4-[(3-hydroxy-phenyl)-thioureido]-phenyl)-amide

2-Fluoro-N-(4-[(3-hydroxy-phenyl)-thioureido]-phenyl)-benzamide

2-Fluoro-N-(4-[(3-hydroxymethyl-phenyl)-thioureido]-phenyl)-benzamide

N-(4-[(3-Acetylamino-phenyl)-thioureido]-phenyl)-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[(3-acetylamino-phenyl)-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[(3-(dimethylamino-phenyl)-thioureido]-phenyl)-amide

Furan-2-carboxylic acid (4-[(3-pyrimidin-4-yl-thioureido)-phenyl]-amide

Furan-2-carboxylic acid (4-[(1H-indazol-5-yl)-thioureido]-phenyl)-amide

Furan-2-carboxylic acid (4-[(3-benzothiazol-5-yl-thioureido)-phenyl]-amide

2-Fluoro-N-(4-[(1H-indazol-5-yl)-thioureido]-phenyl)-benzamide

N-(4-[(3-Benzothiazol-5-yl-thioureido)-phenyl]-2-fluoro-benzamide

5-(3-[(4-[[1,2,3]Thiadiazole-4-carbonyl]-amino]-phenyl)-thioureido)-isophthalic acid dimethyl ester

Furan-2-carboxylic acid (4-[(3-[(4-[(1-azido-ethyl)-3-chloro-phenyl]-thioureido]-phenyl)-amide

2-Fluoro-N-(4-[(3-(methoxy-phenyl)-thioureido]-phenyl)-benzamide

Furan-2-carboxylic acid (4-[(3-(hydroxymethyl-phenyl)-thioureido]-phenyl)-amide

Furan-2-carboxylic acid (4-[(3-(5-chloro-2-(dimethylamino-phenyl)-thioureido]-phenyl)]-amide

N-(4-[(3-Chloro-2-(dimethylamino-phenyl)-thioureido]-phenyl)-2-fluoro-
[3-Chloro-5-(3-[4-[[1,2,3]thiadiazole-4-carbonyl-amino]-phenyl]-thioureido)-phenyl]-carbamic acid tert-butyl ester
N-(4-[3-[4-(1-Azido-ethyl)-3-chloro-phenyl]-thioureido]-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid [4-((1H-thiazolo[5,4-b]pyridin-2-ylideneamino)-phenyl)-amide
Furan-2-carboxylic acid {4-[3-(1H-benzimidazol-5-yl)-thioureido]-phenyl}-amide
Furan-2-carboxylic acid {4-[3-(2-methyl-1H-benzimidazol-5-yl)-thioureido]-phenyl}-amide
N-(4-[3-(1H-Benzimidazol-5-yl)-thioureido]-phenyl)-2-fluoro-benzamide
2-Fluoro-N-(4-[3-(2-methyl-1H-benzimidazol-5-yl)-thioureido]-phenyl)-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid {5-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-2-yl}-amide
Pyridine-2-carboxylic acid {5-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-2-yl}-amide
[1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(5-chloro-2-dimethylamino-phenyl)-thioureido]-phenyl}-amide
[1,2,3]Thiadiazole-4-carboxylic acid {4-[3-[4-(2-amino-pyrimidin-4-yl)-3-chloro-phenyl]-thioureido]-phenyl}-amide
N-(4-[3-[4-(2-Amino-pyrimidin-4-yl)-3-chloro-phenyl]-thioureido]-phenyl)-2-fluoro-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-chloro-2-dimethylamino-phenyl)-thioureido]-phenyl}-amide
N-(4-[3-(3-Chloro-2-dimethylamino-phenyl)-thioureido]-phenyl)-2,6-difluoro-benzamide
Furan-2-carboxylic acid {4-[3-(3-chloro-2-dimethylamino-phenyl)-thioureido]-phenyl}-amide
Pyridine-2-carboxylic acid {6-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-3-yl}-amide
N-(6-[3-(5-Chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-3-yl)-2-fluoro-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-iodo-phenyl)-thioureido]-phenyl}-amide
[1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-tert-butyl-phenyl)-thioureido]-phenyl}-amide
Furan-2-carboxylic acid \{4-[3-(3-chloro-benzyl)-thioureido]-phenyl\}-amide

N-[4-[3-(3-Chloro-benzyl)-thioureido]-phenyl]-2-fluoro-benzamide

Furan-2-carboxylic acid \{6-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-3-yl\}-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-(3-bromo-phenyl)-thioureido]-phenyl\}-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{6-[3-(5-chloro-2,4-dimethoxy-phenyl)-thioureido]-pyridin-3-yl\}-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{5-[3-(3,5-dichloro-phenyl)-thioureido]-pyridin-2-yl\}-amide

Furan-2-carboxylic acid \{4-[3-(3,5-bis-trifluoromethyl-phenyl)-thioureido]-phenyl\}-amide

N-[4-[3-(3,5-Bis-trifluoromethyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

N-[4-[3-(4-Amino-3,5-dichloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

N-[4-[3-(4-Amino-3,5-dibromo-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-(5-chloro-pyridin-3-yl)-thioureido]-phenyl\}-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-(4-amino-3,5-dibromo-phenyl)-thioureido]-phenyl\}-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-(3-chloro-5-dimethylamino-phenyl)-thioureiido]-phenyl\}-amide

N-[4-[3-(3-Chloro-5-dimethylamino-phenyl)-thioureiido]-phenyl]-2-fluoro-benzamide

Furan-2-carboxylic acid \{4-[3-(3-chloro-5-dimethylamino-phenyl)-thioureiido]-phenyl\}-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-(5-bromo-pyridin-3-yl)-thioureiido]-phenyl\}-amide

Furan-2-carboxylic acid \{4-[3-(1H-benzotriazol-5-yl)-thioureiido]-phenyl\}-amide

N-[4-[3-(1H-Benzotriazol-5-yl)-thioureiido]-phenyl]-2,6-difluoro-benzamide

N-[4-{[2-(3-Chloro-phenyl)-hydrazino]-thioxomethyl}-amino]-phenyl]-furan-2-carboxamide

N-[4-{[2-(3-Chloro-phenyl)-hydrazino]-thioxomethyl}-amino]-phenyl]-2-fluoro-benzamide

Furan-2-carboxylic acid \{4-[3-(2-amino-3-chloro-5-trifluoromethyl-phenyl)-
thioureido]-phenyl)-amide

531 513 N-{4-[3-(3-Bromo-5-trifluoromethyl-phenyl)-thioureido]-phenyl}-2-fluoro-
benzamide

532 503 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(bromo-5-trifluoromethyl-
phenyl)-thioureido]-phenyl}-amide

533 374 {4-[(Furan-2-carbonyl)-amino]-phenyl]-thiocarbamic acid O-(3-chloro-phenyl)
ester

534 474 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(2-amino-3-chloro-5-trifluoro-
methyl-phenyl)-thioureido]-phenyl}-amide

535 508 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-piperidin-1-yl-5-trifluoromethyl-
phenyl)-thioureido]-phenyl}-amide

536 380 N-{4-(3-Benzyl-thioureido)-phenyl}-2-fluoro-benzamide

537 439 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3,4-dichloro-benzyl)-thioureido]-
phenyl}-amide

538 449 N-{4-[3-(3-Dichloro-benzyl)-thioureido]-phenyl}-2-fluoro-benzamide

539 370 [1,2,3]Thiadiazole-4-carboxylic acid {4-(3-benzyl-thioureido)-phenyl}-amide

540 424 N-{4-(3-Benzo[1,3]dioxol-5-ylmethyl-thioureido)-phenyl}-2-fluoro-benzamide

541 414 [1,2,3]Thiadiazole-4-carboxylic acid {4-(3-benzo[1,3]dioxol-5-ylmethyl-
thioureido)-phenyl}-amide

542 506 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3,5-bis-trifluoromethyl-benzyl)-
thioureido]-phenyl}-amide

543 516 N-{4-[3-(3,5-Bis-trifluoromethyl-benzyl)-thioureido]-phenyl}-2-fluoro-
benzamide

544 352 Furan-2-carboxylic acid [4-(3-benzyl-thioureido)-phenyl]-amide

545 421 Furan-2-carboxylic acid [4-[3-(3,4-dichloro-benzyl)-thioureido]-phenyl]-amide

546 396 Furan-2-carboxylic acid [4-(3-benzo[1,3]dioxol-5-ylmethyl-thioureido)-
phenyl]-amide

547 488 Furan-2-carboxylic acid [4-[3-(3,5-bis-trifluoromethyl-benzyl)-thioureido]-
phenyl]-amide

548 503 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(4-bromo-3-trifluoromethyl-
phenyl)-thioureido]-phenyl}-amide

549 529 N-{4-[3-(3-Bromo-4-trifluoromethoxy-phenyl)-thioureido]-phenyl}-2-fluoro-
benzamide

550 519 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-bromo-4-trifluoromethoxy-
phenyl)-thioureido]-phenyl)-amide

551 473  Furan-2-carboxylic acid (4-[3-(3-chloro-4-trifluoromethylsulfanyl-phenyl)-thioureido]-phenyl)-amide

552 412  2-Fluoro-N-[4-[3-(2-(3-fluoro-phenyl)-ethy]-thioureido]-phenyl]-benzamide

553 412  2-Fluoro-N-[4-[3-(2-(4-fluoro-phenyl)-ethy]-thioureido]-phenyl]-benzamide

554 402  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(2-(3-fluoro-phenyl)-ethy]-thioureido]-phenyl)-amide

555 402  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(2-(4-fluoro-phenyl)-ethy]-thioureido]-phenyl)-amide

556 495  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-(2-methyl-butyl)-5-trifluoromethyl-phenyl]-thioureido]-phenyl)-amide

557 481  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-isobutyl-5-trifluoromethyl-phenyl]-thioureido]-phenyl)-amide

558 523  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-(4-methyl-pipercasin-1-yl)-5-trifluoromethyl-phenyl]-thioureido]-phenyl)-amide

559 510  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-morpholin-4-yl-5-trifluoromethyl-phenyl]-thioureido]-phenyl)-amide

560 494  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-pyrrolidin-1-yl-5-trifluoromethyl-phenyl]-thioureido]-phenyl)-amide

561 384  Furan-2-carboxylic acid (4-[3-[2-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide

562 419  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-(3-chloro-phenyl)-ethyl]-thioureido]-phenyl)-amide

563 429  N-[4-[3-(2-(3-Chloro-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide

564 401  Furan-2-carboxylic acid (4-[3-[2-(3-chloro-phenyl)-ethyl]-thioureido]-phenyl)-amide

565 402  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide

566 504  2-Fluoro-N-[4-[3-(3-pyrrolidin-1-yl-5-trifluoromethyl-phenyl]-thioureido]-phenyl]-benzamide

567 477  N-[4-[3-(3-Dimethylamino-5-trifluoromethyl-phenyl]-thioureido]-phenyl]-2-fluoro-benzamide

568 520  2-Fluoro-N-[4-[3-(3-morpholin-4-yl-5-trifluoromethyl-phenyl]-thioureido]-phenyl]-benzamide
2-Fluoro-N-(4-[3-(3-methyl-piperazin-1-yl)-5-trifluoromethyl-phenyl]-thioureido)-phenyl)-benzamide

2-Fluoro-N-[4-[3-(3-piperidin-1-yl)-5-trifluoromethyl-phenyl]-thioureido]-phenyl)-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3-dimethylamino-5-trifluoromethyl-phenyl)-thioureido]-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3-chloro-benzyl)-thioureido]-phenyl]-amide

Furan-2-carboxylic acid (4-[3-[2-(3-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide

Furan-2-carboxylic acid [4-(3-phenethyl-thioureido)-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-(3-phenethyl-thioureido)-phenyl]-amide

2-Fluoro-N-[4-(3-phenethyl-thioureido)-phenyl]-benzamide

2-Fluoro-N-[4-[3-(2-methyl-butyl)-5-trifluoromethyl-phenyl]-thioureido]-phenyl)-benzamide

2-Fluoro-N-[4-[3-(isobutyl-5-trifluoromethyl-phenyl)-thioureido]-phenyl]-benzamide

Furan-2-carboxylic acid [4-[3-(3,5-difluoro-benzyl)-thioureido]-phenyl]-amide

N-[4-[3-(3,5-Difluoro-benzyl)-thioureido]-phenyl]-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3,5-difluoro-benzyl)-thioureido]-phenyl]-amide

Furan-2-carboxylic acid [4-[3-(3,5-dichloro-benzyl)-thioureido]-phenyl]-amide

N-[4-[3-(3,5-Dichloro-benzyl)-thioureido]-phenyl]-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3,5-dichloro-benzyl)-thioureido]-phenyl]-amide

Furan-2-carboxylic acid [4-[3-(3-fluoro-5-trifluoromethyl-benzyl)-thioureido]-phenyl]-amide

2-Fluoro-N-[4-[3-(3-fluoro-5-trifluoromethyl-benzyl)-thioureido]-phenyl]-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3-fluoro-5-trifluoromethyl-benzyl)-thioureido]-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(1-phenyl-ethyl)-thioureido]-phenyl]-amide

Furan-2-carboxylic acid [4-[3-(1-phenyl-ethyl)-thioureido]-phenyl]-amide

Furan-2-carboxylic acid [4-[3-(1-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide

2-Fluoro-N-[4-[3-(1-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-benzamide

Furan-2-carboxylic acid [4-[3-(1-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide

2-Fluoro-N-[4-[3-(1-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-benzamide
Furan-2-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-amide
N-{4-[3-(1-tert-Butyl-1H-imidazol-2-yl)-thioureido]-phenyl}-2-fluorobenzamide
[1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[3-(isobutyl-methyl-amino)-5-trifluoromethyl-phenyl]-thiourea}-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[3-(hydroxy-pyridin-1-yl)-5-trifluoromethyl-phenyl]-thiourea}-phenyl)-amide
2-Fluoro-N-{4-[3-[3-(isobutyl-methyl-amino)-5-trifluoromethyl-phenyl]-thiourea}-phenyl)-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[3-(butyl-methyl-amino)-5-trifluoromethyl-phenyl]-thiourea}-phenyl)-amide
N-{4-[3-[3-(Butyl-methyl-amino)-5-trifluoromethyl-phenyl]-thiourea}-phenyl)-2-fluoro-benzamide
[1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-thiourea}-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(4-fluoro-3-trifluoromethyl-phenyl)-thioureido]-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(4-piperidin-1-yl-3-trifluoromethyl-benzyl)-thioureido]-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(4-dimethylamino-3-trifluoromethyl-benzyl)-thioureido]-phenyl)-amide
Furan-2-carboxylic acid (4-{3-[2-(4-amino-phenyl)-ethyl]-thioureido}-phenyl)-amide
Furan-2-carboxylic acid (4-{3-[2-(4-bromo-phenyl)-ethyl]-thioureido}-phenyl)-amide
Furan-2-carboxylic acid (4-[3-{2-p-tolyl-ethyl]-thioureido}-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(4-bromo-phenyl)-ethyl]-thiourea}-phenyl)-amide
Furan-2-carboxylic acid (4-{3-[2-(3-methoxy-phenyl)-ethyl]-thioureido}-phenyl)-amide
[1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[1-(tert-butyl-1H-imidazol-2-yl)-thiourea]-phenyl)-amide
Furan-2-carboxylic acid (4-[3-{1-(tert-butyl-1H-imidazol-2-yl)-thiourea}-phenyl)-amide
N-{4-[3-(4-Dimethylamino-3-trifluoromethyl-benzyl)-thiourea]-phenyl)-2-fluoro-benzamide
Furan-2-carboxylic acid (4-{3-[2-(3,4-dimethoxy-phenyl)-ethyl]-thiourea}-phenyl)-amide
phenyl)-amide

612  380  Furan-2-carboxylic acid {4-[3-(3-phenyl-propyl)-thioureido]-phenyl}-amide

613  399  [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-phenyl-propyl)-thioureido]-phenyl}-amide

614  502  Furan-2-carboxylic acid (4-{3-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-thioureido}-phenyl)-amide

615  550  [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(4-iodo-3-trifluoromethyl-phenyl)-thioureido]-phenyl}-amide

616  532  2-Fluoro-N-{4-[3-(4-piperidin-1-yl-3-trifluoromethyl-benzyl)-thioureido]-phenyl}-benzamide

617  537  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[4-(4-methyl-piperazin-1-yl)-3-trifluoromethyl-benzyl]-thioureido]-phenyl)-amide

618  482  [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-dimethylamino-5-trifluoromethyl-benzyl)-thioureido]-phenyl)-amide

619  488  Furan-2-carboxylic acid {4-[3-(3,5-bis-trifluoromethyl-phenyl)-thioureidomethyl]-phenyl}-amide

620  421  Furan-2-carboxylic acid {4-[3-(3,5-dichloro-phenyl)-thioureidomethyl]-phenyl}-amide

621  421  Furan-2-carboxylic acid {4-[3-(3,4-dichloro-phenyl)-thioureidomethyl]-phenyl}-amide

622  455  Furan-2-carboxylic acid (4-[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureidomethyl]-phenyl)-amide

623  466  2-Fluoro-N-{4-[3-(4-fluoro-3-trifluoromethyl-benzyl)-thioureido]-phenyl}-benzamide

624  456  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(4-fluoro-3-trifluoromethyl-benzyl)-thioureido]-phenyl)-amide

625  410  2-Fluoro-N-{4-[3-(2-phenoxy-ethyl)-thioureido]-phenyl}-benzamide

626  382  Furan-2-carboxylic acid (4-[3-(2-phenoxy-ethyl)-thioureido]-phenyl)-amide

627  400  [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-(2-phenoxy-ethyl)-thioureido]-phenyl)-amide

628  409  2-Fluoro-N-{4-[3-(3-phenyl-propyl)-thioureido]-phenyl}-benzamide

629  425  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(5-trifluoromethyl-pyridin-3-yl)-thioureido]-phenyl)-amide

630  439  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3,4-dichloro-phenyl)-thioureidomethyl]-phenyl)-amide

631  473  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureidomethyl]-phenyl)-amide
2-Fluoro-N-[4-(3-pyridin-3-ylmethyl-thioureido)-phenyl]-benzamide

Furan-2-carboxylic acid [4-(3-pyridin-3-ylmethyl-thioureido)-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-(3-pyridin-3-ylmethyl-thioureido)-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3,5-dichloro-phenyl)-thioureidomethyl]-phenyl]-amide

N-[4-[3-(3-Dimethylamino-5-trifluoromethyl-benzyl)-thioureido]-phenyl]-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(3-methoxy-phenyl)-ethyl]-thioureido}-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-(p-tolyl-ethyl)-thioureido]-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-(3,4-dimethoxy-phenyl)-ethyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-(3,5-bis-trifluoromethyl-phenyl)-thioureidomethyl]-phenyl]-amide

N-[4-[3-(3,5-Bis-trifluoromethyl-phenyl)-thioureidomethyl]-phenyl]-2-fluoro-benzamide

N-[4-[3-(3,5-Dichloro-phenyl)-thioureidomethyl]-phenyl]-2-fluoro-benzamide

N-[4-[3-(3,4-Dichloro-phenyl)-thioureidomethyl]-phenyl]-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[3-acetylamino-5-chloro-phenyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-[3,4-dichloro-phenyl]-ethyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[1-methyl-3-phenyl-propyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[4-phenyl-butyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-(3-indan-1-yl-thioureido)-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(2-methoxy-benzyl)-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-(2-methoxy-phenyl)-ethyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-(4-methoxy-phenyl)-ethyl]-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-[2-(4-methoxy-phenyl)-ethyl]-thioureido]-phenyl)-amide
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653 506 N-(4-(3-[2-(3-Dimethylamino-5-trifluoromethyl-phenyl)-ethyl]-thioureido)-phenyl)-2-fluoro-benzamide

654 510 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(3-dimethylamino-propyl)-5-trifluoromethyl-phenyl]-thioureido}-phenyl)-amide

655 417 [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(2-phenylsulfanyl-ethyl)-thioureido]-phenyl)-amide

656 427 2-Fluoro-N-{4-[3-(2-phenylsulfanyl-ethyl)-thioureido]-phenyl}-benzamide

657 399 Furan-2-carboxylic acid {4-[3-(2-phenylsulfanyl-ethyl)-thioureido]-phenyl}-amide

658 381 2-Fluoro-N-{4-(3-pyridin-4-yml-ethyl)-thioureido}-phenyl]-benzamide

659 353 Furan-2-carboxylic acid [4-(3-pyridin-4-yml-ethyl-thioureido)-phenyl]-amide

660 371 [1,2,3]Thiadiazole-4-carboxylic acid [4-(3-pyridin-4-yml-ethyl-thioureido)-phenyl]-amide

661 506 2-Fluoro-N-{4-[3-(3-iodo-benzyl)-thioureido]-phenyl}-benzamide

662 478 Furan-2-carboxylic acid (4-{3-(3-iodo-benzyl)-thioureido}-phenyl)-amide

663 496 [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-iodo-benzyl)-thioureido]-phenyl)-amide

664 479 N-(4-[3-[2-(3,5-Dichloro-phenoxy)-ethyl]-thioureido]-phenyl)-2-fluorobenzamide

665 451 Furan-2-carboxylic acid (4-{3-[2-(3,5-dichloro-phenoxy)-ethyl]-thioureido}-phenyl)-amide

666 445 N-(4-[3-[2-(3-Chloro-phenoxy)-ethyl]-thioureido]-phenyl)-2-fluorobenzamide

667 417 Furan-2-carboxylic acid (4-{3-[2-(3-chloro-phenoxy)-ethyl]-thioureido}-phenyl)-amide

668 435 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(3-chloro-phenoxy)-ethyl]-thioureido}-phenyl)-amide

669 466 2-Fluoro-N-{4-[3-(2-fluoro-5-trifluoromethyl-benzyl)-thioureido]-phenyl}-benzamide

670 438 Furan-2-carboxylic acid {4-[3-(2-fluoro-5-trifluoromethyl-benzyl)-thioureido]-phenyl}-amide

671 456 [1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(2-fluoro-5-trifluoromethyl-benzyl)-thioureido]-phenyl}-amide

672 416 N-(4-[3-(3,4-Difluoro-benzyl)-thioureido]-phenyl)-2-fluorobenzamide

673 452 N-(4-[3-[2-(4-Dimethylamino-3-methyl-phenyl)-ethyl]-thioureido]-phenyl)-2-fluorobenzamide

674 496 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(3-dimethylamino-5-trifluoromethyl-phenyl)-ethyl]-thioureido}-phenyl)-amide
Furan-2-carboxylic acid \{4-[3-(3,4-difluoro-benzyl)-thioureido]-phenyl\}-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-(3,4-difluoro-benzyl)-thioureido]-phenyl\}-amide

N-\{4-[3-(3-Chloro-4-fluoro-benzyl)-thioureido]-phenyl\}-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(3-bromo-phenylsulfanyl)-ethyl]-thioureido\}-phenyl-amide

Furan-2-carboxylic acid \{4-[3-2-(3-bromo-phenylsulfanyl)-ethyl]-thioureido\}-phenyl-amide

N-\{4-[3-[2-(3-Bromo-phenylsulfanyl)-ethyl]-thioureido\}-phenyl\}-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(3-methoxy-phenyl)-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(5-bromo-2-methoxy-phenyl)-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(2-chloro-phenyl)-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(2-fluoro-phenyl)-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(3-chloro-phenyl)-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-3-diphenyl-propyl]-thioureido\}-phenyl-amide

2-Fluoro-N-\{4-[3-(4-methyl-piperazin-1-yl)-3-trifluoromethyl-benzyl]-thioureido\}-phenyl-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(3,5-dichloro-phenoxy)-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-3-chloro-4-fluoro-benzyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-4-tert-butyl-benzyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-3,5-dimethyl-benzyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-4-dimethylamino-3-methyl-phenyl]-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(3-bromo-phenoxy)-ethyl]-thioureido\}-phenyl-amide

[1,2,3]Thiadiazole-4-carboxylic acid \{4-[3-2-(4-iodo-phenoxo)-ethyl]-}
thioureido)-phenyl)-amide

695  489  N-(4-[[3-2-(4-Bromo-phenoxy)-ethyl]-thioureido]-phenyl)-2-fluorobenzamide

696  536  2-Fluoro-N-(4-[[3-2-(4-iodo-phenoxy)-ethyl]-thioureido]-phenyl)-benzamide

697  461  Furan-2-carboxylic acid (4-[[3-2-(4-bromo-phenoxy)-ethyl]-thioureido]-phenyl)-amide

698  508  Furan-2-carboxylic acid (4-[[3-2-(4-iodo-phenoxy)-ethyl]-thioureido]-phenyl)-amide

699  408  Oxazole-4-carboxylic acid (4-[[3-(3,4-dichloro-phenyl)-thioureido]-phenyl]-amide

700  424  Thiazole-4-carboxylic acid (4-[[3-(3,5-dichloro-phenyl)-thioureido]-phenyl]-amide

701  491  Thiazole-4-carboxylic acid (4-[[3-(3,5-bis-trifluoromethyl-phenyl)-thioureido]-phenyl]-amide

702  408  Oxazole-4-carboxylic acid (4-[[3-(3,5-dichloro-phenyl)-thioureido]-phenyl]-amide

703  469  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-2-(3,4-dichloro-phenoxy)-ethyl]-thioureido]-phenyl)-amide

704  424  Thiazole-4-carboxylic acid (4-[[3-(3,4-dichloro-phenyl)-thioureido]-phenyl]-amide

705  458  Thiazole-4-carboxylic acid (4-[[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureido]-phenyl]-amide

706  400  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-(2-phenylamino-ethyl)-thioureido]-phenyl]-amide

707  453  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-2-(2,4-dichloro-phenyl)-ethyl]-thioureido]-phenyl)-amide

708  452  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-2-(3-trifluoromethyl-phenyl)-ethyl]-thioureido]-phenyl)-amide

709  453  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-2-(2,6-dichloro-phenyl)-ethyl]-thioureido]-phenyl)-amide

710  485  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-2-(3,4-dichloro-phenylsulfanyl)-ethyl]-thioureido]-phenyl)-amide

711  503  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-2-(2-fluoro-5-trifluoromethyl-phenylsulfanyl)-ethyl]-thioureido]-phenyl)-amide

712  668  N-(4-[[3-Chloro-5-[[3-4-[[1,2,3]thiadiazole-4-carbonyl]-amino]-phenyl]-thioureido]-phenyl)-[1,2,3]thiadiazole-4-carboxamide

713  413  [1,2,3]Thiadiazole-4-carboxylic acid (4-[[3-2-(4-ethyl-phenyl)-ethyl]-thioureido]-phenyl)-amide
714 442 Oxazole-4-carboxylic acid \(4\{3-(4-chloro-3-trifluoromethyl-phenyl)thioureido\}phenyl\)-amide
716 420 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-2-(3,4-difluoro-phenyl)ethyl\}thioureido\}phenyl\)-amide
717 452 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-2-(4-trifluoromethyl-phenyl)ethyl\}thioureido\}phenyl\)-amide
718 435 Puran-2-carboxylic acid \(4\{3-2-(3,4-dichloro-phenyl)ethyl\}thioureido\}phenyl\)-amide
719 463 N-(4-(3-[2-(3,4-Dichloro-phenyl)ethyl]-thioureido)-phenyl)-2-fluorobenzamide
720 420 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-2-(3,5-difluoro-phenyl)ethyl\}thioureido\}phenyl\)-amide
721 412 2-Fluoro-N-(4-(3-[2-(2-fluoro-phenyl)ethyl]-thioureido)-phenyl)-benzamide
722 429 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-2-(4-nitro-phenyl)ethyl\}thioureido\}phenyl\)-amide
723 399 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-(1-methyl-2-phenyl-ethyl)thioureido\}phenyl\)-amide
724 437 N-(4-[3-(4-tert-Butyl-benzyl)thioureido]-phenyl)-2-fluoro-benzamide
725 409 N-(4-[3-(3,5-Dimethyl-benzyl)thioureido]-phenyl)-2-fluoro-benzamide
726 400 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-2-hydroxy-1-phenyl-ethyl\}thioureido\}phenyl\)-amide
727 409 2-Fluoro-N-(4-[3-(1-methyl-1-phenyl-ethyl)-thioureido]-phenyl)-benzamide
728 399 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-(1-methyl-1-phenyl-ethyl)thioureido\}phenyl\)-amide
729 405 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-(2-chloro-benzyl)-thioureido\}phenyl\)-amide
730 388 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-(2-fluoro-benzyl)-thioureido\}phenyl\)-amide
731 438 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-(3-trifluoromethyl-benzyl)thioureido\}phenyl\)-amide
732 388 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-(3-fluoro-benzyl)-thioureido\}phenyl\)-amide
733 435 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-2-(2-chloro-phenoxy)-ethyl\}thioureido\}phenyl\)-amide
734 479 \[1,2,3\]Thiadiazole-4-carboxylic acid \(4\{3-2-(3-bromo-phenoxy)-ethyl\}
thioureido)-phenyl)-amide

735 418 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(2-fluoro-phenoxy)-ethyl]-thioureido}-phenyl)-amide

736 418 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(3-fluoro-phenoxy)-ethyl]-thioureido}-phenyl)-amide

737 486 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(2-fluoro-5-trifluoromethyl-phenoxy)-ethyl]-thioureido}-phenyl)-amide

738 384 Furan-2-carboxylic acid (4-{3-[2-(2-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-amide

739 435 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[4-bromo-phenyl]-thioureido}-phenyl)-amide

740 374 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[4-fluoro-phenyl]-thioureido}-phenyl)-amide

741 388 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[4-fluoro-benzyl]-thioureido}-phenyl)-amide

742 405 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[4-chloro-benzyl]-thioureido}-phenyl)-amide

743 449 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[4-bromo-benzyl]-thioureido}-phenyl)-amide

744 332 N-(4-{3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido})-phenyl)-acetamide

745 438 Thiazole-4-carboxylic acid (4-{3-[3,4-dichloro-benzyl]-thioureido}-phenyl)-amide

746 455 Thiazole-4-carboxylic acid (4-{3-[2-fluoro-5-trifluoromethyl-benzyl]-thioureido}-phenyl)-amide

747 426 Thiazole-4-carboxylic acid (4-{3-[4-tert-butyl-benzyl]-thioureido}-phenyl)-amide

748 374 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-fluoro-phenyl]-thioureido}-phenyl)-amide

749 374 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[3-fluoro-phenyl]-thioureido}-phenyl)-amide

750 526 [1,2,3]Thiadiazole-4-carboxylic acid (4-{3-[2-(3-iodo-phenoxy)-ethyl]-thioureido}-phenyl)-amide

751 409 N-(4-{3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido})-phenyl)-2-phenyl-acetamide

752 425 N-(4-{3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido})-phenyl)-2-methoxy-benzamide

753 425 N-(4-{3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido})-phenyl)-3-methoxy-benzamide
N-(4-[(3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido)-phenyl]-4-methoxy-benzamide

2-Chloro-N-(4-[(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenyl]-benzamide

4-Chloro-N-(4-[(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenyl]-benzamide

Acetic acid 4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenylcarbamoyl)-phenyl ester

N-(4-[(3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido)-phenyl]-benzamide

N-(4-[(3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido)-phenyl]-isonicotinamide

N-(4-[(3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido)-phenyl]-4-hydroxy-benzamide

3-Chloro-N-(4-[(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenyl]-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(3-fluoro-5-trifluoromethyl-phenyl)-ethyl]-thioureido)-phenyl-amine

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(2,4-bis-trifluoromethyl-phenyl)-ethyl]-thioureido)-phenyl-amine

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(4-fluoro-3-trifluoromethyl-phenyl)-ethyl]-thioureido)-phenyl-amine

4-Dimethylamino-N-(4-[(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenyl]-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(2-fluoro-3-trifluoromethyl-phenyl)-ethyl]-thioureido)-phenyl-amine

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(2-fluoro-5-trifluoromethyl-phenyl)-ethyl]-thioureido)-phenyl-amine

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(3-iodo-phenyl)-ethyl]-thioureido)-phenyl-amine

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(4-fluoro-2-trifluoromethyl-phenyl)-ethyl]-thioureido)-phenyl-amine

[1,2,3]Thiadiazole-4-carboxylic acid 4-(3-[2-(3-bromo-phenyl)-ethyl]-thioureido)-phenyl-amine

2-Fluoro-N-(4-[(3-[1-(4-fluoro-phenyl)-propyl]-thioureido)-phenyl]-benzamide

2-Fluoro-N-(4-[(3-[4-fluoro-phenyl]-phenyl-methyl]-thioureido)-phenyl]-benzamide

2-Fluoro-N-(4-[(3-[1-(4-fluoro-phenyl)-pentyl]-thioureido)-phenyl]-benzamide

2-Fluoro-N-(4-[(3-[1-(4-fluoro-phenyl)-2-phenyl-ethyl]-thioureido)-phenyl]-benzamide

2-Fluoro-N-(4-[(3-[1-o-tolyl-ethyl]-thioureido)-phenyl]-benzamide
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<td>2-Fluoro-N-{4-[3-(1-m-tolyl-ethyl)-thioureido]-phenyl}-benzamide</td>
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<td>2-Fluoro-N-{4-[3-[1-(4-methoxy-phenyl)-ethyl]-thioureido]-phenyl}-benzamide</td>
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<td>2-Fluoro-N-{4-[3-[1-(2-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-benzamide</td>
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<td>N-4-[3-[1-(3-Chloro-phenyl)-ethyl]-thioureido]-phenyl]-2-fluorobenzamide</td>
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<td>473</td>
<td>N-4-[3-[1-(3-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-2-fluorobenzamide</td>
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<td>429</td>
<td>N-4-[3-[1-(4-Chloro-phenyl)-ethyl]-thioureido]-phenyl]-2-fluorobenzamide</td>
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<td>782</td>
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<td>2-Fluoro-N-{4-[3-(1-p-tolyl-ethyl)-thioureido]-phenyl}-benzamide</td>
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<td>783</td>
<td>473</td>
<td>N-4-[3-[1-(2-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-2-fluorobenzamide</td>
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<td>2-Fluoro-N-{4-[3-[1-(2-trifluoromethyl-phenyl)-ethyl]-thioureido]-phenyl}-benzamide</td>
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<td>2-Fluoro-N-{4-[3-[1-(3-trifluoromethyl-phenyl)-ethyl]-thioureido]-phenyl}-benzamide</td>
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<td>787</td>
<td>462</td>
<td>2-Fluoro-N-{4-[3-[1-(4-trifluoromethyl-phenyl)-ethyl]-thioureido]-phenyl}-benzamide</td>
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<td>425</td>
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<td>441</td>
<td>2-Fluoro-N-{4-[3-[1-(4-fluoro-phenyl)-2-methyl-propyl]-thioureido]-phenyl}-benzamide</td>
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<td>792</td>
<td>419</td>
<td>N-4-[3-[1-(4-Cyano-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide</td>
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<td>793</td>
<td>438</td>
<td>N-4-[3-[1-(4-Dimethylamino-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide</td>
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<td>794</td>
<td>438</td>
<td>N-4-[3-[1-(3-Dimethylamino-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide</td>
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<td>795</td>
<td>473</td>
<td>2-Bromo-N-{4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-benzamide</td>
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<td>Quinoline-2-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide</td>
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2-Fluoro-N-[4-[3-(2-hydroxy-1-phenyl-ethyl)-thioureido]-phenyl]-benzamide
2-Fluoro-N-[4-[3-isopropyl-thioureido]-phenyl]-benzamide
2-Fluoro-N-[4-[3-[1-naphthalen-2-yl-ethyl]-thioureido]-phenyl]-benzamide
3-Fluoro-N-[4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-benzamide
4-Fluoro-N-[4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-benzamide
2-Fluoro-N-[4-[3-[1-furan-2-yl-ethyl]-thioureido]-phenyl]-benzamide
2-Fluoro-N-[4-[3-[1-(1-methyl-1H-pyrrol-2-yl)-ethyl]-thioureido]-phenyl]-benzamide
2-Fluoro-N-[4-[3-[1-thiophen-3-yl-ethyl]-thioureido]-phenyl]-benzamide
N-[4-[3-(3-Chloro-4-ethoxy-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-(3-Chloro-4-propoxy-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-(3-Chloro-4-isopropoxy-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-(3-Bromo-4-chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-(1-iodo-4-methoxy-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-(1-(4-Fluoro-phenyl)-ethyl)-thioureido]-phenyl]-2-iodo-benzamide
N-[4-[3-(1-(4-Fluoro-phenyl)-ethyl)-thioureido]-phenyl]-propionamide
N-[4-[3-(Phenyl-thioureido)-phenyl]-acetamide
N-[4-[3-[1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide
N-[4-[3-[1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-4-fluoro-benzamide
N-[4-[3-[1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-2-methoxy-benzamide
N-[4-[3-[1-(1R)-1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-2-methoxy-benzamide
Isoquinoline-1-carboxylic acid (4-[[3-[1S]-1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl)-amide
Isoquinoline-3-carboxylic acid (4-[[3-[1S]-1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl)-amide
Isoquinoline-1-carboxylic acid (4-[[3-[1S]-1-(4-chloro-phenyl)-ethyl]-
thioureido]-phenyl)-amide

Isoquinoline-1-carboxylic acid (4-{{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-amide

N-[4-{{1S}-1-(4-cyanophenyl)ethyl]amino}carbothioyl]amino[phenyl]-1-nophenyl)ethyl]amino]carbothioyl]amino[phenyl]-1-isooquinolinecarboxamide

EXAMPLE 815 (METHOD 32)

[1,2,3]Thiadiazole-4-carboxylic acid (4-{{3-(2,5-dichloro-phenyl)-thioureido]-phenyl}-amide

To a solution of 2,5-dichloroaniline (0.16 g) in tetrahydrofuran (20 mL) is added freshly prepared 1,1'-thiocarbonyldiimidazole (0.20 g) and the mixture is stirred for approximately 30 minutes at room temperature. [1,2,3]-Thiadiazole-4-carboxylic acid (4-amino-phenyl) amide (0.22 g) is added to the reaction flask and the mixture is stirred for approximately 6 hours. The solvent is then removed by evaporation under reduced pressure and warm acetonitrile (3 mL) is added. After 15 hours the mixture is filtered and the collected precipitate is washed with acetonitrile then diethyl ether, and air dried to provide the desired product as a white powder.

Using the above procedure and appropriate starting materials the following compounds were prepared:

<table>
<thead>
<tr>
<th>EX. NO.</th>
<th>M+H</th>
<th>COMPOUND NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>816</td>
<td>321</td>
<td>N-[4-{3-(3-Chloro-phenyl)-thioureido]-phenyl]-acetamide</td>
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<tr>
<td>817</td>
<td>413</td>
<td>N-[4-{3-(3-Chloro-4-methoxy-phenyl)-thioureido]-phenyl}-benzamide</td>
</tr>
<tr>
<td>818</td>
<td>443</td>
<td>N-[4-{3-(3-Chloro-4-methoxy-phenyl)-thioureido]-phenyl}-2-methoxy-benzamide</td>
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<tr>
<td>819</td>
<td>443</td>
<td>N-[4-{3-(3-Chloro-4-methoxy-phenyl)-thioureido]-phenyl}-3-methoxy-benzamide</td>
</tr>
<tr>
<td>820</td>
<td>443</td>
<td>N-[4-{3-(3-Chloro-4-methoxy-phenyl)-thioureido]-phenyl}-4-methoxy-benzamide</td>
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<td>821</td>
<td>431</td>
<td>N-[4-{3-(3-Chloro-4-methoxy-phenyl)-thioureido]-phenyl}-4-methoxy-benzamide</td>
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<td>N-[4-{3-(3-Chloro-4-methoxy-phenyl)-thioureido]-phenyl}-3-fluoro-benzamide</td>
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<td>N-[4-{3-(3-Chloro-4-methoxy-phenyl)-thioureido]-phenyl}-4-fluoro-benzamide</td>
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<tr>
<td>824</td>
<td>437</td>
<td>Furan-2-carboxylic acid (4-{{3-(3,5-dichloro-4-methoxy-phenyl)-thioureido]-phenyl]-amide</td>
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</tbody>
</table>
825  511  4-[3-(5-Bromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-carbamic acid hexyl ester
826  481  Hexanoic acid 4-[3-(5-bromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-amide
827  505  N-[4-[3-(5-Bromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2-fluorobenzamide
828  477  Furan-2-carboxylic acid 4-[3-(5-bromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-amide
829  501  N-[4-[3-(5-Bromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-2-methylbenzamide
830  517  N-[4-[3-(5-Bromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl]-4-methoxybenzamide
831  395  N-[4-[3-(5-Chloro-2-ethoxy-4-methoxy-phenyl)-thioureido]-phenyl]-acetamide
832  395  N-[4-[3-(5-Chloro-4-ethoxy-2-methoxy-phenyl)-thioureido]-phenyl]-acetamide
833  423  N-[4-[3-(2-Butoxy-5-chloro-4-methoxy-phenyl)-thioureido]-phenyl]-acetamide
834  423  N-[4-[3-(4-Butoxy-5-chloro-2-methoxy-phenyl)-thioureido]-phenyl]-acetamide
835  457  N-[4-[3-(2-Benzylxy-5-chloro-4-methoxy-phenyl)-thioureido]-phenyl]-acetamide
836  457  N-[4-[3-(4-Benzylxy-5-chloro-2-methoxy-phenyl)-thioureido]-phenyl]-acetamide
837  421  [1,2,3]Thiadiazole-4-carboxylic acid 4-[3-(3-chloro-4-methoxy-phenyl)-thioureido]-phenyl]-amide
838  424  2-[(4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-5-methoxy-phenoxyl)-acetamide
839  367  N-[4-[3-(5-Chloro-2-hydroxy-4-methoxy-phenyl)-thioureido]-phenyl]-acetamide
840  367  N-[4-[3-(3-Chloro-4-methylsulfonyl-phenyl)-thioureido]-phenyl]-acetamide
841  447  N-[4-[3-Chloro-4-[methyl-(1-methyl-piperidin-4-yl)-amino]-phenyl]-thiourea]-phenyl]-acetamide
842  426  N-[4-[3-Chloro-4-(methyl-phenyl-amino)-phenyl]-thiourea]-phenyl]-acetamide
843  509  N-[4-[3-[4-[(1-Benzyl-pyrrolidin-3-yl)-methyl-amino]-3-chloro-phenyl]-thiourea]-phenyl]-acetamide
844  418  N-[4-[3-Chloro-4-(cyclopentyl-methyl-amino)-phenyl]-thiourea]-phenyl]-acetamide
845  433  N-[4-[3-Chloro-4-[methyl-(1-methyl-pyrrolidin-3-yl)-amino]-phenyl]-thiourea]-phenyl]-acetamide
846  419  Furan-2-carboxylic acid 4-[3-(3-chloro-4-methylsulfonyl-phenyl)-thiourea]-
phenyl)-amide

N-[(3-Chloro-4-methylsulfonyl-phenyl)-thioureido]-phenyl)-2-fluoro-benzamide

N-[(3-Chloro-4-methylsulfonyl-phenyl)-thioureido]-phenyl)-2,6-difluoro-benzamide

N-[(3-Chloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl)-2-fluoro-benzamide

N-[(3-Chloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl)-2-methyl-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-chloro-4-dimethylamino-phenyl)-thioureido]-phenyl)-amide

N-[(3-Chloro-4-dimethylamino-phenyl)-thioureido]-phenyl)-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[(3-chloro-4-[methyl-(1-methyl-piperidin-4-yl)-amino]-phenyl)-thioureido]-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[(3-chloro-4-[1-benzyl-pyrrolidin-3-yl]-methyl-amin0]-3-chloro-phenyl)-thioureido]-phenyl]-amide

N-[(3-Chloro-4-[methyl-(1-methyl-piperidin-4-yl)-amino]-phenyl)-thioureido]-phenyl)-2-fluoro-benzamide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[(3-Chloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl]-amide

N-[(3-Chloro-4-[1-Benzyl-pyrrolidin-3-yl]-methyl-amin0]-3-chloro-phenyl]-thioureido)-phenyl]-2-fluoro-benzamide

Furan-2-carboxylic acid [4-[3-(3-chloro-2,4-dimethoxy-phenyl)-thioureido]-3-trifluoromethyl-phenyl]-amide

2-Fluoro-N-[4-(3-phenyl-thioureido)-phenyl]-benzamide

Furan-2-carboxylic acid [4-(3-phenyl-thioureido)-phenyl]-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-(3-phenyl-thioureido)-phenyl]-amide

N-[(4-3-Chloro-4-(1-hydroxy-ethyl)-phenyl)-thioureido]-phenyl)-acetamide

[1,2,3]Thiadiazole-4-carboxylic acid [4-[(3-Chloro-4-(1-hydroxy-ethyl)-phenyl)-thioureido]-phenyl]-amide

N-[(4-3-Chloro-4-(2-hydroxy-ethyl)-phenyl)-thioureido]-phenyl)-acetamide

N-[(4-3-Chloro-4-(1-hydroxy-ethyl)-phenyl)-thioureido]-phenyl)-2-fluoro-benzamide

Furan-2-carboxylic acid [4-[(3-Chloro-4-(1-hydroxy-ethyl)-phenyl)-thioureido]-phenyl)-amide

[1,2,3]Thiadiazole-4-carboxylic acid [4-(3-3-amino-phenyl)-thioureido]-phenyl]-
amide
868 501 Furan-2-carboxylic acid [4-[3-(3-bromo-4-trifluoromethoxy-phenyl)-thioureido]-phenyl]-amide
869 423 N-[4-[3-(3-tert-Butyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
870 440 [1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(4-chloro-3,5-dichloro-phenyl)-thioureido]-phenyl]-amide
974 485 N-[4-[3-(1-Benzofuran-2-yl-ethyl)-thioureido]-phenyl]-2-trifluoromethyl-benzamide
975 412 N-[4-(Fluoro-phenyl)-4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-benzamide
976 446 Isoquinoline-1-carboxylic acid [4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide
977 468 Isoquinoline-1-carboxylic acid [4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl]-amide
978 506 Isoquinoline-1-carboxylic acid [4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl]-amide
979 453 Isoquinoline-1-carboxylic acid [4-[3-[1-(4-cyano-phenyl)-ethyl]-thioureido]-phenyl]-amide
980 435 Benzofuran-2-carboxylic acid [4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide
981 457 Benzofuran-2-carboxylic acid [4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl]-amide
982 495 Benzofuran-2-carboxylic acid [4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl]-amide
983 442 Benzofuran-2-carboxylic acid [4-[3-[1-(4-cyano-phenyl)-ethyl]-thioureido]-phenyl]-amide
984 446 Isoquinoline-3-carboxylic acid [4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide
985 468 Isoquinoline-3-carboxylic acid [4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl]-amide
986 453 Isoquinoline-3-carboxylic acid [4-[3-[1-(4-cyano-phenyl)-ethyl]-thioureido]-phenyl]-amide
987 506 Isoquinoline-3-carboxylic acid [4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl]-amide
988 446 Quinoline-3-carboxylic acid [4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide
989 446 Quinoline-4-carboxylic acid [4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide
990 446 Quinoline-6-carboxylic acid [4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-
amide

991 446 Quinoline-8-carboxylic acid (4-[[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-amide

992 462 N-[[4-[[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-2-trifluoromethyl-benzamide

993 419 2-Cyano-N-[[4-[[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl]-benzamide

994 473 N-[[4-[[3-Chloro-4-isobutoxy-phenyl]-thioureido]-phenyl]-2-fluoro-benzamide

995 414 2-Fluoro-N-[[4-[[3-fluoro-4-methoxy-phenyl]-thioureido]-phenyl]-benzamide

996 475 N-[[4-[[3-Chloro-4-(2-methoxy-ethoxy)-phenyl]-thioureido]-phenyl]-2-fluoro-benzamide

997 398 2-Fluoro-N-[[4-[[3-fluoro-4-methyl-phenyl]-thioureido]-phenyl]-benzamide

998 464 2-Fluoro-N-[[4-[[3-[4-methoxy-3-trifluoromethyl-phenyl]-thioureido]-phenyl]-benzamide

999 449 N-[[4-[[3-(2-Amino-5-trifluoromethyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

1000 459 N-[[4-[[1-(3-Chloro-4-methoxy-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide

1001 417 N-[[4-[[3-(5-Chloro-2-hydroxy-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

1002 435 N-[[4-[[3-(1-Benzofuran-2-yl-ethyl)-thioureido]-phenyl]-2-fluoro-benzamide

1003 448 2-Fluoro-N-[[4-[[3-(4-methyl-3-trifluoromethyl-phenyl)-thioureido]-phenyl]-benzamide

1004 473 (S)-N-[[4-[[3-[1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide

1005 473 N-[[4-[[3-[[1(R)]-1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide

1006 494 2-Fluoro-N-[[4-[[3-[[2-methoxy-4-(2,2,2-trifluoro-ethoxy)-phenyl]-thioureido]-phenyl]-benzamide

1007 399 N-[[4-[[3-(2-Amino-5-fluoro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

1008 502 N-[[4-[[3-[[1-(4-Dimethylsulfamoyl-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide

1009 542 2-Fluoro-N-[[4-[[3-[[1-[4-(piperidine-1-sulfonil-phenyl)-ethyl]-thioureido]-phenyl]-benzamide

1010 562 N-[[4-[[2,2-Bis-(2,2,2-trifluoro-ethoxy)-phenyl]-thioureido]-phenyl]-2-fluoro-benzamide

1011 409 2-Fluoro-N-[[4-[[3-[[1(S)]-1-p-tolyl-ethyl]-thioureido]-phenyl]-benzamide

1012 409 2-Fluoro-N-[[4-[[3-[[1(R)]-1-p-tolyl-ethyl]-thioureido]-phenyl]-benzamide

1013 394 2-Fluoro-N-[[4-[[3-[[1(S)]-1-phenyl-ethyl]-thioureido]-phenyl]-benzamide

1014 429 N-[[4-[[3-[[1(R)]-1-(4-Chloro-phenyl)-ethyl]-thioureido]-phenyl]-2-fluoro-benzamide
N-(4-[(3-[(1S)-1-(4-Chloro-phenyl)-ethyl]-thioureido]-phenyl)-2-fluoro-benzamide
2-Fluoro-N-(4-[(3-[(1R)-1-phenyl-ethyl]-thioureido]-phenyl)-benzamide
N-(4-[(3-1-(4-Cyano-phenyl)-ethyl]-thioureido]-phenyl)-2-methoxy-benzamide
N-(4-[(3-1-Benzofuran-2-yl-ethyl]-thioureido]-phenyl)-2-methoxy-benzamide
N-(4-[(3-1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl)-2-methoxy-benzamide
3-Cyano-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-benzamide
N-(4-[(3-1-(4-Fluoro-phenyl)-ethyl]-thioureido]-phenyl)-4-trifluoromethyl-benzamide
4-Cyano-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-benzamide
2-Fluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-2,3,5,6-tetramethyl-phenyl)-benzamide
N-(4-[(3-1-(4-Cyano-phenyl)-ethyl]-thioureido]-2,5-dimethoxy-phenyl)-2-fluoro-benzamide
2-Fluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-2,5-dimethoxy-phenyl)-benzamide
N-(3,5-Dichloro-4-[(3-5-chloro-2,4-dimethoxy-phenyl)-thioureido]-phenyl)-2-fluoro-benzamide
N-(3-Chloro-4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-2-fluoro-benzamide
2,3,4,5-Tetrafluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-3-methyl-phenyl)-benzamide
2,4,5-Trifluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-3-methyl-phenyl)-benzamide
2-Fluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-3-methyl-phenyl)-benzamide
2-Fluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-methoxy-5-methyl-phenyl)-benzamide
2-Fluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-3-methoxy-phenyl)-benzamide
N-(2,6-Dibromo-4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-2-fluoro-benzamide
2-Fluoro-N-(4-[(3-1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-trifluoromethyl-phenyl)-benzamide
N-(4-[(3-1-(4-Bromo-phenyl)-ethyl]-thioureido]-2-trifluoromethyl-phenyl)-2-fluoro-benzamide
N-(4-[(3-1-(4-Cyano-phenyl)-ethyl]-thioureido]-2-trifluoromethyl-phenyl)-2-fluoro-benzamide
1037  503  N-[4-{3-(1-Benzofuran-2-yl-ethyl)-thioureido}-2-trifluoromethyl-phenyl]-2-fluoro- benzamide
1038  447  N-(2-Chloro-4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1039  454  N-(2-Chloro-4-{3-[1-(4-cyano-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1040  437  N-(2-Cyano-4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1041  498  N-(4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido }-2-cyano-phenyl)-2-fluoro- benzamide
1042  445  N-(2-Cyano-4-{3-[1-(4-cyano-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1043  460  N-[4-{3-(1-Benzofuran-2-yl-ethyl)-thioureido }-2-cyano-phenyl]-2-fluoro- benzamide
1044  517  N-(2-Benzoyl-4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1045  427  2-Fluoro-N-(4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-2-methyl-phenyl)- benzamide
1046  487  N-(4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido }-2-methyl-phenyl)-2-fluoro- benzamide
1047  434  N-(4-{3-[1-(4-Cyano-phenyl)-ethyl]-thioureido }-2-methyl-phenyl)-2-fluoro- benzamide
1048  449  N-[4-{3-(1-Benzofuran-2-yl-ethyl)-thioureido }-2-methyl-phenyl]-2-fluoro- benzamide
1049  456  N-(2-Dimethylamino-4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-phenyl)-2- fluoro-benzamide
1050  526  N-(2-Benzoyloxy-4-{3-[1-(4-cyano-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1051  519  N-(2-Benzoyloxy-4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1052  603  N-[4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido }-2-(2-morpholin-4-yl-ethoxy)- phenyl]-2-fluoro-benzamide
1053  603  N-[4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido }-2-(2-morpholin-4-yl-ethoxy)- phenyl]-2-fluoro-benzamide
1054  542  2-Fluoro-N-[4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-2-(2-morpholin-4-yl- ethoxy)-phenyl]-benzamide
1055  485  N-(2-Butoxy-4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido }-phenyl)-2-fluoro- benzamide
1056  492  N-(2-Butoxy-4-(3-[1-(4-cyano-phenyl)-ethyl]-thioureido)-phenyl)-2-fluoro-benzamide
1057  589  N-[4-(3-[1-(4-Bromo-phenyl)-ethyl]-thioureido)-2-(2-diethylamino-ethoxy)-phenyl]-2-fluoro-benzamide
1058  528  N-(2-(2-Diethylamino-ethoxy)-4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenyl)-2-fluoro-benzamide
1059  589  N-[4-(3-[1-(4-Bromo-phenyl)-ethyl]-thioureido)-2-(2-diethylamino-ethoxy)-phenyl]-2-fluoro-benzamide
1060  457  N-(2-Ethoxy-4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenyl)-2-fluoro-benzamide
1061  464  N-[4-(3-[1-(4-Cyano-phenyl)-ethyl]-thioureido)-2-ethoxy-phenyl]-2-fluoro-benzamide
1062  468  2-Fluoro-N-[4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-2-(2-nitrilo-ethoxy)-phenyl]-benzamide
1063  475  N-[4-(3-[1-(4-Cyano-phenyl)-ethyl]-thioureido)-2-(2-nitrilo-ethoxy)-phenyl]-2-fluoro-benzamide
1064  443  2-Fluoro-N-(4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-2-methoxy-phenyl)-benzamide
1065  489  2-Fluoro-N-(5-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-biphenyl-2-yl)-benzamide
1066  514  Isoquinoline-1-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-trifluoromethyl-phenyl)-amide
1067  503  Benzo[f]uran-2-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-trifluoromethyl-phenyl)-amide
1068  514  Isoquinoline-3-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-trifluoromethyl-phenyl)-amide
1069  471  Isoquinoline-1-carboxylic acid (2-cyano-4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido)-phenyl)-amide
1070  460  Benzo[f]uran-2-carboxylic acid (2-cyano-4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide
1071  471  Isoquinoline-3-carboxylic acid (2-cyano-4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide
1072  460  Isoquinoline-1-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-methyl-phenyl)-amide
1073  449  Benzo[f]uran-2-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-methyl-phenyl)-amide
1074  460  Isoquinoline-3-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-2-methyl-phenyl)-amide
1075  396  Pyrazine-2-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-
amide

1076  401  Thiophene-2-carboxylic acid (4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide

1077  401  Thiophene-3-carboxylic acid (4-(3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide

1078  500  2-Isopropyl-thiazole-4-carboxylic acid {4-[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureido]-phenyl}-amide

1079  466  2-Isopropyl-thiazole-4-carboxylic acid {4-[3-(3,5-dichloro-phenyl)-thioureido]-phenyl}-amide

1080  466  2-Isopropyl-thiazole-4-carboxylic acid {4-[3-(3,4-dichloro-phenyl)-thioureido]-phenyl}-amide

1081  534  2-Isopropyl-thiazole-4-carboxylic acid {4-[3-(3,5-bis-trifluoromethyl-phenyl)-thioureido]-phenyl}-amide

1082  480  2-Butyl-thiazole-4-carboxylic acid {4-[3-(3,5-bis-dichloro-phenyl)-thioureido]-phenyl}-amide

1083  480  2-Butyl-thiazole-4-carboxylic acid {4-[3-(3,4-dichloro-phenyl)-thioureido]-phenyl}-amide

1084  480  2-Butyl-thiazole-4-carboxylic acid {4-[3-(3,5-dichloro-phenyl)-thioureido]-phenyl}-amide

1085  548  2-Butyl-thiazole-4-carboxylic acid {4-[3-(3,5-bis-trifluoromethyl-phenyl)-thioureido]-phenyl}-amide

1086  438  2-Methyl-thiazole-4-carboxylic acid {4-[3-(3,5-dichloro-phenyl)-thioureido]-phenyl}-amide

1087  438  2-Methyl-thiazole-4-carboxylic acid {4-[3-(3,4-dichloro-phenyl)-thioureido]-phenyl}-amide

1088  505  2-Methyl-thiazole-4-carboxylic acid {4-[3-(3,5-bis-trifluoromethyl-phenyl)-thioureido]-phenyl}-amide

1089  534  2-Phenyl-thiazole-4-carboxylic acid {4-[3-(4-chloro-3-trifluoromethyl-phenyl)-thioureido]-phenyl}-amide

1090  500  2-Phenyl-thiazole-4-carboxylic acid {4-[3-(3,5-dichloro-phenyl)-thioureido]-phenyl}-amide

1091  500  2-Phenyl-thiazole-4-carboxylic acid {4-[3-(3,4-dichloro-phenyl)-thioureido]-phenyl}-amide

1092  568  2-Phenyl-thiazole-4-carboxylic acid {4-[3-(3,5-bis-trifluoromethyl-phenyl)-thioureido]-phenyl}-amide

1093  401  2-Fluoro-N-(4-[3-(1-thiazol-2-yl-ethyl)-thioureido]-phenyl)-benzamide

1094  588  2-Fluoro-N-[4-[3-(1-toluene-4-sulfonyl)-1H-indol-2-yl]-ethyl]-thioureido]-phenyl]-benzamide
EXAMPLE 871 (METHOD 33)

[1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3,5-dichloro-phenyl)-thioureido]-phenyl)-amide

To a solution of 3,5-dichloroaniline (0.16 g) in tetrahydrofuran (20 mL) is added freshly prepared 1,1’-thiocarbonyl-di-1,2,4-triazole (0.20 g) and the mixture is stirred for approximately 30 minutes at room temperature. [1,2,3]-Thiadiazole-4-carboxylic acid (4-amino-phenyl) amide (0.22 g) is added to the reaction flask and the mixture is stirred for approximately 6 hours. The solvent is then removed by evaporation under reduced pressure and warm acetonitrile (3 mL) is added. After 15 hours the mixture is filtered and the collected precipitate is washed with acetonitrile then diethyl ether, and air dried to provide the desired product as a white powder. [M+H] 424.

Using the above procedure and appropriate starting materials the following compounds were prepared:

<table>
<thead>
<tr>
<th>EX. NO.</th>
<th>M+H</th>
<th>COMPOUND NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>872</td>
<td>465</td>
<td>N-[4-[3-(3,5-Dichloro-4-methoxy-phenyl)-thioureido]-phenyl]-3-fluorobenzamide</td>
</tr>
<tr>
<td>873</td>
<td>477</td>
<td>N-[4-[3-(3,5-Dichloro-4-methoxy-phenyl)-thioureido]-phenyl]-2-methoxybenzamide</td>
</tr>
<tr>
<td>874</td>
<td>465</td>
<td>N-[4-[3-(3,5-Dichloro-4-methoxy-phenyl)-thioureido]-phenyl]-2-fluorobenzamide</td>
</tr>
<tr>
<td>875</td>
<td>477</td>
<td>N-[4-[3-(3,5-Dichloro-4-methoxy-phenyl)-thioureido]-phenyl]-3-methoxy-</td>
</tr>
</tbody>
</table>
benzamide
N-\{4-[3-(3,5-Dichloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(3-Chloro-4-methoxy-5-methyl-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(2-Nitro-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(4-Nitro-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(3,5-Dichloro-4-methoxy-phenyl)-thioureido]-phenyl\}-4-methoxy-benzamide
N-\{4-[3-(2-Chloro-5-methoxy-phenyl)-thioureido]-phenyl\}-acetamide
2-[4-(4-Acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy)-acetamide
\{4-[3-(4-Acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy\}-acetic acid methyl ester
\{4-[3-(4-Acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy\}-acetic acid ethyl ester
N-\{4-[3-(3,5-Dichloro-4-phenoxy-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(3,5-Dichloro-4-(2-nitrito-ethoxy)-phenyl)-thioureido]-phenyl\}-acetamide
\{4-[3-(4-Acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy\}-acetic acid tert-butyl ester
\{1,2,3\}Thiadiazole-4-carboxylic acid \{4-[3-(3,5-dichloro-2-methoxy-4-methyl-phenyl)-thioureido]-phenyl\}-amide
N-\{4-[3-(3-Chloro-4-methyl-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(5-Chloro-2-methyl-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-[4-(4-Acetylamino-phenyl)-thioureido]-2-chloro-phenyl]disulfanyl\]-3-chloro-phenyl\}-thioureido]-phenyl\}-acetamide
N-\{4-[3-(3,5-Dichloro-4-methyl-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(3,5-Diodo-2,4-dimethoxy-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(3,5-Dibromo-2,4-dimethoxy-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(6-Methoxy-pyridin-3-yl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(2,6-Dimethoxy-pyridin-3-yl)-thioureido]-phenyl\}-acetamide
Acetic acid 2-[4-[3-(4-acetylamino-phenyl)-thioureido]-2,6-dichloro-phenoxy]-ethyl ester
4-[3-(4-Acetylamino-phenyl)-thioureido]-2-chloro-benzoic acid
N-\{4-[3-(3-Chloro-4-cyano-phenyl)-thioureido]-phenyl\}-acetamide
N-\{4-[3-(5-Chloro-2-(4-chloro-phenoxy)-4-pyrrol-1-yl-phenyl]-thioureido}-
phenyl)-acetamide

901  355  N-[4-[3-(3,4-Dichloro-phenyl)-thioureido]-phenyl]-acetamide
902  339  N-[4-[3-(3-Chloro-4-fluoro-phenyl)-thioureido]-phenyl]-acetamide
903  447  N-[4-[3-(3-Chloro-4-iodo-phenyl)-thioureido]-phenyl]-acetamide
904  400  N-[4-[3-(4-Bromo-3-chloro-phenyl)-thioureido]-phenyl]-acetamide
905  424  N-[4-[3-(4-[Bis-(2-hydroxy-ethyl)-amino]-3-chloro-phenyl)-thioureido]-phenyl]-acetamide
906  434  N-(4-[3-[3-Chloro-4-(hexyl-methyl-amino)-phenyl]-thioureido]-phenyl)-acetamide
907  406  N-(4-[3-Chloro-4-[(isobutyl-methyl-amino)-phenyl]-thioureido]-phenyl)-acetamide
908  389  N-[4-[3-(3-Chloro-4-trifluoromethyl-phenyl)-thioureido]-phenyl]-acetamide
909  441  Furan-2-carboxylic acid [4-[3-(3-chloro-4-trifluoromethyl-phenyl)-thioureido]-phenyl]-amide
910  459  [1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3-chloro-4-trifluoromethyl-phenyl)-thioureido]-phenyl]-amide
911  469  N-[4-[3-(3-Chloro-4-trifluoromethyl-phenyl)-thioureido]-phenyl]-2-fluorobenzamide
912  435  N-[4-[3-(3,4-Dichloro-phenyl)-thioureido]-phenyl]-2-fluorobenzamide
913  407  Furan-2-carboxylic acid [4-[3-(3,4-dichloro-phenyl)-thioureido]-phenyl]-amide
914  425  [1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3,4-dichloro-phenyl)-thioureido]-phenyl]-amide
915  480  N-[4-[3-(4-Bromo-3-chloro-phenyl)-thioureido]-phenyl]-2-fluorobenzamide
916  527  N-[4-[3-(3-Chloro-4-iodo-phenyl)-thioureido]-phenyl]-2-fluorobenzamide
917  452  Furan-2-carboxylic acid [4-[3-(4-bromo-3-chloro-phenyl)-thioureido]-phenyl]-amide
918  499  Furan-2-carboxylic acid [4-[3-(3-chloro-4-iodo-phenyl)-thioureido]-phenyl]-amide
919  391  Furan-2-carboxylic acid [4-[3-(3-chloro-4-fluoro-phenyl)-thioureido]-phenyl]-amide
920  470  [1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(4-bromo-3-chloro-phenyl)-thioureido]-phenyl]-amide
921  517  [1,2,3]Thiadiazole-4-carboxylic acid [4-[3-(3-chloro-4-iodo-phenyl)-thioureido]-phenyl]-amide
922  419  N-[4-[3-(3-Chloro-4-fluoro-phenyl)-thioureido]-phenyl]-2-fluorobenzamide
923  409  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-chloro-4-fluoro-phenyl)thioureido]-phenyl)-amide
924  388  N-[4-[3-(3-Chloro-4-isoxazol-5-yl-phenyl)-thioureido]-phenyl]-acetamide
925  387  N-[4-[3-Chloro-4-(1H-pyrazol-3-yl)-phenyl]-thioureido]-phenyl)-acetamide
926  355  N-[4-[3-(2,3-Dichloro-phenyl)-thioureido]-phenyl]-acetamide
927  435  N-[4-[3-(2,3-Dichloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
928  407  Furan-2-carboxylic acid (4-[3-(2,3-dichloro-phenyl)-thioureido]-phenyl)-amide
929  425  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(2,3-dichloro-phenyl)-thioureido]-phenyl)-amide
930  355  N-[4-[3-(2,5-Dichloro-phenyl)-thioureido]-phenyl]-acetamide
931  435  N-[4-[3-(2,5-Dichloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
932  407  Furan-2-carboxylic acid (4-[3-(2,5-dichloro-phenyl)-thioureido]-phenyl)-amide
933  355  N-[4-[3-(3,5-Dichloro-phenyl)-thioureido]-phenyl]-acetamide
934  435  N-[4-[3-(3,5-Dichloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
935  407  Furan-2-carboxylic acid (4-[3-(3,5-dichloro-phenyl)-thioureido]-phenyl)-amide
936  390  N-[4-[3-(3,4,5-Trichloro-phenyl)-thioureido]-phenyl]-acetamide
937  470  2-Fluoro-N-[4-[3-(3,4,5-trichloro-phenyl)-thioureido]-phenyl]-benzamide
938  442  Furan-2-carboxylic acid (4-[3-(3,4,5-trichloro-phenyl)-thioureido]-phenyl)-amide
939  460  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3,4,5-trichloro-phenyl)-thioureido]-phenyl)-amide
940  458  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-chloro-4-isoxazol-5-yl-phenyl)thioureido]-phenyl)-amide
941  457  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-chloro-4-(1H-pyrazol-3-yl)-phenyl)-thioureido]-phenyl)-amide
942  391  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(3-chloro-phenyl)-thioureido]-phenyl)-amide
943  373  Furan-2-carboxylic acid (4-[3-(3-chloro-phenyl)-thioureido]-phenyl)-amide
944  401  N-[4-[3-(3-Chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
945  373  Furan-2-carboxylic acid (4-[3-(4-chloro-phenyl)-thioureido]-phenyl)-amide
946  401  N-[4-[3-(4-Chloro-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide
947  391  [1,2,3]Thiadiazole-4-carboxylic acid (4-[3-(4-chloro-phenyl)-thioureido]-phenyl)-amide
N-[4-{3-(2-Chloro-phenyl)-thioureido}-phenyl]-2-fluoro-benzamide

3-(3-{4-[(Furan-2-carbonyl)-amino]-phenyl}-thioureido)-benzoic acid methyl ester

3-{3-[4-(2-Fluoro-benzoylamo)-phenyl]-thioureido}-benzoic acid methyl ester

3-(3-{4-[[1,2,3]Thiadiazole-4-carbonyl]-amino]-phenyl}-thioureido)-benzoic acid methyl ester

N-[4-[[3-(Aminocarbonyl)phenyl]amino(thioxomethyl)amino]phenyl]-2-fluoro-benzamide

Furan-2-carboxylic acid {4-[3-(2-chloro-phenyl)-thioureido]-phenyl}-amide

Furan-2-carboxylic acid {4-[3-(3-carbamoyl-phenyl)-thioureido]-phenyl}-amide

[1,2,3]Thiadiazole-4-carboxylic acid {4-[3-(3-carbamoyl-phenyl)-thioureido]-phenyl}-amide

Furan-2-carboxylic acid {4-[3-(2-chloro-phenyl)-thioureido]-phenyl}-amide

Furan-2-carboxylic acid {4-[3-(3-fluoro-phenyl)-thioureido]-phenyl}-amide

Furan-2-carboxylic acid {4-[3-(3-nitro-phenyl)-thioureido]-phenyl}-amide

2-Fluoro-N-[4-[3-(3-nitro-phenyl)-thioureido]-phenyl]-benzamide

Furan-2-carboxylic acid {4-[3-(3-trifluoromethoxy-phenyl)-thioureido]-phenyl}-amide

2-Fluoro-N-[4-[3-(3-trifluoromethoxy-phenyl)-thioureido]-phenyl]-benzamide

2-Fluoro-N-[4-[3-(3-fluoro-phenyl)-thioureido]-phenyl]-benzamide

3-{3-[4-(2-Fluoro-benzoylamo)-phenyl]-thioureido}-benzoic acid

3-{3-[4-[(Furan-2-carbonyl)-amino]-phenyl]-thioureido}-benzoic acid

N-[4-[3-(3-Acetyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

N-[4-[3-(3-Butylsulfamoyl-phenyl)-thioureido]-phenyl]-2-fluoro-benzamide

Furan-2-carboxylic acid {4-[3-(3-acetyl-phenyl)-thioureido]-phenyl}-amide

Furan-2-carboxylic acid {4-[3-{3-(2-hydroxy-ethanesulfonyl)-phenyl}-thioureido]-phenyl}-amide

2-Fluoro-N-(4-[3-[3-(2-hydroxy-ethanesulfonyl)-phenyl]-thioureido]-phenyl)-benzamide

Furan-2-carboxylic acid {4-[3-(3-butylsulfamoyl-phenyl)-thioureido]-phenyl}-amide
EXAMPLE 971 (METHOD 57)
1-(4-Fluoro-phenyl)-2-methyl-propan-1-ol

To a solution of 4-fluorobenzaldehyde (2.0 g) in diethyl ether (40 mL) at 0 °C is added dropwise isopropylmagnesium bromide (2.0 M, 9.6 mL) with stirring. After 1.5 hours the reaction is quenched with aqueous ammonium chloride and extracted with diethyl ether. The diethyl ether extracts are washed with saturated sodium chloride, dried over anhydrous magnesium sulfate, filtered and evaporated to give an oil. The oil is purified by silica gel chromatography eluting with 10% dichloromethane-hexanes to give the product, a yellow oil (1.76 g).

EXAMPLE 972 (METHOD 58)
1-(4-Fluoro-phenyl)-2-methyl-propan-1-one

To a solution of 1-(4-Fluoro-phenyl)-2-methyl-propan-1-ol (1.6 g) in acetone (10 mL) at 0 °C is added Jones reagent (20 mL) with stirring. After 10 minutes excess Jones reagent is destroyed by addition of isopropyl alcohol. Diethyl ether is added followed by anhydrous magnesium and the mixture is filtered and evaporated to give the product, a yellow oil (1.2 g).

EXAMPLE 973 (METHOD 59)
3-Dimethylamino-5-trifluoromethyl-benzonitrile

To a solution of 3-dimethylamino-5-trifluoromethylbromobenzene (7.3 g) in N,N-dimethylformamide (20 mL) is added cuprous cyanide (2.7 g) and the reaction heated at reflux for 12 hours. The reaction is diluted with water (40 mL) and dichloromethane is added. The dichloromethane fraction is washed with concentrated ammonium hydroxide, then water. The solution is dried over anhydrous magnesium sulfate, filtered and concentrated to give a yellow solid which is recrystallized from hexanes to give a yellow solid, (4.7 g).

The foregoing compounds were tested for activity as herpes virus inhibitors.
HUMAN CYTOMEGALOVIRUS

Yield assay. Monolayer cultures of human foreskin fibroblasts are infected with HCMV wild-type, typically at a multiplicity of infection equal to 0.2, in the presence of inhibitor compound (varying concentrations). At three days post-infection, total virus produced in these cultures (i.e. virus yield) is assessed by harvesting and titrating the virus in 12-well plates of cultured human foreskin fibroblasts (done in the absence of inhibitor). Plaques are quantified at 2 weeks post-infection. An inhibitor of HCMV is identified by the reduction in titer of virus yield in the presence, compared to the titer in the absence of compound. In this assay, the relative anti-HCMV activity of an inhibitor is typically determined by calculating the IC50 or IC90 value, that is, the amount of compound required to reduce the virus yield by 50% or 90%, respectively. Table I describes IC50 data for compounds tested against HCMV.

Microtiter plate assay. Ninety-six well plate cultures of human foreskin fibroblasts are infected in the presence of inhibitor compound with a HCMV recombinant mutant virus whose genome contains the prokaryotic beta-glucuronidase gene (Jefferson, R. A., S. M. Burgess, and D. Hirsch. 1986. Beta-glucuronidase from Escherichia coli as a gene fusion marker. Proc. Natl. Acad. Sci. USA 83:8447-8451) whose expression is controlled by a viral promoter. An example of such a virus is RV145 (Jones, T. R., V. P. Muzithras, and Y. Gluzman. 1991. Replacement mutagenesis of the human cytomegalovirus genome: US10 and US11 gene products are nonessential. J. Virol. 65:5860-5872). Since it is under the control of a viral promoter, beta-glucuronidase expression is an indirect indicator of growth and replication of HCMV in this assay. At 96 hours post-infection, the infected cell lysates are prepared (using 50mM sodium phosphate [pH7.0] containing 0.1% Triton X-100 and 0.1% sarkosyl) and assayed for beta-glucuronidase activity using a substrate for the enzyme which when cleaved yields either a product which can be measured colorimetrically in a spectrophotometer or fluorescently in a microfluorimeter. Examples of such substrates are p-nitrophenyl-beta-D-glucuronide and methylumbelliferylglucuronide, respectively. The presence of an antiviral
compound is indicated by the reduced expression of the HCMV genome resident beta-glucuronidase gene, compared to the absence of inhibitor. Thus, the generation of the chromophore or fluorophore product in this assay is correspondingly reduced. Data from this assay generated using varying amounts of inhibitor compound is also used to estimate the IC₅₀ of an inhibitor compound.

**HSV antiviral (ELISA) assay**

Vero cells (ATCC #CCL-81) are plated on 96-well tissue culture plates at 3.5x10⁴ cells per 100μl tissue culture DMEM (Dulbecco’s modified Eagle media) supplemented with 2% fetal bovine serum (FBS) in each well. After overnight incubation @ 37°C (in 5% CO₂) and 30 minutes prior to infection with HSV-1 (multiplicity of infection equal to 0.006), cells are either untreated, or treated with test compound (multiple concentrations) or reference standard drug control. After approximately 24 hours post-infection incubation @ 37°C (in 5% CO₂), cells are fixed for ELISA assay. The primary antibody is murine anti-HSV glycoprotein D monoclonal primary antibody and the secondary antibody is goat anti-mouse IgG linked to β-galactosidase. Thus the extent of viral replication is determined by assessing β-galactosidase activity by quantifying the generation of the 4-methyl umbelliferone fluorescent cleavage product after addition of the methyl umbelliferyl-β-D-galactoside (Sigma #M1633) substrate on a microfluorimeter (365nm for excitation and 450nm for emission). Antiviral activity (IC₅₀) of the test compound is determined by comparing the fluorescence obtained in absence of compound to that obtained in the presence of compound. Data is shown in Table I.

**VZV antiviral (ELISA) assay**

For the generation of stock VZV to be used in the assay, VZV strain Ellen (ATCC #VR-1367) is used to infect human foreskin fibroblast (HFF) cells at low multiplicity (less than 0.1) and incubated overnight at 37°C in 5% CO₂. After the overnight incubation, the mixture of uninfected and VZV-infected HFF infected cells are then harvested and added to each well of 96-well plates (3.5x10⁴ cells in 100 μl DMEM
supplemented with 2% FBS) which contain test compound or the reference standard
drug control (in 100μl DMEM supplemented with 2% FBS per well). These cells are
incubated for three days at 37°C in 5% CO₂, then fixed for ELISA assay. The
primary antibody is murine anti-VZV glycoprotein II monoclonal antibody (Applied
Biosystems, Inc. #13-145-100) and the secondary antibody is goat anti-mouse IgG
linked to β-galactosidase. Thus the extent of viral replication is determined by
assessing β-galactosidase activity by quantifying the generation of the 4-methyl
umbelliferone fluorescent cleavage product after addition of the methyl umbelliferyl-
β-D-galactoside (Sigma #M1633) substrate on a microfluorimeter (365nm for
excitation and 450nm for emission). Antiviral activity (IC₅₀) of the test compound is
determined by comparing the fluorescence obtained in absence of compound to that
obtained in the presence of compound. Data is shown in Table I.

Table I

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<th>IC₅₀ (ug/ml) HSV</th>
<th>% inhibition 10 ug/ml VZV</th>
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Thus, compounds of the present invention are potent inhibitors of the growth and replication of the herpes viruses, including HCMV, VZV and HSV, effectively inhibiting viral yield.

In accordance with the present invention, compounds of the present invention may be administered to a patient suffering from a herpes virus, including HCMV, VZV and HSV in an amount effective to inhibit the virus. Compounds of the present
invention are thus useful to ameliorate or eliminate the symptoms of the herpes virus infections in mammals including, but not limited to humans.

Compounds of the invention may be administered to a patient either neat or with a conventional pharmaceutical carrier.

Applicable solid carriers can include one or more substances which may also act as flavoring agents, lubricants, solubilizers, suspending agents, fillers, glidants, compression aids, binders or tablet-disintegrating agents or an encapsulating material. In powders, the carrier is a finely divided solid which is in admixture with the finely divided active ingredient. In tablets, the active ingredient is mixed with a carrier having the necessary compression properties in suitable proportions and compacted in the shape and size desired. The powders and tablets preferably contain up to 99% of the active ingredient. Suitable solid carriers include, for example, calcium phosphate, magnesium stearate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, methyl cellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidone, low melting waxes and ion exchange resins.

Liquid carriers may be used in preparing solutions, suspensions, emulsions, syrups and elixirs. The active ingredient of this invention can be dissolved or suspended in a pharmaceutically acceptable liquid carrier such as water, an organic solvent, a mixture of both or pharmaceutically acceptable oils or fats. The liquid carrier can contain other suitable pharmaceutical additives such as solubilizers, emulsifiers, buffers, preservatives, sweeteners, flavoring agents, suspending agents, thickening agents, colors, viscosity regulators, stabilizers or osmo-regulators. Suitable examples of liquid carriers for oral and parenteral administration include water (particularly containing additives as above e.g. cellulose derivatives, preferably sodium carboxymethyl cellulose solution), alcohols (including monohydric alcohols and polyhydric alcohols e.g. glycols) and their derivatives, and oils (e.g. fractionated coconut oil and arachis oil). For parenteral administration the carrier can also be an oily ester such as ethyl oleate and isopropyl myristate. Sterile liquid carriers are used in sterile liquid form compositions for parenteral administration.

Liquid pharmaceutical compositions which are sterile solutions or suspensions can be utilized by, for example, intramuscular, intraperitoneal or
subcutaneous injection. Sterile solutions can also be administered intravenously. Oral administration may be either liquid or solid composition form.

Preferably the pharmaceutical composition is in unit dosage form, e.g. as tablets or capsules. In such form, the composition is sub-divided in unit dose containing appropriate quantities of the active ingredient; the unit dosage forms can be packaged compositions, for example packeted powders, vials, ampoules, prefilled syringes or sachets containing liquids. The unit dosage form can be, for example, a capsule or tablet itself, or it can be the appropriate number of any such compositions in package form.

The therapeutically effective dosage to be used in the treatment of herpes virus infection must be subjectively determined by the attending physician. The variables involved include the the condition, age and weight of the patient. The novel method of the invention for treating herpes virus infection comprises administering to a subject, including humans, an effective amount of at least one compound of Formula 1 or a non-toxic, pharmaceutically acceptable salt thereof. The compounds may be administered orally, rectally, parenterally or topically to the skin and mucosa. The usual daily dose is depending on the specific compound, method of treatment and condition of the patient. The usual daily dose is 0.01 - 1000 mg/Kg for oral application, preferably 0.5 - 500 mg/Kg, and 0.1 - 100 mg/Kg for parenteral application, preferably 0.5 - 50 mg/Kg.
What is claimed:

5 1. A compound having the formula:

![Chemical Structure Image]

I

10 wherein

R₁-R₆ are independently selected from hydrogen, alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 carbon members, aryl, heteroaryl, halogen, -CN, -NO₂, -CO₂R, -COR, -OR, -SR, -SOR, -SO₂R, -CONR₂, -NR₂,N(R,R'), -N(R,R') or W-Y-(CH₃)ₙ-Z provided that at least one of R₁-R₆ is not hydrogen; or R₂ and R₃, or R₄ and R₅, taken together form a 3 to 7 membered heterocycloalkyl or 3 to 7 membered heteroaryl;

20 R₆ and R₇ are independently hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, or aryl;

R₇ is hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 members, aryl or heteroaryl, or

25 R₇ and R₈, taken together may form a 3 to 7 membered heterocycloalkyl;

W is O, NR₈, or is absent;

Y is -(CO)ₖ- or -(CO₂)ₖ-, or is absent;

Z is alkyl of 1 to 4 carbon atoms, -CN, -CO₂R, COR, -CONR₂, -OR, -SR, -SOR, -SO₂R, SR₆N(R₇R₈),

-OR, -SR, -SOR, -SO₂R, SR₆N(R₇R₈),

30 -N(R₉R₈) or phenyl;
G is aryl or fused bicyclic heteroaryl;
X is a bond, -NH, alkyl of 1 to 6 carbon atoms, alkenyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, thioalkyl of 1 to 6 carbon atoms, alkylamino of 1 to 6 carbon atoms, or (CH)J;
J is alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, phenyl or benzyl; and
n is an integer from 1 to 6;
or a pharmaceutical salt thereof.

2. A compound of Claim 1 wherein R₁ through R₇ are independently, alkyl of 1 to 6 carbon atoms, halogen, perhaloalkyl of 1 to 6 carbon atoms, OR₅ or N(R₆R₇).

3. A compound of Claim 1 wherein R₄ is halogen, trifluoromethyl or cyano.

4. A compound of Claim 1 wherein G is substituted by one or more groups selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 carbon members, aryl, heteroaryl, halogen, -CN, -NO₂, -CO₂R₆, -COR₆, -OR₆, -SR₆, -SOR₆, -SO₂R₆, -CONR,R₆, -NR₆N(R₆R₇), -N(R₆R₇) or W-Y-(CH)ₙ-Z.

5. A compound of Claim 1 wherein G is phenyl.

6. A compound of Claim 5 wherein G is substituted phenyl.

7. A compound of Claim 1 wherein G is substituted by one or more groups selected from alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, halogen, -SR₆, -SOR₆, N(R₆R₇) or -W-Y-(CH)ₙn-Z.

8. A compound of Claim 1 wherein G is 2-fluorophenyl.

9. A compound of Claim 1 wherein G is a fused bicyclic heteroaryl.
10. A compound of Claim 9 wherein G is quinoline, isoquinoline or benzofuran.

11. A compound of Claim 1 wherein X is a bond.

12. A compound of Claim 1 wherein X is straight chain alkyl.

13. A compound of Claim 1 wherein X is straight chain alkyl of 1 to 4 carbon atoms.

14. A compound of Claim 1 wherein X is CH(3).

15. A compound of Claim 1 wherein J is methyl.

16. A compound of Claim 1 selected from N-[4-[3-(1-Benzofuran-2-yl-ethyl)-thioureido]-phenyl]-2-trifluoromethyl-benzamide,
N-(4-Fluoro-phenyl)-4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-benzamide,
Isoquinoline-1-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Isoquinoline-1-carboxylic acid [4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl]-amide,
Isoquinoline-1-carboxylic acid (4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Isoquinoline-1-carboxylic acid (4-[3-[1-(4-cyano-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Benzofuran-2-carboxylic acid (4-[3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Benzofuran-2-carboxylic acid (4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl)-amide,
Benzofuran-2-carboxylic acid (4-[3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl)-amide,
Benzofuran-2-carboxylic acid (4-{3-[1-(4-cyano-phenyl)-ethyl]-thioureido]-phenyl}-amide,
Isoquinoline-3-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-amide,
5 Isoquinoline-3-carboxylic acid (4-[3-(1-benzofuran-2-yl-ethyl)-thioureido]-phenyl}-amide,
Isoquinoline-3-carboxylic acid (4-{3-[1-(4-cyano-phenyl)-ethyl]-thioureido]-phenyl}-amide,
Isoquinoline-3-carboxylic acid (4-{3-[1-(4-bromo-phenyl)-ethyl]-thioureido]-phenyl}-amide,
10 Quinoline-3-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-amide,
Quinoline-4-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-amide,
15 Quinoline-6-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-amide,
Quinoline-8-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-amide,
N-(4-{3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido]-phenyl}-2-trifluoromethyl-benzamide,
2-Cyano-N-(4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido]-phenyl}-benzamide,
N-(4-[3-(3-Chloro-4-isobutoxy-phenyl)-thioureido]-phenyl}-2-fluoro-benzamide,
25 2-Fluoro-N-{4-[3-(3-fluoro-4-methoxy-phenyl)-thioureido]-phenyl}-benzamide,
N-(4-{3-[3-Chloro-4-(2-methoxy-ethoxy)-phenyl]-thioureido]-phenyl}-2-fluoro-benzamide,
2-Fluoro-N-{4-[3-(3-fluoro-4-methyl-phenyl)-thioureido]-phenyl}-benzamide,
30 2-Fluoro-N-{4-[3-(4-methoxy-3-trifluoromethyl-phenyl)-thioureido]-phenyl}-benzamide,
N-(4-[3-(2-Amino-5-trifluoromethyl-phenyl)-thioureido]-phenyl}-2-fluoro-benzamide,
N-(4-{3-[1-(3-Chloro-4-methoxy-phenyl)-ethyl]-thioureido]-phenyl})-2-fluoro-benzamide,
N-(4-{2-(5-Chloro-2-hydroxy-phenyl)-thioureido]-phenyl})-2-fluoro-benzamide,
N-(4-{3-(1-Benzofuran-2-yl-ethyl)-thioureido]-phenyl})-2-fluoro-benzamide,
2-Fluoro-N-(4-{3-(4-methyl-3-trifluoromethyl-phenyl)-thioureido]-phenyl})-benzamide,
(S)-N-(4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl})-2-fluoro-benzamide,
N-(4-{3-[(1R)-1-(4-Bromo-phenyl)-ethyl]-thioureido]-phenyl})-2-fluoro-benzamide,
2-Fluoro-N-(4-{3-[2-methoxy-4-(2,2,2-trifluoro-ethoxy)-phenyl]-thioureido]-phenyl})-benzamide,
N-(4-{3-(2-Amino-5-fluoro-phenyl)-thioureido]-phenyl})-2-fluoro-benzamide,
N-(4-{3-[1-(4-Dimethylsulfamoyl-phenyl)-ethyl]-thioureido]-phenyl})-2-fluoro-benzamide,
2-Fluoro-N-(4-{3-[1-[4-(piperidine-1-sulfonyl)-phenyl]-ethyl]-thioureido]-phenyl})-benzamide,
N-(4-{3-[2,4-Bis-(2,2,2-trifluoro-ethoxy)-phenyl]-thioureido]-phenyl})-2-fluoro-benzamide,
2-Fluoro-N-(4-{3-[(1S)-1-p-tolyl-ethyl]-thioureido]-phenyl})-benzamide,
2-Fluoro-N-(4-{3-[(1R)-1-p-tolyl-ethyl]-thioureido]-phenyl})-benzamide,
2-Fluoro-N-(4-{3-[(1S)-1-phenyl-ethyl]-thioureido]-phenyl})-benzamide,
N-(4-{3-[(1R)-1-(4-Chloro-phenyl)-ethyl]-thioureido]-phenyl})-2-fluoro-benzamide,
N-(4-{3-(1S)-1-(4-Chloro-phenyl)-ethyl]-thioureido]-phenyl})-2-fluoro-benzamide,
2-Fluoro-N-{4-3-[(1R)-1-phenyl-ethyl]-thioureido]-phenyl})-benzamide,
N-(4-{3-[1-(4-Cyano-phenyl)-ethyl]-thioureido]-phenyl})-2-methoxy-benzamide,
N-(4-{3-(1-Benzofuran-2-yl-ethyl)-thioureido]-phenyl})-2-methoxy-benzamide,
N-(4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-2-methoxy-benzamide,
3-Cyano-N-(4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-benzamide,
N-(4-{3-[1-(4-Fluoro-phenyl)-ethyl]-thioureido}-phenyl)-4-trifluoromethyl-benzamide,
4-Cyano-N-(4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-benzamide,
N-(4-{3-[1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-2-fluoro-benzamide,
N-(4-{3-[(1S)-1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-4-fluoro-benzamide,
N-(4-{3-[(1S)-1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-2-methoxy-benzamide,
N-(4-{3-[(1R)-1-(4-Bromo-phenyl)-ethyl]-thioureido}-phenyl)-2-methoxy-benzamide,
2-fluoro-N-(4-{[(1-2-fluoro-4-(trifluoromethyl)phenyl)ethyl]amino}phenyl)benzamide,
Isoquinoline-1-carboxylic acid (4-{3-[(1S)-1-(4-bromo-phenyl)-ethyl]-thioureido}-phenyl)-amide,
Isoquinoline-3-carboxylic acid (4-{3-[(1S)-1-(4-bromo-phenyl)-ethyl]-thioureido}-phenyl)-amide,
Isoquinoline-1-carboxylic acid (4-{3-[(1S)-1-(4-chloro-phenyl)-ethyl]-thioureido}-phenyl)-amide,
Isoquinoline-1-carboxylic acid (4-{3-[1-(4-fluoro-phenyl)-ethyl]-thioureido}-phenyl)-amide, and
N-{4-[[{(1S)-1-(4-cyanophenyl)ethyl]amino}carbothiyl]amino}phenyl}-1-nophenyl)ethyl]amino)carbothiyl]amino}phenyl)-1-isoquinolinecarboxamide,
and pharmaceutical salts thereof.
17. A pharmaceutical composition comprising a compound of the formula:

![Chemical structure](image)

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wherein

R₁-R₅ are independently selected from hydrogen, alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 carbon members, aryl, heteroaryl, halogen, -CN, -NO₂, -CO₂R₆, -COR₆, -OR₆, -SR₆, -SOR₆, -SO₂R₆, -CONR₂R₆, -NR₆N(R₇R₈), -N(R₉R₆) or W-Y-(CH₂)ₙ-Z provided that at least one of R₁-R₅ is not hydrogen; or R₂ and R₃ or R₆ and R₇, taken together form a 3 to 7 membered heterocycloalkyl or 3 to 7 membered heteroaryl;

R₆ and R₇ are independently hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, or aryl;

R₈ is hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 members, aryl or heteroaryl, or

R₉ and R₁₀, taken together may form a 3 to 7 membered heterocycloalkyl;

W is O, NR₆, or is absent;

Y is -(CO)- or -(CO₂)-, or is absent;

Z is alkyl of 1 to 4 carbon atoms, -CN, -CO₂R₆, COR₆, -CONR₂R₆, -OCOR₆, -NR₆COR₆, -OCONR₆, -OR₆, -SR₆, -SOR₆, -SO₂R₆, SR₆N(R₇R₈), -

N(R₉R₁₀) or phenyl;

G is aryl or fused bicyclic heteroaryl; and

X is a bond, -NH, alkyl of 1 to 6 carbon atoms, alkenyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, thioalkyl of 1 to 6 carbon atoms, alkylamino of 1 to 6 carbon atoms, or (CH)J;
J is alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, phenyl or benzyl; and

n is an integer from 1 to 6;

or a pharmaceutical salt thereof, and a pharmaceutically acceptable carrier or diluent.

18. A method of inhibiting the replication of a herpes virus comprising contacting a compound of the formula:

\[
\text{R}_1 - \text{R}_5
\]

wherein

\(\text{R}_1 - \text{R}_5\) are independently selected from hydrogen, alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 carbon members, aryl, heteroaryl, halogen, -CN, -NO₂, -CO₂R₆, -COR₆, -OR₆, -SR₆, -SOR₆, -SO₂R₆, -CONR₂R₆, -NR₂N(R₃R₄), -N(R₅R₆), or W-Y-(CH₂)ₙ-Z provided that at least one of \(\text{R}_1 - \text{R}_5\) is not hydrogen; or \(\text{R}_2\) and \(\text{R}_3\) or \(\text{R}_4\) and \(\text{R}_5\), taken together form a 3 to 7 membered heterocycloalkyl or 3 to 7 membered heteroaryl;

\(\text{R}_6\) and \(\text{R}_7\) are independently hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, or aryl;

\(\text{R}_8\) is hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 members, aryl or heteroaryl, or

\(\text{R}_9\) and \(\text{R}_{10}\), taken together may form a 3 to 7 membered heterocycloalkyl;

\(\text{W}\) is O, NR₆, or is absent;

\(\text{Y}\) is -(CO)- or -(CO₂)-, or is absent;
Z is alkyl of 1 to 4 carbon atoms, -CN, -CO₂R₆, COR₆, -CONR₆R₇, -OCOR₆,
-NR₆COR₆, -OCONR₆R₇, -OR₆, -SR₆, -SOR₆, -SO₂R₆, SR₆NR₆R₇R₈,
-N(R₆R₇) or phenyl;
G is aryl or fused bicyclic heteroaryl; and
X is a bond, -NH, alkyl of 1 to 6 carbon atoms, alkenyl of 1 to 6 carbon
atoms, alkoxy of 1 to 6 carbon atoms, thioalkyl of 1 to 6 carbon
atoms, alkylamino of 1 to 6 carbon atoms, or (CH)J;
J is alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, phenyl or
benzyl; and
n is an integer from 1 to 6;
or a pharmaceutical salt thereof, with a herpes virus.

19. The method of Claim 18 wherein the herpes virus is human cytomegalovirus.

20. The method of Claim 18 wherein the herpes virus is varicella zoster virus.

21. The method of Claim 20 wherein the compound is substantially pure (S)
optical isomer.

22. The method of Claim 18 wherein the herpes virus is herpes simplex virus.

23. A method of treating a patient suffering from a herpes virus infection
comprising administering to the patient a therapeutically effective amount of a
compound having the formula:

\[
\begin{align*}
R_1 & \quad \text{are independently selected from hydrogen, alkyl of 1 to 6 carbon atoms,} \\
R_2 \quad \text{alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms,} \\
R_3 \quad \text{perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon} \\
R_4 \quad \text{atoms, heterocycloalkyl of 3 to 10 carbon members, aryl, heteroaryl,} \\
R_5 \quad \text{and (CH)J; and} \\
G \quad \text{n is an integer from 1 to 6; or a pharmaceutical salt thereof, with a herpes virus.}
\end{align*}
\]
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halogen, -CN, -NO₂, -CO₂R₆, -COR₆, -OR₆, -S₆R₆, -SOR₆, -SO₂R₆,
-CONR₆R₆, -NR₆N(R₆R₆), -N(R₆R₆) or W-Y-(CH₂)ₙ-Z provided that at least one of R₁, R₃ is not hydrogen; or R₂ and R₅ or R₅ and R₇, taken together form a 3 to 7 membered heterocycloalkyl or 3 to 7 membered heteroaryl;

R₆ and R₇ are independently hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, or aryl;

R₈ is hydrogen, alkyl of 1 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 10 carbon atoms, heterocycloalkyl of 3 to 10 members, aryl or heteroaryl, or

R₉ and R₁₀, taken together may form a 3 to 7 membered heterocycloalkyl;

W is O, NR₆, or is absent;

Y is -(CO)- or -(CO₂)-, or is absent;

Z is alkyl of 1 to 4 carbon atoms, -CN, -CO₂R₆, COR₆, -CONR₆R₆, -OCOR₆,
-NR₆COR₆, -OCONR₆, -OR₆, -SR₆, -SOR₆, -SO₂R₆, SR₆N(R₇R₈),
-N(R₆R₈) or phenyl;

G is aryl or fused bicyclic heteroaryl; and

X is a bond, -NH, alkyl of 1 to 6 carbon atoms, alkenyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, thioalkyl of 1 to 6 carbon atoms, alkenyl of 1 to 6 carbon atoms, or (CH)J;

J is alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, phenyl or benzyl; and

n is an integer from 1 to 6; or a pharmaceutical salt thereof.

24. The method of Claim 23 wherein the herpes virus is human cytomegalovirus.

25. The method of Claim 23 wherein the herpes virus is varicella zoster virus.

26. The method of Claim 25 wherein the compound is substantially pure (S) isomer.

27. The method of Claim 23 wherein the herpes virus is herpes simplex virus.