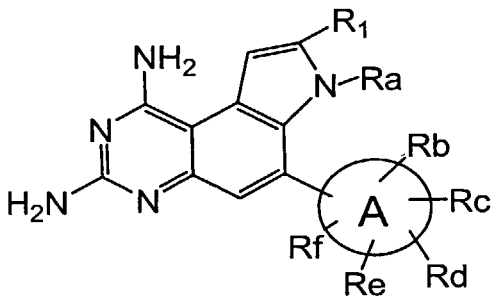
Diaminopyrroloquinazolines Compounds as Protein Tyrosine Phosphatase Inhibitors

The invention relates to diaminopyrroloquinazolines compounds useful for inhibiting protein tyrosine phosphatases, particularly PTP1B, and are useful for lowering blood glucose concentrations in mammals. These compounds are characterised by formula (I)



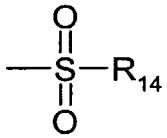
(I)

or pharmaceutically acceptable salts thereof, wherein

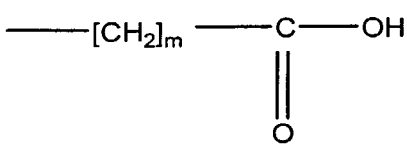
A is a 5- or 6-membered unsaturated or saturated hydrocarbon ring or a 5- or 6-membered unsaturated or saturated ring that contains at least one heteroatom selected from S, N or O,

R1 is hydrogen or lower alkyl,

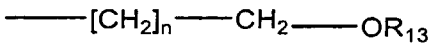
Ra is hydrogen, lower alkyl,



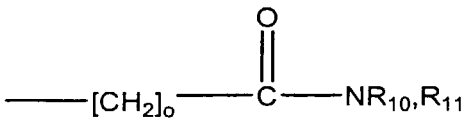
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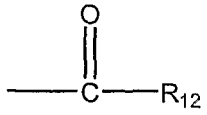


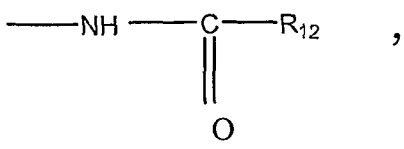
, or



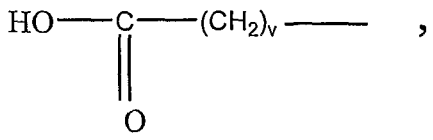
;

Rb, Rc, Rd, Re and Rf are each independently selected from the group consisting of hydrogen, lower alkyl, halogen, amino, lower alkenyl, hydroxy, alkoxy, hydroxy lower alkyl, alkylsulfanyl, perfluoroloweralkyl, perfluoroloweralkoxy, aryl, nitro, lower alkanoyl, $-NR_5R_6$, R_7S-, alkanoyl, alkanoylamino, carboxy, aryloxy, carboxy alkyl, substituted alkyl, or





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or two of Rb, Rc, Rd, Re and Rf, when present on adjacent carbon atoms on the phenyl ring can be taken together to form a lower alkylenedioxy bridge or a ring system fused to the phenyl ring, said ring system containing one or two rings fused to the phenyl ring with at least one of said rings in said system being either an aromatic or heteroaromatic ring and the remainder ring in the system, if any, being a cycloalkyl or heterocycloalkyl ring;

R_5, R_6 and R_{14} independently are hydrogen or lower alkyl;

R_7 is lower alkyl;

R_{13} is hydrogen, lower alkyl, benzyl or phenyl;

R_{10}, R_{11} and R_{12} are independently hydrogen or lower alkyl; and

m, n, o and v are independent integers from 0 to 4.

Protein tyrosine phosphatases (PTPases) are key enzymes in processes that regulate cell growth and differentiation. The inhibition of these enzymes can play

a role in the modulation of multiple signaling pathways in which tyrosine phosphorylation dephosphorylation plays a role. PTP1B is a particular protein tyrosine phosphatases that is often used as a prototypical member of that class of enzymes.

PTPase inhibitors are recognized as potential therapeutic agents for the treatment of diabetes. See, e.g. Moeller et al., **3**(5):527-40, Current Opinion in Drug Discovery and Development, 2000; or Zhang, Zhong-Yin, **5**:416-23, Current Opinion in Chemical Biology, 2001. The utility of PTPase inhibitors as therapeutic agents has been a topic of discussion in several review articles including, for example, Expert *Opin Investig Drugs*, **12(2)**:223-33, Feb. 2003.

Unless otherwise indicated the following definitions are set forth to illustrate and define the meaning and scope of the various terms used to describe the invention herein.

In this specification the term "lower" is used to mean a group consisting of one to six, preferably of one to four carbon atom(s).

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

The term "alkyl", alone or in combination with other groups, refers to a branched or straight-chain monovalent saturated aliphatic hydrocarbon radical of one to twenty carbon atoms, preferably one to sixteen carbon atoms, more preferably one to ten carbon atoms. Alkyl groups can be substituted as defined below for lower alkyl. Lower alkyl groups as defined below are preferred alkyl groups.

As used in the specification, the term "lower alkyl", alone or in combination, means a straight-chain or branched-chain alkyl group containing a maximum of six carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl,

isobutyl, tert-butyl, n-pentyl, n-hexyl and the like. Lower alkyl groups may be unsubstituted or substituted by one or more groups selected independently from cycloalkyl, nitro, aryloxy, aryl, hydroxy, halogen, cyano, lower alkoxy, lower alkanoyl, lower alkylthio, lower alkyl sulfinyl, lower alkyl sulfonyl and substituted amino. An example of substituted lower alkyl groups includes trifluoromethyl.

The term "perfluoroloweralkyl" means any lower alkyl group wherein all the hydrogens of the lower alkyl group are substituted or replaced by fluorine. Among the prefered perfluoroloweralkyl groups are trifluoromethyl, pentafluroethyl, heptafluoropropyl, etc.

The term "perfluoroloweralkoxy" means any lower alkoxy group wherein all the hydrogens of the lower alkoxy group are substituted or replaced by fluorine. Among the prefered perfluoroloweralkyl groups are trifluoromethoxy, pentafluroethoxy, heptafluoropropoxy, etc.

The term "alkanoyl" refers to a group R-C(O)-, wherein R is hydrogen or alkyl and alkyl is as defined above. The term "lower alkanoyl" refers to a R-C(O)-, wherein R is hydrogen or lower alkyl and lower alkyl is as defined above. Examples are formyl, acetyl, etc. Lower alkanoyl groups are preferred alkanoyl groups.

The term "alkenyl", alone or in combination with other groups, stands for a straight-chain or branched hydrocarbon residue comprising an olefinic bond and 2 to 20, preferably 2 to 16 carbon atoms, more preferrably 2 to 10 carbon atoms. Lower-alkenyl groups as described below also are preferred alkenyl groups. The term "lower-alkenyl" refers to a straight-chain or branched hydrocarbon residue comprising an olefinic bond and 2 to 6, preferably 2 to 4 carbon atoms, such as e.g. 2-propenyl.

The term "cycloalkyl" means an unsubstituted or substituted monocylic 3- to 7-membered cycloalkyl ring. Substituents useful in accordance with the present invention are hydroxy, halogen, cyano, lower alkoxy, lower alkanoyl, lower alkyl, aroyl, lower alkylthio, lower alkyl sulfinyl, lower alkyl sulfonyl, aryl, heteroaryl and substituted amino. Unsubstituted cycloalkyl are preferred.

The term "alkoxy" refers to the group R'-O-, wherein R' is an alkyl. The term "lower alkoxy" means a straight-chain or branched-chain alkoxy group containing a maximum of six carbon atoms, such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, tert-butoxy and the like.

The term "aryl" means a mono- or bicyclic aromatic group, such as phenyl or naphthyl, which is unsubstituted or substituted by conventional substituent groups. Preferred substituents are lower alkyl, lower alkoxy, hydroxy lower alkyl, hydroxy, hydroxyalkoxy, halogen, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, cyano, nitro, perfluoroalkyl, alkanyoyl, aroyl, aryl alkynyl, lower alkynyl and lower alkanoylamino. The especially preferred substituents are lower alkyl, lower alkoxy, hydroxy, halogen, cyano and perfluoro lower alkyl. Examples of aryl groups that may be used in accordance with this invention are phenyl, p-tolyl, p-methoxyphenyl, p-chlorophenyl, m-hydroxy phenyl, m-methylthiophenyl, 2-methyl-5-nitrophenyl, 2,6-dichlorophenyl, 1-naphthyl and the like.

The term "lower alkyl-aryl" means a lower alkyl group in which one or more hydrogen atoms is/are replaced by an aryl group. Any conventional lower alkyl-aryl may be used in accordance with this invention, such as benzyl and the like. The term aralkyloxy denotes aryl lower alkoxy groups such as benzyloxy, phenyl ethoxy, etc.

The term "lower alkylenedioxy" denotes a divalent saturated hydrocarbon moiety containing from one to six carbon atoms having terminal oxygens which are placed at the end of the lower alkylene chain and connect to the rest of the molecule. The preferred lower alkylenedioxy moieties are 1,2-ethylene dioxy, methylene dioxy, 1,3-propylene dioxy. Generally, the preferred lower alkylene dioxy moieties are formed in a straight chain.

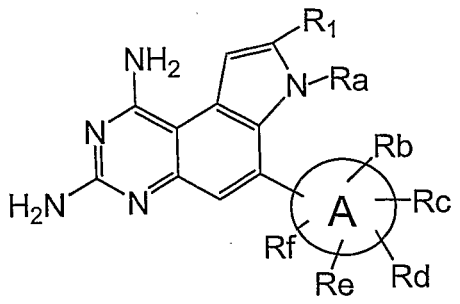
The term "heterocycloalkyl" refers to a 4 to 6 membered monocyclic ring containing 3 to 4 carbon atoms and one or two heteroatoms selected from the group consisting of oxygen, nitrogen or sulfur. Among the heterocyclic alkyl groups are included morpholinyl, tetrahydrothiopyranyl or tetrahydropyranyl.

The term "heteroaromatic ring" refers to a monovalent 5 or 6 membered monocyclic heteroaromatic ring containing from 4 to 5 carbon atoms and from 1 to 2 heteroatoms selected from the group consisting of oxygen, nitrogen or sulfur. Among the preferred heteroaromatic groups are included thiophenyl, thiazolyl, pyridinyl, furanyl, etc.

A "ring system" as used herein, unless otherwise designated, denotes a ring system containing from 1 to 4 fused rings which can be saturated or unsaturated. The rings within the system are selected from aromatic, cycloalkyl, heteroaromatic or heterocycloalkyl rings wherein cycloalkyl, heteroaromatic and heterocycloalkyl rings are defined as above and aromatic is defined as monocyclic unsubstituted aryl, particularly phenyl. In the above given defintions of these terms, the number of ring members in a given ring in the ring system reflects both the fused and the free ring atoms.

The term "pharmaceutically acceptable salts" refers to conventional acid-addition salts or base-addition salts that retain the biological effectiveness and properties of the compounds of formulas I, II, III, IV and V and are formed from suitable non-toxic organic or inorganic acids, or organic or inorganic bases. Sample acid-addition salts include those derived from inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, sulfamic acid, phosphoric acid and nitric acid, and those derived from organic acids such as p-toluenesulfonic acid, salicylic acid, methanesulfonic acid, oxalic acid, succinic acid, citric acid, malic acid, lactic acid, fumaric acid, and the like. Sample base-addition salts include those derived from ammonium, potassium, sodium and, quaternary ammonium hydroxides, such as for example, tetramethylammonium hydroxide. The chemical modification of a pharmaceutical compound (i.e., drug) into a salt is a technique well known to pharmaceutical chemists to obtain improved physical and chemical stability, hygroscopicity, flowability and solubility of compounds. *See, e.g.*, H. Ansel et al., *Pharmaceutical Dosage Forms and Drug Delivery Systems* (6th Ed. 1995) at pp. 196 and 1456-1457.

In detail, the present invention relates to compounds of formula (I)



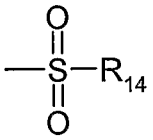
(I)

or pharmaceutically acceptable salts thereof, wherein

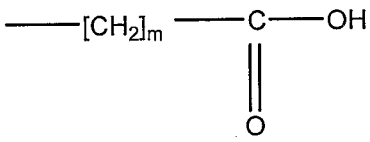
A is a 5- or 6-membered unsaturated or saturated hydrocarbon ring or a 5- or 6-membered unsaturated or saturated ring that contains at least one heteroatom selected from S, N or O,

R1 is hydrogen or lower alkyl,

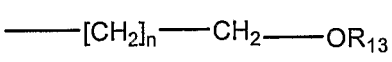
Ra is hydrogen, lower alkyl,



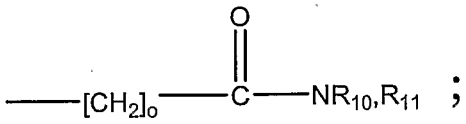
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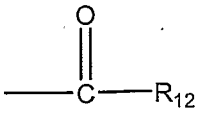


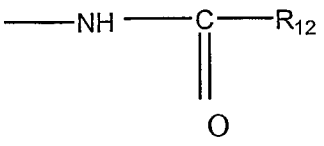
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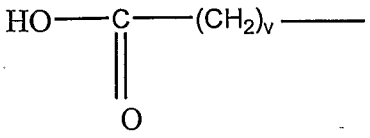
;

Rb, Rc, Rd, Re and Rf are each independently selected from the group consisting of hydrogen, lower alkyl, halogen, amino, lower alkenyl, hydroxy, alkoxy, hydroxy lower alkyl, alkylsulfanyl, perfluoroloweralkyl, perfluoroloweralkoxy, aryl, nitro, lower alkanoyl, -NR_5R_6, R_7S-, alkanoyl, alkanoylamino, carboxy, aryloxy, carboxy alkyl, substituted alkyl, or





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or two of Rb, Rc, Rd, Re and Rf, when present on adjacent carbon atoms on the phenyl ring can be taken together to form a lower alkylenedioxy bridge or a ring system fused to the phenyl ring, said ring system containing one or two rings fused to the phenyl ring with at least one of said rings in said system being either an aromatic or heteroaromatic ring and the remainder ring in the system, if any, being a cycloalkyl or heterocycloalkyl ring;

R_5, R_6 and R_{14} independently are hydrogen or lower alkyl;

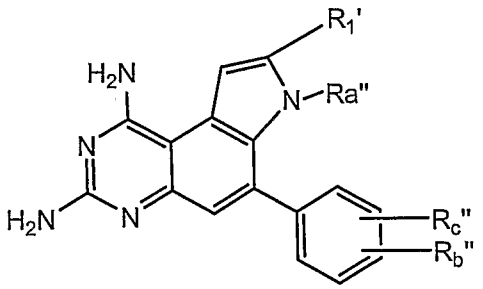
R_7 is lower alkyl;

R_{13} is hydrogen, lower alkyl, benzyl or phenyl;

R_{10}, R_{11} and R_{12} are independently hydrogen or lower alkyl; and

m, n, o and v are independent integers from 0 to 4.

A preferred embodiment of the present invention relates to compounds as defined above, characterised by formula (I-A)

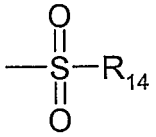


I-A

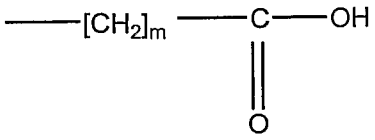
wherein

R_1' is hydrogen or lower alkyl;

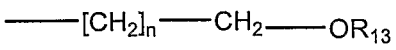
R_a'' is hydrogen, lower alkyl;



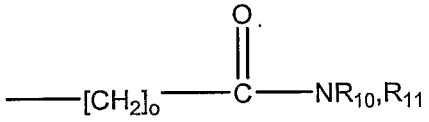
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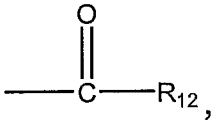


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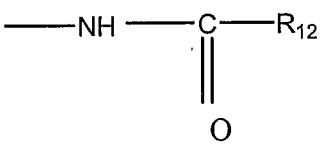


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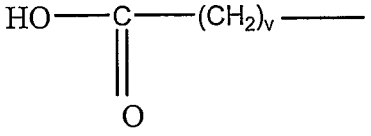
R_b'' and R_c'' are independently hydrogen, lower alkyl, lower alkenyl, lower alkoxy, hydroxy lower alkyl, perfluoroloweralklyl, nitro, halogen, lower alkanoyl, $-NR_5R_6$, R_7S-



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phenyl, hydroxy, perfluoroloweralkoxy, or phenoxy, or R_b'' and R_c'' when present on adjacent carbon atoms on the phenyl ring can be taken together to form a lower alkylenedioxy bridge or a ring system fused to the phenyl ring, said ring system containing one or two rings fused to the phenyl ring with at least one of said rings

in said system being either an aromatic or heteroaromatic ring and the remainder ring in the system, if any, being a cycloalkyl or heterocycloalkyl ring;

R_5, R_6 and R_{14} independently are hydrogen or lower alkyl;

R_7 is lower alkyl;

R_{13} is hydrogen, lower alkyl, benzyl or phenyl;

R_{10}, R_{11} and R_{12} are independently hydrogen or lower alkyl; and

m, n, o and v are independent integers from 0 to 4,

or pharmaceutically acceptable salts thereof.

Preferred compounds as defined above are those, wherein R_1' is hydrogen and R_b'' and R_c'' are substituted on adjacent carbon atoms and form a lower alkylene dioxy bridge.

Other preferred compounds as defined above are those, wherein R_1' is hydrogen and R_b'' and R_c'' are substituted on adjacent carbon atoms and taken together with their attached carbon atoms form a fused aromatic ring.

Other preferred compounds as defined above are those, wherein
R_a'' and R_b'' are substituted on adjacent carbon atoms on the phenyl ring and taken together form a fused heteroaromatic ring; and
R_1' and R_a' are independently hydrogen or lower alkyl.

Other preferred compounds as defined above are those, wherein R_b'' and R_c'' are attached on adjacent carbon atoms on the phenyl ring and form a two membered ring system fused on the phenyl, one of said rings being a heteroaromatic ring or a heterocycloalkyl ring and the other being an aromatic ring

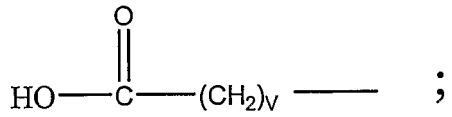
Other preferred compounds as defined above are those, wherein R_1' and Ra" are independently hydrogen or lower alkyl and R_b" and R_c" are independently hydrogen, lower alkyl or lower alkenyl.

Other compounds as defined above are those, wherein R_b" is lower alkenyl and R_c" is hydrogen.

Other compounds as defined above are those, wherein R_b" is lower alkyl or hydrogen and R_c" is lower alkyl.

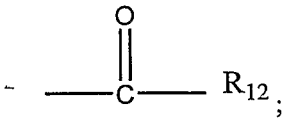
Other preferred compounds as defined above are those, wherein
R_1' and R_a" are hydrogen or lower alkyl,
R_b" and R_c" are individually hydrogen, halogen, trifluoromethyl; and trifluoromethoxy; and
one of R_c" and R_b" is other than hydrogen.

Other preferred compounds as defined above are those, wherein
R_1' and R_a" are hydrogen or lower alkyl;
R_b" is hydrogen or halogen; and
R_c" is halogen, nitro, lower alkoxy, phenoxy, hydroxy, hydroxy lower alkyl



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or

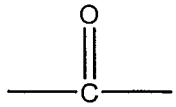


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v is an integer from 0 to 4;
R_{12} is hydrogen or lower alkyl.

Other preferred compounds as defined above are those, wherein R_b" is hydrogen or halogen and R_c" is nitro, halogen, phenoxy, lower alkoxy, hydroxy or hydroxyalkyl.

Other preferred compounds as defined above are those, wherein

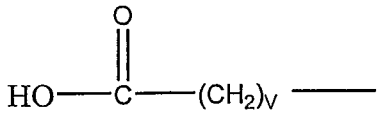
R_a" is hydrogen, R_b" is  ,

R_c" is hydrogen or lower alkyl,

R_{12} is hydrogen or lower alkyl.

Other preferred compounds as defined above are those, wherein

R_b" and R_c" are hydrogen or

 and

v is an integer from 0 to 4;

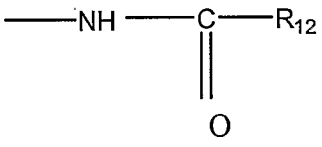
R_1' and R_a" are hydrogen or lower alkyl; and

one of R_b" and R_c" is other than hydrogen.

Other preferred compounds as defined above are those, wherein

R_1' and R_a" are independently hydrogen or lower alkyl;

R_b" and R_c"are hydrogen, R_5 R_6 N-,

 , or

R_7S-;

R_5 and R_6 are independently hydrogen or lower alkyl;

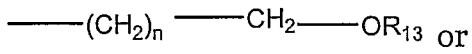
R_7 is lower alkyl;

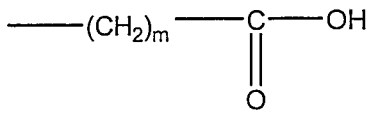
R_{12} is hydrogen or lower alkyl; and

one of R_b" and R_c" is other than hydrogen.

Other preferred compounds as defined above are those, wherein

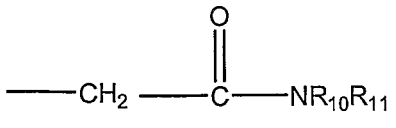
R_a" is

 or

 ;

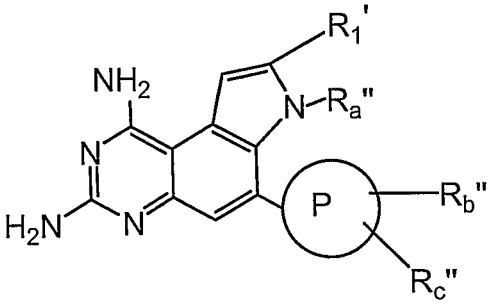
R_{13} is hydrogen, phenyl, benzyl or lower alkyl; and
m and n are independent integers from 0 to 4.

Other preferred compounds as defined above are those, wherein

R_a" is  ;

R_{10} and R_{11} are independently hydrogen or lower alkyl.

Another embodiment of the present invention relates to compounds as defined above, characterised by formula (I-B):



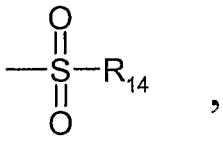
I-B

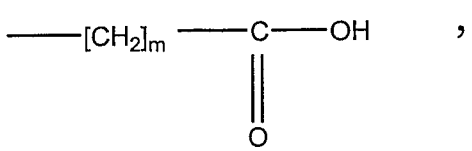
wherein

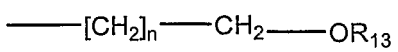
Ⓟ is a 5 or 6 membered heteroaromatic ring containing from 1 to 2 hetero atoms selected from the group consisting of oxygen, sulfur, or nitrogen;

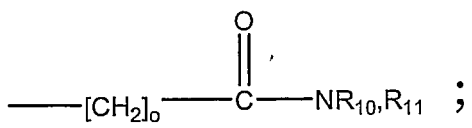
R_1' is hydrogen or lower alkyl;

R_a" is hydrogen, lower alkyl,

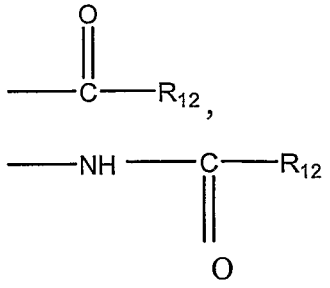
 ,

 ,

 , or

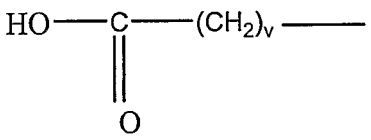
 ;

R_c" and R_b"are independently hydrogen, lower alkyl, lower alkenyl, lower alkoxy, hydroxy lower alkyl, perfluoroloweralklyl, nitro, halogen, lower alkanoyl, $-NR_5R_6$, R_7S-,



,

,



,

phenyl, hydroxy, perfluoroloweralkoxy, or phenoxy, or R_c" and R_b"when present on adjacent carbon atoms on the heteroaromatic ring can be taken together to form a lower alkylene dioxy bridge or a ring system fused to the heteroaromatic ring, said ring system containing one or two rings fused to the heteroaromaticl ring with at least one of said rings in said system being either an aromatic or heteroaromatic ring and the remainder ring in the system, if any, being a cycloalkyl or heterocycloalkyl ring;

R_5, R_6 and R_{14} independently are hydrogen or lower alkyl;

R_7 is lower alkyl;

R_{13} is hydrogen, lower alkyl, benzyl or phenyl;

R_{10}, R_{11} and R_{12} are independently hydrogen or lower alkyl; and

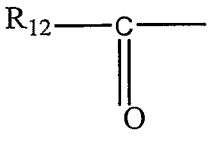
m, n, o and v are independent integers from 0 to 4
or pharmaceutically acceptable salts thereof.

Preferred compounds as defined above are those, wherein Ⓟ is a heteroaromatic ring containing sulfur as the only hetero atom.

Other preferred compounds as defined above are those, wherein $R_{b''}$ and $R_{c''}$ are independently hydrogen, halogen or lower alkyl.

Other preferred compounds as defined above are those, wherein

$R_{c''}$ and $R_{b''}$ is hydrogen, or



;

R_{12} is hydrogen or lower alkyl; and

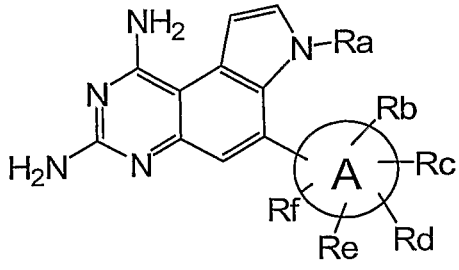
one of $R_{c''}$ and $R_{b''}$ is other than hydrogen.

Other preferred compounds as defined above are those wherein $R_{c''}$ and $R_{b''}$ are attached to the hetero atom ring on adjacent carbon atoms and taken together with their attached carbon atoms a fused phenyl ring.

Other preferred compounds as defined above are those, wherein Ⓟ is a heteroaromatic ring containing an oxygen atom as the only hetero atom.

Other preferred compounds as defined above are those, wherein Ⓟ is a heteroaromatic ring containing a nitrogen hetero atom.

A further embodiment of the present invention relates to compounds as defined above, characterised by formula (II):



(II)

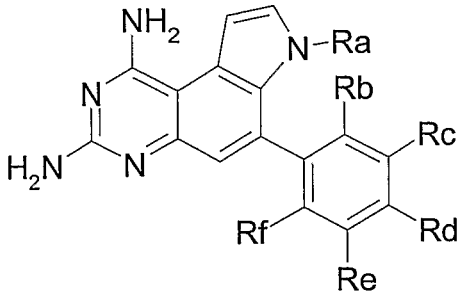
or pharmaceutically acceptable salts thereof, wherein

A is a 5- or 6-membered unsaturated or saturated hydrocarbon or 6-membered unsaturated or saturated ring that contains at least one heteroatom selected from S, N or O;

Ra is hydrogen or lower alkyl; and

Rb, Rc, Rd and Re are each independently selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetyl, acetylamino, hydroxy, alkoxy, carboxy, aryloxy hydroxy methyl, carboxy alkyl, formyl and substituted alkyl, with the proviso that if A is a 6-membered unsaturated or saturated ring, then Rf is selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetyl, acetylamino, hydroxy, alkoxy, carboxy, aryloxy hydroxy methyl, carboxy alkyl, formyl and substituted alkyl.

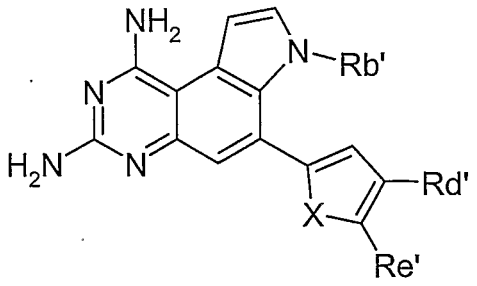
Another embodiment of the present invention relates to compounds as defined above, characterised by formula (III):



(III)

or pharmaceutically acceptable salts thereof, wherein
Ra is hydrogen or lower alkyl;
Rb is selected from the group consisting of hydrogen, lower alkyl, halogen, nitro, acetyl, alkoxy, carboxy, aryloxy and substituted alkyl;
Rc is individually selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetylamino, hydroxy, alkoxy, hydroxy methyl, carboxy alkyl, formyl and substituted alkyl;
Rd is selected from the group consisting of hydrogen, lower alkyl, halogen, hydroxy, alkoxy, carboxyalkyl, alkylsulfanyl and acetyl;
Re is selected from the group consisting of hydrogen, methoxy, halogen and substituted alkyl; and
Rf is hydrogen, alkoxy, lower alkyl or halogen.

Another preferred embodiment of the present invention relates to compounds as defined above, characterised by formula (IV):



(IV)

or pharmaceutical acceptable salt thereof, wherein,

Rb' is selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetylamino, hydroxy, alkoxy, hydroxy methyl, carboxy alkyl, nitro, acetyl, carboxy, aryloxy, formyl and substituted alkyl;

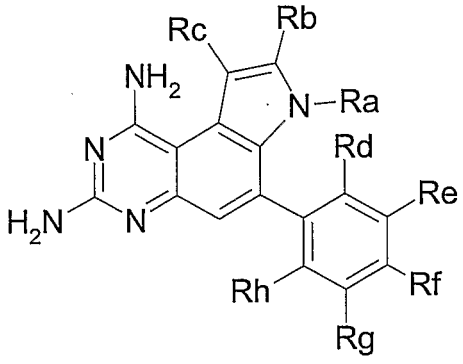
Rd' and Re' are each independently selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetylamino, hydroxy, alkoxy, hydroxy methyl, carboxy alkyl, nitro, acetyl, carboxy, aryloxy, formyl and substituted alkyl; or

Rd' and Re' form a part of a 5- or 6-membered unsaturated or saturated ring that contains at least one hetero atom selected from S, N and O; and

X is selected from the group consisting of S, N and O.

Preferably, Rb' is hydrogen or lower-alkyl.

Still another embodiment of the present invention relates to compounds as defined above, characterised by formula (V):



(V)

or a pharmaceutically acceptable salt thereof, wherein

Ra, Rb and Rc are independently hydrogen or lower alkyl;

Rd is selected from the group consisting of hydrogen, lower alkyl, halogen, nitro, acetyl, alkoxy, carboxy, aryloxy and substituted alkyl;

Re is selected from the group consisting of hydrogen, lower alkyl consisting of individually selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetylamino, hydroxy, alkoxy, hydroxy methyl, carboxy alkyl, formyl and substituted alkyl;

Rf is selected from the group consisting of hydrogen, lower alkyl, halogen, hydroxy, alkoxy, carboxyalkyl, alkylsulfanyl and acetyl;

Rg is selected from the group consisting of hydrogen, methoxy, halogen and substituted alkyl; and

Rh is hydrogen, alkoxy or lower alkyl or halogen.

Preferred compounds as defined above are those, wherein

Ra is selected from hydrogen, methyl, biphenyl-4-ylmethyl, hydroxy benzyl, hydroxy ethyl, carboxy methyl, 2-benzyloxyethyl, and dimethylcarbamoylmethyl;

Rb is hydrogen or methyl;

Rc is hydrogen, isopropyl or methyl;

Rd is selected from the group consisting of hydrogen, acetyl, carboxy-ethyl, chloro, ethoxy, fluoro, methoxy, nitro, phenoxy, trifluoromethyl and methyl;

Re is selected from the group consisting of hydrogen, chloro, amino, methyl, nitro, fluoro, acetylamino, hydroxymethyl, methoxy, hydroxy, carboxymethyl, carboxy-ethyl, ethoxy, formal, trifluoromethyl and isopropyl;

Rf is selected from the group consisting of hydrogen, methoxy, chloro, fluoro, bromo, methyl, phenyl, ethyl, t-butyl, acetyl, ethylsulfanyl, methylsulfanyl, hydroxy, vinyl, ethoxy, carboxy ethyl;

Rg is hydrogen, fluoro, methoxy, trifluoromethyl and chloro; and

Rh is hydrogen, methoxy, methyl or fluoro.

Other preferred compounds as defined above are those, wherein each of Rd and Re, Re and Rf, Rf and Rg and Rg and Rh independently form a part of an cyclic arene or heterocyclic group.

Other preferred compounds as defined above are those, wherein Rd and Re, Re and Rf, Rf and Rg, and Rg and Rh independently form a part of a cyclic ring group selected from the group consisting of thiophene, phenoxantin, indole, pyridine. cycloacetyl, or aryl group.

Preferably among the compounds of formula I, II, II, IV and V are those compounds where

Ra is selected from hydrogen, methyl, biphenyl-4-ylmethyl, hydroxy benzyl, hydroxy ethyl, carboxy methyl, 2-benzyloxyethyl, and dimethylcarbamoylmethyl;

Rb is hydrogen or methyl;

Rc is hydrogen, isopropyl or methyl;

Rd is selected from the group consisting of hydrogen, acetyl, carboxy-ethyl, chloro, ethoxy, fluoro, methoxy, nitro, phenoxy, trifluoromethyl and methyl;

Re is selected from the group consisting of hydrogen, chloro, amino, methyl, nitro, fluoro, acetylamino, hydroxymethyl, methoxy, hydroxy, carboxymethyl, carboxy-ethyl, ethoxy, formal, trifluoromethyl and isopropyl;

Rf is selected from the group consisting of hydrogen, methoxy, chloro, fluoro, bromo, methyl, phenyl, ethyl, t-butyl, acetyl, ethylsulfanyl, methylsulfanyl, hydroxy, vinyl, ethoxy, carboxy ethyl;

Rg is hydrogen, fluoro, methoxy, trifluoromethyl and chloro; and

Rh is hydrogen, methoxy, methyl or fluoro.

Also, preferably, among the compounds of formulas I, II, III, IV and V are those compounds where each of Rd and Re, Re and Rf, Rf and Rg and Rg and Rh independently form a part of an cyclic arene or heterocyclic group. Further, the compound above is where Rd and Re, Re and Rf, Rf and Rg, and Rg and Rh independently form a part of a cyclic ring group selected from the group consisting of thiophene, phenoxantin, indole, pyridine cycloacetyl, or aryl group.

The preferred compounds of the Compounds of Formula I-A and I-B above are those compounds where R_1' is hydrogen. Particularly preferred among those classes of compounds where R_1' is hydrogen are those compounds where R_a'' is hydrogen or lower alkyl.

There are many different embodiments of the compounds of formula I-A. The main embodiments of the compounds of formula I-A are first, those compounds where R_b'' and R_c'' are present on the phenyl ring on the compound of formula I-A on adjacent carbon atoms and taken together form a lower alkylene dioxy bridge. The second major embodiment are those compounds of formula I-A where R_b'' and R_c'' are present on adjacent carbon atoms on the phenyl ring and are taken together

with their adjacent carbon atoms to form a ring system fused to the phenyl ring. The third major embodiment are those compounds where R_b" and R_c" are individually connected to the phenyl ring.

In the first embodiment where R_b" and R_c" form a lower alkylenedioxy bridge, these bridges preferably contain from one to three carbon atoms.

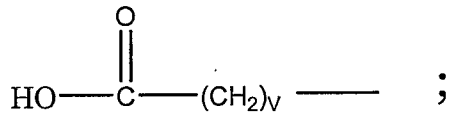
The second major embodiment of the compounds of formula I-A are those compounds where R_b" and R_c" are substituted on adjacent carbon atoms and taken together with their attached carbon atoms form a fused ring system containing from 1 to 3 fused rings fused to the phenyl ring on the compound of formula I-A. One class of compouds in this embodiment are those compounds where the ring system fused to the phenyl ring on the compound of formula I-A, can contain one heteroaromatic or heterocycloalkyl ring and/or one hetero aromatic and/or one aromatic ring. In the embodiment where R_b" and R_c" form a fused aromatic ring system, R_1' is preferably hydrogen and R_a" is preferably hydrogen or lower alkyl. In this second major embodiment of the compounds of formula I-A, another class of compoujnds are those compounds where R_b" and R_c" when taken together with their attached carbon atoms form a single fused heteroaromatic ring or an aromatic ring such as phenyl. In this embodiment R_1' and R_a" are preferably hydrogen or lower alkyl. In this second major embodiment of the compounds of formula I-A, another class of compoujnds are those compounds where R_b" and R_c" when taken together with their attached carbon atoms form a two membered fused ring system which is fused to the phenyl group on the compound of formula I. These two membered ring systems can be both aromatic rings or one hetero aromatic or one heterocycloalkyl ring and one aromatic ring.

In the third major embodiment, R_b" and R_c" are independent groups seperately attached to the phenyl moiety in the compound of formula I-A. One of compounds within this embodiment include compounds where R_b" and R_c" are independently hydrogen or lower alkyl and R_b" and R_c" are independently hydrogen, lower alkyl or lower alkenyl. In this preferred group of compounds, lower alkenyl denotes a monovalent aliphatic hydrocarbon substituent containing from two to six carbon atoms and having an unsubstituted double bond within its structure. The

preferred group of compunds where R_b" is lower alkenyl are those compounds where R_c" is hydrogen and R_1' and R_a" are independently hydrogen or lower alkyl.

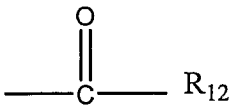
Another class of compounds within the compounds of formula I-A where R_b" and R_c" are independent substituents are those compounds where R_b" and R_c" are individually hydrogen, halogen, trifluoroloweralkyl, preferably trifluoromethyl, and trifluoroloweralkoxy, preferably trifluoromethoxy, with one of R_b" and R_c" being other than hydrogen. Within this class of compounds are those compounds where R_1' and R_a" are either hydrogen or lower alkyl.

Another class of compounds within the embodiment of R_b" and R_c" being individual seperate substituents are those compounds where R_b" is hydrogen or halogen and R_c" is halogen, nitro, lower alkoxy, phenoxy, hydroxy or hydroxyalkyl. Among this class of compounds, compounds where R_1' and R_a" are hydrogen or lower alkyl are preferred. In another class of compounds within this embodiment, are those compounds where R_b" is halogen or hydrogen. Another class of compounds are those where R_c" is:



;

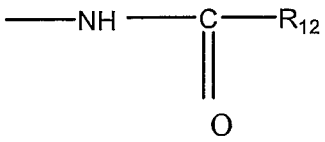
or



v is an integer from 0 to 4;

R_{12} is hydrogen or lower alkyl. In this embodiment, R_c" can be either an aldehyde, where R_{12} is H or a ketone where R_{12} is lower alkyl. Also in this regard, R_b" and R_c" can each be a lower carboxylic acid groups.

In accordance with another embodiment of the compound of formula I-A where R_b" and R_c" are independent substituents there are those compounds where R_1' and R_a" are independently hydrogen or lower alkyl; and R_b" and R_c" are hydrogen, R_7S-, R_5 R_6 N-, or



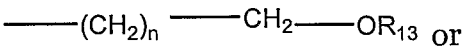
or

R_5 and R_6 are independently hydrogen or lower alkyl;

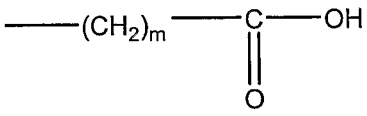
R_7 is lower alkyl; and

one of R_b" and R_c" is other than hydrogen.

Furthermore, in accordance with the embodiment of this invention where R_b" and R_c" in the compund of formula I- A are independent substituents are those class of compounds where Ra" is



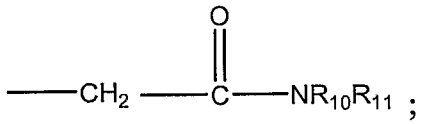
or



R_{13} is hydrogen, phenyl, benzyl, lower alkyl; and

m and n is an integer from 0 to 4. In this case R_1' is generally hydrogen or lower alkyl, preferably hydrogen. In addition, R_b" and R_c" can be halogen or trifluoroalkyl, preferably trifluoromethyl with one of R_b" and R_c" being halogen or hydrogen.

In another class of compounds where R_b" and R_c" are separate independent substituents are those compounds whereR_a" is



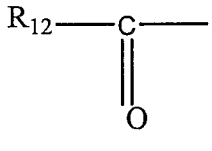
R_{10} and R_{11} are independently hydrogen or lower alkyl. In this group of compounds R_1' is hydrogen or lower alkyl, preferably hydrogen. Also, with respect to this class of compounds, R_b" and R_c" are preferably hydrogen or lower alkoxy.

The compound of formula I-B contains various different embodiments in the same manner as the compound of formula I-A. The first major embodiment are those compounds where R_b" and R_c" taken together form a lower alkylene dioxy bridge. The second are those compounds where R_b" and R_c" taken together with their adjacent carbon atoms to form an ring system which contains one or two aromatic, cycloalkyl or heteroaromatic rings fused to the heteroaromatic ring Ⓟ in the compound of formula I-B. On the other hand, in accordance with a third embodiment of this invention, the compound where R_b" and R_c" in the compound

of formula I-B can be independent, individual substituents. The embodiments formed in this manner are the same as set forth with regard to compounds I-A.

In addition, since the compound of formula I-B contains within its structure a heteroaromatic ring, this heteroaromatic ring can contain sulfur, oxygen and/or nitrogen as the only hetero atom. On the other hand, this structure can contain two hetero atoms with each being the same or each being a different hetero atom such as oxygen or nitrogen. One such embodiment of those compounds, where the hetero aromatic ring contains sulfur as the only hetero atom. In this embodiment, the class of compounds where R_b" and R_c" are independently halogen or lower alkyl are preferred. In addition, those class of compounds where R_b" and R_c" are independently hydrogen, halogen or lower alkyl and R_1' and $R_{a''}$ are hydrogen and lower alkyl are especially preferred.

In addition, with respect to those compounds of formula I-B where the hetero aromatic ring in this compound contains the sulfur atom as the only hetero atom in its ring, the class of compounds where R_b" and R_c" is hydrogen, or



;

R_{12} is hydrogen or lower alkyl; and

R_b" and R_c" is other than hydrogen are preferred. In this embodiment, those compounds where R_1' and $R_{a''}$ are hydrogen and lower alkyl are especially preferred.

As indicated hereinabove, R_b" and R_c" which are present when attached on adjacent carbon atoms on the hetero aromatic ring can be taken together with their attached carbon atoms to form a fused ring system. This ring system can be either a hetero aromatic ring or an aromatic ring. The preferred fused aromatic ring is a phenyl ring.

Preferred compounds are those selected from the group consisting of
6-(3,5-Bis-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine
6-(3-Nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

6-(2,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(5-Chloro-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-o-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[1,3]dioxol-5-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Amino-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-m-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Biphenyl-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(3-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Ethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-tert-Butyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Isopropyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[b]thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Chloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dimethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
1-[5-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone,
6-(3-Amino-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-m-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Biphenyl-4-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(3-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Ethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Isopropyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[b]thiophen-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,5-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

N-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide,
7-Methyl-6-naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
1-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone,
1-[5-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone,
8-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-benzaldehyde,
8-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-methanol,
6-(5-Chloro-2-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,3-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(5-Fluoro-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
1-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone,
6-(5-Chloro-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Furan-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(5-methyl-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
2-[1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-ethanol,
[1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-acetic acid,
(1,3-Diamino-6-thiophen-2-yl-pyrrolo[3,2-f]quinazolin-7-yl)-acetic acid,
1-[4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone,
6-(3,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-trifluoromethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,6-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(3,4,5-trimethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Bromo-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

7-Methyl-6-(3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(4-Ethylsulfanyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-methylsulfanyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-p-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,5-Dimethyl-isoxazol-4-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[b]thiophen-7-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-phenoxathiin-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,3-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophene-2-carbaldehyde,
4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol,
6-Benzo[b]thiophen-3-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(2-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(5-Isopropyl-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol,
7-Methyl-6-(2-phenoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-o-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-vinyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Ethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Chloro-4-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Bromo-2-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,6-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-5-methoxy-benzoic acid,
6-(5-Methoxy-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

6-(2,6-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-(2-Benzyloxy-ethyl)-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methanesulfonyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
N-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide,
2-[1,3-Diamino-6-(3-methoxy-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-N,N-diethyl-acetamide,
6-(2-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Ethyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-(2-Methoxy-ethyl)-6-(3-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzofuran-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
[4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
3-[2-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid, and
3-[4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
and pharmaceutically acceptable salts thereof.

Other preferred compounds are those selected from the group consisting of
6-(3,5-Bis-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3-Nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

6-(5-Chloro-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-o-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[1,3]dioxol-5-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3-Amino-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-m-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Biphenyl-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(3-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Ethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-tert-Butyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3-Isopropyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Benzo[b]thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,4-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2-Chloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,

6-(2,4-Dimethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
1-[5-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone, compound with trifluoro-acetic acid,
6-(3-Amino-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-m-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Biphenyl-4-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(4-methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(3-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Ethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3-Isopropyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Benzo[b]thiophen-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3,5-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
N-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide, compound with trifluoro-acetic acid,
7-Methyl-6-naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,

6-(2,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
1-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone, compound with trifluoro-acetic acid,
1-[5-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone, compound with trifluoro-acetic acid,
8-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-benzaldehyde,
8-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-methanol, compound with trifluoro-acetic acid,
6-(5-Chloro-2-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,3-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,5-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(5-Fluoro-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,5-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
1-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone, compound with trifluoro-acetic acid,
6-(5-Chloro-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Furan-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(5-methyl-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
2-[1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-ethanol, compound with trifluoro-acetic acid,
[1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-acetic acid, compound with trifluoro-acetic acid,

(1,3-Diamino-6-thiophen-2-yl-pyrrolo[3,2-f]quinazolin-7-yl)-acetic acid, compound with trifluoro-acetic acid,
1-[4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone, compound with trifluoro-acetic acid,
6-(3,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(4-trifluoromethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,6-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(3,4,5-trimethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Bromo-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(4-Ethylsulfanyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(4-methylsulfanyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-p-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3,5-Dimethyl-isoxazol-4-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-Benzo[b]thiophen-7-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-phenoxathiin-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,

6-(2,4-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,5-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(2,3-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophene-2-carbaldehyde, compound with trifluoro-acetic acid,
4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol, compound with trifluoro-acetic acid,
6-Benzo[b]thiophen-3-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(2-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(5-Isopropyl-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol, compound with trifluoro-acetic acid,
7-Methyl-6-(2-phenoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-o-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methyl-6-(4-vinyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Ethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(3-Chloro-4-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
6-(4-Bromo-2-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,

6-(2,6-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-5-methoxy-benzoic acid, compound with trifluoro-acetic acid,
6-(5-Methoxy-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,6-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-(2-Benzyloxy-ethyl)-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
7-Methanesulfonyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, compound with trifluoro-acetic acid,
N-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide, compound with trifluoro-acetic acid,
2-[1,3-Diamino-6-(3-methoxy-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-N,N-diethyl-acetamide,
6-(2-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Ethyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-(2-Methoxy-ethyl)-6-(3-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzofuran-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
[4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
3-[2-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid, and
3-[4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
and pharmaceutically acceptable salts thereof.

Particularly preferred compounds as defined above are those selected from the group consisting of
7-ethyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, and
2-(1,3-diamino-6-[2-trifluoromethyl-phenyl]-pyrrolo[3,2-f]quinazoline-7-yl)-ethanol,
and pharmaceutically acceptable salts thereof.

Other particularly preferred compounds as defined above are those selected from the group consisting of
7-ethyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, and
2-(1,3-diamino-6-[2-trifluoromethyl-phenyl]-pyrrolo[3,2-f]quinazoline-7-yl)-ethanol trifluoro acetic acid salt,
and pharmaceutically acceptable salts thereof.

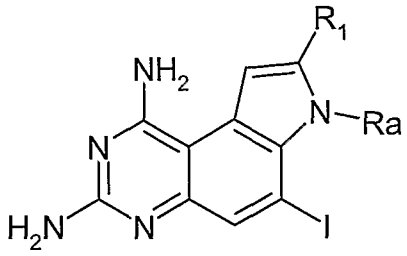
Each of the compounds mentioned above individually constitutes a preferred embodiment of the present invention. Compounds as described above, which are not pharmaceutically acceptable salts and/or pharmaceutically acceptable esters are preferred. Each of the individual substituents exemplified in the above mentioned examples is individually preferred.

Compounds of formula (I) can have one or more asymmetric carbon atoms and can exist in the form of optically pure enantiomers, optically pure diastereoisomers or mixtures of diastereoisomers. The optically active forms can be obtained for example by resolution of the racemates, by asymmetric synthesis or asymmetric chromatography (chromatography with a chiral adsorbens or eluant). The invention embraces all such forms.

It will be appreciated, that the compounds of general formula (I) in this invention may be derivatised at functional groups to provide derivatives which are capable of conversion back to the parent compound in vivo. Physiologically acceptable and metabolically labile derivatives, which are capable of producing the parent

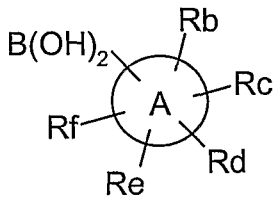
compounds of general formula (I) in vivo are also within the scope of this invention.

A further aspect of the present invention is the process for the manufacture of compounds of formula (I) as defined above, comprising reacting a compound of formula (XXI)



(XXI)

with a compound of formula (XXII)



(XXII)

wherein R1, Ra, Rb, Rc, Rd, Re, Rf and A have the significances given above.

Said reaction of a compound of formula XXI with a compound of formula XXII can be carried out by methods well known to the person skilled in the art, e.g. in analogy to the examples and schemes described below. The reaction can e.g. be carried out with Pd(P(phenyl)3)4 in a solvent such as e.g. DME or ETOH and treating with Na2CO3 and H2O.

Another embodiment of the present invention relates to compounds as defined above, when prepared by a process as defined above.

As described above, the compounds of the present invention can be used as medicaments for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors. Examples of such diseases are diseases which are based on high blood glucose concentration, particularly diabetes. The compounds of the invention inhibit PTP1B *in vitro* and have been shown to lower blood glucose levels *in vivo*. Thus, the compounds of the present invention would be useful for the treatment of diabetes.

The invention therefore also relates to pharmaceutical compositions comprising a compound as defined above and a pharmaceutically acceptable carrier and/or adjuvant.

Further, the invention relates to compounds as defined above for use as therapeutic active substances, particularly as therapeutic active substances for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors. Examples of such diseases are diseases which are based on high blood glucose concentration, particularly diabetes.

In another embodiment, the invention relates to a method for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors, which method comprises administering a compound as defined above to a human or animal. Preferred examples of such diseases are diseases which are based on high blood glucose concentration, particularly diabetes.

The invention further relates to the use of compounds as defined above for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors. Preferred examples of such diseases are diseases which are based on high blood glucose concentration, particularly diabetes.

In addition, the invention relates to the use of compounds as defined above for the preparation of medicaments for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors. Preferred examples of such diseases are diseases which are based on high blood glucose concentration, particularly diabetes. Such medicaments comprise a compound as defined above.

The compounds of the invention can be administered orally, rectally, or parentally, e.g., intravenously, intramuscularly, subcutaneously, intrathecally or transdermally; or sublingually, or as opthalmalogical preparations. Capsules, tablets, suspensions or solutions for oral administration, suppositories, injection solutions, eye drops, salves or spray solutions are examples of administration forms.

Intravenous, intramuscular, oral or inhalation administration are preferred forms of use. The dosages in which the compounds of the invention are administered in effective amount depend on the nature of the specific active ingredient, the age and requirements of the patient and the mode of administration. Dosages may be determined by any conventional means, e.g., by dose-limiting clinical trials. In general, dosages of about 0.1 to 100 mg/kg body weight per day are preferred, with dosages of 1-25 mg/kg per day being particularly preferred.

The invention further comprises pharmaceutical compositions that contain a pharmaceutically effective amount of a compound of the invention and a pharmaceutically acceptable carrier. Such compositions may be formulated by any conventional means. Tablets or granulates can contain a series of binders, fillers, carriers or diluents. Liquid compositions can be, for example, in the form of a sterile water-miscible solution. Capsules can contain a filler or thickener in addition to the active ingredient. Furthermore, flavor-improving additives as well as substances usually used as preserving, stabilizing, moisture-retaining and emulsifying agents as well as salts for varying the osmotic pressure, buffers and other additives can also be present.

The previously mentioned carrier materials and diluents can comprise any conventional pharmaceutically acceptable organic or inorganic substances, e.g., water, gelatine, lactose, starch, magnesium stearate, talc, gum arabic, polyalkylene glycols and the like.

Oral unit dosage forms, such as tablets and capsules, preferably contain from 25 mg to 1000 mg of a compound of this invention. The compounds of the invention may be prepared by conventional means.

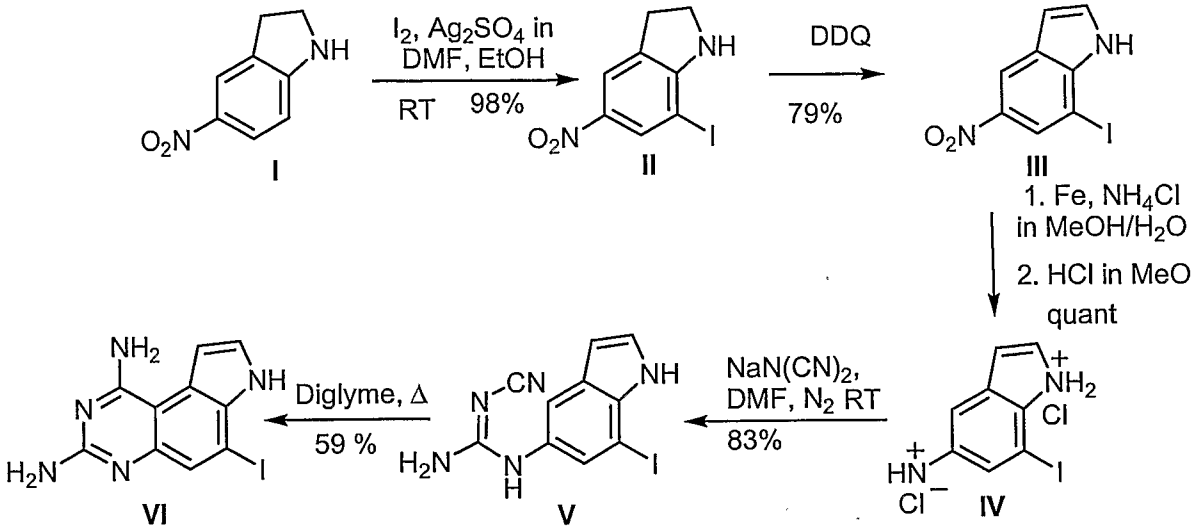
In accordance with this invention, the compounds herein as well as their pharmaceutically acceptable salts are useful in the control or prevention of illnesses associated with high blood glucose concentration. A preferred indication associated with the present invention is that associated with diabetes.

The dosage can vary within wide limits and will, of course, have to be adjusted to the individual requirements in each particular case. In the case of oral administration, the dosage for adults may vary from about 0.01 mg to about 1000 mg per day of a compound of formulas I or II, or of the corresponding amount of a pharmaceutically acceptable salt thereof. The daily dosage may be administered as single dose or in divided doses, and in addition, the upper limit can also be exceeded when this is found to be indicated.

The compounds of formula (I) can be manufactured by the methods given below, by the methods given in the examples or by analogous methods. Appropriate reaction conditions for the individual reaction steps are known to a person skilled in the art. Starting materials are either commercially available or can be prepared by methods analogous to the methods given below, by methods described in references cited in the text or in the examples, or by methods known in the art.

A particular method for preparing the compounds of this invention is described in the following schemes. The examples following each of the schemes provide a detailed description of the schematic methods.

SCHEME 1



Compound **II:** A mixture of silver sulfate (100 g, 0.32 mol) and iodine (82 g, 0.32 mol) in *N,N*-dimethylformamide (700 mL) and ethanol (1400 mL) was treated with 5-nitro-2,3-dihydro-1H-indole **I** (48 g, 0.29 mol). The resulting mixture was stirred at 25°C for 1.5 h, filtered and the filter pad washed with ethyl acetate. The filtrate was concentrated *in vacuo* to a volume of approximately 500 mL. This solution was treated with a 1.0N aqueous sodium thiosulfate solution (100 mL) and a saturated aqueous sodium chloride solution (400 mL). The resulting precipitate was collected by filtration, washed with water and petroleum ether, and dried *in vacuo* to afford 7-iodo-5-nitro-2,3-dihydro-1H-indole **II** (83.9 g, 98.9%) as a white solid: ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.18 (d, J = 2.20 Hz, 1H), 7.80 (d, J = 1.46 Hz, 1H), 7.03 (broad s, 1H), 3.65 (t, J = 8.97 Hz, 2H), 3.17 (t, J = 8.60 Hz, 2H).

Compound **III**: A solution of 7-iodo-5-nitro-2,3-dihydro-1H-indole **II** (15 g, 51.7 mmol) in ethanol (1200 mL) and isopropanol (20 mL) at 25°C was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (13.6 g, 59.9 mmol). The resulting solution was warmed to 65°C and air was bubbled through for 1 h. An additional 0.57 equivalents of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (6.8 g, 29.9 mmol) was added and the reaction was stirred at 65°C for another 2 h before being

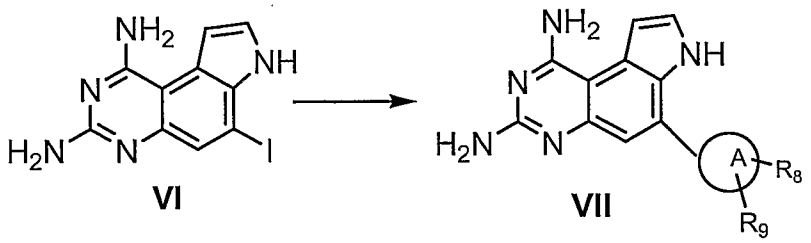
concentrated *in vacuo*. Flash chromatography (Merck Silica gel 60, 230-400 mesh, 90/10 toluene/ethyl acetate) afforded 7-iodo-5-nitro-1H-indole **III** (13.07 g, 79%) as a yellow solid: ^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.82 (broad s, 1H), 8.59 (d, J = 1.83 Hz, 1H), 8.30 (d, J = 1.83 Hz, 1H), 7.61 (t, J = 2.93 Hz, 1H), 6.90 (dd, J_1 = 1.83 Hz, J_2 = 3.30 Hz, 1H).

Compound **IV**: A solution of 7-iodo-5-nitro-1H-indole **III** (20 g, 69.4 mmol) in methanol (650 mL) at 25°C was treated with a solution of ammonium chloride (26.1 g, 485.8 mmol) in water (550 mL) and iron powder (13.6 g, 242.9 mmol). The mixture was heated to 100°C under a nitrogen atmosphere for 5 h. The resulting mixture was filtered through a pad of celite and the celite pad washed with hot methanol. The filtrate was concentrated in vacuo and the residue was partitioned between methylene chloride and water and separated. The pH of the aqueous layer was adjusted to pH=10 with ammonium hydroxide and extracted with methylene chloride. The combined organic layers were dried over sodium sulfate, filtered, and concentrated *in vacuo* to a volume of 250 mL. This solution was treated with a 4.0M aqueous hydrochloric acid solution in dioxane and stirred at 25°C for 2 h. The precipitate was collected by filtration and washed with methylene chloride and petroleum ether to afford 7-iodo-1H-indol-5-ylamine hydrochloride **IV** (24.7 g, quant.) as a gray solid: ^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.34 (broad s, 1H), 9.93 (broad s, 2H), 7.56 (d, J = 1.46 Hz, 1H), 7.48 (t, J = 2.74 Hz, 1H), 7.44 (d, J = 1.83 Hz, 1H), 6.68 (dd, J_1 = 1.83 Hz, J_2 = 2.93 Hz, 1H).

Compound **V:** A solution of 7-iodo-1H-indol-5-ylamine hydrochloride **IV** (24.6 g, 83.7 mmol) in *N,N*-dimethylformamide (400 mL) at 25°C was treated with sodium dicyanamide (18.6 g, 209 mmol). The reaction mixture was warmed to 50°C for 2 h, concentrated *in vacuo*, and the residue treated with water (500 mL). The resulting mixture was allowed to stand at 25°C for 2.5 h during which time a yellow precipitate formed. The precipitate was collected by filtration and washed with water to afford N"-cyano-N-(7-iodo-1H-indol-5-yl)guanidine **V** (22.59 g, 83%) as a light yellow solid: ^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.02 (broad s, 1H), 8.89 (broad s, 1H), 7.46 (d, J = 1.83 Hz, 1H), 7.37 (d, J = 1.83 Hz, 1H), 7.35 (t, J = 2.56 Hz, 1H), 6.85 (broad s, 2H), 6.56 (dd, J_1 = 1.83 Hz, J_2 = 3.10 Hz, 1H).

Compound **VI:** A solution of N"-cyano-N-(7-iodo-1H-indol-5-yl)guanidine **V** (6.08 g, 18.7 mmol) in 2-methoxyethyl ether (50 mL) was heated to 175°C for 32.5 h. The reaction mixture was cooled to 25°C, the resulting solids removed by filtration and washed with methanol. The filtrate was concentrated *in vacuo* to give a brown oil. The residue was dissolved in methanol and then absorbed onto Merck Silica gel 60, 230-400 mesh (25 g). Flash chromatography (Merck Silica gel 60, 230-400 mesh, 90/10/1 methylene chloride/methanol/ammonium hydroxide) afforded 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **VI** (3.61 g, 59%) as a brown solid: ^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.36 (broad s, 1H), 7.45 (broad s, 1H), 7.43 (t, J = 2.93 Hz, 1H), 7.20 (s, 1H), 6.74 (broad s, 2H), 5.78 (broad s, 2H).

Scheme 2



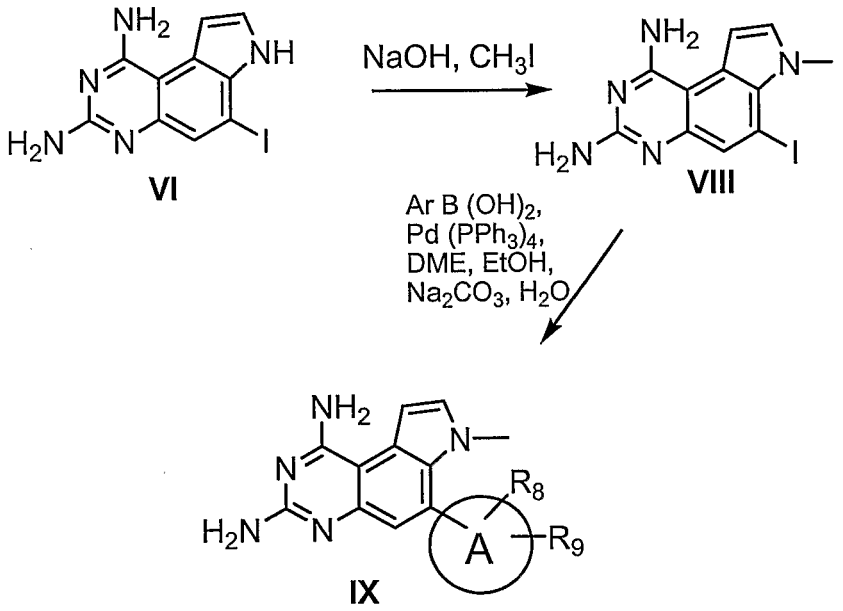
Compound **VII:** The coupling reaction can be carried out by a conventional aryl coupling method, e.g., Suzuki coupling method: (a) Suzuki et *al., synth.commun.* **1981,** *11,* 513, (b) Suzuki *pure and Appl. Chem.* **1985,** *57,* 1749-1758, (c) Suzuki *et al., Chem. Rev.* **1995,** *95,* 2457-2483, (d) Shieh *et al., J. Org. Chem.* **1992,** *57,* 379-381, (e) Martin *et al., Acta Chemica Scandinavica.* **1993,** *47,* 513.

Typical conditions used to carry out the Suzuki coupling of 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **VI** includes the use of either aryl or heteroaromatic boronic acid or esters (e.g., where Ar is defined as aryl) as coupling partner, in aqueous base such as sodium bicarbonate or potassium carbonate or barium hydroxide or triethylamine solution, a palladium catalyst (2-20 mole %) such as tetrakis(triphenylphosphine)-palladium (0) or [1,1'bis(diphenylphosphino)-ferrocene]dichloro-palladium(II), in a suitable solvent such as aqueous ethanol or THF or DMF or ethylene glycol for at temperatures ranging from 25° C to 125° C for 2-18 hr yields compound **VII.**

Alternatively, coupling reaction can be carried out by a conventional aryl or heteroaromatic coupling partner utilizing Stille coupling, *e.g.*, Stille *et al., Angew. Chem. Int. Ed. Engl.*, **1986**, *25*, 508.

Typical conditions used to carry out the Stille reaction include the use of an organostannane as the coupling partner, palladium catalyst (2-20 mole %) such as tetrakis(triphenylphosphine)-palladium (0) or [1,1'bis(diphenylphosphino)-ferrocene]dichloro-palladium(II), a salt such as potassium fluoride or lithium chloride, in a suitable anhydrous solvent such as THF or DMF or ethylene glycol for at temperatures ranging from 25°C to 125°C for 2-18 hr yields compound **VII**.

Scheme 3



Compound **VIII**: A solution of 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **VI**, 400 mg, 1.23 mmol) in tetrahydrofuran (20 mL) at 25°C was treated with sodium hydroxide (98 mg, 2.46 mmol), methyl iodide (0.09 mL, 1.48 mmol), and tetrabutylammonium bromide (198 mg, 0.62 mmol), and the resulting mixture stirred at 25°C for 18 h. The reaction mixture was treated with ethyl acetate, water, and a saturated aqueous sodium chloride solution, shaken and separated. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were dried over sodium sulfate, filtered, and concentrated *in vacuo* to afford 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine (500 mg) as a yellow solid. The product was taken on into the next reaction without further purification 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **VIII**.

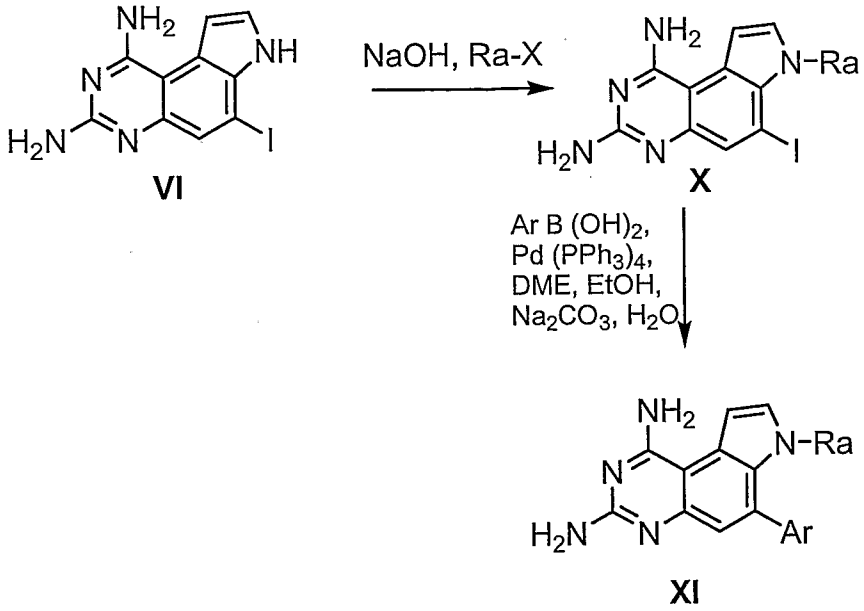
Compound **IX:** The coupling reaction can be carried out by a conventional aryl coupling method, e.g., Suzuki coupling method: (a) Suzuki et *al., synth.commun.* **1981,** *11,* 513, (b) Suzuki *pure and Appl. Chem.* **1985,** *57,* 1749-1758, (c) Suzuki *et al., Chem. Rev.* **1995,** *95,* 2457-2483, (d) Shieh *et al., J. Org. Chem.* **1992,** *57,* 379-381, (e) Martin *et al., Acta Chemica Scandinavica.* **1993,** *47,* 513.

Typical conditions used to carry out the Suzuki coupling of **VIII** includes the use of either aryl or heteroaromatic boronic acid or esters (e.g., where Ar is defined as aryl) as coupling partner, in aqueous base such as sodium bicarbonate or potassium carbonate or barium hydroxide or triethylamine solution, a palladium catalyst (2-20 mole %) such as tetrakis(triphenylphosphine)-palladium (0) or [1,1'-bis(diphenylphosphino)-ferrocene]dichloro-palladium(II), in a suitable solvent such as aqueous ethanol or THF or DMF or ethylene glycol for at temperatures ranging from 25 °C to 125 °C for 2-18 hr yields 6-Aryl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **X.**

Alternatively, coupling reaction can be carried out by a conventional aryl or heteroaromatic coupling partner utilizing Stille coupling, e.g., Stille *et al., Angew. Chem. Int. Ed. Engl.,* **1986,** *25,* 508.

Typical conditions used to carry out the Stille reaction include the use of an organostannane as the coupling partner, palladium catalyst (2-20 mole %) such as tetrakis(triphenylphosphine)-palladium (0) or [1,1'bis(diphenylphosphino)-ferrocene]dichloro-palladium(II), a salt such as potassium fluoride or lithium chloride, in a suitable anhydrous solvent such as THF or DMF or ethylene glycol for at temperatures ranging from 25°C to 125°C for 2-18 hr yields compound 6-Aryl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **IX.**

Scheme 4:



Compound **X**: Typical condition used to carry out alkylation of 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **VI** and phase transfer catalyst such as tetrabutylammonium bromide, with variety of halides (e.g. RaBr or RaI, where Ra is defined above) is carried out with suitable solvent such as tetrahydrofuran, DMF using suitable base such as sodium hydroxide at temperatures ranging from -78° C to 25° C to provide the 6-iodo-7-alkyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **XI**.

6-Aryl-7-alkyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **XI:** The coupling reaction can be carried out by a conventional aryl coupling method, e.g., Suzuki coupling method: (a) Suzuki et *al.*, *synth.commun.* **1981,** *11,* 513, (b) Suzuki, *Pure and Appl. Chem.* **1985,** *57,* 1749-1758, (c) Suzuki *et al.*, *Chem. Rev.* **1995,** *95,* 2457-2483, (d) Shieh *et al.*, *J. Org. Chem.* **1992,** *57,* 379-381, (e) Martin *et al.*, *Acta Chemica Scandinavica.* **1993,** *47,* 513.

Typical conditions used to carry out the Suzuki coupling of 6-iodo-7-alkyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **X** includes the use of either aryl or heteroaromatic boronic acid or esters (e.g. where Ar is defined as aryl) as coupling partner, in aqueous base such as sodium bicarbonate or potassium carbonate or barium hydroxide or triethylamine solution, a palladium catalyst (2-20 mole %) such as tetrakis(triphenylphosphine)-palladium (0) or

[1,1'bis(diphenylphosphino)-ferrocene]dichloro-palladium(II), in a suitable solvent such as aqueous ethanol or THF or DMF or ethylene glycol for at temperatures ranging from 25° C to 125° C for 2-18 hr yields compound **X**.

Alternatively, coupling reaction can be carried out by a conventional aryl or heteroaromatic coupling partner utilizing Stille coupling. e.g., Stille *et al., Angew. Chem. Int. Ed. Engl.,* **1986,** *25,* 508.

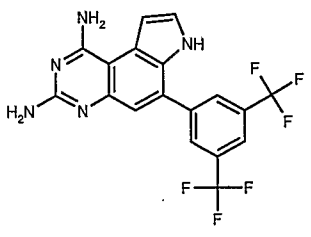
Typical conditions used to carry out the Stille reaction include the use of an organostannane as the coupling partner, palladium catalyst (2-20 mole%) such as tetrakis(triphenylphosphine)-palladium (0) or [1,1'bis(diphenylphosphino)-ferrocene]dichloro-palladium(II), a salt such as potassium fluoride or lithium chloride, in a suitable anhydrous solvent such as THF or DMF or ethylene glycol for at temperatures ranging from 25° C to 125° C for 2-18 hr yields 6-Aryl-7-alkyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **XI**.

This invention is illustrated by the following Examples. In the Examples, the procedures of Examples 2-28 were carried out by the procedure of Example 1. In the Examples, the procedures of Examples 30-33 were carried out by the procedure of Example 29. In the Examples, the procedures of Examples 35-104 were carried out by the procedure of Example 34. In the Examples, the procedures of Examples 106-112 were carried out by the procedure of Example 105. In the Examples, the procedure of Example 114 was carried out by the procedure of Example 113.

EXAMPLES

Example 1

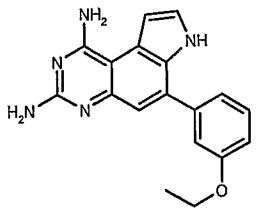
6-(3,5-Bis-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine



A solution of 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine (322 mg, 0.99 mmol) in ethylene glycol dimethyl ether (3.0 mL) and ethanol (3.0 mL)at 25°C was treated with 3,5-bis(trifluoromethyl)benzene boronic acid (510 mg, 1.98 mmol), a saturated aqueous sodium bicarbonate solution (1.5 mL), and tetrakis(triphenylphosphine)-palladium (0) (115 mg, 0.1 mmol). The resulting mixture was heated to 80°C for 18 h, cooled, filtered and the isolated solids washed with ethyl acetate. The filtrate was pre-absorbed onto silica gel and purified by flash chromatography (Merck Silica gel 60, 230-400 mesh, 90/10/1 methylene chloride/methanol/ammonium hydroxide) to give 6-(3,5-bis-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine (218 mg, 53.5%) as a yellow solid ; EI-HRMS m/e calcd for $C_{18}H_{11}F_6N_5$ (M^+) 411.0918, found 411.0921.

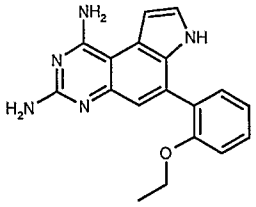
In an analogous manner, there were obtained:

Example 2



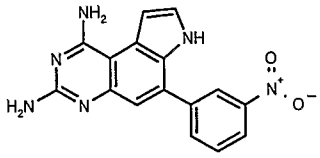
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-ethoxyphenylboronic acid there was produced 6-(3-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{17}N_5O$ $(M+H)^+$ at m/z = 320.

Example 3



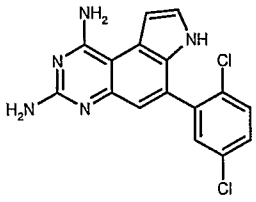
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-ethoxyphenylboronic acid there was produced 6-(2-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{17}N_5O$ $(M+H)^+$ at m/z = 320.

Example 4



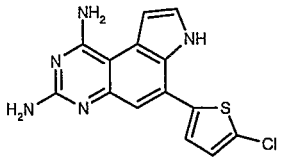
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-nitrophenylboronic acid there was produced 6-(3-Nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine; EI-HRMS m/e calcd for $C_{16}H_{12}N_6O_2$ (M^+) 320.1022, found 320.1020.

Example 5



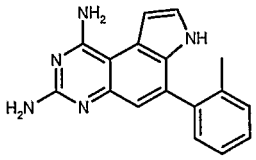
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,5-dichlorophenylboronic acid there was produced 6-(2,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine; EI-HRMS m/e calcd for $C_{16}H_{11}Cl_2N_5$ (M^+) 343.0391, found 343.0392.

Example 6



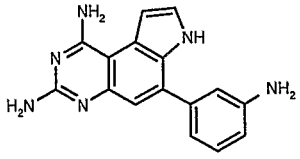
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-chlorothiophene-2-boronic acid there was produced 6-(5-Chloro-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; $(ES)^+$-HRMS m/e calcd for $C_{14}H_{10}ClN_5S$ (M+H) 316.0418, found 316.0422.

Example 7



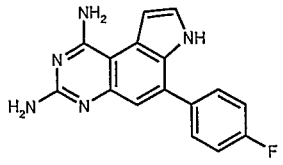
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and o-tolylboronic acid there was produced 6-o-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as an off-white solid; EI-HRMS m/e calcd for $C_{17}H_{15}N_5$ $(M+H)^+$ 290.1400, found 290.1399.

Example 8



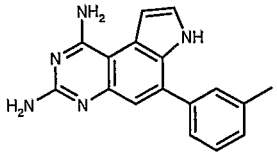
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-aminobenzeneboronic acid there was produced 6-(3-Amino-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{16}H_{14}N_6$ $(M+H)^+$ at m/z = 291.

Example 9



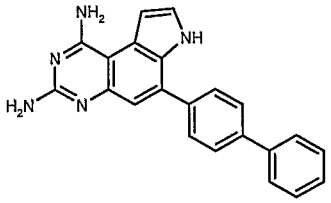
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-fluorophenylboronic acid there was produced 6-(4-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{16}H_{12}FN_5$ $(M+H)^+$ at m/z = 294.

Example 10



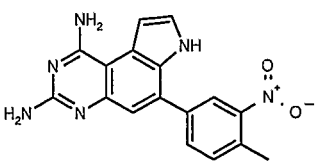
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-methylphenylboronic acid there was produced 6-m-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid;. LRMS for $C_{17}H_{15}N_5$ $(M+H)^+$ at m/z = 290

Example 11



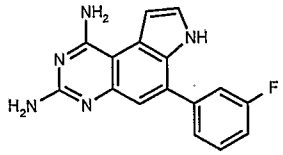
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-biphenylphenylboronic acid there was produced 6-Biphenyl-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{22}H_{17}N_5$ $(M+H)^+$ at m/z = 352.

Example 12



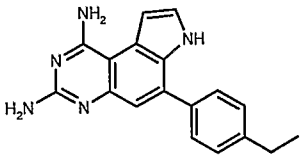
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-methyl-3-nitrophenylboronic acid there was produced 6-(4-methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{14}N_6O_2$ $(M+H)^+$ at m/z = 335.

Example 13



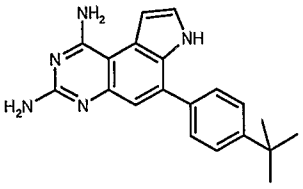
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-fluorophenylboronic acid there was produced 6-(3-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{16}H_{12}FN_5$ $(M+H)^+$ at m/z = 294.

Example 14



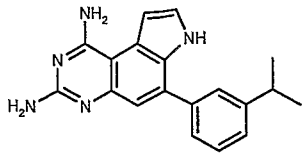
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-ethylphenylboronic acid there was produced 6-(4-Ethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{18}H_{17}N_5$ $(M+H)^+$ at m/z = 335.

Example 15



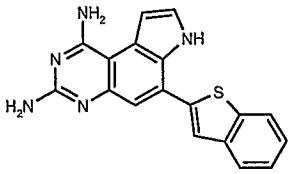
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-*tert*-butylbenzeneboronic acid there was produced 6-(4-tert-Butyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{20}H_{21}N_5$ $(M+H)^+$ at m/z = 332.

Example 16



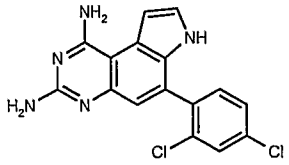
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (3-isopropylphenyl)boronic acid there was produced 6-(3-Isopropyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt a white solid; LRMS for $C_{19}H_{19}N_5$ $(M+H)^+$ at m/z = 318.

Example 17



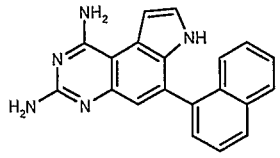
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and benzo(B)thiophene-2-boronic acid there was produced 6-Benzo[b]thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as white solid; LRMS for $C_{18}H_{13}N_5S$ $(M+H)^+$ at m/z = 332.

Example 18



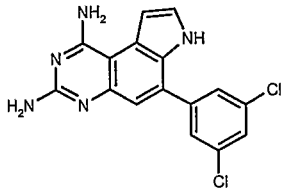
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,4-dichlorophenylboronic acid there was produced 6-(2,4-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{16}H_{11}Cl_2N_5$ $(M+H)^+$ at m/z = 344.

Example 19



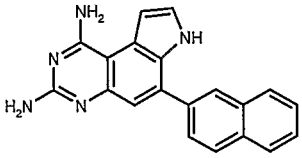
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 1-naphthaleneboronic acid there was produced 6-Naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{20}H_{15}N_5$ $(M+H)^+$ at m/z = 326.

Example 20



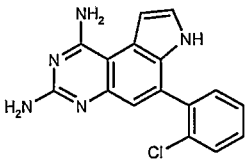
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3,5-dichlorophenylboronic acid there was produced 6-(3,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{16}H_{11}Cl_2N_5$ $(M+H)^+$ at m/z = 344.

Example 21



From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and naphthalene-2-boronic acid there was produced 6-Naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{20}H_{15}N_5$ $(M+H)^+$ at m/z = 326.

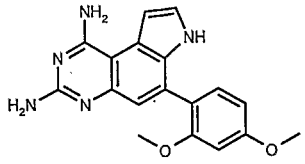
Example 22



From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-chlorophenylboronic acid there was produced 6-(2-Chloro-phenyl)-7H-

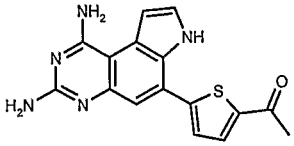
pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{16}H_{12}ClN_5$ $(M+H)^+$ at m/z = 310.

Example 23



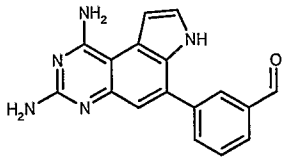
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,4-dimethoxyphenylboronic acid there was produced 6-(2,4-Dimethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{18}H_{17}N_5O_2$ $(M+H)^+$ at m/z = 336.

Example 24



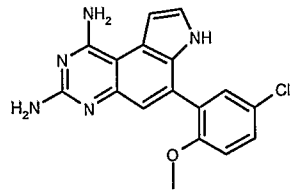
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-acetyl-2-thiopheneboronic acid there was produced 1-[5-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone trifluoro-acetic acid salt as a white solid; LRMS for $C_{16}H_{13}N_5OS$ $(M+H)^+$ at m/z = 324.

Example 25



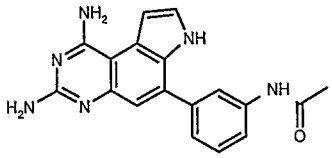
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-formylphenylboronic acid there was produced 3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-benzaldehyde as a yellow solid; $(ES)^+$-HRMS m/e calcd for $C_{17}H_{13}N_5O$ $(M+H)^+$ 304.1193, found 304.1195.

Example 26



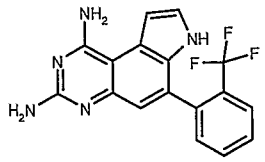
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-chloro-2-methoxyphenylboronic acid there was produced 6-(5-Chloro-2-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{14}ClN_5O$ $(M+H)^+$ at m/z = 340.

Example 27



From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (3-acetylaminophenyl)boronic acid there was produced N-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide trifluoro-acetic acid salt as a white solid; LRMS for $C_{18}H_{16}N_6O$ $(M+H)^+$ at m/z = 333.

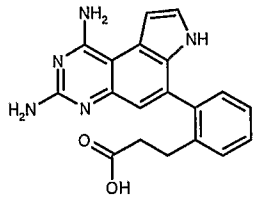
Example 28



From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-(trifluoromethylbenzene)boronic acid there was produced 6-(2-Trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a light brown solid; LRMS for $C_{17}H_{12}F_3N_5$ $(M+H)^+$ at m/z = 344.

Example 29

3-[2-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid

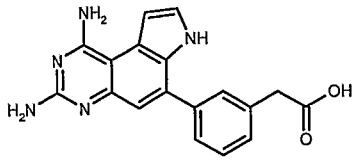


A mixture of 3-(2-bromo-phenyl)-propionic acid (458 mg, 2.0 mmol), 4,4,5,5,4',4',5',5'-octamethyl-[2,2']bi[[1,3,2]dioxaborolanyl] (558 mg, 2.20 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium (II) (132 mg, 0.18 mmol), and potassium acetate (589 mg, 6.0 mmol) was heated to 95°C for 2 d. The resulting mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with a saturated aqueous sodium chloride solution, filtered through a pad of silca gel and sodium sulfate, and concentrated *in vacuo* to afford 3-[2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionic acid. A solution of 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine (prepared as in Example 1, 100 mg, 0.31 mmol), 3-[2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionic acid (102 mg, 0.37 mmol), tetrakis(triphenylphosphine)palladium(0) (71 mg, 0.06 mmol) in a 2.0M aqueous sodium carbonate solution (0.5 mL), ethanol (1.5 mL), and ethylene glycol dimethyl ether (1.5 mL) was heated to 95°C for 18 h. The resulting mixture was cooled to 25°C, dissolved in methanol and tetrahydrofuran, and filtered through a pad of silica gel and sodium sulfate. The filtrate was concentrated *in vacuo*. HPLC purification (Shimadzu HPLC, ODSA column from Medchem, 2x10 cm, 10 micro, 10-90% CH3CN/H2O with 0.1% TFA.) afforded 3-[2-(1,3-diamino-7H-pyrrolo[3,2-

f]quinazolin-6-yl)-phenyl]-propionic acid (12.5 mg, 12.1%); LRMS for $C_{19}H_{17}N_5O_2$ $(M+H)^+$ at m/z = 348.

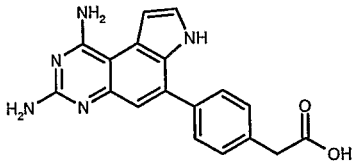
(B) In an analogous manner, there were obtained:

Example 30



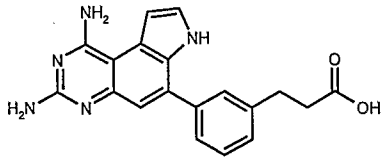
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and [3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-acetic acid there was produced [3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid; LRMS for $C_{18}H_{15}N_5O_2$ $(M+H)^+$ at m/z = 334.

Example 31



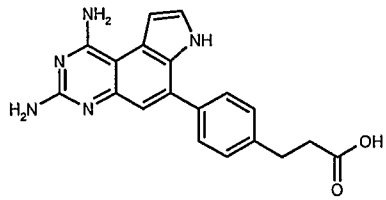
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and [4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-acetic acid there was produced [4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid; LRMS for $C_{18}H_{15}N_5O_2$ $(M+H)^+$ at m/z = 334.

Example 32



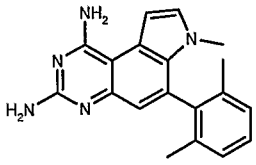
From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-[3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionic acid there was produced 3-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid; LRMS for $C_{19}H_{17}N_5O_2$ $(M+H)^+$ for m/z = 348.

Example 33



From 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionic acid there was produced 3-[4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid; LRMS for $C_{19}H_{17}N_5O_2$ $(M+H)^+$ at m/z = 348.

Example 34



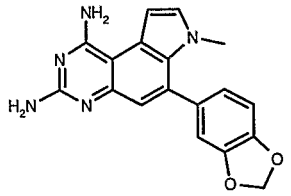
6-(2,6-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine.

A solution of 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine (1.68 g, 5.00 mmol) in ethylene glycol dimethyl ether (10 mL) at 25°C was treated with 2,6-dimethylbenzene boronic acid (1.50 g, 10.0 mmol) in ethanol (10 mL), sodium bicarbonate (2.84 g, 26.80 mmol), and tetrakis(triphenylphosphine)-palladium (0) (3.31 g, 2.86 mmol). The resulting mixture was heated to 80°C for 3 h. The

resulting mixture was filtered through a pad of celite and the filtrate diluted with water (100 mL). This solution was extracted with a 95/5/0.5 solution of methylene chloride/methanol/ammonium hydroxide (3 x 100 mL) and the combined organic layers dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Flash chromatography (Merck Silica gel 60, 230-400 mesh, 90/5/0.5 methylene chloride/methanol/ammonium hydroxide) afforded 6-(2,6-dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine (100 mg, 6.34%) as an off-white solid; EI-HRMS m/e calcd for $C_{19}H_{19}N_5$ (M^+) 317.1640, found 317.1632.

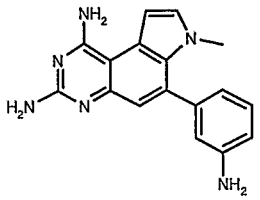
(B) In an analogous manner, there were obtained:

Example 35



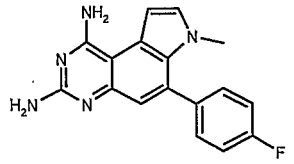
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3,4-methylenedioxyphenylboronic acid there was produced 6-Benzo[1,3]dioxol-5-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{15}N_5O_2$ $(M+H)^+$ at m/z = 334.

Example 36



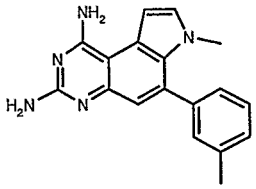
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-aminobenzeneboronic acid there was produced 6-(3-Amino-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{16}N_6$ $(M+H)^+$ at m/z = 305.

Example 37



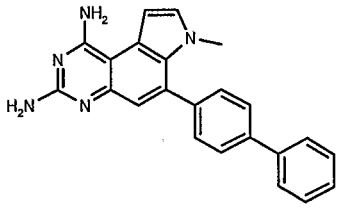
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-fluorophenylboronic acid there was produced 6-(4-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{14}FN_5$ $(M+H)^+$ at m/z = 308.

Example 38



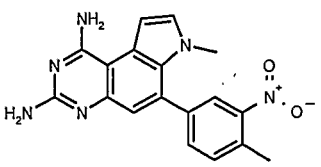
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-methylphenylboronic acid there was produced 7-Methyl-6-m-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{18}H_{17}N_5$ $(M+H)^+$ at m/z = 304.

Example 39



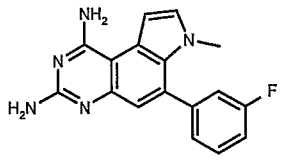
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-biphenylboronic acid there was produced 6-Biphenyl-4-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{23}H_{19}N_5$ $(M+H)^+$ at m/z = 366.

Example 40



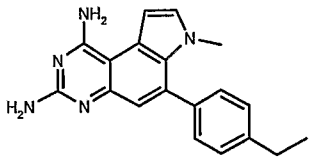
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-methyl-3-nitrophenylboronic acid there was produced 7-methyl-6-(4-methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{18}H_{16}N_6O_2$ $(M+H)^+$ for m/z = 349.

Example 41



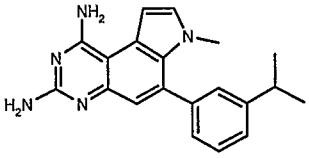
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-fluorophenylboronic acid there was produced 6-(3-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{14}FN_5$ $(M+H)^+$ at m/z = 308.

Example 42



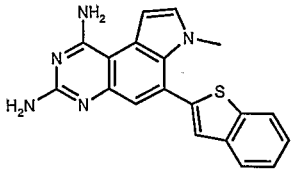
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-ethylphenylboronic acid there was produced 6-(4-Ethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{19}H_{19}N_5$ $(M+H)^+$ at m/z = 318.

Example 43



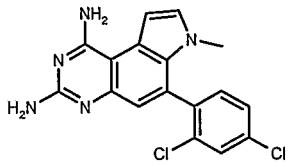
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (3-isopropylphenyl)boronic acid there was produced 6-(3-Isopropyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{20}H_{21}N_5$ $(M+H)^+$ at m/z = 332.

Example 44



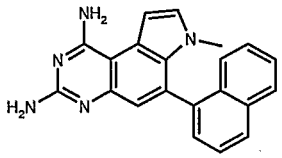
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and benzo[B]thiphene-2-boronic acid there was produced 6-Benzo[b]thiophen-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{19}H_{15}N_5S$ $(M+H)^+$ at m/z = 346.

Example 45



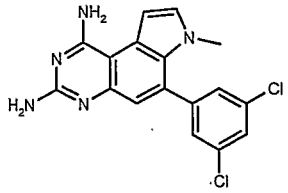
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,4-dichlorophenylboronic acid there was produced 6-(2,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{13}Cl_2N_5$ $(M+H)^+$ at m/z = 358.

Example 46



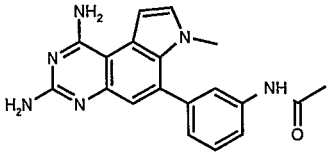
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3diamine and 1-naphthaleneboronic acid there was produced 7-Methyl-6-naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{21}H_{17}N_5$ $(M+H)^+$ at m/z = 340.

Example 47



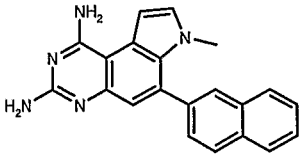
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3,5-dichlorophenylboronic acid there was produced 6-(3,5-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{13}Cl_2N_5$ $(M+H)^+$ at m/z = 358.

Example 48



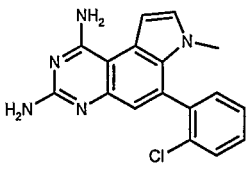
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (3-acetylaminophenyl)boronic acid there was produced N-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide trifluoro-acetic acid salt as a white solid; LRMS for $C_{19}H_{18}N_6O$ $(M+H)^+$ at m/z = 347.

Example 49



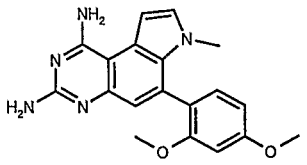
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and naphthalene-2-boronic acid there was produced 7-Methyl-6-naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{21}H_{17}N_5$ $(M+H)^+$ at m/z = 340.

Example 50



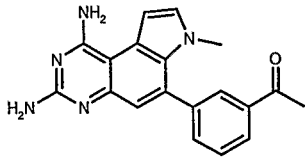
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-chlorophenylboronic acid there was produced 6-(2-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{14}ClN_5$ $(M+H)^+$ at m/z = 324.

Example 51



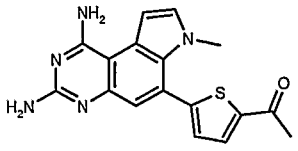
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,4-dimethoxyphenylboronic acid there was produced 6-(2,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a white solid; LRMS for $C_{19}H_{19}N_5O_2$ $(M+H)^+$ at m/z = 350.

Example 52



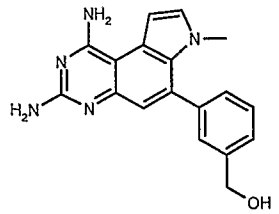
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-acetylphenylboronic acid there was produced 1-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone trifluoro-acetic acid salt as a white solid; LRMS for $C_{19}H_{17}N_5O$ $(M+H)^+$ at m/z = 332.

Example 53



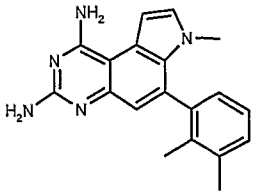
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-acetyl-2-thiopheneboronic acid there was produced 1-[5-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone trifluoro-acetic acid salt as a white solid; LRMS for $C_{17}H_{15}N_5OS$ $(M+H)^+$ at m/z = 338.

Example 54



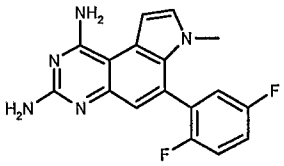
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (3-hydroxymethylphenyl)boronic acid there was produced [3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-methanol trifluoro-acetic acid salt; LRMS for $C_{18}H_{17}N_5O$ $(M+H)^+$ at m/z = 320.

Example 55



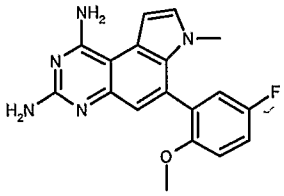
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,3-dimethylphenylboronic acid there was produced 6-(2,3-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{19}N_5$ $(M+H)^+$ at m/z = 318.

Example 56



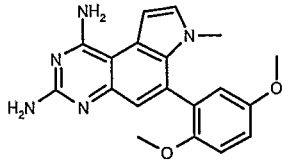
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,5-difluorophenylboronic acid there was produced 6-(2,5-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{13}F_2N_5$ $(M+H)^+$ at m/z = 326.

Example 57



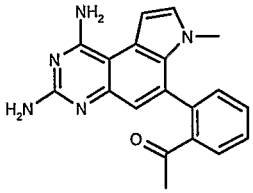
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-fluoro-2-methoxyphenylboronic acid there was produced 6-(5-Fluoro-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{16}FN_5O$ $(M+H)^+$ at m/z = 338.

Example 58



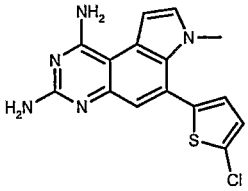
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,5-dimethoxyphenylboronic acid there was produced 6-(2,5-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS m/z calcd for $C_{19}H_{19}N_5O_2$ $(M+H)^+$ at m/z = 350.

Example 59



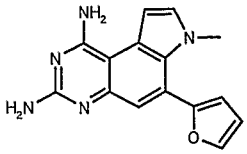
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-acetylphenylboronic acid there was produced 1-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone trifluoro-acetic acid salt; LRMS for $C_{19}H_{17}N_5O$ $(M+H)^+$ at m/z = 332.

Example 60



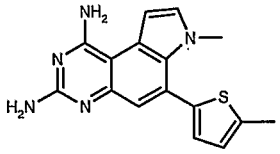
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-chlorothiophene-2-boronic acid there was produced 6-(5-Chloro-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{15}H_{12}ClN_5S$ $(M+H)^+$ at m/z = 330.

Example 61



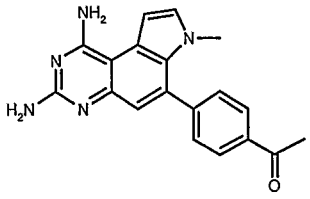
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and furan-2-boronic acid there was produced 6-Furan-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{15}H_{13}N_5O$ $(M+H)^+$ at m/z = 280.

Example 62



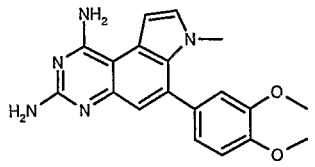
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-methylthiophene-2-boronic acid there was produced 7-Methyl-6-(5-methyl-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as an off-white solid; EI-HRMS m/e calcd. for $C_{16}H_{15}N_5S$ $(M+H)^+$ 310.1121, found 310.1125.

Example 63



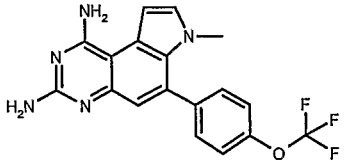
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-acetylphenylboronic acid there was produced 1-[4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone trifluoro-acetic acid salt; LRMS for $C_{19}H_{17}N_5O$ $(M+H)^+$ at m/z = 332.

Example 64



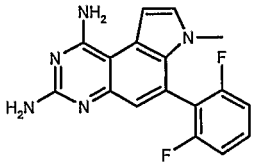
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3,4-dimethoxyphenylboronic acid there was produced 6-(3,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{19}N_5O_2$ $(M+H)^+$ at m/z = 350.

Example 65



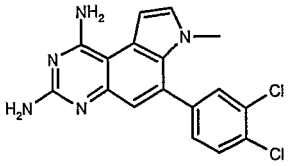
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-(trifluoromethoxy)benzeneboronic acid there was produced 7-Methyl-6-(4-trifluoromethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{14}F_3N_5O$ $(M+H)^+$ at m/z = 374.

Example 66



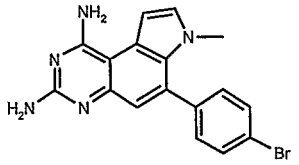
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,6-difluorophenylboronic acid there was produced 6-(2,6-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{13}F_2N_5$ $(M+H)^+$ at m/z = 326.

Example 67



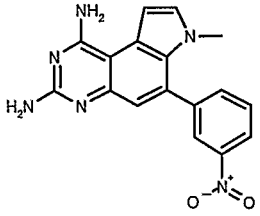
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3,4-dichlorophenylboronic acid there was produced 6-(3,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{13}Cl_2N_5$ $(M+H)^+$ at m/z = 358.

Example 68



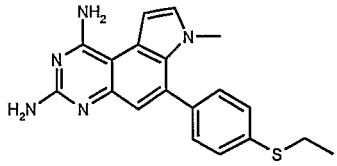
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-bromophenylboronic acid there was produced 6-(4-Bromo-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{14}BrN_5$ $(M+H)^+$ at m/z = 368.

Example 69



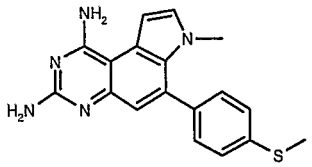
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-nitrophenylboronic acid there was produced 7-methyl-6-(3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{14}N_6O_2$ $(M+H)^+$ at m/z = 335.

Example 70



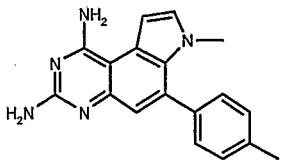
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-(ethylthio)phenylboronic acid there was produced 6-(4-Ethylsulfanyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{19}N_5S$ $(M+H)^+$ at m/z = 350.

Example 71



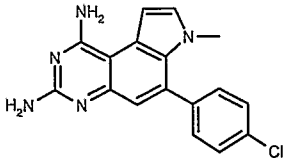
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-(methylthio)phenylboronic acid there was produced 7-Methyl-6-(4-methylsulfanyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{17}N_5S$ $(M+H)^+$ at m/z = 336.

Example 72



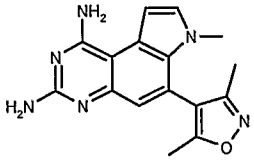
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-methylphenylboronic acid there was produced 7-Methyl-6-p-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{17}N_5$ $(M+H)^+$ at m/z = 304.

Example 73



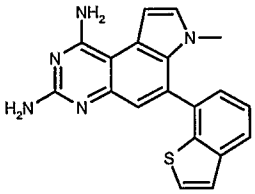
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-chlorophenylboronic acid there was produced 6-(4-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{14}ClN_5$ $(M+H)^+$ at m/z = 324.

Example 74



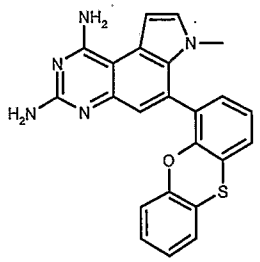
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3,5-dimethylisoxazole-4-boronic acid there was produced 6-(3,5-Dimethyl-isoxazol-4-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{16}H_{16}N_6O$ $(M+H)^+$ at m/z = 309.

Example 75



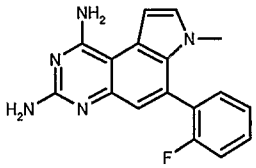
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and benzothiophene-7-boronic acid there was produced 6-(3,5-6-Benzo[b]thiophen-7-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{15}N_5S$ $(M+H)^+$ at m/z = 346.

Example 76



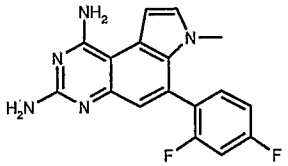
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and phenoxathiin-4-boronic acid there was produced 7-Methyl-6-phenoxathiin-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{23}H_{17}N_5OS$ $(M+H)^+$ at m/z = 412.

Example 77



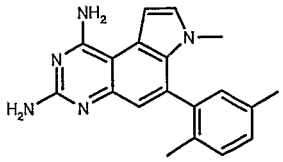
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-fluorophenylboronic acid there was produced 6-(2-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{14}FN_5$ $(M+H)^+$ at m/z = 308.

Example 78



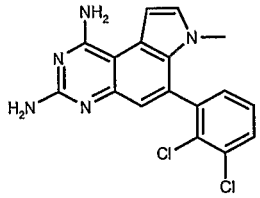
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,4-difluorobenzeneboronic acid there was produced 6-(2,4-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{13}F_2N_5$ $(M+H)^+$ at m/z = 326.

Example 79



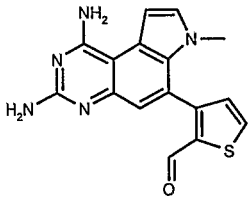
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,5-dimethylphenylboronic acid there was produced 6-(2,5-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{19}N_5$ $(M+H)^+$ at m/z = 318.

Example 80



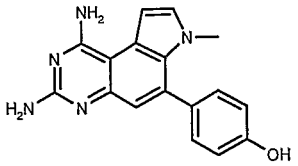
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,3-dichlorophenylboronic acid there was produced 6-(2,3-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{13}Cl_2N_5$ $(M+H)^+$ at m/z = 358.

Example 81



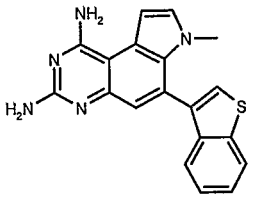
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-formyl-3-thiopheneboronic acid there was produced 3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophene-2-carbaldehyde trifluoro-acetic acid salt; LRMS for $C_{16}H_{13}N_5OS$ $(M+H)^+$ at m/z = 324.

Example 82



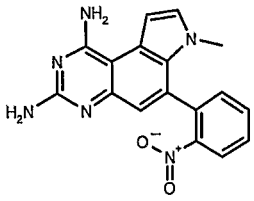
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (4-hydroxyphenyl)boronic acid there was produced 4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol trifluoro-acetic acid salt; LRMS for $C_{17}H_{15}N_5O$ $(M+H)^+$ at m/z = 306.

Example 83



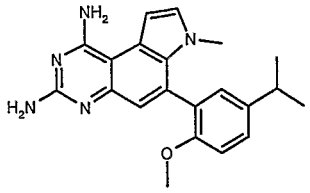
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 1-benzothiophen-3-ylboronic acid there was produced 6-Benzo[b]thiophen-3-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{15}N_5S$ $(M)^+$ at m/z = 345.

Example 84



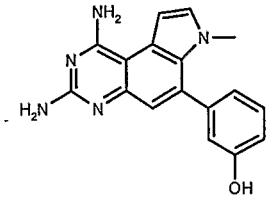
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (2-nitrophenyl)boronic acid there was produced 7-methyl-6-(2-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{14}N_6O_2$ $(M+H)^+$ at m/z = 335.

Example 85



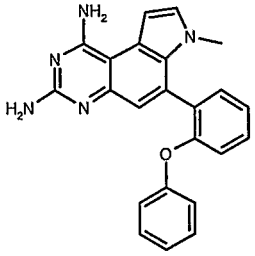
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-isopropyl-2-methoxybenzeneboronic acid there was produced 6-(5-Isopropyl-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{21}H_{23}N_5O$ $(M+H)^+$ at m/z = 362.

Example 86



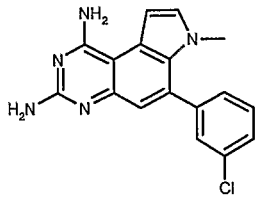
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and (3-hydroxyphenyl)boronic acid there was produced 3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol trifluoro-acetic acid salt; LRMS for $C_{17}H_{15}N_5O$ $(M+H)^+$ at m/z = 306.

Example 87



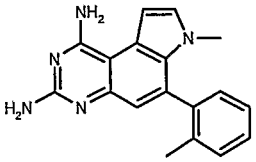
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-(phenoxy)phenylboronic acid there was produced 7-Methyl-6-(2-phenoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{23}H_{19}N_5O$ $(M+H)^+$ at m/z = 382.

Example 88



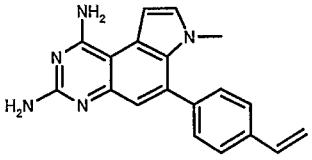
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-chlorophenylboronic acid there was produced 6-(3-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{14}ClN_5$ $(M+H)^+$ at m/z = 324.

Example 89



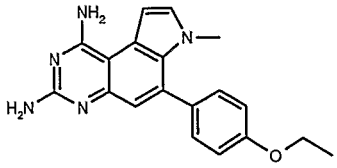
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and o-tolylboronic acid there was produced 7-Methyl-6-o-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{17}N_5$ $(M+H)^+$ at m/z = 304.

Example 90



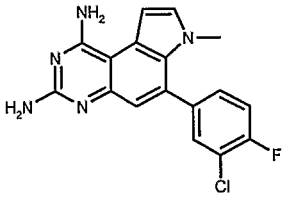
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-vinylphenylboronic acid there was produced 7-Methyl-6-(4-vinyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{17}N_5$ $(M+H)^+$ at m/z = 316.

Example 91



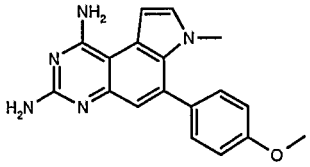
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-ethoxyphenylboronic acid there was produced 6-(4-Ethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{19}N_5O$ $(M+H)^+$ at m/z = 334.

Example 92



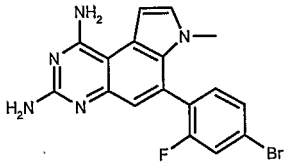
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-chloro-4-fluorophenylboronic acid there was produced 6-(3-Chloro-4-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{13}ClFN_5$ $(M+H)^+$ at m/z = 342.

Example 93



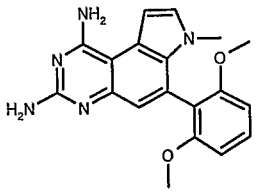
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-methoxyphenylboronic acid there was produced 6-(4-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{18}H_{17}N_5O$ $(M+H)^+$ at m/z = 320.

Example 94



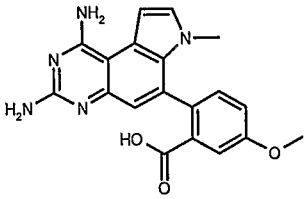
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 4-bromo-2-fluorobenzeneboronic acid there was produced 6-(4-Bromo-2-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{17}H_{13}BrFN_5$ $(M+H)^+$ at m/z = 386.

Example 95



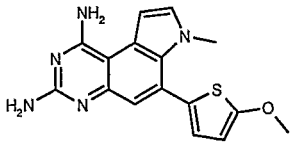
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2,6-dimethoxyphenylboronic acid there was produced 6-(2,6-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt; LRMS for $C_{19}H_{19}N_5O_2$ $(M+H)^+$ at m/z = 350.

Example 96



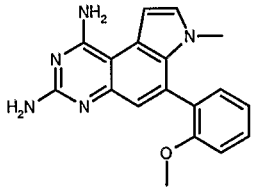
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-*tert*-butoxycarbonyl-4-methoxyphenylboronic acid there was produced 2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-5-methoxy-benzoic acid trifluoro-acetic acid salt; LRMS for $C_{19}H_{17}N_5O_3$ $(M+H)^+$ at m/z = 364.

Example 97



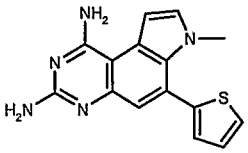
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 5-methoxy thiopheneboronic acid there was produced 6-(5-Methoxy-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a light yellow solid; EI-HRMS m/e calcd for $C_{16}H_{15}N_5OS$ (M^+) 325.0997, found 325.0994.

Example 98



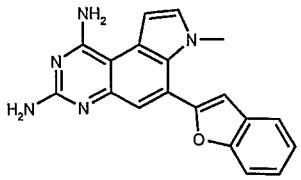
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-methoxyphenylboronic acid there was produced 6-(2-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a light brown solid; LRMS for $C_{18}H_{17}N_5O$ $(M+H)^+$ at m/z = 320.

Example 99



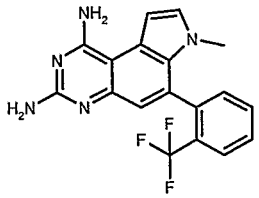
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and thiophene-2-boronic acid there was produced 7-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a light yellow solid; LRMS for $C_{15}H_{13}N_5S$ $(M+Na)^+$ at m/z = 318.

Example 100



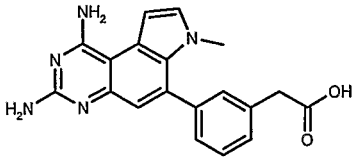
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and benzo[B]furan-2-boronic acid there was produced 6-Benzofuran-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a yellow solid; LRMS for $C_{19}H_{15}N_5O$ $(M+H)^+$ at m/z = 330.

Example 101



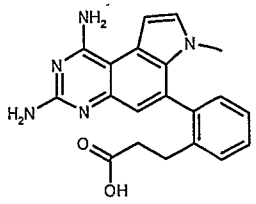
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-(trifluoromethyl)benzeneboronic acid there was produced 7-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a yellow solid; LRMS for $C_{18}H_{14}F_3N_5$ $(M+H)^+$ at m/z = 358.

Example 102



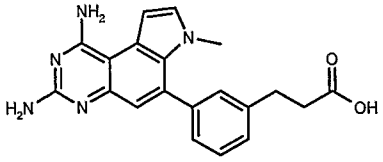
From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and [3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-acetic acid there was produced [3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid; LRMS for $C_{19}H_{17}N_5O_2$ $(M+H)^+$ at m/z = 348.

Example 103



From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-[2-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionic acid there was produced 3-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid; LRMS for $C_{20}H_{19}N_5O_2$ $(M+H)^+$ at m/z = 362.

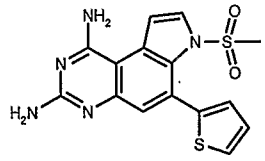
Example 104



From 6-iodo-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-[3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionic acid there was produced 3-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid; LRMS for $C_{20}H_{19}N_5O_2$ $(M+H)^+$ at m/z = 362.

Example 105

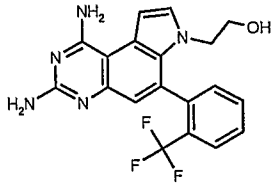
7-Methanesulfonyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt



To a slurry of 6-Thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine (example 100), prepared as described in example 1 from 6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **VI** and 2-thiopheneboronic acid, (50 mg, 0.178 mmole) in anhydrous DMF (3 ml) at room temperature was added sodium hydride (60% in mineral oil, 8 mg, 0.20 mmole) and the mixture was stirred at room temperature for 45 minutes. The above mixture was cooled in an ice bath, methanesulfonyl chloride was slowly added dropwise (0.016 ml, 0.207 mmole) and stirred at 0°C

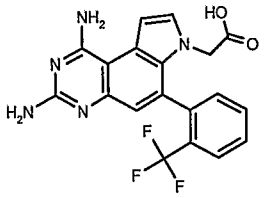
for 30 minutes. The mixture was then warmed up to room temperature and stirred overnight. Additional amounts of sodium hydride (8 mg) and methanesulfonyl chloride (0.016 ml) was added the next day to drive the reaction to completion and the mixture was stirred at room temperature for an additional 20 hours. The mixture was evaporated to dryness and the crude mixture was purified by reversed phase HPLC to give 7-Methanesulfonyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a light brown solid; LRMS m/z calcd for $C_{15}H_{13}N_5O_2S_2$ $(M+H)^+$ at m/z = 360.

Example 106



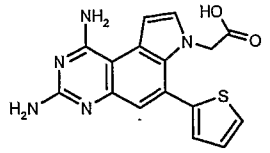
From 2-(1,3-Diamino-6-iodo-pyrrolo[3,2-f]quinazolin-7-yl)-ethanol and 2-(trifluoromethyl)benzeneboronic acid there was produced 2-[1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-ethanol trifluoro-acetic acid salt as an off-white solid; LRMS for $C_{19}H_{16}F_3N_5O$ $(M+H)^+$ at m/z = 388.

Example 107



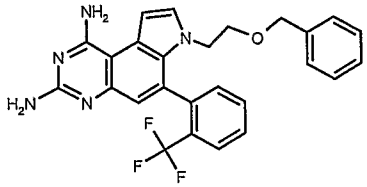
From (1,3-Diamino-6-iodo-pyrrolo[3,2-f]quinazolin-7-yl)-acetic acid and 2-(trifluoromethyl)benzeneboronic acid there was produced [1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-acetic acid trifluoro-acetic acid salt as an off-white solid; LRMS for $C_{19}H_{14}F_3N_5O_2$ $(M+H)^+$ at m/z = 402.

Example 108



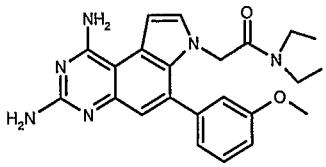
From (1,3-Diamino-6-iodo-pyrrolo[3,2-f]quinazolin-7-yl)-acetic acid and thiophene-2-boronic acid there was produced (1,3-Diamino-6-thiophen-2-yl-pyrrolo[3,2-f]quinazolin-7-yl)-acetic acid trifluoro-acetic acid salt as an off-white solid; LRMS for $C_{16}H_{13}N_5O_2S$ $(M+H)^+$ at m/z = 340.

Example 109



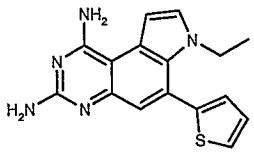
From 7-(2-Benzyloxy-ethyl)-6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 2-(trifluoromethyl)benzeneboronic acid there was produced 7-(2-Benzyloxy-ethyl)-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt as a light brown solid; LRMS for $C_{26}H_{22}F_3N_5O$ $(M+H)^+$ at m/z = 478.

Example 110



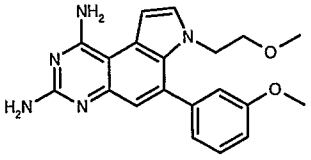
From 2-(1,3-Diamino-6-iodo-pyrrolo[3,2-f]quinazolin-7-yl)-N,N-diethyl-acetamide and 3-methoxyphenylboronic acid there was produced 2-[1,3-Diamino-6-(3-methoxy-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-N,N-diethyl-acetamide as a yellow solid; LRMS for $C_{23}H_{26}N_6O_2$ $(M+H)^+$ at m/z = 419.

Example 111



From 7-Ethyl-6-iodo-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and thiophene-2-boronic acid there was produced 7-Ethyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as an off-white solid; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.69 (d, J = 5.13 Hz, 1H), 7.49 (d, J = 2.56 Hz, 1H), 7.27 (m, 1H), 7.18 (m, 1H), 7.14 (d, J = 2.56 Hz, 1H), 6.91 (s, 1H), 6.81 (broad s, 2H), 5.82 (broad s, 2H), 3.82 (q, J = 6.96 Hz, 2H), 0.99 (t, J = 6.96 Hz, 3H).

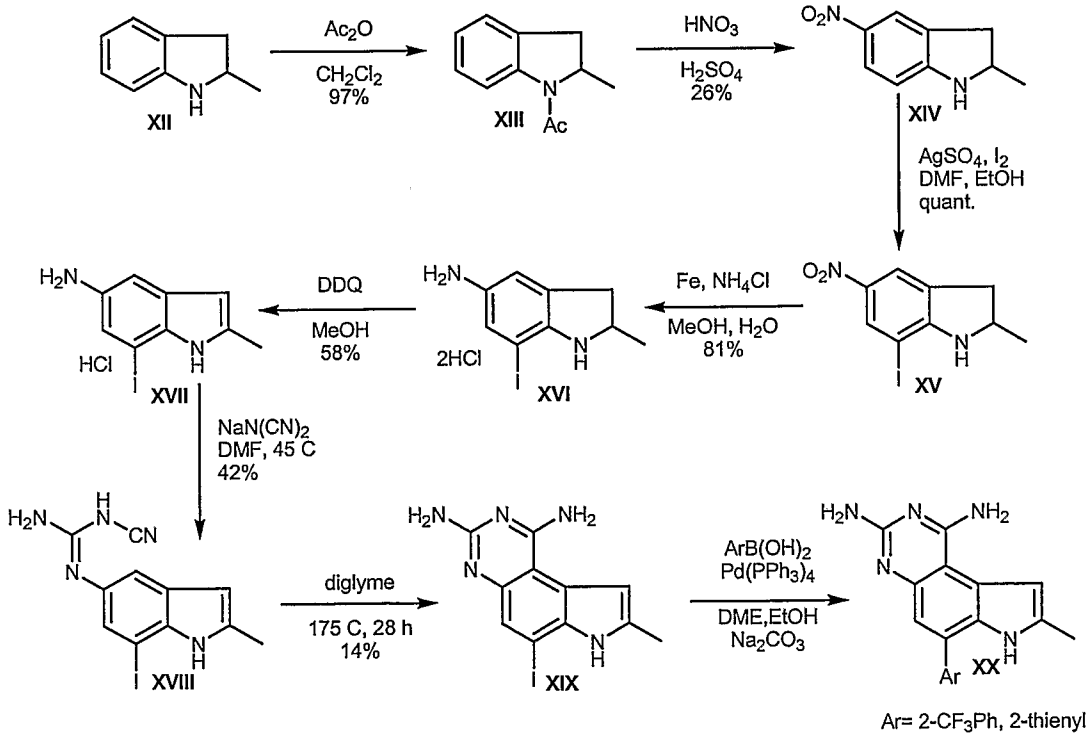
Example 112



From 6-Iodo-7-(2-methoxy-ethyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine and 3-methoxyphenylboronic acid there was produced 7-(2-Methoxy-ethyl)-6-(3-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a light-brown solid; LRMS for $C_{20}H_{21}N_5O_2$ $(M+H)^+$ at m/z = 364.

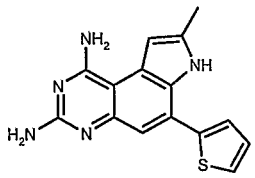
Scheme 5 is directed to the synthesis of 8 methyl derivatives.

SCHEME 5



Example 113

8-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoroacetic acid salt



To a cooled (0-10C) mixture of concentrated nitric acid (12 mL) and concentrated sulfuric acid (40 mL) was added 1-acetyl-2-methyl-indoline **XII** (12.5g, 0.0713 moles), prepared by an analgous method to that described in *Chem.Ber.*; 14; **1881**; 890, in small portions so that the internal temperature of the reaction remained between 10-20°C. The resulting mixture was allowed to stir at 5-10°C overnight. The mixture was poured slowly into 300 mL of cold water and the precipitate that formed was collected by filtration, washed with water and redissolved in an ethanol-6N HCl solution and warmed to reflux for 30 minutes. The resulting solution was concentrated, EtOAc was added and the Ph of the solution adjusted to 10. The organic phase was separated and dried over $MgSO_4$. The mixture was filtered, and evaporated and the crude material purified by column chromatography (50% EtOAc-Hexane) to give 3.31g, 26% of 2-methyl-5-nitro-2,3-dihydro-1H-indole **XIII**: LRMS for $C_9H_{10}N_2O_2$ $(M+H)^+$ at m/z = 179.

A mixture of silver sulfate (4.92 g, 0.0157 mol) and iodine (4 g, 0.0.0157 mol) in *N,N*-dimethylformamide (50 mL) and ethanol (100 mL) was treated with 2-methyl-5-nitro-2,3-dihydro-1H-indole **XIII** (3.31 g, 0.015 mol) and the resulting mixture was stirred at 25°C for 30 min before an additional 1 g of iodine was added and the stirring continued for 2 h. The resulting reaction mixture was filtered and the solids washed with ethyl acetate before being concentrated *in vacuo* to a volume of approximately 50 mL. This solution was treated with a 1.0N aqueous sodium thiosulfate solution (100 mL) and a saturated aqueous sodium chloride solution (200 mL). The resulting precipitate was collected by filtration, washed with water and petroleum ether, and dried *in vacuo* to 7-iodo-2-methyl-5-nitro-2,3-dihydro-1H-indole **XIV** as a yellow solid: LRMS for $C_9H_9IN_2O_2$ $(M+H)^+$ at m/z = 305.

A solution of 7-iodo-2-methyl-5-nitro-2,3-dihydro-1H-indole **XIV** (4.75 g, 0.0156 mol) in methanol (150 mL) at 25°C was treated with a solution of ammonium chloride (5.22 g, 0.0976 mol) in water (150 mL) and iron powder (3 g, 0.0534 mol). The mixture was heated to 100°C under a nitrogen atmosphere for 6 h. The reaction mixture was filtered hot through a pad of celite and washed with hot methanol. The filtrate was concentrated in vacuo and the residue partitioned between methylene chloride and water. The layers were separated and the pH of the aqueous layer was adjusted to pH=10 with ammonium hydroxide. The aqueous layer was extracted with methylene chloride and the combined organic layers were dried over sodium sulfate, filtered, and concentrated *in vacuo* to a volume of 50 mL. The resulting solution was treated with a 4.0M aqueous hydrochloric acid solution in dioxane and then stirred at 25°C for 1 h. The precipitate was collected by filtration and washed with methylene chloride and petroleum ether to afford 7-iodo-2-methyl-1H-indol-5-ylamine hydrochloride **XV** (4.37 g, 81%) as a gray solid: LRMS for freebase $C_9H_{11}IN_2$ $(M+H)^+$ at m/z = 275.

A solution of 7-iodo-2-methyl-1H-indol-5-ylamine hydrochloride **XV** (4.3 g, 12.39 mmol) in methanol (200 mL) at 25°C was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (2.8 g, 12.39 mmol) in portions. The resulting dark solution was concentrated *in vacuo* and partitioned between water and methylene chloride, the pH was adjusted to 10 by the addition of with ammonium hydroxide, the organic layer separated and filtered and the aqueous layer extracted 3x100 mL with methylene chloride. The organic layers were combined, dried over magnesium sulfate and charcoal. The mixture was filtered and concentrated to 100 mL in volume before 20 mL of a 4.0 M HCL in dioxane solution was added. The resulting mixture was stirred at room temperature for 1 h and the precipitate formed was isolated by filtration, washed well with ether and dried to give 7-iodo-2-methyl-1H-indol-5-ylamine hydrochloride **XVI** (1.94 g, 58%) as a grey solid: LRMS for freebase $C_9H_9IN_2$ $(M+H)^+$ at m/z = 273.

A solution of 7-iodo-2-methyl-1H-indol-5-ylamine hydrochloride **XVII** (1.9 g, 6.158 mmol) in *N,N*-dimethylformamide (30 mL) at 25°C was treated with sodium dicyanamide (1.37 g, 15.397 mmol) and then warmed to 45°C for 4 h. The resulting mixture filtered and concentrated *in vacuo* and the residue treated with

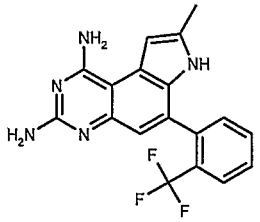
water (20 mL). The resulting mixture was allowed to stand at 25°C for 2.5 h during which time a solid formed. The solid was collected by filtration and washed with water, resuspended in methanol, filtered and dried to give N''-cyano-N-(7-iodo-2-methyl-1H-indol-5-yl)guanidine **XVIII** (0.88 g, 42%) as a light grey solid: LRMS for $C_{11}H_{10}IN_5$ $(M-H)^+$ at m/z = 338.

A solution of N''-cyano-N-(7-iodo-2-methyl-1H-indol-5-yl)guanidine **XVIII** (0.86 g, 2.54 mmol) in 2-methoxyethyl ether (20 mL) was heated to 175°C for 28 h. The reaction mixture was cooled to 25°C and the solid formed was removed by filtration and washed with methanol. The filtrate was concentrated *in vacuo* and the residue triturated with methanol and ether to give a brown solid which was isolated by filtration and dried to give 6-iodo-8-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **XIX** (120 mg, 14%) as a brown solid: LRMS for $C_{11}H_{10}IN_5$ $(M+H)^+$ at m/z = 340.

A solution of 6-iodo-8-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine **XIX** (20 mg, 0.06 mmol) in ethylene glycol dimethyl ether (5.0 mL) and ethanol (2.5 mL) at 25°C was treated with 2-thiopheneboronic acid (11 mg, 0.09 mmol), a 2 M aqueous sodium carbonate solution (2.5 mL), and tetrakis(triphenylphosphine)-palladium (0) (0.3 mg, 0.0026 mmol). The resulting mixture was heated to 80°C for 3 h, cooled and pre-absorbed onto silica gel and purified by flash chromatography (Merck Silica gel 60, 230-400 mesh, 90/10/1 methylene chloride/methanol/ammonium hydroxide) followed by reversed phase HPLC (Zorbax 21.2 x 100 mmSB C18 column, 15 min 95/5 to 5/95 water/acetonitrile 0.075% TFA gradient) to afford 8-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine trifluoro-acetic acid salt **XX** (4 mg, 25%) as a lyophilized solid; LRMS for freebase $C_{15}H_{13}N_5S_2$ $(M+H)^+$ at m/z = 296.

(B) In an analogous manner, there were obtained:

Example 114



From 6-iodo-8-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine 2-(trifluoromethylbenzene)boronic acid 8-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine as a lyophilized solid; LRMS for $C_{18}H_{14}F_3N_5$ $(M+H)^+$ at m/z = 358.

Example 115

In vitro inhibition of PTP1B

Enzymes

Human PTP1B (1-321) was cloned from a human cDNA library using conventional molecular biology techniques. The cDNA sequence was identical to the published human PTP1B sequence (Accession number M33689). The protein was expressed and purified from E. coli as described by Barford D. et.al, *J. Mol Biol* (1994) 239, 726-730).

Example 116

PTPase assays

The measurement of PTPase activity was carried out using one of two methods:

The first method for the measurement of PTP1B inhibitory activity a tyrosine phosphorylated peptide based on the amino acid sequence of insulin receptor tyrosine autophosphorylation site 1146 (TRDI(pY)E) was used as substrate. The reaction conditions were as follows:

PTP1B (0.5-2nM) was incubated with compound for 15 min in buffer containing 37.5 mM Bis-Tris buffer pH 6.2, 140mMNaCl, 0.05% BSA and 2mM DTT. The reaction was started by the addition of 50μM substrate. After 20 min at room temperature (22-25°C) the reaction was stopped with KOH and the amount of free phosphate measured using Malachite Green as previously described. (Harder et al. 1994 *Biochem J.* 298; 395).

The second method was used for the measurement of general PTPase inhibitory activity across a panel of PTPases the substrate (6,8-difluoro-4-methylumbelliferyl phosphate (DiFMUP; from Molecular Probes) was used at the Km for each enzyme. The buffer conditions were identical as in the Malachite Green assay. The reaction was stopped with KOH. In this case the dephosphoryated product

becomes fluorescent and the fluorescence read. (Excitiation:360mM/Emmission: 460nM).

For kinetic experiments the same buffer conditions were used except that the reaction was started using enzyme and the reaction stopped after 10 minutes.

The IC50 values (in μM) for the PTP1B inhibitory activity of the compounds in the present application are in the range of 0.1 μM to 500 μM, preferably 1 μM to 100 μM. The most preferred compounds show an IC50 of < 30.0 μM.

Examples of the some compounds with its corresponding IC50 values are

Example	IC50 (μM)
2	23.79
6	29.22
8	24.11

Example 117

Glucose Uptake Assay

The day before the assay the SKMC media was changed to high glucose DMEM , 25mM Hepes, pH 7.0 and 2% Charcoal/dextran treated FBS for 19 hours.

On the morning of the assay, cells were starved for max. 2 hours in low glucose (5.5mM glucose) DMEM, 25 mM Hepes, pH 7.0 and 0.5% BSA. The starvation medium was removed and replaced with test medium (150mMNaCl, 25mM Hepes, pH 7.0) containing either 1% DMSO, or test compound diluted in DMSO or Porcine Insulin to a final concentrations of 1, 0.1, 0.05, 0.01 and 0.01μM. Each assay point was performed in triplicate. The cells were incubated for 45 min at 37°C. 10μM Cytochalasin B (CB) was added to appropriate wells to stop the active glucose transport (i.e. GLUT 1 & 4). At this point 2-Deoxy-D(U-^{14}C) glucose (Amersham, Code CFB195, 200uCi/ml) was added to all wells to a final concentration of 0.8 μCi/ml. The cells were incubated for an additional 45 minutes at 37°C in an incubator. Cells were then very gently washed for three times in PBS (RT). The cells were then lysed with the addition of 0.05% NaOH solution for 20min at RT. The lysate was transferred to a scintillation vial containing 5 ml of scintillation fluid and counted in a Beckman LS6500 Scintillation counter. Analysis of results: The counts obtained with CB (passive

glucose transport values) were subtracted from every value obtained with PI (or compounds) in order to evaluate only active glucose transport. Fold increase was calculated by dividing values in the presence of PI (or compounds) by the value obtained in the presence of DMSO (control). Compounds were considered to be active when they increase glucose uptake at least 25% of the Porcine Insulin response at 0.05µM.

Example 118

In vivo inhibition of PTP1B: Effects of compounds on blood glucose levels in mouse model

To measure the anti-diabetic effect compounds were tested in well established rodent *in vivo* models of type 2 diabetes and obesity.

Diet induced obese C57BL6/J mice (DIO mice)

Mice that have type 2 diabetes were be generated by maintaining them on a high fat diet for a 4-6 months (Diabetes vol. 37 Sept 1988). Male C57Bl6/J mice (age 3 - 4 weeks) were placed on high fat diet for 4-6 months. At this time, they were hyperglycemic and hyperinsulinemic and weighed 40-50 g. DIO mice (n=10) were weighed and fasted for a two hour period prior to oral treatment. Immediately prior to dosing a pre-dose blood glucose reading was taken by snipping off a portion of the tail and collecting blood from the tail vein. Mice were treated either with a single dose of compound (acute) or once a day for 5 days (sub- chronic). For the acute studies glucose was generally measured at 2h, 4h, 6h, 8h post treatment. Compounds were considered active if they showed a statistically significant ($p \leq 0,05$) glucose lowering (>15%) compared to the vehicle treated animals.

For sub-chronic (5 day) studies mice were dosed once a day by gavage as described above. On day five, glucose was measured prior to dosing (0 time) and 2 hours after dosing. Insulin and triglycerides were measured at 2 hour post dose. Compounds were considered active if they showed a statistically significant ($p \leq 0,05$) glucose, insulin and triglyceride lowering compared to the vehicle treated animals.

Example A

Tablets containing the following ingredients can be manufactured in a conventional manner:

Ingredients	Per tablet
Compound of formula (I)	10.0 - 100.0 mg
Lactose	125.0 mg
Maize starch	75.0 mg
Talc	4.0 mg
Magnesium stearate	1.0 mg

Example B

Capsules containing the following ingredients can be manufactured in a conventional manner:

Ingredients	Per capsule
Compound of formula (I)	25.0 mg
Lactose	150.0 mg
Maize starch	20.0 mg
Talc	5.0 mg

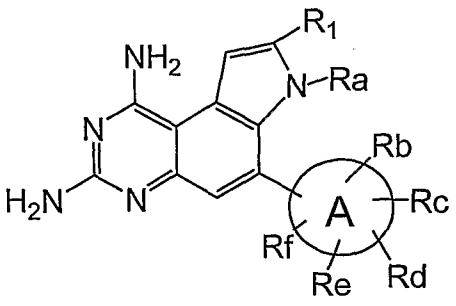
Example C

Injection solutions can have the following composition:

Compound of formula (I)	3.0 mg
Gelatine	150.0 mg
Phenol	4.7 mg
Sodium carbonate	to obtain a final pH of 7
Water for injection solutions	ad 1.0 ml

Claims

1. Compounds of the formula (I):



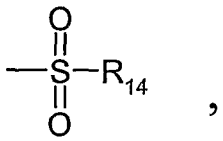
(I)

or pharmaceutically acceptable salts thereof, wherein

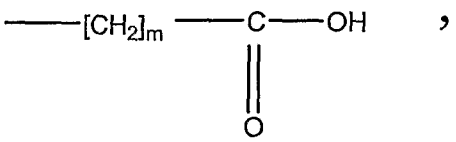
A is a 5- or 6-membered unsaturated or saturated hydrocarbon ring or a 5- or 6-membered unsaturated or saturated ring that contains at least one heteroatom selected from S, N or O,

R1 is hydrogen or lower alkyl,

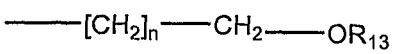
Ra is hydrogen, lower alkyl,



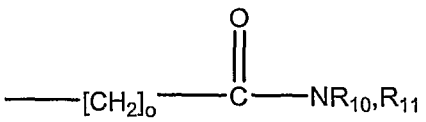
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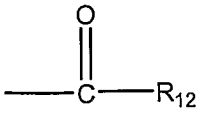


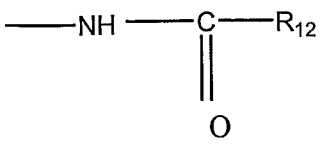
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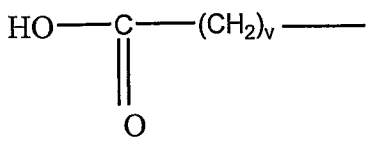
;

Rb, Rc, Rd, Re and Rf are each independently selected from the group consisting of hydrogen, lower alkyl, halogen, amino, lower alkenyl, hydroxy, alkoxy, hydroxy lower alkyl, alkylsulfanyl, perfluoroloweralkyl, perfluoroloweralkoxy, aryl, nitro, lower alkanoyl, -NR_5R_6, R_7S-, alkanoyl, alkanoylamino, carboxy, aryloxy, carboxy alkyl, substituted alkyl, or





,



,

or two of Rb, Rc, Rd, Re and Rf, when present on adjacent carbon atoms on the phenyl ring can be taken together to form a lower alkylenedioxy bridge or a ring system fused to the phenyl ring, said ring system containing one or two rings fused to the phenyl ring with at least one of said rings in said system being either an aromatic or heteroaromatic ring and the remainder ring in the system, if any, being a cycloalkyl or heterocycloalkyl ring;

R_5, R_6 and R_{14} independently are hydrogen or lower alkyl;

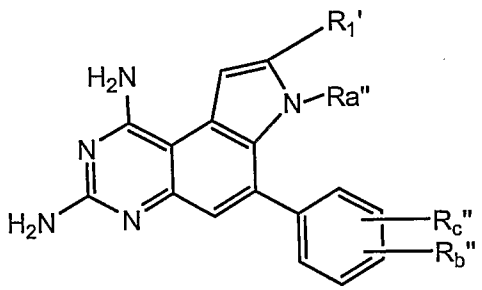
R_7 is lower alkyl;

R_{13} is hydrogen, lower alkyl, benzyl or phenyl;

R_{10}, R_{11} and R_{12} are independently hydrogen or lower alkyl; and

m, n, o and v are independent integers from 0 to 4.

2. Compounds according to claim 1, characterised by formula (I-A)

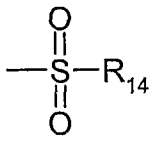


I-A

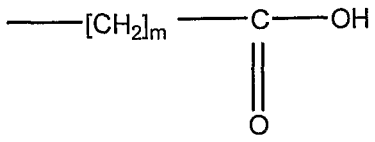
wherein

R_1' is hydrogen or lower alkyl;

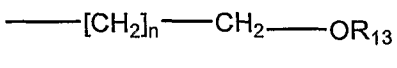
R_a'' is hydrogen, lower alkyl;



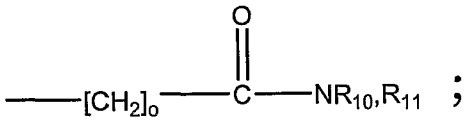
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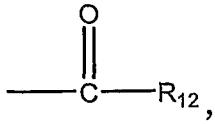


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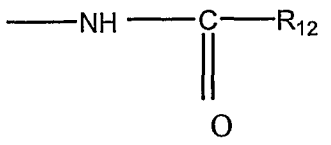


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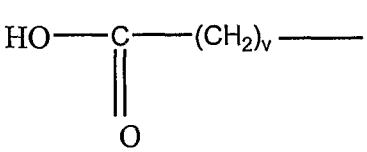
R_b'' and R_c'' are independently hydrogen, lower alkyl, lower alkenyl, lower alkoxy, hydroxy lower alkyl, perfluoroloweralklyl, nitro, halogen, lower alkanoyl, $-NR_5R_6$, R_7S-



,



,



,

phenyl, hydroxy, perfluoroloweralkoxy, or phenoxy, or R_b'' and R_c'' when present on adjacent carbon atoms on the phenyl ring can be taken together to form a lower alkylenedioxy bridge or a ring system fused to the phenyl ring, said ring system containing one or two rings fused to the phenyl ring with at least one of said rings

in said system being either an aromatic or heteroaromatic ring and the remainder ring in the system, if any, being a cycloalkyl or heterocycloalkyl ring;

R_5, R_6 and R_{14} independently are hydrogen or lower alkyl;

R_7 is lower alkyl;

R_{13} is hydrogen, lower alkyl, benzyl or phenyl;

R_{10}, R_{11} and R_{12} are independently hydrogen or lower alkyl; and

m, n, o and v are independent integers from 0 to 4,

or pharmaceutically acceptable salts thereof.

3. Compounds according to claim 2, wherein R_1' is hydrogen and R_b'' and R_c'' are substituted on adjacent carbon atoms and form a lower alkylene dioxy bridge.

4. Compounds according to claim 3, wherein R_1' is hydrogen and R_b'' and R_c'' are substituted on adjacent carbon atoms and taken together with their attached carbon atoms form a fused aromatic ring.

5. Compounds according to claim 2, wherein
R_a'' and R_b'' are substituted on adjacent carbon atoms on the phenyl ring and taken together form a fused heteroaromatic ring; and
R_1' and R_a' are independently hydrogen or lower alkyl.

6. Compounds according to claim 2, wherein R_b'' and R_c'' are attached on adjacent carbon atoms on the phenyl ring and form a two membered ring system fused on the phenyl, one of said rings being a heteroaromatic ring or a heterocycloalkyl ring and the other being an aromatic ring

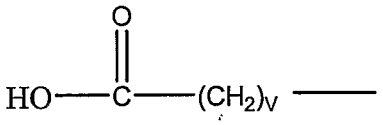
7. Compounds according to claim 2, wherein R_1' and Ra'' are independently hydrogen or lower alkyl and R_b'' and R_c'' are independently hydrogen, lower alkyl or lower alkenyl.

8. Compounds according to claim 7, wherein R_b" is lower alkenyl and R_c" is hydrogen.

9. Compounds according to claim 7, wherein R_b" is lower alkyl or hydrogen and R_c" is lower alkyl.

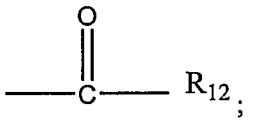
10. Compounds according to claim 2, wherein
R_1' and R_a" are hydrogen or lower alkyl,
R_b" and R_c" are individually hydrogen, halogen, trifluoromethyl; and trifluoromethoxy; and
one of R_c" and R_b" is other than hydrogen.

11. Compounds acording to claim 2, wherein
R_1' and R_a" are hydrogen or lower alkyl;
R_b" is hydrogen or halogen; and
R_c" is halogen, nitro, lower alkoxy, phenoxy, hydroxy, hydroxy lower alkyl



;

or

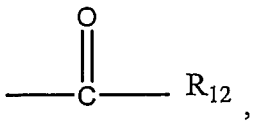


;

v is an integer from 0 to 4;
R_{12} is hydrogen or lower alkyl.

12. Compounds acording to claim 11, wherein R_b" is hydrogen or halogen and R_c" is nitro, halogen, phenoxy, lower alkoxy, hydroxy or hydroxyalkyl.

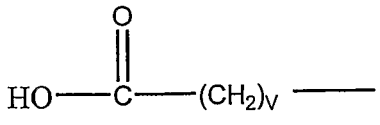
13. Compounds according to claim 11, wherein

R_a" is hydrogen, R_b" is ,

R_c" is hydrogen or lower alkyl,

R_{12} is hydrogen or lower alkyl.

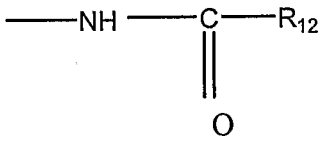
14. Compounds according to claim 11, wherein
R_b" and R_c" are hydrogen or



and

v is an integer from 0 to 4;
R_1' and R_a" are hydrogen or lower alkyl; and
one of R_b" and R_c" is other than hydrogen.

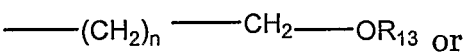
15. Compounds according to claim 2, wherein
R_1' and R_a" are independently hydrogen or lower alkyl;
R_b" and R_c"are hydrogen, R_5 R_6 N-,



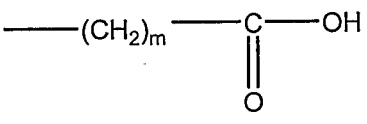
, or

R_7S-;
R_5 and R_6 are independently hydrogen or lower alkyl;
R_7 is lower alkyl;
R_{12} is hydrogen or lower alkyl; and
one of R_b" and R_c" is other than hydrogen.

16. Compounds according to claim 2, wherein
R_a" is



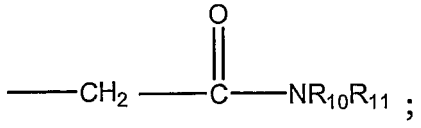
or



;

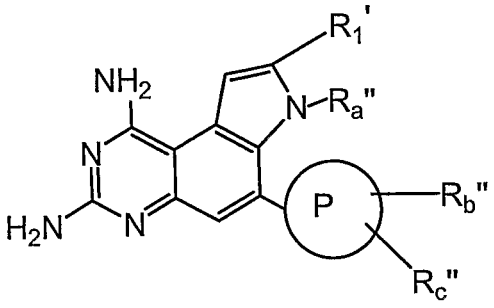
R_{13} is hydrogen, phenyl, benzyl or lower alkyl; and
m and n are independent integers from 0 to 4.

17. Compounds according to claim 2, wherein

R_a" is  ;

R_{10} and R_{11} are independently hydrogen or lower alkyl.

18. Compounds according to claim 1, characterised by formula (I-B):



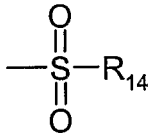
I-B

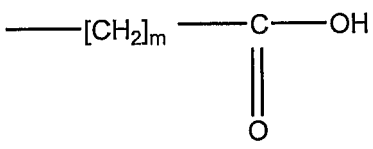
wherein

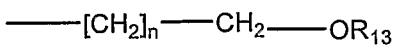
Ⓟ is a 5 or 6 membered heteroaromatic ring containing from 1 to 2 hetero atoms selected from the group consisting of oxygen, sulfur, or nitrogen;

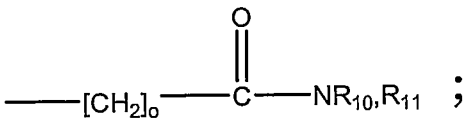
R_1' is hydrogen or lower alkyl;

R_a" is hydrogen, lower alkyl,

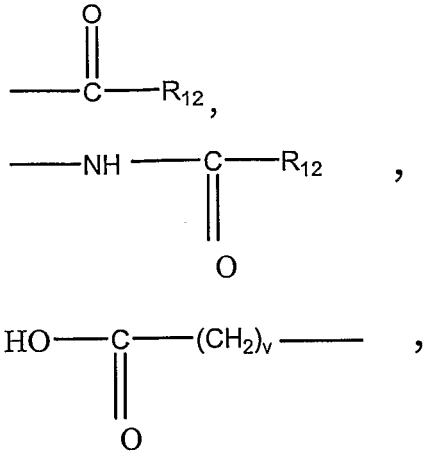
 ,

 ,

 , or

 ;

R_c" and R_b"are independently hydrogen, lower alkyl, lower alkenyl, lower alkoxy, hydroxy lower alkyl, perfluoroloweralklyl, nitro, halogen, lower alkanoyl, -NR_5R_6, R_7S-,



phenyl, hydroxy, perfluoroloweralkoxy, or R_c" and R_b"when present on adjacent carbon atoms on the heteroaromatic ring can be taken together to form a lower alkylene dioxy bridge or a ring system fused to the heteroaromatic ring, said ring system containing one or two rings fused to the heteroaromaticl ring with at least one of said rings in said system being either an aromatic or heteroaromatic ring and the remainder ring in the system, if any, being a cycloalkyl or heterocycloalkyl ring;

R_5, R_6 and R_{14} independently are hydrogen or lower alkyl;

R_7 is lower alkyl;

R_{13} is hydrogen, lower alkyl, benzyl or phenyl;

R_{10}, R_{11} and R_{12} are independently hydrogen or lower alkyl; and

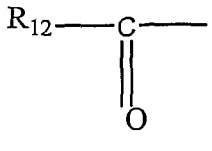
m, n, o and v are independent integers from 0 to 4
or pharmaceutically acceptable salts thereof.

19. Compounds according to claim 18, wherein Ⓟ is a heteroaromatic ring containing sulfur as the only hetero atom.

20. Compounds according to claim 19, wherein R_b" and R_c" are independently hydrogen, halogen or lower alkyl.

21. Compounds according to claim 19, wherein

R_c" and R_b" is hydrogen, or



;

R_{12} is hydrogen or lower alkyl; and

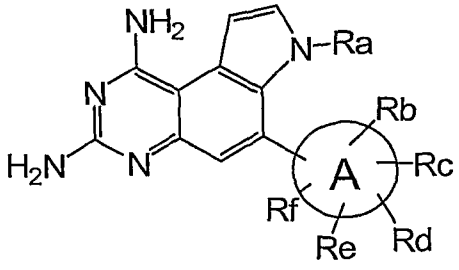
one of R_c" and R_b" is other than hydrogen.

22. Compounds according to claim 19, wherein R_c" and R_b" are attached to the hetero atom ring on adjacent carbon atoms and taken together with their attached carbon atoms a fused phenyl ring.

23. Compounds according to claim 18, wherein Ⓟ is a heteroaromatic ring containing an oxygen atom as the only hetero atom.

24. Compounds according to claim 18, wherein Ⓟ is a heteroaromatic ring containing a nitrogen hetero atom.

25. Compounds according to claim 1, characterised by formula (II):



(II)

or pharmaceutically acceptable salts thereof, wherein

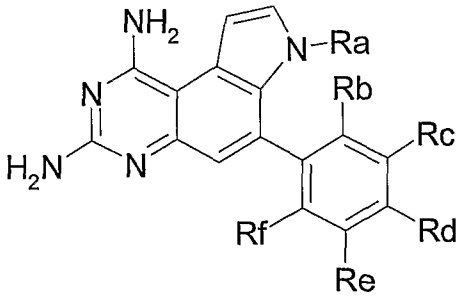
A is a 5- or 6-membered unsaturated or saturated hydrocarbon or 6-membered unsaturated or saturated ring that contains at least one heteroatom selected from S, N or O;

Ra is hydrogen or lower alkyl; and

Rb, Rc, Rd and Re are each independently selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetyl, acetylamino, hydroxy, alkoxy, carboxy, aryloxy hydroxy methyl, carboxy alkyl, formyl and substituted alkyl, with the proviso that if A is a 6-membered unsaturated or saturated ring, then

Rf is selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetyl, acetylamino, hydroxy, alkoxy, carboxy, aryloxy hydroxy methyl, carboxy alkyl, formyl and substituted alkyl.

26. Compounds according to claim 1, characterised by formula (III):



(III)

or pharmaceutically acceptable salts thereof, wherein

Ra is hydrogen or lower alkyl;

Rb is selected from the group consisting of hydrogen, lower alkyl, halogen, nitro, acetyl, alkoxy, carboxy, aryloxy and substituted alkyl;

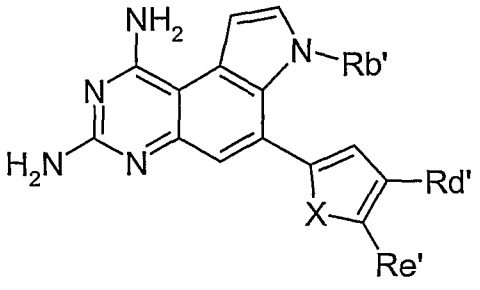
Rc is individually selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetylamino, hydroxy, alkoxy, hydroxy methyl, carboxy alkyl, formyl and substituted alkyl;

Rd is selected from the group consisting of hydrogen, lower alkyl, halogen, hydroxy, alkoxy, carboxyalkyl, alkylsulfanyl and acetyl;

Re is selected from the group consisting of hydrogen, methoxy, halogen and substituted alkyl; and

Rf is hydrogen, alkoxy, lower alkyl or halogen.

27. Compounds according to claim 1, characterised by formula (IV):



(IV)

or pharmaceutical acceptable salt thereof, wherein,

Rb' is selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetylamino, hydroxy, alkoxy, hydroxy methyl, carboxy alkyl, nitro, acetyl, carboxy, aryloxy, formyl and substituted alkyl;

Rd' and Re' are each independently selected from the group consisting of hydrogen, lower alkyl, halogen, amino, acetylamino, hydroxy, alkoxy, hydroxy methyl, carboxy alkyl, nitro, acetyl, carboxy, aryloxy, formyl and substituted alkyl;

or

Rd' and Re' form a part of a 5- or 6-membered unsaturated or saturated ring that contains at least one hetero atom selected from S, N and O; and

X is selected from the group consisting of S, N and O.

28. Compounds according to any of claims 1 to 27, selected from the group consisting of

6-(3,5-Bis-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Ethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine
6-(3-Nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(5-Chloro-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-o-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[1,3]dioxol-5-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Amino-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-m-Tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Biphenyl-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(3-Fluoro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Ethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-tert-Butyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Isopropyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[b]thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,5-Dichloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

6-Naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Chloro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dimethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
1-[5-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone,
6-(3-Amino-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-m-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Biphenyl-4-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-methyl-3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(3-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Ethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Isopropyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[b]thiophen-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-naphthalen-1-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,5-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
N-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide,
7-Methyl-6-naphthalen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
1-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone,
1-[5-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophen-2-yl]-ethanone,
8-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-benzaldehyde,
8-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-methanol,
6-(5-Chloro-2-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,3-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(5-Fluoro-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

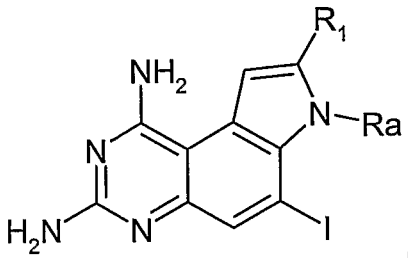
1-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone,
6-(5-Chloro-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Furan-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(5-methyl-thiophen-2-yl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
2-[1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-ethanol,
[1,3-Diamino-6-(2-trifluoromethyl-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-acetic acid,
(1,3-Diamino-6-thiophen-2-yl-pyrrolo[3,2-f]quinazolin-7-yl)-acetic acid,
1-[4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-ethanone,
6-(3,4-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-trifluoromethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,6-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(3,4,5-trimethoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,4-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Bromo-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(3-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(4-Ethylsulfanyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-methylsulfanyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-p-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3,5-Dimethyl-isoxazol-4-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzo[b]thiophen-7-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-phenoxathiin-4-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,4-Difluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,5-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,3-Dichloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-thiophene-2-carbaldehyde,
4-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol,
6-Benzo[b]thiophen-3-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,

7-Methyl-6-(2-nitro-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diaminetrifluoro-acetic acid,
6-(5-Isopropyl-2-methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenol,
7-Methyl-6-(2-phenoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Chloro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-o-tolyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(4-vinyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Ethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(3-Chloro-4-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(4-Bromo-2-fluoro-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,6-Dimethoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-5-methoxy-benzoic acid,
6-(5-Methoxy-thiophen-2-yl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2,6-Dimethyl-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-(2-Benzyloxy-ethyl)-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methanesulfonyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
N-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetamide,
2-[1,3-Diamino-6-(3-methoxy-phenyl)-pyrrolo[3,2-f]quinazolin-7-yl]-N,N-diethyl-acetamide,
6-(2-Methoxy-phenyl)-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Ethyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-(2-Methoxy-ethyl)-6-(3-methoxy-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-(2-Trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
6-Benzofuran-2-yl-7-methyl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-Methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,
[4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-acetic acid,

3-[2-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[2-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[3-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
3-[3-(1,3-Diamino-7-methyl-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid, and
3-[4-(1,3-Diamino-7H-pyrrolo[3,2-f]quinazolin-6-yl)-phenyl]-propionic acid,
and pharmaceutically acceptable salts thereof.

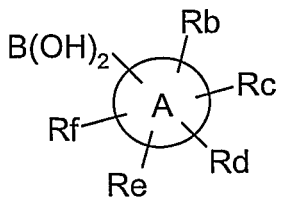
29. Compounds according to any of claims 1 to 28, selected from the group consisting of
7-ethyl-6-thiophen-2-yl-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine,
7-methyl-6-(2-trifluoromethyl-phenyl)-7H-pyrrolo[3,2-f]quinazoline-1,3-diamine, and
2-(1,3-diamino-6-[2-trifluoromethyl-phenyl]-pyrrolo[3,2-f]quinazoline-7-yl)-ethanol,
and pharmaceutically acceptable salts thereof.

30. A process for the preparation of compounds according to any of claims 1 - 29, comprising reacting a compound of formula (XXI)



(XXI)

with a compound of formula (XXII)



(XXII)

wherein R1, Ra, Rb, Rc, Rd, Re, Rf and A have the significances given in any of claims 1 to 29.

31. Compounds according to any of claims 1 - 29, when prepared by a process according to claim 30.

32. Pharmaceutical compositions comprising a compound according to any one of claims 1 to 29 and a pharmaceutically acceptable carrier and/or adjuvant.

33. Compounds according to any one of claims 1 to 29 for use as therapeutic active substances.

34. Compounds according to any one of claims 1 to 29 for use as therapeutic active substances for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors.

35. A method for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors, which method comprises administering a compound according to any one of claims 1 to 29 to a human being or animal.

36. The use of compounds according to any one of claims 1 to 29 for the treatment and/or prevention of diseases which are modulated by PTP1B inhibitors.

37. The use of compounds according to any one of claims 1 to 29 for the preparation of medicaments for the treatment and/or prevention of diseases which are modulated PTP1B inhibitors.

38. The uses or methods according to any of claims 34 - 37, wherein the disease is diabetes.

39. The novel compounds, processes and methods as well as the use of such compounds substantially as described herein before.

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