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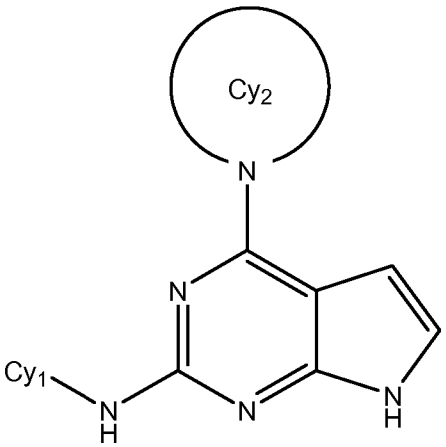

(I)

(57) Abstract: Pyrrolopyrimidine derivatives of formula (I), wherein the meanings for the various substituents are as disclosed in the description. These compounds are useful as JAK3 kinase inhibitors.

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PYRROLOPYRIMIDINE DERIVATIVES AS JAK3 INHIBITORS

Field of the invention

The present invention relates to a new series of pyrrolopyrimidine derivatives, as well as to processes for their preparation, to pharmaceutical compositions comprising them and to their use in therapy.

Background of the invention

The Janus kinases (JAKs) are cytoplasmic protein tyrosine kinases that play pivotal roles in pathways that modulate cellular functions in the lympho-hematopoietic system that are critical for cell proliferation and cell survival. JAKs are involved in the initiation of cytokine-triggered signaling events by activating through tyrosine phosphorylation the signal transducers and activators of transcription (STAT) proteins. JAK/STAT signaling has been implicated in the mediation of many abnormal immune responses such as transplant rejection and autoimmune diseases, as well as in solid and hematologic malignancies such as leukemias and lymphomas and in myeloproliferative disorders, and has thus emerged as an interesting target for drug intervention.

Four members of the JAK family have been identified so far: JAK1, JAK2, JAK3 and Tyk2. Unlike JAK1, JAK2 and Tyk2, whose expression is ubiquitous, JAK3 is mainly found in hematopoietic cells. JAK3 is associated in a non-covalent manner with the γc subunit of the receptors of IL-2, IL-4, IL-7, IL-9, IL-13 and IL-15. These cytokines play an important role in the proliferation and differentiation of T lymphocytes. JAK3-deficient mouse T cells do not respond to IL-2. This cytokine is fundamental in the regulation of T lymphocytes. In this regard, it is known that antibodies directed against the IL-2 receptor are able to prevent transplant rejection. In patients with X severe combined immunodeficiency (X-SCID), very low levels of JAK3 expression as well as genetic defects in the γc subunit of the receptor have been identified, which indicates that immunosuppression is a consequence of an alteration in the JAK3 signaling pathway.

Animal studies have suggested that JAK3 not only plays a critical role in T and B lymphocyte maturation, but also that JAK3 is required to maintain lymphocyte function. Modulation of the immunological activity through this new mechanism can prove useful in the treatment of T cell proliferative disorders such as transplant rejection and autoimmune diseases.

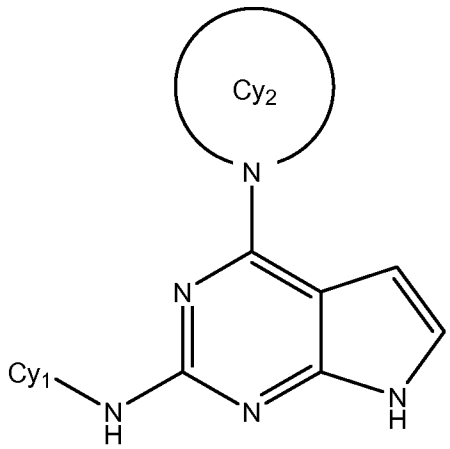
JAK3 has also been shown to play an important role in mast cells, because antigen-induced degranulation and mediator release have been found to be substantially reduced in mast cells from JAK3 deficient mice. JAK3 deficiency does not affect mast cell proliferation nor IgE receptor expression levels. On the other hand, JAK3-/- and JAK3+/+ mast cells contain the same intracellular mediators. Therefore, JAK3 appears to be essential in the IgE-induced release of mediators in mast cells and its inhibition would be, thus, an effective treatment for allergic reactions.

In conclusion, JAK3 kinase inhibitors have been recognised as a new class of effective immunosuppresive agents useful for transplant rejection prevention and in the treatment of immune, autoimmune, inflammatory and proliferative diseases such as psoriasis, psoriatic arthritis, rheumatoid arthritis, multiple sclerosis, inflammatory bowel diseases, systemic lupus erythematosus, type I diabetes and complications from diabetes, allergic reactions and leukemia (see e.g. O'Shea J.J. et al, Nat. Rev. Drug. Discov. 2004, 3(7):555-64; Cetkovic-Cvrlje M. et al, Curr. Pharm. Des. 2004, 10(15):1767-84; Cetkovic-Cvrlje M. et al, Arch. Immunol. Ther. Exp. (Warsz), 2004, 52(2):69-82).

Accordingly, it would be desirable to provide novel compounds that are capable of inhibiting JAK/STAT signaling pathways, and in particular which are capable of inhibiting JAK3 activity, and which are good drug candidates. Compounds should exhibit good activity in *in vivo* pharmacological assays, good oral absorption when administered by the oral route, as well as be metabolically stable and exhibit a favourable pharmacokinetic profile. Moreover, compounds should not be toxic and exhibit few side effects.

Description of the invention

One aspect of the invention relates to a compound of formula I



I

wherein:

Cy_1 represents phenyl or a 5- or 6-membered aromatic heterocycle bonded to the NH group through a C atom, each of which can be optionally fused to a 5- or 6-membered saturated, partially unsaturated or aromatic carbocyclic or heterocyclic ring, wherein Cy_1 can contain from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms of the optional 5- or 6-membered fused ring can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_1 can be optionally substituted with one or more R_1;

Cy_2 represents a 3- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated or partially unsaturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2;

each R_1 and R_2 independently represent C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, halogen, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-COCONR_3R_3$, $-OR_3$, $-OCOR_4$, $-OCONR_4R_4$, $-OCO_2R_4$, $-SR_3$, $-SOR_4$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5CO_2R_4$, $-NR_5SO_2R_4$, $-C(=N\text{-}OH)R_4$ or Cy_3, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7;

R_3 represents hydrogen or R_4;

R_4 represents C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, or Cy_4, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_4 can be optionally substituted with one or more R_8;

R_5 represents hydrogen or C_{1-4}alkyl;

R_6 represents halogen, -CN, -NO_2, -COR_9, -CO_2R_9, -$CONR_9R_9$, -OR_9, -$OCOR_{10}$, -$OCONR_{10}R_{10}$, -OCO_2R_{10}, -SR_9, -SOR_{10}, -SO_2R_{10}, -$SO_2NR_9R_9$, -$SO_2NR_5COR_{10}$, -NR_9R_9, -NR_5COR_9, -$NR_5CONR_9R_9$, -$NR_5CO_2R_{10}$, -$NR_5SO_2R_{10}$, -C(=N-OH)R_{10} or Cy_4, wherein Cy_4 can be optionally substituted with one or more R_8;

R_7 represents C_{1-4}alkyl that can be optionally substituted with one or more R_{11}, or R_7 represents any of the meanings described for R_{12};

R_8 represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, cyanoC_{1-4}alkyl or any of the meanings described for R_{12};

R_9 represents hydrogen or R_{10};

R_{10} represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, cyanoC_{1-4}alkyl, Cy_5-C_{1-4}alkyl or Cy_4, wherein Cy_4 can be optionally substituted with one or more R_8;

R_{11} represents halogen, -CN, -NO_2, -COR_9, -CO_2R_9, -$CONR_9R_9$, -OR_9, -$OCOR_{10}$, -$OCONR_{10}R_{10}$, -OCO_2R_{10}, -SR_9, -SOR_{10}, -SO_2R_{10}, -$SO_2NR_9R_9$, -$SO_2NR_5COR_{10}$, -NR_9R_9, -NR_5COR_9, -$NR_5CONR_9R_9$, -$NR_5CO_2R_{10}$, -$NR_5SO_2R_{10}$, or -C(=N-OH)R_{10};

R_{12} represents halogen, -CN, -NO_2, -COR_{13}, -CO_2R_{13}, -$CONR_{13}R_{13}$, -OR_{13}, -$OCOR_{14}$, -$OCONR_{14}R_{14}$, -OCO_2R_{14}, -SR_{13}, -SOR_{14}, -SO_2R_{14}, -$SO_2NR_{13}R_{13}$, -$SO_2NR_5COR_{14}$, -$NR_{13}R_{13}$, -NR_5COR_{13}, -$NR_5CONR_{13}R_{13}$, -$NR_5CO_2R_{14}$, -$NR_5SO_2R_{14}$ or -C(=N-OH)R_{14};

R_{13} represents hydrogen or R_{14};

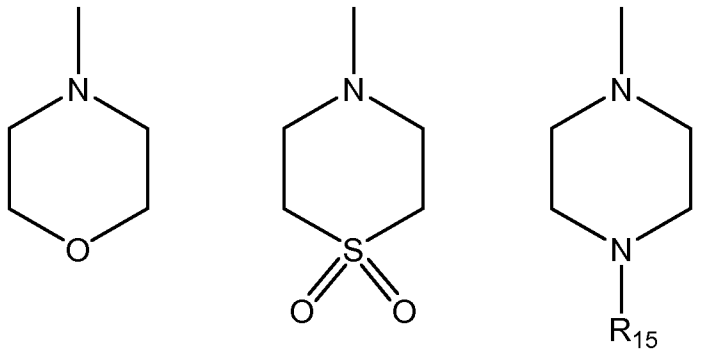
R_{14} represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl or hydroxyC_{1-4}alkyl;

or two R_{13} groups or two R_{14} groups on the same N atom can be bonded completing, together with the N atom, a 5- or 6-membered saturated ring, which can additionally contain one or two heteroatoms selected from N, S and O and which can be optionally substituted with one or more C_{1-4}alkyl groups;

each Cy_3 and Cy_4 independently represent a 3- to 7-membered monocyclic or 6- to 11-membered bicyclic ring which can be carbocyclic or heterocyclic, in which case it can contain from 1 to 4 heteroatoms selected from N, S and O, wherein each Cy_3 and Cy_4 can be saturated, partially unsaturated or aromatic, and

can be bonded to the rest of the molecule through any available C or N atom, and wherein one or more C or S atoms of the ring can be optionally oxidized forming CO, SO or SO_2 groups;

Cy_5 represents a ring selected from (a)-(c):



(a) (b) (c) ; and

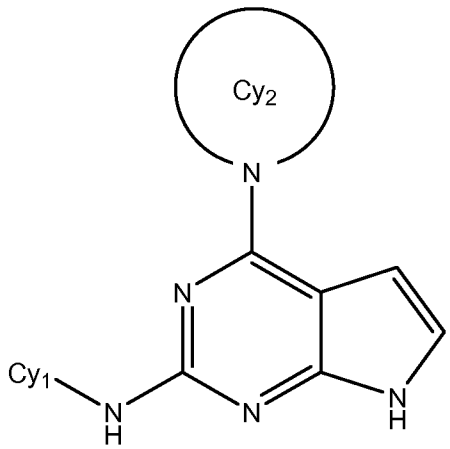
R_{15} represents hydrogen or C_{1-4}alkyl.

The present invention also relates to the salts and solvates of the compounds of formula **I**.

Some compounds of formula **I** can have chiral centers that can give rise to various stereoisomers. The present invention relates to each of these stereoisomers and also mixtures thereof.

The compounds of formula **I** are JAK, particularly JAK3, kinase inhibitors and therefore can be useful for the treatment of any disease mediated by this kinase.

Thus, another aspect of the invention relates to a compound of formula **I**



I

wherein:

Cy_1 represents phenyl or a 5- or 6-membered aromatic heterocycle bonded to the NH group through a C atom, each of which can be optionally fused to a 5- or 6-membered saturated, partially unsaturated or aromatic carbocyclic or heterocyclic ring, wherein Cy_1 can contain from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms of the optional 5- or 6-membered fused ring can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_1 can be optionally substituted with one or more R_1;

Cy_2 represents a 3- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated or partially unsaturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2;

each R_1 and R_2 independently represent C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, halogen, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-COCONR_3R_3$, $-OR_3$, $-OCOR_4$, $-OCONR_4R_4$, $-OCO_2R_4$, $-SR_3$, $-SOR_4$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5CO_2R_4$, $-NR_5SO_2R_4$, $-C(=N\text{-}OH)R_4$ or Cy_3, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7;

R_3 represents hydrogen or R_4;

R_4 represents C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, or Cy_4, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_4 can be optionally substituted with one or more R_8;

R_5 represents hydrogen or C_{1-4}alkyl;

R_6 represents halogen, -CN, $-NO_2$, $-COR_9$, $-CO_2R_9$, $-CONR_9R_9$, $-OR_9$, $-OCOR_{10}$, $-OCONR_{10}R_{10}$, $-OCO_2R_{10}$, $-SR_9$, $-SOR_{10}$, $-SO_2R_{10}$, $-SO_2NR_9R_9$, $-SO_2NR_5COR_{10}$, $-NR_9R_9$, $-NR_5COR_9$, $-NR_5CONR_9R_9$, $-NR_5CO_2R_{10}$, $-NR_5SO_2R_{10}$, $-C(=N\text{-}OH)R_{10}$ or Cy_4, wherein Cy_4 can be optionally substituted with one or more R_8;

R_7 represents C_{1-4}alkyl that can be optionally substituted with one or more R_{11}, or R_7 represents any of the meanings described for R_{12};

R_8 represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl,

cyanoC_{1-4}alkyl or any of the meanings described for R_{12};

R_9 represents hydrogen or R_{10};

R_{10} represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, cyanoC_{1-4}alkyl, Cy_5-C_{1-4}alkyl or Cy_4, wherein Cy_4 can be optionally substituted with one or more R_8;

R_{11} represents halogen, -CN, -NO_2, -COR_9, -CO_2R_9, -$CONR_9R_9$, -OR_9, -$OCOR_{10}$, -$OCONR_{10}R_{10}$, -OCO_2R_{10}, -SR_9, -SOR_{10}, -SO_2R_{10}, -$SO_2NR_9R_9$, -$SO_2NR_5COR_{10}$, -NR_9R_9, -NR_5COR_9, -$NR_5CONR_9R_9$, -$NR_5CO_2R_{10}$, -$NR_5SO_2R_{10}$, or -C(=N-OH)R_{10};

R_{12} represents halogen, -CN, -NO_2, -COR_{13}, -CO_2R_{13}, -$CONR_{13}R_{13}$, -OR_{13}, -$OCOR_{14}$, -$OCONR_{14}R_{14}$, -OCO_2R_{14}, -SR_{13}, -SOR_{14}, -SO_2R_{14}, -$SO_2NR_{13}R_{13}$, -$SO_2NR_5COR_{14}$, -$NR_{13}R_{13}$, -NR_5COR_{13}, -$NR_5CONR_{13}R_{13}$, -$NR_5CO_2R_{14}$, -$NR_5SO_2R_{14}$ or -C(=N-OH)R_{14};

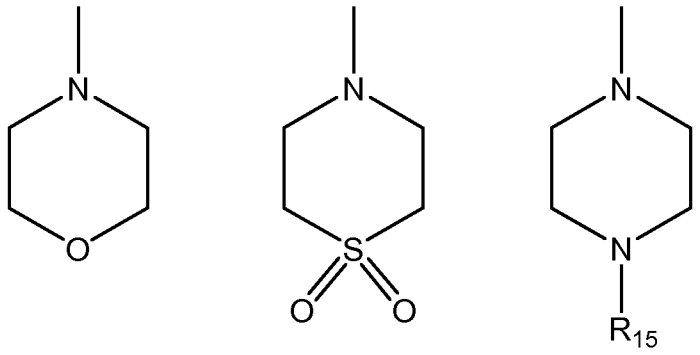
R_{13} represents hydrogen or R_{14};

R_{14} represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl or hydroxyC_{1-4}alkyl;

or two R_{13} groups or two R_{14} groups on the same N atom can be bonded completing, together with the N atom, a 5- or 6-membered saturated ring, which can additionally contain one or two heteroatoms selected from N, S and O and which can be optionally substituted with one or more C_{1-4}alkyl groups;

each Cy_3 and Cy_4 independently represent a 3- to 7-membered monocyclic or 6- to 11-membered bicyclic ring which can be carbocyclic or heterocyclic, in which case it can contain from 1 to 4 heteroatoms selected from N, S and O, wherein each Cy_3 and Cy_4 can be saturated, partially unsaturated or aromatic, and can be bonded to the rest of the molecule through any available C or N atom, and wherein one or more C or S atoms of the ring can be optionally oxidized forming CO, SO or SO_2 groups;

Cy_5 represents a ring selected from (a)-(c):



(a) (b) (c) ; and

R_{15} represents hydrogen or C_{1-4}alkyl,

for use in therapy.

Another aspect of the invention relates to a pharmaceutical composition which comprises a compound of formula I or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.

Another aspect of the present invention relates to the use of a compound of formula I or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of a disease mediated by JAKs, particularly JAK3.

Another aspect of the present invention relates to the use of a compound of formula I or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of at least one disease selected from transplant rejection, immune, autoimmune and inflammatory diseases, neurodegenerative diseases, and proliferative disorders. In a preferred embodiment, the disease is selected from transplant rejection and immune, autoimmune and inflammatory diseases.

Another aspect of the present invention relates to the use of a compound of formula I or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of a disease selected from transplant rejection, rheumatoid arthritis, psoriatic arthritis, psoriasis, type I diabetes, complications from diabetes, multiple sclerosis, systemic lupus erythematosus, atopic dermatitis, mast cell-mediated allergic reactions, leukemias, lymphomas, and thromboembolic and allergic complications associated with leukemias and lymphomas.

Another aspect of the present invention relates to a compound of formula I or a pharmaceutically acceptable salt thereof for the treatment of a disease

mediated by JAKs, particularly JAK3.

Another aspect of the present invention relates to a compound of formula **I** or a pharmaceutically acceptable salt thereof for the treatment of at least one disease selected from transplant rejection, immune, autoimmune and inflammatory diseases, neurodegenerative diseases, and proliferative disorders. In a preferred embodiment, the disease is selected from transplant rejection and immune, autoimmune and inflammatory diseases.

Another aspect of the present invention relates to a compound of formula **I** or a pharmaceutically acceptable salt thereof for the treatment of a disease selected from transplant rejection, rheumatoid arthritis, psoriatic arthritis, psoriasis, type I diabetes, complications from diabetes, multiple sclerosis, systemic lupus erythematosus, atopic dermatitis, mast cell-mediated allergic reactions, leukemias, lymphomas, and thromboembolic and allergic complications associated with leukemias and lymphomas.

Another aspect of the present invention relates to the use of a compound of formula **I** or a pharmaceutically acceptable salt thereof for the treatment of a disease mediated by JAKs, particularly JAK3.

Another aspect of the present invention relates to the use of a compound of formula **I** or a pharmaceutically acceptable salt thereof for the treatment of at least one disease selected from transplant rejection, immune, autoimmune and inflammatory diseases, neurodegenerative diseases, and proliferative disorders. In a preferred embodiment, the disease is selected from transplant rejection and immune, autoimmune and inflammatory diseases.

Another aspect of the present invention relates to the use of a compound of formula **I** or a pharmaceutically acceptable salt thereof for the treatment of a disease selected from transplant rejection, rheumatoid arthritis, psoriatic arthritis, psoriasis, type I diabetes, complications from diabetes, multiple sclerosis, systemic lupus erythematosus, atopic dermatitis, mast cell-mediated allergic reactions, leukemias, lymphomas, and thromboembolic and allergic complications associated with leukemias and lymphomas.

Another aspect of the present invention relates to a method of treating a disease mediated by JAKs, particularly JAK3, in a subject in need thereof, especially a human being, which comprises administering to said subject a

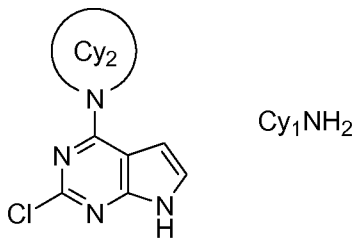
compound of formula **I** or a pharmaceutically acceptable salt thereof.

Another aspect of the present invention relates to a method of treating at least one disease selected from transplant rejection, immune, autoimmune and inflammatory diseases, neurodegenerative diseases, and proliferative disorders in a subject in need thereof, especially a human being, which comprises administering to said subject a compound of formula **I** or a pharmaceutically acceptable salt thereof. In a preferred embodiment, the disease is selected from transplant rejection and immune, autoimmune and inflammatory diseases.

Another aspect of the present invention relates to a method of treating a disease selected from transplant rejection, rheumatoid arthritis, psoriatic arthritis, psoriasis, type I diabetes, complications from diabetes, multiple sclerosis, systemic lupus erythematosus, atopic dermatitis, mast cell-mediated allergic reactions, leukemias, lymphomas, and thromboembolic and allergic complications associated with leukemias and lymphomas in a subject in need thereof, especially a human being, which comprises administering to said subject a compound of formula **I** or a pharmaceutically acceptable salt thereof.

Another aspect of the present invention relates to a process for the preparation of a compound of formula **I** as defined above, which comprises:

(a) reacting a compound of formula **IV** with a compound of formula **V**



IV **V**

wherein Cy_1 and Cy_2 have the previously described meaning; or

(b) converting, in one or a plurality of steps, a compound of formula **I** into another compound of formula **I**.

In the above definitions, the term C_{1-4} alkyl, as a group or part of a group, means a straight or branched alkyl chain which contains from 1 to 4 carbon atoms and includes the groups methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *sec*-butyl and *tert*-butyl.

A C_{2-4}alkenyl group means a straight or branched alkyl chain which

contains from 2 to 4 C atoms, and also contains one or two double bonds. Examples include the groups ethenyl, 1-propenyl, 2-propenyl, isopropenyl, 1-butenyl, 2-butenyl, 3-butenyl and 1,3-butadienyl.

A C_{2-4}alkynyl group means straight or branched alkyl chain which contains from 2 to 4 C atoms, and also contains one or two triple bonds. Examples include the groups ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl and 1,3-butadiynyl.

A C_{1-4}alkoxy group, as a group or part of a group, means a group of formula -OC_{1-4}alkyl, wherein the C_{1-4}alkyl moiety has the same meaning as previously described. Examples include methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, *sec*-butoxy and *tert*-butoxy.

Halogen or its abbreviation halo means fluoro, chloro, bromo or iodo.

A C_{1-4}alkoxyC_{1-4}alkyl group means a group resulting from the replacement of one or more hydrogen atoms from a C_{1-4}alkyl group with one or more C_{1-4}alkoxy groups as defined above, which can be the same or different. Examples include, among others, the groups methoxymethyl, ethoxymethyl, propoxymethyl, isopropoxymethyl, butoxymethyl, isobutoxymethyl, *sec*-butoxymethyl, *tert*-butoxymethyl, dimethoxymethyl, 1-methoxyethyl, 2-methoxyethyl, 2-ethoxyethyl, 1,2-diethoxyethyl, 1-butoxyethyl, 2-*sec*-butoxyethyl, 3-methoxypropyl, 2-butoxypropyl, 1-methoxy-2-ethoxypropyl, 3-*tert*-butoxypropyl and 4-methoxybutyl.

A haloC_{1-4}alkyl group means a group resulting from the replacement of one or more hydrogen atoms from a C_{1-4}alkyl group with one or more halogen atoms (i.e. fluoro, chloro, bromo or iodo), which can be the same or different. Examples include, among others, the groups trifluoromethyl, fluoromethyl, 1-chloroethyl, 2-chloroethyl, 1-fluoroethyl, 2-fluoroethyl, 2-bromoethyl, 2-iodoethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, 3-fluoropropyl, 3-chloropropyl, 2,2,3,3-tetrafluoropropyl, 2,2,3,3,3-pentafluoropropyl, heptafluoropropyl, 4-fluorobutyl and nonafluorobutyl.

A hydroxyC_{1-4}alkyl group means a group resulting from the replacement of one or more hydrogen atoms from a C_{1-4}alkyl group with one or more hydroxy groups. Examples include, among others, the groups hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 1,2-dihydroxyethyl, 3-hydroxypropyl, 2-hydroxypropyl, 1-hydroxypropyl, 2,3-dihydroxypropyl, 4-hydroxybutyl, 3-

hydroxybutyl, 2-hydroxybutyl and 1-hydroxybutyl.

A cyanoC_{1-4}alkyl group means a group resulting from the replacement of one or more hydrogen atoms from a C_{1-4}alkyl group with one or more cyano groups. Examples include, among others, the groups cyanomethyl, dicyanomethyl, 1-cyanoethyl, 2-cyanoethyl, 3-cyanopropyl, 2,3-dicyanopropyl and 4-cyanobutyl.

A Cy_5-C_{1-4}alkyl group means a group resulting from the replacement of one hydrogen atom from a C_{1-4}alkyl group with one Cy_5 group. Examples include, among others, the groups (morpholin-4-yl)methyl, 2-(morpholin-4-yl)ethyl, 3-(morpholin-4-yl)propyl, 4-(morpholin-4-yl)butyl, (piperazin-1-yl)methyl, (4-methylpiperazin-1-yl)methyl, 2-(4-methylpiperazin-1-yl)ethyl, 3-(4-methylpiperazin-1-yl)propyl, 4-(4-methylpiperazin-1-yl)butyl, (4-ethylpiperazin-1-yl)methyl, (4-propylpiperazin-1-yl)methyl, (4-butylpiperazin-1-yl)methyl, (1,1-dioxothiomorpholin-4-yl)methyl, 2-(1,1-dioxotiomorpholin-4-yl)ethyl, 3-(1,1-dioxothiomorpholin-4-yl)propyl and 4-(1,1-dioxothiomorpholin-4-yl)butyl.

A Cy_4-C_{1-4}alkyl group means a group resulting from the replacement of one hydrogen atom from a C_{1-4}alkyl group with one Cy_4 group as defined above.

A group $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, R_9CO-C_{1-4}alkyl, NR_9R_9-C_{1-4}alkyl, $R_{10}SO_2NR_5$-C_{1-4}alkyl or $NR_9R_9CONR_5$-C_{1-4}alkyl means a group resulting from the replacement of one hydrogen atom from a C_{1-4}alkyl group with one $-SO_2NR_9R_9$, $-CONR_9R_9$, $-SO_2NR_5COR_{10}$, $-NR_5COR_9$, $-COR_9$, $-NR_9R_9$, $-NR_5SO_2R_{10}$ or $-NR_5CONR_9R_9$ group, respectively. For example, examples of a group $NR_9R_9SO_2$-C_{1-4}alkyl include, among others, the groups sulfamoylmethyl, 1-sulfamoylethyl, 2-sulfamoylethyl, 1-sulfamoylpropyl, 2-sulfamoylpropyl, 3-sulfamoylpropyl, 1-sulfamoylbutyl, 2-sulfamoylbutyl, 3-sulfamoylbutyl, 4-sulfamoylbutyl, *N*-methylsulfamoylmethyl, *N*,*N*-dimethylsulfamoylmethyl and *N*-ethyl-*N*-methylsulfamoylmethyl.

The term Cy_1 refers to a phenyl group or a 5- or 6-membered aromatic heterocycle that must be bonded to the NH group through a C atom, wherein both the phenyl group and the 5- or 6-membered aromatic heterocycle can be optionally fused to a 5- or 6-membered carbocycle or heterocycle which can be saturated, partially unsaturated or aromatic. The Cy_1 group, as a whole, can contain from 1 to 4 heteroatoms in total selected from N, O and S. When the second ring, i.e. the optional 5- or 6-membered carbocyclic or heterocyclic fused

ring, is saturated or partially unsaturated, one or more C or S atoms of said ring can be optionally oxidized forming CO, SO or SO_2 groups. The Cy_1 group can be optionally substituted as disclosed above in the definition of a compound of formula **I**; said substituents can be the same or different and can be placed on any available position of any of the rings. Examples of Cy_1 groups include, among others, phenyl, naphthyl, thienyl, furyl, pyrrolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, tetrazolyl, 1,3,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,4-oxadiazolyl, 1,2,4-thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, benzimidazolyl, benzooxazolyl, benzofuranyl, isobenzofuranyl, indolyl, isoindolyl, benzothiophenyl, benzothiazolyl, quinolinyl, isoquinolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, cinolinyl, naphthyridinyl, indazolyl, imidazopyridinyl, pyrrolopyridinyl, thienopyridinyl, imidazopyrimidinyl, imidazopyrazinyl, imidazopyridazinyl, pyrazolopyrazinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, benzo[1,3]dioxolyl, phtalimidyl, 1-oxo-1,3-dihydroisobenzofuranyl, 1,3-dioxo-1,3-dihydroisobenzofuranyl, 2-oxo-2,3-dihydro-1*H*-indolyl, 1-oxo-2,3-dihydro-1*H*-isoindolyl, 1,2,3,4-tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1-oxo-1,2,3,4-tetrahydroisoquinolinyl, 1-oxo-1,2-dihydroisoquinolinyl and 4-oxo-3,4-dihydroquinazolinyl.

The term Cy_2 refers to a 3- to 7-membered monocyclic or a 6- to 11-membered bicyclic heterocycle, with the proviso that the ring directly bonded to the pyrrolopyrimidine is saturated or partially unsaturated. When Cy_2 is bicyclic, the second ring can be saturated, partially unsaturated or aromatic. Cy_2 contains from 1 to 4 heteroatoms in total selected from N, O and S including the N atom bonding Cy_2 to the pyrrolopyrimidine ring, so that Cy_2 always contains at least one N atom. When Cy_2 is a bicyclic ring, this can be formed by two rings fused through two adjacent C or N atoms, or through two non-adjacent C or N atoms forming a bridged ring, or else it can be formed by two rings sharing a C atom as a single common atom thus forming a spiro ring. In Cy_2 one or more C or S atoms in any saturated or partially unsaturated ring can be optionally oxidized forming CO, SO or SO_2 groups. The Cy_2 group can be optionally substituted as disclosed above in the definition of a compound of formula **I**; said substituents can be the same or different and can be placed on any available position of the ring system. Examples of Cy_2 groups include, among others, azepanyl, aziridinyl, azetidinyl, 1,4-

diazepanyl, pyrrolidinyl, imidazolidinyl, isoxazolidinyl, oxazolidinyl, pyrazolidinyl, thiazolidinyl, isothiazolidinyl, imidazolinyl, pyrrolinyl, pyrazolinyl, piperidinyl, homopiperidinyl, morpholinyl, thiomorpholinyl, 1,1-dioxothiomorpholinyl, piperazinyl, homopiperazinyl, 2-oxo-azepanyl, 2-oxo-azetidinyl, 2-oxo-1,4-diazepanyl, 2-oxo-pyrrolidinyl, 2-oxo-piperazinyl, 2-oxo-piperidinyl, 3-oxo-piperidinyl, 4-oxo-piperidinyl, 2-oxo-imidazolidinyl, 2-oxo-oxazolidinyl, 2-oxo-1,2-dihydropyridinyl, 2-oxo-1,2-dihydropyrazinyl, 2-oxo-1,2-dihydropyrimidinyl, 3-oxo-2,3-dihydropyridazinyl, 1,2,3,6-tetrahydropyridinyl, perhydroisoquinolinyl, 1-oxo-1,2-dihydroisoquinolinyl, 4-oxo-3,4-dihydroquinazolinyl, 5-aza-bicyclo[2.1.1]hexanyl, 2-aza-bicyclo[2.2.1]heptanyl, 6-aza-bicyclo[3.2.1]octanyl, octahydro-pyrrolo[1,2-a]pyrazinyl, 2*H*-spiro[benzofuran-3,4'-piperidinyl], 3*H*-spiro[isobenzofuran-1,4'-piperidinyl], 2,8-diazaspiro[4.5]decan-1-onyl, 2,7-diazaspiro[4.5]decan-1-onyl, 2-aza-bicyclo[2.2.1]heptan-6-onyl and 6-aza-bicyclo[3.2.1]octan-7-onyl.

The term Cy_3 or Cy_4 refers to a 3- to 7-membered monocyclic or 6- to 11-membered bicyclic carbocyclic or heterocyclic ring. When heterocyclic, it can contain from 1 to 4 heteroatoms selected from N, S and O. Bicyclic rings may be formed either by two rings fused through two adjacent C or N atoms, or through two non-adjacent C or N atoms forming a bridged ring, or else they can be formed by two rings bonded through a single common C atom forming a spiro ring. A Cy_3 or Cy_4 group can be saturated, partially unsaturated or aromatic. Cy_3 and Cy_4 can be bonded to the rest of the molecule through any available C or N atom. In Cy_3 or Cy_4 one or more C or S atoms of a saturated or partially unsaturated ring can be optionally oxidized forming CO, SO or SO_2 groups. Cy_3 and Cy_4 can be optionally substituted as disclosed above in the definition of a compound of formula **I**; if substituted, said substituents can be the same or different and can be placed on any available position of the ring system. Examples of Cy_3 or Cy_4 groups include, among others, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, azetidinyl, aziridinyl, oxiranyl, oxetanyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, oxazolidinyl, pyrazolidinyl, pyrrolidinyl, thiazolidinyl, dioxanyl, morpholinyl, thiomorpholinyl, 1,1-dioxothiomorpholinyl, piperazinyl, homopiperazinyl, piperidinyl, pyranyl, tetrahydropyranyl, homopiperidinyl, oxazinyl, oxazolinyl, pyrrolinyl, thiazolinyl, pyrazolinyl, imidazolinyl, isoxazolinyl,

isothiazolinyl, 2-oxo-pyrrolidinyl, 2-oxo-piperidinyl, 4-oxo-piperidinyl, 2-oxo-piperazinyl, 2-oxo-1,2-dihydropyridinyl, 2-oxo-1,2-dihydropyrazinyl, 2-oxo-1,2-dihydropyrimidinyl, 3-oxo-2,3-dihydropyridazyl, phenyl, naphthyl, thienyl, furyl, pyrrolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, tetrazolyl, 1,3,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,4-oxadiazolyl, 1,2,4-thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, benzimidazolyl, benzooxazolyl, benzofuranyl, isobenzofuranyl, indolyl, isoindolyl, benzothiophenyl, benzothiazolyl, quinolinyl, isoquinolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, cinolinyl, naphthyridinyl, indazolyl, imidazopyridinyl, pyrrolopyridinyl, thienopyridinyl, imidazopyrimidinyl, imidazopyrazinyl, imidazopyridazinyl, pyrazolopyrazinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, benzo[1,3]dioxolyl, phtalimidyl, 1-oxo-1,3-dihydroisobenzofuranyl, 1,3-dioxo-1,3-dihydroisobenzofuranyl, 2-oxo-2,3-dihydro-1*H*-indolyl, 1-oxo-2,3-dihydro-1*H*-isoindolyl, perhydroquinolinyl, 1-oxo-perhydroisoquinolinyl, 1-oxo-1,2-dihydroisoquinolinyl, 4-oxo-3,4-dihydroquinazolinyl, 2-aza-bicyclo[2.2.1]heptanyl, 5-aza-bicyclo[2.1.1]hexanyl, 2*H*-spiro[benzofuran-3,4'-piperidinyl], 3*H*-spiro[isobenzofuran-1,4'-piperidinyl], 2,8-diazaspiro[4.5]decan-1-onyl and 2,7-diazaspiro[4.5]decan-1-onyl.

In the above definitions of Cy_1, Cy_2, Cy_3 and Cy_4, when the examples listed refer to a bicycle in general terms, all possible dispositions of the atoms are included. Thus, for example, the term pyrazolopyridinyl can include groups such as 1*H*-pyrazolo[3,4-*b*]pyridinyl, 1*H*-pyrazolo[1,5-*a*]pyridinyl, 1*H*-pyrazolo[3,4-*c*]pyridinyl, 1*H*-pyrazolo[4,3-*c*]pyridinyl and 1*H*-pyrazolo[4,3-*b*]pyridinyl, the term imidazopyrazinyl can include groups such as 1*H*-imidazo[4,5-*b*]pyrazinyl, imidazo[1,2-*a*]pyrazinyl and imidazo[1,5-*a*]pyrazinyl and the term pyrazolopyrimidinyl can include groups such as 1*H*-pyrazolo[3,4-*d*]pyrimidinyl, 1*H*-pyrazolo[4,3-*d*]pyrimidinyl, pyrazolo[1,5-*a*]pyrimidinyl and pyrazolo[1,5-*c*]pyrimidinyl.

When in the definitions used throughout the present specification for cyclic groups the examples given refer to a radical of a ring in general terms, for example pyridyl, thienyl or indolyl, all the available bonding positions are included, unless a limitation is indicated in the corresponding definition for said cyclic group, for example that the ring is bonded through a C atom in Cy_1 or through a N atom

in Cy_2, in which case such limitation applies. Thus for example, in the definitions of Cy_3 and Cy_4, which do not include any limitation regarding the bonding position, the term pyridyl includes 2-pyridyl, 3-pyridyl and 4-pyridyl; thienyl includes 2-thienyl and 3-thienyl; and indolyl includes 1-indolyl, 2-indolyl, 3-indolyl, 4-indolyl, 5-indolyl, 6-indolyl and 7-indolyl.

The expression "optionally substituted with one or more" means that a group can be substituted with one or more, preferably with 1, 2, 3 or 4 substituents, more preferably with 1, 2 or 3 substituents, and still more preferably with 1 or 2 substituents, provided that said group has enough positions susceptible of being substituted. The substituents can be the same or different and can be placed on any available position.

When a non-aromatic ring is present as a substituent of a non-aromatic ring, it can replace one hydrogen atom, or it can replace two hydrogen atoms on the same C atom thus forming a spiro ring. Likewise, when a non-aromatic ring is present as a substituent of an alkyl, alkenyl or alkynyl group, it can either replace one hydrogen atom, or it can replace two hydrogen atoms on the same C atom.

When in the definition of a substituent two or more groups with the same numbering are indicated (e.g. $-NR_5CONR_3R_3$, $-NR_9R_9$, $-CONR_{13}R_{13}$, etc.), this does not mean that they must be the same. Each of them is independently selected from the list of possible meanings given for said group, and therefore they can be the same or different.

In certain embodiments of the invention, Cy_1 represents a phenyl group substituted at one or two of positions 3, 4 and 5 with a R_1 group. This means that the phenyl group is either substituted with one R_1 group at position 3, 4 or 5 of the phenyl ring, or with two R_1 groups (which can be the same or different) at positions 3 and 4, positions 4 and 5 or positions 3 and 5 of the phenyl ring.

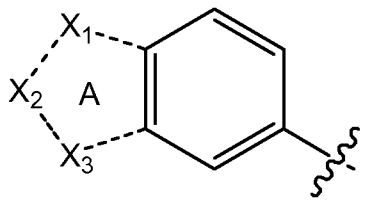
Throughout the present specification, the expressions “treatment” of a disease, “treating” a disease and the like refer both to curative treatment as well as palliative treatment or prophylactic treatment of said disease. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation or amelioration of one or more symptoms, diminishment of extent of disease, stabilized (i.e. not worsening) state of disease, preventing the disease from occurring in a patient that is predisposed or does not yet display symptoms of

the disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total). Those in need of treatment include those already with the disease or disorder as well as those prone to have the disease or disorder or those in which the disease or disorder is to be prevented.

The invention thus relates to the compounds of formula **I** as defined above.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl or pyridyl, which can be optionally fused to a 5- or 6-membered saturated, partially unsaturated or aromatic carbocyclic or heterocyclic ring, wherein Cy_1 can contain from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms of the 5- or 6-membered fused ring can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_1 can be optionally substituted with one or more R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl, pyridyl or a ring of formula Cy_{1a},



Cy_{1a}

wherein in ring A X_1, X_2 and X_3 are selected from C, N, O and S and the dashed lines represent single or double bonds, wherein one or two C or S atoms of ring A can be optionally oxidized forming CO, SO or SO_2 groups, and wherein the phenyl, pyridyl and Cy_{1a} groups can be optionally substituted with one or more R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl, 3-pyridyl, 4-pyridyl or a ring of formula Cy_{1a}, each of which can be optionally substituted with one or more R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl, pyridyl, benzo[1,3]dioxolyl or benzooxazolyl, each

of which can be optionally substituted with one or more R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl, 3-pyridyl, 4-pyridyl, 5-benzo[1,3]dioxolyl or 6-benzooxazolyl, which can be optionally substituted with one or more R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl optionally substituted with one or more R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl substituted with one or more R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl substituted with one, two or three R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl substituted with one or two R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl substituted at one or two of positions 3, 4 and 5 with an R_1.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_1 represents phenyl substituted with one R_1, which is placed at position 3 or 4 of the phenyl ring.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, halogen, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-COCONR_3R_3$, $-OR_3$, $-OCOR_4$, $-OCONR_4R_4$, $-OCO_2R_4$, $-SR_3$, $-SOR_4$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5CO_2R_4$, $-C(=N\text{-}OH)R_4$ or Cy_3, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-COCONR_3R_3$, $-OR_3$, $-SR_3$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$,

-COCONR$_3$R$_3$, -OR$_3$, -SR$_3$, -SO$_2$R$_4$, -SO$_2$NR$_3$R$_3$, -SO$_2$NR$_5$COR$_4$, -NR$_3$R$_3$, -NR$_5$COR$_3$, -NR$_5$CONR$_3$R$_3$ or Cy$_3$, wherein the C$_{1-4}$alkyl group can be optionally substituted with one or more R$_6$ and Cy$_3$ can be optionally substituted with one or more R$_7$.

In another embodiment, the invention relates to the compounds of formula I wherein each R$_1$ represents C$_{1-4}$alkyl, halogen, -CN, -OR$_3$, -SO$_2$R$_4$, -SO$_2$NR$_3$R$_3$, -SO$_2$NR$_5$COR$_4$, -NR$_3$R$_3$, -NR$_5$COR$_3$, -NR$_5$SO$_2$R$_4$ or Cy$_3$, wherein the C$_{1-4}$alkyl group can be optionally substituted with one or more R$_6$ and Cy$_3$ can be optionally substituted with one or more R$_7$.

In another embodiment, the invention relates to the compounds of formula I wherein each R$_1$ represents C$_{1-4}$alkyl, halogen, haloC$_{1-4}$alkyl, hydroxyC$_{1-4}$alkyl, C$_{1-4}$alkoxyC$_{1-4}$alkyl, -CN, -OR$_3$, -SO$_2$R$_4$, -SO$_2$NR$_3$R$_3$, -SO$_2$NR$_5$COR$_4$, -NR$_3$R$_3$, -NR$_5$COR$_3$, -NR$_5$SO$_2$R$_4$ or Cy$_3$, wherein Cy$_3$ can be optionally substituted with one or more R$_7$.

In another embodiment, the invention relates to the compounds of formula I wherein Cy$_3$ in R$_1$ represents Cy$_{3a}$, and Cy$_{3a}$ represents a 5- or 6-membered saturated monocyclic heterocycle which contains 1 or 2 heteroatoms selected from N, S and O, wherein said ring can be bonded to the rest of the molecule through any available C or N atom, and wherein one or more C or S atoms of the ring can be optionally oxidized forming CO, SO or SO$_2$ groups, wherein said Cy$_{3a}$ can be optionally substituted with one or more R$_7$.

In another embodiment, the invention relates to the compounds of formula I wherein Cy$_3$ in R$_1$ represents Cy$_{3b}$, and Cy$_{3b}$ represents a 5- or 6-membered saturated monocyclic heterocycle which contains 1 or 2 heteroatoms selected from N, S and O with the proviso that it contains at least 1 N atom, wherein said ring is bonded to the rest of the molecule through a N atom, wherein one or more C or S ring atoms can be optionally oxidized forming CO, SO or SO$_2$ groups, and wherein said Cy$_{3b}$ can be optionally substituted with one or more R$_7$.

In another embodiment, the invention relates to the compounds of formula I wherein Cy$_4$ in R$_1$ represents Cy$_{4a}$, and Cy$_{4a}$ represents a 5- or 6-membered saturated monocyclic heterocycle which contains 1 or 2 heteroatoms selected from N, S and O and which can be bonded to the rest of the molecule through any available C or N atom, wherein one or more C or S ring atoms can be optionally

oxidized forming CO, SO or SO_2 groups, and wherein said Cy_{4a} can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_{3a}, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_{3a} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_{3b}, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_{3b} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_{4a}-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$,

-NR_5COR_3 or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7 and wherein Cy_{4a} can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_{4a}-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, -$CONR_3R_3$, -OR_3, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_5COR_3 or Cy_{3b}, wherein Cy_{3b} can be optionally substituted with one or more R_7 and wherein Cy_{4a} can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, -$CONR_3R_3$, -OR_3, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_5COR_3 or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, -$CONR_3R_3$, -OR_3, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_5COR_3 or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_{4a}-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, -$CONR_3R_3$, -OR_3, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_5COR_3 or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7 and wherein Cy_{4a} can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_{4a}-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, -$CONR_3R_3$, -OR_3, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_5COR_3 or Cy_{3b}, wherein Cy_{3b} can be optionally substituted with one or more R_7 and wherein Cy_{4a} can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I

wherein each R_1 represents C_{1-4}alkyl, halogen, haloC_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, -CN, -OR_3, -SO_2R_4, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_3R_3, -NR_5COR_3, -$NR_5SO_2R_4$ or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein R_3 in R_1 represents hydrogen or R_4 and R_4 in R_1 represents C_{1-4}alkyl or Cy_4, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein R_3 in R_1 represents hydrogen or R_4 and R_4 in R_1 represents C_{1-4}alkyl, Cy_4-C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl or Cy_4, wherein any Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1, preferably one or two R_1; and

each R_1 represents C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, halogen, -CN, -NO_2, -COR_3, -CO_2R_3, -$CONR_3R_3$, -$COCONR_3R_3$, -OR_3, -$OCOR_4$, -$OCONR_4R_4$, -OCO_2R_4, -SR_3, -SOR_4, -SO_2R_4, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_3R_3, -NR_5COR_3, –$NR_5CONR_3R_3$, -$NR_5CO_2R_4$, -C(=N-OH)R_4 or Cy_3, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1, preferably one or two R_1; and

each R_1 represents C_{1-4}alkyl, halogen, -CN, -COR_3, -CO_2R_3, -$CONR_3R_3$, -$COCONR_3R_3$, -OR_3, -SR_3, -SO_2R_4, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_3R_3, -NR_5COR_3, -$NR_5CONR_3R_3$, -$NR_5SO_2R_4$ or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1, preferably one or two R_1; and

each R_1 represents C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1, preferably one or two R_1; and

each R_1 represents C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_{3a}, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_{3a} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1, preferably one or two R_1; and

each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

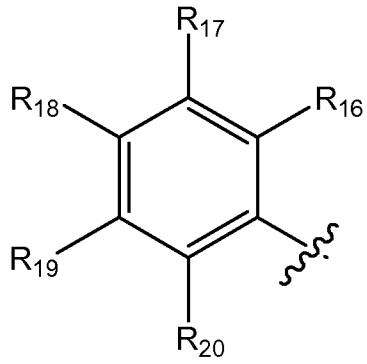
In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1, preferably one or two R_1; and

each R_1 represents C_{1-4}alkyl, halogen, haloC_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, -CN, $-OR_3$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5SO_2R_4$ or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents a ring of formula Cy_{1b}:



Cy_{1b}

one of R_{17}, R_{18} or R_{19} represents hydroxyC_{1-4}alkyl, -CN, -OR_3, -SO_2R_4, -$SO_2NR_3R_3$, -NR_5COR_3, -$NR_5SO_2R_4$ or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7; and

the remainder of R_{17}, R_{18} and R_{19} as well as R_{16} and R_{20} are selected from hydrogen, C_{1-4}alkyl, halogen and C_{1-4}alkoxy.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted at one or two of positions 3, 4 and 5 with an R_1; and

each R_1 represents C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, halogen, -CN, -NO_2, -COR_3, -CO_2R_3, -$CONR_3R_3$, -$COCONR_3R_3$, -OR_3, -$OCOR_4$, -$OCONR_4R_4$, -OCO_2R_4, -SR_3, -SOR_4, -SO_2R_4, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_3R_3, -NR_5COR_3, –$NR_5CONR_3R_3$, -$NR_5CO_2R_4$, -C(=N-OH)R_4 or Cy_3, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted at one or two of positions 3, 4 and 5 with an R_1; and

each R_1 represents C_{1-4}alkyl, halogen, -$CONR_3R_3$, -OR_3, -$SO_2NR_3R_3$, -$SO_2NR_5COR_4$, -NR_5COR_3 or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I

wherein:

Cy_1 represents phenyl substituted at one or two of positions 3, 4 and 5 with an R_1; and

each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one R_1, which is placed at position 3 or 4 of the phenyl ring; and

R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one R_1, which is placed at position 3 or 4 of the phenyl ring; and

R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one R_1, which is placed at position 3 or 4 of the phenyl ring; and

R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_{4a}-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_{3b},

wherein Cy_{3b} can be optionally substituted with one or more R_7 and wherein Cy_{4a} can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one R_1, which is placed at position 3 or 4 of the phenyl ring;

R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8;

R_3 in R_1 represents hydrogen or R_4; and

R_4 in R_1 represents C_{1-4}alkyl or Cy_4, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine is saturated or partially unsaturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

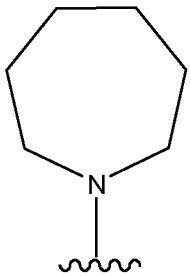
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally

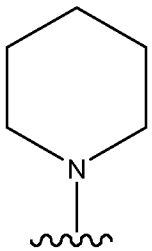
oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents a saturated 5- to 7-membered monocyclic heterocycle which contains from 1 to 2 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

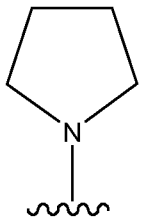
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 is selected from (a)-(i):



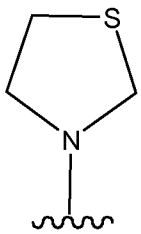
(a)



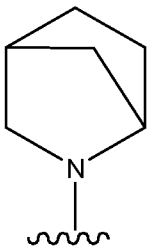
(b)



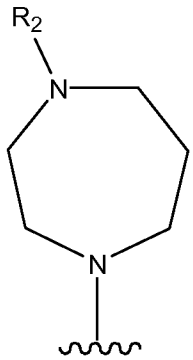
(c)



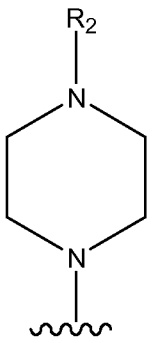
(d)



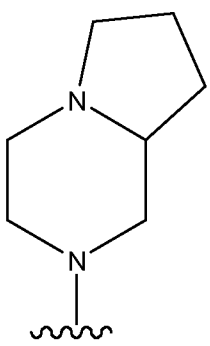
(e)



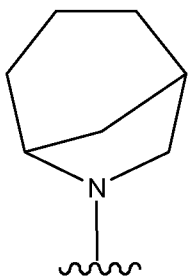
(f)



(g)



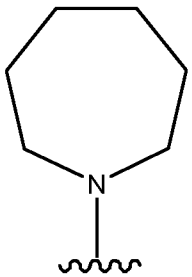
(h)



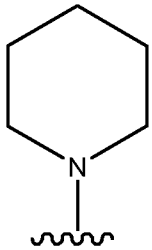
(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 is selected from (a)-(g):



(a)



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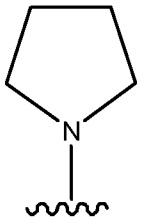

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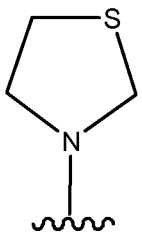
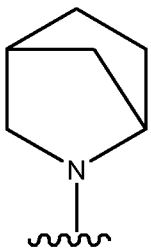


(d)



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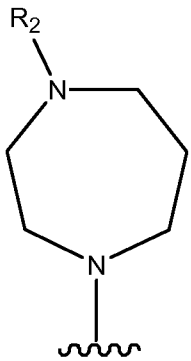

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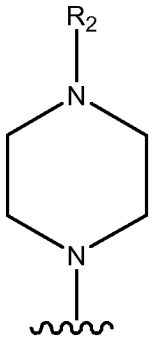
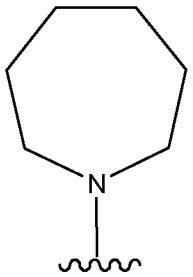


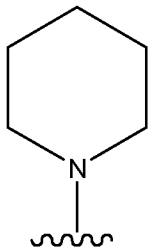
(g) ,

wherein Cy_2 can be optionally substituted with one or more R_2.

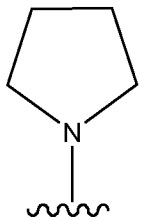
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 is selected from (a)-(f):



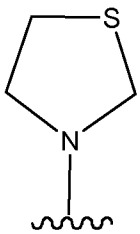
(a)



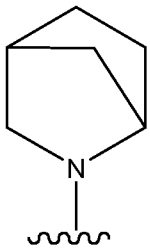
(b)



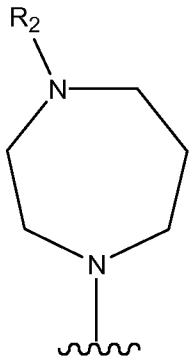
(c)



(d)



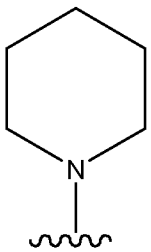
(e)



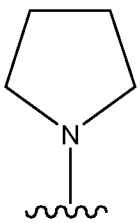
(f) ,

wherein Cy_2 can be optionally substituted with one or more R_2.

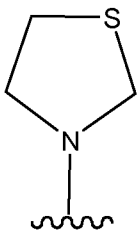
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 is selected from (b), (c), (d), (e), (h) and (i):



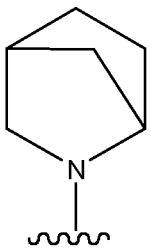
(b)



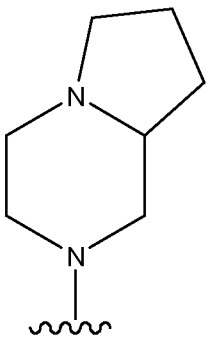
(c)



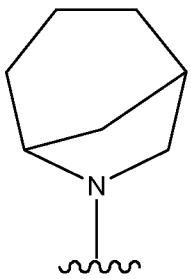
(d)



(e)



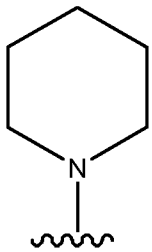
(h)



(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

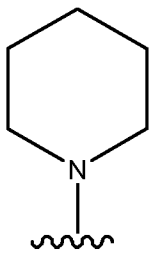
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (b):



(b) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

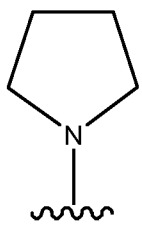
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (b):



(b) ,

which can be optionally substituted with one or more R_2.

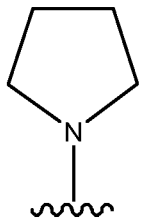
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (c):



(c) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

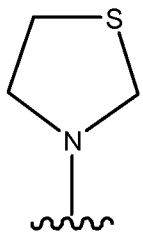
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (c):



(c) ,

which can be optionally substituted with one or more R_2.

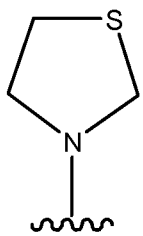
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (d)



(d) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

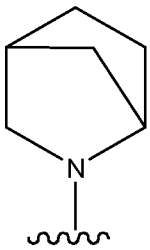
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (d)



(d) ,

which can be optionally substituted with one or more R_2.

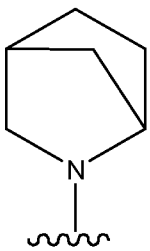
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (e):



(e) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

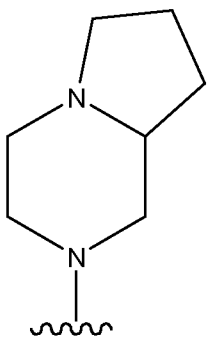
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (e):



(e) ,

which can be optionally substituted with one or more R_2.

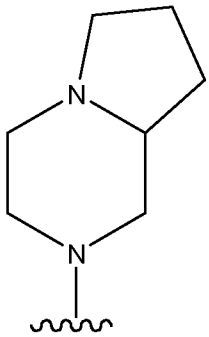
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (h):



(h) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

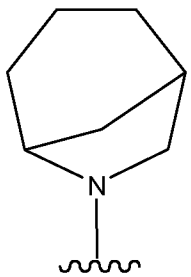
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (h):



(h) ,

which can be optionally substituted with one or more R_2.

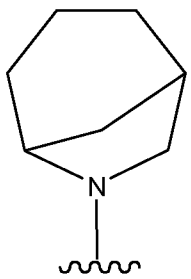
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (i):



(i) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (i):



(i) ,

which can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 is optionally substituted with one, two, three or four R_2.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents $C_{1\text{-}4}$alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$,

$-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_3 in R_2 represents Cy_{3c}, and Cy_{3c} represents a saturated 3- to 7-membered monocyclic or 6- to 11-membered bicyclic ring which can be carbocyclic or heterocyclic, in which case it can contain from 1 to 4 heteroatoms selected from N, S and O, wherein Cy_{3c} can be bonded to the rest of the molecule through any available C or N atom, wherein one or more C or S atoms of the ring can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_{3c} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_{3c}, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_{3c} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, R_9CO-C_{1-4}alkyl, NR_9R_9-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $R_{10}SO_2NR_5$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $NR_9R_9CONR_5$-C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, R_9CO-C_{1-4}alkyl, NR_9R_9-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $R_{10}SO_2NR_5$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $NR_9R_9CONR_5$-C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_{3c}, wherein Cy_{3c} can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with

one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, R_9CO-C_{1-4}alkyl, NR_9R_9-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $R_{10}SO_2NR_5$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $NR_9R_9CONR_5$-C_{1-4}alkyl, -COR_3, -OR_3, -NR_3R_3, -NR_5COR_3, –$NR_5CONR_3R_3$ or -$NR_5SO_2R_4$, wherein Cy_4 can be optionally substituted with one or more R_8.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, halogen, -CN, -COR_3, -CO_2R_3, -$CONR_3R_3$, -OR_3, -NR_3R_3, -NR_5COR_3 or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, halogen, -CN, -COR_3, -CO_2R_3, -$CONR_3R_3$, -OR_3, -NR_3R_3, -NR_5COR_3 or Cy_{3a}, wherein Cy_{3a} can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein each R_2 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, halogen, -COR_3, -$CONR_3R_3$, -OR_3 or -NR_3R_3.

In another embodiment, the invention relates to the compounds of formula I wherein R_3 in R_2 represents represents hydrogen or R_4 and R_4 in R_2 represents C_{1-4}alkyl optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein R_3 in R_2 represents hydrogen or R_4 and R_4 in R_2 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl or haloC_{1-4}alkyl.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, -COR_3, -CO_2R_3, -$CONR_3R_3$,

$-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$,

$-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7.

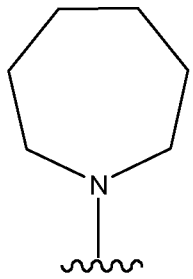
In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

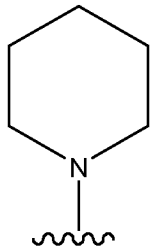
each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein:

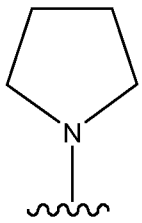
Cy_2 is selected from (a)-(i):



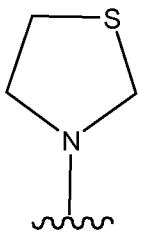
(a)



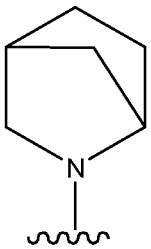
(b)



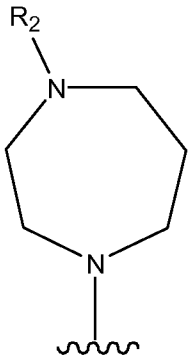
(c)



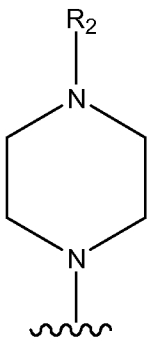
(d)



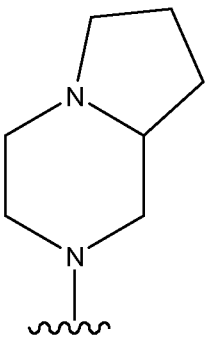
(e)



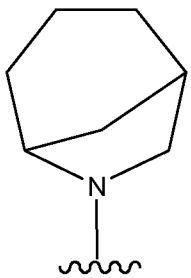
(f)



(g)



(h)



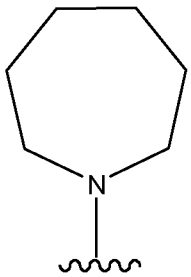
(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

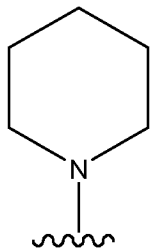
each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $–NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

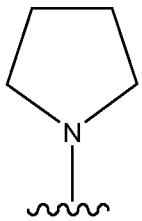
Cy_2 is selected from (a)-(i):



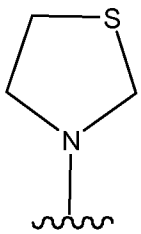
(a)



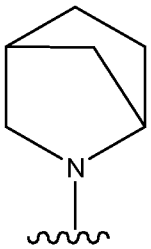
(b)



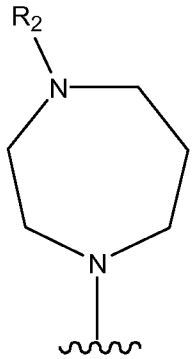
(c)



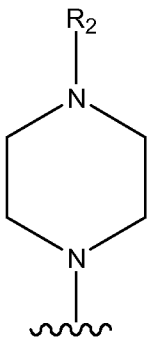
(d)



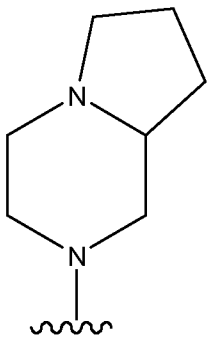
(e)



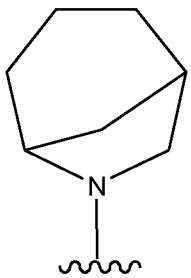
(f)



(g)



(h)



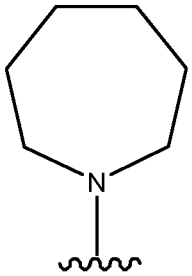
(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

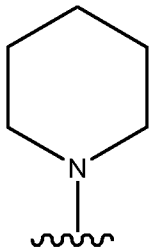
each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein:

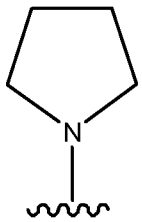
Cy_2 is selected from (a)-(g):



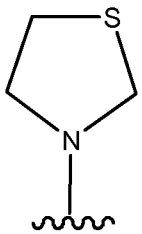
(a)



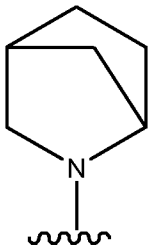
(b)



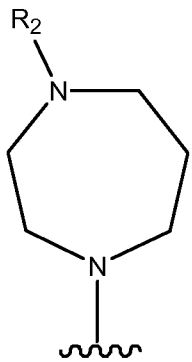
(c)



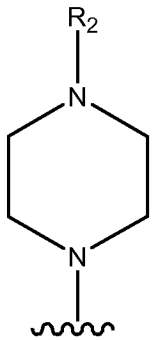
(d)



(e)



(f)

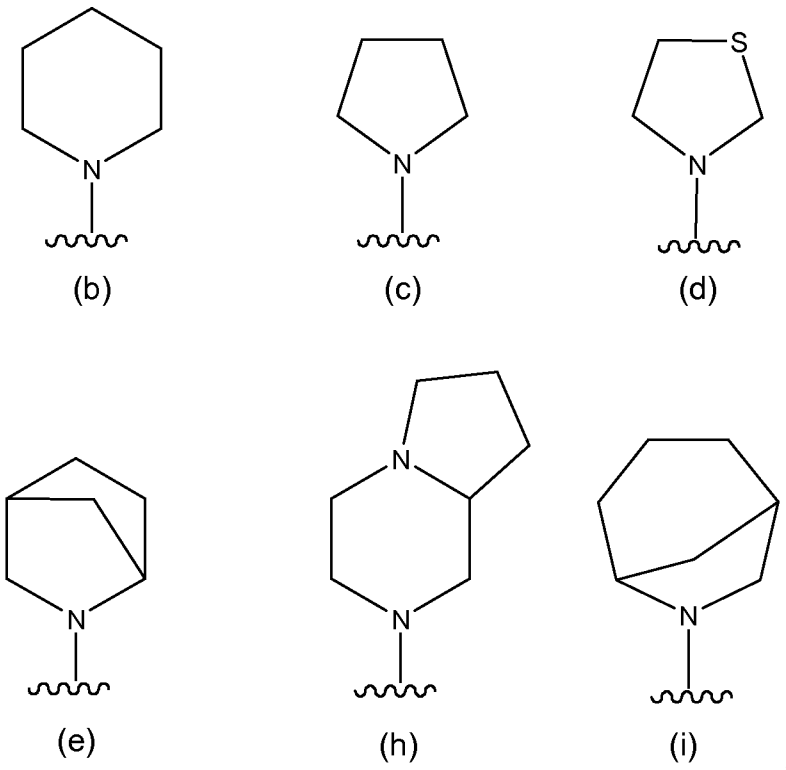


(g) ,

wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 is selected from (b), (c), (d), (e), (h) and (i):

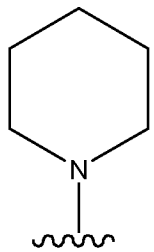


,

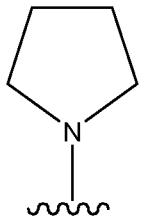
wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

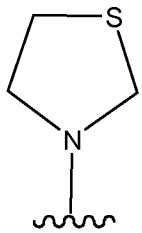
In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 is selected from (b), (c), (d), (e), (h) and (i):



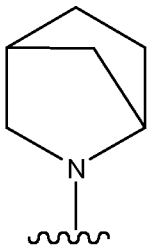
(b)



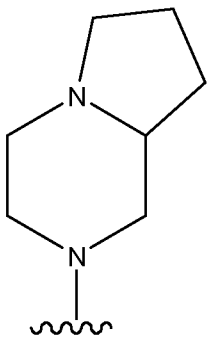
(c)



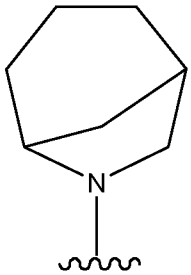
(d)



(e)



(h)

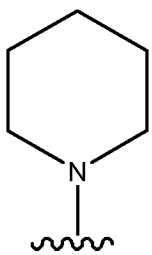


(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (b):



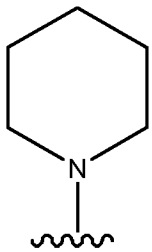
(b) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl

can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (b):

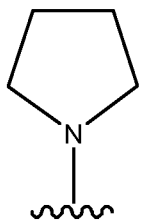


(b) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (c):

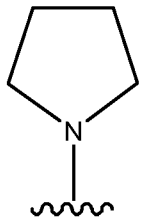


(c) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (c):

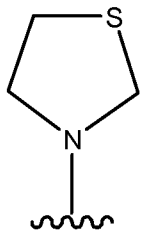


(c) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (d)

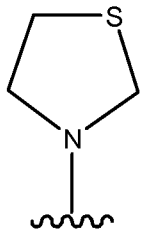


(d) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (d)

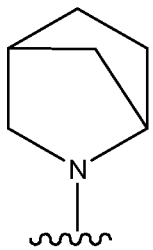


(d) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (e):

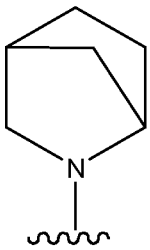


(e) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (e):

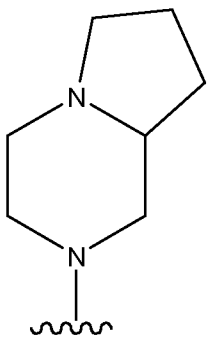


(e) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (h)

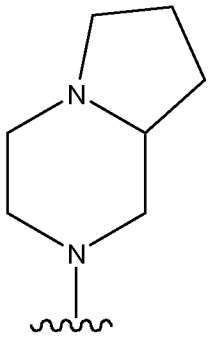


(h) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (h)

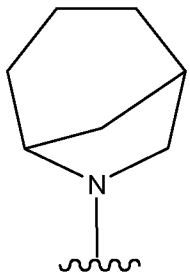


(h) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (i)

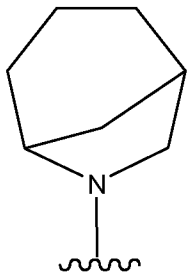


(i) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein Cy_2 represents (i)



(i) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2; and

each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine is saturated or partially unsaturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

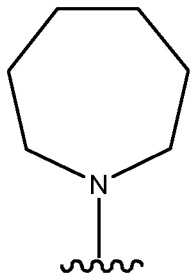
Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents a 5- to 7-membered saturated monocyclic heterocycle which contains from 1 to 2 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

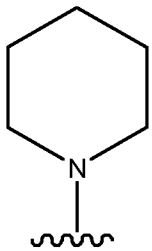
In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

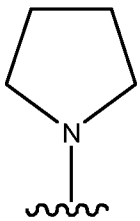
Cy_2 is selected from (a)-(g):



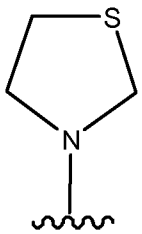
(a)



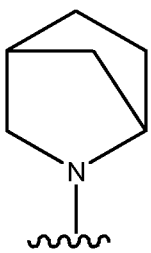
(b)



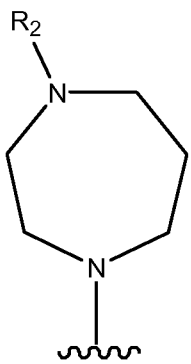
(c)



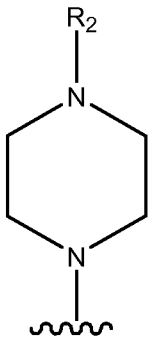
(d)



(e)



(f)



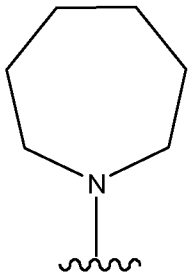
(g) ,

wherein Cy_2 can be optionally substituted with one or more R_2.

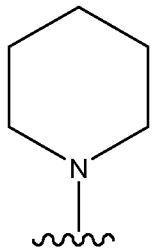
In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 is selected from (a)-(i):



(a)



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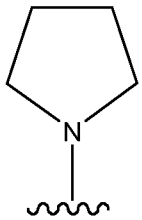

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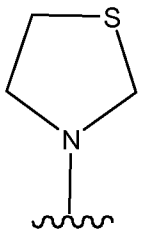
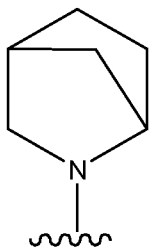
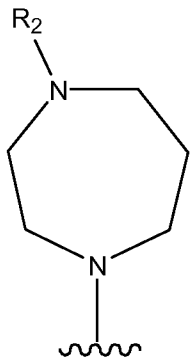


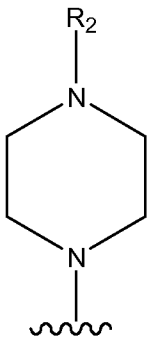
(d)



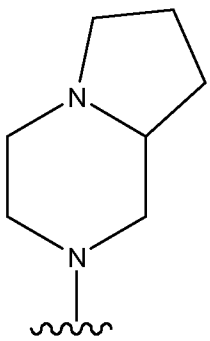
(e)



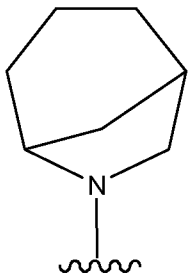
(f)



(g)



(h)



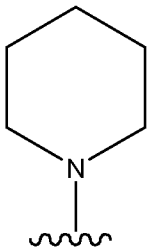
(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 is selected from (b), (c), (d), (e), (h) and (i):



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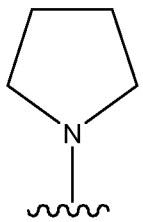
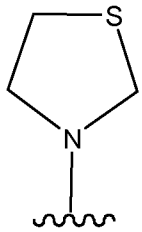
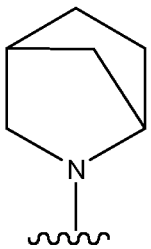


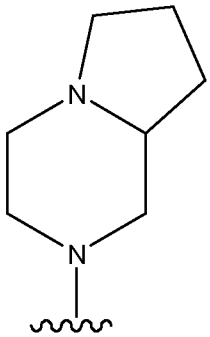
(c)



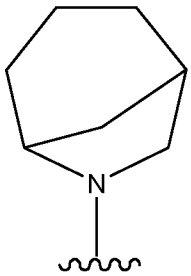
(d)



(e)



(h)



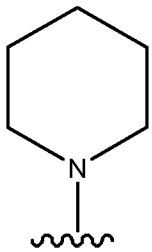
(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents (b):



(b) ,

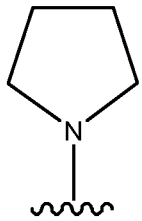
wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I

wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents (c):



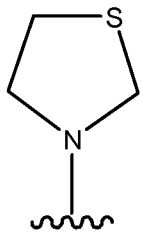
(c) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents (d)



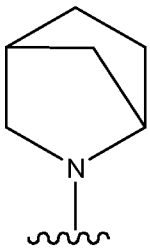
(d) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents (e):



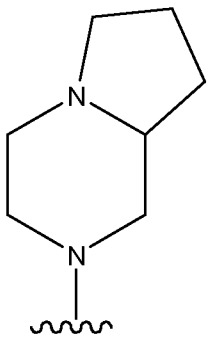
(e) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents (h)



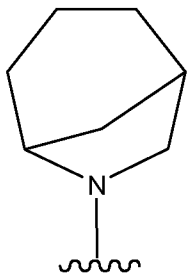
(h) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1; and

Cy_2 represents (i):



(i) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1;

Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2;

each R_1 represents C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7; and

each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $–NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

In another embodiment, the invention relates to the compounds of formula I wherein:

Cy_1 represents phenyl substituted with one or more R_1;

Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2;

each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8; and

each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, R_9CO-C_{1-4}alkyl, NR_9R_9-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl,

$R_{10}SO_2NR_5$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $NR_9R_9CONR_5$-C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

Furthermore, the present invention covers all possible combinations of the particular and preferred embodiments described above.

In another embodiment, the invention relates to a compound of formula **I**, which provides more than 50% inhibition of JAK3 activity at 10 μM, more preferably at 1 μM and still more preferably at 0.1 μM, in a JAK3 assay such as the one described in example 14.

In another embodiment, the invention relates to a compound of formula **I** selected from the list of compounds described in examples 1 to 13.

The compounds of the present invention contain one or more basic nitrogens and may, therefore, form salts with organic or inorganic acids. Examples of these salts include: salts with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, nitric acid, perchloric acid, sulfuric acid or phosphoric acid; and salts with organic acids such as methanesulfonic acid, trifluoromethanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, *p*-toluenesulfonic acid, fumaric acid, oxalic acid, acetic acid, maleic acid, ascorbic acid, citric acid, lactic acid, tartaric acid, malonic acid, glycolic acid, succinic acid and propionic acid, among others. Some of the compounds of the present invention may contain one or more acidic protons and, therefore, they may also form salts with bases. Examples of these salts include: salts with inorganic cations such as sodium, potassium, calcium, magnesium, lithium, aluminium, zinc, etc; and salts formed with pharmaceutically acceptable amines such as ammonia, alkylamines, hydroxylalkylamines, lysine, arginine, *N*-methylglucamine, procaine and the like.

There is no limitation on the type of salt that can be used, provided that these are pharmaceutically acceptable when they are used for therapeutic purposes. The term pharmaceutically acceptable salt represents those salts which are, according to medical judgment, suitable for use in contact with the tissues of humans and other mammals without undue toxicity, irritation, allergic response and the like. Pharmaceutically acceptable salts are well known in the art.

The salts of a compound of formula I can be obtained during the final isolation and purification of the compounds of the invention or can be prepared by treating a compound of formula I with a sufficient amount of the desired acid or base to give the salt in the conventional manner. The salts of the compounds of formula I can be converted into other salts of the compounds of formula I by ion exchange using ionic exchange resins.

The compounds of formula I and their salts may differ in some physical properties but they are equivalent for the purposes of the present invention. All salts of the compounds of formula I are included within the scope of the invention.

The compounds of the present invention may form complexes with solvents in which they are reacted or from which they are precipitated or crystallized. These complexes are known as solvates. As used herein, the term solvate refers to a complex of variable stoichiometry formed by a solute (a compound of formula I or a salt thereof) and a solvent. Examples of solvents include pharmaceutically acceptable solvents such as water, ethanol and the like. A complex with water is known as a hydrate. Solvates of compounds of the invention (or salts thereof), including hydrates, are included within the scope of the invention.

The compounds of formula I may exist in different physical forms, i.e. amorphous and crystalline forms. Moreover, the compounds of the invention may have the ability to crystallize in more than one form, a characteristic which is known as polymorphism. Polymorphs can be distinguished by various physical properties well known in the art such as X-ray diffraction pattern, melting point or solubility. All physical forms of the compounds of formula I, including all polymorphic forms ("polymorphs") thereof, are included within the scope of the invention.

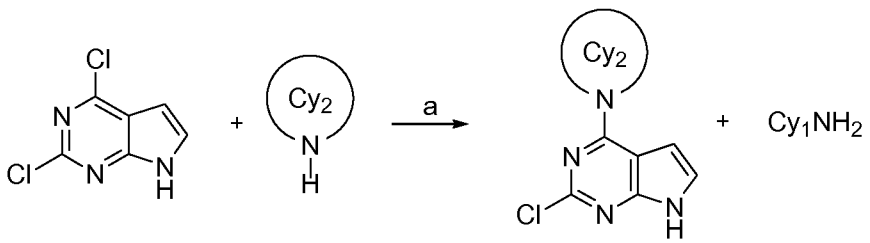
Some of the compounds of the present invention may exist as several diastereoisomers and/or several optical isomers. Diastereoisomers can be separated by conventional techniques such as chromatography or fractional crystallization. Optical isomers can be resolved by conventional techniques of optical resolution to give optically pure isomers. This resolution can be carried out on any chiral synthetic intermediate or on products of formula I. Optically pure isomers can also be individually obtained using enantiospecific synthesis. The present invention covers all individual isomers as well as mixtures thereof (for

example racemic mixtures or mixtures of diastereomers), whether obtained by synthesis or by physically mixing them.

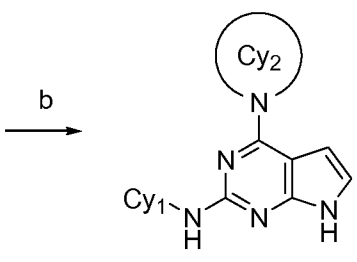
The compounds of formula **I** can be obtained by following the processes described below. As it will be obvious to one skilled in the art, the exact method used to prepare a given compound may vary depending on its chemical structure. Moreover, in some of the processes described below it may be necessary or advisable to protect the reactive or labile groups with conventional protecting groups. Both the nature of these protecting groups and the procedures for their introduction and removal are well known in the art (see for example Greene T.W. and Wuts P.G.M, "Protecting Groups in Organic Synthesis", John Wiley & Sons, 3rd edition, 1999). As an example, as protecting group of an amino function the *tert*-butoxycarbonyl (BOC) group can be used. Whenever a protecting group is present, a later deprotection step will be required, which can be performed under standard conditions in organic synthesis, such as those described in the above-mentioned reference.

Unless otherwise stated, in the methods described below the meanings of the different substituents are the meanings described above with regard to a compound of formula **I**.

In general, compounds of formula **I** can be obtained in two steps by the method described in Scheme 1:



II **III** **IV** **V**



I

Scheme 1

wherein Cy_1 and Cy_2 have the meaning previously described in relation with a compound of formula **I**.

In a first step (step a), the reaction between a compound of formula **II** and a compound of formula **III** may be carried out in the presence of a base such as triethylamine, K_2CO_3, Cs_2CO_3 or diisopropylethylamine, a solvent such as ethanol, tetrahydrofuran/H_2O or any polar solvent, and heating preferably at reflux to obtain a compound of formula **IV**.

Step b may be carried out by the reaction between a compound of formula **IV** and an amine of formula **V** in the presence of 4M dioxane/$HCl_{(g)}$ solution, a solvent such as n-butanol or methoxyethanol, and irradiating with a microwave oven preferably at around 170 ºC to obtain a compound of formula **I**.

Alternatively, step b may be carried out by the reaction between a compound of formula **IV** and an amine of formula **V** in the presence of a Pd catalyst such as $Pd_2(dba)_3$, a phosphine such as 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl, and a base such as potassium carbonate, in a solvent such as tert-butanol, and heating preferably at reflux to obtain a compound of formula **I**.

The compounds of formula **II**, **III** and **V** are commercially available or can be prepared by well-known methods described in the literature, and can be protected with suitable protecting groups.

Furthermore, some compounds of the present invention can also be obtained from other compounds of formula **I** by appropriate conversion reactions of functional groups in one or several steps, using well-known reactions in organic chemistry under the standard experimental conditions.

Said transformations can be carried out upon Cy_1 or Cy_2 groups and include, for example:

the reduction of a nitro group to give an amino group, for example by treatment with hydrogen, hydrazine or formic acid in the presence of a suitable catalyst such as Pd/C; or by treatment with sodium borohydride in the presence of $NiCl_2$, or $SnCl_2$;

the substitution of a primary or secondary amine by treatment with an

alkylating agent under standard conditions, or by reductive amination, i.e. by treatment with an aldehyde or a ketone in the presence of a reducing agent such as sodium cyanoborohydride or sodium triacetoxyborohydride;

the conversion of an amine into a sulfonamide by reaction with a sulfonyl halide, such as sulfonyl chloride, optionally in the presence of catalytic amounts of a base such as 4-dimethylaminopyridine, in a suitable solvent such as dioxane, chloroform, dichloromethane or pyridine, optionally in the presence of a base such as triethylamine or pyridine;

the conversion of an amine into an amide, carbamate or urea under standard conditions;

the alkylation of an amide by treatment with an alkylating agent under basic conditions;

the conversion of an alcohol into an ether, ester or carbamate under standard conditions;

the alkylation of a thiol to give a thioeter under standard conditions;

the partial or total oxidation of an alcohol to give ketones, aldehydes or carboxylic acids under standard oxidizing conditions;

the reduction of an aldehyde or a ketone to an alcohol by treatment with a reducing agent such as sodium borohydride;

the reduction of a carboxylic acid or a carboxylic acid derivative to an alcohol by treatment with a reducing agent such as diisobutylaluminium hydride or $LiAlH_4$;

the oxidation of a thioeter to a sulfoxide or sulfone under standard conditions;

the conversion of an alcohol into a halogen by reaction with $SOCl_2$, PBr_3, tetrabutylammonium bromide in the presence of P_2O_5, or PI_3;

the conversion of a halogen atom into an amine by reaction with an amine, optionally in the presence of a suitable solvent, and preferably heating;

the conversion of a primary amide into a –CN group or vice versa, under standard conditions.

Likewise, any of the aromatic rings of the compounds of the present invention can undergo electrophilic aromatic substitution reactions or nucleophilic aromatic substitution reactions, widely described in the literature.

Some of these interconversion reactions are explained in greater detail in the examples.

As it will be obvious to those skilled in the art, these interconversion reactions can be carried out upon the compounds of formula **I** as well as upon any suitable synthesis intermediate thereof.

As mentioned above, the compounds of the present invention act by inhibiting JAK/STAT signaling pathways, particularly by inhibiting JAK3 activity. Therefore, the compounds of the invention are expected to be useful to treat diseases in which JAKs, particularly JAK3, play a role in mammals, including human beings. These diseases include, but are not limited to, transplant rejection; immune, autoimmune and inflammatory diseases; neurodegenerative diseases; and proliferative disorders (see e.g. O'Shea J.J. et al, Nat. Rev. Drug. Discov. 2004, 3(7):555-64; Cetkovic-Cvrlje M. et al, Curr. Pharm. Des. 2004, 10(15):1767-84; Cetkovic-Cvrlje M. et al, Arch. Immunol. Ther. Exp. (Warsz), 2004, 52(2):69-82).

Acute or chronic transplant rejection reactions that can be treated with the compounds of the present invention include any kind of cell, tissue or organ xenotransplants or allografts, such as of heart, lung, liver, kidney, pancreas, uterus, joints, pancreatic islets, bone marrow, limbs, cornea, skin, hepatocytes, pancreatic beta cells, pluripotential cells, neuronal cells and myocardial cells, as well as graft-versus-host reactions (see e.g. Rousvoal G. et al, Transpl. Int. 2006, 19(12):1014-21; Borie DC. et al, Transplantation 2005, 79(7):791-801; Paniagua R. et al, Transplantation 2005, 80(9):1283-92; Higuchi T. et al, J. Heart Lung Transplant. 2005, 24(10):1557-64; Säemann MD. et al, Transpl Int. 2004, 17(9):481-89; Silva Jr HT. et al, Drugs 2006, 66(13):1665-1684).

Immune, autoimmune and inflammatory diseases that can be treated with the compounds of the present invention include among others, rheumatic diseases (e.g. rheumatoid arthritis and psoriatic arthritis), autoimmune hematological disorders (e.g. hemolytic anemia, aplastic anemia, idiopathic thrombocytopenia, and neutropenia), autoimmune gastritis and inflammatory bowel diseases (e.g. ulcerative colitis and Crohn's disease), scleroderma, type I diabetes and complications from diabetes, type B hepatitis, type C hepatitis, primary biliary cirrhosis, myasthenia gravis, multiple sclerosis, systemic lupus erythematosus,

psoriasis, atopic dermatitis, contact dermatitis, eczema, skin sunburns, suppression of HIV replication, infertility of autoimmune origin, autoimmune thyroid disease (Grave's disease), interstitial cystitis, and mast cell-mediated allergic reactions such as asthma, angiodema, anaphylaxis, bronchitis, rhinitis and sinusitis (see e.g. Sorbera LA. et al, Drugs of the Future 2007, 32(8):674-680; O'Shea J.J. et al, Nat. Rev. Drug. Discov. 2004, 3(7):555-64; Cetkovic-Cvrlje M. et al, Curr. Pharm. Des. 2004, 10(15):1767-84; Muller-Ladner U. et al, J. Immunol. 2000, 164(7): 3894-3901; Walker JG. et al, Ann. Rheum. Dis. 2006, 65(2):149-56; Milici AJ. et al, Arthritis Rheum .2006, 54 (9, Suppl): abstr 789; Kremer JM. et al, Arthritis Rheum. 2006, 54, 4116, presentation no. L40; Cetkovic-Cvrlje M. et al, Arch Immunol. Ther. Exp. (Warsz), 2004, 52(2):69-82; Malaviya R. et al, J. Pharmacol. Exp. Ther. 2000, 295(3):912-26; Malaviya R. et al, J. Biol. Chem. 1999, 274(38):27028-38; Wilkinson B et al, Ann. Rheum. Dis. 2007, 66(Suppl 2): Abst. THU0099; Matsumoto M. et al, J. Immunol. 1999, 162(2):1056-63).

Neurodegenerative diseases that can be treated with the compounds of the present invention include, among others, amyotrophic lateral sclerosis and Alzheimer's disease (see e.g. Trieu VN. et al, Biochem. Biophys. Res. Commun. 2000, 267(1):22-5).

Proliferative disorders that can be treated with the compounds of the present invention include, among others, leukemias, lymphomas, glioblastoma multiforme, colon carcinoma, as well as thromboembolic and allergic complications associated with these diseases (see e.g. Sudbeck EA. et al, Clin. Cancer Res. 1999, 5(6):1569-82; Narla RK. et al, Clin. Cancer Res. 1998, 4(10):2463-71; Lin Q. et al, Am J. Pathol. 2005, 167(4):969-80; Tibbles HE. et al, J. Biol. Chem. 2001, 276(21):17815-22).

Biological assays that can be used to determine the ability of a compound to inhibit JAKs, particularly JAK3, are well known in the art. For example, a compound to be tested can be incubated in the presence of JAK3 to determine whether inhibition of JAK3 enzymatic activity occurs, as described in the assay of example 14. Other *in vitro* useful assays that can be used to measure JAK3-inhibitory activity include cellular assays, for example IL-2-induced proliferation of human T lymphocytes. The immunosuppressive activity of the compounds of the invention can be tested using standard *in vivo* animal models for immune and

autoimmune diseases, which are well known in the art. For example, the following assays can be used: delayed-type hypersensitivity (DTH) (see e.g. the method disclosed in Kudlacz E. et al, Am J. Transplant. 2004, 4(1):51-7, the contents of which are incorporated herein by reference), rheumatoid arthritis models such as collagen-induced arthritis (see e.g. the method disclosed in Holmdahl R et al, APMIS, 1989, 97(7):575-84, the contents of which are incorporated herein by reference), multiple sclerosis models such as experimental autoimmune encephalomyelitis (EAE) (see e.g. the method disclosed in González-Rey et al, Am. J. Pathol. 2006, 168(4): 1179-88, the contents of which are incorporated herein by reference) and transplant rejection models (see e.g. the various animal models disclosed in the references listed above in relation to the treatment of transplant rejection, incorporated herein by reference).

For selecting active compounds, testing at 10 μM must result in an activity of more than 50% inhibition of JAK3 activity in the test provided in example 14. More preferably, when tested in this assay compounds should exhibit more than 50% inhibition at 1 μM, and still more preferably, they should exhibit more than 50% inhibition at 0.1 μM.

The present invention also relates to a pharmaceutical composition that comprises a compound of the present invention (or a pharmaceutically acceptable salt or solvate thereof) and one or more pharmaceutically acceptable excipients. The excipients must be “acceptable” in the sense of being compatible with the other ingredients of the composition and not deleterious to the recipients thereof.

The compounds of the present invention can be administered in the form of any pharmaceutical formulation, the nature of which, as it is well known, will depend upon the nature of the active compound and its route of administration. Any route of administration may be used, for example oral, parenteral, nasal, ocular, rectal and topical administration.

Solid compositions for oral administration include tablets, granulates and capsules. In any case the manufacturing method is based on a simple mixture, dry granulation or wet granulation of the active compound with excipients. These excipients can be, for example, diluents such as lactose, microcrystalline cellulose, mannitol or calcium hydrogenphosphate; binding agents such as for example starch, gelatin or povidone; disintegrants such as sodium carboxymethyl

starch or sodium croscarmellose; and lubricating agents such as for example magnesium stearate, stearic acid or talc. Tablets can be additionally coated with suitable excipients by using known techniques with the purpose of delaying their disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period, or simply to improve their organoleptic properties or their stability. The active compound can also be incorporated by coating onto inert pellets using natural or synthetic film-coating agents. Soft gelatin capsules are also possible, in which the active compound is mixed with water or an oily medium, for example coconut oil, mineral oil or olive oil.

Powders and granulates for the preparation of oral suspensions by the addition of water can be obtained by mixing the active compound with dispersing or wetting agents; suspending agents and preservatives. Other excipients can also be added, for example sweetening, flavoring and colouring agents.

Liquid forms for oral administration include emulsions, solutions, suspensions, syrups and elixirs containing commonly used inert diluents, such as purified water, ethanol, sorbitol, glycerol, polyethylene glycols (macrogols) and propylene glycol. Said compositions can also contain coadjuvants such as wetting, suspending, sweetening, flavoring agents, preservatives and buffers.

Injectable preparations, according to the present invention, for parenteral administration, comprise sterile solutions, suspensions or emulsions, in an aqueous or non-aqueous solvent such as propylene glycol, polyethylene glycol or vegetable oils. These compositions can also contain coadjuvants, such as wetting, emulsifying, dispersing agents and preservatives. They may be sterilized by any known method or prepared as sterile solid compositions, which will be dissolved in water or any other sterile injectable medium immediately before use. It is also possible to start from sterile materials and keep them under these conditions throughout all the manufacturing process.

For the rectal administration, the active compound can be preferably formulated as a suppository on an oily base, such as for example vegetable oils or solid semisynthetic glycerides, or on a hydrophilic base such as polyethylene glycols (macrogol).

The compounds of the invention can also be formulated for their topical application for the treatment of pathologies occurring in zones or organs

accessible through this route, such as eyes, skin and the intestinal tract. Formulations include creams, lotions, gels, powders, solutions and patches wherein the compound is dispersed or dissolved in suitable excipients.

For the nasal administration or for inhalation, the compound can be formulated as an aerosol and it can be conveniently released using suitable propellants.

The dosage and frequency of doses will depend upon the nature and severity of the disease to be treated, the age, the general condition and body weight of the patient, as well as the particular compound administered and the route of administration, among other factors. A representative example of a suitable dosage range is from about 0.01 mg/Kg to about 100 mg/Kg per day, which can be administered as a single or divided doses.

The following examples illustrate the scope of the invention.

Examples

The following abbreviations have been used in the examples:

AcN: acetonitrile
n-BuOH: 1-butanol
DIEA: *N,N*-diisopropylethylamine
DMAP: 4-(dimethylamino)pyridine
DMF: *N,N*-dimethylformamide
EDC: *N*-[3-(dimethylamino)propyl]-*N'*-ethylcarbodiimide
EtOAc: ethyl acetate
EtOH: ethanol
HBTU: *O*-(benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate
HOBT: 1-hydroxybenzotriazole
HPLC: high performance liquid chromatography
LC-MS: liquid chromatography-mass spectroscopy
MeOH: methanol
$Pd_2(dba)_3$: tris(dibenzylideneacetone)dipalladium(0)
TEA: triethylamine

THF: tetrahydrofuran

t_R: retention time

X-Phos: 2-dicyclohexylphosphino-2',4',6'-triisopropyl-biphenyl

LC-MS spectra have been performed using the following chromatographic methods:

Method 1: Column X-Terra, MS C18 5 μm (100 mm x 2.1 mm), temperature: 30 ºC, flow: 0.35 mL/min, eluent: A = AcN, B = NH_4HCO_3 10 mM, gradient: 0 min 10% A; 10 min 90% A; 15 min 90% A; 15.01 min 10% A.

Method 2: Column Waters Acquity UPLC BEH C18 (1.7 μm, 2.1 mm x 50 mm), temperature: 40 ºC, flow: 0.5 mL/min, eluent: ACN (A) / ammonium bicarbonate 10mM (B), gradient: 0 min 10% A – 3.75 min 90% A.

Method 3: Column Tracer Excel 120, ODSB 5 μm (10 mm x 0.21 mm), temperature: 30 ºC, flow: 0.35 mL/min, eluent: A = AcN, B = 0.1% HCOOH, gradient: 0 min 10% A - 10 min 90% A.

Method 4: Column YMC, 3 μm (50 mm x 4.6), temperature: 30 ºC, flow: 2.6 mL/min, eluent: A = H_2O (0.1% HCOOH) B = AcN (0.1% HCOOH), gradient: 0 min 5% B; 4.8 min 95% B; 6 min 95% B.

Method 5: Column Symmetry C_{18} 3.5 μm (4.6 x 75 mm), temperature: 30 ºC, flow: 1.0 mL/min, eluent: A = H_2O (0.1% HCOOH) B = AcN (0.07% HCOOH), gradient: 0 min 5% B; 7 min 100% B.

REFERENCE EXAMPLE 1

[4-(3-Hydroxypiperidin-1-yl)phenyl]amine

a) 4-(3-Hydroxypiperidin-1-yl)nitrobenzene

To a 4-fluoronitrobenzene solution (1 g, 7.09 mmol) in AcN (16 mL), 3-hydroxypiperidine hydrochloride (1.04 g, 7.57 mmol) and DIEA (1.32 mL, 7.57 mmol) were added. The mixture was stirred and refluxed for 18 h. The resulting mixture was cooled until room temperature and concentrated to dryness. The crude product obtained was chromatographed over silica gel using hexane/EtOAc

mixtures of increasing polarity as eluent, to afford 1.15 g of the desired compound (51 % yield).

b) Title compound

To a $NiCl_2.6H_2O$ (222 mg, 0.93 mmol) suspension in MeOH (50 mL) $NaBH_4$ (74 mg, 1.95 mmol) was added at room temperature and a solution of the compound obtained in the previous section (0.51 g, 2.33 mmol) in THF (30 mL). The resulting mixture was stirred for 1 h at room temperature and concentrated to dryness. The residue obtained was divided between a 1N NaOH solution and EtOAc. Phases were separated and the aqueous phase was extracted with EtOAc. The combined organic phases were dried over Na_2SO_4 and concentrated to dryness. The crude product obtained was chromatographed over silica gel using hexane/EtOAc mixtures of increasing polarity as eluent, to afford 450 mg of the desired compound (99 % yield).

LC-MS (method 1): t_R = 3.06 min; m/z = 193 (MH^+).

Following a similar procedure to that described in reference example 1, but using in each case the corresponding starting materials, these compounds are obtained:

Reference Example	Compound name	Starting Material	HPLC method	t_R (min)	m/z
1a	[4-(3-*tert*-butoxycarbonylaminopyrrolidin-1-yl)phenyl]amine	3-*tert*-butoxycarbonylaminopyrrolidine	1	5.41	308
1b	[4-(3-hydroxypyirrolidin-1-yl) phenyl]amine	3-hydroxypyirrolidine	1	2.53	179

REFERENCE EXAMPLE 2

4-(4-aminophenyl)-1-[2-(trimethylsylanyl)ethoxymethyl]-pyrazol

a) 4-(4-nitrophenyl)-1-[2-(trimethylsylanyl)ethoxymethyl]-pyrazol

To a 4-(4-nitrophenyl)-1*H*-pyrazol (0.2 g, 1.05 mmol) and DIEA (0.55 mL, 3.15 mmol) solution in $CHCl_3$ (3 mL) (2-trimethylsylanyl)ethoxymethyl chloride is added. The resulting mixture was stirred for 18 h at room temperature. H_2O was added and extracted thrice with $CHCl_3$. The organic phase was dried over Na_2SO_4 and concentrated to dryness. The crude product obtained was chromatographed over silica gel using hexane/EtOAc mixtures of increasing polarity as eluent, to afford 320 mg of the desired compound (95 % yield).

b) Title compound

Following a similar procedure to that described in reference example 1 section b, but starting with the compound obtained in previous section, the desired compound was obtained (83 % yield).

LC-MS (method 1): t_R = 8.31 min; m/z = 290 (MH^+).

Following a similar procedure to that described in reference example 2, but using in each case the corresponding starting materials, these compounds are obtained:

Reference Example	Compound name	Starting material	HPLC method	t_R (min)	m/z
2a	3-(4-aminophenyl)-1-[2-(trimethylsylanyl)ethoxymethyl]-pyrazol	3-(4-nitrophenyl)-1*H*-pyrazol	1	8.54	290.17

REFERENCE EXAMPLE 3

N-(3-Aminophenyl)-N-methylacetamide

a) N-(3-Nitrophenyl)-N-methylacetamide

To a solution of 3-nitro-*N*-methylaniline (650 mg, 4.27 mmol) in CH_2Cl_2 (10 mL) under Ar-atmosphere, acetyl chloride (0.33 mL, 4.7 mmol), a catalytic amount of DMAP and DIEA (1.49 mL, 8.5 mmol) were added. The resulting mixture was stirred at room temperature overnight. The resulting residue was diluted with H_2O, the phases were separated and the aqueous phase extracted with CH_2Cl_2. The

combined organic phases were dried over Na_2SO_4 and concentrated to dryness. The crude product thus obtained was directly used in the next step.

LC-MS (method 5): t_R = 1.43 min; m/z = 195 (MH^+).

b) Title compound

To a solution of the compound obtained in the previous section (0.96 g, 4.97 mmol) in MeOH (13 mL) under Ar-atmosphere, 10 % Pd/C (128 mg) was added at room temperature. The resulting mixture was stirred under H_2 overnight, filtered and the filtrate was concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using Hexane/EtOAc mixtures of increasing polarity as eluent, to afford 0.45 g of the desired compound (56 % yield).

LC-MS (method 2): t_R = 1.02 min; m/z = 165 (MH^+).

Following a similar procedure to that described in reference example 3, but using the corresponding starting material, the following compound was obtained:

Reference example	Compound name	Starting material	HPLC method	t_R (min)	m/z
3a	N-(3-aminophenyl)-N-methylcyclopropanecarboxamide	cyclopropane carbonyl chloride	5	1.38	191

REFERENCE EXAMPLE 4

4-(Imidazol-1-ylmethyl)piperidine

a) 4-Piperidylmethanol

To a mixture of $LiAlH_4$ (8.82 g, 0.23 mol) and THF (125 mL), cooled at 0 °C, a solution of ethyl isonipecotate (18 mL, 0.117 mol) in THF (325 mL) was added dropwise under Ar-atmosphere, the mixture was stirred at room temperature overnight. A mixture of H_2O (12.03 mL) and THF (25 mL), followed by a mixture of 15 % NaOH (10.03 mL) and H_2O (32.4 mL) were slowly added at 0 °C. The resulting mixture was washed with THF, filtered and concentrated to dryness. The residue was partitioned between H_2O and $CHCl_3$, the phases were separated, the aqueous phase was extracted with $CHCl_3$ and the combined organic phases were

dried over Na_2SO_4 and concentrated to afford 8.2 g of the desired product (61 % yield).

b) (1-*tert*-Butoxycarbonylpiperidin-4-yl)methanol

To a solution of the compound obtained in the previous section (15.3 g, 133 mmol) in DMF (160 mL), at 0 °C and under Ar-atmosphere, di-*tert*-butyl dicarbonate (29 g, 133 mmol) in DMF (80 mL) was added. The solution was stirred at room temperature overnight, and concentrated to dryness. The residue was dissolved in a mixture of THF (100 mL), MeOH (100 mL) and 1N NaOH (100 mL) and stirred at room temperature for 18 h. The organic phase was evaporated and the aqueous phase was extracted thrice with $CHCl_3$. The combined organic phases were dried over Na_2SO_4 and concentrated to dryness to afford 23.0 g of the desired product (80 % yield).

c) (1-*tert*-Butoxycarbonylpiperidin-4-yl)methyl mesylate

To a solution of the product obtained in the previous section (6.8 g, 31 mmol) and DIEA (5.75 mL, 33 mmol) in CH_2Cl_2 (50 mL), at 0 °C and under Ar-atmosphere, methanesulfonyl chloride (2.4 mL, 31 mmol) was added dropwise. The reaction mixture was stirred at room temperature overnight and treated with H_2O, the phases were separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and concentrated to afford the title compound in quantitative yield.

^1H NMR (300 MHz, $CDCl_3$) δ (TMS): 4.12 (broad d, J = 11.8 Hz, 2 H), 4.04 (d, J = 6.5 Hz, 2 H), 2.98 (s, 3 H), 2.69 (broad t, J = 12.4 Hz, 2 H), 1.89 (m, 1 H), 1.72 (broad d, J = 12.9 Hz, 2 H), 1.43 (s, 9 H), 1.25 (m, 2 H).

d) 1-*tert*-Butoxycarbonyl-4-(imidazol-1-ylmethyl)piperidine

To a solution of the compound obtained in the previous section (400 mg, 1.36 mmol) in THF (5 mL), K_2CO_3 (188 mg, 1.36 mmol) and imidazole (93 mg, 1.36 mmol) were added. The mixture was stirred and refluxed overnight. The crude product obtained was partitioned between EtOAc and 0.05 N aqueous NaOH solution. The phases were separated and the organic phase was dried over Na_2SO_4 and concentrated to dryness. The crude product thus obtained was

chromatographed over silica gel using $CHCl_3$/MeOH/NH_3 mixtures of increasing polarity as eluent, to afford 170 mg of the desired product (47 %).

e) Title compound

The compound obtained in the previous section (170 mg, 0.64 mmol) and a 4 M dioxane/$HCl_{(g)}$ mixture (5 mL) were mixed in a flask under Ar-atmosphere. The mixture was stirred at room temperature overnight and concentrated to dryness, to afford the title compound in quantitative yield.

^{1}H NMR (300 MHz, MeOD) δ (TMS): 8.96 (s, 1H), 7.61 (s, 1H), 7.53 (s, 1H), 4.18 (d, J = 7.2 Hz, 2 H), 3.36-3.32 (m, 2H), 2.95-2.87 (m, 2H), 2.25-2.10 (m, 1H), 1.78-1.74 (m, 2H), 1.49-1.44 (m, 2H).

REFERENCE EXAMPLE 5

N-tert-Butyl-*N'*-(4-piperidylmethyl)urea hydrochloride

a) 4-Aminomethyl-1-*tert*-butoxycarbonylpiperidine

To a solution of 4-(aminomethyl)piperidine (100 g, 0.88 mol) in $CHCl_3$ (550 mL), cooled at 0 °C and under Ar-atmosphere, a solution of di-*tert*-butyl dicarbonate (98 g, 0.45 mol) in $CHCl_3$ (350 mL) was added. The resulting mixture was stirred at room temperature for 48 h, washed with H_2O and the aqueous phase extracted with $CHCl_3$. The combined organic phases were dried over Na_2SO_4 and the solvents were removed to afford 84.5 g of the title compound (88 % yield).

^{1}H NMR (80MHz, $CDCl_3$) δ (TMS): 4.11 (broad d, J = 13.4 Hz, 2 H), 2.69 (m, 4 H), 1.45 (s, 9 H), 1.8-0.8 (complex signal, 7 H).

b) *N-tert*-Butyl-*N'*-[(1-*tert*-butoxycarbonylpiperidin-4-yl)methyl]urea

To a solution of 4-aminomethyl-1-*tert*-butoxycarbonylpiperidine (5 g, 23 mmol) obtained in the previous section in DMF (20 mL), *tert*-butyl isocyanate (2.63 mL, 23 mmol) was added dropwise under Ar-atmosphere. The reaction mixture was stirred at room temperature overnight and concentrated to dryness to afford the desired compound in quantitative yield.

c) Title compound

Following a similar procedure to that described in section e of reference example 4, but using the compound obtained in the previous section, the title compound of the example was obtained in quantitative yield.

^{1}H NMR (300 MHz, CD_3OD) δ (TMS): 4.92 (s, 4 H), 3.37 (m, 2 H), 2.97 (m, 4 H), 1.95 (m, 2 H), 1.80 (m, 1 H), 1.43 (m, 2 H), 1.31 (s, 9 H).

REFERENCE EXAMPLE 6

4-Hydroxy-2-methylpiperidine

To a solution of 2-methyl-4-piperidone (250 mg, 2.21 mmol) in MeOH (8 mL), $NaBH_4$ (175 mg, 4.62 mmol) was added at 0 ºC. The resulting mixture was stirred at room temperature overnight. The crude product was partitioned between H_2O and EtOAc and the phases were separted. The organic phase was dried over Na_2SO_4 and concentrated to dryness to afford the desired compound in quantitative yield.

LC-MS (method 2): t_R = 0.31 min; m/z = 116 (MH^+). 1807/78

REFERENCE EXAMPLE 7

(6*S*,8*R*)-8-Hydroxy-1,4-diazabicyclo[4.3.0]nonane dihydrochloride

a) (2*S*,4*R*)-N-*tert*-Butoxycarbonylaminoacetyl-4-hydroxyproline methyl ester

To a mixture of *N*-(*tert*-butoxycarbonyl)glycine (950 mg, 5.368 mmol), DIEA (2.82 mL, 16.10 mmol) and HBTU (2.07 g, 5.368 mmol) in 30 mL DMF at 0 ºC, *L*-4-hydroxyproline methyl ester hydrochloride (995 mg, 5.368 mmol) was added and the suspension thus obtained was stirred at room temperature overnight. The mixture was concentrated to dryness and partitioned between $CHCl_3$ and 0.2 M $NaHCO_3$ solution. The combined organic phases were dried over Na_2SO_4 and concentrated to dryness to afford the desired compound (80 %).

LC-MS (method 2): t_R = 1.25 min; m/z = 303.3 (MH^+).

b) (6*S*,8*R*)-2,5-Dioxo-8-hydroxy-1,4-diazabicyclo[4.3.0]nonane

To a solution of the compound obtained in the previous section (1.3 g, 4.30 mmol) in CH_2Cl_2 (2 mL), trifluoroacetic acid (1 mL) was added. The solution was stirred at

room temperature for 2 h. A 2N aqueous $NaHCO_3$ solution (2 mL) was added and the mixture evaporated to dryness. The crude product was diluted with a mixture of $CHCl_3$/MeOH/NH_3 (10:5:1, 10 mL) and the solution thus obtained was filtered over silica gel. The filtrate was concentrated to dryness to afford the desired compound in quantitative yield.

LC-MS (method 2): t_R = 0.28 min; m/z = 171.2 (MH^+).

c) Title compound

A solution of the compound obtained in the previous section (914 mg, 5.37 mmol) in THF (10 mL) was added to a solution of $LiAlH_4$ (815 mg, 21.48 mmol) in THF (21 mL) and under Ar-atmosphere. The resulting mixture was refluxed for 1 h and stirred at room temperature overnight. H_2O (0.82 mL), 15 % aqueous NaOH solution (0.82 mL) and H_2O (2.45 mL) were added in this order to the resulting solution. The resulting suspension was stirred for 1 h at room temperature and after the addition of THF (9 mL) the resulting solid was filtered and washed with EtOH. The filtrate was neutralized with a mixture of 2N HCl and Dowex 50w x 8 (10 g), and stirred at room temperature overnight. The suspension thus obtained was filtered and washed with a mixture of H_2O/MeOH. NH_4OH/25 % MeOH (75 mL) was added stirred for 2 h at room temperature. The resulting suspension was filtered and washed with MeOH. The resulting crude product was redisolved in 4M HCl in 1,4-dioxane (5 mL) and concentrated to dryness to afford the desired product (26 %).

LC-MS (method 2): t_R = 0.28 min; m/z = 143 (MH^+).

Following a similar procedure to that described in reference example 7 sections a, b, and c, but using the corresponding starting materials, the next compounds were obtained:

Reference Example	Compound name	Reagents for step a)	HPLC method	t_R (min)	m/z
7a	(*S*)-1,4-diazabicyclo[4.3.0] nonane dihydrochloride	*L*-proline methyl ester hydrochloride *N*-(*tert*-butoxycarbonyl)glycine	2	0.34	127

7b	(6*S*,3*S*)-3-methyl-1,4-diazabicyclo[4.3.0] nonane dihydrochloride	*L*-proline methyl ester hydrochloride *N*-(*tert*-butoxycarbonyl)-*L*-alanine	2	0.35	141

EXAMPLE 1

2-[4-(4-morpholino)phenyl]amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

a) 2-Chloro-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

To a 2,4-dichloro-7*H*-pyrrolo[2,3-d]pyrimidine solution (0.16 g, 0.86 mmol) in EtOH (2 mL), piperidine (0.085 mL, 0.86 mmol) and TEA (0,24 mL, 1.7 mmol) were added. The reaction was stirred and refluxed for 18 h. The resulting mixture was cooled until room temperature and evaporated to dryness. The crude product obtained was chromatographed over silica gel using hexane/EtOAc mixtures of increasing polarity as eluent, to afford 0.18 g of the desired compound (88 % yield).

b) Title compound

A mixture of the compound obtained in previous section (90 mg, 0.38 mmol), [4-(4-morpholino)phenyl]amine (123 mg, 0.57 mmol) and a 4M dioxane/$HCl_{(g)}$ solution (0.1 mL) in n-BuOH (2 mL) was irradiated in a microwave oven at 170 °C for 40 min. n-BuOH was evaporated and the residue was purified by preparative HPLC. 26.5 mg (18% yield) of the title compound was obtained

LC-MS (method 1): t_R = 8.03 min; m/z = 379 (MH^+).

Following a similar procedure to that described in example 1, but using in each case the corresponding starting materials, these compounds are obtained:

Example	Compound name	Reagent for step a)	Reagent for step b)	HPLC method	t_R (min)	m/z
1a	4-(4-methylpiperidin-1-yl)-2-[4-(4-morpholino)phenyl]amino-7*H*-pyrrolo[2,3-d]pyirimidine	4-methylpiperidine	[4-(4-morpholino)phenyl]amine	1	8.69	393.2
1b	2-(3-aminosulfonylphenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	7.62	387.1
1c	2-(3-*tert*-butylaminosulfonylphenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	9.44	443.2
1d	2-[4-(3-hydroxypyrrolidin-1-yl)phenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyirimidine	4-methylpiperidine	Reference example 1b	1	8.10	393.2
1e	4-(4-methylpiperidin-1-yl)-2-[4-(piperidin-3-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	*N*-*tert*-butoxycarbonyl-3-(4-aminophenyl)piperidine	1	8.14	391.2
1f	2-(3-methyltiophenyl)amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	piperidine	3-methyltiophenylamine	1	9.56	340.1
1g	2-(3-ethoxyphenyl)amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	piperidine	3-ethoxyphenylamine	1	9.41	338.1
1h	2-[4-(3-aminopyrrolidin-1-yl)phenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	Reference example 1a	1	7.50	392.2
1i	2-(3-aminosufonilphenyl)amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	piperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	6.99	373.1
1j	2-(3-*tert*-butylaminosufonilphenyl)amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	piperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	8.87	429.1

1k	2-[4-(3-aminopyrrolidin-1-yl)phenyl]amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	piperidine	Reference example 1a	1	6.99	378.2
1l	2-[4-(3-*tert*-butoxycarbonyl aminopyrrolidin-1-yl)phenyl]amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	piperidine	Reference example 1a	1	9.69	478.2
1m	4-(piperidin-1-yl)- 2-[4-(3-piperidinil)phenyl]amino-7H-pyrrolo[2,3-d]pyrimidine	piperidine	*N-tert*-butoxycarbonyl-3-(4-aminophenyl)piperidine	1	7.45	377.2
1n	2-[3-acetylphenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-acetylphenylamine	3	6.99	350.2
1o	4-(4-methylpiperidin-1-yl)-2-[(3-piperidin-1-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-(piperidin-1-yl)phenylamine	1	10.75	391.2
1p	4-(4-methylpiperidin-1-yl)-2-[3-(4-morpholino)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	[3-(4-morpholino)phenyl]amine	1	8.94	393.2
1q	2-(3-cyanophenyl)amino-4-(4-methylpiperidin-1-yl)- 7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-aminobenzonitrile	1	9.37	333.1
1r	4-(4-methylpiperidin-1-yl)-2-(3,4-dimethoxyphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3,4-dimethoxyphenylamine	1	8.60	368.1
1s	2-[(3,4-methylendioxy)phenyl] amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3,4-(methylendioxy)phenylamine	1	9.22	352.1
1t	2-[(3-acetylamino)phenyl] amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	(3-acetylamino)phenylamine	1	7.70	365.1

1u	2-(4-aminosufonilphenyl) amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-amino-*N*-*tert*-butylbenzenesulfonamide	1	7.56	387.0
1v	2-[(4-carbamoíl)phenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	(4-carbamoíl)phenyl amine	1	7.05	351.1
1w	4-(4-acetylpiperazine-1-yl)-2-(3-aminosulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	1-acetylpiperazine	3-amino-*N*-*tert*-butylbenzenesulfonamide	4	1.43	416.2
1x	2-(3-aminosulfonylphenyl)amino-4-(2-methyl-1-pyrrolidinil)-7*H*-pyrrolo[2,3-d]pyrimidine	2-methylpyrrolidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	1.8	373.2
1y	2-(3-aminosulfonylphenyl)amino-4-(4-phenylpiperazin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	1-phenylpiperazine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	7.72	449.9
1z	2-(3-aminosulfonylphenyl)amino-4-(4-phenyl-1,2,3,6-tetrahidropyridin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-phenyl-1,2,3,6-tetrahidropyridine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	8.31	446.9
1aa	2-[4-(2-hydroxyethyl)phenyl] amino-4-(homopiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperidine	2-(4-aminophenyl)ethanol	1	7.73	352.0
1ab	2-[4-(3-piperidinyl)phenyl]amino-4-(homopiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperidine	*N*-*tert*-butoxycarbonyl-3-(4-aminophenyl)piperidine	1	7.07	391.1
1ac	2-(3-aminosulfonylphenyl)amino-4-(homopiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	7.43	387.0

1ad	2-(3-aminosulfonylphenyl)amino-4-(3-acetamidopiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	3-acetamidopiperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	4	1.42	430.2
1ae	2-(3-aminosulfonylphenyl)amino-4-([1,4]diazepan-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperazine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	4.19	388.0
1af	2-(3-aminosulfonylphenyl)amino-4-(4-hydroxypiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxypiperidine	3-amino-benzenesulfonamide	4	1.32	389.2
1ag	2-(3-aminosulfonylphenyl)amino-4-(3-hydroxypiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	3-hydroxypiperidine	3-amino-benzenesulfonamide	4	1.43	389.2
1ah	2-(3-aminosulfonylphenyl)amino-4-(4-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethyl piperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	2	1.41	403
1ai	2-(3-aminosulfonylphenyl)amino-4-(4-benzilpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-benzylpiperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	4	2.58	463.2
1aj	2-(3-aminosulfonylphenyl)amino-4-(4-phenylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-phenylpiperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	4	2.43	449.2
1ak	2-(3-aminosulfonylphenyl)amino-4-(3-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	3-hydroxymethyl piperidine	3-amino-benzenesulfonamide	4	1.50	403.2
1al	2-(3-aminosulfonylphenyl)amino-4-(2-azabiciclo[2,2,1]heptan-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	2-azabiciclo[2,2,1]heptane	3-amino-benzenesulfonamide	4	1.80	385.2

1am	2-(3-aminosulfonylphenyl)amino-4-(perhydroisoquinolin-2-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	perhydroisoquinoline	3-amino-benzenesulfonamide	4	2.52	427.2
1an	2-[(4-*N,N*-diethylamine)phenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	*N,N*-diethyl-1,4-phenylendiamine	1	10.39	379.2
1ao	4-(3-methylpiperidin-1-yl)-2-[4-(4-morpholino)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	3-methylpiperidine	[4-(4-morpholino)phenyl]amine	1	8.64	393
1ap	2-(3-aminosulfonylphenyl)amino-4-(3-methylaminoazetidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	3-(*N*-*tert*-butoxycarbonyl-*N*-methylamino)azetidine	3-amino-benzenesulfonamide	2	1.23	374.3
1aq	2-[4-(3-hydroxypiperidin-1-yl)phenyl]amino-4-(piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	piperidine	Reference example 1	1	7.49	393.1
1ar	2-[4-(3-hydroxypiperidin-1-yl)phenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	Reference example 1	1	8.13	407.1
1as	2-(3-phenylaminophenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-(phenylaminophenyl)amine	1	10.34	399.1
1at	2-(4-hydroxyphenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-aminophenol	1	7.62	324.1
1au	2-[4-(2-hydroxyethyl)phenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	2-(4-aminophenyl)ethanol	1	7.84	352.1

1av	4-(4-methylpiperidin-1-yl)-2-[4-(piperidin-1-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-(piperidin-1-yl)aniline	1	10.51	391.1
1aw	4-(4-methylpiperidin-1-yl)-2-[3-(pyridin-4-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-(pyiridyn-4-yl)aniline	1	9.00	385.1
1ax	2-(3-hydroxyphenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-aminophenol	1	8.05	324.1
1ay	2-(benzofuran-5-yl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	(benzofuran-5-yl)amine	1	9.49	348.1
1az	2-(3-aminosulfonylphenyl)amino-4-[(*R*)-3-hydroxypyrrolidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-hydroxypyrrolidine	3-amino-benzenosulfonamide	4	1.27	375.1
1ba	4-(4-methylpiperidin-1-yl)-2-[4-(1,1-dioxotiomorpholin-4-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-(1,1-dioxotiomorpholin-4-yl)aniline	1	8.10	441.1
1bb	2-(3-aminosulfonylphenyl)amino-4-(pyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	pyrrolidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	4	1.63	359.2
1bc	4-(4-methylpiperidin-1-yl)-2-[4-(methylsulfonyl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-(methylsulfonyl)aniline	1	8.24	386.1
1bd	4-(4-methylpiperidin-1-yl)-2-[3-(methylsulfonyl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-(methylsulfonyl)aniline	1	8.12	386.0

1be	4-(4-methylpiperidin-1-yl)-2-[3-(methylsulfonylamino)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	*N*-(3-aminophenyl)methanosulfonamide	1	8.06	401.0
1bf	2-(4-cyanophenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-aminobenzonitrile	1	9.33	333.1
1bg	4-(4-methylpiperidin-1-yl)-2-[4-(pirazol-4-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	Reference example 2	1	7.99	374.1
1bh	4-(4-methylpiperidin-1-yl)-2-[4-(pirazol-3-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	Reference example 2a	1	8.22	374.1
1bi	2-(3-aminosulfonylphenyl)amino-4-(4-trifluoromethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-trifluoromethyl piperidine	3-amino-benzenesulfonamide	4	2.23	441.2
1bj	2-(3-aminosulfonylphenyl)amino-4-[3-(n-butoxycarbonyl)pyrrolidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	3-(n-butoxycarbonyl)pyrrolidine	3-amino-benzenesulfonamide	4	2.22	459.2
1bk	2-(3-aminosulfonylphenyl)amino-4-[4-(ethoxymethyl)piperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	4-(ethoxymethyl) piperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	4	1.98	431.2
1bl	2-(3-hydroxyphenyl)amino-4-(homopiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperidine	(3-hydroxyphenyl)amine	1	7.84	324.1
1bm	2-(3-acetylaminophenyl)amino-4-(homopiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperidine	(3-acetylaminophenyl)amine	2	2.14	365

1bn	2-(3-aminosulfonylphenyl)amino-4-[4-(2-hydroxyethyl)piperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	4-(2-hydroxyethyl)piperidine	3-amino-benzenesulfonamide	4	1.52	417.2
1bo	2-(3-aminosulfonylphenyl)amino-4-[(*S*)-2-(hydroxymethyl)pyrrolidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-2-(hydroxymethyl)pyrrolidine	3-amino-benzenesulfonamide	4	1.45	389.2
1bp	2-(3-aminosulfonylphenyl)amino-4-(4,4-difluoropiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4,4-difluoropiperidine	3-amino-benzenesulfonamide	4	2.13	409.2
1bq	2-(3-acetylaminophenyl)amino-4-(3-acetylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	3-acetylpiperidine	3-acetylaminophenylamine	2	1.75	393.3
1br	2-(3-aminosulfonylphenyl)amino-4-[(S)-3-hydroxypiperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-3-hydroxypiperidine	3-amino-benzenesulfonamide	4	1.42	389.2
1bs	2-(3-aminosulfonylphenyl)amino-4-(4-methoxypiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methoxypiperidine	3-amino-benzenesulfonamide	4	1.67	403.1
1bt	2-(3-aminosulfonylphenyl)amino-4-[(*R*)-3-hydroxypiperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-hydroxypiperidine	3-amino-benzenesulfonamide	4	1.43	389.2
1bu	2-(3-aminosulfonylphenyl)amino-4-[(*R*)-2-(hydroxymethyl)pyrrolidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-2-(hydroxymethyl)pyrrolidine	3-amino-benzenesulfonamide	4	1.45	389.2

1bv	2-(3-aminosulfonylphenyl)amino-4-(thiazolidin-3-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	thiazolidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	2	1.72	377.2
1bw	4-(3-acetylpiperidin-1-yl)- 2-(3-aminosulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	3-acetylpiperidine	3-amino-*N*-*tert*-butylbenzenesulfonamide	1	6.26	415
1bx	2-(3-aminosulfonylphenyl)amino-4-(4-fluoropiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-fluoropiperidine	3-amino-benzenesulfonamide	4	1.83	391.1
1by	2-(3-aminosulfonylphenyl)amino-4(4-hydroxyethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxyethylpiperidine	3-amino-benzenesulfonamide	4	1.70	431
1bz	2-(3-aminosulfonylphenyl)amino-4-(3-dimethylaminopyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	3-dimethylamino pyrrolidine	3-amino-benzenesulfonamide	2	1.46	402
1aa	2-(3-acetylaminophenyl)amino-4-(thiazolidin-3-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	thiazolidine	3-aminoacetanilide	2	1.78	355

EXAMPLE 2

4-(2-Azabicyclo[2.2.1]heptan-2-yl)-2-(3-fluoro-4-methoxyphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine

a) 4-(2-Azabicyclo[2.2.1]heptan-2-yl)-2-chloro-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 1 section a, but using 2-aza-bicyclo[2.2.1]heptane hydrochloride instead of piperidine, the desired compound was obtained (78 % yield).

LC-MS (method 2): t_R = 2.04 min; m/z = 249 (MH^+).

b) Title compound

To a solution of the compound obtained in the previous section (100 mg, 0.402 mmol) in *tert*-butanol (2 mL), K_2CO_3 (167 mg, 1.20 mmol), X-Phos (19 mg, 0.04 mmol), $Pd_2(dba)_3$ (18 mg, 0.02mmol) and 3-fluoro-4-methoxyphenylamine (69 mg, 0.48 mmol) were added at room temperature and under Ar-atmosphere. The reaction mixture was heated at 100 °C overnight and the crude product thus obtained was diluted with MeOH and filtered over Celite®. The filtrate was concentrated to dryness and chromatographed over silica gel using $CHCl_3$/MeOH mixtures of increasing polarity as eluent, to afford 24 mg of the desired compound (17 % yield).

LC-MS (method 2): t_R = 2.53 min; m/z = 354 (MH^+).

Following a similar procedure to that described in example 2, but using in each case the corresponding starting materials, the following compounds were obtained:

Example	Compound name	Regeant for step a)	Regeant for step b)	HPLC method	t_R (min)	m/z
2a (1)	2-(3-aminosulfonylphenyl)amino-4-(2-benzyl-2,8-diaza-spiro[4.5]decan-1-one-8-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	2-benzyl-2,8-diaza-spiro[4.5]decan-1-one hydrochloride	3-amino-benzenesulfonamide	4	2.22	532
2b (1)	2-(3-aminosulfonylphenyl)amino-4-(2-methyl-2,8-diaza-spiro[4.5]decan-1-one-8-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	2-methyl-2,8-diaza-spiro[4.5]decan-1-one hydrochloride	3-amino-benzenesulfonamide	4	1.60	456
2c (1)	2-[4-(2-hydroxyethylaminosulfonyl)phenyl]amino-4-(4-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethyl piperidine	4-amino-1-(2-hydroxyethyl)benzenesulfonamide	4	1.47	447

2d (1)	4-(4-hydroxymethylpiperidin-1-yl)-2-[4-(2-(morpholin-4-yl)ethylaminosulfonyl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethylpiperidine	4-amino-N-(2-(morpholin-4-yl)ethyl)benzenesulfonamide	4	1.28	516
2e (1)	(*S*)-2-(3-aminosulfonylphenyl)amino-4-[(2-methyloxycarbonyl)pyrrolidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-methyl pyrrolidine-2-carboxylate hydrochloride	3-amino-benzenesulfonamide	4	1.70	417
2f (1)	2-(4-(1,1-dioxothiomorpholin-4-yl)phenyl)amino-4-(4-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethylpiperidine	4-(1,1-dioxothiomorpholin-4-yl)-phenylamine	4	1.58	457
2g (1)	2-(3-acetylaminophenyl)amino-4-(4-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethylpiperidine	3-aminoacetanilide	4	1.48	381
2h (1)	4-(4-hydroxymethylpiperidin-1-yl)-2-(3-(1,3-oxazol-5-yl)phenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethylpiperidine	3-(1,3-oxazol-5-yl)phenylamine	4	1.78	391
2i (1)	4-(4-hydroxymethylpiperidin-1-yl)-2-(3-(1*H*-imidazol-1-ylmethyl)phenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethylpiperidine	3-(1*H*-imidazol-1-ylmethyl)phenylamine	4	1.17	404
2j (1)	(*R*)-2-(3-aminosulfonylphenyl)amino-4-(3-dimethylaminopyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-dimethylaminopyrrolidine	3-amino-benzenesulfonamide	4	0.90	402

2k	2-[4-(2-hydroxyethylaminosulfonyl)phenyl]amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-amino-1-(2-hydroxyethyl)benzenesulfonamide	2	2.13	431
2l	2-(4-(4-methylpiperazin-1-yl)phenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	4-(4-methylpiperazino)phenylamine	2	2.34	406
2m	4-(4-methylpiperidin-1-yl)-2-(3-pyrrolidin-1-ylmethylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-methylpiperidine	3-pyrrolidin-1-ylmethylphenylamine	2	2.50	391
2n	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-(3-pyrrolidin-1-ylmethylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	3-pyrrolidin-1-ylmethylphenylamine	2	2.26	389
2o (1)	4-(4-hydroxymethylpiperidin -1-yl)-2-(4-(4-methylpiperazin-1-yl)phenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethyl piperidine	4-(4-methylpiperazino)phenylamine	4	1.13	422
2p (1)	2-(3-hydroxyethylphenyl)amino-4-(4-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethyl piperidine	3-hydroxyethylphenylamine	4	1.58	368
2q (1)	2-(3-aminosulfonylphenyl)amino-4-(4-[(2-methyl-1*H*-imidazol-1-yl)methyl]piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-[(2-methyl-1*H*-imidazol-1-yl)methyl]piperidine	3-amino-benzenesulfonamide	4	1.18	467
2r (1)	4-(4-hydroxymethylpiperidin-1-yl)-2-[3-(*N*-methylaminosulfonyl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethyl piperidine	3-amino-*N*-methylbenzenesulfonamide	4	1.60	417

2s (1)	4-(4-(3-hydroxypropylpiperidin-1-yl)-2-(3-pyrrolidin-1-ylmethylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-(3-hydroxypropyl) piperidine	3-pyrrolidin-1-ylmethylphenylamine	4	1.45	435
2t (1)	(*R*)-2-(3-aminosulfonylphenyl)amino-4-(2-methylpyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-2-methylpyrrolidine	3-amino-benzenesulfonamide	4	1.83	373
2u (1)	(*S*)-2-(3-aminosulfonylphenyl)amino-4-[(2-methyl)piperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-2-methyl piperidine	3-amino-benzenesulfonamide	4	2.03	387
2v	2-(3-aminosulfonylphenyl)amino-4-(1,4-diazabicyclo[4.3.0]nonan-4-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	1,4-diazabicyclo[4.3.0]nonane	3-amino-benzenesulfonamide	2	1.62	414
2w (1)	2-(3-aminosulfonylphenyl)amino-4-[(3,3-dimethyl)piperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	3,3-dimethyl piperidine	3-amino-benzenesulfonamide	4	2.27	401
2x (1)	(*S*)-4-(2-hydroxymethylpyrrolidin-1-yl)-2-(4-pyrrolidin-1-ylmethylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-2-hydroxymethyl pyrrolidine	4-pyrrolidin-1-ylmethylphenylamine	4	1.25	393
2y (1)	(*R*)-2-(3-aminosulfonylphenyl)amino-4-([2-methyl]piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-2-methyl piperidine	3-amino-benzenesulfonamide	4	2.12	387
2z (1)	(*S*)-2-[(3-cyclopropylcarbonylamino)phenyl]amino-4-(3-hydroxypiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-3-hydroxypiperidine	*N*-(3-aminophenyl)cyclopropanecarboxamide	4	1.75	393

2aa (1)	(*S*)-4-(3-hydroxypiperidin-1-yl)- 2-(3-pyrrolidin-1-ylmethylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-3-hydroxypiperidine	3-pyrrolidin-1-ylmethylphenylamine	4	1.18	393
2ab	4-(homopiperidin-1-yl)-2-(3-pyrrolidin-1-ylmethylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperidine	3-pyrrolidin-1-ylmethylphenylamine	2	2.42	391
2ac	4-(homopiperidin-1-yl)-2-[4-(4-methylpiperazin-1-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	homopiperidine	4-(4-methylpiperazin-1-ylphenylamine	2	2.27	406
2ad (1)	2-[3-(aminosulfonylmethyl)phenyl]amino-4-(4-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethyl piperidine	(3-amino-phenyl)-methanesulfonamide	4	1.47	417
2ae	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-(4-hydroxyethylphenyl) amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	4-hydroxyethylphenylamine	2	2.09	350
2af	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-(3-hydroxyethylphenyl) amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	3-hydroxyethylphenylamine	2	2.12	350
2ag (1)	(*R*)-4-(3-(*N,N*-dimethylamino)pyrrolidin-1-yl)-2-(3-methylamino-sulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-(*N,N*-dimethylamino) pyrrolidine	3-amino-*N*-methylbenzenesulfonamide	4	1.03	416
2ah (1)	(*R*)-2-(3-acetylaminophenyl)amino-4-(3-(*N,N*-dimethylamino)pyrrolidin-1-yl)- 7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-(*N,N*-dimethylamino) pyrrolidine	3-aminoacetanilide	4	0.9	380

2ai (1)	(*R*)-2-[3-(phenylamino)phenyl]amino-4-(3-(*N,N*-dimethylamino)pyrrolidin-1-yl)- 7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-(*N,N*-dimethylamino) pyrrolidine	3-(phenylamino)phenylamine	4	1.47	414
2aj (1)	(*R*)-4-(3-(*N,N*-dimethylamino)pyrrolidin-1-yl)-2-[4-(morpholin-4-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-(*N,N*-dimethylamino) pyrrolidine	[4-(4-morpholino)phenyl]amine	4	0.92	408
2ak (1)	(*R*)-4-(3-*(N,N*-dimethylamino)pyrrolidin-1-yl)-2-(3-fluoro-4-methoxyphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	*(R)*-3-(*N,N*-dimethylamino) pyrrolidine	3-fluoro-4-methoxyphenylamine	4	1.03	371
2al	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-[(4-morpholin-4-yl)methylphenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	4-(morpholin-4-yl)methylphenylamine	2	2.23	405
2am	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-(4-(1-methylpiperazin-4-yl)methylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	4-(1-methylpiperazin-4-yl)methylphenylamine	2	1.99	418
2an	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-[3-(*N*-methylacetamido)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	Reference example 3	2	2.11	377
2ao	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-[3-(N-methylcyclopropanecarbonylamino)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	Reference example 3a	2	2.32	404

2ap (1), (2)	4-(4-hydroxymethylpiperidin-1-yl)-2-[4-(piperidin-4-yl)-phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-hydroxymethyl piperidine	4-(1-*tert*-butoxycarbonylpiperidin-4-yl)-phenylamine	4	1.18	407
2aq	2-(3-aminosulfonylphenyl)amino-4[4-(imidazol-1-ylmethyl)piperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	Reference example 4	3-amino-benzenesulfonamide	2	1.51	453
2ar	2-(3-aminosulfonylphenyl)amino-4-[4-[(N'-*tert*-butylureido)methyl]piperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	Reference example 5	3-amino-benzenesulfonamide	1	6.48	501
2as	4-(3-acetamidopyrrolidin-1-yl)-2-(3-aminosulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	3-acetamidopyrrolidine	3-amino-benzenesulfonamide	2	1.24	416
2at	2-(3-aminosulfonylphenyl)amino-4-(3,3-dimethyl-4-hydroxypiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	3,3-dimethylpiperidin-4-ol (3)	3-amino-benzenesulfonamide	2	1.57	417
2au	4-(1'-acetyl-[4,4']-bipiperidin-1-yl)-2-(3-aminosulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	1-(4,4'-bipiperidin-1-yl)ethanone	3-amino-benzenesulfonamide	4	1.85	498
2av	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-(4-[4-methylpiperazin-1-yl]phenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	4-(4-methylpiperazin-1-ylphenylamine	2	2.07	404
2aw	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-[4-(piperazin-1-yl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	4-(piperazin-1-yl)phenylamine	2	1.78	390

2ax	4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-[4-(2-(pyrrolidin-1-yl)ethoxyphenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-aza-bicyclo[2.2.1]heptane hydrochloride	4-(2-pyrrolidin-1-yl)ethoxyaniline	2	2.11	419
2ay	(*S*)-2-(3-aminosulfonylphenyl)amino-4-[3-(*tert*-butoxycarbonylaminomethyl)pyrrolidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	(*S*)-3-(*tert*-butoxycarbonylaminomethyl)pyrrolidine	3-amino-benzenesulfonamide	2	1.99	488
2az	*trans*-2-(3-aminosulfonylphenyl)amino-4-(4-dimethylamino-3-hydroxypyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	*trans*-4-dimethylamino pyrrolidin-3-ol (4)	3-amino-benzenesulfonamide	2	1.22	418
2ba	(*R*)-2-(3-aminosulfonylphenyl)amino-4-(3-methylpyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-3-methylpyrrolidine	3-amino-benzenesulfonamide	4	1.85	373
2bb	(*R*)-2-(3-aminosulfonylphenyl)amino-4-[3-(N-*tert*-butoxycarbonyl-N-methylamino)pyrrolidin1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	3-(*R*)-(N-*tert*-butoxycarbonyl-N-methylamino)pyrrolidine	3-amino-benzenesulfonamide	2	2.14	488
2bc	(*R*)-4-[3-(N-*tert*-butoxycarbonyl-N-methylamino)pyrrolidin1-yl]-2-(3-fluoro-4-methoxyphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	3-(*R*)-(N-*tert*-butoxycarbonyl-N-methylamino)pyrrolidine	3-fluoro-4-methoxyphenylamine	4	2.50	457
2bd	(*R*)-2-(3-aminosulfonylphenyl)amino-4-[3-(N-*tert*-butoxycarbonylamino)pyrrolidin1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	3-(*R*)-(N-*tert*-butoxycarbonylamino)pyrrolidine	3-amino-benzenesulfonamide	2	1.98	474

2be	(*R*)-4-(3-acetamidopyrrolidin 1-yl)-2-(3-aminosulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	3-(*R*)-acetamidopyrrolidine	3-amino-benzenesulfonamide	2	1.27	416
2bf	2-(3-aminosulfonylphenyl)amino-4-(4-hydroxy-2-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	Reference example 6	3-amino-benzenesulfonamide	2	1.46	403
2bg	*trans*-2-(3-aminosulfonylphenyl)amino-4-(3-hydroxy-4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	*trans*-4-methylpiperidin-3-ol (5)	3-amino-benzenesulfonamide	5	3.13	403
2bh	*cis*-2-(3-aminosulfonylphenyl)amino-4-(3-hydroxy-2-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	*cis*-2-methylpiperidin-3-ol (6)	3-amino-benzenesulfonamide	5	3.04	403
2bi	*cis*-2-(3-aminosulfonylphenyl)amino-4-(3-hydroxy-6-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	*cis*-6-methylpiperidin-3-ol (6)	3-amino-benzenesulfonamide	5	3.09	403
2bj	*cis*-2-(3-aminosulfonylphenyl)amino-4-(3-hydroxy-5-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	*cis*-5-methylpiperidin-3-ol (6)	3-amino-benzenesulfonamide	5	3.22	403
2bk	(6*S*,8*R*)-2-(3-aminosulfonylphenyl)amino-4-(8-hydroxy-1,4-diazabicyclo[4.3.0]nonan-4-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	Reference example 7	3-amino-benzenesulfonamide	2	1.20	555.6
2bl	(*S*)-2-(3-aminosulfonylphenyl)amino-4-(1,4-diazabicyclo[4.3.0]nonan-4-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	Reference example 7a	3-amino-benzenesulfonamide	2	1.62	414.4

2bm	*(S)*-2-(4-hydroxyethylphenyl)amino-4-(1,4-diazabicyclo[4.3.0]nonan-4-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	Reference example 7a	4-hydroxyethylphenylamine	2	1.70	379.5
2bn	(6*S*,3*S*)-2-(3-aminosulfonylphenyl)amino-4-(3-methyl-1,4-diazabicyclo[4.3.0]nonan-4-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	Reference example 7b	3-amino-benzenesulfonamide	2	1.88	428.4
2bo	2-(3-aminosulfonylphenyl)amino-4-[(2-methyl)piperidin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine	2-methylpiperidine	3-amino-benzenesulfonamide	4	2.05	387.3
2bp	2-(3-aminosulfonylphenyl)amino-4-[(2-hydroxymethyl)piperidin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine	2-(hydroxymethyl)piperidine	3-amino-benzenesulfonamide	4	1.62	403.2
2bq	4-[(4-hydroxymethyl)piperidin-1-yl]-2-[4-(methoxyethyl)aminosulfonylphenyl]amino-7H-pyrrolo[2,3-d]pyrimidine	4-(hydroxymethyl)piperidine	4-amino-N-(2-methoxyethyl)benzenesulfonamide	4	1.67	461.3
2br	4-[(4-hydroxymethyl)piperidin-1-yl]-2-(3-pyrrolidin-1-ylmethylphenyl)amino-7H-pyrrolo[2,3-d]pyrimidine	4-(hydroxymethyl)piperidine	3-pyrrolidin-1-ylmethylphenylamine	4	1.18	407.3

(1) First step using 1,4-dioxane instead of ethanol

(2) An additional deprotection step was necessary: over a solution of the product obtained, 4M dioxane/ $HCl_{(g)}$ (2 mL) were added to afford the desired product.

(3) Described in WO/2005/026145

(4) Described in WO/2007/146759

(5) Described in WO/2001/087866

(6) Described in WO/2007/122103

EXAMPLE 3

(R)-2-(3-Aminosulfonylphenyl)amino-4-(3-(1-methylureido)pyrrolidin1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

a) (R)-2-(3-Aminosulfonylphenyl)amino-4-(3-(N-methylamino)pyrrolidin1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

A mixture of the compound obtained in example 2bb (390 mg, 0.8 mmol), 4M dioxane/$HCl_{(g)}$ (7 mL), and methanol (3 mL) was stirred under Ar-atmosphere for 2 h at room temperature. The resulting mixture was concentrated to dryness and the residue thus obtained was partitioned between 0.2 N $NaHCO_3$ and $CHCl_3$. The phases were separated and the combined organic phases were dried over Na_2SO_4 and concentrated to dryness to afford 225 mg of the desired product.

LC-MS (method 2): t_R = 1.27 min; m/z = 388 (MH^+).

b) Title compound

To a solution of the compound obtained in the previous section (40 mg, 0.1 mmol) in DMF (1 mL), trimethylsilyl isocyanate (14 mg, 0.12 mmol) was added under Ar-atmosphere and the mixture was stirred at room temperature overnight. The resulting solution was concentrated to dryness, diluted with EtOAc and washed twice with NH_4Cl saturated aqueous solution. The combined organic phases were dried over Na_2SO_4 and concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using EtOAc/MeOH/NH_3 mixtures of increasing polarity as eluent, to afford 18 mg of the desired compound (43 % yield).

LC-MS (method 2): t_R = 1.23 min; m/z = 431 (MH^+).

Following a similar procedure to that described in example 3, but using the corresponding starting material, the following compounds were obtained:

Example	Compound name	Reagent for step a)	Reagent for step b)	HPLC method	t_R (min)	m/z
3a	(*R*)-2-(3-aminosulfonylphenyl)amino-4-[3-(N-methylmethanesulfonylamino)pyrrolidin1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	Example 2bb	methanesulfonyl chloride (1)	2	1.55	466

3b	(*R*)-2-(3-aminosulfonylphenyl)amino-4-[3-(N-phenoxycarbonylamino)pyrrolidin1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	Example 2bh	phenyl chloroformate (1)	2	1.91	494
3c	(*R*)-2-(3-aminosulfonylphenyl)amino-4-[3-(N-methanesulfonylamino)pyrrolidin1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine	Example 2bh	methanesulfonyl chloride	2	1.38	452
3d	(*R*)-2-(3-aminosulfonylphenyl)amino-4-(3-ureidopyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	Example 2bh	trimethylsilyl isocyanate	2	1.15	417

(1) Using pyridine instead of DMF as a solvent

EXAMPLE 4

(*R*)-2-(3-Aminosulfonylphenyl)amino-4-(3-(3-methylureido)pyrrolidin1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

To a solution of the compound obtained in example 3c (27 mg, 0.05 mmol) in pyridine (2 mL), a 2 M solution of methylamine in THF (0.27 mL, 0.54 mmol) was added under Ar-atmosphere. The resulting mixture was heated at 100 °C overnight and concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using $CHCl_3$/MeOH/NH_3 mixtures of increasing polarity as eluent, to afford the desired compound in quantitative yield.

LC-MS (method 2): t_R = 1.24 min; m/z = 431 (MH^+).

Following a similar procedure to that described in example 4, but using the corresponding starting material, the following compound were obtained:

Example	Compound name	Starting material	HPLC method	t_R (min)	m/z
4a	(*R*)-2-(3-aminosulfonylphenyl)amino-4-{3-[3-(2,2,2-trifluoro)ethylureido]pyrrolidin1-yl}-7*H*-pyrrolo[2,3-d]pyrimidine	2,2,2-trifluoroethylamine	2	1.58	499

4b	(*R*)-2-(3-aminosulfonylphenyl)amino-4-(3-((3,3-diethylureido)pyrrolidin1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	diethylamine	2	1.65	473

EXAMPLE 5

(*S*)-2-(3-Aminosulfonylphenyl)amino-4-(3-aminomethylpyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 3 section a, but using 2ay instead of example 2bb, the product was obtained (44 % yield).

LC-MS (method 2): t_R = 1.08 min; m/z = 388.3 (MH^+).

EXAMPLE 6

2-(3-Acetylaminosulfonylphenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

A mixture of the compound obtained in example 1b (34 mg, 0.088 mmol), acetic anhydride (0.025 mL, 0.264 mmol) and triethylamine (0.011 mL, 0.088 mmol) in $CHCl_3$ (2 mL) was stirred at room temperature overnight. The resulting solution was diluted with $CHCl_3$ and washed with water and brine. The combined organic phases were dried over Na_2SO_4 and concentrated to dryness. The crude product obtained was chromatographed over silica gel using CH_2Cl_2/MeOH mixtures of increasing polarity as eluent, to afford 25 mg of the desired compound (55 % yield).

LC-MS (method 2): t_R = 1.71 min; m/z = 429 (MH^+).

Following a similar procedure to that described in example 6, but using the corresponding starting material, the following compound is obtained:

Example	Compound name	Starting material	HPLC method	t_R (min)	m/z
6a	4-(4-methylpiperidin-1-yl)-2-(3-propionylaminosulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine	propionyl chloride	2	1.75	443.5

EXAMPLE 7

2-(3-Acetylaminosulfonylphenyl)amino-4-(4-methylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine sodium salt

To a solution of example 6 (16 mg, 0.039 mmol) in EtOH (1.5 mL), a 0.05 M aqueous solution of NaOH in EtOH (0.78 mL) was added. The mixture was stirred at room temperature for 30 min and concentrated to dryness to afford 18 mg of the desired product (100% yield).

LC-MS (method 2): t_R = 1.71 min; m/z = 429 (MH^+).

EXAMPLE 8

(2*S*,4*S*)-2-(3-Aminosulfonylphenyl)amino-4-(2-hydroxymethyl-4-hydroxypyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

a) (2*S*,4*S*)-2-Chloro-4-(2-methoxycarbonyl-4-hydroxypyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 1 section a, but using (2*S*, 4*S*)-methyl-4-hydroxy-2-pyrrolidincarboxylate instead of piperidine the desired product was obtained (61%).

LC-MS (method 2): t_R = 1.19 min; m/z = 297 (MH^+).

b) (2*S*,4*S*)-2-(3-Amino-N-*tert*-butylsulfonylphenyl)amino-4-(2-methoxycarbonyl-4-hydroxypyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 2 section b, but using 3-amino-N-*tert*-butylbenzenesulfonamide instead of 3-fluoro-4-methoxyphenylamine, the desired product was obtained (52 % yield).

LC-MS (method 2): t_R = 1.78 min; m/z = 489.3 (MH^+).

c) (2*S*,4*S*)-2-(3-Amino-N-*tert*-butylsulfonylphenyl)amino-4-(2-hydroxymethyl-4-hydroxypyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

A solution of the compound obtained in the previous section (357 mg, 0.731 mmol) in THF (8 mL) was added to a suspension of $LiAlH_4$ (56 mg, 1.462 mmol) in THF (4 mL) under Ar-atmosphere. The mixture was refluxed overnight, cooled and diluted with CH_2Cl_2 (0.766 mL) The resulting mixture was treated with a saturated solution of sodium tartrate (0.076 mL). The organic phase was dried over Na_2SO_4 and concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using hexane/EtOAc mixtures of increasing polarity as eluent, to afford 79 mg of the desired compound (35 % yield).

LC-MS (method 2): t_R = 1.67 min; m/z = 461 (MH^+).

d) Tiltle compound

A mixture of the compound obtained in the previous section (107 mg, 0.233 mmol), THF (2 mL) and 6N $HCl_{(g)}$ (4 mL) was stirred at reflux overnight. The solvent was concentrated and the residue was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The combined organic phases were dried over Na_2SO_4 and concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using hexane/EtOAc mixtures of increasing polarity as eluent, to afford 25 mg of the desired compound (25 % yield).

LC-MS (method 2): t_R = 1.22 min; m/z = 405 (MH^+).

Following a similar procedure to that described in example 8 but using the corresponding starting material, the following compound is obtained:

Example	Compound name	Reagent for step a)	Reagent for step b)	HPLC method	t_R (min)	m/z
8a	(*R*)-2-(3-aminosulfonylphenyl)amino-4-(3-hydroxymethylpyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine	(*R*)-methyl 3-pyrrolidinecarboxylate	3-aminobenzenesulfonamide	4	1.42	389

EXAMPLE 9

2-(3-Aminosulfonylphenyl)amino-4-[3-(1-hydroxyliminoethyl)piperidin-1-yl]-7*H*-pyrrolo[2,3-d]pyrimidine

a) 2-Chloro-4-(3-acetylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 1 section a, but using 1-(piperidin-3-yl)ethanone instead of piperidine, the desired product was obtained (39 %).

LC-MS (method 2): t_R = 1.75 min; m/z = 279 (MH^+).

b) 4-(3-Acetylpiperidin-1-yl)-2-(3-aminosulfonylphenyl)amino-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 2 section b, but using 3-aminobenzenesulfonamide, instead of 3-fluoro-4-methoxyphenylamine the product was obtained (37 % yield).

LC-MS (method 1): t_R = 6.26 min; m/z = 415 (MH^+).

c) Title compound

To a solution of the compound obtained in previous section (96 mg, 0.233 mmol) in MeOH (3 mL) hydroxylamine hydrochloride (16.2 mg, 0.233 mmol) and sodium acetate (4 mg, 0.023 mmol) were added under Ar-atmosphere. The mixture was stirred at room temperature overnight and the resulting solution was evaporated to dryness, diluted with EtOAc and washed twice with H_2O. The combined organic phases were dried over Na_2SO_4 and concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using hexane/EtOAc mixtures of increasing polarity as eluent, to afford 17 mg of the desired compound (13 % yield).

LC-MS (method 1): t_R = 6.13 min; m/z = 430 (MH^+).

EXAMPLE 10

(*S*)-2-(3-Aminosulfonylphenyl)amino-4-(2-methoxymethylpyrrolidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

a) (*S*)-2-Chloro-4-(2-methoxymethylpyrrolidin-1-yl)-7*H*-pyrrolo[2,3-

d]pyrimidine

Following a similar procedure to that described in example 1 section a, but using (S)-2-methoxymethylpyrrolidine, instead of piperidine, and 1,4-dioxane instead of EtOH, 150 mg of the desired product were obtained (83 % yield).

b) (S)-2-(3-Amino-N-*tert*-butylsulfonylphenyl)amino-4-(2-methoxymethylpyrrolidin-1-yl)-7H-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 2 section b, but using 3-amino-*N*-*tert*-butylbenzenesulfonamide instead of 3-fluoro-4-methoxyphenylamine, the desired product was obtained (35 % yield).

c) Title compound

To a solution of the compound obtained in the previous section (0.088 g, 0.19 mmol)) in AcN (2 mL), trifluoromethanesulfonic acid (0.16 mL) was added under Ar-atmosphere and the mixture was stirred at room temperature overnight. The resulting solution was concentrated to dryness, diluted with EtOAc and washed twice with H_2O. The organic phase was dried over Na_2SO_4 and concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using hexane/EtOAc mixtures of increasing polarity as eluent, to obtain 7 mg of the desired compound (22 % yield).

LC-MS (method 4): t_R = 1.77 min; m/z = 403 (MH^+).

EXAMPLE 11

2-[4-(2-Hydroxyethylaminocarbonyl)phenyl]amino-4-(4-hydroxymethylpiperidin-1-yl)- 7*H*-pyrrolo[2,3-d]pyrimidine

a) 2-(4-Ethoxycarbonylphenyl)amino-4-(4-hydroxymethylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example example 2 section b, but using the compound obtained in example 2c section a and ethyl 4-aminobenzoate instead of 4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-chloro-7*H*-

pyrrolo[2,3-d]pyrimidine and 3-fluoro-4-methoxyphenylamine, the desired compound was obtained.

b) 2-(4-Carboxyphenyl)amino-4-(4-hydroxymethylpiperidin-1-yl)- 7*H*-pyrrolo[2,3-d]pyrimidine

To a solution of 354 mg of the compound obtained in the previous section in DME (9 mL), a solution of $LiOH.H_2O$ (188 mg) in 4.5 mL of H_2O was added. The mixture was stirred at room temperature for 40 h. and cooled to 0 ºC. A 1N aqueous HCl solution (4 mL) was added and the mixture was concentrated. The crude product thus obtained was chromatographed over a SCX-2 column to afford 53 mg of the desired compound.

LC-MS (method 4): t_R = 1.55 min; m/z = 368 (MH^+).

c) Title compound

To a solution of the compound obtained in the previous section (100 mg, 0.2 mmol) in DMF (3 mL), a mixture of EDC.HCl (117 mg, 0.60 mmol), HOBT (82 mg, 0.60 mmol), DIEA (87 μL, 0.60 mmol) and 2-aminoethanol (61 μL, 1.0 mmol) was added under Ar-atmposphere. The resulting mixture was stirred at room temperature overnight and concentrated to dryness. The crude product thus obtained was chromatographed over silica gel using CH_2Cl_2/MeOH/NH_3 mixtures of increasing polarity as eluent, to afford 51 mg of the desired compound (62% yield).

LC-MS (method 4): t_R = 1.35 min; m/z = 411 (MH^+)

Example	Compound name	Starting material	HPLC method	t_R (min)	m/z
11a	4-(4-hydroxymethylpiperidin-1-yl)-2-[4-(2-methoxyethylaminocarbonyl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-methoxyethylamine	4	1.53	425

11b	4-(4-hydroxymethylpiperidin-1-yl)-2-[(4-(2-(1-methylpyrrolidin-2-yl)ethyl)aminocarbonyl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	2-(2-aminoethyl)-1-methylpyrrolidine	4	1.25	478
11c	4-(4-hydroxymethylpiperidin-1-yl)-2-[(4-(2-(morpholin-4-yl)ethyl)aminocarbonyl)phenyl]amino-7*H*-pyrrolo[2,3-d]pyrimidine	4-(2-aminoethyl)morpholine	4	1.18	480

EXAMPLE 12

(S)-2-(3-Aminosulfonylphenyl)amino-4-(3-(2-hydroxypropan-2-yl)piperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

a) (S)-2-Chloro-4-(3-ethoxycarbonylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example 1 section a, but using (*S*)-ethyl 3-piperidinecarboxylate instead of piperidine, the desired compound was obtained.

LC-MS (method 4): t_R = 3.01 min; m/z = 309 (MH^+).

b) (S)-2-(3-Aminosulfonylphenyl)amino-4-(3-ethoxycarbonylpiperidin-1-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

Following a similar procedure to that described in example example 2 section b, but using the compound obtained in the previous section and 3-aminobenzenesulfonamide instead of 4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-chloro-7*H*-pyrrolo[2,3-d]pyrimidine and 3-fluoro-4-methoxyphenylamine, the desired compound was obtained.

LC-MS (method 4): t_R = 2.05 min; m/z = 445 (MH^+).

c) Title compound

To a solution of the compound obtained in the previous section (65 mg, 0.15 mmol) in THF (3 mL), a 1.4 M solution of methylmagnesium bromide in THF (0.75

mL, 1.05 mmol) was added at 0 ºC. The resulting mixture was stirred under Ar-atmoshere at room temperature overnight. The mixture was concentrated to dryness and the residue thus obtained was chromatographed over silica gel using CH_2Cl_2/MeOH/NH_3 mixtures of increasing polarity as eluent, to afford 17 mg of the desired compound (26% yield).

LC-MS (method 4): t_R = 1.78 min; m/z = 431 (MH^+)

EXAMPLE 13

2-(3-Aminosulfonylphenyl)amino-4-(7-oxo-6-azabicyclo[3.2.1]octan-6-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

a) 4-(3-Carboxycyclohexylamino)-2-chloro-7*H*-pyrrolo[2,3-d]pyrimidine

To a solution of 2,4-dichloro-7*H*-pyrrolo[2,3-d]pyrimidine (0.50 g, 2.66 mmol) in THF/H_2O (1:1) (7 mL), 3-aminocyclohexane carboxylic acid (0.38 g, 2.66 mmol) and K_2CO_3 (0.55 g, 3.98 mmol) were added. The reaction was stirred at 110ºC in a sealed tube for 10 h. The resulting mixture was diluted with H_2O and the phases were separated. Aqueous 1N HCl was added at 0 °C until pH = 3 and extracted thrice with EtOAc/MeOH (9:1). The combined organic phases were dried over Na_2SO_4 and concentrated to dryness and the crude product thus obtained was directly used in the next step.

LC-MS (method 2): t_R = 0.94 min; m/z = 295 (MH^+).

a) 2-Chloro-4-(7-oxo-6-azabicyclo[3.2.1]octan-6-yl)-7*H*-pyrrolo[2,3-d]pyrimidine

To a solution of the product obtained in the previous section in DMF (25 mL), HBTU (1.14 g, 3.00 mmol) and DIEA (0.65 mL, 3.73 mmol) were added. The reaction was stirred under Ar-atmosphere at room temperature for 18 h. The resulting mixture was concentrated to dryness and the residue was dissolved in DMF (20 mL). DIEA (0.65 mL, 3.73 mmol) was added and the mixture was stirred overnight at 120 ºC. The resulting mixture was evaporated to dryness and the crude product thus obtained was chromatographed over silica gel using $CHCl_3$/MeOH mixtures of increasing polarity as eluent, to afford 0.15 g of the desired compound (20 % yield).

LC-MS (method 2): t_R = 1.95 min; m/z = 277 (MH^+).

b) Title compound

Following a similar procedure to that described in example 2 section b, but using the compound obtained in the previous section, and 3-aminobenzenesulfonamide instead of 4-(2-azabicyclo[2.2.1]heptan-2-yl)-2-chloro-7*H*-pyrrolo[2,3-d]pyrimidine and 3-fluoro-4-methoxyphenylamine, the desired product was obtained (19% yield).

LC-MS (method 2): t_R = 1.72 min; m/z = 413 (MH^+).

EXAMPLE 14

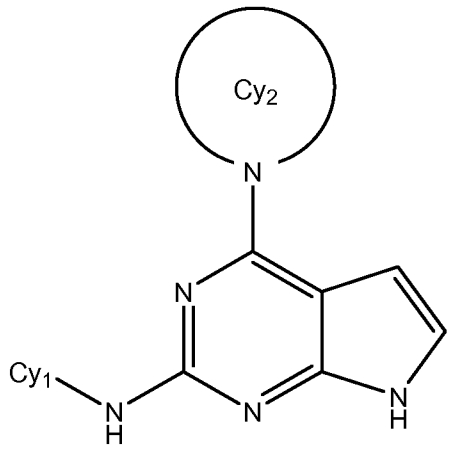
Biological assay 1: JAK3 kinase inhibition

In a final volume of 50 µL, 5 µL of the test product dissolved in 10% DMSO (final concentration, 0.001-10 µM), was incubated with 4 µg/mL of human JAK3 781-1124, 1 µg/mL of Poly-L-Ala, L-Glu, L-Lys, L-Tyr and ATP (0.2 µM, approximately $2x10^5$ cpm of γ^{33}P-ATP) in HEPES buffer (60 mM, pH 7.5) with Mg^{2+} chloride (3 mM), Mn^{2+} chloride (3 mM), sodium orthovanadate (3µM) and dithiotreitol (1.2 mM). The reaction was started by adding Mg^{2+}[γ^{33}P-ATP]. After incubation for 50 min at room temperature, the reaction was quenched by the addition of 50 µL of 2% phosphoric acid solution. The reaction mixture was filtered in vacuo and washed three times with a 150 mM phosphoric acid solution. 200 µL of liquid scintillation was added before drying it and counting it.

The compounds of all examples showed more than 50% of inhibition of JAK3 activity at 10 µM in this assay.

CLAIMS

1.- A compound of formula **I**:



I

wherein:

Cy_1 represents phenyl or a 5- or 6-membered aromatic heterocycle bonded to the NH group through a C atom, each of which can be optionally fused to a 5- or 6-membered saturated, partially unsaturated or aromatic carbocyclic or heterocyclic ring, wherein Cy_1 can contain from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms of the optional 5- or 6-membered fused ring can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_1 can be optionally substituted with one or more R_1;

Cy_2 represents a 3- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated or partially unsaturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2;

each R_1 and R_2 independently represent C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, halogen, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-COCONR_3R_3$, $-OR_3$, $-OCOR_4$, $-OCONR_4R_4$, $-OCO_2R_4$, $-SR_3$, $-SOR_4$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5CO_2R_4$, $-NR_5SO_2R_4$, $-C(=N-OH)R_4$ or Cy_3, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7;

R_3 represents hydrogen or R_4;

R_4 represents C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, or Cy_4, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_4 can be optionally substituted with one or more R_8;

R_5 represents hydrogen or C_{1-4}alkyl;

R_6 represents halogen, -CN, $-NO_2$, $-COR_9$, $-CO_2R_9$, $-CONR_9R_9$, $-OR_9$, $-OCOR_{10}$, $-OCONR_{10}R_{10}$, $-OCO_2R_{10}$, $-SR_9$, $-SOR_{10}$, $-SO_2R_{10}$, $-SO_2NR_9R_9$, $-SO_2NR_5COR_{10}$, $-NR_9R_9$, $-NR_5COR_9$, $-NR_5CONR_9R_9$, $-NR_5CO_2R_{10}$, $-NR_5SO_2R_{10}$, $-C(=N\text{-}OH)R_{10}$ or Cy_4, wherein Cy_4 can be optionally substituted with one or more R_8;

R_7 represents C_{1-4}alkyl that can be optionally substituted with one or more R_{11}, or R_7 represents any of the meanings described for R_{12};

R_8 represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, cyanoC_{1-4}alkyl or any of the meanings described for R_{12};

R_9 represents hydrogen or R_{10};

R_{10} represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, cyanoC_{1-4}alkyl, Cy_5-C_{1-4}alkyl or Cy_4, wherein Cy_4 can be optionally substituted with one or more R_8;

R_{11} represents halogen, -CN, $-NO_2$, $-COR_9$, $-CO_2R_9$, $-CONR_9R_9$, $-OR_9$, $-OCOR_{10}$, $-OCONR_{10}R_{10}$, $-OCO_2R_{10}$, $-SR_9$, $-SOR_{10}$, $-SO_2R_{10}$, $-SO_2NR_9R_9$, $-SO_2NR_5COR_{10}$, $-NR_9R_9$, $-NR_5COR_9$, $-NR_5CONR_9R_9$, $-NR_5CO_2R_{10}$, $-NR_5SO_2R_{10}$, or $-C(=N\text{-}OH)R_{10}$;

R_{12} represents halogen, -CN, $-NO_2$, $-COR_{13}$, $-CO_2R_{13}$, $-CONR_{13}R_{13}$, $-OR_{13}$, $-OCOR_{14}$, $-OCONR_{14}R_{14}$, $-OCO_2R_{14}$, $-SR_{13}$, $-SOR_{14}$, $-SO_2R_{14}$, $-SO_2NR_{13}R_{13}$, $-SO_2NR_5COR_{14}$, $-NR_{13}R_{13}$, $-NR_5COR_{13}$, $-NR_5CONR_{13}R_{13}$, $-NR_5CO_2R_{14}$, $-NR_5SO_2R_{14}$ or $-C(=N\text{-}OH)R_{14}$;

R_{13} represents hydrogen or R_{14};

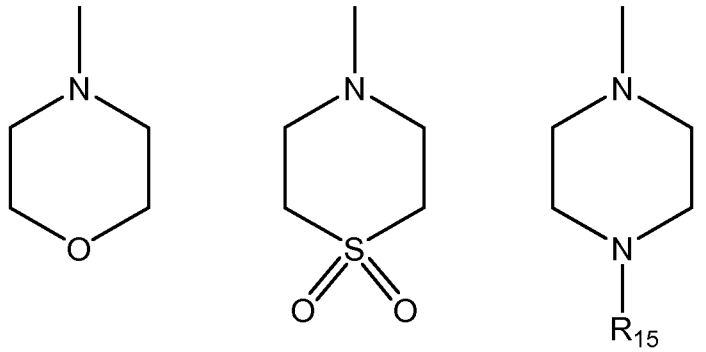
R_{14} represents C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl or hydroxyC_{1-4}alkyl;

or two R_{13} groups or two R_{14} groups on the same N atom can be bonded completing, together with the N atom, a 5- or 6-membered saturated ring, which can additionally contain one or two heteroatoms selected from N, S and O and which can be optionally substituted with one or more C_{1-4}alkyl groups;

each Cy_3 and Cy_4 independently represent a 3- to 7-membered monocyclic

or 6- to 11-membered bicyclic ring which can be carbocyclic or heterocyclic, in which case it can contain from 1 to 4 heteroatoms selected from N, S and O, wherein each Cy_3 and Cy_4 can be saturated, partially unsaturated or aromatic, and can be bonded to the rest of the molecule through any available C or N atom, and wherein one or more C or S atoms of the ring can be optionally oxidized forming CO, SO or SO_2 groups;

Cy_5 represents a ring selected from (a)-(c):



(a) (b) (c) ; and

R_{15} represents hydrogen or C_{1-4}alkyl;

or a salt thereof.

2.- A compound according to claim 1 wherein Cy_1 represents phenyl or pyridyl, which can be optionally fused to a 5- or 6-membered saturated, partially unsaturated or aromatic carbocyclic or heterocyclic ring, wherein Cy_1 can contain from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms of the 5- or 6-membered fused ring can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_1 can be optionally substituted with one or more R_1.

3.- A compound according to claim 1 wherein Cy_1 represents phenyl optionally substituted with one or more R_1.

4.- A compound according to claim 1 wherein Cy_1 represents phenyl substituted with one or more R_1.

5.- A compound according to claim 1 wherein Cy_1 represents phenyl substituted with one or two R_1.

6.- A compound according to claim 1 wherein Cy_1 represents phenyl substituted at

one or two of positions 3, 4 and 5 with an R_1.

7.- A compound according to claim 1 wherein Cy_1 represents phenyl substituted with one R_1, which is placed at position 3 or 4 of the phenyl ring.

8.- A compound according to any of claims 1 to 7 wherein each R_1 represents C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, halogen, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-COCONR_3R_3$, $-OR_3$, $-OCOR_4$, $-OCONR_4R_4$, $-OCO_2R_4$, $-SR_3$, $-SOR_4$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5CO_2R_4$, $-C(=N\text{-}OH)R_4$ or Cy_3, wherein C_{1-4}alkyl, C_{2-4}alkenyl and C_{2-4}alkynyl can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

9.- A compound according to any of claims 1 to 7 wherein each R_1 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-COCONR_3R_3$, $-OR_3$, $-SR_3$, $-SO_2R_4$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

10.- A compound according to any of claims 1 to 7 wherein each R_1 represents C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein the C_{1-4}alkyl group can be optionally substituted with one or more R_6 and Cy_3 can be optionally substituted with one or more R_7.

11.- A compound according to any of claims 1 to 7 wherein each R_1 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, halogen, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

12.- A compound according to any of claims 1 to 7 wherein each R_1 represents hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, $NR_9R_9SO_2$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $R_{10}CONR_5SO_2$-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $-CONR_3R_3$, $-OR_3$, $-SO_2NR_3R_3$, $-SO_2NR_5COR_4$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

13.- A compound according to any of claims 1 to 12 wherein Cy_3 in R_1 represents Cy_{3a}, and Cy_{3a} represents a 5- or 6-membered saturated monocyclic heterocycle

which contains 1 or 2 heteroatoms selected from N, S and O, wherein said ring can be bonded to the rest of the molecule through any available C or N atom, and wherein one or more C or S atoms of the ring can be optionally oxidized forming CO, SO or SO_2 groups, wherein said Cy_{3a} can be optionally substituted with one or more R_7.

14.- A compound according to any of claims 1 to 12 wherein Cy_3 in R_1 represents Cy_{3b}, and Cy_{3b} represents a 5- or 6-membered saturated monocyclic heterocycle which contains 1 or 2 heteroatoms selected from N, S and O with the proviso that it contains at least 1 N atom, wherein said ring is bonded to the rest of the molecule through a N atom, wherein one or more C or S ring atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein said Cy_{3b} can be optionally substituted with one or more R_7.

15.- A compound according to any of claims 1 to 14 wherein Cy_4 in R_1 represents Cy_{4a}, and Cy_{4a} represents a 5- or 6-membered saturated monocyclic heterocycle which contains 1 or 2 heteroatoms selected from N, S and O and which can be bonded to the rest of the molecule through any available C or N atom, wherein one or more C or S ring atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein said Cy_{4a} can be optionally substituted with one or more R_8.

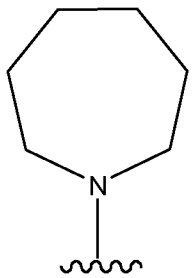
16.- A compound according to any of claims 1 to 15 wherein R_3 in R_1 represents hydrogen or R_4 and R_4 in R_1 represents C_{1-4}alkyl or Cy_4, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_4 can be optionally substituted with one or more R_8.

17.- A compound according to any of claims 1 to 15 wherein R_3 in R_1 represents hydrogen or R_4 and R_4 in R_1 represents C_{1-4}alkyl, Cy_4-C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl or Cy_4, wherein any Cy_4 can be optionally substituted with one or more R_8.

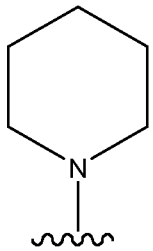
18.- A compound according to any of claims 1 to 17 wherein Cy_2 represents a 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein the ring which contains the N atom which is bonded to the pyrrolopyrimidine moiety is saturated, wherein Cy_2 contains from 1 to 4 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

19.- A compound according to any of claims 1 to 17 wherein Cy_2 represents a saturated 5- to 7-membered monocyclic or 6- to 11-membered bicyclic heterocycle, wherein Cy_2 contains from 1 to 3 heteroatoms selected from N, O and S, wherein one or more C or S atoms can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

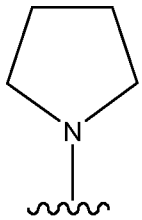
20.- A compound according to any of claims 1 to 17 wherein Cy_2 is selected from (a)-(i):



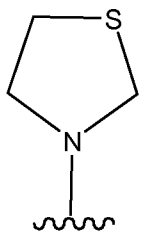
(a)



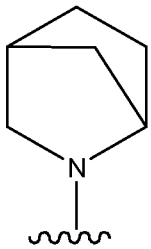
(b)



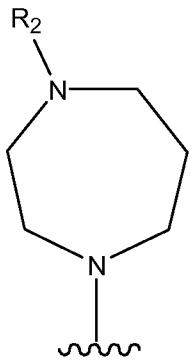
(c)



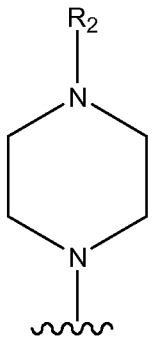
(d)



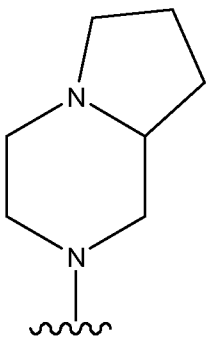
(e)



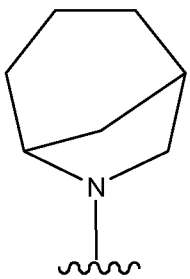
(f)



(g)



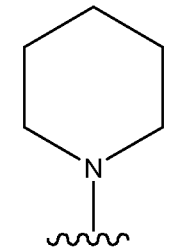
(h)



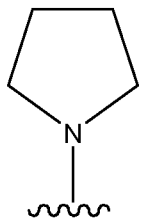
(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

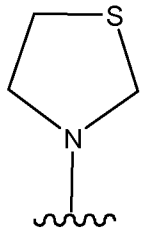
21.- A compound according to any of claims 1 to 17 wherein Cy_2 is selected from (b), (c), (d), (e), (h) and (i):



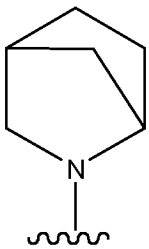
(b)



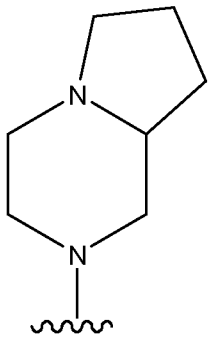
(c)



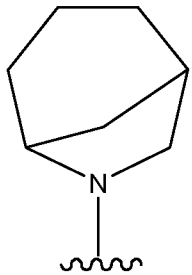
(d)



(e)



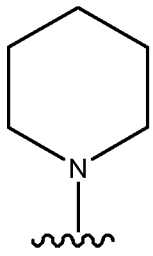
(h)



(i) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

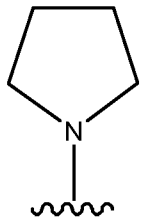
22.- A compound according to any of claims 1 to 17 wherein Cy_2 represents (b):



(b) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

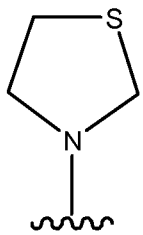
23.- A compound according to any of claims 1 to 17 wherein Cy_2 represents (c):



(c) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

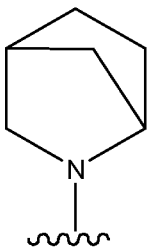
24.- A compound according to any of claims 1 to 17 wherein Cy_2 represents (d):



(d) ,

wherein one or more C or S atoms of Cy_2 can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

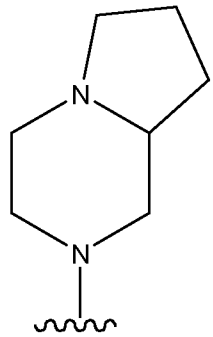
25.- A compound according to any of claims 1 to 17 wherein Cy_2 represents (e):



(e) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

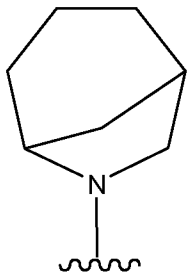
26.- A compound according to any of claims 1 to 17 wherein Cy_2 represents (h)



(h) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

27.- A compound according to any of claims 1 to 17 wherein Cy_2 represents (i):



(i) ,

wherein one or more C atoms of Cy_2 can be optionally oxidized forming CO groups, and wherein Cy_2 can be optionally substituted with one or more R_2.

28.- A compound according to any of claims 1 to 27 wherein each R_2 represents C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6 and wherein Cy_3 can be optionally substituted with one or more R_7.

29.- A compound according to any of claims 1 to 27 wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, R_9CO-C_{1-4}alkyl, NR_9R_9-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $R_{10}SO_2NR_5$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $NR_9R_9CONR_5$-C_{1-4}alkyl, halogen, -CN, $-COR_3$, $-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$, $-NR_5SO_2R_4$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7 and wherein Cy_4 can be optionally substituted with one or more R_8.

30.- A compound according to any of claims 1 to 27 wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, halogen, -CN, $-COR_3$,

$-CO_2R_3$, $-CONR_3R_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$ or Cy_3, wherein Cy_3 can be optionally substituted with one or more R_7.

31.- A compound according to any of claims 1 to 30 wherein Cy_3 in R_2 represents Cy_{3c}, and Cy_{3c} represents a saturated 3- to 7-membered monocyclic or 6- to 11-membered bicyclic ring which can be carbocyclic or heterocyclic, in which case it can contain from 1 to 4 heteroatoms selected from N, S and O, wherein Cy_{3c} can be bonded to the rest of the molecule through any available C or N atom, wherein one or more C or S atoms of the ring can be optionally oxidized forming CO, SO or SO_2 groups, and wherein Cy_{3c} can be optionally substituted with one or more R_7.

32.- A compound according to any of claims 1 to 27 wherein each R_2 represents C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein C_{1-4}alkyl can be optionally substituted with one or more R_6.

33.- A compound according to any of claims 1 to 27 wherein each R_2 represents C_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, Cy_4-C_{1-4}alkyl, R_9CO-C_{1-4}alkyl, NR_9R_9-C_{1-4}alkyl, R_9CONR_5-C_{1-4}alkyl, $R_{10}SO_2NR_5$-C_{1-4}alkyl, NR_9R_9CO-C_{1-4}alkyl, $NR_9R_9CONR_5$-C_{1-4}alkyl, $-COR_3$, $-OR_3$, $-NR_3R_3$, $-NR_5COR_3$, $-NR_5CONR_3R_3$ or $-NR_5SO_2R_4$, wherein Cy_4 can be optionally substituted with one or more R_8.

34.- A compound according to any of claims 1 to 33 wherein R_3 in R_2 represents hydrogen or R_4 and R_4 in R_2 represents C_{1-4}alkyl optionally substituted with one or more R_6.

35.- A compound according to any of claims 1 to 33 wherein R_3 in R_2 represents hydrogen or R_4 and R_4 in R_2 represents C_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl or haloC_{1-4}alkyl.

36.- A pharmaceutical composition which comprises a compound of formula **I** according to any of claims 1 to 35 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.

37.- Use of a compound of formula **I** according to any of claims 1 to 35 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of a disease mediated by JAK3.

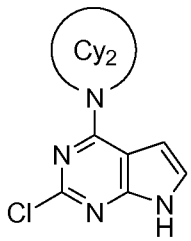
38.- Use of a compound of formula **I** according to any of claims 1 to 35 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of at least one disease selected from transplant rejection, immune, autoimmune and inflammatory diseases, neurodegenerative diseases, and

proliferative disorders.

39.- Use according to claim 38 wherein the disease is selected from transplant rejection, rheumatoid arthritis, psoriatic arthritis, psoriasis, type I diabetes, complications from diabetes, multiple sclerosis, systemic lupus erythematosus, atopic dermatitis, mast cell-mediated allergic reactions, leukemias, lymphomas, and thromboembolic and allergic complications associated with leukemias and lymphomas.

40.- A process for the preparation of a compound of formula **I** according to claim 1, which comprises :

(a) reacting a compound of formula **IV** with a compound of formula **V**



IV

Cy_1NH_2

V

wherein Cy_1 and Cy_2 have the meaning described in claim 1; or

(b) converting, in one or a plurality of steps, a compound of formula **I** into another compound of formula **I**.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/053842

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D487/04 A61K31/519 A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 635 762 B1 (BLUMENKOPF TODD A [US] ET AL) 21 October 2003 (2003-10-21) column 1, paragraph 1 claim 1	1-40
A	WO 99/65909 A (PFIZER PROD INC [US]; BLUMENKOPF TODD ANDREW [US]; FLANAGAN MARK EDWAR) 23 December 1999 (1999-12-23) page 1, paragraph 1 claim 1	1,40
A	WO 99/65908 A (PFIZER PROD INC [US]; BLUMENKOPF TODD ANDREW [US]; FLANAGAN MARK EDWAR) 23 December 1999 (1999-12-23) page 1, paragraph 1 claim 1	1-40

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 September 2008	17/09/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fanni, Stefano

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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2006/096270 A (VERTEX PHARMA [US]; LEDEBOER MARK W [US]; PIERCE ALBERT C [US]; BEMIS) 14 September 2006 (2006-09-14) page 2, paragraph 105 claim 1	1-40
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Information on patent family members

International application No
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