PYRIDOPYRAZINE DERIVATIVES AND USE THEREOF AS MODULATORS OF THE SIGNAL TRANSDUCTION PATHS

Description

Technical field

The present invention relates to pyridopyrazine derivatives with new biological action and their use for the treatment of physiological and/or pathophysiological states mediated and/or modulated by signal transduction pathways in mammals and in particular in humans.

Prior art

The signal transduction cascades ras-Raf-Mek-Erk and PI3K-Akt play a central role in cell growth, cell proliferation, apoptosis, adhesion, migration and glucose metabolism. Consequently, the fundamental involvement in the pathogenesis of diseases such as cancer, neurodegeneration and inflammatory diseases is proven both for the ras-Raf-Mek-Erk and for the PI3K-Akt signal pathway. The individual components of these signal cascades are therefore important therapeutic points of attack for intervention in various disease processes (Weinstein-Oppenheimer C.R. et al. 2000, Chang F. et al. 2003, Katso R. et al 2001 and Lu Y. et al 2003).

The molecular and biochemical properties of both signal pathways are first described separately hereinafter.

A plurality of growth factors, cytokines and oncogenes transduce their growth-promoting signals via the activation of G-protein coupled ras which leads to the activation of serine threonine kinase Raf and to the activation of mitogen-activated protein kinase kinase 1 and 2 (MAPKK1/2 or Mek1/2) and results in the phosphorylation and activation of MAPK 1 and 2 - also known as extracellular signal regulated kinase (Erk1 and 2). Compared to other signal pathways, the ras-Raf-

Mek-Erk signal pathway combines a large number of proto-oncogenes, including ligands, tyrosine kinase receptors, G-proteins, kinases and nuclear transcription factors. Tyrosine kinases such as, for example, EGFR (Mendelsohn J. et al., 2000) frequently mediate constitutively active signals to the downstream ras-Raf-Mek-Erk signal pathway in tumour events caused by overexpression and mutation. Ras mutations are mutated in 30% of all human tumours (Khleif S.N. et al., 1999, Marshall C., 1999), the highest incidence of 90% being found in pancreatic carcinomas (Friess H. et al., 1996, Sirivatanauksorn V. et al., 1998). For c-Raf a deregulated expression and/or activation has been described in various tumours (Hoshino R. et al., 1999, McPhillips F. et al., 2001). B-Raf point mutants were detected in 66% of all human malignant melanomas, 14% of ovarian carcimomas and 12% of carcinomas of the colon (Davies H. et al., 2002). It is therefore not surprising that Erk1/2 is primarily involved in many cellular processes such as cell growth, cell profileration and cell differentiation (Lewis T.S. et al., 1998, Chang F. et al., 2003).

In addition, the members of the Raf kinases also have Mek-Erk-indepedent anti-apoptotic functions whose molecular steps have not yet been fully described. Ask1, Bcl-2, Akt and Bag1 have been described as possible interaction partners for the Mek-Erk-independent Raf activity (Chen J et al., 2001, Troppmaier J. et al., 2003, Rapp U.R. et al., 2004, Gotz R. et al., 2005). It is assumed nowadays that both Mek-Erk-dependent and Mek-Erk-independent signal transduction mechanisms control the activation of the upstream ras and Raf stimuli.

The isoenzymes of the phosphatidylinositol 3-kinases (PI3Ks) function predominantly as lipid kinases and catalyse the D3 phosphorylation of the second-messenger lipids PtdIns (phosphatidylinositol) to PtdIns(3)P,

PtdIns(3,4)P_2, PtdIns(3,4,5)P_3 phosphatidylinositol phosphates. The class I PI3Ks are composed structurally of the catalytic (p110alpha, beta, gamma, delta) and the regulatory (p85alpha, beta or p101gamma) subunits. Furthermore, the class II (PI3K-C2alpha, PI3K-C2beta) and class III (Vps34p) enzymes belong to the family of the P13 kinases (Wymann M.P. et al., 1998, VanHaesebroeck B. et al., 2001). The PIP increase triggered by the PI3Ks activates the proliferative ras-Raf-Mek-Erk signal pathway via the coupling of ras on the one hand (Rodriguez-Viciana P. et al., 1994) and on the other hand stimulates the anti-apoptotic signal pathway by recruiting Akt to the cell membrane and consequent overactivation of this kinase (Alessi D.R. et al., 1996, Chang H.W. et al., 1997, Moore S.M. et al., 1998). Consequently, the activation of PI3Ks fulfils at least two crucial mechanisms for tumour formation, namely the activation of cell growth and cell differentiation and the inhibition of apoptosis. In addition, PI3K also have protein-phosphorylating properties (Dhand et al., 1994, Bondeva T. et al., 1998, Bondev A. et al., 1999, VanHaesebroeck B. et al., 1999) which can trigger a PI3Ks-intrinsically regulating serine autophosphorylation for example. In addition, it is known that PI3Ks also have kinase-independent regulating effector properties, e.g. during control of cardiac contraction (Crackower M.A. et al., 2002, Patrucco et al., 2004). It is furthermore proven that PI3Kdelta and PI3Kgamma are specifically expressed on hematopoietic cells and therefore constitute potential points of attack for isoenzyme-specific PI3Kdelta and PI3Kgamma inhibitors in the treatment of inflammatory diseases such as rheumatism, asthma and allergies and in the treatment of B and T cell lymphomas (Okkenhaug K. et al., 2003, Ali K. et al., 2004, Sujobert P. et al., 2005). PI3Kalpha, which was recently identified as a proto-oncogene (Shayesteh L. et al., 1999, Ma Y.Y. et al., 2000, Samuels Y. et al., 2004, Campbell I.G. et al., 2004, Levine D.A., 2005) is

considered to be an important target in the treatment of tumour diseases. The importance of PI3K species as a target for the development of active substances is therefore extremely diverse (Chang F. & Lee J.T. et al, 2003).

The kinases related to PI3K (PIKK), which include the serine/threonine kinases mTOR, ATM, ATR, h-SMG-1 and DNA-PK (Chiang G.G. et al 2004) are also of great interest. Their catalytic domains have a high sequence homology to the catalytic domains of PI3Ks.

In addition, the loss of the tumour suppressor protein PTEN (Li J. et al., 1997, Steck P.A. et al., 1997) - whose function is the reversion of the phosphorylation initiated by the PI3K - contributes to an overactivation of Akt and its downstream cascade components and thereby emphasise the causal importance of PI3K as a target molucule for tumour therapy.

Various inhibitors of individual components of the ras-Raf-Mek-Erk and PI3K-Akt signal pathways have already been published and patented.

The present state of development in the field of kinase inhibitors, in particular of the ras-Raf-Mek-Erk and PI3K-Akt pathway, is described in the reviews of J.S. Sebolt-Leopold et al., 2004, and R. Wetzker et al., 2004. These publications contain comprehensive listings of the published patent specifications which describe the synthesis and use of low-molecular ras-Raf-Mek-Erk- and PI3K inhibitors.

The kinase inhibitor Bay 43-9006 (WO 99/32111, WO 03/068223) which is already undergoing clinical trials, shows a relatively non-specific inhibition pattern of serine/threonine and of tyrosine kinases such as Raf, VEGFR2/3, Flt-3, PDGFR, c-Kit and other kinases. Great

importance is attached to this inhibitor in angiogenesis-induced advanced tumour diseases (e.g. in renal cell carcinoma) and also in melanomas having a high B-Raf mutation rate. The clinical effect of Bay 43-9006 is currently also being determined in patients presenting with refractory solid tumours in combination with, for example, Docetaxel. Mild side effects and promising anti-tumoral effects have been described so far. No inhibition of the kinases in the PI3K-Akt signal pathway has been described for Bay 43-9006.

The Mek1/2 inhibitor PD0325901 (WO 02/06213) is currently undergoing a Phase I clinical trial. The precursor substance CI-1040 (WO 00/35435, WO 00/37141) was striking because of its high Mek specificity and target affinity. However, this compound proved to be metabolically unstable in Phase I/II trials. No clinical data are available yet for the current successor substance PD0325901. However, no interaction with Erk1 or Erk2 nor any PI3K-Akt signal pathway inhibiting function or its simultaneous modulation has yet been disclosed for this Mek inhibitor.

Patent specifications WO 04/104002 and WO 04/104003 describe pyrido[2,3-b]pyrazines, which can be substituted in the 6- or 7-position with urea, thiourea, amidine or guanidine groups. These compounds possess properties as inhibitors or modulators of kinases, in particular of tyrosine and serine/threonine kinases, and a use as a medicinal product is specified. However, no use of these compounds as modulators of lipid kinases, alone or in combination with tyrosine and serine/threonine kinases has been described.

In addition, patent specification WO 99/17759 describes pyrido[2,3-b]pyrazines which, among other things, carry alkyl-, aryl- and heteroaryl-substituted carbamates in

the 6-position. These compounds are to be used to modulate serine threonine protein kinases.

Patent specification WO 05/007099 describes, among other things, urea-substituted pyrido[2,3-b]pyrazines as inhibitors of the serine/threonine kinase PKB. A use in the treatment of cancer diseases is specified for these compounds. However, no specific examples of urea-substituted pyridopyrazines with these biological properties are given.

Further examples of pyrido[2,3-b]pyrazines substituted with urea in the 6- and 7-position are given in patent specification WO 05/056547. The compounds in this patent specification are described as inhibitors of protein kinases, in particular GSK-3, Syk und JAK-3. A use in the treatment of proliferative diseases is given for these compounds among other things. No use of these compounds as modulators of lipid kinases, alone or in combination with serine/threonine kinases is described.

The patent application WO 04/005472 describes, among other things pyrido[2,3-b]pyrazines substituted with carbamate in the 6-position which inhibit the growth of bacteria as antibacterial substances. No antitumour effect is described.

Certain diphenyl quinoxalines and pyrido[2,3-b]pyrazines with special alkylpyrrolidine, alkylpiperidine or alkyl sulfonamides group at a phenyl ring which can additionally also bear urea or carbamate substitutions in the 6- or 7-position are described in patent specifications WO 03/084473, WO 03/086394 and WO 03/086403 as inhibitors of the activity of the serine/threonine kinase Akt. A use in the treatment of cancer diseases is specified for these compounds. No

defined indication of a biological effect is given for the pyrido[2,3-b]pyrazine compounds described therein as examples.

Patent specification WO 03/024448 describes amide and acrylamide-substituted pyrido[2,3-b]pyrazines which can also contain carbamates as additional substituents and can be used as histone deacetylase inhibitors for the treatment of cell proliferation diseases.

In another publication (Temple C. et al. 1990) the synthesis of a 6-ethylcarbamate-substituted pyrido[2,3-b]pyrazine derivative is described as one example. No antitumour effect is disclosed or made obvious.

The synthesis of further derivatives of 6-ethylcarbamate-substituted pyrido[2,3-b]pyrazine is described in a publication by R. D. Elliott (J. Org. Chem. 1968). No biological effect of these compounds is described or disclosed.

The publication by C. Temple (1968) describes the synthesis and investigation of 6-ethylcarbamate-substituted pyrido[2,3-b]pyrazines as potential antimalarial drugs. No antitumour effect is disclosed or made obvious.

The PI3K inhibitors published so far are undergoing preclinical trials. ICOS disclosed a PI3K inhibitor IC87114 with high PI3Kdelta isoenzyme specificity (WO 01/81346). For PI103 (WO 04/017950) Yamanouchi/Piramed describe a selectivity versus the PI3Kalpha isoform. In addition, a research environment which has attracted a great deal of attention exists in the early development

of PI3K inhibitors (see the review of R. Wetzker et al., 2004).

Inhibitors of the SAPK signal pathway, either of Jnk or of p38 have been described in the literature (Gum R.J., 1998, Bennett B.L. et al 2001, Davies S.P. et al 2000). However, no PI3K-inhibiting function and also no specific inhibition of Erk1 or Erk2 or simultaneous inhibition of SAPKs, Erk1, Erk2, or PI3Ks is disclosed for these SAPK inhibitors.

Summary of the invention

In one aspect, there is provided the use of compound as referred to in claim 1.

In another aspect, there is provided a pyridopyrazine selected from the group consisting of compounds 38 to 136 and 138 to 269 as described herein.

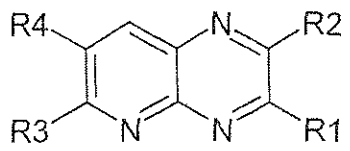
In another aspect, there is provided a pharmaceutical composition comprising a pharmacologically active quantity of at least one compound as described herein, and at least one pharmaceutically compatible excipient.

In another aspect, there is provided a kit comprising a pharmacologically active quantity of at least one compound as described herein and a pharmacologically active quantity of at least one further pharmacologically active substance as described herein.

Description of the invention

The object of the present invention is to provide new compounds which can be used for the treatment or prevention of physiological and/or pathophysiological states in mammals, in particular in humans, which are mediated by signal transduction pathways selected from the group consisting of: "ras-Raf-Mek-Erk signal transduction pathway, PI3K-Akt signal transduction pathway and/or SAPK signal transduction pathway". A further object of the invention is to provide new compounds for the aforesaid uses by modulation of said signal transduction pathways. It is further the object of the present invention to provide new compounds which can be used for the treatment or prevention of physiological and/or pathophysiological states in mammals, in particular in humans, which are mediated by enzymes selected from the group consisting of: "ATM, ATR, mTOR, DNA-PK, hSMG-1". A further object of the invention is to provide new compounds for the aforesaid uses by modulation of said enzymes.

The inventive object was surprisingly achieved in one aspect by preparing a compound according to the general formula (I)



(I)

wherein the substituents R1, R2, R3, R4 have the following meaning:

R1 and R2 can be independently of one another

(i) hydrogen

(ii) hydroxyl

(iii) halogen

(iv) alkyl, wherein the alkyl group is saturated and can consists of 1 to 8 C atoms,

(v) unsubstituted or substituted aryl, wherein the alkyl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, NH-alkyl-NH_2, NH-alkyl-OH, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, NHC(O)-alkyl-aryl, NHC(O)-alkyl-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-heterocyclyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, $NHSO_2$-alkyl-aryl, $NHSO_2$-alkyl-heteroaryl, NO_2, SH, S-alkyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-heterocyclyl, O-alkyl-aryl, O-alkyl-heteroaryl, O-alkyl-OH, O-$(CH_2)_n$-O, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OC(O)-alkyl-aryl, OC(O)-alkyl-heteroaryl, OSO_3H, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-heterocyclyl, OSO_2-aryl, OSO_2-heteroaryl, OSO_2-alkyl-aryl, OSO_2-alkyl-heteroaryl, $OP(O)(OH)_2$, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-

cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, C(O)N$(alkyl)_2$, C(O)N$(cycloalkyl)_2$, C(O)N$(aryl)_2$, C(O)N$(heteroaryl)_2$, SO-alkyl, SO-aryl, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO_2NH-alkyl-aryl, SO_3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-alkyl-aryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl, n can have the value 1, 2 or 3 and the alkyl-, cycloalkyl-, heterocyclyl-, aryl-, heteroaryl-, alkyl-cycloalkyl-, alkyl-heterocyclyl-, alkyl-aryl- and alkyl-heteroaryl substituents for their part can in turn be substituted,

(vi) unsubstituted or substituted heteroaryl, wherein the heteroaryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, NH-alkyl-NH_2, NH-alkyl-OH, N$(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, NHC(O)-alkyl-aryl, NHC(O)-alkyl-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-heterocyclyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, $NHSO_2$-alkyl-aryl, $NHSO_2$-alkyl-heteroaryl, NO_2, SH, S-alkyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-heterocyclyl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OC(O)-alkyl-aryl, OC(O)-alkyl-heteroaryl, OSO_3H, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-heterocyclyl, OSO_2-aryl, OSO_2-heteroaryl, OSO_2-alkyl-aryl, OSO_2-alkyl-heteroaryl, OP(O)$(OH)_2$, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-

heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, C(O)N(alkyl)$_2$, C(O)N(cycloalkyl)$_2$, C(O)N(aryl)$_2$, C(O)N(heteroaryl)$_2$, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO_2NH-alkyl-aryl, SO3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-alkyl-aryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl, and the alkyl-, cycloalkyl-, heterocyclyl-, aryl- and heteroaryl substituents for their part can in turn be substituted,

(vii) OR5, wherein R5 can be alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl, and the alkyl-, cycloalkyl-, heterocyclyl-, aryl-, heteroaryl-, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl substituents for their part can in turn be substituted,

(viii) SR6, wherein R6 can be alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl and the alkyl-, cycloalkyl-, heterocyclyl-, aryl- and heteroaryl-, alkyl-cycloalkyl-, alkyl-heterocyclyl-, alkyl-aryl- or alkyl-heteroaryl substituents for their part can in turn be substituted,

(ix) NR7R8, wherein R7 and R8 independently of one another can be hydrogen, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl and the alkyl-, cycloalkyl-, heterocyclyl-, aryl- and heteroaryl-, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl substituents for their part can in turn be substituted,

or R7 and R8 together mean cycloalkyl or heterocyclyl, wherein cycloalkyl and heterocyclyl for their part can in turn be substituted.

R3 and R4 can independently of one another mean hydrogen or NR9R10 assuming that if R3 = NR9R10, R4 = H, and if R4 = NR9R10, R3 = H,
wherein R9 can be hydrogen, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl and the alkyl-, cycloalkyl-, heterocyclyl-, aryl- and heteroaryl-, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl substituents for their part can in turn be substituted,

and R10:
can mean -C(Y)NR11R12, wherein Y = O, S and R11 and R12 can be independently of one another

(i) hydrogen,

(ii) unsubstituted or substituted alkyl wherein the alkyl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, NHC(O)-alkyl-aryl, NHC(O)-alkyl-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-heterocyclyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, $NHSO_2$-alkyl-aryl, $NHSO_2$-alkyl-heteroaryl, NO_2, SH, S-alkyl, S-cycloalkyl, S-heterocyclyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-heterocyclyl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OC(O)-alkyl-aryl, OC(O)-alkyl-heteroaryl, OSO_3H, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-heterocyclyl,

OSO_2-aryl, OSO_2-heteroaryl, OSO_2-alkyl-aryl, OSO_2-alkyl-heteroaryl, $OP(O)(OH)_2$, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO-alkyl, SO-aryl, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO_2NH-alkyl-aryl, SO_3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-alkyl-aryl, cycloalkyl, heterocyclyl, aryl or heteroaryl,

(iii) unsubstituted or substituted cycloalkyl, wherein the cycloalkyl group can be substituted with one or more, the same or different F, Cl, Br, I, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, NHC(O)-alkyl-aryl, NHC(O)-alkyl-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-heterocyclyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, $NHSO_2$-alkyl-aryl, $NHSO_2$-alkyl-heteroaryl, OH, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OC(O)-alkyl-aryl, OC(O)-alkyl-heteroaryl, OSO_3H, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-heterocyclyl, OSO_2-aryl, OSO_2-heteroaryl, OSO_2-alkyl-aryl, OSO_2-alkyl-heteroaryl, $OP(O)(OH)_2$, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-

heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, alkyl, or aryl,

(iv) unsubstituted or substituted heterocyclyl, wherein the heterocyclyl group can be substituted with one or more, the same or different OH, O-alkyl, O-aryl, NH_2, NH-alkyl, NH-aryl, alkyl, alkyl-aryl or aryl,

(v) unsubstituted or substituted aryl, wherein the aryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, NH-alkyl-NH_2, NH-alkyl-OH, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, NHC(O)-alkyl-aryl, NHC(O)-alkyl-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-heterocyclyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, $NHSO_2$-alkyl-aryl, $NHSO_2$-alkyl-heteroaryl, NO_2, SH, S-alkyl, S-cycloalkyl, S-heterocyclyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-heterocyclyl, O-alkyl-aryl, O-alkyl-heteroaryl, O-alkyl-OH, O-$(CH_2)_n$-O, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OC(O)-alkyl-aryl, OC(O)-alkyl-heteroaryl, OSO_3H, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-heterocyclyl, OSO_2-aryl, OSO_2-heteroaryl, OSO_2-alkyl-aryl, OSO_2-alkyl-heteroaryl, $OP(O)(OH)_2$, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO-alkyl, SO-aryl, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO_2NH-alkyl-aryl, SO3H,

SO_2O-alkyl, SO_2O-aryl, SO_2O-alkyl-aryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl, and n can have the value 1, 2 or 3,

(vi) unsubstituted or substituted heteroaryl, wherein the heteroaryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, NH-alkyl-NH_2, NH-alkyl-OH, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, NHC(O)-alkyl-aryl, NHC(O)-alkyl-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-heterocyclyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, $NHSO_2$-alkyl-aryl, $NHSO_2$-alkyl-heteroaryl, NO_2, SH, S-alkyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-heterocyclyl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OC(O)-alkyl-aryl, OC(O)-alkyl-heteroaryl, OSO_3H, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-heterocyclyl, OSO_2-aryl, OSO_2-heteroaryl, OSO_2-alkyl-aryl, OSO_2-alkyl-heteroaryl, $OP(O)(OH)_2$, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, $C(O)-NH_2$, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO_2NH-alkyl-aryl, SO_3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-alkyl-aryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl,

(vii) -C(O)-R17, wherein R17 can be alkyl, aryl or heteroaryl and the alkyl and aryl substituents for their part can in turn be substituted,

(viii) or R11 and R12 together can mean cycloalkyl or heterocyclyl,

can mean -C(Y)NR13R14 wherein Y = NH and R13 and R14 can be independently of one another,

(i) hydrogen,

(ii) unsubstituted or substituted aryl, wherein the aryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, NO_2, SH, S-alkyl, S-cycloalkyl, S-heterocyclyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, C(O)-alkyl, C(O)-aryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, $C(O)-NH_2$, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO-alkyl, SO-aryl, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_3H, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl,

(iii) unsubstituted or substituted cycloalkyl, wherein the cycloalkyl group can be substituted with one or more, the same or different F, Cl, Br, I, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl,

NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, OH, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, $C(O)-NH_2$, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, alkyl, or aryl,

(iv) unsubstituted or substituted heterocyclyl, wherein the heterocyclyl group can be substituted with one or more, the same or different OH, O-alkyl, O-aryl, NH_2, NH-alkyl, NH-aryl, alkyl, or aryl,

(v) unsubstituted or substituted aryl, wherein the aryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, NH-alkyl-NH_2, NH-alkyl-OH, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, NO_2, SH, S-alkyl, S-cycloalkyl, S-heterocyclyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-heterocyclyl, O-alkyl-aryl, O-alkyl-heteroaryl, O-alkyl-OH, $O-(CH_2)_n-O$, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, $C(O)-NH_2$, C(O)NH-alkyl,

C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO-alkyl, SO-aryl, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-heteroaryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl, and n can have the value 1, 2 or 3,

(vi) unsubstituted or substituted heteroaryl, wherein the heteroaryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, NO_2, SH, S-alkyl, S-aryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, $C(O)-NH_2$, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-heteroaryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl,

(vii) or R13 and R14 together can mean cycloalkyl or heterocyclyl,

can mean -C(NR15)R16, wherein R15 = H and R16 can be

(i) unsubstituted or substituted alkyl, wherein the alkyl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, NO_2, SH, S-alkyl, S-cycloalkyl, S-heterocyclyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, C(O)-alkyl, C(O)-aryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO-alkyl, SO-aryl, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_3H, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl,

(ii) unsubstituted or substituted cycloalkyl, wherein the cycloalkyl group can be substituted with one or more, the same or different F, Cl, Br, I, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, OH, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-aryl, O-alkyl-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl,

OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, alkyl, or aryl,

(iii) unsubstituted or substituted heterocyclyl, wherein the heterocyclyl group can be substituted with one or more, the same or different OH, O-alkyl, O-aryl, NH_2, NH-alkyl, NH-aryl, alkyl or aryl,

(iv) unsubstituted or substituted aryl, wherein the aryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, NH-alkyl-NH_2, NH-alkyl-OH, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, NO_2, SH, S-alkyl, S-cycloalkyl, S-heterocyclyl, S-aryl, S-heteroaryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, O-alkyl-cycloalkyl, O-alkyl-heterocyclyl, O-alkyl-aryl, O-alkyl-heteroaryl, O-alkyl-OH, O-$(CH_2)_n$-O, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, C(O)-NH_2, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO-alkyl, SO-aryl, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-

heteroaryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl, and n can have the value 1, 2 or 3,

(v) unsubstituted or substituted heteroaryl, wherein the heteroaryl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-aryl, NH-alkyl-heteroaryl, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-aryl, $NHSO_2$-heteroaryl, NO_2, SH, S-alkyl, S-aryl, OH, OCF_3, O-alkyl, O-cycloalkyl, O-heterocyclyl, O-aryl, O-heteroaryl, OC(O)-alkyl, OC(O)-cycloalkyl, OC(O)-heterocyclyl, OC(O)-aryl, OC(O)-heteroaryl, OSO_2-alkyl, OSO_2-cycloalkyl, OSO_2-aryl, OSO_2-heteroaryl, C(O)-alkyl, C(O)-aryl, C(O)-heteroaryl, CO_2H, CO_2-alkyl, CO_2-cycloalkyl, CO_2-heterocyclyl, CO_2-aryl, CO_2-heteroaryl, CO_2-alkyl-cycloalkyl, CO_2-alkyl-heterocyclyl, CO_2-alkyl-aryl, CO_2-alkyl-heteroaryl, $C(O)-NH_2$, C(O)NH-alkyl, C(O)NH-cycloalkyl, C(O)NH-heterocyclyl, C(O)NH-aryl, C(O)NH-heteroaryl, C(O)NH-alkyl-cycloalkyl, C(O)NH-alkyl-heterocyclyl, C(O)NH-alkyl-aryl, C(O)NH-alkyl-heteroaryl, $C(O)N(alkyl)_2$, $C(O)N(cycloalkyl)_2$, $C(O)N(aryl)_2$, $C(O)N(heteroaryl)_2$, SO_2-alkyl, SO_2-aryl, SO_2NH_2, SO_2NH-alkyl, SO_2NH-aryl, SO_2NH-heteroaryl, SO3H, SO_2O-alkyl, SO_2O-aryl, SO_2O-heteroaryl, alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

which can be used for the production of a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals mediated by signal transduction pathways selected from the group consisting of: the "ras-Raf-Mek-Erk signal transduction pathway, the PI3K-Akt signal transduction pathway and/or the SAPK signal transduction pathway.

In a preferred embodiment, compounds according to the general formula (I) are prepared, wherein the alkyl group is selected from the group consisting of: "methyl, ethyl, n-propyl, 2-propyl, n-butyl, sec.-butyl, tert.-butyl, n-pentyl, iso-pentyl, neo-pentyl, n-hexyl, 2-hexyl, n-octyl, ethylenyl (vinyl), ethynyl, propenyl (-CH2CH=CH2; -CH=CH-CH3, -C(=CH2)-CH3), propinyl (-CH2-C≡CH, -C≡C-CH3), butenyl, butinyl, pentenyl, pentinyl, hexenyl, hexinyl, heptenyl, heptinyl, octenyl, octinyl" which can be used for the production of a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals mediated by signal transduction pathways selected from the group consisting of: the "ras-Raf-Mek-Erk signal transduction pathway, the PI3K-Akt signal transduction pathway and/or the SAPK signal transduction pathway.

In a further preferred embodiment, compounds according to the general formula (I) are prepared for the aforementioned use, wherein the heterocyclyl group is selected from the group consisting of: "tetrahydrofuryl, tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl".

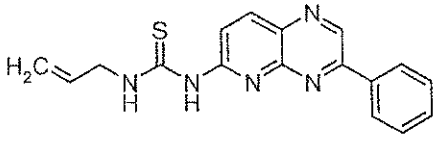
In a further preferred embodiment, compounds according to the general formula (I) are prepared for the aforementioned use, wherein the heteroaryl group is selected from the group consisting of: "pyrrolyl, furyl, thienyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, phthalazinyl, indolyl, indazolyl, indolizinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, carbazolyl, phenazinyl, phenothiazinyl, acridinyl".

In a further preferred embodiment compounds according to the general formula (I) are prepared for the

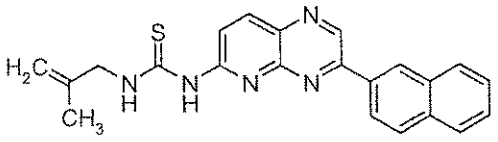
aforementioned use, wherein the alkyl group is selected from the group consisting of: "methyl, ethyl, n-propyl, 2-propyl, n-butyl, sec.-butyl, tert.-butyl, n-pentyl, iso-pentyl, neo-pentyl, n-hexyl, 2-hexyl, n-octyl, ethylenyl (vinyl), ethynyl, propenyl (-CH2CH=CH2; -CH=CH-CH3, -C(=CH2)-CH3), propinyl (-CH2-C≡CH, -C≡C-CH3), butenyl, butinyl, pentenyl, pentinyl, hexenyl, hexinyl, heptenyl, heptinyl, octenyl, octinyl" and/or wherein the heterocyclyl group is selected from the group consisting of: "tetrahydrofuryl, tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl" and/or the heteroaryl group is selected from the group consisting of: "pyrrolyl, furyl, thienyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, phthalazinyl, indolyl, indazolyl, indolizinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, carbazolyl, phenazinyl, phenothiazinyl, acridinyl".

The inventive object was surprisingly achieved in a further aspect by preparing pyridopyrazine compounds selected from the group consisting of:

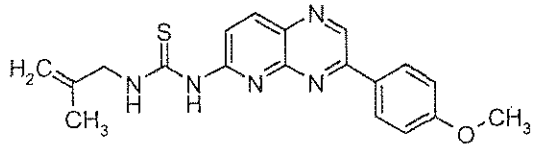
Compound (1) 1-allyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



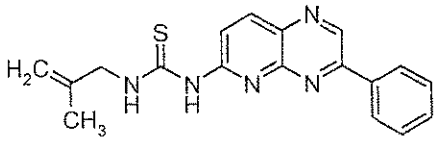
Compound (2) 1-(2-methyl-allyl)-3-(3-naphth-2-yl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



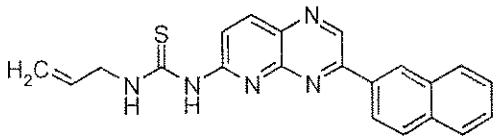
Compound (3) 1-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(2-methyl-allyl)-thiourea



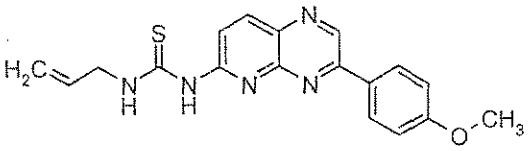
Compound (4) 1-(2-methyl-allyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



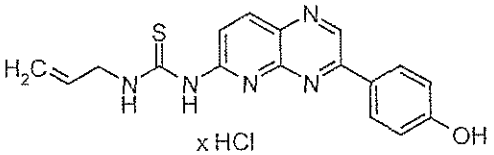
Compound (5) 1-allyl-3-(3-naphth-2-yl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



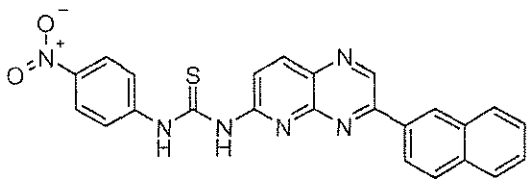
Compound (6) 1-allyl-3-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



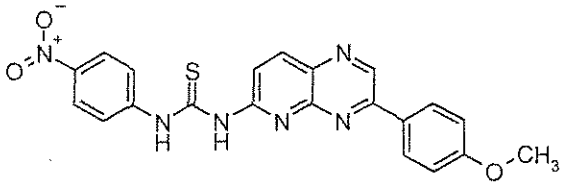
Compound (7) 1-allyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea hydrochloride



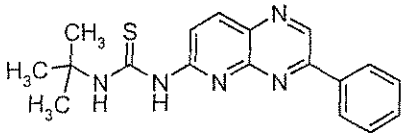
Compound (8) 1-(3-naphth-2-yl-pyrido[2,3-b]pyrazin-6-yl)-3-(4-nitro-phenyl)-thiourea



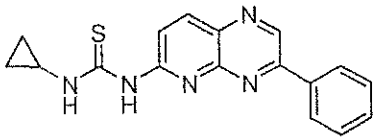
Compound (9) 1-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(4-nitro-phenyl)-thiourea



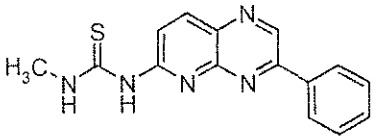
Compound (10) 1-tert-butyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



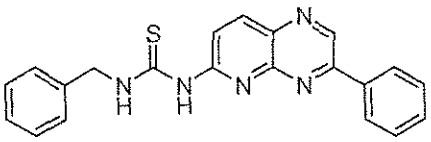
Compound (11) 1-cyclopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



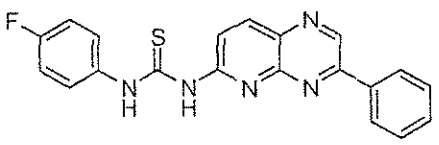
Compound (12) 1-methyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



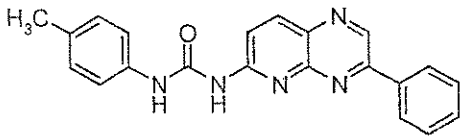
Compound (13) 1-benzyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



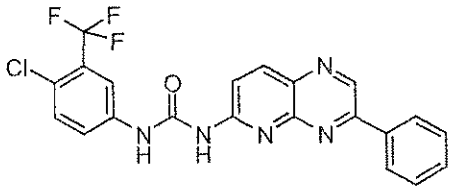
Compound (14) 1-(4-fluoro-phenyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



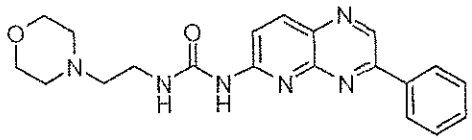
Compound (15) 1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-3-p-tolyl-urea



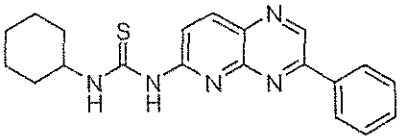
Compound (16) 1-(4-chloro-3-trifluormethyl-phenyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



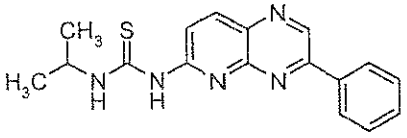
Compound (17) 1-(2-morpholin-4-yl-ethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



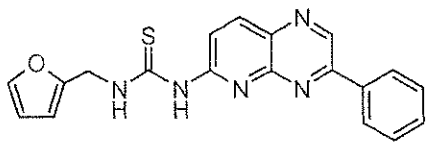
Compound (18) 1-cyclohexyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



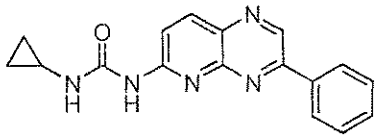
Compound (19) 1-isopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



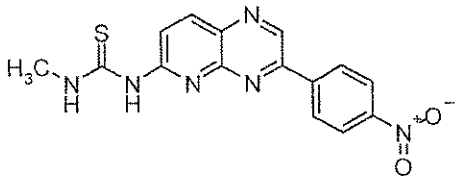
Compound (20) 1-furan-2-ylmethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



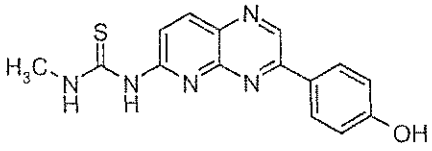
Compound (21) 1-cyclopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



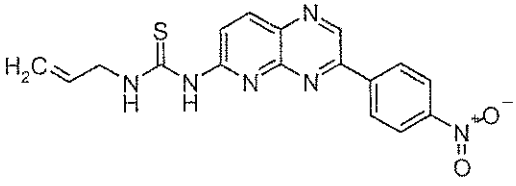
Compound (22) 1-methyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



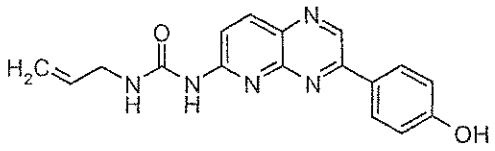
Compound (23) 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-thiourea



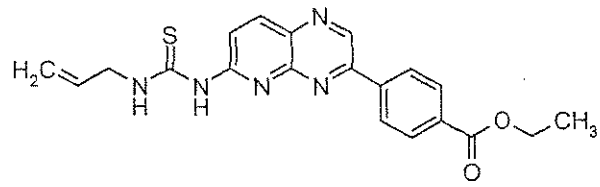
Compound (24) 1-allyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



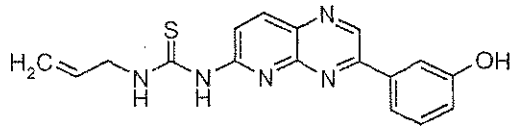
Compound (25) 1-allyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



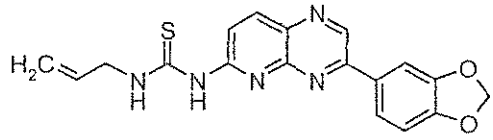
Compound (26) 4-[6-(3-allyl-thioureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid-ethyl ester



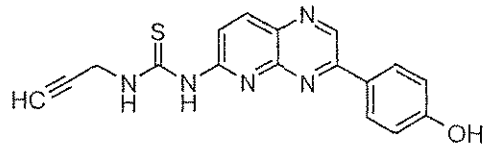
Compound (27) 1-allyl-3-[3-(3-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



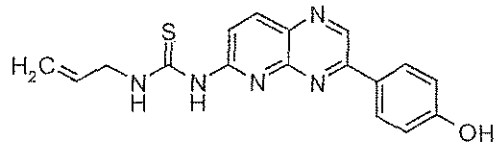
Compound (28) 1-allyl-3-(3-benzo[1,3]dioxol-5-yl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



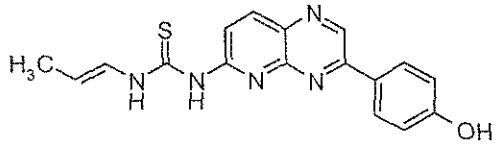
Compound (29) 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-prop-2-inyl-thiourea



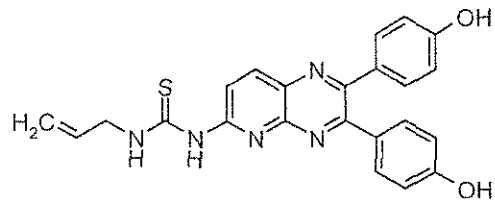
Compound (30) 1-allyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



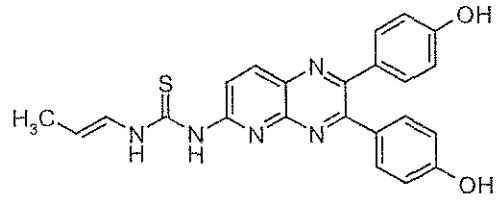
Compound (31) 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-((e)-propenyl)-thiourea



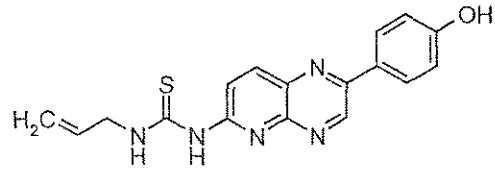
Compound (32) 1-allyl-3-[2,3-bis-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



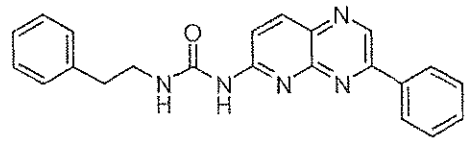
Compound (33) 1-[2,3-bis-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-((e)-propenyl)-thiourea



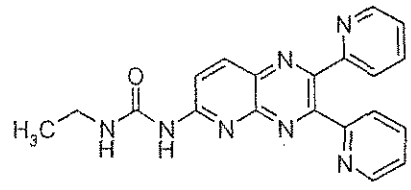
Compound (34) 1-allyl-3-[2-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



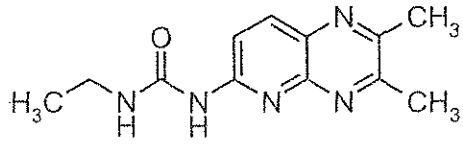
Compound (35) 1-phenethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



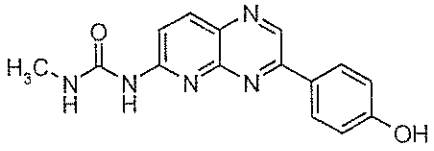
Compound (36) 1-(2,3-di-pyridin-2-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



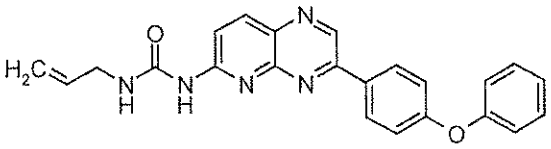
Compound (37) 1-(2,3-dimethyl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



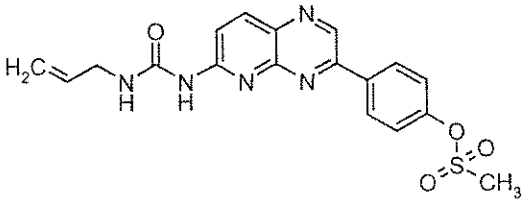
Compound (38) 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-urea



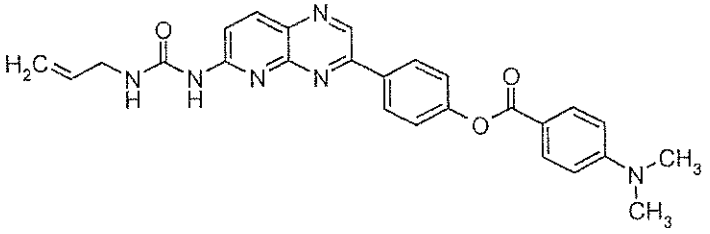
Compound (39) 1-allyl-3-[3-(4-phenoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



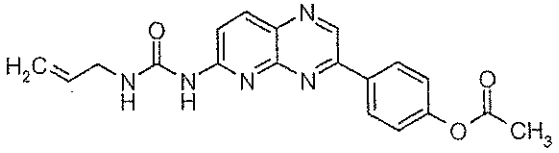
Compound (40) methane sulfonic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl ester



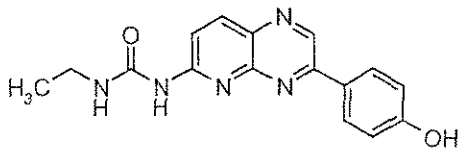
Compound (41) 4-dimethylamino-benzoic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl ester



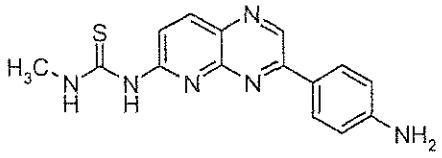
Compound (42) acetic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl ester



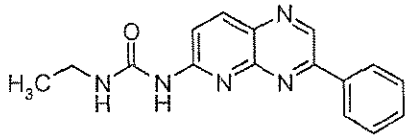
Compound (43) 1-ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



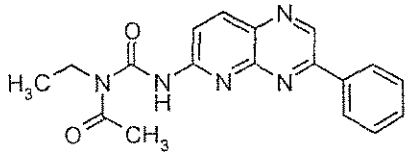
Compound (44) 1-[3-(4-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-thiourea



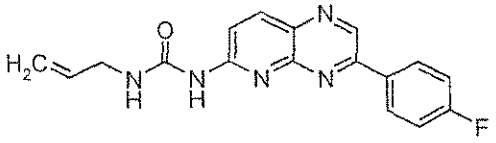
Compound (45) 1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



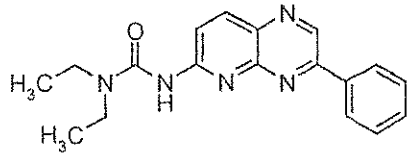
Compound (46) 1-acetyl-1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



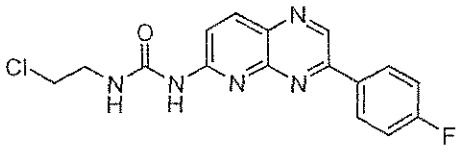
Compound (47) 1-allyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



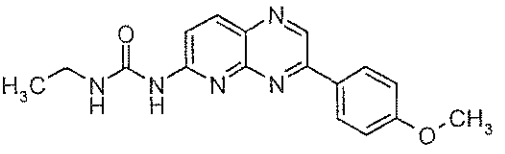
Compound (48) ,1-diethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



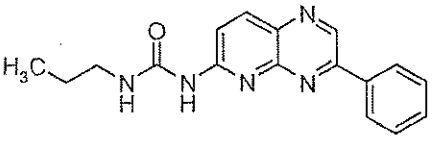
Compound (49) 1-(2-chloro-ethyl)-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



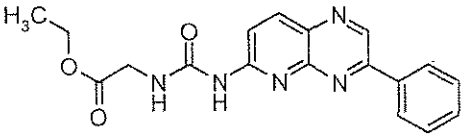
Compound (50) 1-ethyl-3-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



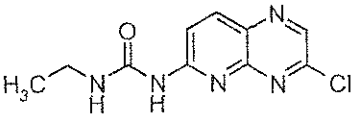
Compound (51) 1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-3-propyl-urea



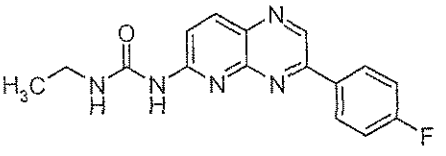
Compound (52) [3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-acetic acid-ethyl ester



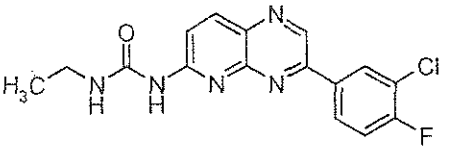
Compound (53) 1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



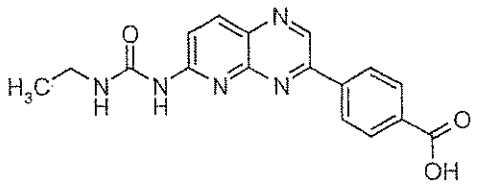
Compound (54) 1-ethyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



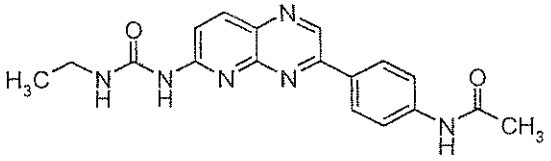
Compound (55) 1-[3-(3-chloro-4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



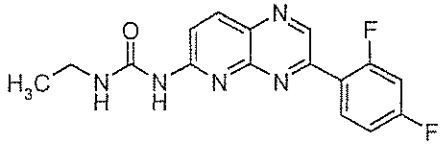
Compound (56) 4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid



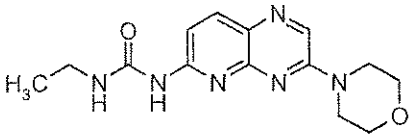
Compound (57) n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acetamide



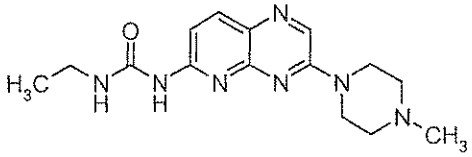
Compound 58) 1-[3-(2,4-difluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



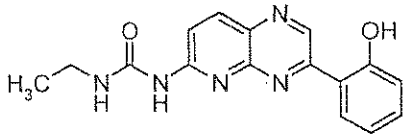
Compound (59) 1-ethyl-3-(3-morpholin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



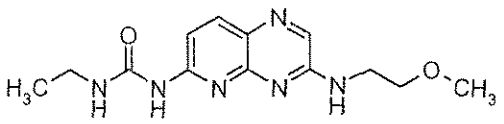
Compound (60) 1-ethyl-3-[3-(4-methyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



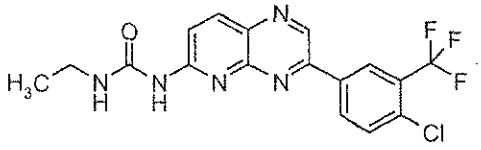
Compound (61) 1-ethyl-3-[3-(2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



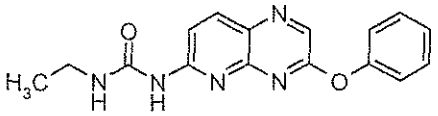
Compound (62) 1-ethyl-3-[3-(2-methoxy-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



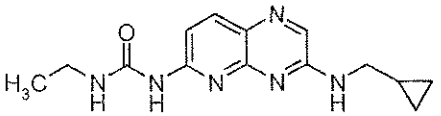
Compound (63) 1-[3-(4-chloro-3-trifluormethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



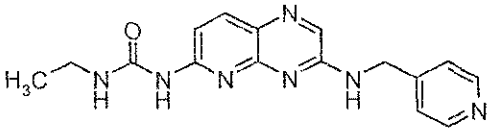
Compound (64) 1-ethyl-3-(3-phenoxy-pyrido[2,3-b]pyrazin-6-yl)-urea



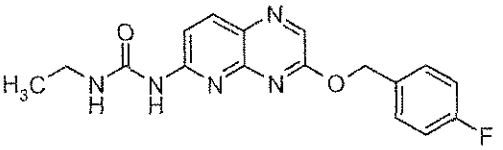
Compound (65) 1-[3-(cyclopropylmethyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



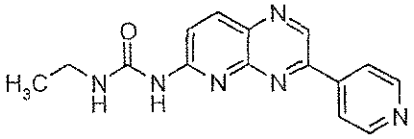
Compound (66) 1-ethyl-3-{3-[(pyridin-4-ylmethyl)-amino]-pyrido[2,3-b]pyrazin-6-yl}-urea



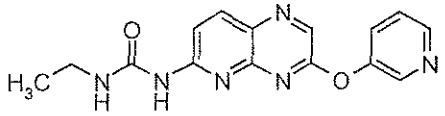
Compound (67) 1-ethyl-3-[3-(4-fluoro-benzyloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



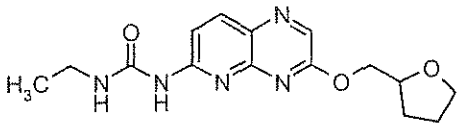
Compound (68) 1-ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



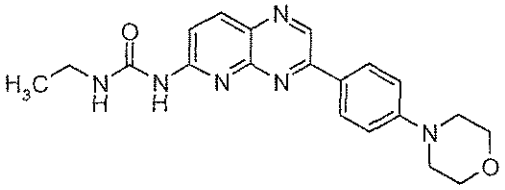
Compound (69) 1-ethyl-3-[3-(pyridin-3-yloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



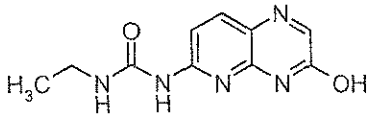
Compound (70) 1-ethyl-3-[3-(tetrahydro-furan-2-ylmethoxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



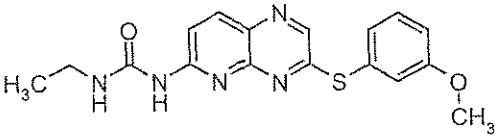
Compound (71) 1-ethyl-3-[3-(4-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



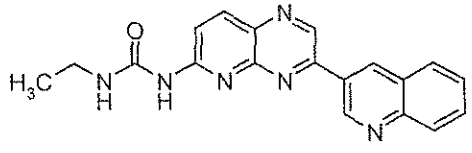
Compound (72) 1-ethyl-3-(3-hydroxy-pyrido[2,3-b]pyrazin-6-yl)-urea;



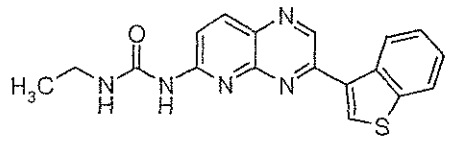
Compound (73) 1-ethyl-3-[3-(3-methoxy-phenylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



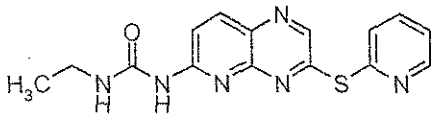
Compound (74) 1-ethyl-3-(3-quinolin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



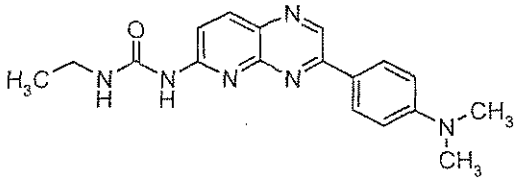
Compound (75) -(3-benzo[b]thiophen-3-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



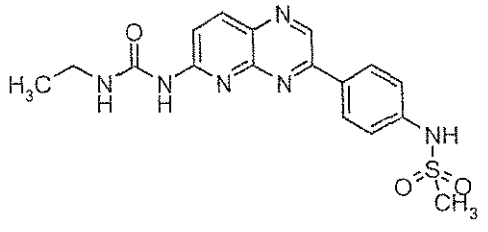
Compound (76) 1-ethyl-3-[3-(pyridin-2-ylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



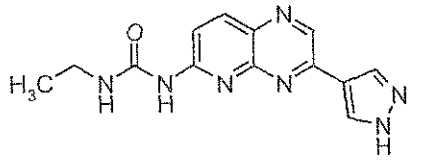
Compound (77) 1-[3-(4-dimethylamino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea;



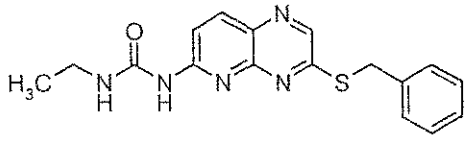
Compound (78) n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-methane sulfonamide



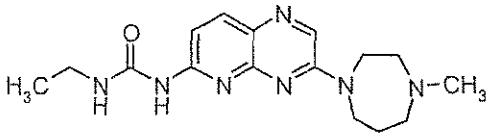
Compound (79) 1-ethyl-3-[3-(1h-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



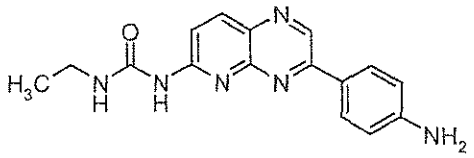
Compound (80) 1-(3-benzylsulfanyl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea;



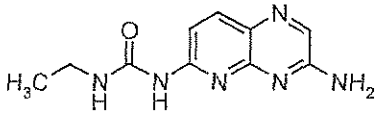
Compound (81) 1-ethyl-3-[3-(4-methyl-[1,4]diazepan-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea;



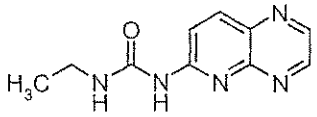
Compound (82) 1-[3-(4-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



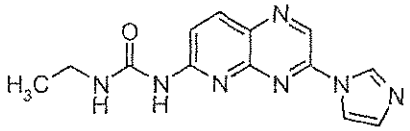
Compound (83) 1-(3-amino-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



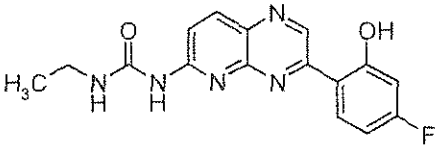
Compound (84) 1-ethyl-3-pyrido[2,3-b]pyrazin-6-yl-urea



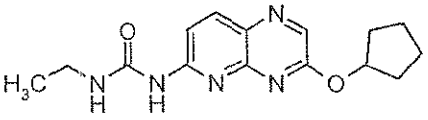
Compound (85) 1-ethyl-3-(3-imidazol-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



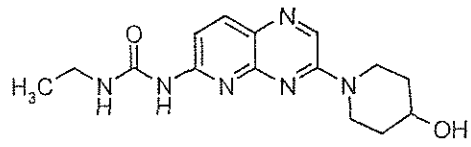
Compound (86) 1-ethyl-3-[3-(4-fluoro-2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



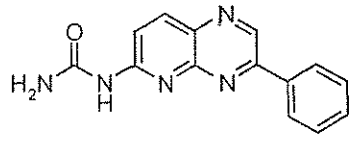
Compound (87) 1-(3-cyclopentyloxy-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



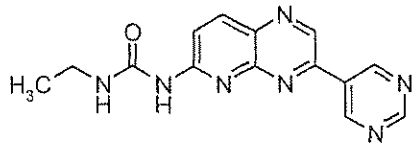
Compound (88) 1-ethyl-3-[3-(4-hydroxy-piperidin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



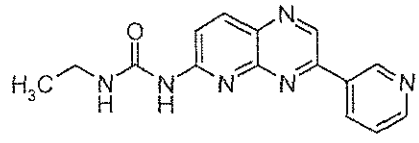
Compound (89) (3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



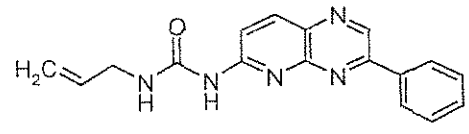
Compound (90) 1-ethyl-3-(3-pyrimidin-5-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



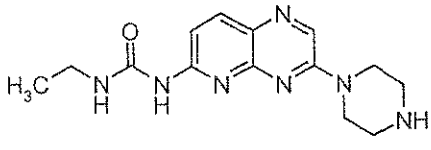
Compound (91) 1-ethyl-3-(3-pyridin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



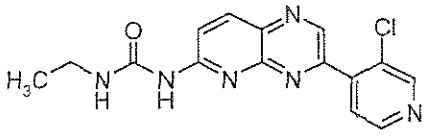
Compound (92) 1-allyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



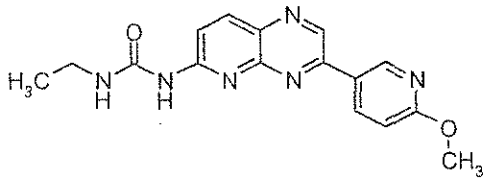
Compound (93) 1-ethyl-3-(3-piperazin-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



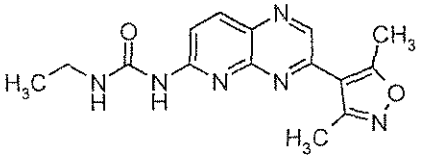
Compound (94) 1-[3-(3-chloro-pyridin-4-ylmethyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



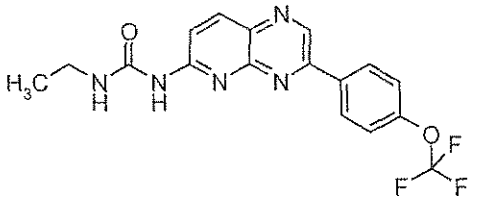
Compound (95) -ethyl-3-[3-(6-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



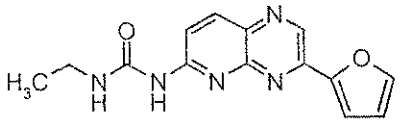
Compound (96) 1-[3-(3,5-dimethyl-isoxazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



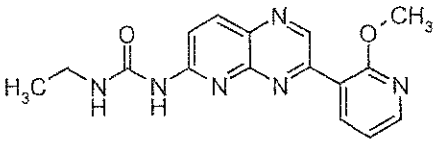
Compound (97) 1-ethyl-3-[3-(4-trifluormethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



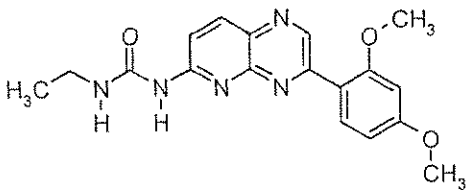
Compound (98) 1-ethyl-3-(3-furan-2-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



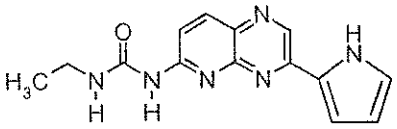
Compound (99) 1-ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



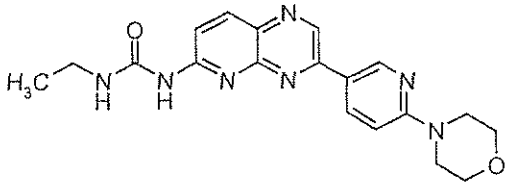
Compound (100) 1-[3-(2,4-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea;



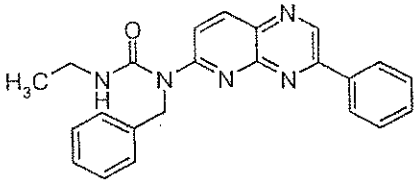
Compound (101) 1-ethyl-3-[3-(1h-pyrrol-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



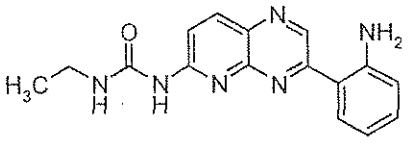
Compound (102) 1-ethyl-3-[3-(6-morpholin-4-yl-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



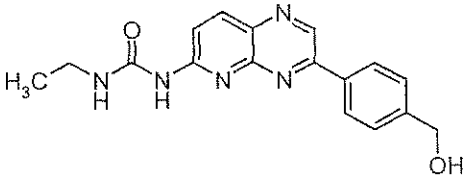
Compound (103) 1-benzyl-3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



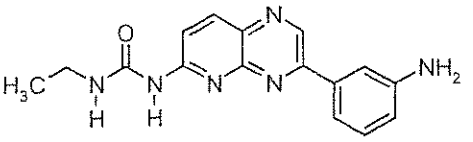
Compound (104) 1-[3-(2-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea;



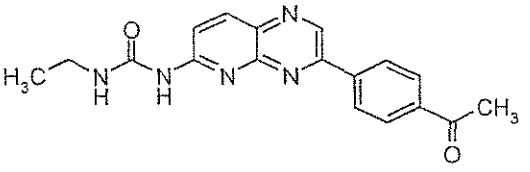
Compound (105) 1-ethyl-3-[3-(4-hydroxymethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



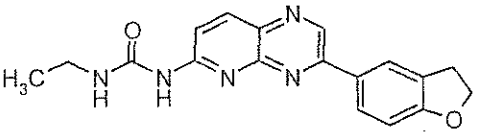
Compound (106) 1-[3-(3-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



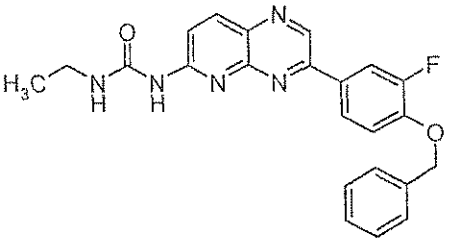
Compound (107) 1-[3-(4-acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



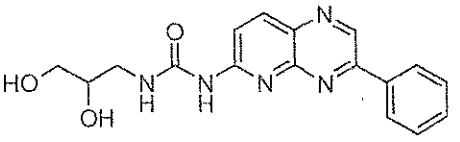
Compound (108) 1-[3-(2,3-dihydro-benzofuran-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



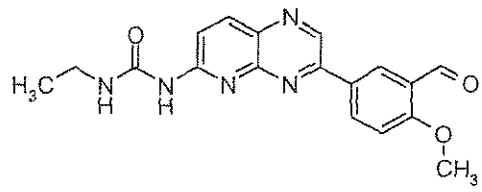
Compound (109) 1-[3-(4-benzyloxy-3-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



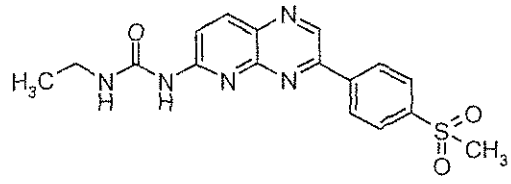
Compound (110) 1-(2,3-dihydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



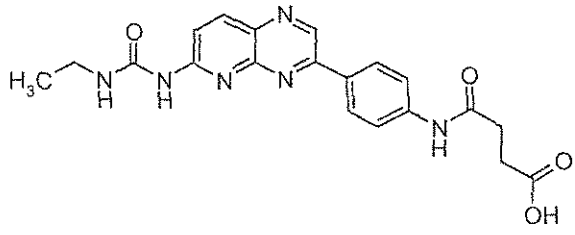
Compound (111) 1-ethyl-3-[3-(3-formyl-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



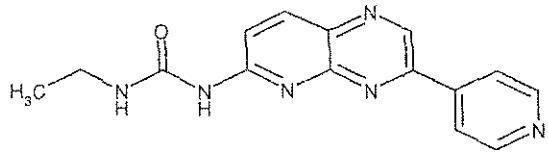
Compound (112) 1-ethyl-3-[3-(4-methansulfonyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea

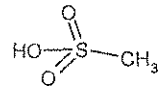


Compound (113) n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-succinamic acid

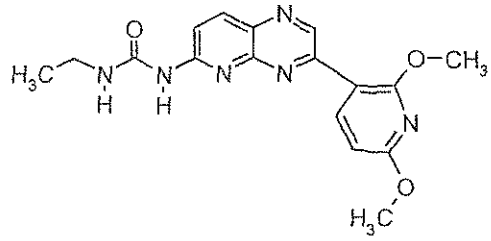


Compound (114) 1-ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea methane sulfonic acid salt (free base)

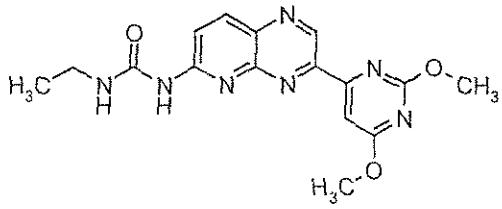




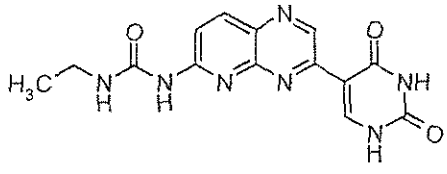
Compound (115) 1-[3-(2,6-dimethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



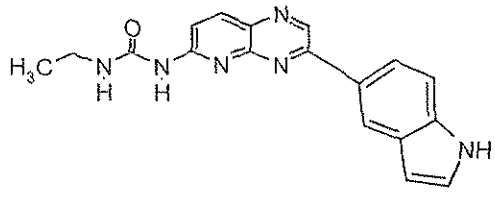
Compound (116) 1-[3-(2,6-dimethoxy-pyrimidin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



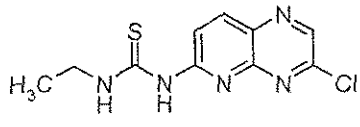
Compound (117) 1-[3-(2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



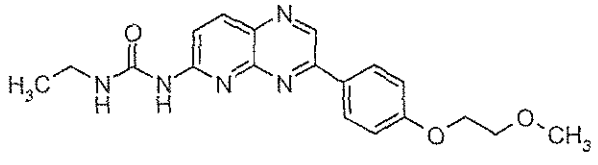
Compound (118) 1-ethyl-3-[3-(1h-indol-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



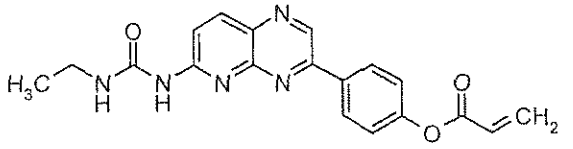
Compound (119) 1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-thiourea



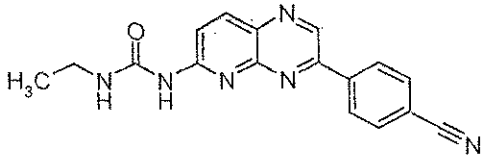
Compound (120) 1-ethyl-3-{3-[4-(2-methoxy-ethoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea



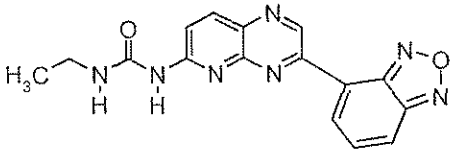
Compound (121) acrylic acid-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl ester



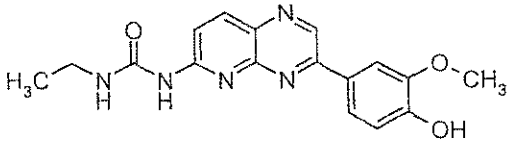
Compound (122) 1-[3-(4-cyano-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



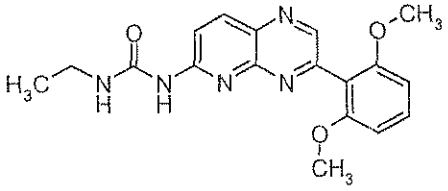
Compound (123) 1-(3-benzo[1,2,5]oxadiazol-4-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



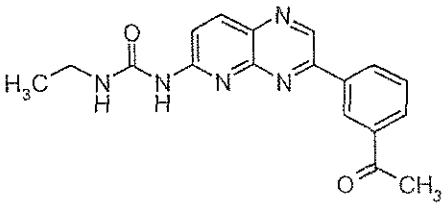
Compound (124) 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



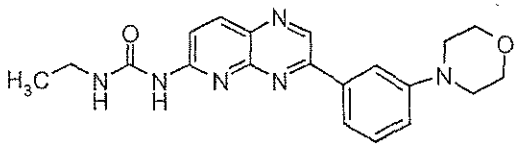
Compound (125) 1-[3-(2,6-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



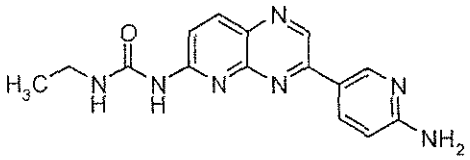
Compound (126) 1-[3-(3-acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



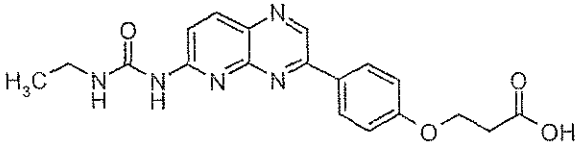
Compound (127) 1-ethyl-3-[3-(3-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



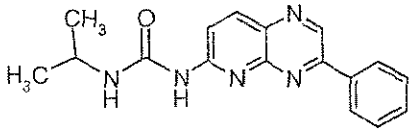
Compound (128) 1-[3-(6-amino-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



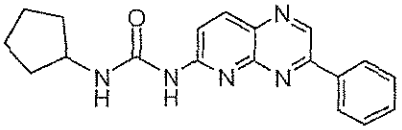
Compound (129) 3-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenoxy}-propionic acid



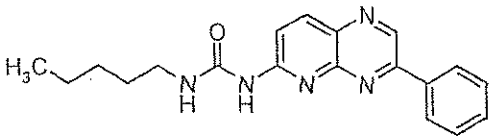
Compound (130) 1-isopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



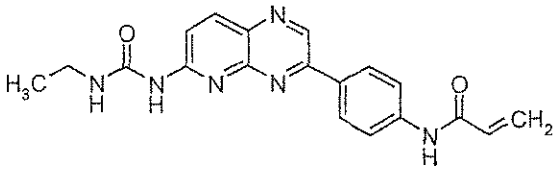
Compound (131) 1-cyclopentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



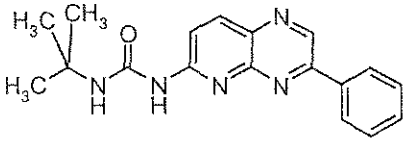
Compound (132) 1-pentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



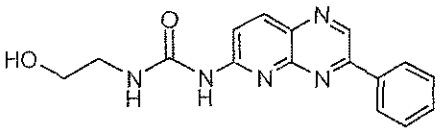
Compound (133) n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acrylamide



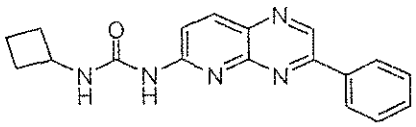
Compound (134) 1-tert-butyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



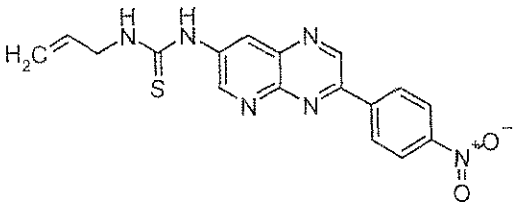
Compound (135) 1-(2-hydroxy-ethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



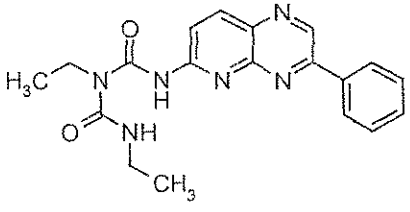
Compound (136) 1-cyclobutyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



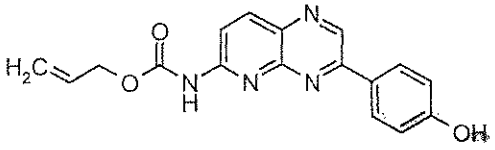
Compound (137) 1-allyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-7-yl]-thiourea



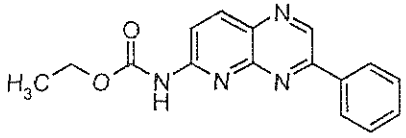
Compound (138) 1-ethyl-1-(ethylcarbamoyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



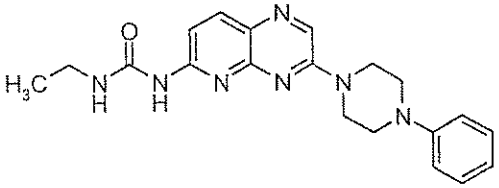
Compound (139) [3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-carbaminic acid-allyl ester



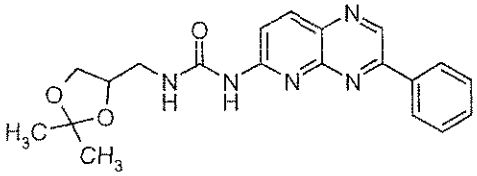
Compound (140) (3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-carbaminic acid-ethyl ester



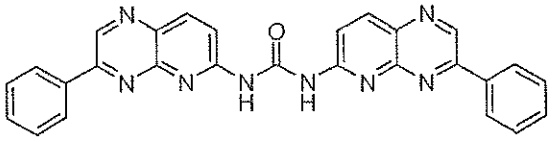
Compound (141) 1-ethyl-3-[3-(4-phenyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



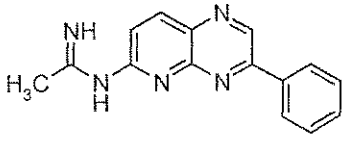
Compound (142) 1-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



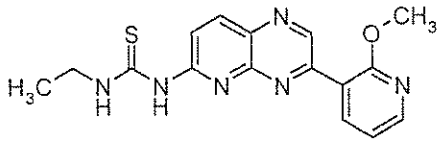
Compound (143) 1,3-bis-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



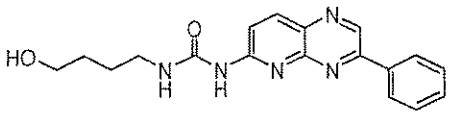
Compound (144) n-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-acetamidine



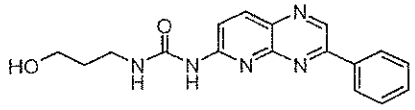
Compound (145) 1-ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea".



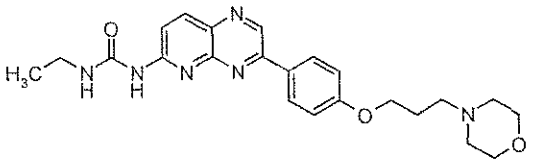
Compound (146) 1-(4-hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



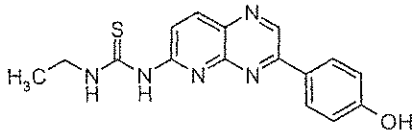
Compound (147) 1-(3-hydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



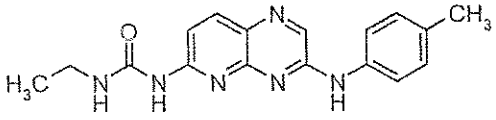
Compound (148) 1-ethyl-3-{3-[4-(3-morpholin-4-yl-propoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea



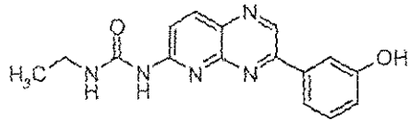
Compound (149) 1-ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



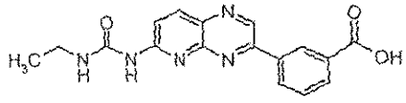
Compound (150) 1-ethyl-3-(3-p-tolylamino-pyrido[2,3-b]pyrazin-6-yl)-urea



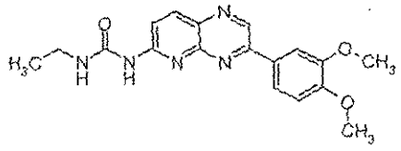
Compound (151) 1-ethyl-3-[3-(3-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



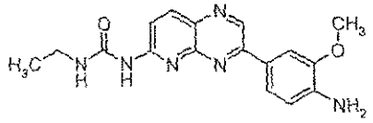
Compound 152 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid



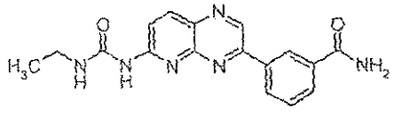
Compound 153 1-[3-(3,4-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



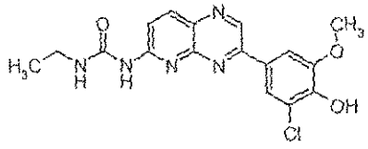
Compound 154 1-[3-(4-amino3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



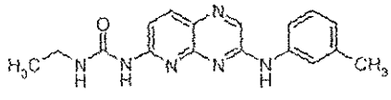
Compound 155 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-benzamid



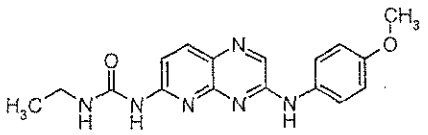
Compound 156 1-[3-(3-chloro-4-hydroxy-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



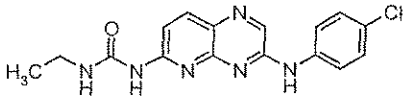
Compound 157 1-ethyl-3-(3-m-tolylamino-pyrido-[2,3-b]pyrazin-6-yl)-urea



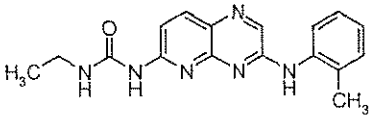
Compound 158 1-ethyl-3-[3-(4-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



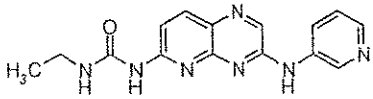
Compound 159 1-[3-(4-chlorophenylamino)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea



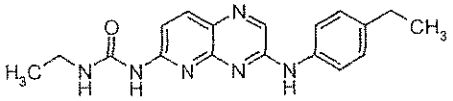
Compound 160 1-ethyl-3-(3-o-tolylamino-pyrido[2,3-b]-pyrazin-6-yl)-urea



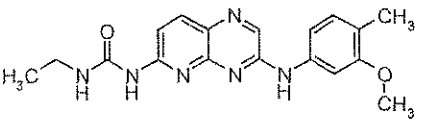
Compound 161 1-ethyl-3-[3-(pyridin-3-ylamino)-pyrido-[2,3-b]pyrazin-6-yl]-urea



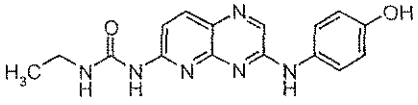
Compound 162 1-ethyl-3-[3-(4-ethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



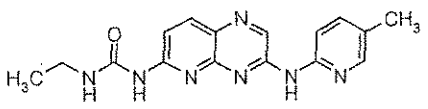
Compound 163 1-ethyl-3-[3-(3-methoxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



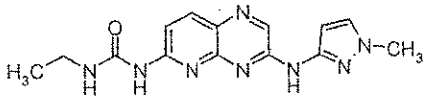
Compound 164 1-ethyl-3-[3-(4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



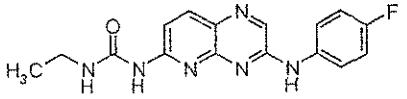
Compound 165 1-ethyl-3-[3-(5-methyl-pyridin-2-yl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



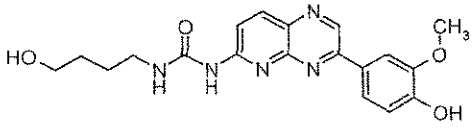
Compound 166 1-ethyl-3-[3-(1-methyl-1H-pyrazol-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



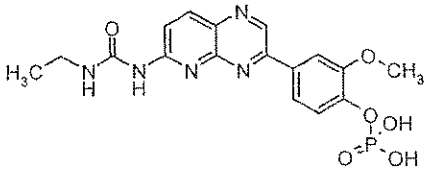
Compound 167 1-ethyl-3-[3-(4-fluoro-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



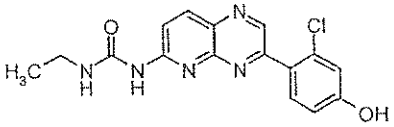
Compound 168 1-(4-hydroxy-butyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



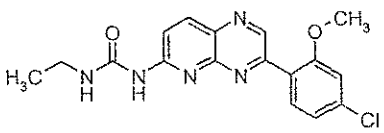
Compound 169 phosphoric acid-mono-{4-[6-(3-ethyl-ureido)-pyrido-[2,3-b]pyrazin-3-yl]-2-methoxy-phenyl}ester



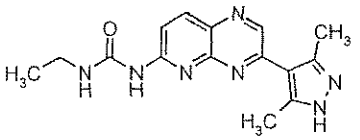
Compound 170 1-[3-(2-chloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



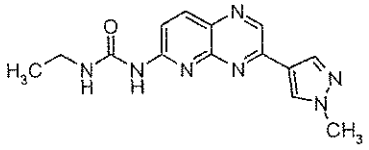
Compound 171 1-[3-(4-chloro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



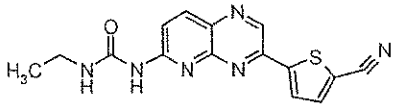
Compound 172 1-[3-(3,5-dimethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



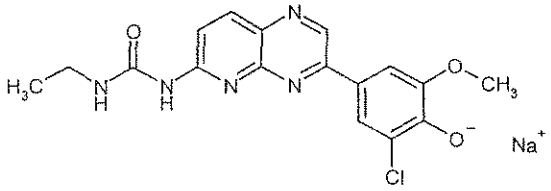
Compound 173 1-ethyl-3-[3-(1-methyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



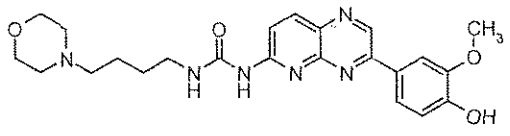
Compound 174 1-[3-(5-cyano-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



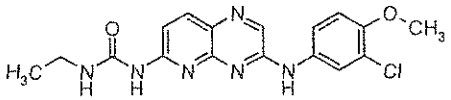
Compound 175 sodium 2-chloro-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-6-methoxy-phenoxide



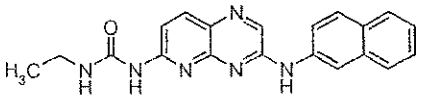
Compound 176 1-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(4-morpholin-4-yl-butyl)-urea



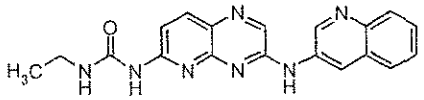
Compound 177 1-[3-(3-chloro-4-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



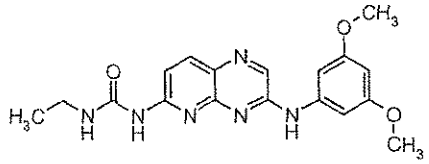
Compound 178 1-ethyl-3-[3-(naphthalen-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



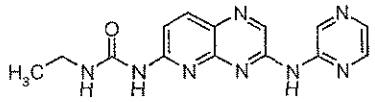
Compound 179 1-ethyl-3-[3-(quinolin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



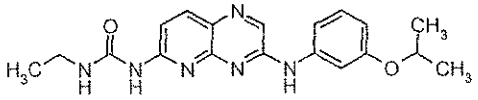
Compound 180 1-[3-(3,5-dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



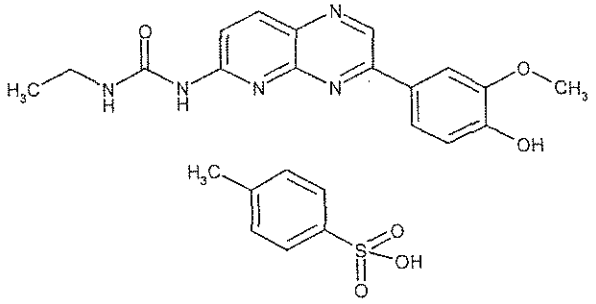
Compound 181 1-ethyl-3-[3-(pyrazin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



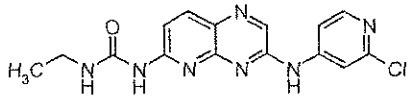
Compound 182 1-ethyl-3-[3-(3-isopropoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



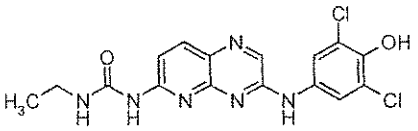
Compound 183 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea p-toluenesulfonate



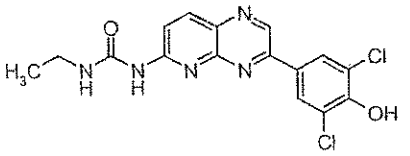
Compound 184 1-[3-(2-chloro-pyridin-4-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



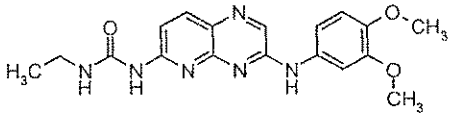
Compound 185 1-[3-(3,5-dichloro-4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



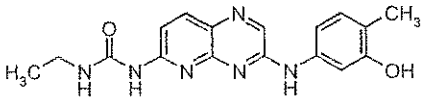
Compound 186 1-[3-(3,5-dichloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



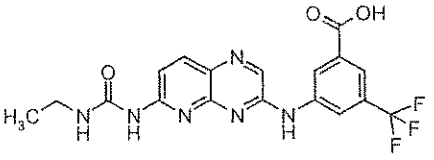
Compound 187 1-[3-(3,4-dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



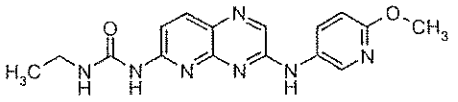
Compound 188 1-ethyl-3-[3-(3-hydroxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



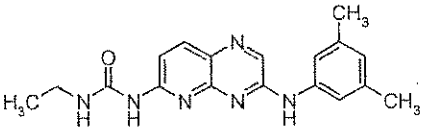
Compound 189 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-ylamino]-5-trifluormethyl-benzoic acid



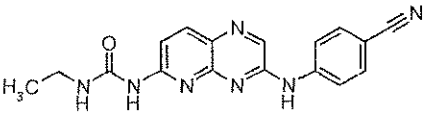
Compound 190 1-ethyl-3-[3-(6-methoxy-pyridin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



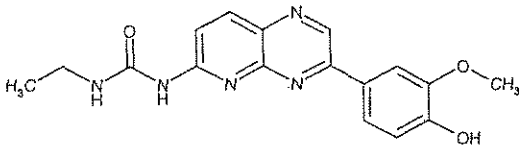
Compound 191 1-[3-(3,5-dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea

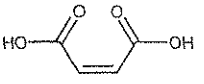


Compound 192 1-[3-(4-cyano-phenylamino)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea

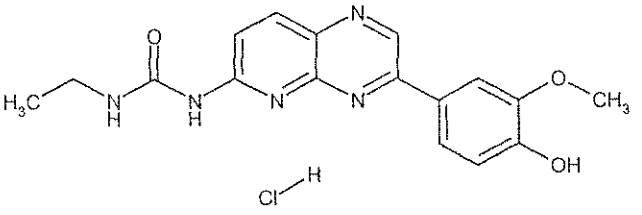


Compound 193 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea (Z)-but-2-enedicarboxylic acid salt

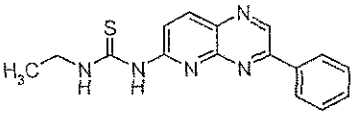




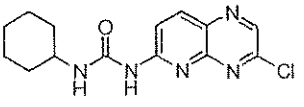
Compound 194 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea hydrochloride



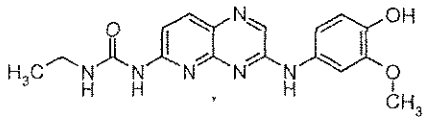
Compound 195 1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



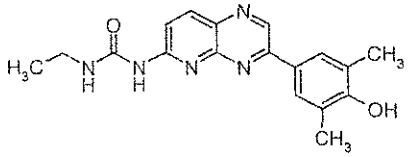
Compound 196 1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-cyclohexyl-urea



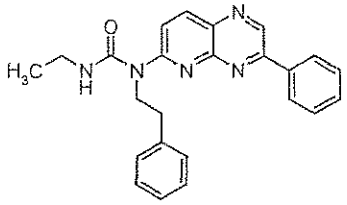
Compound 197 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



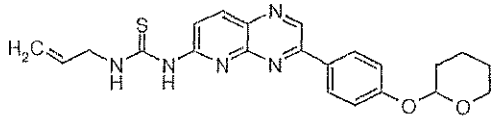
Compound 198 1-ethyl-3-[3-(4-hydroxy-3,5-dimethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



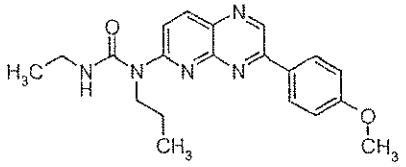
Compound 199 3-ethyl-1-phenethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



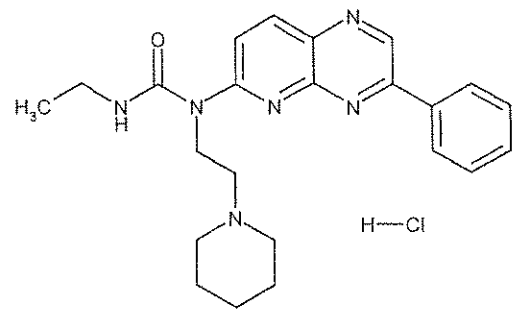
Compound 200 1-allyl-3-{3-[4-(tetrahydro-pyran-2-yloxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



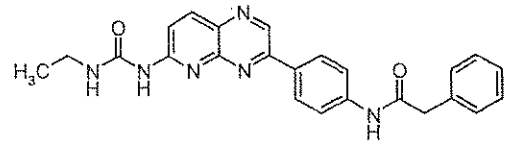
Compound 201 3-ethyl-1-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-1-propyl-urea



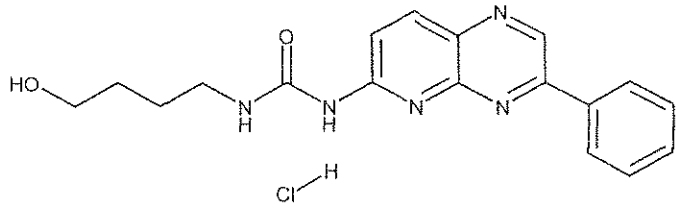
Compound 202 3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-1-(2-piperidin-1-yl-ethyl)-urea hydrochloride



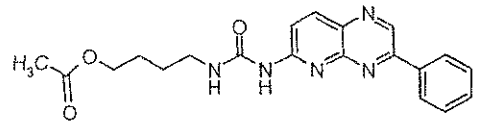
Compound 203 N-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl}-2-phenyl-acetamide



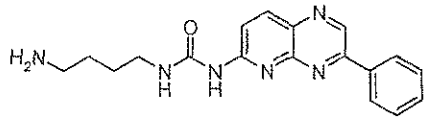
Compound 204 1-(4-hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea hydrochloride



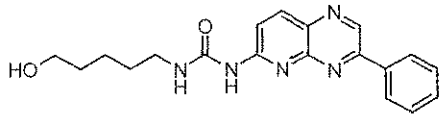
Compound 205 Acetic acid-4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl ester



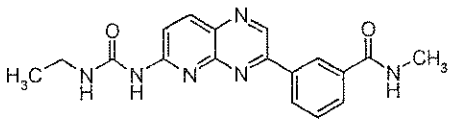
Compound 206 1-(4-aminobutyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



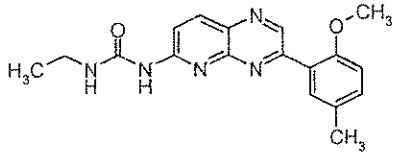
Compound 207 1-(5-hydroxy-pentyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



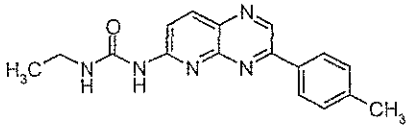
Compound 208 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-N-methyl-benzamide



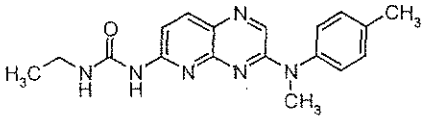
Compound 209 1-ethyl-3-[3-(2-methoxy-5-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



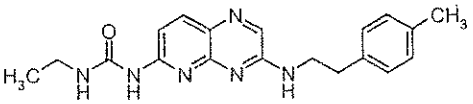
Compound 210 1-ethyl-3-(3-p-tolyl-pyrido[2,3-b]pyrazin-6-yl)-urea



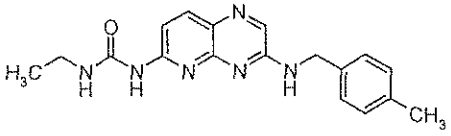
Compound 211 1-ethyl-3-[3-(methyl-p-tolyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



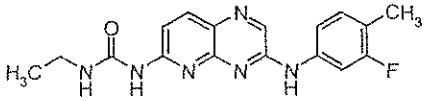
Compound 212 1-ethyl-3-[3-(2-p-tolyl-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



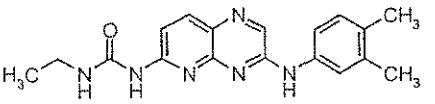
Compound 213 1-ethyl-3-[3-(4-methyl-benzylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



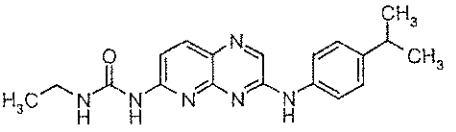
Compound 214 1-ethyl-3-[3-(3-fluoro-4-methyl-phenyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



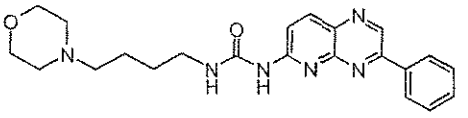
Compound 215 1-[3-(3,4-dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



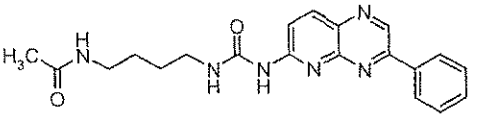
Compound 216 1-ethyl-3-[3-(4-isopropyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



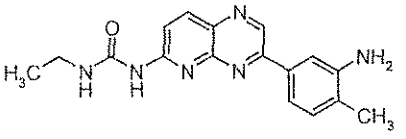
Compound 217 1-(4-morpholin-4-yl-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



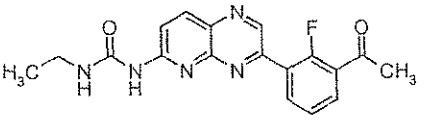
Compound 218 N-{4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-acetamid



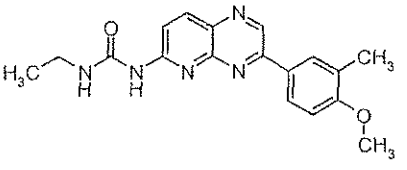
Compound 219 1-[3-(3-amino-4-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



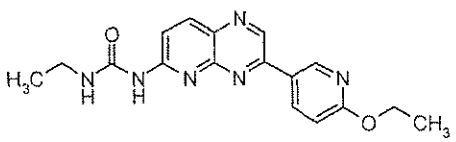
Compound 220 1-[3-(3-acetyl-2-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



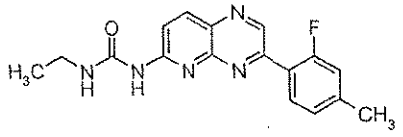
Compound 221 1-ethyl-3-[3-(4-methoxy-3-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



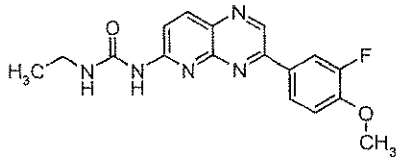
Compound 222 1-[3-(6-ethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



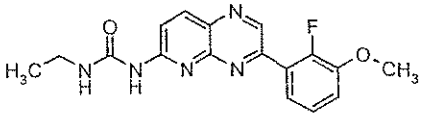
Compound 223 1-ethyl-3-[3-(2-fluoro-4-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



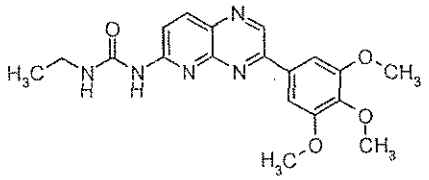
Compound 224 1-ethyl-3-[3-(3-fluoro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



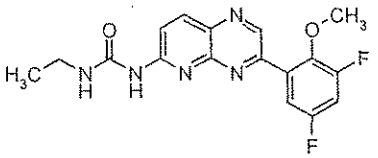
Compound 225 1-ethyl-3-[3-(2-fluoro-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



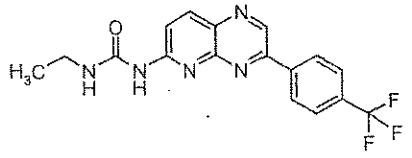
Compound 226 1-ethyl-3-[3-(3,4,5-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



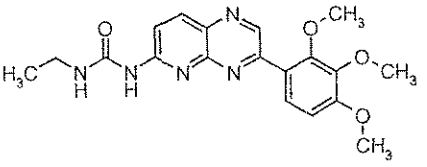
Compound 227 1-[3-(3,5-difluoro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



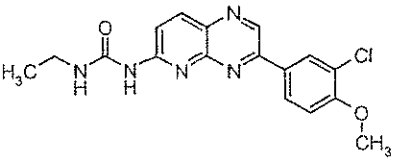
Compound 228 1-ethyl-3-[3-(4-trifluoromethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



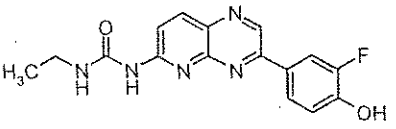
Compound 229 1-ethyl-3-[3-(2,3,4-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



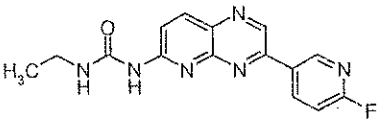
Compound 230 1-[3-(3-chloro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



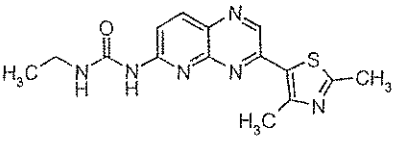
Compound 231 1-ethyl-3-[3-(3-fluoro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



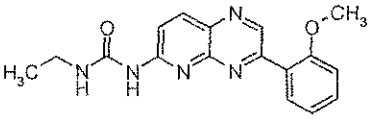
Compound 232 1-ethyl-3-[3-(6-fluoro-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



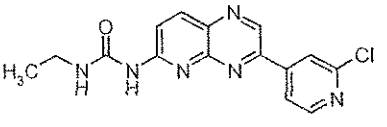
Compound 233 1-[3-(2,4-dimethyl-thiazol-5-yl)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea



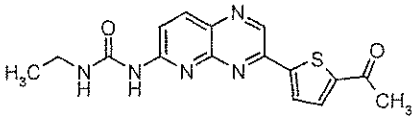
Compound 234 1-ethyl-3-[3-(2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



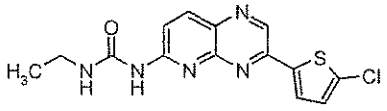
Compound 235 1-[3-(2-chloro-pyridin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



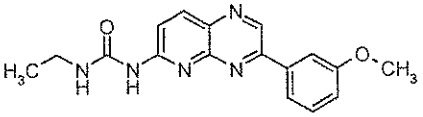
Compound 236 1-[3-(5-acetyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



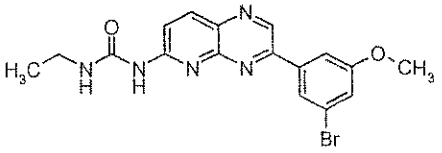
Compound 237 1-[3-(5-chloro-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



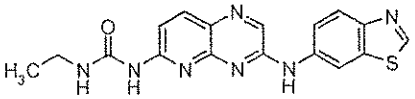
Compound 238 1-ethyl-3-[3-(3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



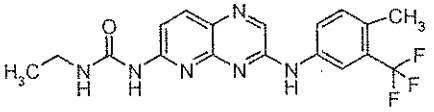
Compound 239 1-[3-(3-bromo-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



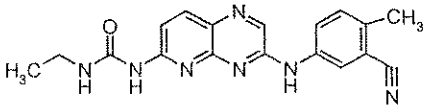
Compound 240 1-[3-(benzothiazol-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



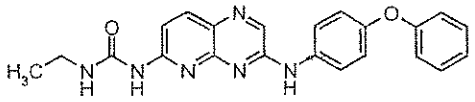
Compound 241 1-ethyl-3-[3-(4-methyl-3-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



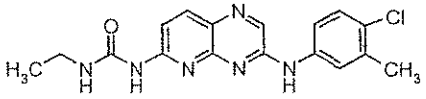
Compound 242 1-[3-(3-cyano-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



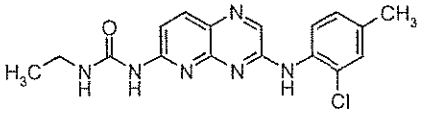
Compound 243 1-ethyl-3-[3-(4-phenoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



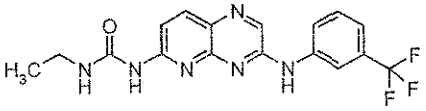
Compound 244 1-[3-(4-chloro-3-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



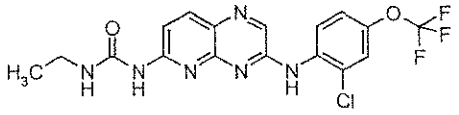
Compound 245 1-[3-(2-chloro-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



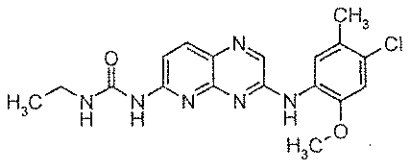
Compound 246 1-ethyl-3-[3-(3-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



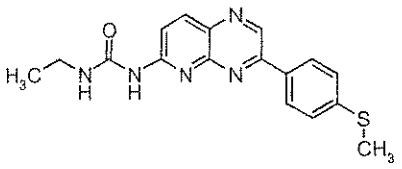
Compound 247 1-[3-(2-chloro-4-trifluoromethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



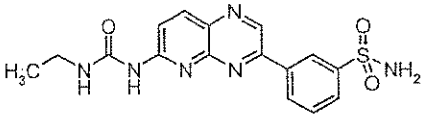
Compound 248 1-[3-(4-chloro-2-methoxy-5-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



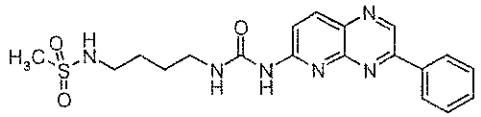
Compound 249 1-ethyl-3-[3-(4-methylsulfanyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



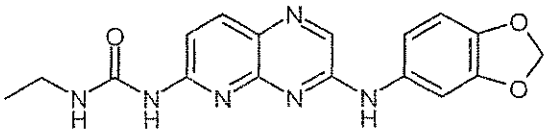
Compound 250 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzenesulfonamide



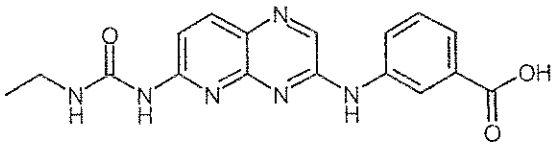
Compound 251 N-{4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-methanesulfonamide



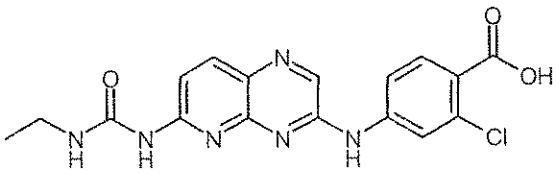
Compound 252 1-[3-(benzo[1,3]dioxol-5-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



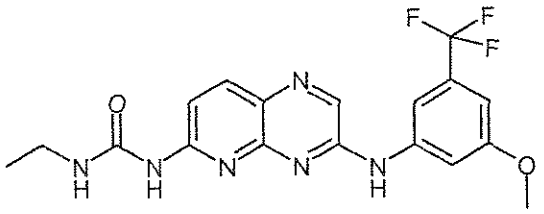
Compound 253 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-benzoic acid



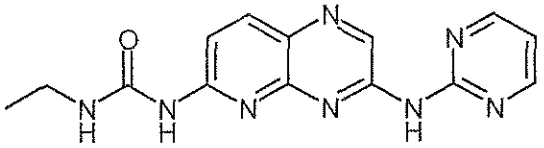
Compound 254 2-chloro-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-benzo ic acid



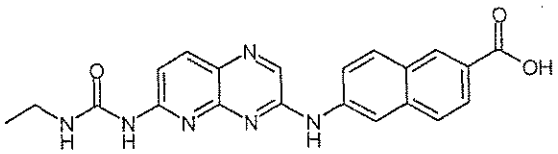
Compound 255 1-ethyl-3-[3-(3-methoxy-5-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



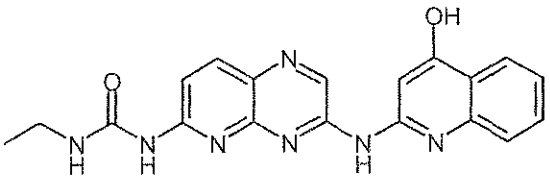
Compound 256 1-ethyl-3-[3-(pyrimidin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



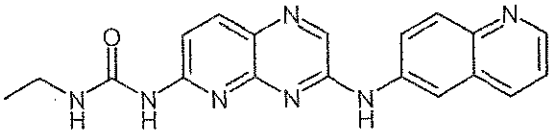
Compound 257 6-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-naphthalene-2-carboxylic acid



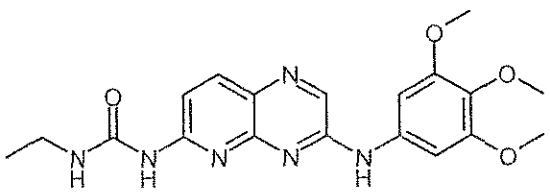
Compound 258 1-ethyl-3-[3-(4-hydroxy-quinolin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



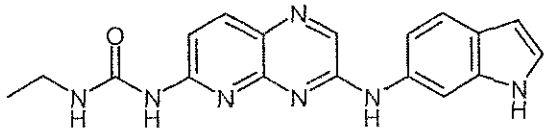
Compound 259 1-ethyl-3-[3-(quinolin-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



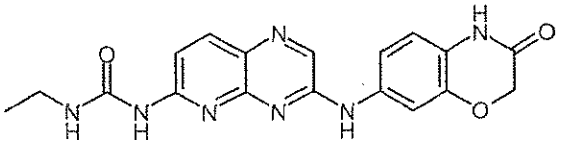
Compound 260 1-ethyl-3-[3-(3,4,5-trimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



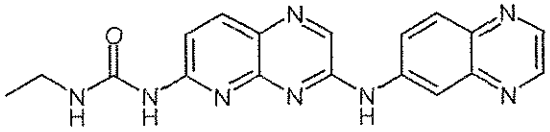
Compound 261 1-ethyl-3-[3-(1H-indol-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



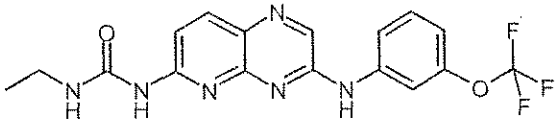
Compound 262 1-ethyl-3-[3-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



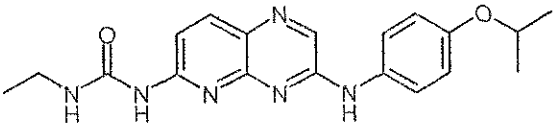
Compound 263 1-ethyl-3-[3-(quinoxalin-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



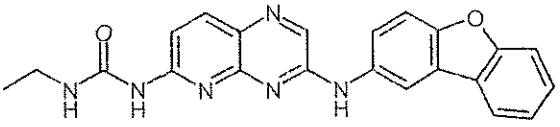
Compound 264 1-ethyl-3-[3-(3-trifluoromethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



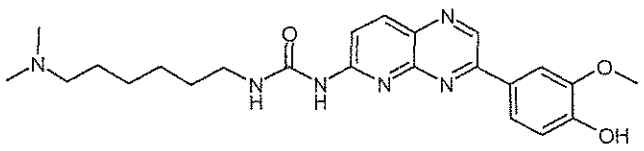
Compound 265 1-ethyl-3-[3-(4-isopropoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



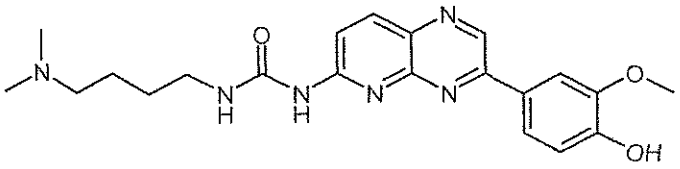
Compound 266 1-[3-(dibenzofuran-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



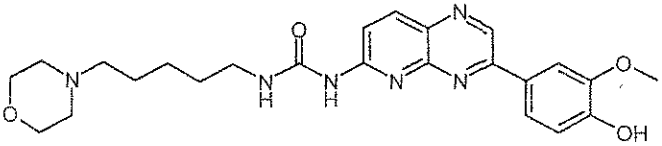
Compound 267 1-(6-dimethylamino-hexyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



Compound 268 1-(4-dimethylamino-butyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



Compound 269 1-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(5-morpholin-4-yl-pentyl)-urea



which can be used for the production of a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals mediated by signal transduction pathways selected from the group consisting of: the "ras-Raf-Mek-Erk signal transduction pathway, the PI3K-Akt signal transduction pathway and/or the SAPK signal transduction pathway.

In order to avoid ambiguities: if chemical structure and chemical name of the explicit compounds shown above erroneously do not match one another, the chemical structure shall unambiguously define the particular explicit compound.

The afore-mentioned generic compounds having the general formula (I) and preferred embodiments as well as the explicitly specified pyridopyrazine compounds 1

to 269 are hereinafter designated jointly as "compounds according to the invention".

The expressions and terms specified to explain the compounds according to the invention basically have the following meanings unless specified otherwise in the description and the claims:

The expression "alkyl" in the sense of this invention comprises acyclic saturated or unsaturated hydrocarbon groups which can be branched or straight-chain, with 1 to 8 C atoms, i.e. C_{1-8}-alkanyls, C_{2-8}-alkenyls and C_{2-8}-alkynyls. In this context, alkenyls have at least one C-C double bond and alkynyls have at least one C-C triple bond. Alkynyls may, though, additionally also have at least one C-C double bond. Preferred alkyl groups are methyl, ethyl, *n*-propyl, 2-propyl, *n*-butyl, *sec.*-butyl, *tert.*-butyl, *n*-pentyl, *iso*-pentyl, *neo*-pentyl, *n*-hexyl, 2-hexyl, n-heptyl, n-nonyl, n-decyl, n-undecyl, n-dodecyl, *n*-octyl, ethylenyl (vinyl), ethynyl, propenyl ($-CH_2CH=CH_2$; $-CH=CH-CH_3$, $-C(=CH_2)-CH_3$), propinyl ($-CH_2-C\equiv CH$, $-C\equiv C-CH_3$), butenyl, butinyl, pentenyl, pentinyl, hexenyl, hexinyl, heptenyl, heptinyl, octenyl, octadienyl and octinyl.

The expression "cycloalkyl" means for the purposes of this invention cyclic, nonaromatic hydrocarbons having from 1 to 3 rings with 3 to 20, preferably 3 to 12 carbons which can be saturated or unsaturated, more preferably (C_3-C_8)-cycloalkyl. The cycloalkyl group can also be part of a bi- or polycyclic system, where for example, the cycloalkyl group is fused to an aryl, heteroaryl or heterocyclyl group as defined herein via any possible and desired ring member(s). Binding to the compounds having the general formula (I) can take place via any arbitrary and possible ring member of the cycloalkyl group. Preferred cycloalkyl groups are

cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclodecyl, cyclohexenyl, cyclopentenyl and cyclooctadienyl.

The expression "heterocyclyl" stands for a three- to fourteen-membered, preferably three-, four-, five-, six-, seven- or eight-membered cyclic organic group which contains at least 1, optionally 2, 3, 4 or 5 heteroatoms, in particularly nitrogen, oxygen and/or sulphur, the heteroatoms being the same or different and the cyclic group being saturated or unsaturated but not aromatic. The heterocyclyl group can also be part of a bi- or polycyclic system, where, for example, the heterocyclic group is fused to an aryl, heteroaryl or cycloalkyl group as defined herein via any possible and desired ring member(s). Binding to the compounds having the general formula (I) can take place via any arbitrary and possible ring member of the heterocyclyl group. Preferred heterocyclyl groups are tetrahydrofuryl, pyrrolidinyl, imidazolidinyl, thiazolidinyl, tetrahydropyranyl, piperidinyl, piperazinyl, morpholinyl, thiapyrrolidinyl, oxapiperazinyl, oxapiperidinyl and oxadizaolyl.

The expression "aryl" in the sense of this invention means aromatic hydrocarbons with 3 to 14 C atoms, preferably 5 to 14 C atoms, more preferably 6 to 14 C atoms. The aryl group can also be part of a bi- or polycyclic system where, for example, the aryl group is fused to a heterocyclyl, heteroaryl or cycloalkyl group as defined herein via any possible and desired ring member(s), for example via terahydrofuran, tetrahydrothiophen, pyrrolidine, imidazolidine, thiazolidine, tetrahydropyran, dihydropyran, piperidine, furan, thiophene, imidazole, thiazole, oxazole, isoxazole. Binding to the compounds having the general formula (I) can take place via any arbitrary

and possible ring member of the aryl group. Preferred aryl groups are phenyl, biphenyl, naphthyl and anthracenyl, but also indanyl, indenyl or 1,2,3,4-tetrahydronaphthyl.

The expression "heteroaryl" stands for any five-, six- or seven-membered cyclic aromatic group containing 1, optionally 2, 3, 4 or 5 heteroatoms, in particular nitrogen, oxygen and/or sulphur, the heteroatoms being the same or different. The number of nitrogen atoms is preferably 0 to 3, that of oxygen and sulfur atoms preferably 0 to 1. The heterocycle can also be part of a bi- or polycyclic system where for example the heteroaryl group is fused to a heterocyclyl, aryl or cycloalkyl group as defined herein via any possible and desired ring member(s). Binding to the compounds having the general formula (I) can take place via any arbitrary and possible ring member of the heteroaryl group. Preferred heteroaryl groups are pyrrolyl, furyl, thienyl, thiazolyl, isothiazolyl, oxazolyl, oxadiazolyl, isoxazolyl, pyrazolyl, imidazolyl, triazole, tetrazole, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazine, phthalazinyl, indolyl, indazolyl, indolizinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, pteridinyl, carbazolyl, phenazinyl, phenoxazinyl, phenothiazinyl, and acridinyl.

For the purposes of the present invention the expressions "alkyl-cycloalkyl", "cycloalkylalkyl", "alkyl-heterocyclyl", "heterocyclylalkyl", "alkyl-aryl", "arylalkyl", "alkyl-heteroaryl" and "alkyl-heteroaryl" mean that alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl have the meanings defined above and the cycloalkyl, heterocyclyl, aryl and heteroaryl group is bound to compounds having the general formula (I)

via an alkyl group, preferably C_{1-8}-alkyl group, more preferably C_1-C_4-alkyl group.

In connection with "alkyl", "cycloalkyl", "heterocyclyl", "aryl", "heteroaryl", alkyl-cycloalkyl", "alkyl-heterocyclyl", "alkyl-aryl" and "alkyl-heteroaryl" the term substituted is understood in the sense of this invention unless defined explicitly above in the description and the claims as the substitution of one or more hydrogen groups by F, Cl, Br, I, CN, CF_3, NH_2, NH-alkyl, NH-aryl, $N(alkyl)_2$, NO_2, SH, S-alkyl, OH, OCF_3, O-alkyl, O-aryl, OSO_3H, $OP(O)(OH)_2$, CHO, CO_2H, SO_3H or alkyl. The substituents can be the same or different and the substitutions can take place in any arbitrary and possible position of the alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl group.

The expression "halogen" encompasses, in the context of this invention, the halogen atoms fluorine, chlorine, bromine and iodine.

Multiply substituted groups are to be understood as those which are multiply, e.g. doubly, triply, substituted either at different or at the same atoms, for example, triply substituted at the same C atoms as in the case of CF_3,
$-CH_2CF_3$ or at different positions as in the case of $-CH(OH)-CH=CH-CHCl_2$. The multiple substitution can take place with the same or different substituents.

Insofar as the compounds according to the invention have at least one centre of asymmetry, they can be present in the form of their racemates, in the form of the pure enantiomers and/or diastereomers or in the form of mixtures of these enantiomers and/or diastereomers. The mixtures can be present in any arbitrary mixture ratio of the stereoisomers.

Thus, for example, the compounds according to the invention which have one or a plurality of centres of chirality and which occur as their racemates can be separated into their optical isomers, that is enantiomers or diastereomers, by methods known per se. The separation can be performed by column separation at chiral phases or by recrystallisation from an optically active solvent or by using an optically active acid or base or by derivatisation with an optically active reagent, such as for example, an optically active alcohol and subsequent separation of the residue.

The inventive compounds may be present in the form of their double bond isomers as "pure" E or Z isomers, or in the form of mixtures of these double bond isomers.

As far as possible, the compounds according to the invention can be present in the form of tautomers.

If they possess a sufficiently basic group, such as for example, a primary, secondary or tertiary amine, the compounds according to the invention can be converted into their physiologically compatible salts using inorganic and organic acids. The pharmaceutically acceptable salts of the compounds according to the invention are preferably formed with hydrochloric acid, bromic acid, sulphuric acid, phosphoric acid, methane sulfonic acid, p-toluene sulfonic acid, carbonic acid, formic acid, acetic acid, trifluoroacetic acid, sulfoacetic acid, oxalic acid, malonic acid, maleic acid, succinic acid, tartaric acid, racemic acid, malic acid, embonic acid, mandelic acid, fumaric acid, lactic acid, citric acid, glutamic acid or asparaginic acid. The salts formed include, among others, hydrochloride, hydrobromide, sulfate, hydrogen sulfate, phosphate, methane sulfonate, tosylate, carbonate, hydrogen carbonate, formiate, acetate, triflate, sulfoacetate, oxalate, malonate, maleate, succinate, tartrate,

malate, embonate, mandelate, fumarate, lactate, citrate, glutaminate and aspartate. The stoichiometry of the salts of the compounds according to the invention which are formed can be integer or non-integer multiples of one.

If they contain a sufficiently acidic group, such as the carboxy group, for example, the compounds according to the invention can be converted into their physiologically compatible salts using inorganic and organic bases. Possible inorganic bases are, for example, sodium hydroxide, potassium hydroxide, calcium hydroxide, possible organic bases are ethanol amine, diethanol amine, triethanol amine, cyclohexylamine, dibenzylethylene diamine and lysine. The stoichiometry of the salts of the compounds according to the invention which are formed can be integer or non-integer multiples of one.

Likewise preferred are solvates and in particular hydrates of the compounds according to the invention, which can be obtained, for example, by crystallisation from a solvent or from aqueous solution. In this context, one, two, three or an arbitrary number of solvate or water molecules can combine with the compounds according to the invention to form solvates and hydrates.

It is known that chemical substances form solids which are present in various states of order, which are designated as polymorphous forms or modifications. The various modifications of a polymorphous substance can differ strongly in respect of their physical properties. The compounds according to the invention can be present in various polymorphous forms, in which case certain modifications can be metastable.

The compounds according to the invention can likewise be present in the form of any prodrugs such as, for

example, esters, carbonates, carbamates, ureas, amides or phosphates wherein the actually biologically active form is only released by catabolism.

It is further known that chemical substances are converted to metabolites in the body which optionally can likewise induce the desired biological effect, possibly even in a more distinct form.

Corresponding prodrugs and metabolites of the compounds according to the invention should also be considered as pertaining to the invention.

It was now surprisingly and advantageously determined that the compounds according to the invention can act simultaneously or have a modulating or inhibiting effect on two or more signal transduction pathways or enzymes. In this context, it has been found that the compounds according to the invention can act or have a modulating or inhibiting effect with high selectivity.

Such a simultaneous, for example, dual modulation or inhibition of two or more signal transduction pathways, e.g. the ras-Raf-Mek-Erk signal pathway, the PI3K-Akt signal pathway and/or the SAPK signal pathway, more especially Erk1/Erk2 and/or PI3K and/or Jnk and/or p38, is advantageous compared with merely single modulation or inhibition of a signal transduction pathway since synergistic therapeutic effects can be brought about, such as for example, intensified apoptosis and faster and more efficient tumour regression.

The surprising advantageous effects of the compounds according to the invention allow multiple therapy approaches to be pursued in physiological and/or pathophysiological states or clinical pictures which are sensitive for the treatment or modulation of, or are mediated by, two or more signal transduction pathways.

It was further surprisingly and advantageously determined that the compounds according to the invention can also act with high selectivity or have a modulating or inhibiting effect on the PI3K-Akt signal transduction pathway or enzymes thereof and that the multiple mechanisms of action and therapy approaches described above can also be used with this signal pathway or enzymes.

It was further surprisingly and advantageously determined that the compounds according to the invention can also act with high selectivity or have a modulating or inhibiting effect on the SAPK signal transduction pathway or enzymes thereof and that the multiple mechanisms of action and therapy approaches described above can also be used with this signal pathway or enzymes.

It was further surprisingly and advantageously determined that the compounds according to the invention can also act with high selectivity or have a modulating or inhibiting effect on enzymes such as ATM, ATR, mTOR, DNA-PK and/or hSMG-1 and that the multiple mechanisms of action and therapy approaches described above can also be used with this signal pathway or enzymes.

The term "modulation" is understood according to the invention as follows: "activation, partial activation, inhibition, partial inhibition". In this case, it is within the specialist knowledge of the average person skilled in the art to measure and determine such activation, partial activation, inhibition, partial inhibition by means of the usual methods of measurement and determination. Thus, a partial activation can be measured and determined in relation to a complete activation; likewise, a partial inhibition in relation to a complete inhibition.

The terms "inhibiting, inhibition and/or retardation" are understood as follows according to the invention: "partial or complete inhibiting, inhibition and/or retardation". In this case, it is within the specialist knowledge of the average person skilled in the art to measure and determine such inhibiting, inhibition, and/or retardation by means of the usual methods of measurement and determination. Thus, a partial inhibiting, inhibition and/or retardation, for example, can be measured and determined in relation to a complete inhibiting, inhibition and/or retardation.

The terms "modulation" and "inhibiting, inhibition and/or retardation" in connection with "enzymes" and/or "kinases" within the scope of this invention relate both to the inactive form (enzymatically inactive) and/or active form (enzymatically active) of the respective enzyme and/or kinase. This means within the scope of this invention that the compound according to the invention can have a modulating effect on the inactive form, active form or both forms of the enzyme and/or kinase.

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds according to the invention which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the treatment or prevention is effected by modulation of the signal transduction pathway or pathways selected from the group consisting of: the "ras-Raf-Mek-Erk signal transduction pathway, the PI3K-Akt signal transduction pathway and/or the SAPK signal transduction pathway.

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds

according to the invention which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, mediated by enzymes selected from the group consisting of: "ATM, ATR, mTOR, DNA-PK, hSMG-1".

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds according to the invention which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the treatment or prevention is effected by modulation of one or more enzymes selected from the group consisting of: "ATM, ATR, mTOR, DNA-PK, hSMG-1".

In a preferred embodiment, the compounds according to the invention are prepared for use to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals mediated by the ras-Raf-Mek-Erk signal transduction pathway, the PI3K-Akt signal transduction pathway and/or use to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the treatment or prevention is effected by modulation of the ras-Raf-Mek-Erk signal transduction pathway and the PI3K-Akt signal transduction pathway.

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds according to the invention which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, mediated by the PI3K-Akt signal transduction pathway.

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds according to the invention which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the treatment or prevention is effected by modulation of the PI3K-Akt signal transduction pathway.

In a preferred embodiment, the compounds according to the invention are prepared for use to produce a medicinal product for the treatment and/or prevention of physiological and/or pathophysiological states in mammals mediated by the SAPK signal transduction pathway and the PI3K-Akt signal transduction pathway and/or to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the treatment or prevention is effected by modulation of the SAPK signal transduction pathway and the PI3K-Akt signal transduction pathway.

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds according to the invention which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, mediated by the SAPK signal transduction pathway.

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds according to the invention which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in

mammals, wherein the treatment or prevention is effected by modulation of the SAPK signal transduction pathway.

In a preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein the modulation of the ras-Raf-Mek-Erk signal transduction pathway is effected by modulation of one or more enzymes selected from the group consisting of: "tyrosine kinase, serine/threonine kinase, receptor tyrosine kinase, cytoplasmic tyrosine kinase, cytoplasmic serine/threonine kinase" and preferably selected from the group consisting of: "Erk, Erk1, Erk2".

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein the modulation of the P13K-Akt signal transduction pathway is effected by modulation of one or more enzymes selected from the group consisting of: "PI3K, PI3Kalpha, PI3Kbeta, PI3Kgamma, PI3Kdelta, PI3K-C2alpha, PI3K-C2beta, PI3K-Vps34p".

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein the modulation of the SAPK signal transduction pathway is effected by modulation of one or more enzymes selected from the group consisting of: "tyrosine kinase, serine/threonine kinase, receptor tyrosine kinase, cytoplasmic tyrosine kinase, cytoplasmic serine/threonine kinase" and is preferably selected from the group consisting of: "Jnk, Jnk1, Jnk2, Jnk3, p38, p38alpha, p38beta, p38gamma, p38delta".

In a further aspect, the inventive object was surprisingly achieved by preparing the compounds according to the invention according to the aspects, preferred embodiments and uses described above which can be used to produce a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the treatment or prevention is effected by modulation of two or more enzymes.

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein in the treatment or prevention effected by modulation of two or more enzymes, at least one enzyme is selected from the group consisting of: "Erk, Erk1, Erk2" and at least one enzyme is selected from the group consisting of: "PI3K, PI3Kalpha, PI3Kbeta, PI3Kgamma, PI3Kdelta, PI3K-C2alpha, PI3K-C2beta, PI3K-Vps34p".

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein in the treatment or prevention effected by modulation of two or more enzymes at least one enzyme is selected from the group consisting of: "Jnk, Jnk1, Jnk2, Jnk3, p38, p38alpha, p38beta, p38gamma, p38delta" and at least one enzyme is selected from the group consisting of: "PI3K, PI3Kalpha, PI3Kbeta, PI3Kgamma, PI3Kdelta, PI3K-C2alpha, PI3K-C2beta, PI3K-Vps34p".

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein in the treatment or prevention effected by modulation of two or more enzymes, at least one enzyme is selected from the group consisting of: "Erk, Erk1, Erk2" and at least one enzyme is selected

from the group consisting of: "ATM, ATR, mTOR, DNA-PK, hSMG-1".

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein in the treatment or prevention effected by modulation of two or more enzymes, at least one enzyme is selected from the group consisting of: "Jnk, Jnk1, Jnk2, Jnk3, p38, p38alpha, p38beta, p38gamma, p38delta" and at least one enzyme is selected from the group consisting of: "ATM, ATR, mTOR, DNA-PK, hSMG-1".

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein in the treatment or prevention effected by modulation of two or more enzymes, at least one enzyme is selected from the group consisting of: "PI3K, PI3Kalpha, PI3Kbeta, PI3Kgamma, PI3Kdelta, PI3K-C2alpha, PI3K-C2beta, PI3K-Vps34p" and at least one enzyme is selected from the group consisting of: "ATM, ATR, mTOR, DNA-PK, hSMG-1".

In a further preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein the modulation is an inhibition.

The compounds according to the invention can be administered within the scope of this invention to all known mammals, in particular, humans, for the treatment and/or prevention.

In another preferred embodiment, the compounds according to the invention are prepared for the uses

described above, wherein the mammal is selected from the group consisting of: "human, domesticated animal, cattle, pet, beef cattle, cow, sheep, pig, goat, horse, pony, donkey, hinny, mule, hare, rabbit, cat, dog, guinea pig, hamster, rat, mouse" and is preferably a human.

The compounds according to the invention can be used within the scope of this invention for the treatment and/or prevention of all known physiological and/or pathophysiological states.

In a preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein the physiological and/or pathophysiological states are selected from the group consisting of: "malignant tumours, benign tumours, inflammatory diseases, inflammations, pain, rheumatic diseases, arthritic diseases, HIV infections, neurological or neurodegenerative diseases, rheumatism, arthritis, AIDS, ARC (AIDS related complex), Kaposi's sarcoma, tumours originating from the brain and/or nervous system and/or meninges, dementia, Alzheimer's disease, hyperproliferative diseases, psoriasis, endometriosis, scarring, benign prostatahyperplasia (BPH), diseases of the immune system, autoimmune diseases, immunodeficiency diseases, colon tumour, gastric tumour, intestinal tumour, pulmonary tumour, pancreatic tumour, ovarian tumour, prostatic tumour, leukaemia, melanoma, hepatic tumour, renal tumour, head tumour, throat tumour, glioma, breast tumour, uterine cancer, endometrial cancer, cervico-uterine carcinoma, brain tumour, adeno-acanthoma, cancer of the bladder, gastric tumour, colorectal tumour, oesophageal cancer, gynocological tumour, ovarian tumour, cancer of the thyroid, lymphoma, chronic leukaemia, acute leukaemia, restenosis, diabetes, diabetic nephropathy, fibrotic

diseases, cystic fibrosis, malignant nephrosclerosis, thrombotic microangiopathy syndrome, organ transplant rejection, glomerulopathy, metabolilc diseases, solid/fixed tumours, rheumatic arthritis, diabetic retinopathy, asthma, allergies, allergic diseases, chronic obstructive pulmonary diseases, inflammatory bowel disease, fibrosis, atheriosclerosis, heart diseases, cardiovascular diseases, diseases of the myocardium, vascular diseases, angiogenetic diseases, kidney diseases, rhinitis, Grave's disease, focal ischaemia, cardiac failure, ischaemia, cardiac hypertrophia, renal failure, cardiac myocytic malfunction, high blood pressure, vasoconstriction, stroke, anaphylactic shock, platelet agglutination, skeletomuscular atrophy, obesity, overweight, glucosis homeostasis, congestive cardiac insufficiency, angina, heart attack, cardiac infarction, hyperglycaemia, hypoglycaemia, hypertension".

In a further aspect of the present invention, the inventive object was surprisingly achieved by preparing the compounds according to the aspects, preferred embodiments and uses described above, for use for the production of a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the medicinal product comprises at least one further pharmacologically active substance.

In a further aspect of the present invention, the inventive object was surprisingly achieved by preparing the compounds according to the aspects, preferred embodiments and uses described above, for use for the production of a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the medicinal product is administered with at least one further pharmacologically

active substance before and/or during and/or after treatment.

In a further aspect of the present invention, the inventive object was surprisingly achieved by preparing the compounds according to the aspects, preferred embodiments and uses described above, for use for the production of a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in mammals, wherein the medicinal product is administered before and/or during and/or after treatment with radiation therapy and/or surgery.

The compounds according to the invention can be administered within the scope of this invention with all known pharmacologically active substances in a combination therapy as described.

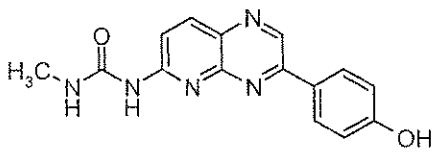
In a preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein the further pharmacologically active substance is selected from the group consisting of: "DNA topoisomerase I and/or II inhibitors, DNA intercalators, alkylating agents, microtubuli destabilisors, hormone and/or growth factor receptor agonists and/or antagonists, antibodies against growth factors and their receptors, kinase inhibitors, antimetabolites".

In a preferred embodiment, the compounds according to the invention are prepared for the uses described above, wherein the further pharmacologically active substance is selected from the group consisting of: "asparaginase, bleomycin, carboplatin, carmustin, chlorambucil, cisplatin, colaspase, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, daunorubicin,

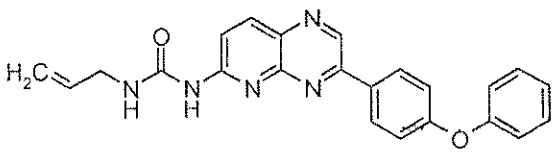
doxorubicin(adriamycin), epirubicin, etoposide, 5-fluorouracil, hexamethylmelamine, hydroxurea, ifosfamide, irinotecan, leucovorin, lomustine, mechlorethamine, 6-mercaptopurine, mesna, methotrexate, mitomycin C, mitoxantrone, prednisolone, prednisone, procarbazine, raloxifene, streptozocin, tamoxifen, thioguanine, topotecan, vinblastine, vincristine, vindesine, aminoglutethimide, L-asparaginase, azathioprine, 5-azacytidine cladribine, busulfan, diethylstilbestrol, 2', 2'-difluorodeoxycytidine, docetaxel, erythrohydroxynonyladenine, ethinylestradiol, 5-fluorodeoxyuridin, 5-fluorodeoxyuridin monophosphate, fludarabine phosphate, fluoxymesterone, flutamide, hydroxyprogesterone caproate, idarubicin, interferon, medroxyprogesteronr acetate, megestrol acetate, melphalan, mitotane, paclitaxel, oxaliplatin, pentostatin, N-phosphonoacetyl-L-aspartate (PALA), plicamycin, semustine, teniposide, testosterone propionate, thiotepa, trimethylmelamine, uridine, vinorelbin, epothilone, gemcitabine, Taxotere, BCNU, CCNU, DTIC, 5-fluorouarcil, Herceptin, Avastin, Erbitux, Sorafenib, Gleevec, Iressa, Tarceva, rapamycin, actinomycin D".

In a further aspect of the present invention, the inventive object was surprisingly achieved by preparing the pyridopyrazine selected from the group consisting of:

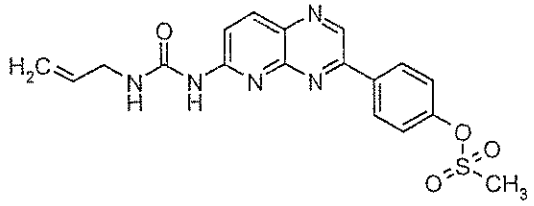
Compound (38) 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-urea



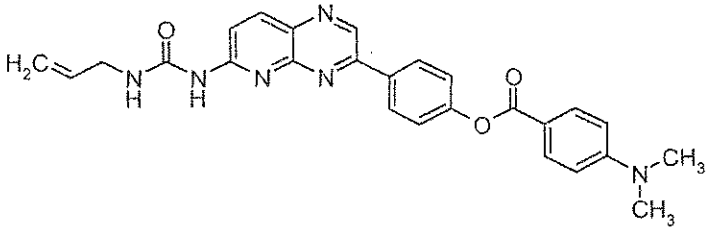
Compound 39 1-allyl-3-[3-(4-phenoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



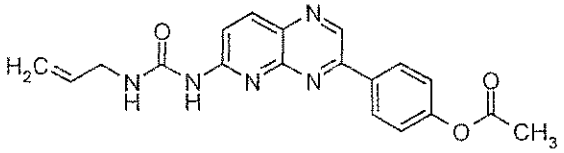
Compound 40 methansulfonic acid -4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl-ester



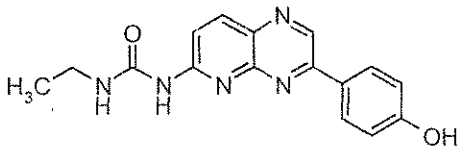
Compound 41 4-dimethylamino-benzoic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl-ester



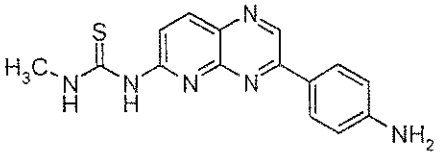
Compound 42 acetic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl-ester



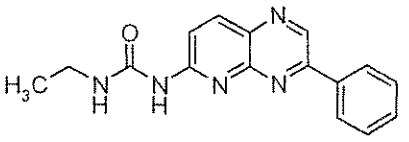
Compound 43 1-ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



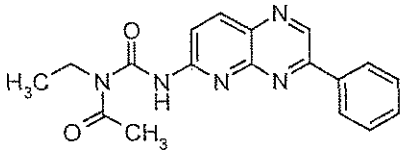
Compound 44 1-[3-(4-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-thiourea



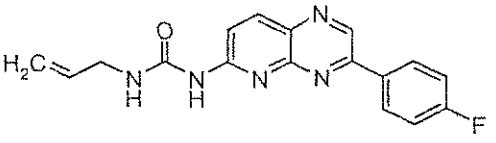
Compound 45 1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



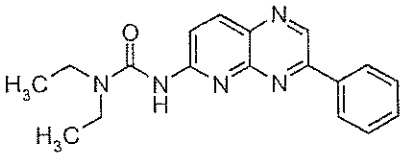
Compound 46 1-acetyl-1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



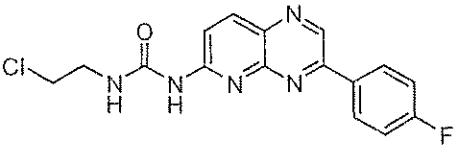
Compound 47 1-allyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



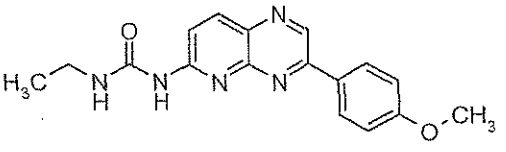
Compound 48 1,1-diethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



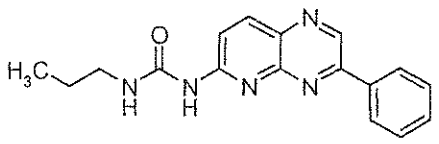
Compound 49 1-(2-chloro-ethyl)-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



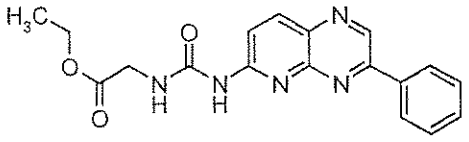
Compound 50 1-ethyl-3-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



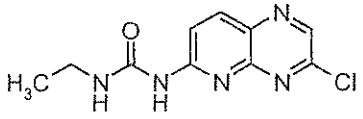
Compound 51 1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-3-propyl-urea



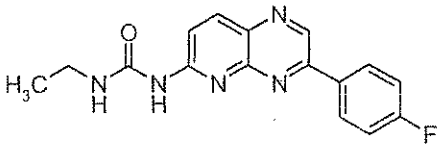
Compound 52 [3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-acetic acid-ethyl-ester



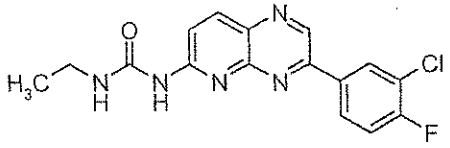
Compound 53 1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



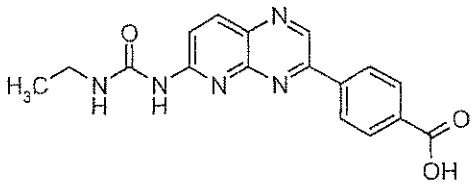
Compound 54 1-ethyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



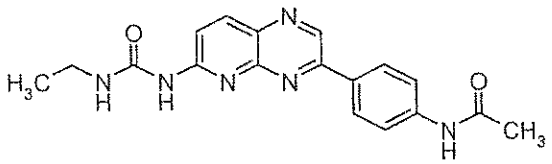
Compound 55 1-[3-(3-chloro-4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



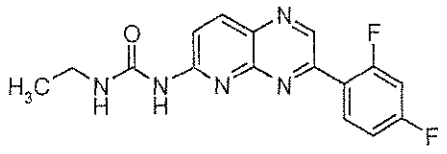
Compound 56 4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid



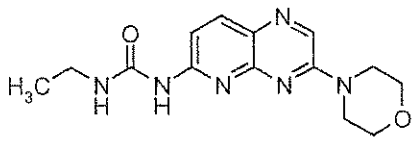
Compound 57 N-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acetamide



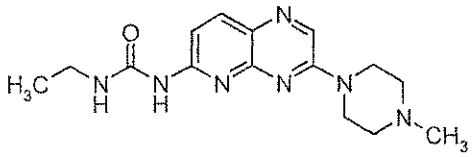
Compound 58 1-[3-(2,4-difluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



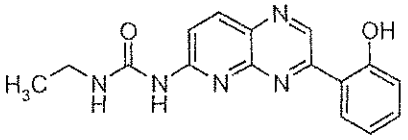
Compound 59 1-ethyl-3-(3-morpholin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



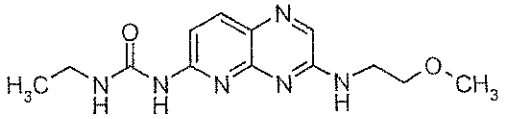
Compound 60 1-ethyl-3-[3-(4-methyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



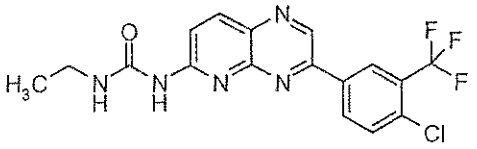
Compound 61 1-ethyl-3-[3-(2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



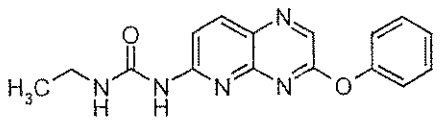
Compound 62 1-ethyl-3-[3-(2-methoxy-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



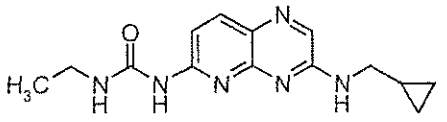
Compound 63 1-[3-(4-chloro-3-trifluoromethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



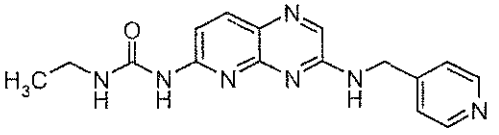
Compound 64 1-ethyl-3-(3-phenoxy-pyrido[2,3-b]pyrazin-6-yl)-urea



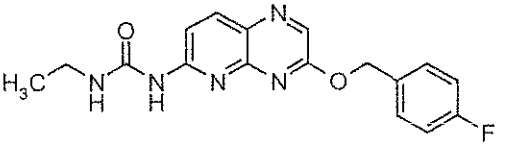
Compound 65 1-[3-(cyclopropylmethyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



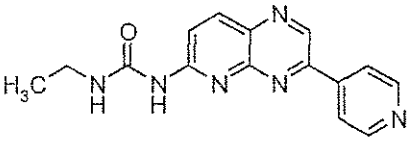
Compound 66 1-ethyl-3-{3-[(pyridin-4-ylmethyl)-amino]-pyrido[2,3-b]pyrazin-6-yl}-urea



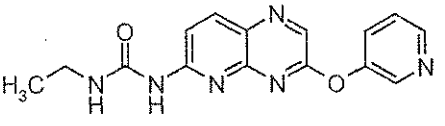
Compound 67 1-ethyl-3-[3-(4-fluoro-benzyloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



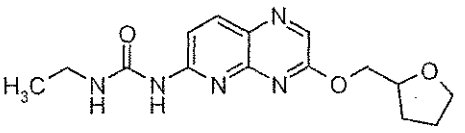
Compound 68 1-ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



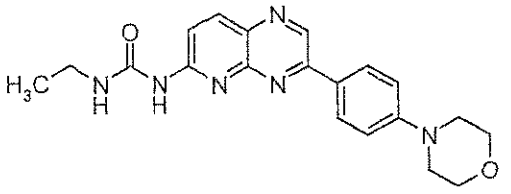
Compound 69 1-ethyl-3-[3-(pyridin-3-yloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



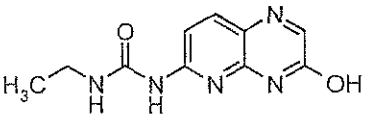
Compound 70 1-ethyl-3-[3-(tetrahydro-furan-2-ylmethoxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



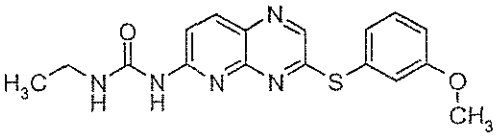
Compound 71 -ethyl-3-[3-(4-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



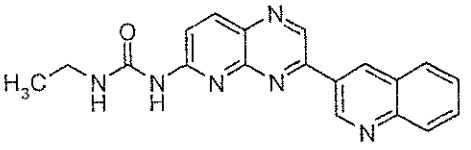
Compound 72 1-ethyl-3-(3-hydroxy-pyrido[2,3-b]pyrazin-6-yl)-urea



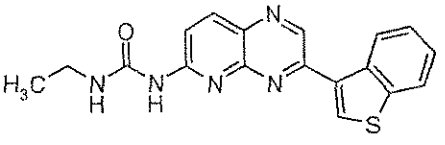
Compound 73 1-ethyl-3-[3-(3-methoxy-phenylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



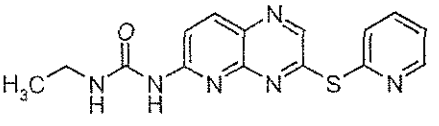
Compound 74 1-ethyl-3-(3-quinolin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



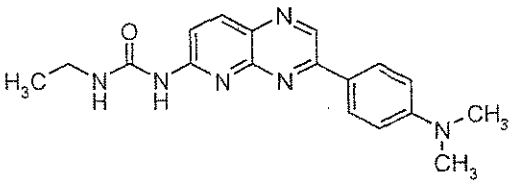
Compound 75 1-(3-benzo[b]thiophen-3-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



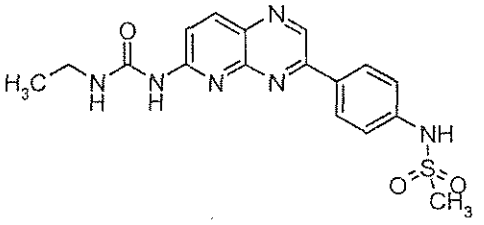
Compound 76 1-ethyl-3-[3-(pyridin-2-ylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



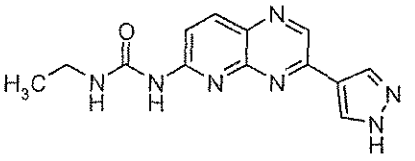
Compound 77 1-[3-(4-dimethylamino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



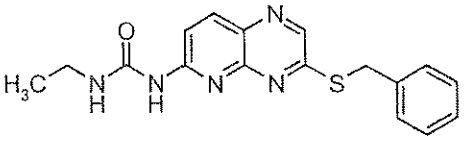
Compound 78 N-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-methanesulfonamide



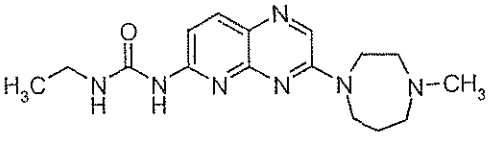
Compound 79 -ethyl-3-[3-(1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



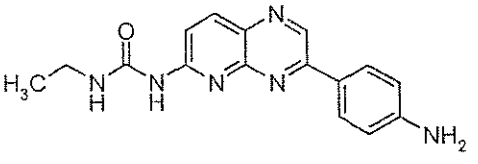
Compound 80 1-(3-benzylsulfanyl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



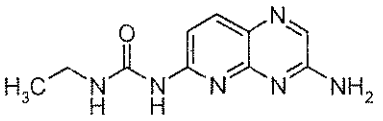
Compound 81 1-ethyl-3-[3-(4-methyl-[1,4]diazepan-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



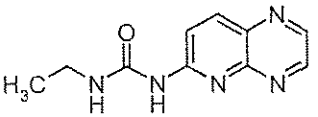
Compound 82 1-[3-(4-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



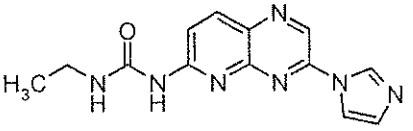
Compound 83 1-(3-amino-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



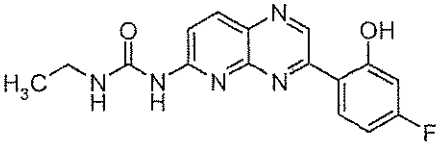
Compound 84 1-ethyl-3-pyrido[2,3-b]pyrazin-6-yl-urea



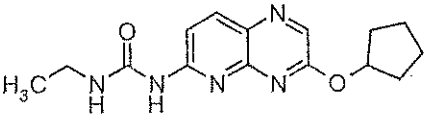
Compound 85 1-ethyl-3-(3-imidazol-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



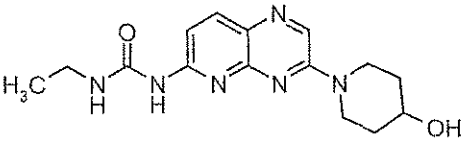
Compound 86 1-ethyl-3-[3-(4-fluoro-2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



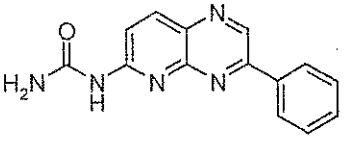
Compound 87 1-(3-cyclopentyloxy-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



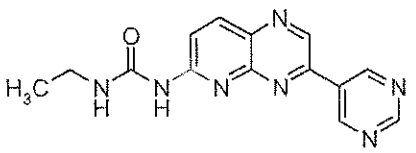
Compound 88 1-ethyl-3-[3-(4-hydroxy-piperidin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



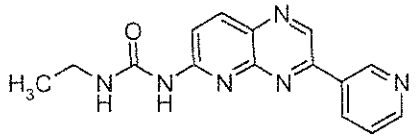
Compound 89 (3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



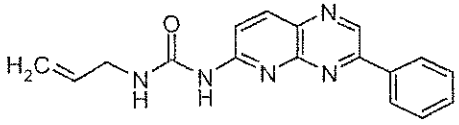
Compound 90 1-ethyl-3-(3-pyrimidin-5-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



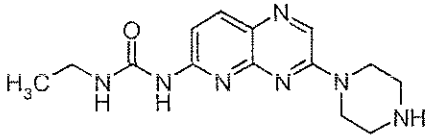
Compound 91 1-ethyl-3-(3-pyridin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



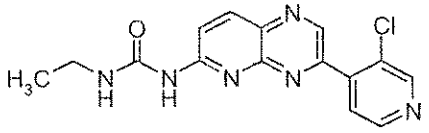
Compound 92 1-allyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



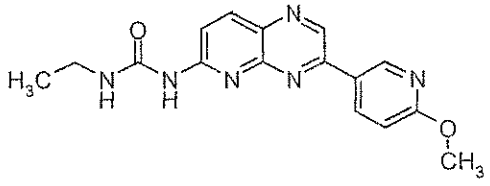
Compound 93 1-ethyl-3-(3-piperazin-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



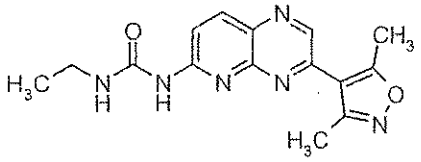
Compound 94 1-[3-(3-chloro-pyridin-4-ylmethyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



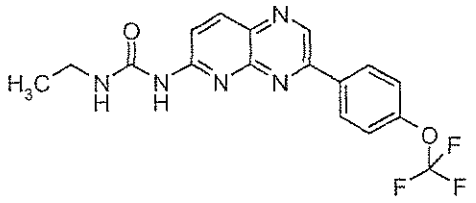
Compound 95 1-ethyl-3-[3-(6-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



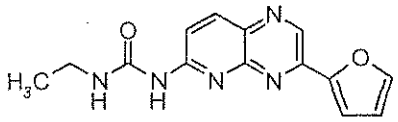
Compound 96 1-[3-(3,5-dimethyl-isoxazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



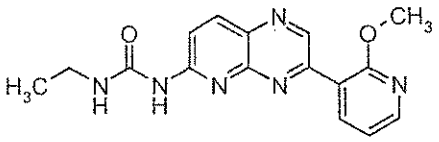
Compound 97 1-ethyl-3-[3-(4-trifluoromethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



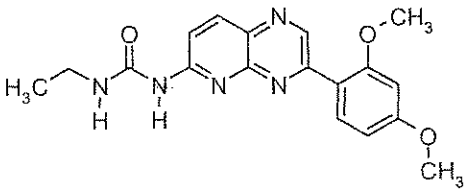
Compound 98 1-ethyl-3-(3-furan-2-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



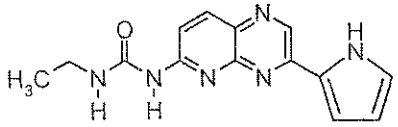
Compound 99 1-ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



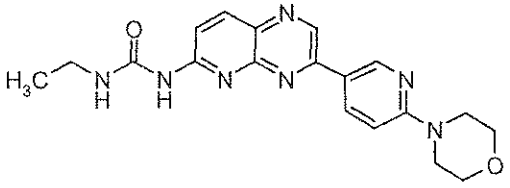
Compound 100 1-[3-(2,4-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



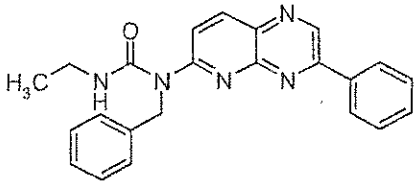
Compound 101 1-ethyl-3-[3-(1H-pyrrol-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



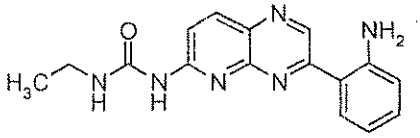
Compound 102 1-ethyl-3-[3-(6-morpholin-4-yl-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



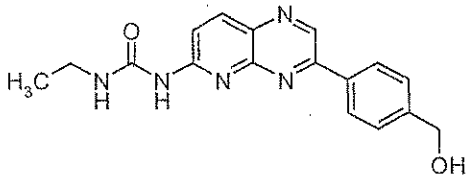
Compound 103 1-benzyl-3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



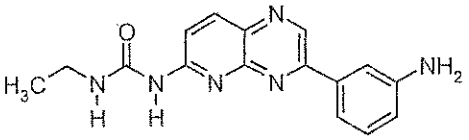
Compound 104 1-[3-(2-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



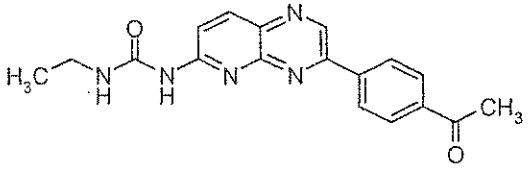
Compound 105 1-ethyl-3-[3-(4-hydroxymethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



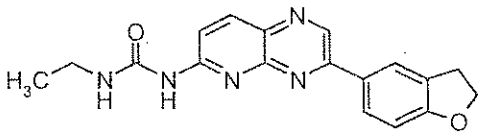
Compound 106 1-[3-(3-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



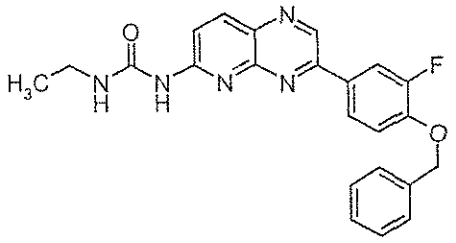
Compound 107 1-[3-(4-acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



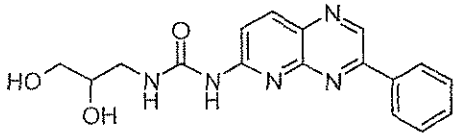
Compound 108 1-[3-(2,3-dihydro-benzofuran-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



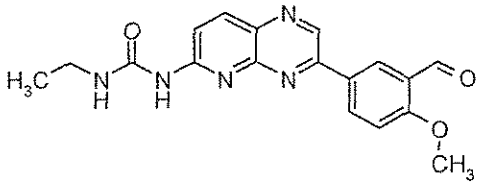
Compound 109 1-[3-(4-benzyloxy-3-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



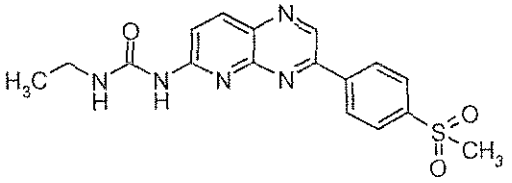
Compound 110 1-(2,3-dihydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



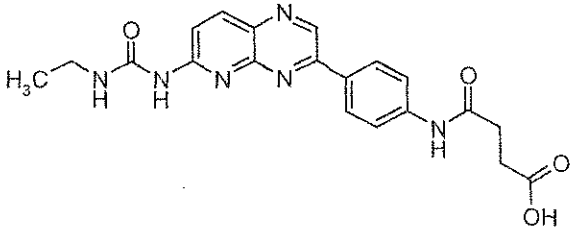
Compound 111 1-ethyl-3-[3-(3-formyl-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



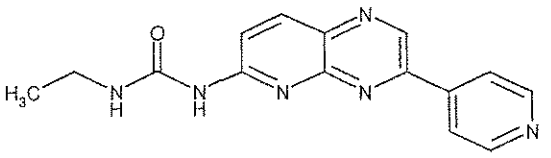
Compound 112 1-ethyl-3-[3-(4-methanesulfonyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea

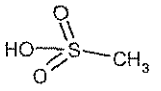


Compound 113 N-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-succinamic acid

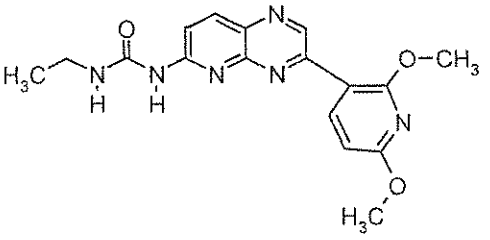


Compound 114 1-ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea methane sulfonic acid salt (free base)

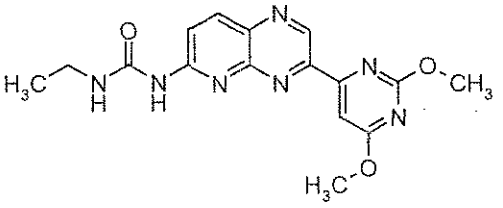




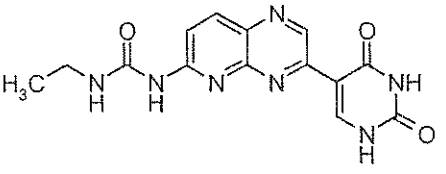
Compound 115 1-[3-(2,6-dimethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



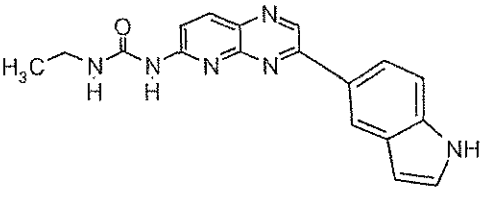
Compound 116 1-[3-(2,6-dimethoxy-pyrimidin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



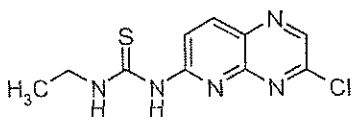
Compound 117 1-[3-(2,4-Dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



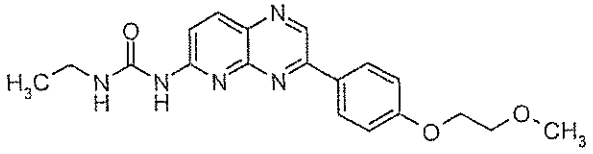
Compound 118 1-ethyl-3-[3-(1H-indol-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



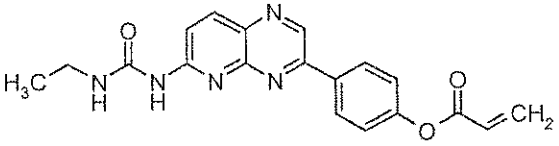
Compound 119 1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-thiourea



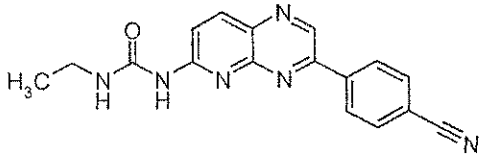
Compound 120 1-ethyl-3-{3-[4-(2-methoxy-ethoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea



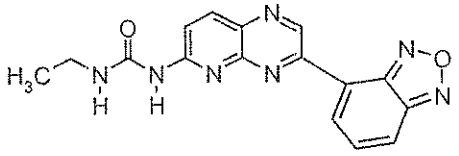
Compound 121 acrylic acid-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl-ester



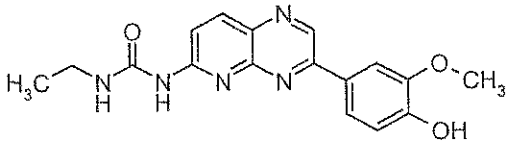
Compound 122 1-[3-(4-cyano-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



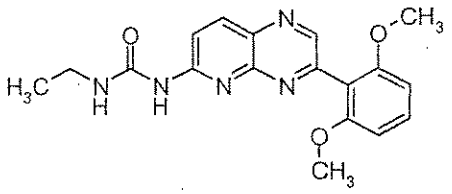
Compound 123 1-(3-benzo[1,2,5]oxadiazol-4-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



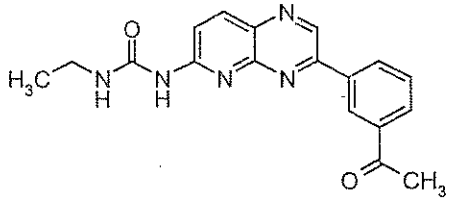
Compound 124 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



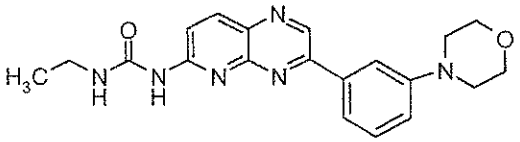
Compound 125 1-[3-(2,6-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



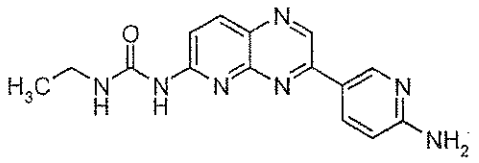
Compound 126 1-[3-(3-acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



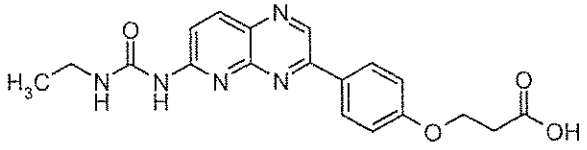
Compound 127 1-ethyl-3-[3-(3-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



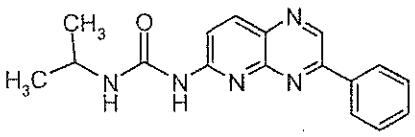
Compound 128 1-[3-(6-amino-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



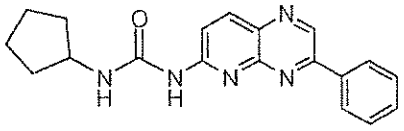
Compound 129 3-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenoxy}-propionic acid



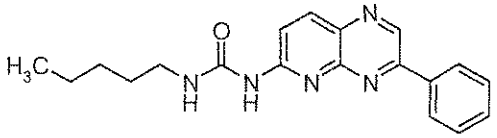
Compound 130 1-isopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



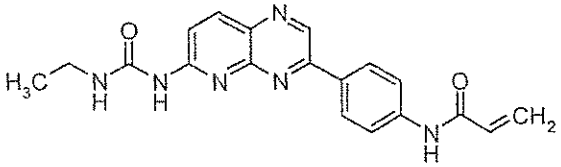
Compound 131 1-cyclopentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



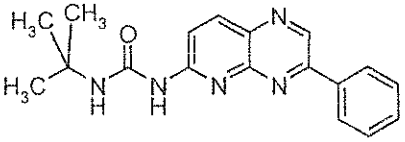
Compound 132 1-pentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



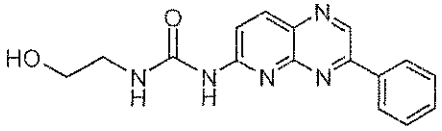
Compound 133 N-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acrylamid



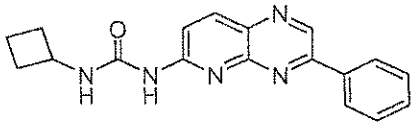
Compound 134 1-tert-butyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



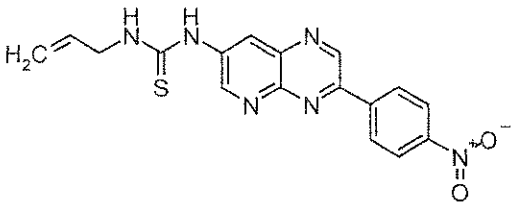
Compound 135 1-(2-hydroxy-ethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



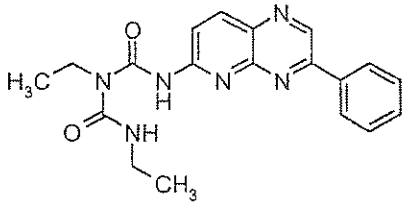
Compound 136 1-cyclobutyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



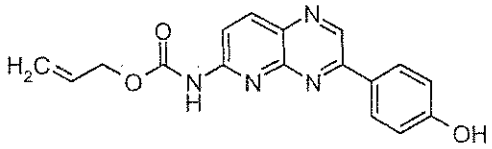
Compound 137 1-allyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-7-yl]-thiourea



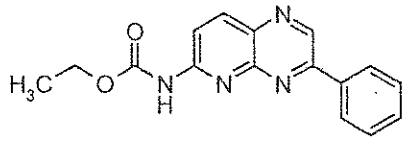
Compound 138 1-ethyl-1-(ethylcarbamoyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



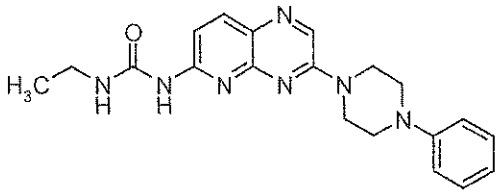
Compound 139 [3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-carbamic acid-allyl-ester



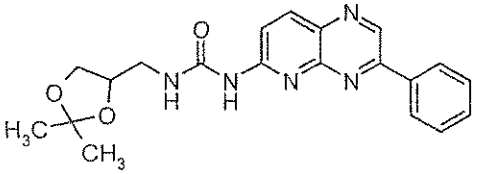
Compound 140 (3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-carbamic acid-ethyl-ester



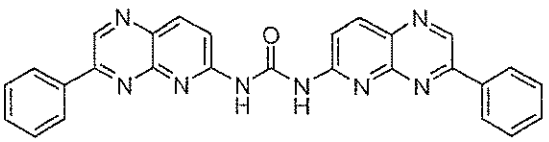
Compound 141 1-ethyl-3-[3-(4-phenyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



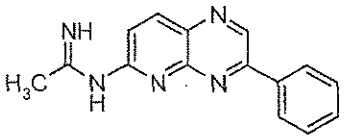
Compound 142 1-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



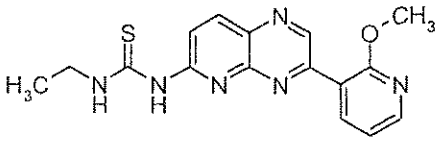
Compound 143 1,3-Bis-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



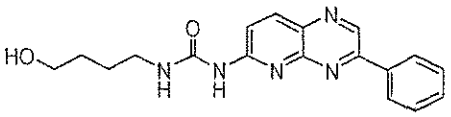
Compound 144 N-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-acetamidin



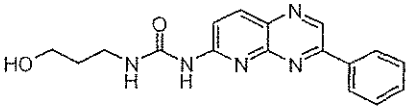
Compound 145 1-ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



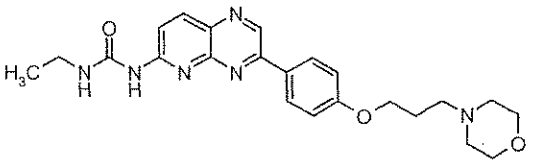
Compound 146 1-(4-hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



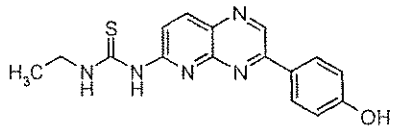
Compound 147 1-(3-hydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



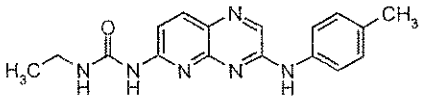
Compound 148 1-ethyl-3-{3-[4-(3-morpholin-4-yl-propoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea



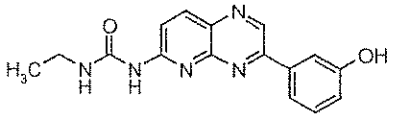
Compound 149 1-ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



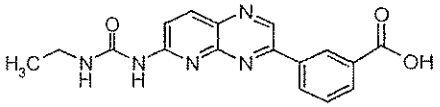
Compound 150 1-ethyl-3-(3-p-tolylamino-pyrido[2,3-b]pyrazin-6-yl)-urea



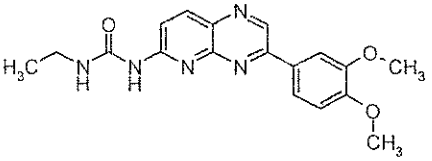
Compound 151 1-ethyl-3-[3-(3-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



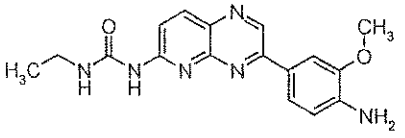
Compound 152 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid



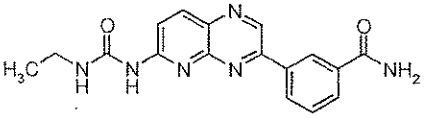
Compound 153 1-[3-(3,4-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



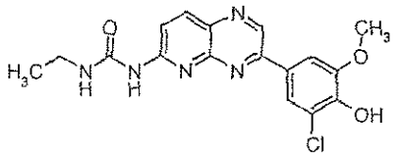
Compound 154 1-[3-(4-amino-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



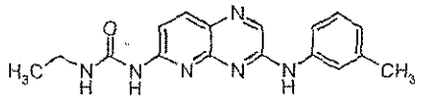
Compound 155 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-benzamid



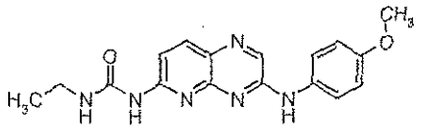
Compound 156 1-[3-(3-chloro-4-hydroxy-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



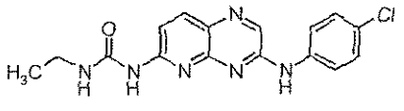
Compound 157 1-ethyl-3-(3-m-tolylamino-pyrido-[2,3-b]pyrazin-6-yl)-urea



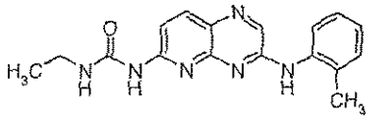
Compound 158 1-ethyl-3-[3-(4-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



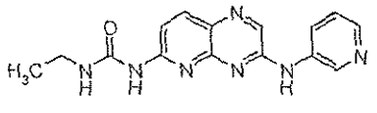
Compound 159 1-[3-(4-chloro-phenylamino)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea



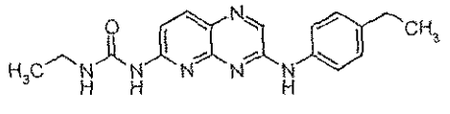
Compound 160 1-ethyl-3-(3-o-tolylamino-pyrido[2,3-b]-pyrazin-6-yl)-urea



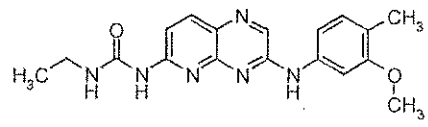
Compound 161 1-ethyl-3-[3-(pyridin-3-ylamino)-pyrido-[2,3-b]pyrazin-6-yl]-urea



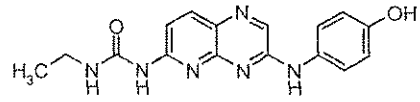
Compound 162 1-ethyl-3-[3-(4-ethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



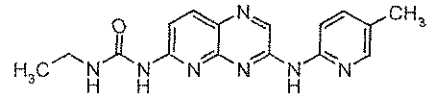
Compound 163 1-ethyl-3-[3-(3-methoxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



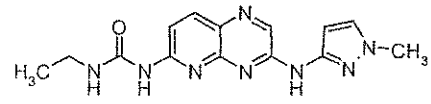
Compound 164 1-ethyl-3-[3-(4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



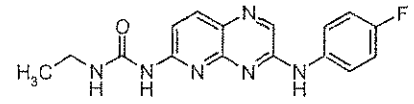
Compound 165 1-ethyl-3-[3-(5-methyl-pyridin-2-yl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



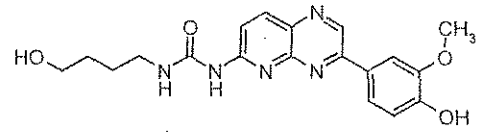
Compound 166 1-ethyl-3-[3-(1-methyl-1H-pyrazol-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



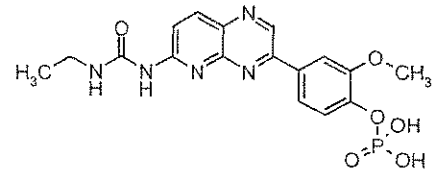
Compound 167 1-ethyl-3-[3-(4-fluoro-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



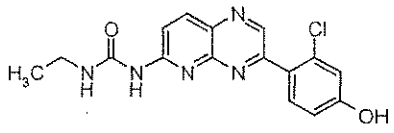
Compound 168 1-(4-hydroxy-butyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



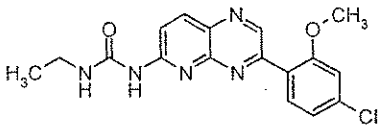
Compound 169 Phosphoric acid-mono-{4-[6-(3-ethyl-ureido)-pyrido-[2,3-b]pyrazin-3-yl]-2-methoxy-phenyl}ester



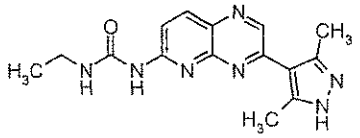
Compound 170 1-[3-(2-chloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



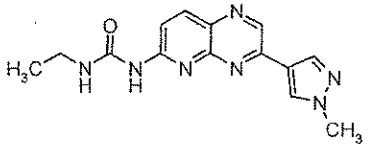
Compound 171 1-[3-(4-chloro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



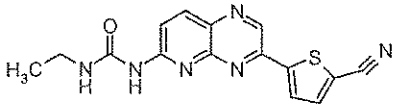
Compound 172 1-[3-(3,5-dimethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



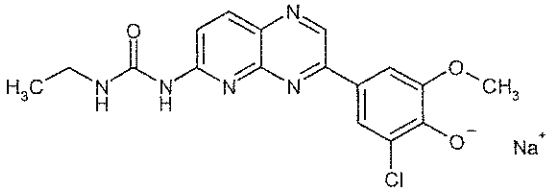
Compound 173 1-ethyl-3-[3-(1-methyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



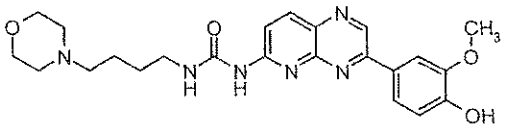
Compound 174 1-[3-(5-cyano-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



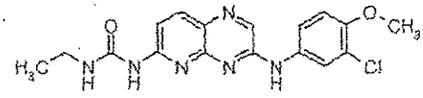
Compound 175 Sodium 2-chloro-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-6-methoxy-phenolate



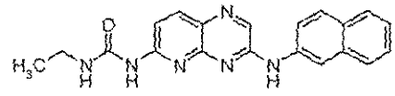
Compound 176 1-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(4-morpholin-4-yl-butyl)-urea



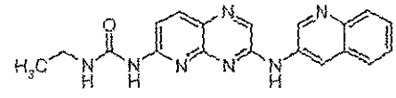
Compound 177 1-[3-(3-chloro-4-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



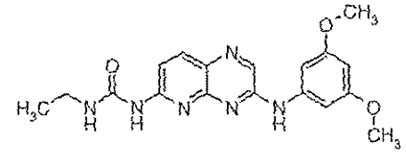
Compound 178 1-ethyl-3-[3-(naphthalen-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



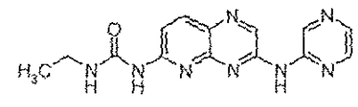
Compound 179 1-ethyl-3-[3-(quinolin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



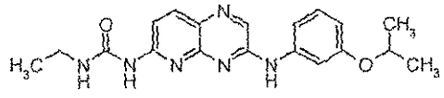
Compound 180 1-[3-(3,5-dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



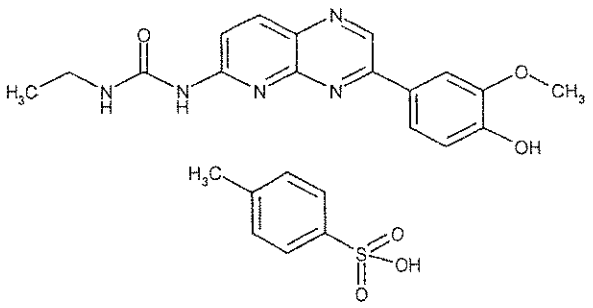
Compound 181 1-ethyl-3-[3-(pyrazin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



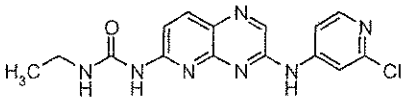
Compound 182 1-ethyl-3-[3-(3-isopropoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



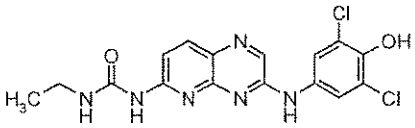
Compound 183 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea p-toluenesulfonate



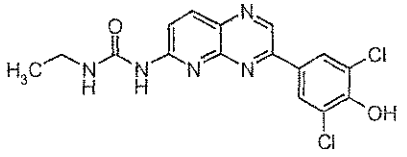
Compound 184 1-[3-(2-chloro-pyridin-4-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



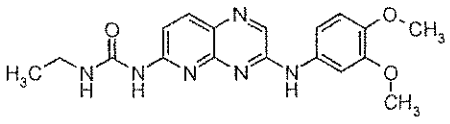
Compound 185 1-[3-(3,5-dichloro-4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



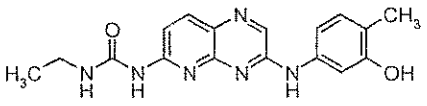
Compound 186 1-[3-(3,5-dichloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



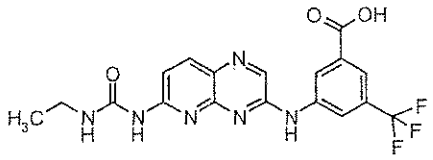
Compound 187 1-[3-(3,4-dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



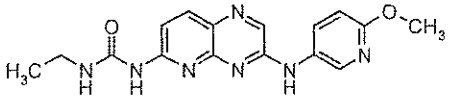
Compound 188 1-ethyl-3-[3-(3-hydroxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



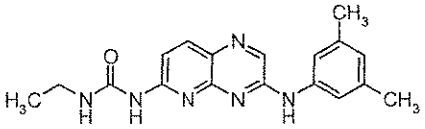
Compound 189 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-ylamino]-5-trifluoromethyl-benzoic acid



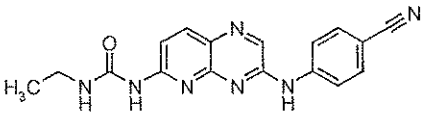
Compound 190 1-ethyl-3-[3-(6-methoxy-pyridin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



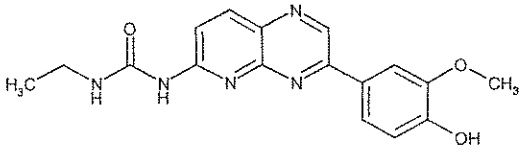
Compound 191 1-[3-(3,5-dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea

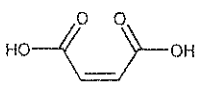


Compound 192 1-[3-(4-cyano-phenylamino)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea

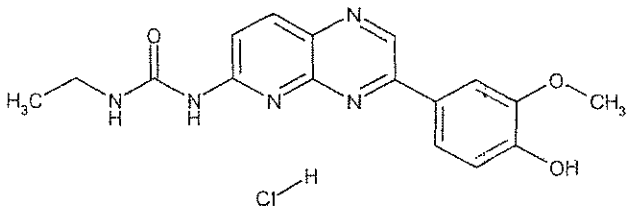


Compound 193 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea (Z)-but-2-enedicarboxylic acid-salt

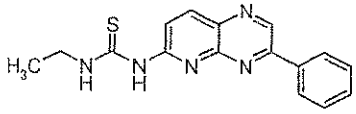




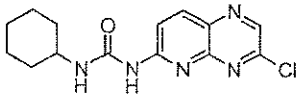
Compound 194 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea hydrochloride



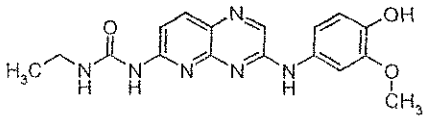
Compound 195 1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



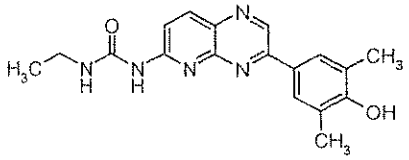
Compound 196 1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-cyclohexyl-urea



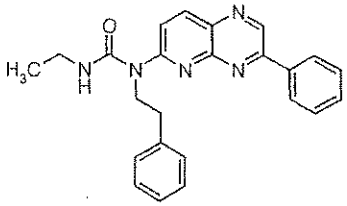
Compound 197 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



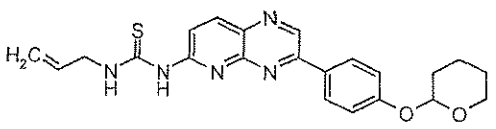
Compound 198 1-ethyl-3-[3-(4-hydroxy-3,5-dimethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



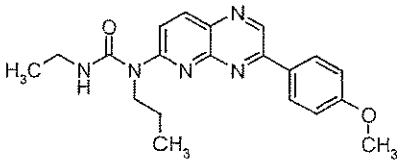
Compound 199 3-ethyl-1-phenethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



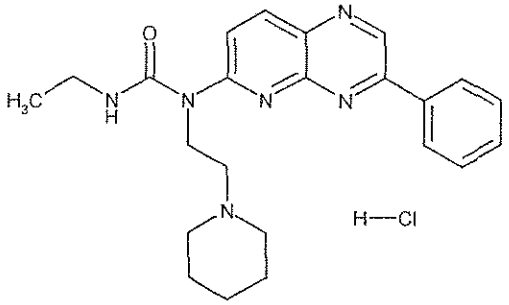
Compound 200 1-allyl-3-{3-[4-(tetrahydro-pyran-2-yloxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



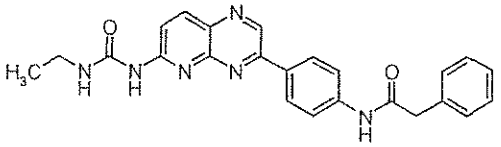
Compound 201 3-ethyl-1-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-1-propyl-urea



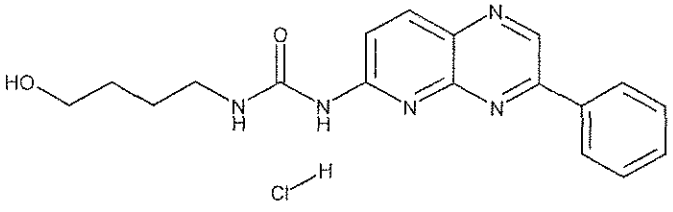
Compound 202 3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-1-(2-piperidin-1-yl-ethyl)-urea hydrochloride



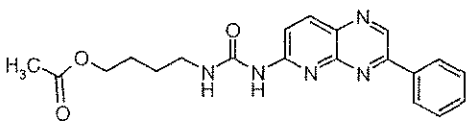
Compound 203 N-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl}-2-phenyl-acetamide



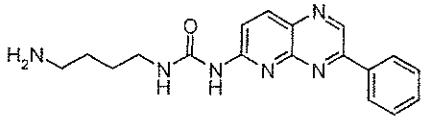
Compound 204 1-(4-hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea hydrochloride



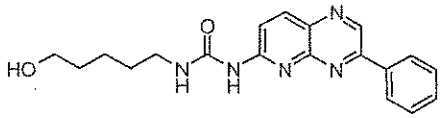
Compound 205 Acetic acid-4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl ester



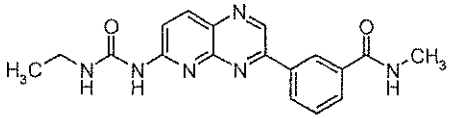
Compound 206 1-(4-amino-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



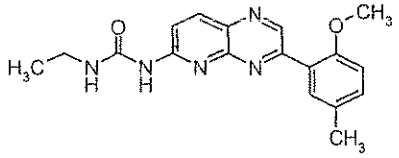
Compound 207 1-(5-hydroxy-pentyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



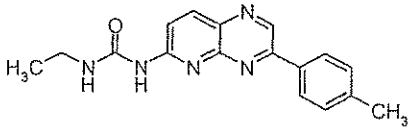
Compound 208 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-N-methyl-benzamide



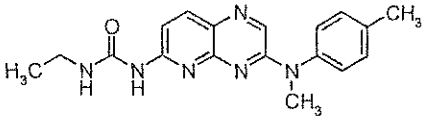
Compound 209 1-ethyl-3-[3-(2-methoxy-5-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



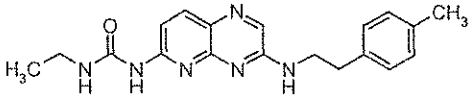
Compound 210 1-ethyl-3-(3-p-tolyl-pyrido[2,3-b]pyrazin-6-yl)-urea



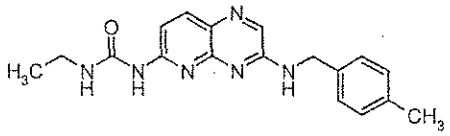
Compound 211 1-ethyl-3-[3-(methyl-p-tolyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



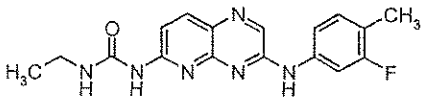
Compound 212 1-ethyl-3-[3-(2-p-tolyl-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



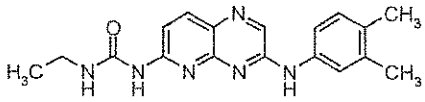
Compound 213 1-ethyl-3-[3-(4-methyl-benzylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



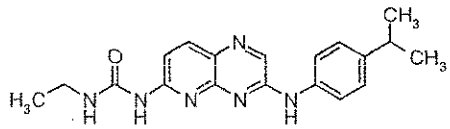
Compound 214 1-ethyl-3-[3-(3-fluoro-4-methyl-phenyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



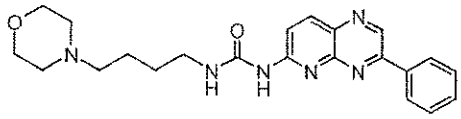
Compound 215 1-[3-(3,4-dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



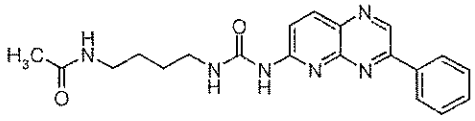
Compound 216 1-ethyl-3-[3-(4-isopropyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



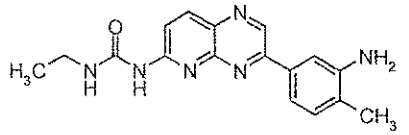
Compound 217 1-(4-morpholin-4-yl-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



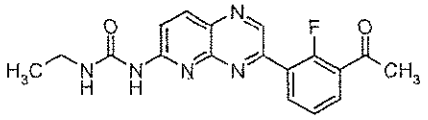
Compound 218 N-{4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-acetamide



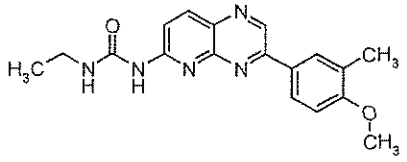
Compound 219 1-[3-(3-amino-4-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



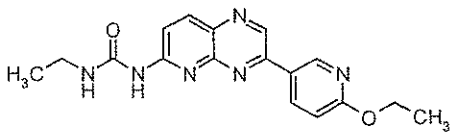
Compound 220 1-[3-(3-acetyl-2-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



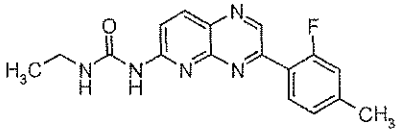
Compound 221 1-ethyl-3-[3-(4-methoxy-3-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



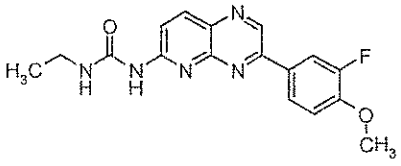
Compound 222 1-[3-(6-ethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



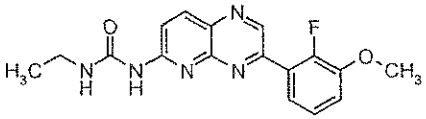
Compound 223 1-ethyl-3-[3-(2-fluoro-4-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



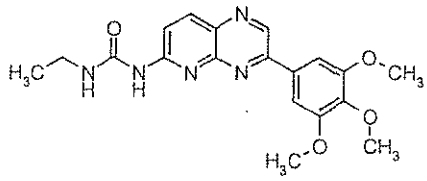
Compound 224 1-ethyl-3-[3-(3-fluoro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



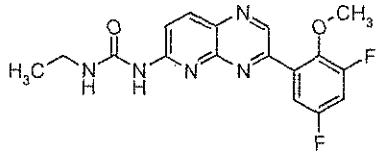
Compound 225 1-ethyl-3-[3-(2-fluoro-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



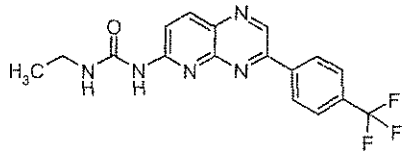
Compound 226 1-ethyl-3-[3-(3,4,5-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



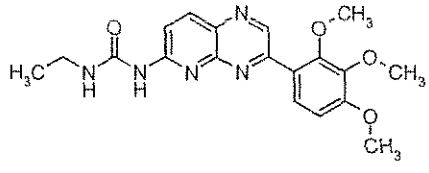
Compound 227 1-[3-(3,5-difluoro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



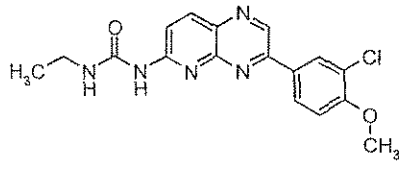
Compound 228 1-ethyl-3-[3-(4-trifluoromethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



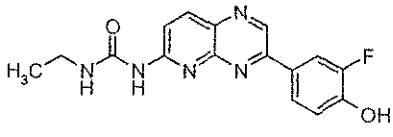
Compound 229 1-ethyl-3-[3-(2,3,4-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



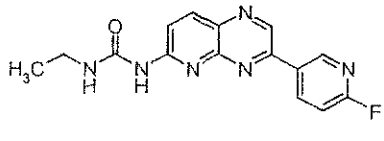
Compound 230 1-[3-(3-chloro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



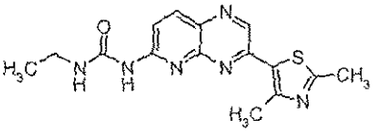
Compound 231 1-ethyl-3-[3-(3-fluoro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



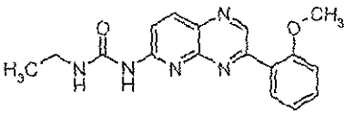
Compound 232 1-ethyl-3-[3-(6-fluoro-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



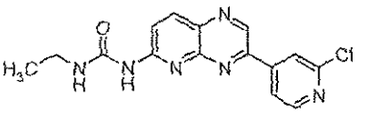
Compound 233 1-[3-(2,4-dimethyl-thiazol-5-yl)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea



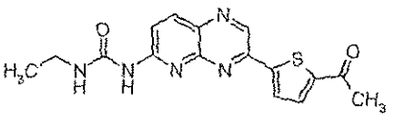
Compound 234 1-ethyl-3-[3-(2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



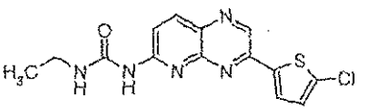
Compound 235 1-[3-(2-chloro-pyridin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



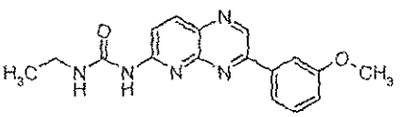
Compound 236 1-[3-(5-acetyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



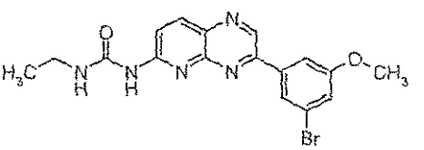
Compound 237 1-[3-(5-chloro-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



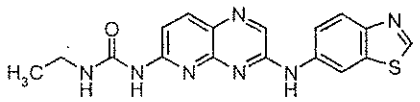
Compound 238 1-ethyl-3-[3-(3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



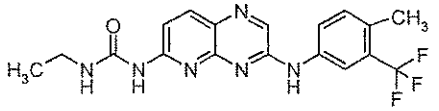
Compound 239 1-[3-(3-bromo-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



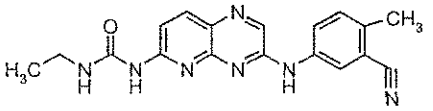
Compound 240 1-[3-(benzothiazol-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



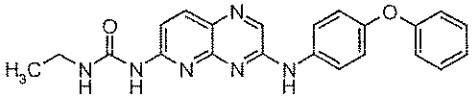
Compound 241 1-ethyl-3-[3-(4-methyl-3-trifluoroomethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



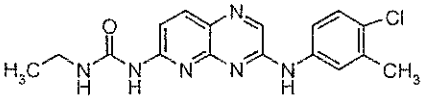
Compound 242 1-[3-(3-cyano-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



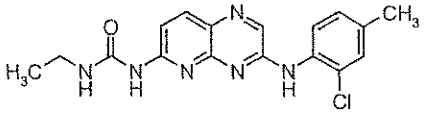
Compound 243 1-ethyl-3-[3-(4-phenoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



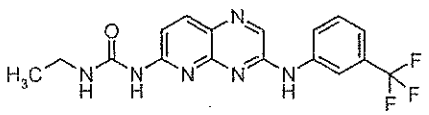
Compound 244 1-[3-(4-chloro-3-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



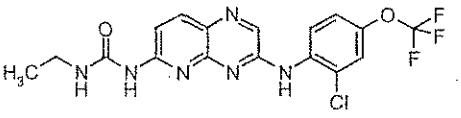
Compound 245 1-[3-(2-chloro-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



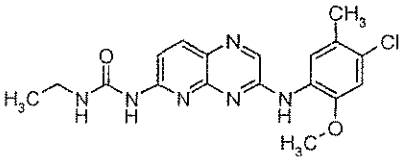
Compound 246 1-ethyl-3-[3-(3-trifluoroomethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



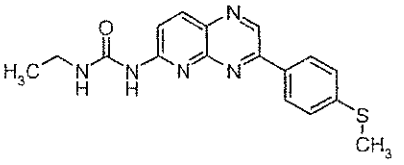
Compound 247 1-[3-(2-chloro-4-trifluoromethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



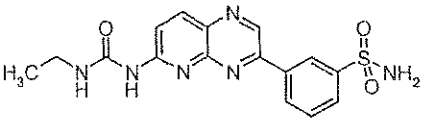
Compound 248 1-[3-(4-chloro-2-methoxy-5-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



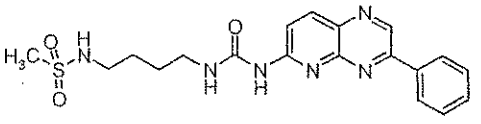
Compound 249 1-ethyl-3-[3-(4-methylsulfanyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



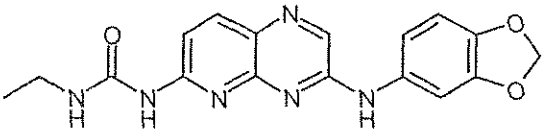
Compound 250 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzenesulfonamide



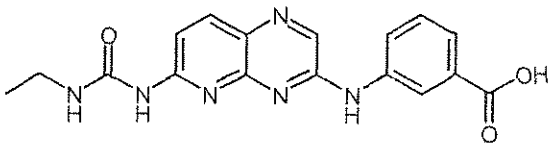
Compound 251 N-{4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-methanesulfonamide



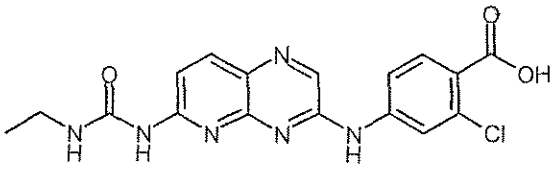
Compound 252 1-[3-(benzo[1,3]dioxol-5-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



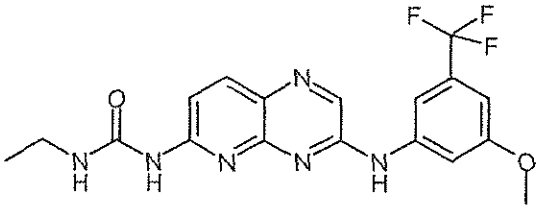
Compound 253 3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-benzoic acid



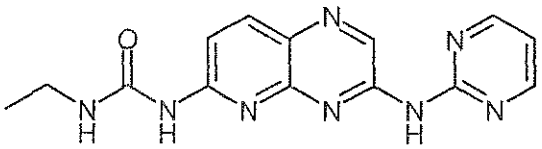
Compound 254 2-chloro-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-benzoic acid



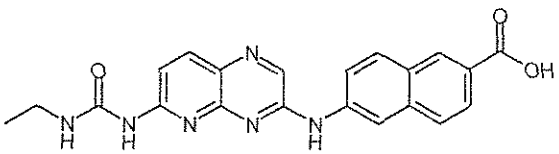
Compound 255 1-ethyl-3-[3-(3-methoxy-5-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



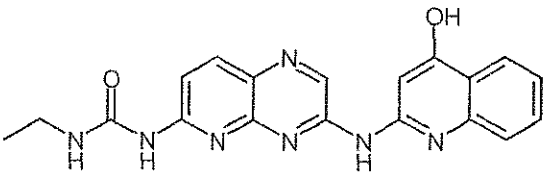
Compound 256 1-ethyl-3-[3-(pyrimidin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



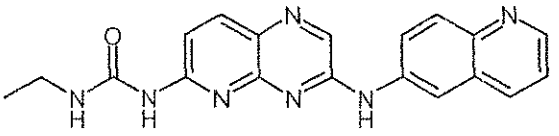
Compound 257 6-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-naphthalene-carboxylic acid



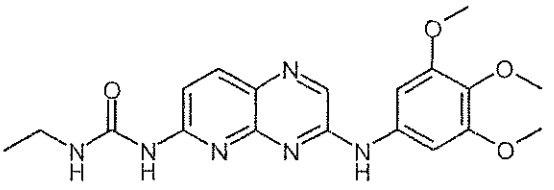
Compound 258 1-ethyl-3-[3-(4-hydroxy-chinolin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



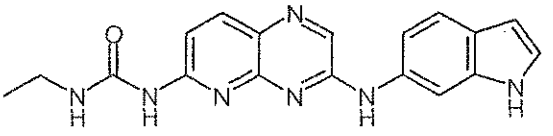
Compound 259 1-ethyl-3-[3-(quinolin-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



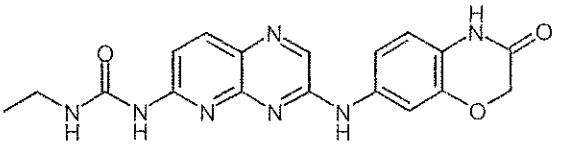
Compound 260 1-ethyl-3-[3-(3,4,5-trimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



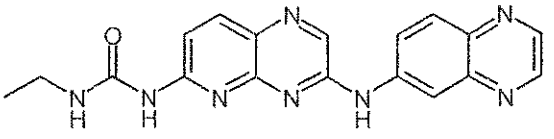
Compound 261 1-ethyl-3-[3-(1H-indol-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



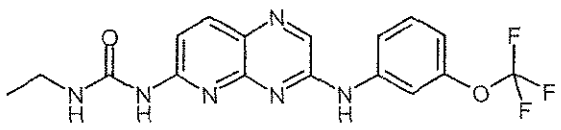
Compound 262 1-ethyl-3-[3-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



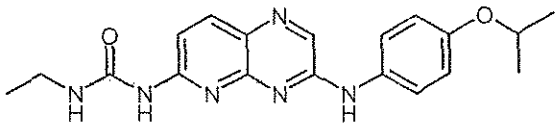
Compound 263 1-ethyl-3-[3-(quinoxalin-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



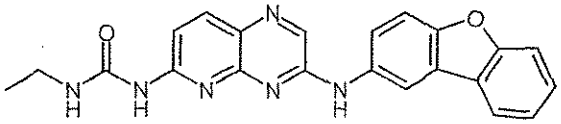
Compound 264 1-ethyl-3-[3-(3-trifluoromethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



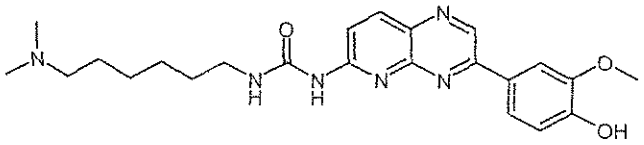
Compound 265 1-ethyl-3-[3-(4-isopropoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



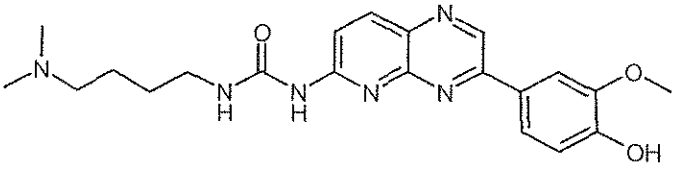
Compound 266 1-[3-(dibenzofuran-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



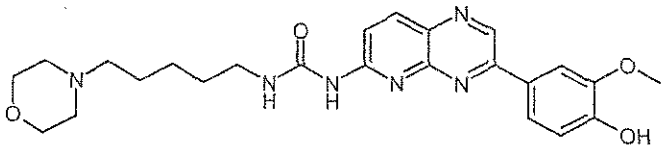
Compound 267 1-(6-dimethylamino-hexyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



Compound 268 1-(4-dimethylamino-butyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



Compound 269 1-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(5-morpholin-4-yl-pentyl)-urea



Oral administration can take place, for example, in solid form as tablet, capsule, gel capsule, dragee,

granule or powder but also in the form of a potable solution. For oral administration, the new compounds according to the invention, as defined hereinbefore, can be combined with known physiologically compatible adjuvants and excipients usually used, such as gum Arabic, talc, starch, sugar such as, for example, mannite, methyl cellulose, lactose, gelatine, surfactants, magnesium stearate, cyclodextrin, aqueous or non-aqueous excipients, diluents, dispersants, emulsifiers, lubricants, preservatives and flavourings (e.g. ether oils). The compounds according to the invention can also be dispersed in a microparticle, e.g. nanoparticle composition.

Non-oral administration can be effected, for example, by intravenous, subcutaneous or intramuscular injection of sterile aqueous or oily solutions, suspensions or emulsions, by means of implants or by ointments, creams or suppositories. Optionally, administration can be effected as a retard form. Implants can contain inert materials, e.g. biologically degradable polymers or synthetic silicones such as, for example, silicone rubber. Intravaginal administration can be effected by means of vaginal rings, for example. Intrauterine administration can take place, for example, by means of diaphragms or other suitable intrauterine devices. In addition, transdermal administration can be provided, in particular by means of a formulation suitable for this purpose and/or suitable means such as plasters, for example.

As has already been explained, the new compounds according to the invention can also be combined with further pharmaceutically active substances. Within the framework of a combination therapy, the individual active constituents cam be administered simultaneously or separately and either by the same pathway (e.g.

oral) or by separate pathways (e.g. oral and as injection). They can be present or administered in the same or different quantities in a unit dose. A certain dosage regime can be applied insofar as this seems appropriate. In this way, a plurality of the new compounds according to the invention can be combined with one another.

The dosage can vary according to the type of indication, the severity of the disease, the type of administration, the age, sex, body weight and sensitivity of the subject to be treated over a wide range. It is within the capabilities of a person skilled in the art to determine a "pharmacologically effective quantity" of the combined pharmaceutical composition. The administration can be made in a single dose or a plurality of separate doses.

A suitable unit dose is 0.001 mg to 100 mg of the active substance, i.e. at least one compound according to the invention and optionally a further pharmaceutically active substance, per kg body weight of a patient.

In a further aspect of the present invention, accordingly pharmaceutical compositions comprising a pharmacologically active quantity of at least one compound selected from the group consisting of: "compound 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148,

149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268 and/or compound 269" and optionally pharmaceutically compatible excipients and/or adjuvants are covered by the present invention.

Preferred and particularly preferred pharmaceutical compositions are those which comprise at least one of the aforesaid preferred compounds according to the invention. Pharmaceutical compositions according to the present invention can also contain, in addition to at least one compound according to the invention, as defined previously, at least one further pharmaceutically active substance, as has been described in detail hereinbefore.

The pharmaceutical compositions according to the invention contain at least one of the new compounds according to the invention, as defined hereinbefore, in a pharmacologically active quantity, preferably in a unit dose, e.g. the aforesaid unit dose and preferably in an administration form which allows oral administration.

With regard to pharmaceutical compositions comprising compounds according to the invention and with regard to the use of the compounds according to the invention as medicinal products, reference is made to the statements made in connection with the use of the new compounds

according to the invention themselves with regard to the possibilities for usage and administration.

In a further aspect of the present invention, the inventive object was surprisingly solved by preparing a kit comprising a pharmacologically active quantity of at least one preferred compound according to the invention as presented above and a pharmacologically active quantity of at least one further pharmacologically active substance as defined hereinbefore.

The naming of the compounds according to the invention having the general formula (I) together with preferred exemplary embodiments and in particular compounds **1** to **269** was made using AutoNom 2000 - Software (ISIS ™/ Draw 2.5; MDL).

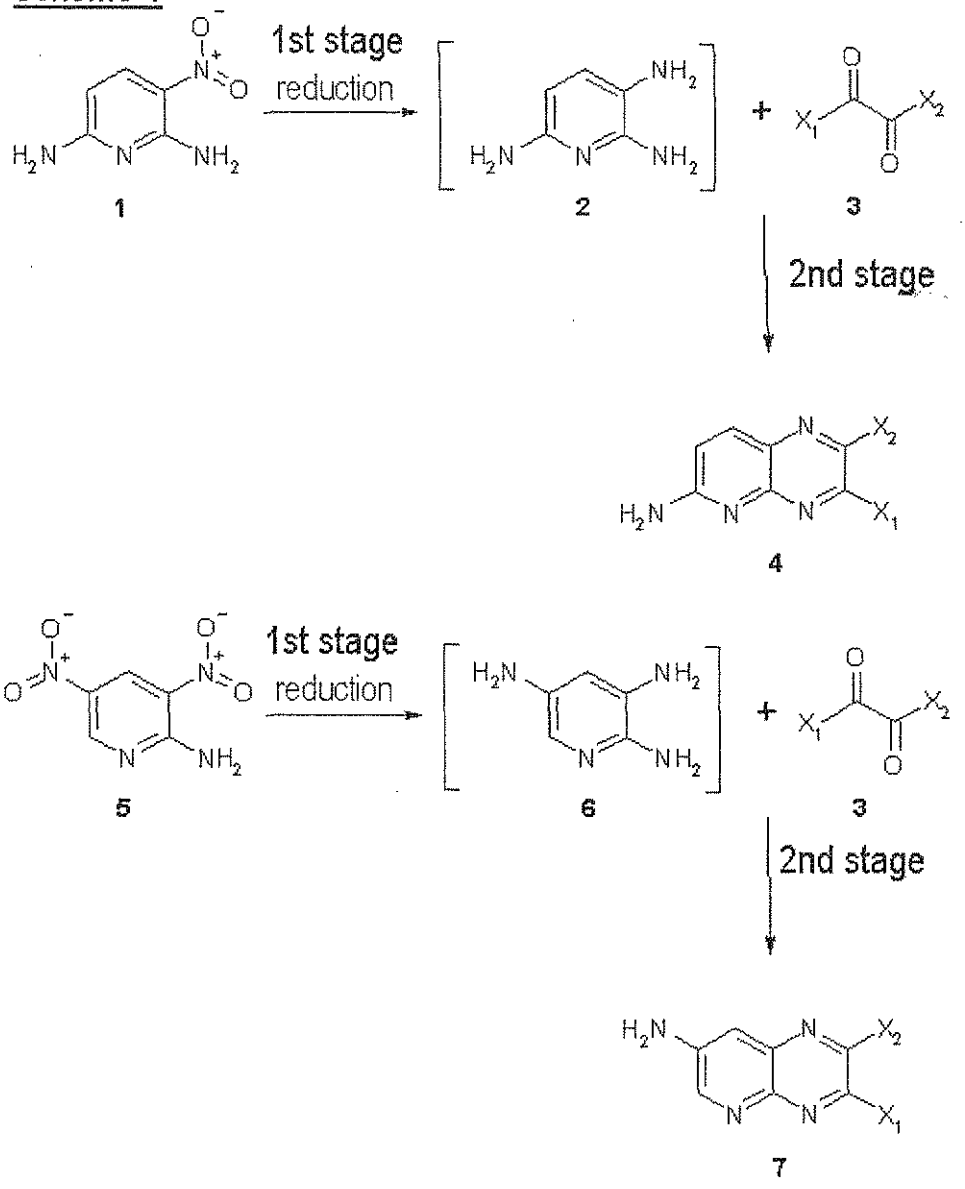
General synthesis methods for the inventive compounds

The processes for preparing inventive substituted pyrido[2,3-b]pyrazines are explained below.

The inventive compounds are obtainable according to the following schemes (scheme 1-7) or corresponding processes known to those skilled in the art. For the preparation of the inventive compounds, reference is also made to patents WO 2004/104002 and WO 2004/104003 and to corresponding methods known from the literature.

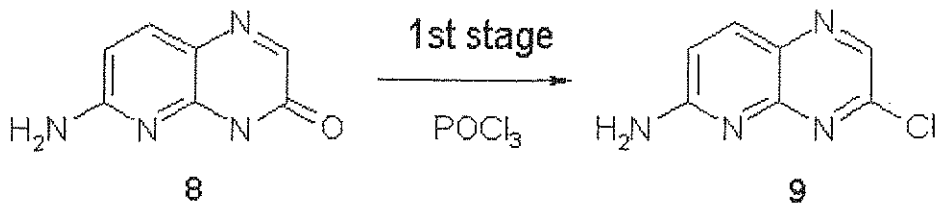
The definition of the X1 to X21 radicals shown in the following schemes corresponds to the substituents defined above in connection with the general formula (I), for example R radicals etc. The individual assignment can be accomplished in a simple manner by the person skilled in the art on the basis of his or her average technical knowledge.

Scheme 1



Precursors for selected examples of the inventive pyrido[2,3-b]pyrazines in which the substituents R2 and R4 are to be substituted with hydrogen are obtainable, for example, by the process in scheme 2 or a corresponding process known to those skilled in the art.

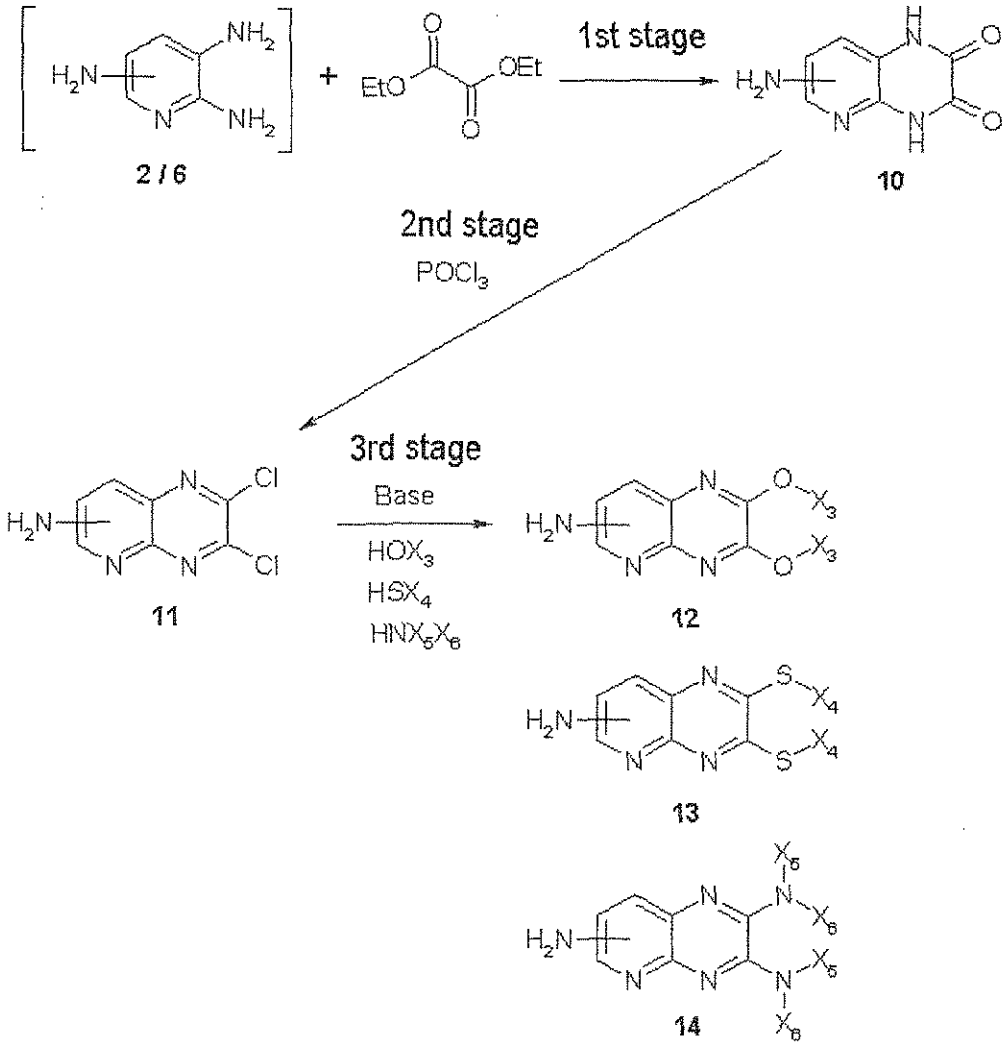
Scheme 2



8 9

Precursors for selected examples of the inventive pyrido[2,3-b]pyrazines in which the substituents R3 and/or R4 are to be the OX_3, SX_4, NX_5X_6 radicals are obtainable, for example, by the process in scheme 3 or a corresponding process known to those skilled in the art.

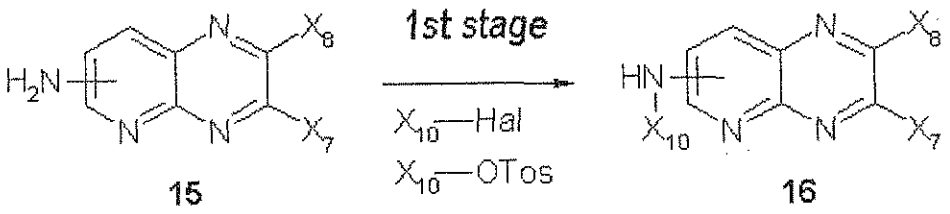
Scheme 3



For the precursor 11 shown above, the intermediate 9 from scheme 2 or else the intermediate 21 from scheme 6 or a correspondingly substituted intermediate can be used.

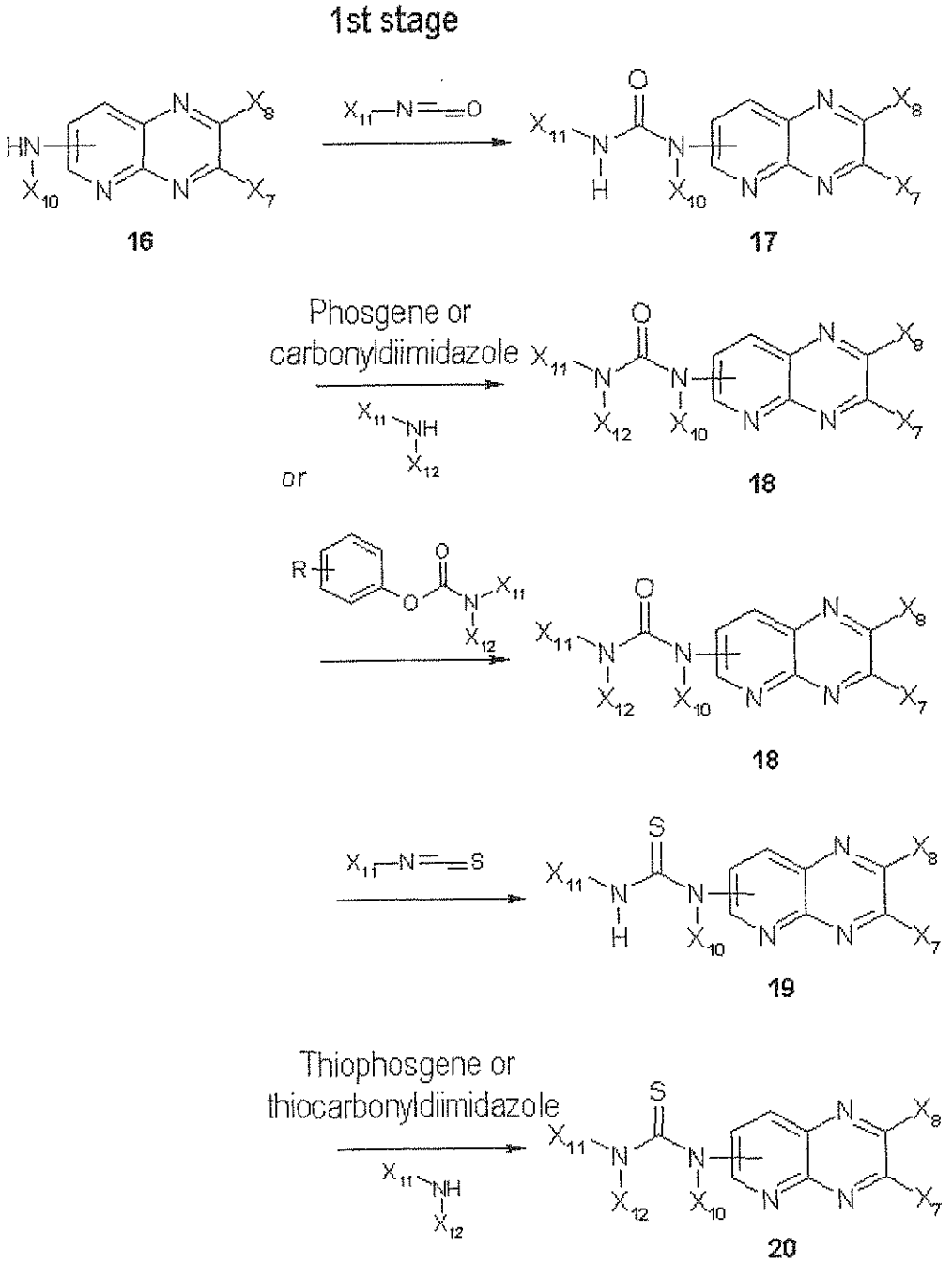
Substituted precursors for selected examples of the inventive pyrido[2,3-b]pyrazines are obtainable, for example, by the process in scheme 4 or a corresponding process known to those skilled in the art.

Scheme 4



The precursor 16 from scheme 4 can be converted to the inventive substituted pyrido[2,3-b]pyrazines, for example, by the process in scheme 5 or a corresponding process known to those skilled in the art.

Scheme 5

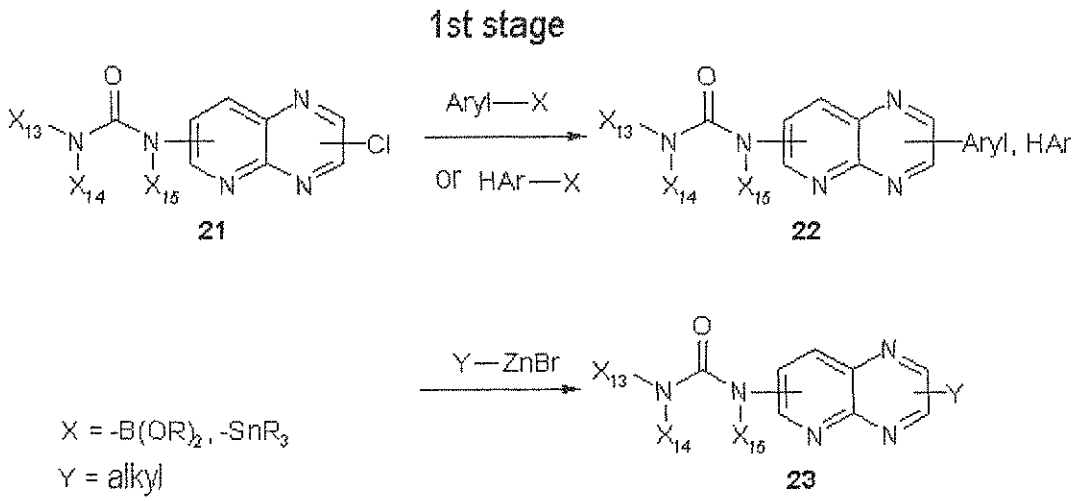


For the precursor 16 shown above, the intermediate 15 from scheme 4 can also be used.

Selected examples of the inventive pyrido[2,3-b]-pyrazines in which the substituents R3 and/or R4 may be selected alkyl, aryl or heteroaryl radicals are obtainable, for example, by the process in scheme 6 or

corresponding processes known to those skilled in the art.

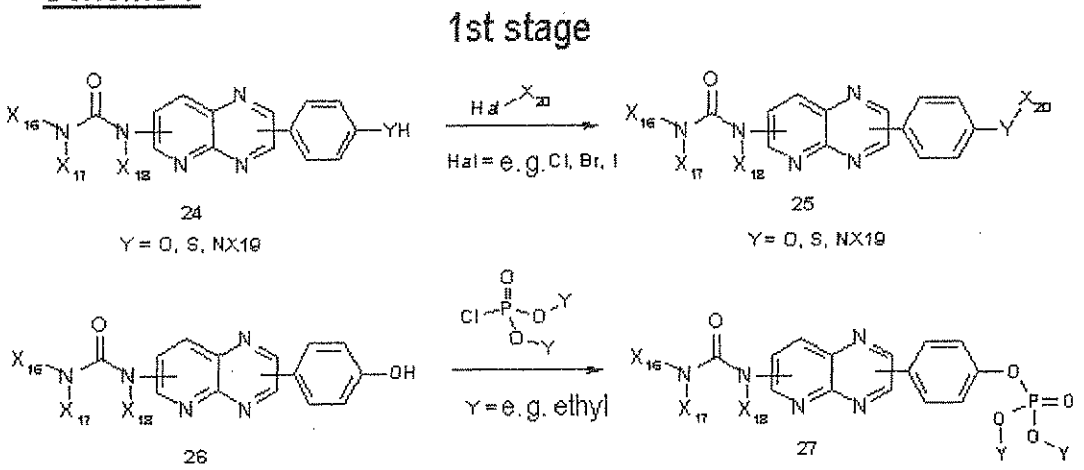
Scheme 6



In the preparation of the inventive aryl/heteroaryl-substituted pyridopyrazines, the intermediate 9 from scheme 2 or else the intermediate 11 from scheme 3 or a correspondingly substituted intermediate can also be used for the precursor 21 shown above.

Selected examples of the inventive pyrido[2,3-b]pyrazines in which the substituents R3 and/or R4 may be selected O-, S-, N-substituted radicals are obtainable, for example, by the process in scheme 7 or corresponding processes known to those skilled in the art.

Scheme 7



The cleavage of the corresponding phosphoric esters can be carried out by procedures which are known per se or are known to those skilled in the art via methods known from the literature.

The starting compounds and intermediates are either commercially available or can be prepared by procedures known per se or known to those skilled in the art. The reactants 4, 7, 9-16, 21, 24 and 26 are valuable intermediates for the preparation of the inventive pyridopyrazines.

For the preparation of the starting compounds, intermediates and the inventive pyridopyrazines, reference is made, inter alia, to the following primary literature, whose contents are hereby incorporated into the disclosure of the present application:

1) Houben-Weyl, Methoden der Organischen Chemie, Volume 4/1a, p. 343-350

2) Houben-Weyl, Methoden der Organischen Chemie, fourth ed., Volume E 7b (part 2), p. 579; Degussa GB 1184848 (1970); S. Seko, et al. EP 735025 (1996)

3) D. Catarzi, et al.; *J. Med. Chem.* **1996**, 1330-1336; J. K. Seydel, et al.; *J. Med. Chem.* **1994**, 3016-3022

4) Houben-Weyl, Methods of Organic Chemistry, Volume E 9c, p.231-235

5) Houben-Weyl/Science of Synthesis, Volume 16, p. 1269

6) C. L. Leese, H. N. Rydon *J. Chem. Soc.* **1955**, 303-309; T. S. Osdene, G. M. Timmis *J. Chem. Soc.* **1955**, 2033-2035

7) W. He, et al. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3097-3100

8) M. S. A. El-Gaby, et al. *Indian J. Chem. Sect. B* **2001**, *40*, 195- 200; M. R. Myers, et al. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3091-3096 ; A. R. Renslo, et al. *J. Amer. Chem. Soc.* **1999**, *121*, 7459-7460 ; C. O. Okafor, et al. *J. Heterocyclic Chem.* **1983**, *20*, 199-203; C. R. Hopkins, et al. *Tet. Lett.* **2004**, *45*, 8631-8633

9) J. Yin, et al. *Org. Lett.* **2002**, *4*, 3481-3484 ; O. A. El-Sayed, et al. *Arch. Pharm.* **2002**, *335*, 403-410 ; C. Temple, et al. *J. Med. Chem.* **1992**, *35*, 988-993

10) A. M. Thompson, et al. *J. Med. Chem.* **2000**, *43*, 4200-4211; N. A. Dales, et al. *Org. Lett.* **2001**, 2313-2316; G. Dannhardt, et al. *Arch. Pharm.* **2000**, 267-274; G. S. Poindexter, et al. *Bioorg. Med. Chem.* **2004**, *12*, 507-521; J.-M. Receveur, et al. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5075-5080

11) G. Heinisch, et al. *Arch. Pharm.* **1997**, 207-210; K. Matsuno, et al. *J. Med. Chem.* **2002**, *45*, 4513-4523; A. M. Papini, et al. *J. Med. Chem.* **2004**, *47*, 5224-5229

12) L. Mao, et al. *Synthesis* **2004**, *15*, 2535-2539; M. Darabantu, et al. *Tetrahedron* **2005**, *61*, 2897-2905; E. Ford, et al. *Tet. Lett.* **2000**, *41*, 3197-3198; T. Shiota, et al. *J. Org. Chem.* **1999**, *64*, 453-457

13) J. F. Miravet, et al. *Org. Lett.* **2005**, 7, 4791-4794; A. L. Castelhano, et al. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1501-1504.

14) J. W. Huffmann, et al. *Bioorg. Med. Chem.* 2006, 14, 247-262; T. Liu, et al. *Org. & Biomolecular Chem.* **2005**, 3, 1525-1533

General methods for the preparation of the inventive compounds:

Scheme 1: 1st stage

2,6-Diamino-3-nitropyridine or 2-amino-3,5-dinitropyridine are dissolved in a suitable inert solvent, for example methanol, ethanol, dimethylformamide or dioxane. After adding a catalyst, for example Raney nickel, palladium on carbon or platinum(IV) dioxide, the reaction mixture is placed under a hydrogen atmosphere, and a pressure between 1 and 5 bar is established. The reaction mixture is allowed to react for several hours, for example 1-16 hours, within a temperature range between 20°C and 60°C. Once the reaction has ended, the insoluble residues are filtered off, for which the filter medium may consist, for example, of silica gel, Celite or commercial glass fibre filters, and they are washed with the appropriate solvent. The crude product, present in solution, is used for the next reaction without further purification.

2nd stage

The 1,2-dione derivative is initially charged in a suitable inert solvent, for example methanol, ethanol, dioxane, toluene or dimethylformamide. 2,3,6-Triaminopyridine or 2,3,5-triaminopyridine, directly after the reduction, as a solution of the crude products in one of the abovementioned solvents, are added to the initially charged 1,2-dione, optionally with addition of an acid, for example acetic acid or a base, for example potassium hydroxide. The reaction mixture is allowed to react within a temperature range of 20°C to 80°C for a certain time, for example 20 minutes to 40 hours. Once the reaction has ended, any precipitated solid is filtered off, for which the

filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed of solvent under reduced pressure. When dimethylformamide is used, the reaction mixture is stirred into a large amount of water and the precipitated solid is filtered off, or the aqueous phase is extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phases are concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example dioxane, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Scheme 2: 1st stage

The pyridopyrazinone derivative 8 is initially charged in a suitable inert solvent, for example dimethylformamide, dioxane or toluene, or without solvent. A chlorinating agent, for example phosphoryl chloride or thionyl chloride, is added at room temperature and the reaction mixture is allowed to react within a temperature range of from 20°C to 100°C for a certain time, for example 1 hour to 24 hours. Once the reaction has ended, the reaction mixture is poured onto water and neutralized with a suitable aqueous base, for example sodium hydroxide solution. Any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the aqueous phase is extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phases are concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example dioxane or toluene, or by column or flash chromatography on silica gel or

alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Scheme 3: 1st stage

2,3,6-Triaminopyridine or 2,3,5-triaminopyridine are, directly after the reduction, as a solution of the crude products, initially charged in one of the abovementioned solvents. After an oxalic acid derivative has been added, for example diethyl oxalate or oxalyl chloride, the reaction mixture, optionally with addition of an acid, for example hydrochloric acid, sulphuric acid or glacial acetic acid, is allowed to react within a temperature range of 20°C to 150°C for a certain time, for example 10 minutes to 24 hours. After the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed from the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid can be filtered off, or the aqueous phase, after neutralization with a suitable aqueous base, for example sodium hydroxide solution, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example dioxane or toluene, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

2nd stage

The dione derivative 10 is initially charged in a suitable inert solvent, for example dimethylformamide, dioxane or toluene, or without solvent. A chlorinating agent, for example phosphoryl chloride or thionyl

chloride, is added at room temperature and the reaction mixture is allowed to react within a temperature range of from 20°C to 100°C for a certain time, for example 1 hour to 24 hours. Once the reaction has ended, the reaction mixture is poured onto water and neutralized with a suitable aqueous base, for example sodium hydroxide solution. Any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the aqueous phase is extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phases are concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example dioxane or toluene, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

3rd stage

The intermediate 11 can be reacted with an appropriate alcohol, thiol or amine and optionally with a suitable base, preferably sodium hydride, pyridine, triethylamine, potassium carbonate or sodium methoxide in methanol, in a suitable inert solvent, for example dimethylformamide, dimethyl sulphoxide, methanol, toluene, or in a base as the solvent, for example pyridine or triethylamine, or without solvent. The reaction mixture is allowed to react for a certain time, for example 30 minutes to 2 days, in a temperature range between 20°C and 140°C. Alternatively, the intermediate 11 can be reacted with an appropriate amine and a suitable catalyst, for example tris(dibenzylideneacetone)dipalladium(0) or tetrakis(triphenylphosphine)palladium(0), and a suitable ligand, for example 2-(dicyclohexyl-phosphanyl)biphenyl or BINAP, and a suitable base, for

example sodium tert-butoxide or potassium carbonate, in a suitable solvent, for example toluene, dioxane or dimethylformamide. The reaction mixture is allowed to react for a certain time, for example 2 hours to 30 hours, in a temperature range between 60°C and 120°C. After the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed from the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid can be filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example dioxane, ethyl acetate or toluene, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Scheme 4: 1st stage

The intermediate 15 can be reacted with an appropriate, suitable chloride, bromide, iodide or tosylate and optionally with a suitable base, preferably sodium hydride, pyridine, triethylamine, potassium carbonate or sodium methoxide in methanol, in a suitable inert solvent, for example dimethylformamide, dimethyl sulphoxide, methanol, or in a base as a solvent, for example pyridine or triethylamine, or without solvent. The reaction mixture is allowed to react for a certain time, for example 1 hour to 24 hours, in a temperature range between 20°C and 150°C. Alternatively, the intermediate 15 can be reacted with an appropriate aryl bromide or iodide and

a suitable catalyst, for example tris(dibenzylideneacetone)dipalladium(0), or tetrakis(triphenylphosphine)palladium(0), and a suitable ligand, for example 2-(dicyclohexylphosphanyl)biphenyl or BINAP, and a suitable base, for example potassium carbonate or sodium tert-butoxide, in a suitable solvent, for example toluene, dioxane or dimethylformamide. The reaction mixture is allowed to react for a certain time, for example 10 hours to 30 hours, in a temperature range between 60°C and 120°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or any catalyst residues are filtered off and washed with the appropriate solvent, and the solvent is removed under reduced pressure, or the reaction mixture is freed of the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid can be filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example ethanol or toluene, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Scheme 5: 1st stage

After the basic processes, the products formed by the basic process can be converted in conversion reactions to inventive conversion products in a procedure known to the person skilled in the art.

For instance, when the product is to be a derivative of compound 17 according to scheme 5, the reaction product 16 can be reacted with an appropriate isocyanate and optionally a suitable base, preferably sodium hydride, potassium hexamethyldisilazide, pyridine, triethylamine or potassium carbonate, in a suitable inert solvent, for example dimethylformamide, dimethyl sulphoxide, acetonitrile, dichloromethane, 1,2-dichloroethane or dioxane, or in a base as the solvent, for example pyridine or triethylamine, or without solvent. The reaction mixture is allowed to react for several hours, for example 1 - 24 hours, within a temperature range between 0 and 80°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed of the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid can be filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example ethanol or ethyl acetate, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Or, alternatively, when the product is to be a derivative of compound 18 according to scheme 5, the reaction product 16 may be reacted with phosgene or carbonyldiimidazole and an appropriate amine in a suitable inert solvent, for example dimethylformamide, tetrahydrofuran, toluene, dichloromethane or

acetonitrile. If appropriate, a suitable base, preferably pyridine, sodium hydrogencarbonate, triethylamine, N-methylmorpholine or sodium acetate, is used. The reaction mixture is allowed to react for a certain time, for example 15 minutes to 24 hours, in a temperature range between 0 and 60°C. Alternatively, the reaction product 16 can be reacted with an appropriate amine-phenyl-carbamate reagent and optionally with a suitable base, preferably pyridine, sodium carbonate, triethylamine or sodium hydride, in a suitable inert solvent, for example tetrahydrofuran, dioxane, dichloromethane, dimethylformamide or acetonitrile, or in a base as a solvent, for example pyridine or triethylamine, or without solvent. The reaction mixture is allowed to react for a certain time, for example 1 hour to 18 hours, within a temperature range between 0°C and 120°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed of the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid can be filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example ethanol or ethyl acetate, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

For instance, when the product is to be a derivative of compound 19 according to scheme 5, the reaction

product 16 can be reacted with an appropriate isothiocyanate and optionally a suitable base, preferably sodium hydride, triethylamine, potassium carbonate or pyridine, in a suitable inert solvent, for example dimethylformamide, tetrahydrofuran, acetone or toluene, or in a base as a solvent, for example pyridine or triethylamine, or without solvent. The reaction mixture is allowed to react for a certain time, for example 30 minutes to 90 hours, within a temperature range between 0 and 115°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed of the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid can be filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example ethanol or ethyl acetate, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Or, alternatively, when the product is to be a derivative of the compound 20 according to scheme 5, the reaction product 16 can be reacted with thiophosgene or thiocarbonyldiimidazole and an appropriate amine in a suitable inert solvent, for example dimethylformamide, tetrahydrofuran, toluene, dichloromethane, ethanol or acetonitrile. Optionally, a suitable base, preferably pyridine, sodium hydrogencarbonate, potassium carbonate, triethylamine

or imidazole is used. The reaction mixture is allowed to react for several hours, for example 1 to 24 hours, in a temperature range between -10 and 80°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed of the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid can be filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example ethanol or ethyl acetate, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Scheme 6: 1st stage

After the basic process, the products formed by the basic process can be converted to inventive conversion products in conversion reactions in a procedure known to those skilled in the art.

For instance, when the product is to be a derivative of compound 22 according to scheme 6, the reaction product 21 can be reacted with appropriate aryl/heteroarylboronic acid derivatives or aryl/heteroarylorganotin compounds and a suitable catalyst, for example $Pd(PPh_3)_4$, [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) or $Pd_2(dba)_3$, and a suitable base, for example sodium carbonate, caesium carbonate or triethylamine, in a suitable solvent, for example dimethylformamide,

dimethylformamide/water, toluene, acetonitrile, dimethoxyethane or dioxane. The reaction mixture is allowed to react for a certain time, for example 6 hours to several days, within a temperature range between 60°C and 120°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or any catalyst residues present are filtered off and washed with the appropriate solvent, and the solvent is removed under reduced pressure, or the reaction mixture is freed from the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example ethanol or ethyl acetate, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

For instance, when the product is to be a derivative of the compound 23 according to scheme 6, the reaction product 21 can be reacted with appropriate alkylzinc halides and a suitable catalyst, for example $Pd(PPh_3)_4$, [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) or $PdCl_2(PPh_3)_2$ in a suitable solvent, for example dimethylformamide, tetrahydrofuran, toluene, dimethoxyethane or dioxane. The reaction mixture is allowed to react for a certain time, for example 30 minutes to 48 hours, within a temperature range between room temperature and 120°C. Once the reaction has ended, any precipitated solid is filtered off, for

which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or any catalyst residues present are filtered off and washed with the appropriate solvent, and the solvent is removed under reduced pressure, or the reaction mixture is freed from the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid filtered off, or the aqueous phase can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example ethanol or ethyl acetate, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Scheme 7: 1st stage

After the basic process, the products formed by the basic process can be converted to inventive conversion products in conversion reactions in a procedure known to those skilled in the art.

For instance, when the product is to be a derivative of the compound 25 according to scheme 7, the reaction product 24 can be reacted, for example, with an appropriate chloride, bromide or iodide and optionally with a suitable base, preferably sodium hydride, pyridine, triethylamine, potassium carbonate or sodium methoxide in methanol, in a suitable inert solvent, for example dimethylformamide, dimethyl sulphoxide, methanol, dioxane, tetrahydrofuran, toluene, or in a base as a solvent, for example pyridine or triethylamine, or without solvent. The reaction mixture is allowed to react for a certain time, for example 30 minutes to 2 days, in a temperature range between 0°C

and 140°C. Alternatively, an amino-substituted intermediate 24 can be reacted, for example, with an appropriate chloride, bromide or iodide and a suitable catalyst, for example tris(dibenzylidene-acetone)dipalladium(0) or tetrakis(triphenylphosphine)-palladium(0), and a suitable ligand, for example 2-(dicyclohexylphosphanyl)biphenyl or BINAP, and a suitable base, for example sodium tert-butoxide or potassium carbonate, in a suitable solvent, for example toluene, dioxane or dimethylformamide. The reaction mixture is allowed to react for a certain time, for example 2 hours to 30 hours, within a temperature range between 60°C and 120°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed from the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example dioxane, ethyl acetate or toluene, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

For instance, when the product is to be a derivative of the compound 27 according to scheme 7, the reaction product 26 can be reacted, for example, with an appropriate chlorophosphoric ester and optionally with a suitable base, preferably sodium hydride, pyridine, triethylamine, potassium carbonate or lithium diisopropylamide, in a suitable inert solvent, for

example dimethylformamide, dimethyl sulphoxide, methanol, dioxane, tetrahydrofuran, toluene, or in a base as a solvent, for example pyridine or triethylamine, or without solvent. The reaction mixture is allowed to react for a certain time, for example 1 hour to 24 hours, within a temperature range between 0°C and 100°C. Once the reaction has ended, any precipitated solid is filtered off, for which the filter medium may consist, for example, of commercial filter paper, and washed with the appropriate solvent, and the remaining solid is dried under reduced pressure, or the reaction mixture is freed from the solvent under reduced pressure. Alternatively, the reaction mixture can be stirred into a large amount of water and the precipitated solid filtered off, or the aqueous phase, after neutralization with a suitable aqueous acid, for example hydrochloric acid, can be extracted with a suitable organic solvent, for example dichloromethane or ethyl acetate, and the organic phase concentrated under reduced pressure. The remaining crude product is purified by recrystallization from a suitable solvent, for example dioxane, ethyl acetate or ethanol, or by column or flash chromatography on silica gel or alumina. The eluent used is, for example, a mixture of methanol and dichloromethane.

Under some of the reaction conditions specified, OH, SH and NH_2 groups may possibly enter into undesired side reactions. It is therefore preferred to provide them with protecting groups or, in the case of NH_2, to replace it with NO_2, and then to eliminate the protecting group or to reduce the NO_2 group. For instance, in a modification of the above-described processes, at least one OH group in the starting compounds can be replaced, for example, by a benzyloxy group, and/or at least one SH group can be replaced, for example, by an S-benzyl group and/or at least one NH_2 group can be replaced by an NH-benzyl group or by an NO_2 group. Subsequently, at least one - preferably all -

benzyloxy group(s) or NH-benzyl group(s) can be eliminated, for example, with hydrogen and palladium on carbon, and/or at least one - preferably all - S-benzyl group(s) can be eliminated, for example, with sodium in ammonia, and/or at least one - preferably all - NO_2 group(s) can be reduced, for example, with hydrogen and Raney nickel to NH_2.

Under some of the reaction conditions mentioned, OH, NH_2 and COOH groups may possibly enter into undesired side reactions. It is therefore preferred to convert starting compounds and intermediates which contain at least one OH group and/or at least one NH_2 group and/or at least one COOH group to corresponding carboxylic ester and carboxamide derivatives. In a modification of the above-described processes, starting compounds and intermediates which have at least one OH group and/or which have at least one NH_2 group can be converted to carboxylic ester or carboxamide derivatives by reaction with an activated carboxylic acid group, for example a carbonyl chloride group. In a modification of the above-described processes, starting compounds and intermediates which have at least one COOH group can be converted to carboxylic ester or carboxamide derivatives by reaction with an activating agent, for example thionyl chloride or carbonyldiimidazole, and subsequent reaction with a suitable alcohol or amine. Subsequently, at least one - preferably all - carboxylic ester or carboxamide group(s) in the starting compounds and intermediates can be detached, for example, with dilute aqueous acids or bases, in order to release at least one - preferably all - OH group(s) and/or NH_2 group(s) and/or COOH group(s).

The invention will be explained in detail with reference to the following examples without being restricted to these examples.

Examples

I. Preparation of inventive compounds

The general synthesis methods which are based on the synthesis schemes 1-7 were used to synthesize the following inventive compounds.

The precursors used for the preparation of the inventive compounds can - unless stated otherwise - be synthesized by processes known to those skilled in the art.

The chemicals and solvents used have been purchased commercially from the conventional suppliers (Acros, Aldrich, Fluka, Lancaster, Maybridge, Merck, Sigma, TCI, etc.) or synthesized.

Example 1:

1-Ethyl-3-[3-(3-hydroxyphenyl)pyrido[2,3-b]pyrazin-6-yl]urea (compound 151)

Preparation of 1-(3-chloropyrido[2,3-b]pyrazin-6-yl)-3-ethylurea (reaction according to scheme 5)

100 mg of 3-chloropyrido[2,3-b]pyrazin-6-ylamine (0.55 mmol) were initially charged in 5 ml of predried pyridine, and 44 µl of ethyl isocyanate (0.55 mmol) were added at room temperature. The mixture was left to stir at 75°C for 3 h and then another 132 µl in total of ethyl isocyanate (1.65 mmol) were added to the reaction mixture in small portions over 18 h. The volatile constituents were then removed under reduced pressure. The resulting solid was purified by means of column chromatography on silica gel (eluent: dichloromethane/methanol). This gave a bright yellow solid.

For the preparation of 3-chloropyrido[2,3-b]pyrazin-6-ylamine, reference is hereby made to the following literature and to the processes known to those skilled in the art:

1) T. S. Osdene, et al. *J. Chem. Soc.* **1955**, 2033-2035 ; C. L. Leese, et al. *J. Chem . Soc.* **1955**, 303-309

2) C. M. Atkinson, et al. *J. Chem. Soc.* **1956**, 26-30 ; S. Goswami, et al. *Molecules* **2005**, *10*, 929-936

Preparation of 1-ethyl-3-[3-(3-hydroxyphenyl)pyrido[2,3-b]pyrazin-6-yl]urea (reaction according to scheme 6)

100 mg of 1-(3-chloropyrido[2,3-b]pyrazin-6-yl)-3-ethylurea (0.40 mmol) were initially charged in a DMF/water mixture under nitrogen as a protective gas. Subsequently, 60.3 mg of 3-hydroxyphenylboronic acid (0.44 mmol), 126 mg of sodium carbonate (1.19 mmol) and 23 mg of tetrakis(triphenylphosphine)palladium(0) (0.02 mmol) were added. The reaction mixture was stirred at 90°C for 4 h. For workup, the mixture was admixed with water and the precipitated solid was washed with dichloromethane. The resulting crude product was stirred once again in warm DCM, filtered off and dried. This gave a yellow solid.

According to this method, further inventive compounds were prepared: for example compounds 152, 153, 154, 208, 209 and 210.

Example 2:

1-Ethyl-3-(3-o-tolylaminopyrido[2,3-b]pyrazin-6-yl)urea (compound 160)

Preparation of 1-ethyl-3-(3-o-tolylaminopyrido[2,3-b]-pyrazin-6-yl)urea (reaction according to scheme 3)

55 mg of 1-(3-chloropyrido[2,3-b]pyrazin-6-yl)-3-ethylurea (0.22 mmol), 60 mg of o-toluidine (0.56 mmol), 33 mg of sodium tert-butoxide (0.33 mmol), 29 mg of tris(dibenzylideneacetone)dipalladium(0) (0.03 mmol) and 78 mg of 2-(dicyclohexylphosphanyl)biphenyl (0.22 mmol) were initially charged in 1.5 ml of predried toluene in a microwave reaction vessel under nitrogen as a protective gas. The reaction mixture was heated to 100°C (100 watts) in the microwave for 30 minutes. Thereafter, the volatile constituents were removed under reduced pressure and the crude product was purified by column chromatography on silica gel (eluent: dichloromethane/methanol). This gave a yellow solid.

According to this method, further inventive compounds were prepared: for example compounds 161, 180, 211, 212 and 213.

Example 3:

1-Ethyl-3-(3-phenoxypyrido[2,3-b]pyrazin-6-yl)urea (compound 64)

Preparation of 1-ethyl-3-(3-phenoxypyrido[2,3-b]pyrazin-6-yl)urea (reaction according to scheme 3)

19 mg of sodium hydride (0.48 mmol) (60% suspension in mineral oil) were initially charged in 10 ml of predried dimethylformamide. At 0°C, 37 mg of phenol (0.40 mmol) were added dissolved in a little predried dimethylformamide. The mixture was stirred at 0°C for 1 h. Subsequently, 100 mg of 1-(3-chloropyrido[2,3-b]pyrazin-6-yl)-3-ethylurea (0.40 mmol) were dissolved in a little predried dimethylformamide and added dropwise at 0°C. The reaction mixture was stirred at room temperature overnight. After the reaction had ended, the reaction solution was added to ice-water and neutralized with 1 N HCl. The precipitated crude product was purified by column chromatography on

silica gel (eluent: dichloromethane/methanol). This gave a white solid.

According to this method, further inventive compounds were prepared: for example compounds 67, 69, 73, 80 and 87.

The reaction with amines can be carried out with triethylamine as the base in dioxane, or without base in dioxane. According to this method, further inventive compounds were prepared: for example compounds 59, 62, 65, 81 and 88.

II. Physico-chemical characterisation

II.1 ESI MS data for selected compounds

Table 1: New pyrido[2,3-b]pyrazine derivatives with relevant MS data according to the general formula I

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
1	1-allyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea	322.0
17	1-(2-morpholin-4-yl-ethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	379.1
29	1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-prop-2-inyl-thiourea	336.2
31	1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-((e)-propenyl)-thiourea	338.3
35	1-phenethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	370.2
36	1-(2,3-di-pyridin-2-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea	372.1
37	1-(2,3-dimethyl-pyrido[2,3-b]pyrazin-6-yl)-	246.2

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
	3-ethyl-urea	
38	1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-urea	296.1
39	1-allyl-3-[3-(4-phenoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	398.1
40	Methane sulfonic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl ester	400.0
41	4-dimethylamino-benzoic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl ester	469.3
42	Acetic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl ester	364.1
43	1-ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	310.2
44	1-[3-(4-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-thiourea	311.1
45	1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	294.2
46	1-acetyl-1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	336.3
47	1-allyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	324.0
48	1,1-diethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	322.0
49	1-(2-chloro-ethyl)-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	346.3
50	1-ethyl-3-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	324.2
51	1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-3-propyl-urea	308.0
52	[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-	352.0

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
	ureido]-acetic acid-ethyl ester	
53	1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea	252.1
54	1-ethyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	312.2
55	1-[3-(3-chloro-4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	346.2
56	4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid	338.1
57	n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acetamide	350.9
58	1-[3-(2,4-difluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	329.9
59	1-ethyl-3-(3-morpholin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea	303.1
60	1-ethyl-3-[3-(4-methyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	316.3
61	1-ethyl-3-[3-(2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	310.2
62	1-ethyl-3-[3-(2-methoxy-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	291.2
63	1-[3-(4-chloro-3-trifluoromethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	294.9
64	1-ethyl-3-(3-phenoxy-pyrido[2,3-b]pyrazin-6-yl)-urea	310.2
65	1-[3-(cyclopropylmethyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	287.2
66	1-ethyl-3-{3-[(pyridin-4-ylmethyl)-amino]-pyrido[2,3-b]pyrazin-6-yl}-urea	324.2
67	1-ethyl-3-[3-(4-fluoro-benzyloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea	341.9

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
68	1-ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea	295.3
69	1-ethyl-3-[3-(pyridin-3-yloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea	311.3
70	1-ethyl-3-[3-(tetrahydro-furan-2-ylmethoxy)-pyrido[2,3-b]pyrazin-6-yl]-urea	318.2
71	1-ethyl-3-[3-(4-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	379.4
72	1-ethyl-3-(3-hydroxy-pyrido[2,3-b]pyrazin-6-yl)-urea	234.3
73	1-ethyl-3-[3-(3-methoxy-phenylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	355.9
74	1-ethyl-3-(3-quinolin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea	345.1
75	1-(3-benzo[b]thiophen-3-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea	350.1
76	1-ethyl-3-[3-(pyridin-2-ylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	327.3
77	1-[3-(4-dimethylamino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	337.2
78	n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-methane sulfonamide	387.3
79	1-ethyl-3-[3-(1h-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	284.2
80	1-(3-benzylsulfanyl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea	340.0
81	1-ethyl-3-[3-(4-methyl-[1,4]diazepan-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	330.5
82	1-[3-(4-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	309.4
83	1-(3-amino-pyrido[2,3-b]pyrazin-6-yl)-3-	233.3

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
	ethyl-urea	
84	1-ethyl-3-pyrido[2,3-b]pyrazin-6-yl-urea	218.3
86	1-ethyl-3-[3-(4-fluoro-2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	328.2
87	1-(3-cyclopentyloxy-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea	302.3
88	1-ethyl-3-[3-(4-hydroxy-piperidin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	317.2
89	(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	266.2
90	1-ethyl-3-(3-pyrimidin-5-yl-pyrido[2,3-b]pyrazin-6-yl)-urea	296.3
91	1-ethyl-3-(3-pyridin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea	295.3
92	1-allyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	306.3
93	1-ethyl-3-(3-piperazin-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea	302.3
94	1-[3-(3-chloro-pyridin-4-ylmethyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	329.3
95	1-ethyl-3-[3-(6-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	325.3
96	1-[3-(3,5-dimethyl-isoxazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	313.3
97	1-ethyl-3-[3-(4-trifluormethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	378.3
98	1-ethyl-3-(3-furan-2-yl-pyrido[2,3-b]pyrazin-6-yl)-urea	284.2
99	1-ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	325.3
100	1-[3-(2,4-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	353.9

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
101	1-ethyl-3-[3-(1h-pyrrol-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	383.3
102	1-ethyl-3-[3-(6-morpholin-4-yl-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	380.3
103	1-benzyl-3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	384.0
104	1-[3-(2-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	309.2
105	1-ethyl-3-[3-(4-hydroxymethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	324.2
106	1-[3-(3-amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	309.2
107	1-[3-(4-acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	336.1
108	1-[3-(2,3-dihydro-benzofuran-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	336.2
109	1-[3-(4-benzyloxy-3-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	418.3
110	1-(2,3-dihydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	340.0
111	1-ethyl-3-[3-(3-formyl-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	352.1
112	1-ethyl-3-[3-(4-methanesulfonyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	372.1
113	n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-succinamic acid	409.3
114	1-ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea methane sulfonic acid salt	295.3
115	1-[3-(2,6-dimethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	354.9

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
116	1-[3-(2,6-dimethoxy-pyrimidin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	356.1
117	1-[3-(2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	328.4
118	1-ethyl-3-[3-(1h-indol-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	333.0
119	1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-thiourea	268.0
120	1-ethyl-3-{3-[4-(2-methoxy-ethoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea	368.4
121	Acrylic acid-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl ester	364.1
122	1-[3-(4-cyano-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	319.1
123	1-(3-benzo[1,2,5]oxadiazol-4-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea	336.0
124	1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	340.0
125	1-[3-(2,6-dimethoxy-phenyl)-pyrido [2,3-b]pyrazin-6-yl]-3-ethyl-urea	354.2
126	1-[3-(3-acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	336.2
127	1-ethyl-3-[3-(3-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	379.2
128	1-[3-(6-amino-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	310.2
129	3-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenoxy}-propionsäure	382.3
130	1-isopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	308.2

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
131	1-cyclopentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	333.9
132	1-pentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	336.2
133	n-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acrylamide	363.2
134	1-tert-butyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	322.1
135	1-(2-hydroxy-ethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	310.2
136	1-cyclobutyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	319.8
137	1-allyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-7-yl]-thiourea	367.1
138	1-ethyl-1-(ethylcarbamoyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	365.1
139	[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-carbamic acid-allyl ester	323.0
140	(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-carbamic acid-ethyl ester	295.3
141	1-ethyl-3-[3-(4-phenyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	378.3
142	1-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	380.2
143	1,3-bis-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	471.3
144	n-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-acetamidine	264.8
145	1-ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea	341.2
146	1-(4-hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-	338.2

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
	b]pyrazin-6-yl)-urea	
147	1-(3-hydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	324.2
148	1-ethyl-3-{3-[4-(3-morpholin-4-yl-propoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea	437.3
149	1-ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea	326.1
150	1-ethyl-3-(3-p-tolylamino-pyrido[2,3-b]pyrazin-6-yl)-urea	323.2
151	1-ethyl-3-[3-(3-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	310.2
152	3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid	338.2
153	1-[3-(3,4-dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	354.1
154	1-[3-(4-amino-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	339.1
155	3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-benzamid	337.1
156	1-[3-(3-chloro-4-hydroxy-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	374.2
157	1-ethyl-3-(3-m-tolylamino-pyrido-[2,3-b]pyrazin-6-yl)-urea	323.3
158	1-ethyl-3-[3-(4-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	339.0
159	1-[3-(4-chloro-phenylamino)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea	343.1
160	1-ethyl-3-(3-o-tolylamino-pyrido[2,3-b]-pyrazin-6-yl)-urea	323.2
161	1-ethyl-3-[3-(pyridin-3-ylamino)-pyrido-[2,3-b]pyrazin-6-yl]-urea	310.2

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
162	1-ethyl-3-[3-(4-ethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	337.2
163	1-ethyl-3-[3-(3-methoxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	353.3
164	1-ethyl-3-[3-(4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	325.3
165	1-ethyl-3-[3-(5-methyl-pyridin-2-yl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea	324.3
166	1-ethyl-3-[3-(1-methyl-1H-pyrazol-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	313.4
167	1-ethyl-3-[3-(4-fluoro-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	327.4
168	1-(4-hydroxy-butyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	384.3
169	Phosphoric acid-mono-{4-[6-(3-ethyl-ureido)-pyrido-[2,3-b]pyrazin-3-yl]-2-methoxy-phenyl}-ester	420.2
170	1-[3-(2-chloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	344.3
171	1-[3-(4-chloro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	358.1
172	1-[3-(3,5-dimethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	312.2
173	1-ethyl-3-[3-(1-methyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	298.4
174	1-[3-(5-cyano-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	325.3
176	1-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(4-morpholin-4-yl-butyl)-urea	453.4
177	1-[3-(3-chloro-4-methoxy-phenylamino)-	373.4

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
	pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	
178	1-ethyl-3-[3-(naphthalen-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	359.3
179	1-ethyl-3-[3-(quinolin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	360.3
180	1-[3-(3,5-dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	369.3
181	1-ethyl-3-[3-(pyrazin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	311.3
182	1-ethyl-3-[3-(3-isopropoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	367.2
183	1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea p-toluenesulfonate	340.3 (free base)
184	1-[3-(2-chloro-pyridin-4-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	344.3
185	1-[3-(3,5-dichloro-4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	393.2
186	1-[3-(3,5-dichloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	369.2
187	1-[3-(3,4-dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	369.2
188	1-ethyl-3-[3-(3-hydroxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	339.1
189	3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-ylamino]-5-trifluoromethyl-benzoic acid	421.3
190	1-ethyl-3-[3-(6-methoxy-pyridin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	340.3
191	1-[3-(3,5-dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	337.3
192	1-[3-(4-cyano-phenylamino)-pyrido-[2,3-	334.1

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
	b]pyrazin-6-yl]-3-ethyl-urea	
194	1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea hydrochloride	340.1 (free base)
195	1-ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea	310.2
196	1-(3-chloro-pyrido[2,3-b]pyrazin-6-yl)-3-cyclohexyl-urea	306.2
197	1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	355.3
198	1-ethyl-3-[3-(4-hydroxy-3,5-dimethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	338.3
199	3-ethyl-1-phenethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	398.2
200	1-Allyl-3-{3-[4-(tetrahydro-pyran-2-yloxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea	422.2
201	3-ethyl-1-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-1-propyl- urea	366.3
202	3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-1-(2-piperidin-1-yl-ethyl)-urea hydrochloride	405.4 (free base)
203	N-{4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl}-2-phenyl-acetamide	427.3
204	1-(4-hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea hydrochloride	338.3 (free base)
205	Acetic acid-4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl ester	380.4
206	1-(4-amino-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	337.3
207	1-(5-hydroxy-pentyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	352.3

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
208	3-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-N-methyl-benzamide	351.2
209	1-ethyl-3-[3-(2-methoxy-5-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	338.1
210	1-ethyl-3-(3-p-tolyl-pyrido[2,3-b]pyrazin-6-yl)-urea	308.2
211	1-ethyl-3-[3-(methyl-p-tolyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea	337.1
212	1-ethyl-3-[3-(2-p-tolyl-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	351.1
213	1-ethyl-3-[3-(4-methyl-benzylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	337.2
214	1-ethyl-3-[3-(3-fluoro-4-methyl-phenyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea	341.2
215	1-[3-(3,4-dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	337.1
216	1-ethyl-3-[3-(4-isopropyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	351.1
217	1-(4-morpholin-4-yl-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea	407.3
218	N-{4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-acetamide	379.3
219	1-[3-(3-amino-4-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	323.3
220	1-[3-(3-acetyl-2-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	354.2
221	1-ethyl-3-[3-(4-methoxy-3-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	338.3
222	1-[3-(6-ethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	339.3
223	1-ethyl-3-[3-(2-fluoro-4-methyl-phenyl)-	326.2

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
	pyrido[2,3-b]pyrazin-6-yl]-urea	
224	1-ethyl-3-[3-(3-fluoro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	342.1
225	1-ethyl-3-[3-(2-fluoro-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	342.1
226	1-ethyl-3-[3-(3,4,5-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	384.2
227	1-[3-(3,5-difluoro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	360.3
228	1-ethyl-3-[3-(4-trifluoromethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	362.3
229	1-ethyl-3-[3-(2,3,4-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	384.3
230	1-[3-(3-chloro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	358.2
231	1-ethyl-3-[3-(3-fluoro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	328.3
232	1-ethyl-3-[3-(6-fluoro-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea	313.3
233	1-[3-(2,4-dimethyl-thiazol-5-yl)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea	329.4
234	1-ethyl-3-[3-(2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	324.3
235	1-[3-(2-chloro-pyridin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	329.3
236	1-[3-(5-acetyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	342.3
237	1-[3-(5-chloro-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	334.1
238	1-ethyl-3-[3-(3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	324.1

Comp.	Pyridopyrazine derivative	MS m/z ($M+H^+$)
239	1-[3-(3-bromo-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	402.3
240	1-[3-(benzothiazol-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	366.3
241	1-ethyl-3-[3-(4-methyl-3-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	391.4
242	1-[3-(3-cyano-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	348.3
243	1-ethyl-3-[3-(4-phenoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	401.3
244	1-[3-(4-chloro-3-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	357.3
245	1-[3-(2-chloro-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	357.1
246	1-ethyl-3-[3-(3-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea	377.4
247	1-[3-(2-chloro-4-trifluoromethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	427.3
248	1-[3-(4-chloro-2-methoxy-5-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea	387.4
249	1-ethyl-3-[3-(4-methylsulfanyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea	340.3
250	3-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzenesulfonamide	373.3
251	N-{4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-methanesulfonamide	415.3

II.2 NMR spectroscopic data and melting points for selected compounds

Compound 1: 1-allyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Melting point: 239-240°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.40 (m, 2H), 5.30 (d, 1H), 5.60 (d, 1H), 6.07-6.17 (m, 1H), 7.55-7.70 (m, 4H), 8.35 (d, 2H), 8.45 (d, 1H), 9.50 (s, 1H), 11.35 (s, 1H), 12.55 (m, 1H).

Compound 2: 1-(2-methyl-allyl)-3-(3-naphth-2-yl-pyrido[2,3-b]pyrazin-6-yl)-thiohurea

Mp.: 239-240°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 1.94 (s, 3H), 4.32 (m, 2H), 5.07 (s, 1H), 5.28 (s, 1H), 7.60-7.69 (m, 3H), 8.00-8.05 (m, 1H), 8.07-8.12 (m, 1H), 8.14 (d, 1H), 8.42-8.51 (m, 2H), 8.98 (s, 1H), 9.68 (s, 1H), 11.32 (s, 1H), 12.78 (m, 1H).

Compound 3: 1-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(2-methyl-allyl)-thio-urea

Mp.: 251-252°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 1.92 (s, 3H), 3.85 (s, 3H), 4.27-4.35 (m, 2H), 5.02 (s, 1H), 5.24 (s, 1H), 7.15 (d, 2H), 7.58 (d, 1H), 8.31 (d, 2H), 8.41 (d, 1H), 9.46 (s, 1H), 11.29 (s, 1H), 12.68 (m, 1H).

Compound 4: 1-(2-methyl-allyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 225-226°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 1.90 (s, 3H), 4.30-4.35 (m, 2H), 5.01 (s, 1H), 5.22 (s, 1H), 7.55-7.80 (m, 4H), 8.30-8.38 (m, 2H), 8.45 (d, 1H), 9.52 (s, 1H), 11.32 (s, 1H), 12.65 (m, 1H).

Compound 5: 1-allyl-3-(3-naphth-2-yl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 242-243°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.42 (m, 2H), 5.37 (d, 1H), 5.65 (d, 1H), 6.07-6.19 (m, 1H), 7.57-7.68 (m, 3H), 7.97-8.05 (m, 1H), 8.07-8.19 (m, 2H), 8.40-8.52 (m, 2H), 8.99 (s, 1H), 9.70 (s, 1H), 11.36 (s, 1H), 12.56 (t, 1H).

Compound 6: 1-allyl-3-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea

Mp.: 240-241°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 3.87 (s, 3H), 4.36-4.42 (m, 2H), 5.32 (d, 1H), 5.60 (d, 1H), 6.06-6.16 (m, 1H), 7.16 (d, 2H), 7.60 (d, 1H), 8.32 (d, 2H), 8.42 (d, 1H), 9.56 (s, 1H), 11.29 (s, 1H), 12.56 (m, 1H).

Compound 7: 1-allyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea-hydrochloride

Mp.: 160-161°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.36-4.43 (m, 2H), 5.31 (d, 1H), 5.59 (d, 1H), 6.05-6.16 (m, 1H), 6.97 (d, 2H), 7.57 (d, 1H), 8.20 (d, 2H), 8.40 (d, 1H), 9.41 (s, 1H), 10.17 (bs, 1H), 11.24 (s, 1H), 12.56 (m, 1H).

Compound 8: 1-(3-naphth-2-yl-pyrido[2,3-b]pyrazin-6-yl)-3-(4-nitro-phenyl)-thiourea

Mp.: 260-261°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 7.61-7.68 (m, 3H), 7.72 (d, 2H), 7.75 (d, 1H), 8.01-8.06 (m, 1H), 8.16 (m, 2H), 8.26 (d, 2H), 8.53 (d, 1H), 8.58 (d, 1H), 9.04 (s, 1H), 9.62 (s, 1H), 9.76 (s, 1H), 11.81 (s, 1H).

Compound 9: 1-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(4-nitro-phenyl)-thio-urea

Mp.: 250-251°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 3.85 (s, 3H), 7.17 (d, 2H), 7.71 (d, 2H), 8.21 (d, 2H), 8.22-8.27 (m, 1 H), 8.36-8.42 (m, 3H), 9.53 (s, 1H), 9.65 (s, 1H), 11.77 (s, 1H).

Compound 10: 1-tert.butyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 227°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 1.65 (s, 9H), 7.53-7.69 (m, 4H), 8.34 (d, 2H), 8.41 (d, 1H), 9.51 (s, 1H), 10.98 (s, 1H), 12.75 (s, 1H).

Compound 11: 1-cyclopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 233-234°C

^{1}H-NMR (d_6-DMSO): δ = 0.70-0.80 (m, 2H), 0.91-1.00 (m, 2H), 3.20-3.28 (m, 1H), 7.51-7.72 (m, 4H), 8.36 (d, 2H), 8.45 (d, 1H), 9.52 (s, 1H), 11.31 (s, 1H), 12.45 (s, 1H).

Compound 12: 1-methyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 253-254°C

^{1}H-NMR (d_6-DMSO): δ = 3.25 (s, 3H), 7.59-7.67 (m, 4H), 8.38 (d, 2H), 8.46 (d, 1H), 9.52 (s, 1H), 11.31 (s, 1H), 12.10 (s, 1H).

Compound 13: 1-benzyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 232-233°C

^{1}H-NMR (d_6-DMSO): δ = 4.96 (m, 2H), 7.37-7.48 (m, 3H), 7.54-7.67 (m, 6H), 8.32 (d, 2H), 8.47 (d, 1H), 9.52 (s, 1H), 11.43 (s, 1H), 12.91 (s, 1H).

Compound 14: 1-(4-fluoro-phenyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 225-226°C

^{1}H-NMR (d_6-DMSO): δ = 7.33 (m, 2H), 7.57-7.65 (m, 3H), 7.70-7.81 (m, 3H), 8.34 (d, 2H), 8.54 (d, 1H), 9.57 (s, 1H), 11.62 (s, 1H).

Compound 15: 1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-3-p-tolyl-urea

Mp.: 298-299°C

^{1}H-NMR (d_6-DMSO): δ = 2.29 (s, 3H), 7.20 (d, 2H), 7.52 (d, 2H), 7.59-7.67 (m, 3H), 7.80 (d, 1H), 8.38 (d, 2H), 8.44 (d, 1H), 9.59 (s, 1H), 10.36 (s, 1H), 11.46 (s, 1H).

Compound 16: 1-(4-chloro-3-trifluoromethyl-phenyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea

Mp.: 250°C

^{1}H-NMR (d_6-DMSO): δ = 7.58-7.67 (m, 3H), 7.74 (d, 1H), 7.80 (d, 1H), 7.87 (d, 1H), 8.21 (s, 1H), 8.39 (d, 2H), 8.48 (d, 1H), 9.53 (s, 1H), 10.55 (s, 1H), 11.82 (s, 1H).

Compound 17: 1-(2-morpholin-4-yl-ethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea

Mp.: 226°C

^{1}H-NMR (d_6-DMSO): δ = 2.45-2.67 (m, 6H), 3.40-3.48 (m, 2H), 3.60-3.69 (m, 4H), 7.55-7.70 (m, 4H), 8.30-8.40 (m, 3H), 9.29 (s, 1H), 9.42 (s, 1H), 10.18 (s, 1H).

Compound 18: 1-cyclohexyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 230-232°C

^{1}H-NMR (d_6-DMSO): δ = 1.50-1.75 (m, 6H), 1.80-2.00 (m, 4H), 7.55-7.70 (m, 4H), 8.37 (d, 2H), 8.45 (d, 1H), 9.55 (s, 1H), 11.20 (s, 1H), 12.80 (s, 1H).

Compound 19: 1-isopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 229-230°C

^{1}H-NMR (d_6-DMSO): δ = 1.40 (d, 6H), 4.40-4.50 (m, 1H), 7.58-7.66 (m, 4H), 8.36 (d, 2H), 8.44 (d, 1H), 9.52 (s, 1H), 11.20 (s, 1H), 12.48 (s, 1H).

Compound 20: 1-furan-2-ylmethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 250°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.95 (s, 2H), 6.55 (m, 1H), 6.68 (d, 1H), 7.59-7.68 (m, 4H), 7.74 (d, 1H), 8.37 (d, 2H), 8.48 (d, 1H), 9.55 (s, 1H), 11.45 (s, 1H), 12.83 (s, 1H).

Compound 21: 1-cyclopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea

Mp.: 158-160 °C

^{1}H-NMR (d_6-DMSO): δ = 0.52-0.60 (m, 2H), 0.72-0.82 (m, 2H), 2.70-2.79 (m, 1H), 7.57-7.65 (m, 3H), 7.71 (d, 1H), 8.34 (d, 2H), 8.38 (d, 1H), 9.21 (s, 1H), 9.46 (s, 1H), 10.12 (s, 1H).

Compound 22: 1-methyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea

Mp.: 270°C

^{1}H-NMR (d_6-DMSO): δ = 3.25 (s, 3H), 7.70 (d, 1H), 8.44 (d, 2H), 8.50 (d, 1H), 8.64 (d, 2H), 9.64 (s, 1H), 11.38 (s, 1H), 12.03 (s, 1H).

Compound 23: 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-]pyrazin-6-yl]-3-methyl-thiourea

Mp.: 282°C

^{1}H-NMR (d_6-DMSO): δ = 3.25 (s, 3H), 6.98 (d, 2H), 7.57 (d, 1H), 8.26 (d, 2H), 8.40 (d, 1H), 9.45 (s, 1H), 10.18 (s, 1H), 11.25 (s, 1H), 12.10 (s, 1H).

Compound 24: 1-allyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea

Mp.: 244°C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.40 (s, 2H), 5.36 (d, 1H), 5.59 (d, 1H), 6.08-6.15 (m, 1H), 7.71 (d, 1H), 8.46 (d, 2H), 8.51 (d, 1H), 8.60 (d, 2H), 9.64 (s, 1H), 11.45 (s, 1H), 12.51 (t, 1H).

Compound 25: 1-allyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea

Mp.: 240 °C (Decomp.)
^{1}H-NMR (d_6-DMSO): δ = 3.98 (s, 2H), 5.19 (d, 1H), 5.37 (d, 1H), 5.96-6.05 (m, 1H), 6.97 (d, 2H), 7.59 (d, 1H), 8.22 (d, 2H), 8.33 (d, 1H), 9.38 (s, 1H), 9.45 (s, 1H), 10.13 (s, 1H), 10.18 (s, 1H).

Compound 26: 4-[6-(3-allyl-thioureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid ethyl ester

Mp.: 223-224°C
^{1}H-NMR (d_6-DMSO): δ = 1.39 (t, 3H), 4.35-4.42 (m, 4H), 5.35 (d, 1H), 5.60 (d, 1H), 6.08-6.15 (m, 1H), 7.68 (d, 1H), 8.17 (d, 2H), 8.47 (d, 2H), 8.50 (d, 1H), 9.60 (s, 1H), 11.40 (s, 1H), 12.52 (t, 1H).

Compound 27: 1-allyl-3-[3-(3-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea

Mp.: 205°C (Decomp.)
^{1}H-NMR (d_6-DMSO): δ = 4.41 (s, 2H), 5.33 (d, 1H), 5.58 (d, 1H), 6.07-6.15 (m, 1H), 6.99 (d, 1H), 7.42 (t, 1H), 7.64 (d, 1H), 7.72 (s, 1H), 7.77 (d, 1H), 8.46 (d, 1H), 9.45 (s, 1H), 9.80 (s, 1H), 11.37 (s, 1H), 12.55 (s, 1H).

Compound 28: 1-allyl-3-(3-benzo[1,3]dioxol-5-yl-pyrido[2,3-b]pyrazin-6-yl)-thiourea

Mp.: 218-220°C (Decomp.)
^{1}H-NMR (d_6-DMSO): δ = 4.40 (s, 2H), 5.31 (d, 1H), 5.60 (d, 1H), 6.08-6.20 (m, 3H), 7.16 (d, 1H), 7.61 (d, 1H), 7.90 (s, 1H), 7.96 (d, 1H), 8.43 (d, 1H), 9.49 (s, 1H), 11.34 (s, 1H), 12.58 (s, 1H).

Compound 29: 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-prop-2-inyl-thio-urea

Mp.: 350 °C (Decomp.)
^{1}H-NMR (d_6-DMSO): δ = 2.09 (s, 1H), 2.44 (s, 2H), 6.99 (d, 2H), 7.19 (s, 1H), 7.44 (s, 1H), 8.24 (d, 2H), 8.26 (d, 1H), 9.29 (s, 1H), 10.08 (s, 1H), 11.81 (s, 1H).

Compound 30: 1-allyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea

Mp.: 230 °C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.40 (s, 2H), 5.34 (d, 1H), 5.60 (d, 1H), 6.07-6.15 (m, 1H), 6.98 (d, 2H), 7.58 (d, 1H), 8.24 (d, 2H), 8.42 (d, 1H), 9.45 (s, 1H), 10.19 (s, 1H), 11.34 (s, 1H), 12.60 (s, 1H).

Compound 31: 1-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-((E)-propenyl)-thio-urea

^{1}H-NMR (d_6-DMSO): δ = 2.12 (d, 3H), 5.17 (m, 1H), 6.96 (d, 2H), 7.22-7.26 (m, 1H), 7.59 (d, 1H), 8.25 (d, 2H), 8.45 (d, 1H), 9.48 (s, 1H), 10.20 (s, 1H), 11.56 (s, 1H), 14.67 (s, 1H).

Compound 32: 1-allyl-3-[2,3-bis-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea

Mp.: 270 °C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.40 (s, 2H), 5.25 (d, 1H), 5.50 (d, 1H), 6.02-6.13 (m, 1H), 6.74 (d, 2H), 6.76 (d, 2H), 7.31 (d, 2H), 7.36 (d, 2H), 7.62 (d, 1H), 8.42 (d, 1H), 9.78 (s, 1H), 9.85 (s, 1H), 11.30 (s, 1H), 12.47 (s, 1H).

Compound 33: 1-[2,3-bis-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-((E)-propenyl)-thiourea

Mp.: 240 °C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 2.05 (d, 3H), 5.10-5.18 (m, 1H), 6.74 (d, 2H), 6.76 (d, 2H), 7.20-7.26 (m, 1H), 7.34 (d, 2H), 7.39 (d, 2H), 7.63 (d, 1H), 8.45 (d, 1H), 9.79 (s, 1H), 9.89 (s, 1H), 11.55 (s, 1H), 14.56 (d, 1H).

Compound 34: 1-allyl-3-[2-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea

Mp.: 260 °C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.40 (s, 2H), 5.28 (d, 1H), 5.48 (d, 1H), 6.03-6.12 (m, 1H), 6.96 (d, 2H), 7.66 (d, 1H), 8.16

(d, 2H), 8.43 (d, 1H), 9.52 (s, 1H), 10.06 (s, 1H), 11.31 (s, 1H), 12.40 (s, 1H).

Compound 35: 1-phenethyl-3-(3-phenyl-pyrido[2,3-]pyrazin-6-yl)-urea

Mp.: 250 °C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 2.88-2.95 (m, 2H), 3.52-3.60 (m, 2H), 7.18 (t, 1H), 7.28 (t, 2H), 7.42 (d, 2H), 7.58-7.68 (m, 4H), 8.37 (d, 3H), 9.25 (s, 1H), 9.48 (s, 1H), 10.18 (s, 1H).

Compound 36: 1-(2,3-di-pyridin-2-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea

Mp.: 236-237 °C

^{1}H-NMR (d_6-DMSO): δ = 1.13-1.22 (m, 3H), 3.28-3.39 (m, 2H), 3.60-3.69 (m, 4H), 7.31-7.39 (m, 2H), 7.79 (d, 1H), 7.91-7.99 (m, 4H), 8.26 (d, 1H), 8.29 (d, 1H), 8.47 (d, 1H), 9.08 (s, 1H), 10.20 (s, 1H).

Compound 37: 1-(2,3-dimethyl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea

Mp.: 246-248 °C

^{1}H-NMR (d_6-DMSO): δ = 1.17 (t, 3H), 2.64 (s, 3H), 2.67 (s, 3H), 3.24-3.40 (m, 2H), 7.55 (d, 1H), 8.24 (d, 1H), 9.14 (s, 1H), 9.91 (s, 1H).

Compound 64: 1-ethyl-3-(3-phenoxy-pyrido[2,3-b]pyrazin-6-yl)-urea

Mp.: 256-258 °C

^{1}H-NMR (d_6-DMSO): δ = 1.09 (t, 3H), 3.15 - 3.22 (m, 2H), 7.31 - 7.38 (m, 3H), 7.48 - 7.53 (m, 2H), 7.72 (d, 1H), 8.32 (d, 1H), 8.34 (bs, 1H), 8.71 (s, 1H), 9.90 (s, 1H).

Compound 85: 1-ethyl-3-(3-imidazol-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea

^{1}H-NMR (d_6-DMSO): δ = 1.20 (t, 3H), 3.26 - 3.32 (m, 2H), 7.26 (s, 1H), 7.75 (d, 1H), 8.20 (s, 1H), 8.40 (d, 1H), 8.79 (s, 1H), 8.84 (s, 1H), 9.39 (s, 1H), 10.16 (s, 1H) ppm.

Compound 137: 1-allyl-3-[3-(4-nitro-phenyl)-pyrido[2,3-b]pyrazin-7-yl]-thiourea

Mp.: 250 °C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 4.23 (s, 2H), 5.19 (d, 1H), 5.29 (d, 1H), 5.90-6.00 (m, 1H), 8.46 (d, 2H), 8.55 (s, 1H), 8.64 (d, 2H), 8.92 (s, 1H), 9.23 (s, 1H), 9.77 (s, 1H), 10.35 (s, 1H).

Compound 151: 1-ethyl-3-[3-(3-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea

^{1}H-NMR (d_6-DMSO): δ = 1.20 (t, 3H), 3.32 - 3.38 (m, 2H), 6.98 (d, 1H), 7.40 (t, 1H), 7.68 (d, 1H), 7.73 (s, 1H), 7.76 (d, 1H), 8.37 (d, 1H), 9.12 (bs, 1H), 9.37 (s, 1H), 9.80 (bs, 1H), 10.12 (s, 1H).

Compound 160: 1-ethyl-3-(3-o-tolylamino-pyrido[2,3-b]-pyrazin-6-yl)-urea

Mp.: 221-223 °C

^{1}H-NMR (d_6-DMSO): δ = 1.12 (t, 3H), 2.31 (s, 3H), 3.20 - 3.26 (m, 2H), 7.12 (t, 1H), 7.23 (t, 1H), 7.29 (d, 1H), 7.33 (d, 1H), 7.86 (d, 1H), 8.07 (d, 1H), 8.43 (s, 1H), 8.81 (bs, 1H), 9.26 (s, 1H), 9.75 (s, 1H).

Compound 169: Phosphoric acid-mono-{4-[6-(3-ethyl-ureido)-pyrido-[2,3-b]pyrazin-3-yl]-2-methoxy-phenyl}-ester

^{1}H-NMR (d_6-DMSO): δ = 1.20 (t, 3H), 3.25 - 3.35 (m, 2H), 3.95 (s, 3H), 7.51 (d, 1H), 7.22 (d, 1H), 7.92 (d, 1H),

7.98 (s, 1H), 8.36 (d, 1H), 8.94 (bs, 1H), 9.47 (s, 1H), 10.09 (s, 1H) ppm.

Compound 175: Sodium 2-chloro-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-6-methoxy-phenoxide

Mp.: 260 °C (Decomp.)

^{1}H-NMR (d_6-DMSO): δ = 1.19 (t, 3H), 3.25 - 3.35 (m, 2H), 3.81 (s, 3H), 7.45 (bs, 1H), 7.64 (bs, 1H) 7.92 (s, 1H), 8.16 (bs, 1H), 9.10 (bs, 1H), 9.23 (bs, 1H), 9.89 (bs, 1H) ppm.

Compound 183: 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea p-toluenesulfonate

Mp.: 193-196 °C

^{1}H-NMR (d_6-DMSO): δ = 1.20 (t, 3H), 2.29 (s, 3H), 3.28 - 3.35 (m, 2H), 3.93 (s, 3H), 6.97 (d, 1H), 7.11 (d, 2H), 7.47 (d, 2H), 7.65 (d, 1H), 7.85 (d, 1H), 7.91 (s, 1H), 8.31 (d, 1H), 9.00 (bs, 1H), 9.41 (s, 1H), 9.71 (bs, 1H), 10.04 (s, 1H) ppm.

Compound 193: 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea (Z)-but-2-enedicarboxylic acid salt

Mp.: 200-204 °C

^{1}H-NMR (d_6-DMSO): δ = 1.20 (t, 3H), 3.25 - 3.35 (m, 2H), 3.92 (s, 3H), 6.24 (s, 2H), 6.98 (d, 1H), 7.65 (d, 1H), 7.85 (d, 1H), 7.91 (s, 1H), 8.32 (d, 1H), 9.00 (bs, 1H), 9.41 (s, 1H), 9.71 (bs, 1H), 10.04 (s, 1H) ppm.

Compound 194: 1-ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea hydrochloride

Mp.: 236-239 °C

^{1}H-NMR (d_6-DMSO): δ = 1.20 (t, 3H), 3.32 (quint, 2H), 3.93 (s, 3H), 6.98 (d, 1H), 7.65 (d, 1H), 7.85 (d, 1H), 7.91 (s, 1H), 8.31 (d, 1H), 9.00 (bs, 1H), 9.41 (s, 1H), 9.71 (bs, 1H), 10.05 (s, 1H) ppm.

Compound 202: 3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-1-(2-piperidin-1-yl-ethyl)-urea hydrochloride

Mp.: 187-190 °C

^{1}H-NMR (d_6-DMSO): δ = 1.19 (t, 3H), 1.46 (m, 1H), 1.76 (d, 1H), 1.89 (m, 4H), 3.06 (m, 2H), 3.28 - 3.35 (m, 4H), 3.75 (d, 2H), 4.43 (t, 2H), 7.60-7.66 (m, 3H), 7.92 (d, 1H), 8.36 (d, 2H), 8.46 (d, 1H), 8.59 (t, 1H), 9.58 (s, 1H), 9.73 (bs, 1H) ppm.

Compound 204: 1-(4-hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea hydrochloride

^{1}H-NMR (DMSO-d_6) δ = 1.58-1.64 (m, 4H), 3.30-3.34 (m, 2H), 3.48-3.51 (m, 2H), 7.57-7.63 (m, 3H), 7.66 (d, 1H), 8.34-8.39 (m, 3H), 9.32 (s, 1H), 9.47 (s, 1H), 10.15 (s, 1H) ppm.

III. Evidence of the kinase inhibition of compounds according to the invention

III.1 Cell-free kinase assays (using ALPHA technology)

The inhibitory effect of the compounds according to the invention was tested on various serine/threonine, tyrosine and lipid kinases in enzymatic assays. Recombinant human kinases such as, for example, Erk2, PI3Kalpha, -beta, -gamma, -delta, p38alpha, p38gamma, Jnk1, Jnk2 and others were used in this case, partly as full-length kinases, partly as shortened fragments, but at least consisting of the functional kinase domains. The commercial kinase proteins (Proqinase, Upstate) were used as recombinant fusion proteins with GST (glutathion-S-transferase) or His-Tag. Depending on the type of substrate, the various kinase reactions were quantified by means of suitable ALPHA™ beads (Perkin-Elmer).

Testing

The substance testing is described in detail hereinafter for the Erk assay. Selected test results of the Erk2, PI3Kalpha, p38alpha and Jnk2 assays are given below. To determine the IC_{50} value, the potential inhibitor substances were investigated in 10 semi-logarithmically graded concentrations of 3.16 nM-100 µM.

a) MAPK-ALPHAs (e.g. Erk2): the test substance, 0.625 ng Erk2 (#14-173, Upstate), 10µM ATP and 15nM biotinylated MBP (myelin basic protein) substrate were incubated on a 384-well Optiplate (Perkin-Elmer) in a volume of 15 µl for 1h in 25mM Tris, 10mM $MgCl_2$, 0.1% Tween-20, 100µM $NaVO_4$, 2mM DTT at pH 7.5. The kinase reaction was then stopped by adding 10µl of the ALPHA bead mixes (10 µg/ml, #6760617/ Perkin-Elmer) pre-incubated with anti-phospho MBP antibody

(320pM, #05-429/ Upstate) in 25mM Tris, 200mM NaCl, 100mM EDTA and 0.3% BSA and left to stand overnight.

b) PI3K-ALPHAs (e.g. PI3Kalpha): the test substance, 1 ng PI3Kalpha (#14-602, Upstate), 100µM ATP and 20µM PIP_2 substrate (#P4508, Echelon) were incubated on a 384-well Optiplate (Perkin-Elmer) for 1h in 50mM Hepes, 50mM NaCl, 5mM $MgCl_2$, 0.05% Chaps, 5mM DTT at pH 7.4. The kinase reaction was then stopped by adding ALPHA bead mixes (10µg/ml, #6760603/ Perkin-Elmer) pre-incubated with 1nM GST:Grp1 fusion protein (Upstate) and 15nM biotinylated PIP3 (#C-39B6/ Echelon) in 50mM Hepes, 50mM NaCl, 50mM EDTA and 0.1% BSA and left to stand overnight.

The fluorescence was detected the following morning in a Fusion$^{TMa}\alpha$-system (Perkin-Elmer).

Evaluation

The %-inhibition values per substance concentration were calculated by means of the following formula from the raw data determined in the Fusion$^{TM}\alpha$:

$$\%\ \text{Kinase inhibition}_{(\text{Sample})} = 100 - \left(100x\ \frac{\text{Mean}_{(\text{Sample})} - \text{Mean}_{(0\%\ \text{Control})}}{\text{Mean}_{(100\%\ \text{Control})} - \text{Mean}_{(0\%\ \text{Control})}}\right)$$

Eight determinations were made for each control and two for the substance samples. The 0% control either contains no ATP or no substrate, the 100% control (fully active kinase) contains no test substance. The IC_{50} values were determined using GraphPadPrism.

The compounds according to the invention showed effective inhibition of Erk, PI3K, p38alpha and Jnk1 + Jnk2 with IC_{50} values of up to 6nM (see Table 2).

Table 2: MAPK and PI3Kalpha kinase assay test results (IC_{50} [µM] at 10µM or 100µM* ATP)

Compound	Erk2	PI3Kalph	p38alpha	Jnk1 + Jnk2
1	1	0.9	>31.6	>31.6
25	0.076	1.5	>100	>31.6
30	0.392	0.37	>100	21.8
43	0.006	6.2	>100	5.5
44	2.5	3.8	>100	1.5
46	9.5	>100	0.495	>100
82	0.944	6.4	>31.6	1.1
124	0.062	0.49	>100	1.0
146	0.155	1.1	>100	3.3
147	0.711	4.1	>100	14.2
148	1.8	1.4	>100	13.7
149	0.954	3.5	>100	>31.6
150	18.7	0.129	18.1	>100
151	0.104	1.5	>100	2.9
152	1.9	5.3	>100	12.1
153	0.939	0.612	>100	6.7
154	0.592	0.984	>31.6	2.8
155	>100	5	>100	7.8
156	0.138	0.425	>100	2.1
157	>100	0.348	>100	28.5
158	>100	0.186	>100	>31.6
159	>100	0.147	>100	12.6
160	5.8	2.9	>31.6	>31.6
161	>100	1.1	>100	>100
162	>100	0.19	>100	>31.6
163	26.9	0.096	>100	>31.6
164	19.6	0.444	>100	24.3
165	19.4	1.2	>100	27.1
166	13.7	1.3	>100	21.9
167	>100	1.1	>100	27.3
168	0.15	0.612	>100	2.5

169	2.7	3.7	>100	9.5
170	0.103	2.4	>31.6	1.1
171	0.084	3	>100	1.4
172	0.41	4	>100	4
173	0.107	2.4	>100	2.9
174	4.9	3	>31.6	4.6
175	0.191	0.458	>100	2.5
177	>31.6	0.295	>100	3.9
178	>100	0.164	>31.6	2.3
179	8	0.202	1.4	8.1
180	15.7	1.1	>100	8.6
181	1.7	0.739	>100	4.3
182	>31.6	1.1	>100	21
183	0.203	2.8	>100	4.7
184	>100	0.133	>100	6.3
185	>31.6	0.154	>100	4.3
186	0.223	3.8	>100	2.5
187	16.6	0.712	>31.6	>100
188	>100	2.8	>100	>31.6
189	20.3	0.237	>100	6.2
190	>100	0.271	>100	31
192	31.6	0.422	>100	1.8
193	0.212	2.2	>100	1.5

III.2A Cellular assay: testing for anti-proliferative effect (XTT assay)

The principle of this test is based on the intracellular reduction of the tetrazolium dye XTT (sodium 3'-[1-(phenylaminocarbonyl)-3,4-tetrazolium]-bis(4-methoxy-6-nitro)benzene sulfonic acid, Sigma) to a formazan dye by mitochondrial dehydrogenases. The dye is only formed by metabolically active cells and its photometrically measurable intensity is a quantitative indicator for the presence of living cells. The reduction of dye formation by

incubation of the cells with substances serves as a parameter for the anti-proliferative effect.

Testing

The tumour cell lines (ATCC) were injected into 96-well microtitre plates in a defined cell number (5000 cells/ well for BxPC3 and Hct116; 10000 cells/ well for MDA MB468) and then incubated overnight in an incubator at 37°C, 5% CO_2 and 95% air humidity. The test substances were prepared as stock solutions (10mM) in DMSO. To determine the EC_{50} values the potential inhibitor substances were added to the cells in quarter-logarithmically graded dilutions, resulting in final concentrations of 0.28µM-50µM. The cell plates were then incubated for 45 h in an incubator at 37°C, 5% CO_2 and 95% air humidity.

For the detection reaction the substrate XTT was mixed with PMS (N-Methyl dibenzopyrazine methylsulfate, Sigma) and added to the cells so that a final concentration of 325 µg XTT/ml and 2.5 µg PMS/ml was obtained. It was then incubated for 3h at 37°C, 95% air humidity. The formazan salt formed by the cellular dehydrogenases could then be quantified by adsorption at 490 nm.

Evaluation

The % inhibition value was evaluated by means of the following formula from the values for the optical densities measured in each case at 490 nm:

$$\%\ \text{Inhibition of cell proliferation}_{(\text{Sample})} = 100 - \left(100x \frac{\text{Mean}_{(\text{Sample})} - \text{Mean}_{(0\%\ \text{Control})}}{\text{Mean}_{(100\%\ \text{Control})} - \text{Mean}_{(0\%\ \text{Control})}} \right)$$

Eight determinations were made for each control and two for the substance samples. The 0% control contains no cells, the 100% control (proliferation control) contains no test substance. The EC_{50} values were determined using GraphPadPrism.

The compounds according to the invention showed partly effective inhibition of the cell proliferation with EC_{50} values of < 1 µM (see Table 3).

Table 3: XTT assay test results (EC50 [µM])

Compound	BxPC3	MDA-MB468	Hct116
30	12	4	6
124	10	10	1,5
146	>50	ca. 20	9.3
150	0.9	4.3	2.3
153	>25	24	6
156	8.9	15	1.4
157	>25	3.5	4.4
164	>50	5.2	>25
169	not tested	5.7	2.8
173	not tested	>25	9
175	not tested	>50	4.4
176	not tested	17	11.8
183	not tested	4.3	2.1
191	not tested	8.5	5.5
193	not tested	4.4	2.1
Ly294002	25	20	17

It was surprisingly found that the PI3K inhibitor Ly294002 known from the literature only showed weak anti-proliferative effects on the cell lines used compared to the Exemplary Embodiments.

III.2B Cellular assay: testing for substrate inhibition (Western Blotting)

This method can be used to predict whether the kinase modulator under study also achieves the desired effect in a cellular context, i.e. in this case, a substrate protein downstream of the target kinase is investigated for its phosphorylation status. For this purpose, the cells incubated with substance are lysed and the total protein separated on a reducing polyacrylamide gel. The proteins are then transferred to a PVDF membrane by means of Western Blotting and the substrate bands sought are made visible with specific antibodies and a suitable detection method. The substrate proteins downstream of the target kinases are detected simultaneously with a respectively special anti-phospho-antibody and at the same time a total antibody which recognizes the substrate total protein. This simultaneous measurement can be made using the duplex technology of the ODYSSEY imagers (LiCOR). The intensity of the total substrate bands is used for normalising or quantifying the phosphorylation inhibition or activation.

Testing

Suitable tumour cell lines (e.g. BxPC3, Hct116 or MDA MB468) were injected into six-well microtitre plates in a defined cell number (e.g. 350 000 cells/ well for BxPC3 and Hct116) in the respective standard complete medium and then incubated overnight at 37°C, 5% CO_2 and 95% air humidity. The cells were then incubated for a further 24 h under serum-reduced conditions i.e. in the respective medium but with only 0.25% serum. The test substances were prepared as stock solutions (10mM) in DMSO and incubated with the cells in final concentrations of 5, 15.8 and 50µM for 5 h. This was followed by cell lysis in 25mM Tris, 150mM NaCl, 10mM Na-pyrophosphate, 2mM EGTA, 25mM ß-glycerophosphate, 25mM

NaF, 10% glycerine, 0.75% NP-40, 100µM $NaVO_4$ buffer. Following protein quantification by means of BCA (bicinchonic acid protein assay kit, Sigma) Assay, protein quantities of about 20 µg per track were separated on a Lämmli polyacrylamide gel and then transferred to a PVDF membrane (Millipore) by means of Semi-Dry Western-Blotting at 0.8 mA/cm^2 for 1h. This was followed by pre-hybridisation of the membrane for 1 hour in I-block reagent (Applied Biosystems) and incubation overnight with the specific antibodies. To determine the Erk and PI3K inhibition, the respectively downstream substrates Rsk1 were detected with the total antibody (Rsk #sc-231g C-21, Santa Cruz) and the phospho-antibody (Phospho-p90RSK (S380) #9341, NEB Cell Signalling) and Akt was detected with the total antibody (Akt1 #sc-1618 C-20, Santa Cruz) and the phospho-antibody (Phospho-Akt (Ser 473) #9271, NEB Cell Signaling). After washing the membrane, secondary antibody incubation was carried out with anti-rabbit IR Dye 800 (#611-732-127, Rockland) for the phospho-antibody and anti-goat Alexa Fluor 680 (#A-21081, Molecular Probes) for the total protein-antibody. After incubating for 30 min at room temperature in the dark, the hybridisation of the detection antibody on the membrane was detected by scanning in the ODYSSEY imager (LiCOR).

Evaluation

At concentrations of 5-50 µM, the compounds according to the invention exhibited dual inhibition of Erk (MAPK1/2) and PI3K (see Table 4) which are indicated by inhibition of the band intensity of both corresponding phospho-substrate proteins Rsk1 and Akt. The reduction of the fluorescence intensity of the phospho-substrate bands (pRsk and pAkt) is given in the table below as % inhibition and relates to the following formula:

$$\%\ Inhibition\ of\ Substrate\ phosphorylation_{(Sample)} = 100 - \left(100x \frac{Sample}{100\%Control}\right)$$

The band intensity (fluorescence intensity) of the respective non-inhibited (without substance) phospho-substrates was used as 100% control.

Table 4: Inhibition of cellular substrate phosphorylation (at 50 µM)

Compound	Erk →pRsk	PI3K →pAkt
30	90%	100%
124	90%	90%
146	100%	10%
150	0%	90%
173	90%	50%
183	80%	80%
Ly294002	0%	40%
Wortmannin	0%	100%

The PI3K inhibitor Ly294002 known from the literature showed only weak PI3K inhibition compared to the pyridopyrazine derivatives, i.e. inhibition of the PI3K substrate p-Akt and as predicted, no Erk inhibition or inhibition of the Erk substrate p-Rsk. Wortmannin - a further PI3K inhibitor known from the literature - showed complete inhibition of the PI3K substrate pAkt, but no Erk or p-RSK inhibition.

In contrast to the Exemplary Embodiments, both reference substances used here showed no dual inhibition, i.e. of Erk and PI3K simultaneously but only a PI3K inhibition.

Abbreviations

Akt of: murine Akt8 retrovirus or protein kinase B (PKB)
Ask1 apoptosis signal-regulating kinase
ATR ataxia-telangiectasia and Rad3-related
ATM Ataxia-telangiectasia mutated
Bag1 Bcl-2 associated athanogene-1
Bcl-2 B-cell leukemia/lymhoma-2 gene
DNA-PK DNA-dependent protein kinase
Erk extracellular signal-regulated kinase
Flt-3 fms like tyrosine kinase 3
GSK-3 Glycogen synthase kinase-3
hSMG-1 human ortholog of product of seven nematode gene-1
JAK-3 Janus kinase 3
JNK c-jun N-terminal kinase
MAPK mitogen activated protein kinase
Mek MAP or Erk kinase
mTOR mammalian target of rapamycin
PDGFR platelet derived growth factor receptor
PI3K phosphoinositol 3-kinase
PIKK phosphoinositol 3-kinase related kinase
PIP_2 phosphatidylinositol-biphosphate
PIP_3 phosphatidylinositol-triphosphate
PtdIns phosphatidylinositol
Raf rapid accelerated fibrosarcoma
Ras rat sarcoma
RTK receptor tyrosine kinase
SAPK stress-activated protein kinase
Ser Serine
Syk spleen tyrosine kinase
Thr Threonine
Tyr Tyrosine
VEGFR vascular endothelial growth factor receptor

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proliferation in acute myeloid leukemia. Blood. 2005 Aug 1;106(3):1063-6.

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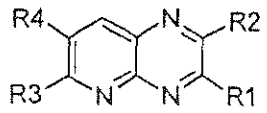
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The claims defining the invention are as follows:

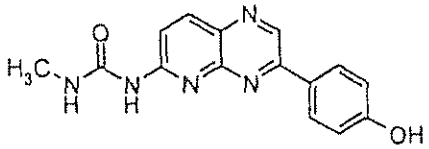
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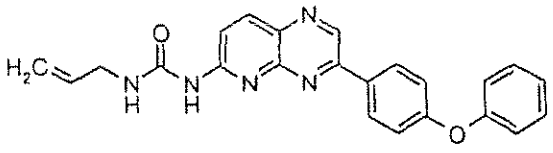
(I)

selected from the group consisting of

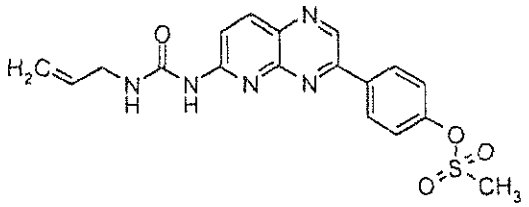
Compound 38 1-[3-(4-Hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-methyl-urea



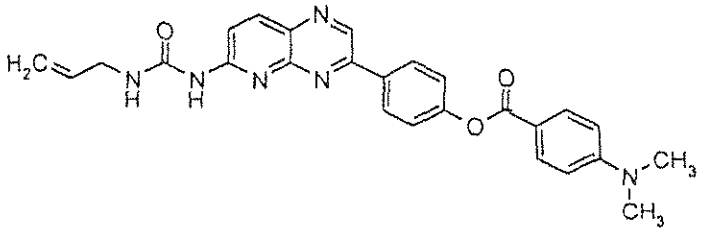
Compound 39 1-Allyl-3-[3-(4-phenoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



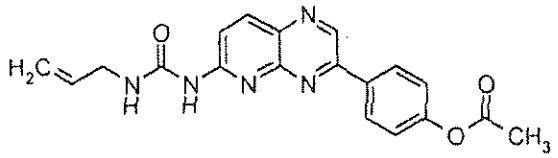
Compound 40 Methane sulfonic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl-ester



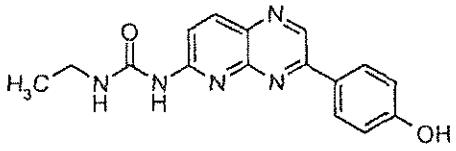
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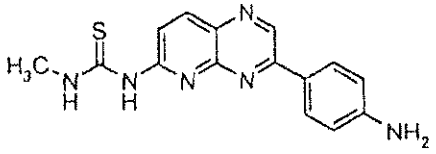
Compound 42 Acetic acid-4-[6-(3-allyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl-ester



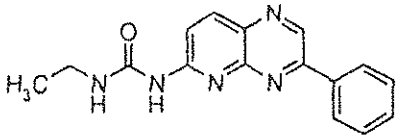
Compound 43 1-Ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



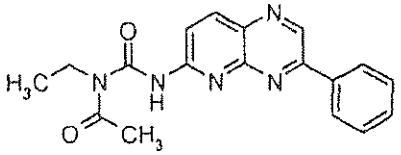
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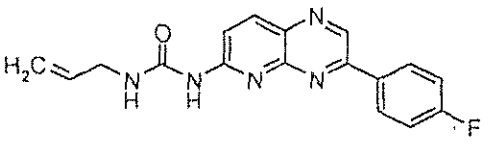
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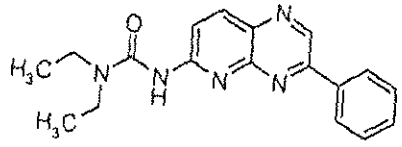
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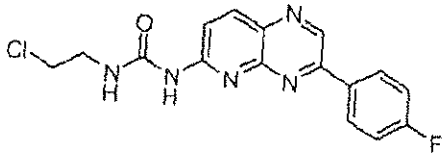
Compound 47 1-Allyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



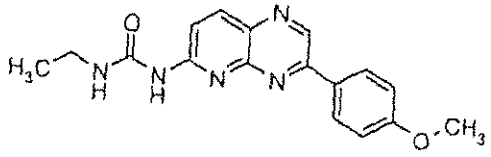
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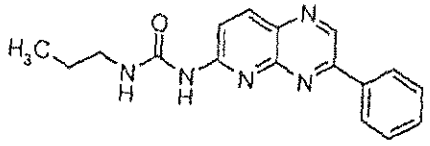
Compound 49 1-(2-Chloro-ethyl)-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



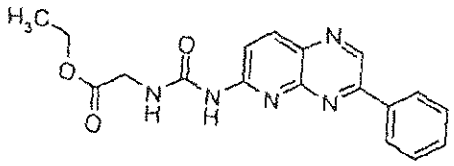
Compound 50 1-Ethyl-3-[3-(4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



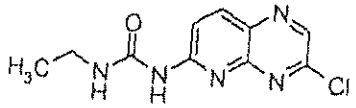
Compound 51 1-(3-Phenyl-pyrido[2,3-b]pyrazin-6-yl)-3-propyl-urea



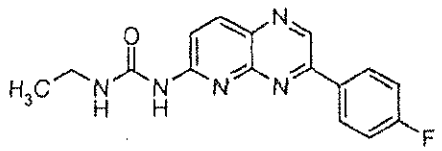
Compound 52 [3-(3-Phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-acetic acid-ethyl-ester



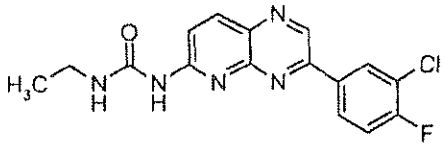
Compound 53 1-(3-Chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



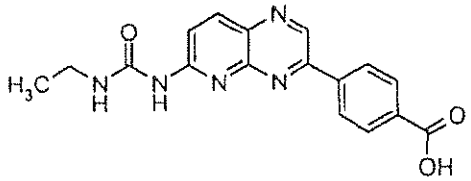
Compound 54 1-Ethyl-3-[3-(4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



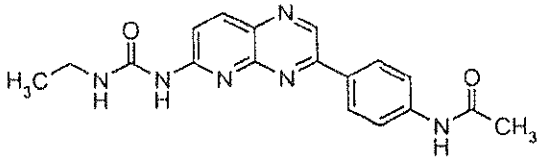
Compound 55 1-[3-(3-Chloro-4-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



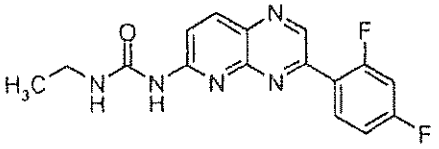
Compound 56 4-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid



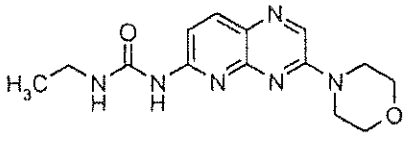
Compound 57 N-{4-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acetamide



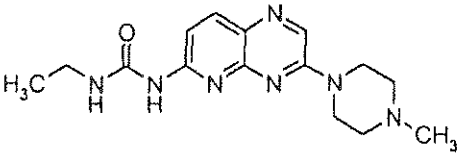
Compound 58 1-[3-(2,4-Difluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



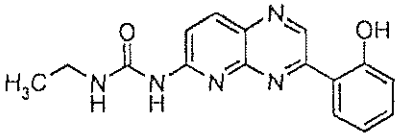
Compound 59 1-Ethyl-3-(3-morpholin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



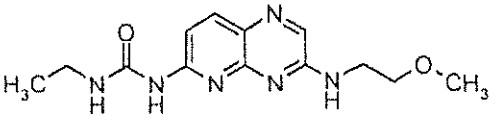
Compound 60 1-Ethyl-3-[3-(4-methyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



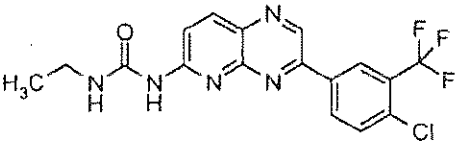
Compound 61 1-Ethyl-3-[3-(2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



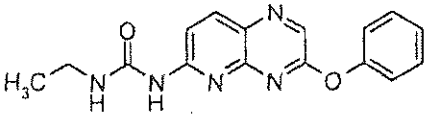
Compound 62 1-Ethyl-3-[3-(2-methoxy-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



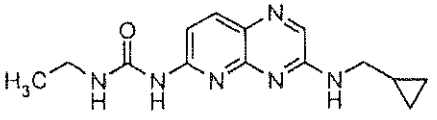
Compound 63 1-[3-(4-Chloro-3-trifluoromethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



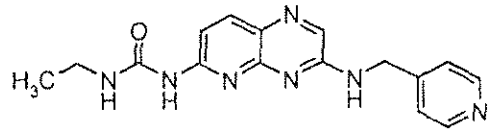
Compound 64 1-Ethyl-3-(3-phenoxy-pyrido[2,3-b]pyrazin-6-yl)-urea



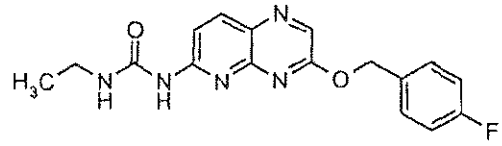
Compound 65 1-[3-(Cyclopropylmethyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



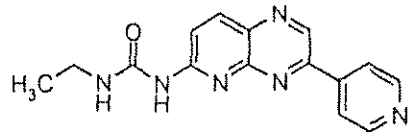
Compound 66 1-Ethyl-3-{3-[(pyridin-4-ylmethyl)-amino]-pyrido[2,3-b]pyrazin-6-yl}-urea



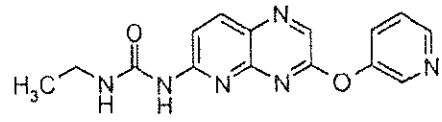
Compound 67 1-Ethyl-3-[3-(4-fluoro-benzyloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



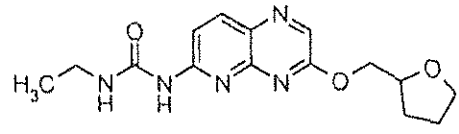
Compound 68 1-Ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



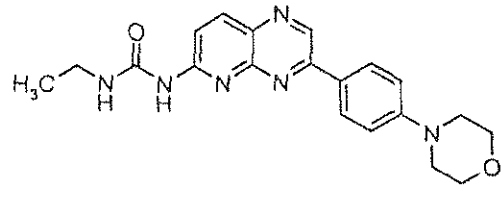
Compound 69 1-Ethyl-3-[3-(pyridin-3-yloxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



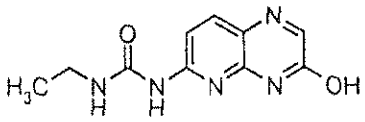
Compound 70 1-Ethyl-3-[3-(tetrahydro-furan-2-ylmethoxy)-pyrido[2,3-b]pyrazin-6-yl]-urea



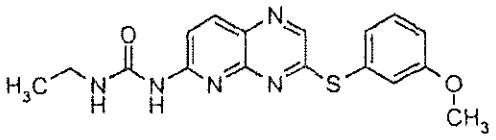
Compound 71 1-Ethyl-3-[3-(4-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



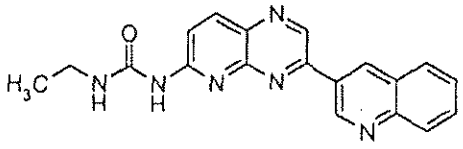
Compound 72 1-Ethyl-3-(3-hydroxy-pyrido[2,3-b]pyrazin-6-yl)-urea



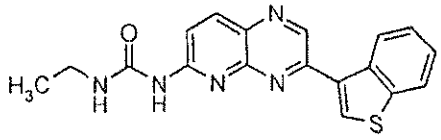
Compound 73 1-Ethyl-3-[3-(3-methoxy-phenylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



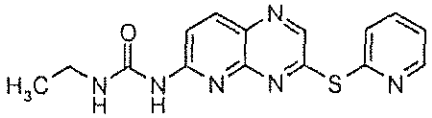
Compound 74 1-Ethyl-3-(3-quinolin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



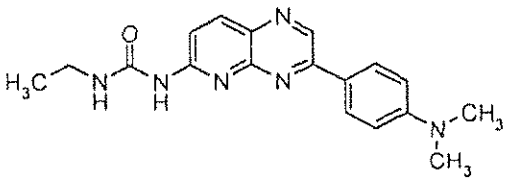
Compound 75 1-(3-Benzo[b]thiophen-3-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



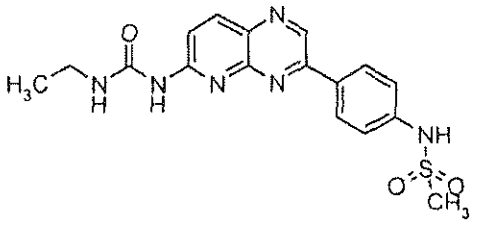
Compound 76 1-Ethyl-3-[3-(pyridin-2-ylsulfanyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



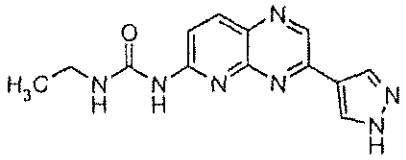
Compound 77 1-[3-(4-Dimethylamino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



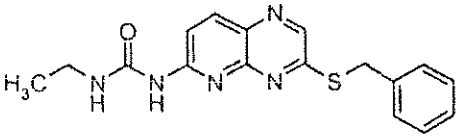
Compound 78 N-{4-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-*methansulfonamide*



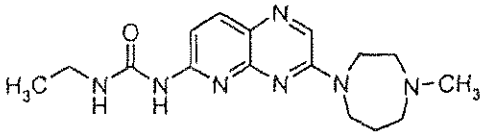
Compound 79 1-Ethyl-3-[3-(1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



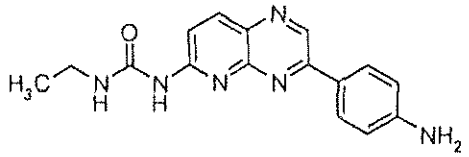
Compound 80 1-(3-Benzylsulfanyl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



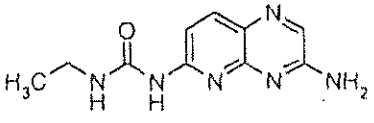
Compound 81 1-Ethyl-3-[3-(4-methyl-[1,4]diazepan-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



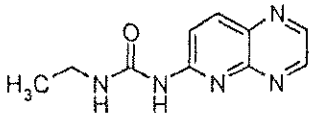
Compound 82 1-[3-(4-Amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



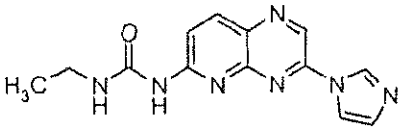
Compound 83 1-(3-Amino-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



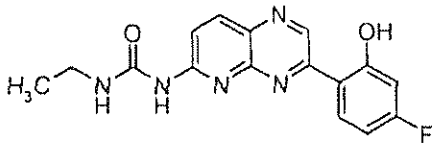
Compound 84 1-Ethyl-3-pyrido[2,3-b]pyrazin-6-yl-urea



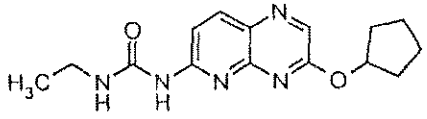
Compound 85 1-Ethyl-3-(3-imidazol-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



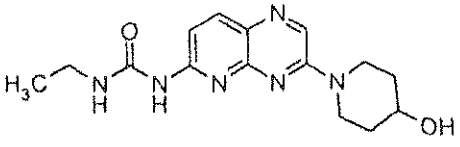
Compound 86 1-Ethyl-3-[3-(4-fluoro-2-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



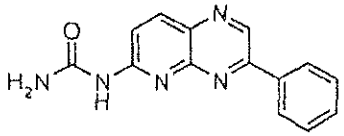
Compound 87 1-(3-Cyclopentyloxy-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



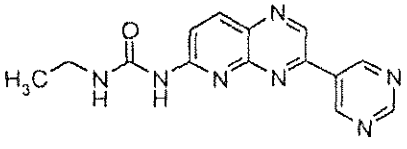
Compound 88 1-Ethyl-3-[3-(4-hydroxy-piperidin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



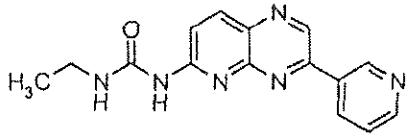
Compound 89 (3-Phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



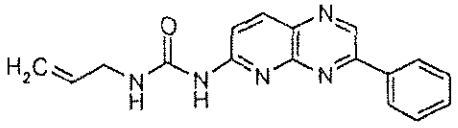
Compound 90 1-Ethyl-3-(3-pyrimidin-5-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



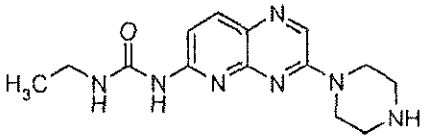
Compound 91 1-Ethyl-3-(3-pyridin-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



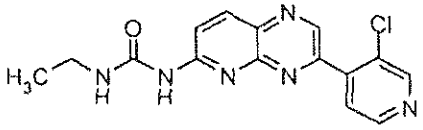
Compound 92 1-Allyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



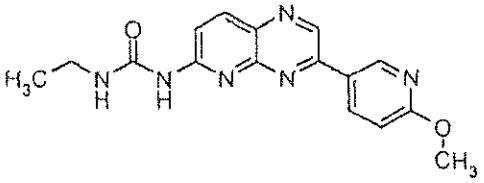
Compound 93 1-Ethyl-3-(3-piperazin-1-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



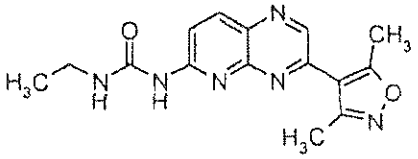
Compound 94 1-[3-(3-Chloro-pyridin-4-ylmethyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



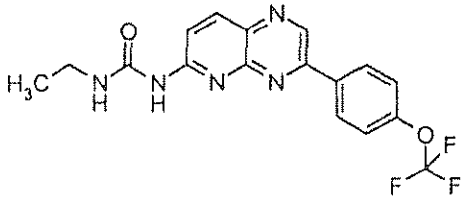
Compound 95 1-Ethyl-3-[3-(6-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



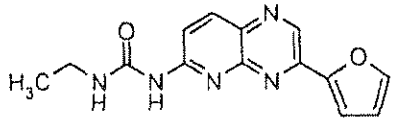
Compound 96 1-[3-(3,5-Dimethyl-isoxazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



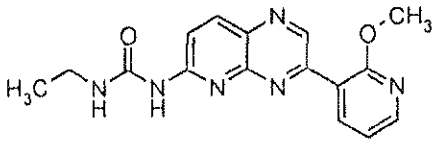
Compound 97 1-Ethyl-3-[3-(4-trifluoromethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



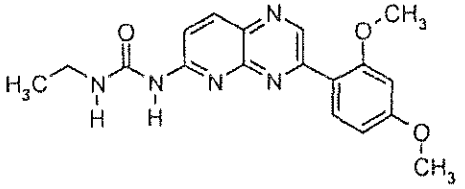
Compound 98 1-Ethyl-3-(3-furan-2-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



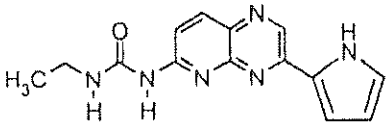
Compound 99 1-Ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



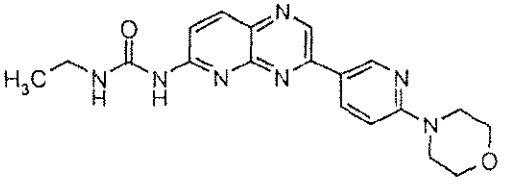
Compound 100 1-[3-(2,4-Dimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



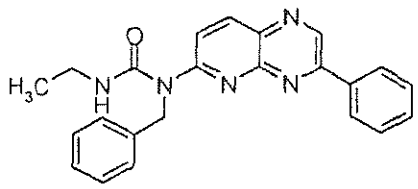
Compound 101 1-Ethyl-3-[3-(1H-pyrrol-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



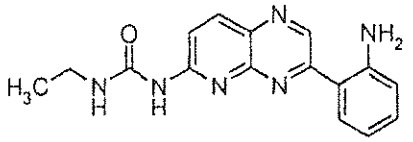
Compound 102 1-Ethyl-3-[3-(6-morpholin-4-yl-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



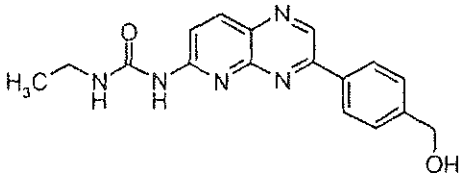
Compound 103 1-Benzyl-3-ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



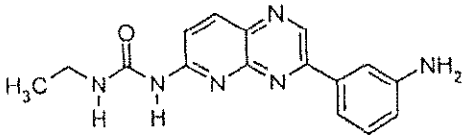
Compound 104 1-[3-(2-Amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



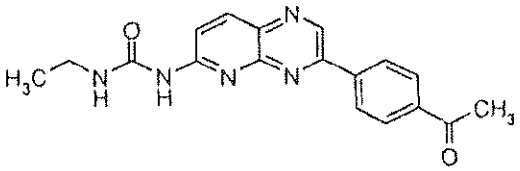
Compound 105 1-Ethyl-3-[3-(4-hydroxymethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



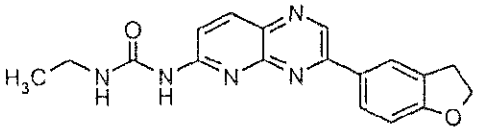
Compound 106 1-[3-(3-Amino-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



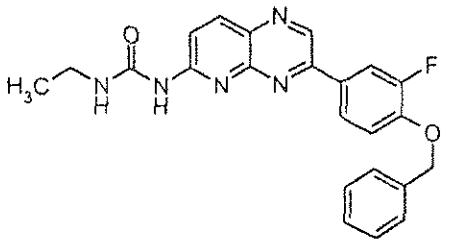
Compound 107 1-[3-(4-Acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



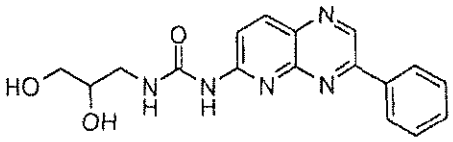
Compound 108 1-[3-(2,3-Dihydro-benzofuran-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



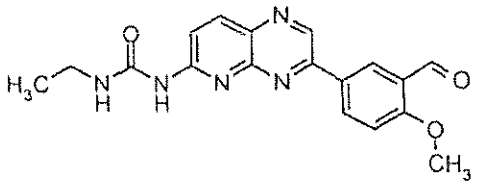
Compound 109 1-[3-(4-Benzyloxy-3-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



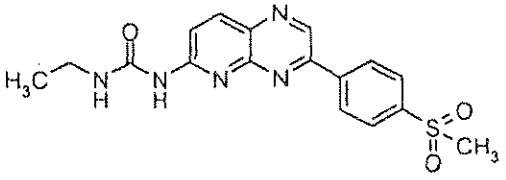
Compound 110 1-(2,3-Dihydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



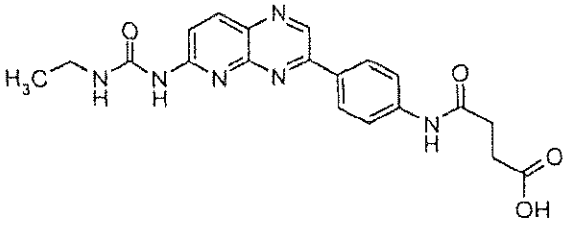
Compound 111 1-Ethyl-3-[3-(3-formyl-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



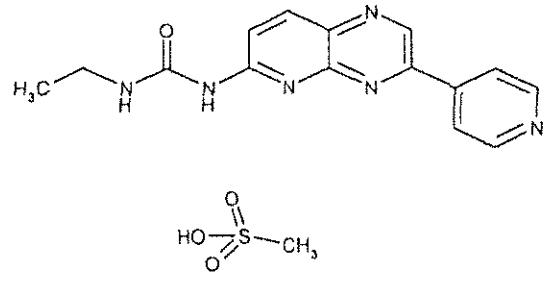
Compound 112 1-Ethyl-3-[3-(4-methansulfonyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



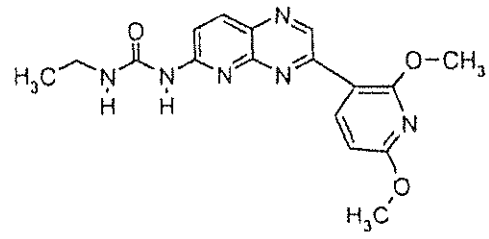
Compound 113 N-{4-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-succinamid acid



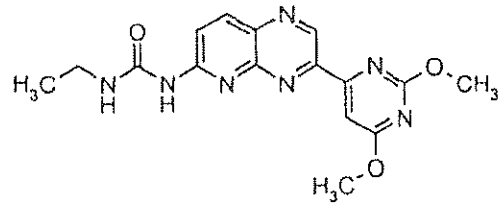
Compound 114 1-Ethyl-3-(3-pyridin-4-yl-pyrido[2,3-b]pyrazin-6-yl)-urea Methane sulfonic acid salt (free base)



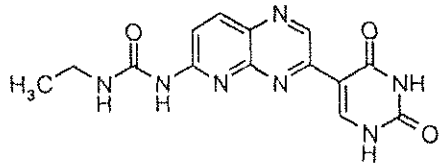
Compound 115 1-[3-(2,6-Dimethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



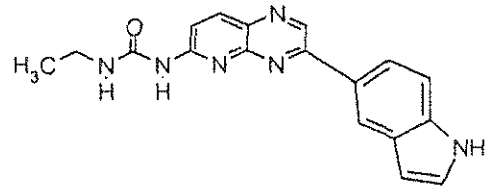
Compound 116 1-[3-(2,6-Dimethoxy-pyrimidin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



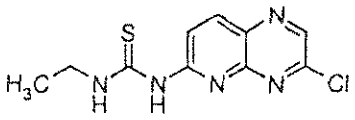
Compound 117 1-[3-(2,4-Dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



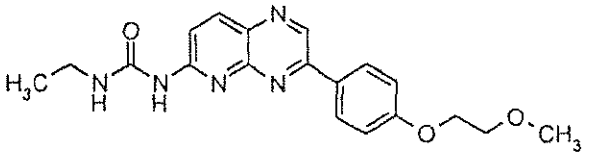
Compound 118 1-Ethyl-3-[3-(1H-indol-5-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



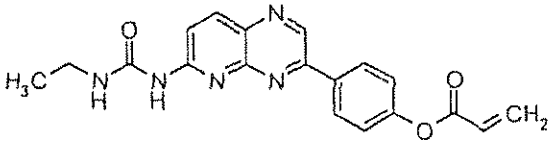
Compound 119 1-(3-Chloro-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-thiourea



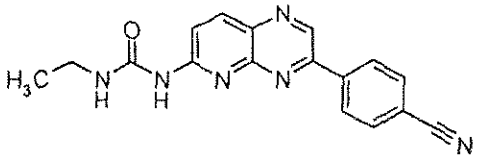
Compound 120 1-Ethyl-3-{3-[4-(2-methoxy-ethoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea



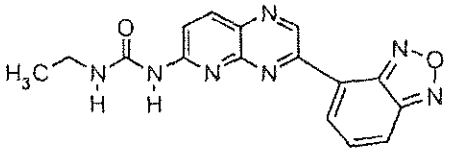
Compound 121 Acrylic acid-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl-ester



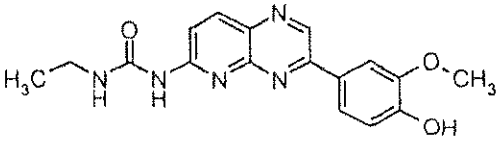
Compound 122 1-[3-(4-Cyano-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



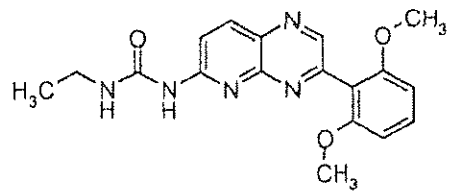
Compound 123 1-(3-Benzo[1,2,5]oxadiazol-4-yl-pyrido[2,3-b]pyrazin-6-yl)-3-ethyl-urea



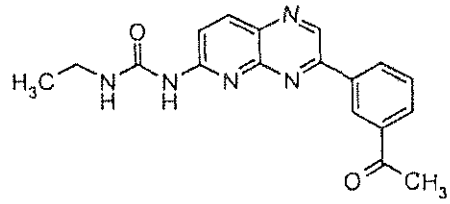
Compound 124 1-Ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



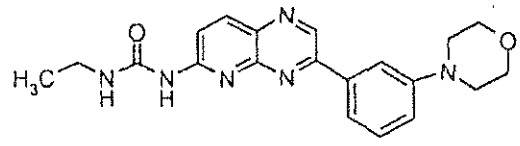
Compound 125 1-[3-(2,6-Dimethoxy-phenyl)-pyrido [2,3-b]pyrazin-6-yl]-3-ethyl-urea



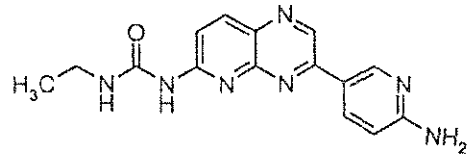
Compound 126 1-[3-(3-Acetyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



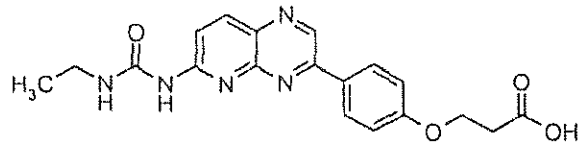
Compound 127 1-Ethyl-3-[3-(3-morpholin-4-yl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



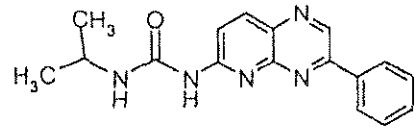
Compound 128 1-[3-(6-Amino-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



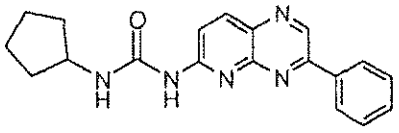
Compound 129 3-{4-[6-(3-Ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenoxy}-propionic acid



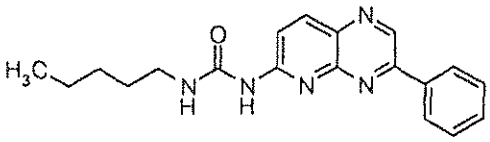
Compound 130 1-Isopropyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



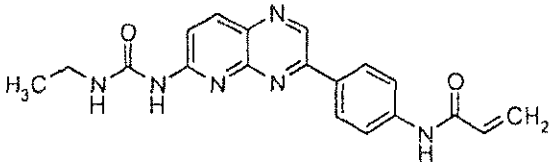
Compound 131 1-Cyclopentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



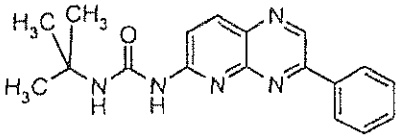
Compound 132 1-Pentyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



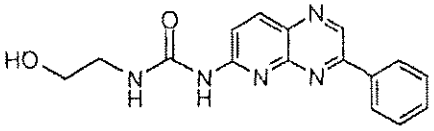
Compound 133 N-{4-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-phenyl}-acrylamide



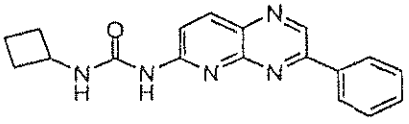
Compound 134 1-tert-Butyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



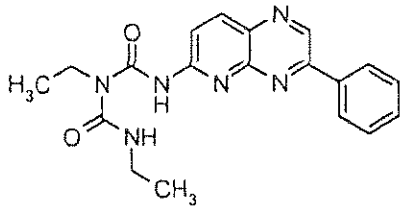
Compound 135 1-(2-Hydroxy-ethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



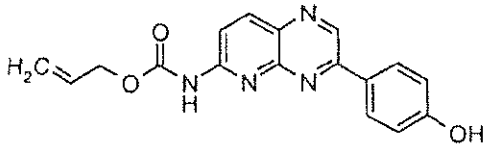
Compound 136 1-Cyclobutyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



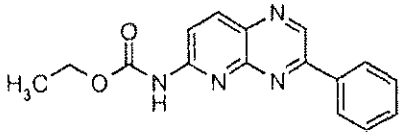
Compound 138 1-Ethyl-1-(Ethylcarbamoyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



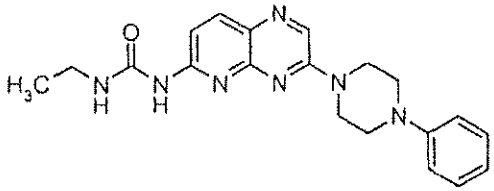
Compound 139 [3-(4-Hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-carbamic acid-allyl-ester



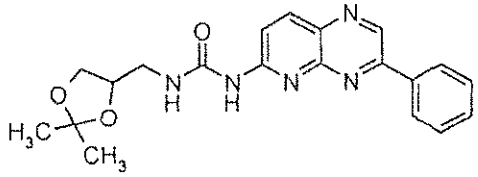
Compound 140 (3-Phenyl-pyrido[2,3-b]pyrazin-6-yl)-carbamic acid-ethyl-ester



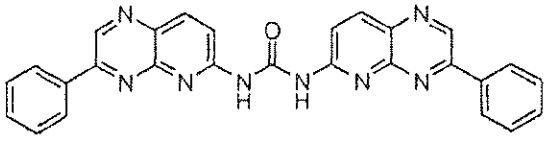
Compound 141 1-Ethyl-3-[3-(4-phenyl-piperazin-1-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



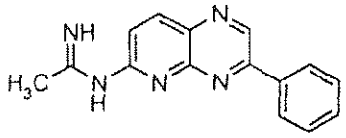
Compound 142 1-(2,2-Dimethyl-[1,3]dioxolan-4-ylmethyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



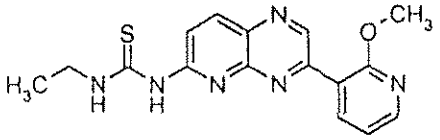
Compound 143 1,3-Bis-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



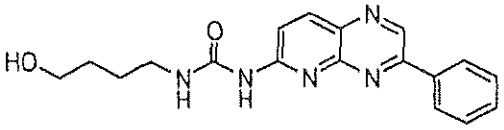
Compound 144 N-(3-Phenyl-pyrido[2,3-b]pyrazin-6-yl)-acetamidine



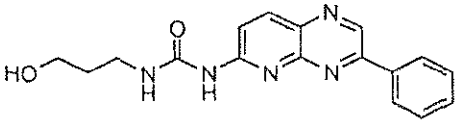
Compound 145 1-Ethyl-3-[3-(2-methoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



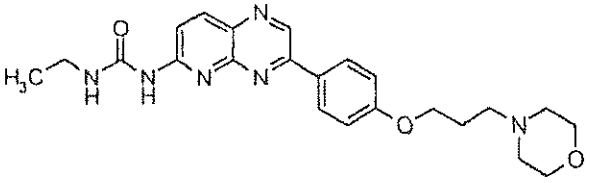
Compound 146 1-(4-Hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



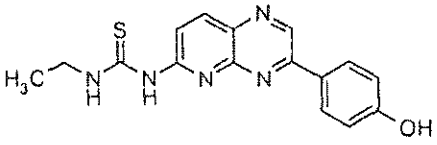
Compound 147 1-(3-Hydroxy-propyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



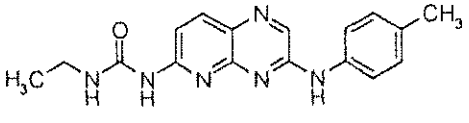
Compound 148 1-Ethyl-3-{3-[4-(3-morpholin-4-yl-propoxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-urea



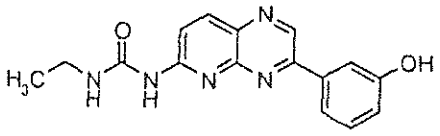
Compound 149 1-Ethyl-3-[3-(4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



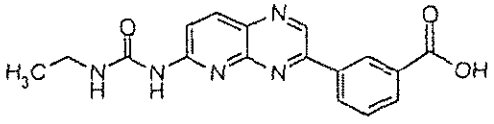
Compound 150 1-Ethyl-3-(3-p-tolylamino-pyrido[2,3-b]pyrazin-6-yl)-urea



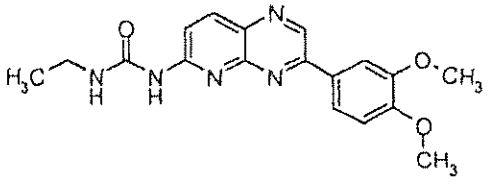
Compound 151 1-Ethyl-3-[3-(3-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



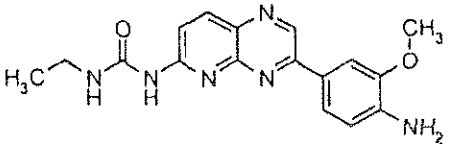
Compound 152 3-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzoic acid



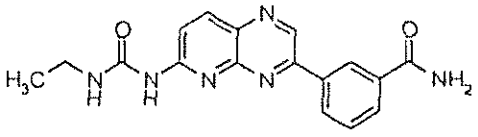
Compound 153 1-[3-(3,4-Dimethoxy-phenyl)-pyrido [2,3-b]pyrazin-6-yl]-3-ethyl-urea



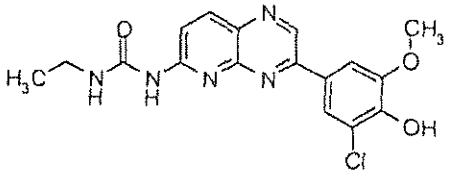
Compound 154 1-[3-(4-Amino-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



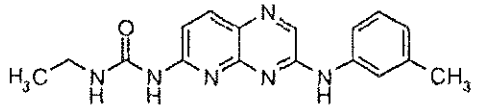
Compound 155 3-[6-(3-Ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-benzamide



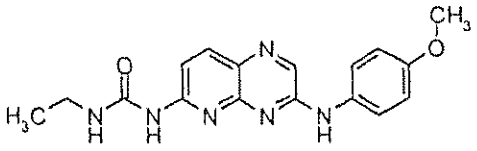
Compound 156 1-[3-(3-Chloro-4-hydroxy-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



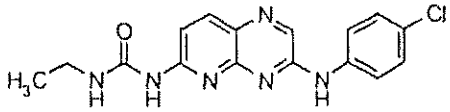
Compound 157 1-Ethyl-3-(3-m-tolylamino-pyrido-[2,3-b]pyrazin-6-yl)-urea



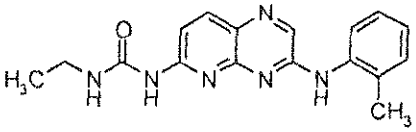
Compound 158 1-Ethyl-3-[3-(4-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



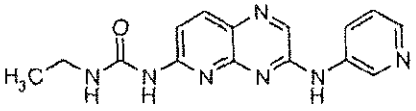
Compound 159 1-[3-(4-Chloro-phenylamino)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea



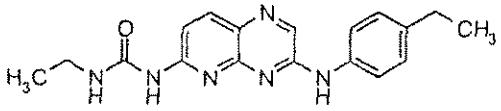
Compound 160 1-Ethyl-3-(3-o-tolylamino-pyrido[2,3-b]-pyrazin-6-yl)-urea



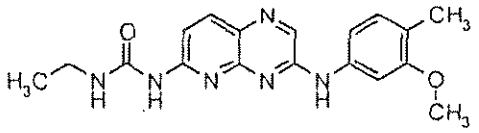
Compound 161 1-Ethyl-3-[3-(pyridin-3-ylamino)-pyrido-[2,3-b]pyrazin-6-yl]-urea



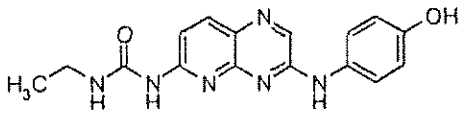
Compound 162 1-Ethyl-3-[3-(4-ethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



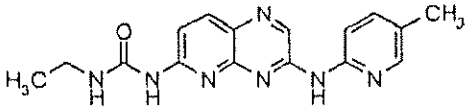
Compound 163 1-Ethyl-3-[3-(3-methoxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



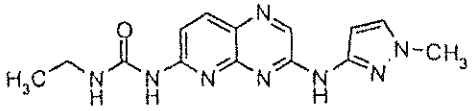
Compound 164 1-Ethyl-3-[3-(4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



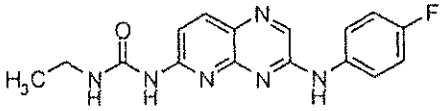
Compound 165 1-Ethyl-3-[3-(5-methyl-pyridin-2-yl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



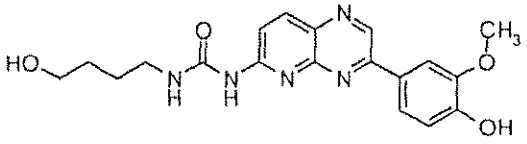
Compound 166 1-Ethyl-3-[3-(1-methyl-1H-pyrazol-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



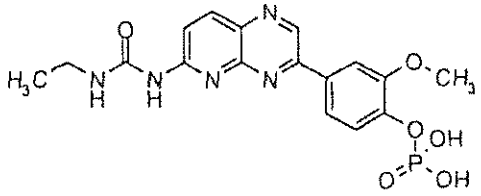
Compound 167 1-Ethyl-3-[3-(4-fluoro-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



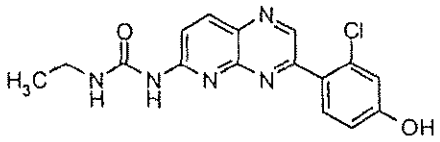
Compound 168 1-(4-Hydroxy-butyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



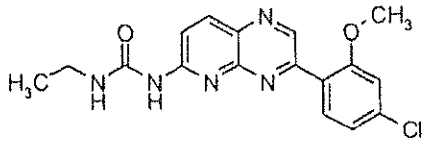
Compound 169 Phosphoric acid-mono-{4-[6-(3-ethyl-ureido)-pyrido-[2,3-b]pyrazin-3-yl]-2-methoxy-phenyl}-ester



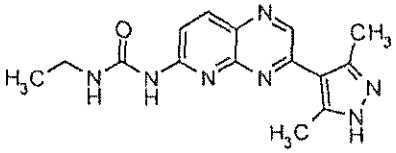
Compound 170 1-[3-(2-Chloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



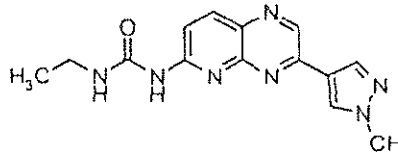
Compound 171 1-[3-(4-Chloro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



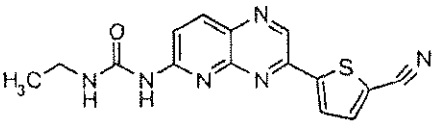
Compound 172 1-[3-(3,5-Dimethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



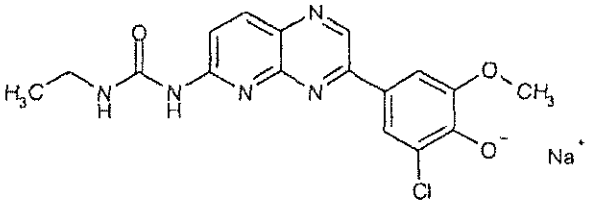
Compound 173 1-Ethyl-3-[3-(1-methyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



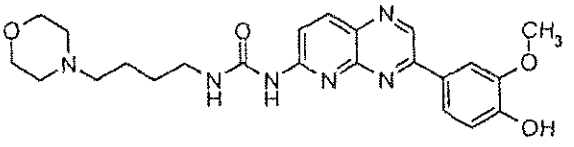
Compound 174 1-[3-(5-Cyano-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



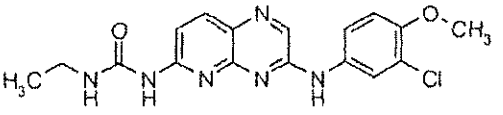
Compound 175 Sodium 2-chloro-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-6-methoxy-phenolate



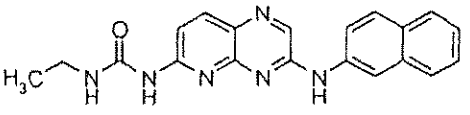
Compound 176 1-[3-(4-Hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(4-morpholin-4-yl-butyl)-urea



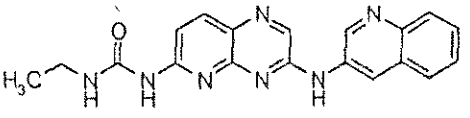
Compound 177 1-[3-(3-Chloro-4-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



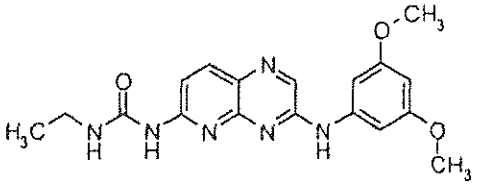
Compound 178 1-Ethyl-3-[3-(naphthalin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



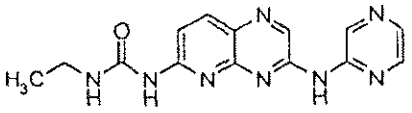
Compound 179 1-Ethyl-3-[3-(quinolin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



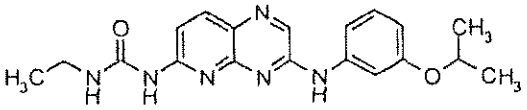
Compound 180 1-[3-(3,5-Dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



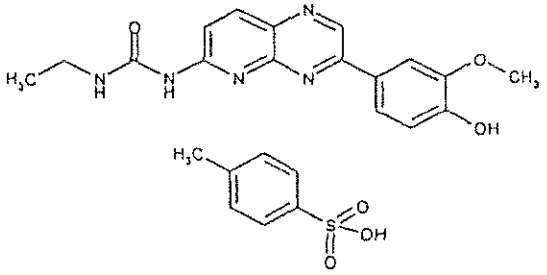
Compound 181 1-Ethyl-3-[3-(pyrazin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



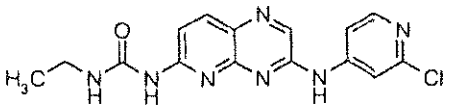
Compound 182 1-Ethyl-3-[3-(3-isopropoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



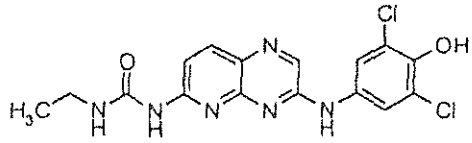
Compound 183 1-Ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea p-Toluolsulfonat



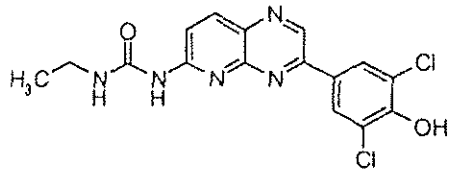
Compound 184 1-[3-(2-Chloro-pyridin-4-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



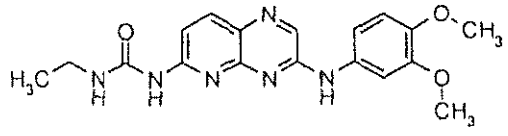
Compound 185 1-[3-(3,5-Dichloro-4-hydroxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



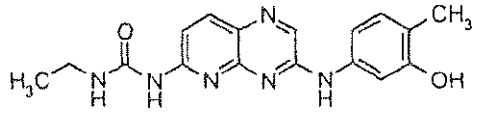
Compound 186 1-[3-(3,5-Dichloro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



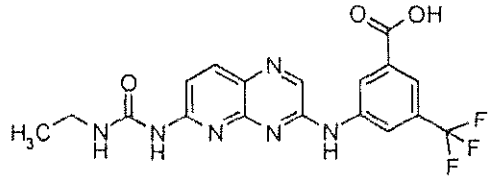
Compound 187 1-[3-(3,4-Dimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



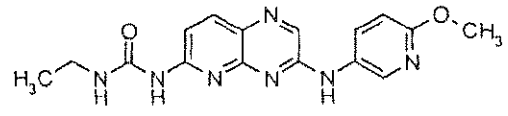
Compound 188 1-Ethyl-3-[3-(3-hydroxy-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



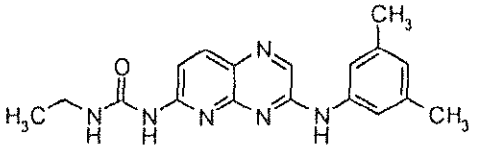
Compound 189 3-[6-(3-Ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-ylamino]-5-trifluoromethyl-benzoic acid



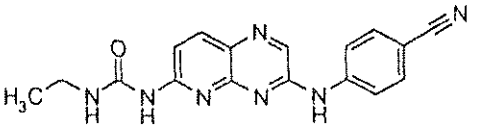
Compound 190 1-Ethyl-3-[3-(6-methoxy-pyridin-3-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



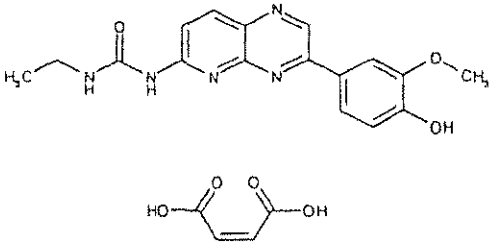
Compound 191 1-[3-(3,5-Dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



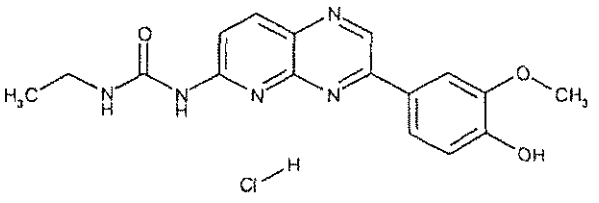
Compound 192 1-[3-(4-Cyano-phenylamino)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea



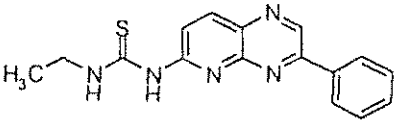
Compound 193 1-Ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea (Z)-but-2-endicarbonic acid salt



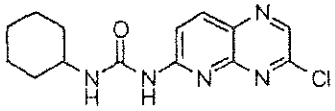
Compound 194 1-Ethyl-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea Hydrochloride



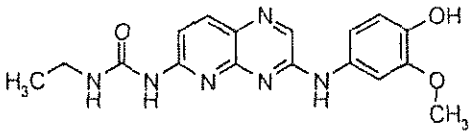
Compound 195 1-Ethyl-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-thiourea



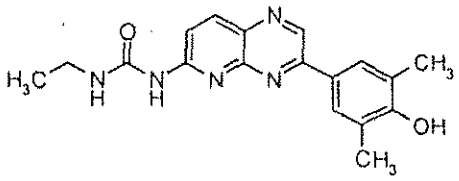
Compound 196 1-(3-Chloro-pyrido[2,3-b]pyrazin-6-yl)-3-cyclohexyl-urea



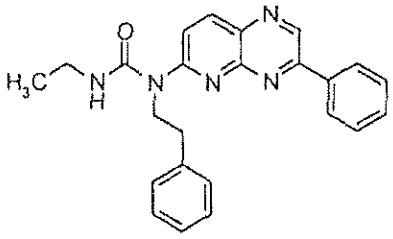
Compound 197 1-Ethyl-3-[3-(4-hydroxy-3-methoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



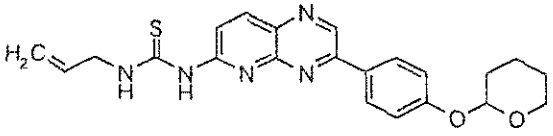
Compound 198 1-Ethyl-3-[3-(4-hydroxy-3,5-dimethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



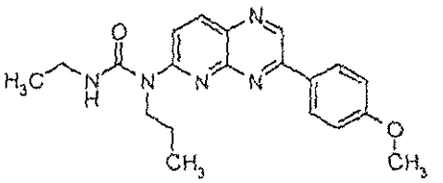
Compound 199 3-Ethyl-1-phenethyl-1-(3-phenyl- pyrido[2,3-b]pyrazin-6-yl)-urea



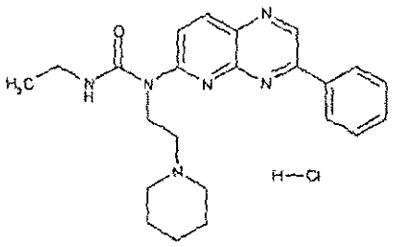
Compound 200 1-Allyl-3-{3-[4-(tetrahydro-pyran-2-yloxy)-phenyl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



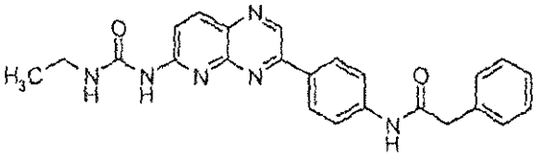
Compound 201 3-Ethyl-1-[3-(4-methoxy-phenyl)- pyrido[2,3-b]pyrazin-6-yl]-1-propyl-urea



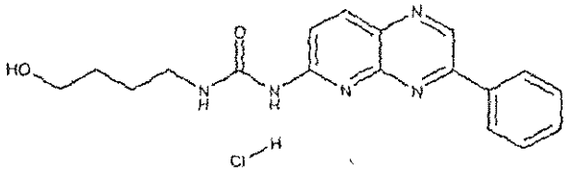
Compound 202 3-Ethyl-1-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-1-(2-piperidin-1-yl-ethyl)-urea Hydrochloride



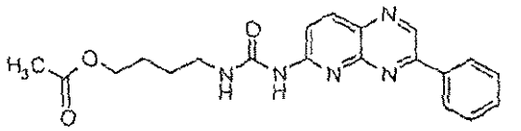
Compound 203 N-{4-[6-(3-Ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-phenyl}-2-phenyl acetamide



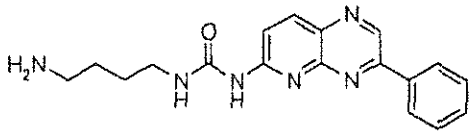
Compound 204 1-(4-Hydroxy-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea Hydrochloride



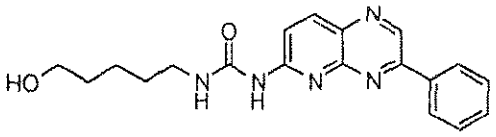
Compound 205 Acetic acid-4-[3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl ester



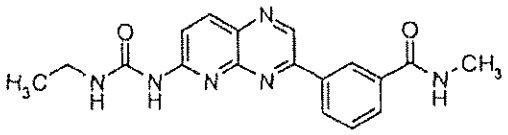
Compound 206 1-(4-Amino-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



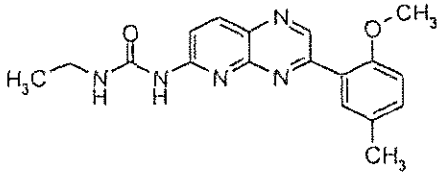
Compound 207 1-(5-Hydroxy-pentyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



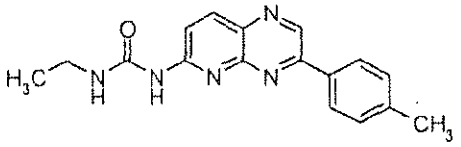
Compound 208 3-[6-(3-Ethyl-ureido)-pyrido[2,3-b]-pyrazin-3-yl]-N-methyl-benzamide



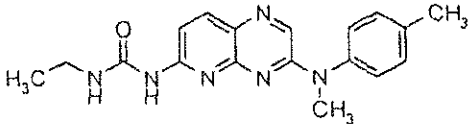
Compound 209 1-Ethyl-3-[3-(2-methoxy-5-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



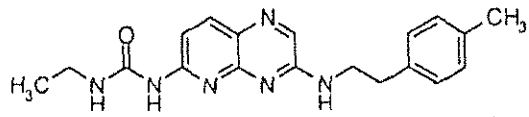
Compound 210 1-Ethyl-3-(3-p-tolyl-pyrido[2,3-b] pyrazin-6-yl)-urea



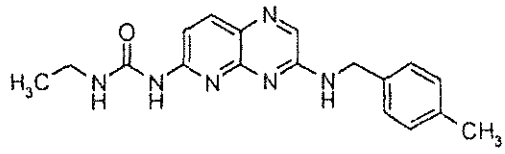
Compound 211 1-Ethyl-3-[3-(methyl-p-tolyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



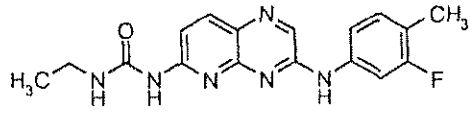
Compound 212 1-Ethyl-3-[3-(2-p-tolyl-ethylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



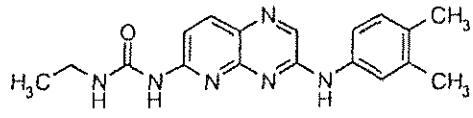
Compound 213 1-Ethyl-3-[3-(4-methyl-benzylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



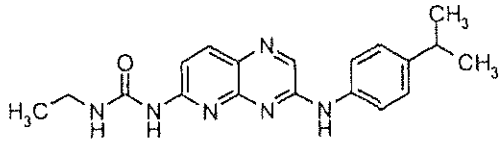
Compound 214 1-Ethyl-3-[3-(3-fluoro-4-methyl-phenyl-amino)-pyrido[2,3-b]pyrazin-6-yl]-urea



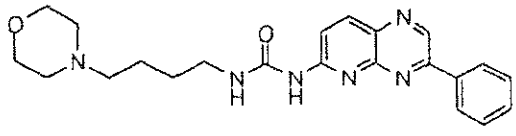
Compound 215 1-[3-(3,4-Dimethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



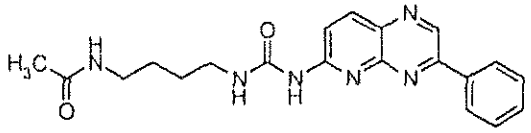
Compound 216 1-Ethyl-3-[3-(4-isopropyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



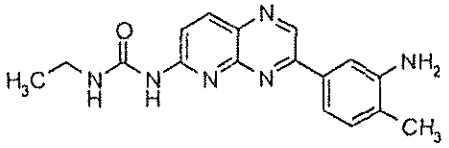
Compound 217 1-(4-Morpholin-4-yl-butyl)-3-(3-phenyl-pyrido[2,3-b]pyrazin-6-yl)-urea



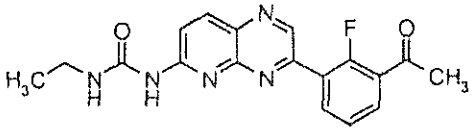
Compound 218 N-{4-[3-(3-Phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-acetamide



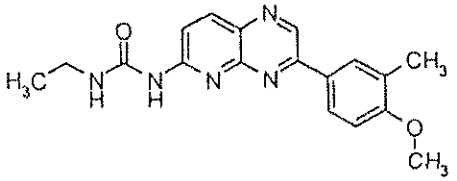
Compound 219 1-[3-(3-Amino-4-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



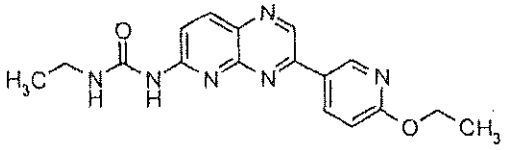
Compound 220 1-[3-(3-Acetyl-2-fluoro-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



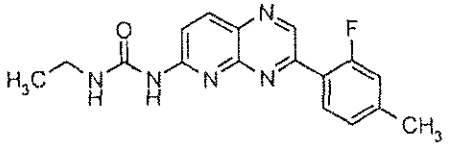
Compound 221 1-Ethyl-3-[3-(4-methoxy-3-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



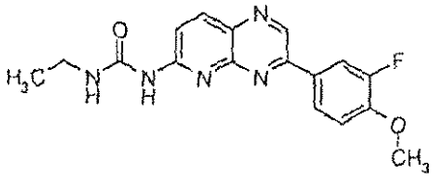
Compound 222 1-[3-(6-Ethoxy-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



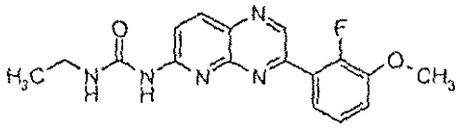
Compound 223 1-Ethyl-3-[3-(2-fluoro-4-methyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



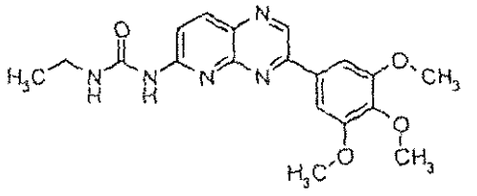
Compound 224 1-Ethyl-3-[3-(3-fluoro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



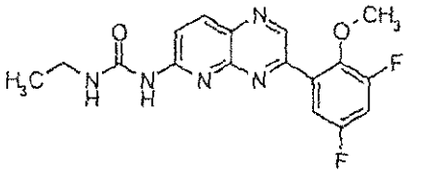
Compound 225 1-Ethyl-3-[3-(2-fluoro-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



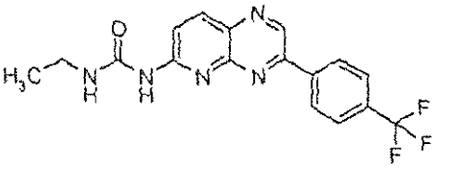
Compound 226 1-Ethyl-3-[3-(3,4,5-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



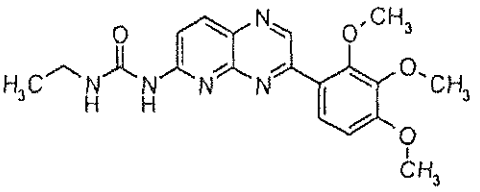
Compound 227 1-[3-(3,5-Difluoro-2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



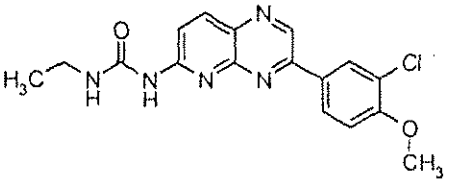
Compound 228 1-Ethyl-3-[3-(4-trifluoromethyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



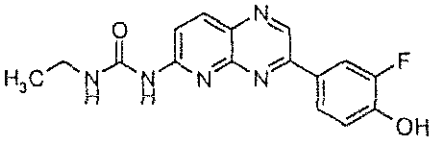
Compound 229 1-Ethyl-3-[3-(2,3,4-trimethoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



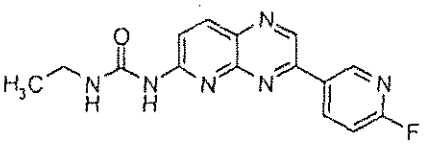
Compound 230 1-[3-(3-Chloro-4-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



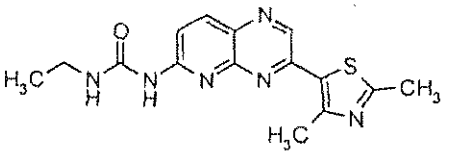
Compound 231 1-Ethyl-3-[3-(3-fluoro-4-hydroxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



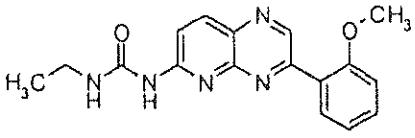
Compound 232 1-Ethyl-3-[3-(6-fluoro-pyridin-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



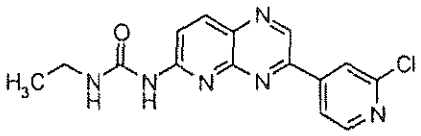
Compound 233 1-[3-(2,4-Dimethyl-thiazol-5-yl)-pyrido-[2,3-b]pyrazin-6-yl]-3-ethyl-urea



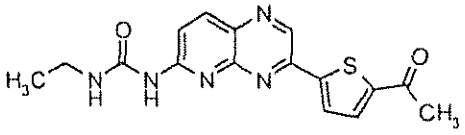
Compound 234 1-Ethyl-3-[3-(2-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



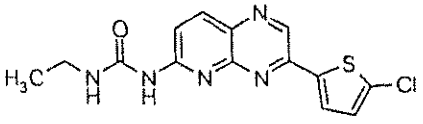
Compound 235 1-[3-(2-Chloro-pyridin-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



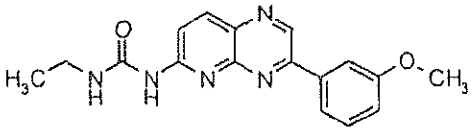
Compound 236 1-[3-(5-Acetyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



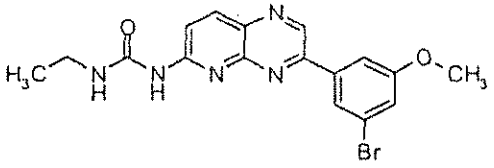
Compound 237 1-[3-(5-Chloro-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



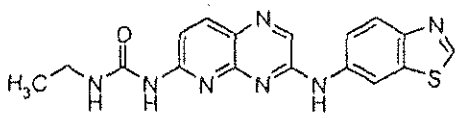
Compound 238 1-Ethyl-3-[3-(3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



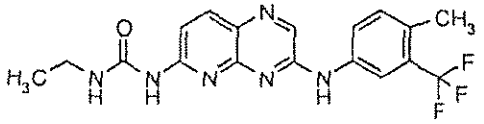
Compound 239 1-[3-(3-Bromo-5-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



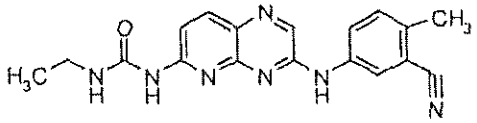
Compound 240 1-[3-(Benzothiazol-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



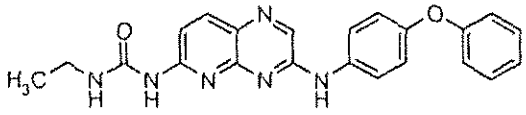
Compound 241 1-Ethyl-3-[3-(4-methyl-3-trifluoroomethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



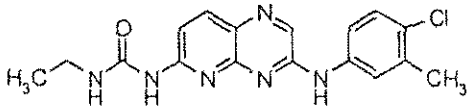
Compound 242 1-[3-(3-Cyano-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



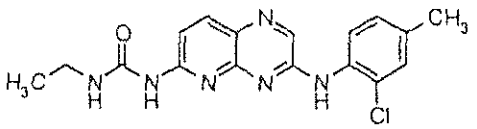
Compound 243 1-Ethyl-3-[3-(4-phenoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



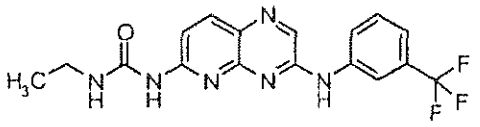
Compound 244 1-[3-(4-Chloro-3-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



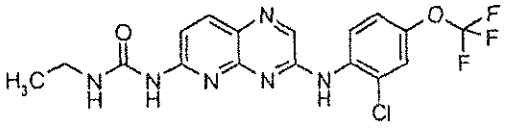
Compound 245 1-[3-(2-Chloro-4-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



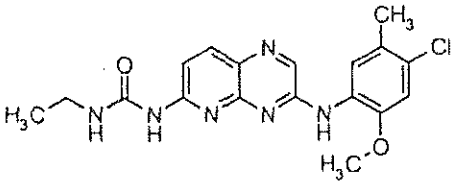
Compound 246 1-Ethyl-3-[3-(3-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



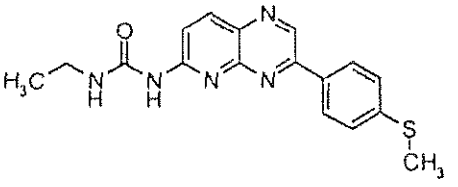
Compound 247 1-[3-(2-Chloro-4-trifluoromethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



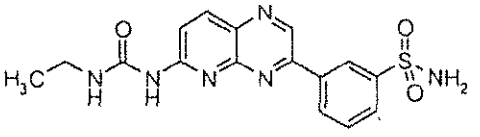
Compound 248 1-[3-(4-Chloro-2-methoxy-5-methyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



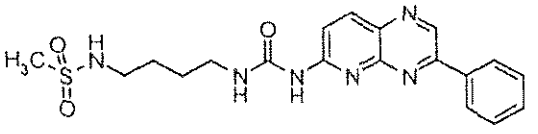
Compound 249 1-Ethyl-3-[3-(4-methylsulfanyl-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



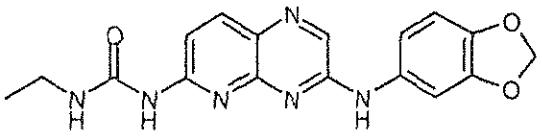
Compound 250 3-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-benzenesulfonamide



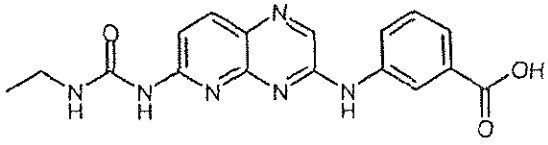
Compound 251 N-{4-[3-(3-Phenyl-pyrido[2,3-b]pyrazin-6-yl)-ureido]-butyl}-methansulfonamide



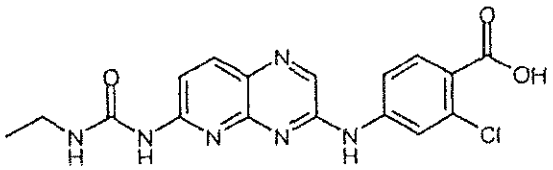
Compound 252 1-[3-(Benzo[1,3]dioxol-5-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



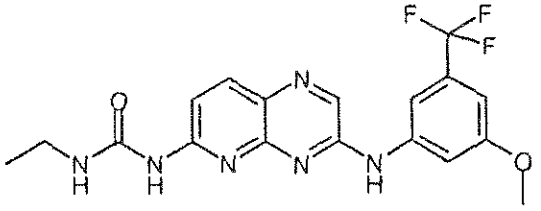
Compound 253 3-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-benzoic acid



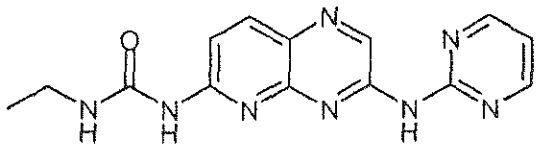
Compound 254 2-Chloro-4-[6-(3-ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-benzoic acid



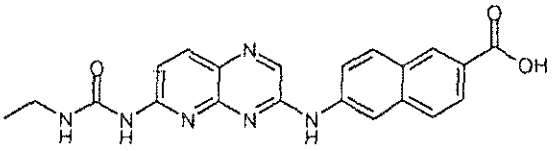
Compound 255 1-Ethyl-3-[3-(3-methoxy-5-trifluoromethyl-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



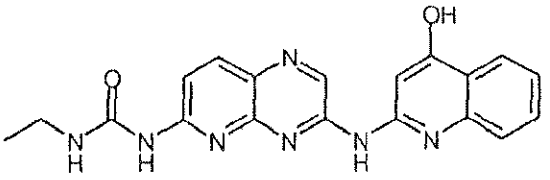
Compound 256 1-Ethyl-3-[3-(pyrimidin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



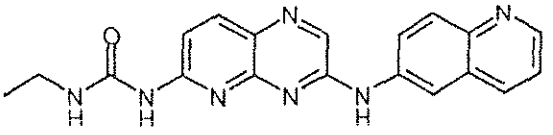
Compound 257 6-[6-(3-Ethyl-ureido)-pyrido[2,3-b]pyrazin-3-ylamino]-naphthalin-2-carbonic acid



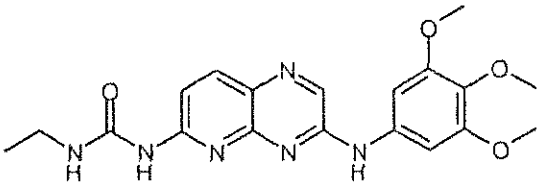
Compound 258 1-Ethyl-3-[3-(4-hydroxy-quinolin-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



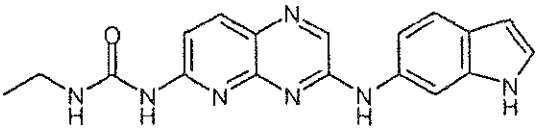
Compound 259 1-Ethyl-3-[3-(quinolin-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



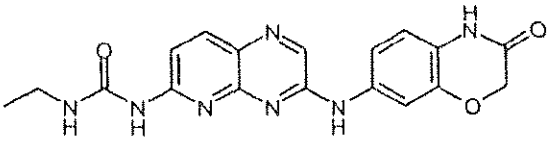
Compound 260 1-Ethyl-3-[3-(3,4,5-trimethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



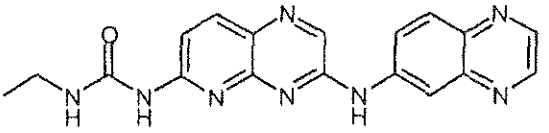
Compound 261 1-Ethyl-3-[3-(1H-indol-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



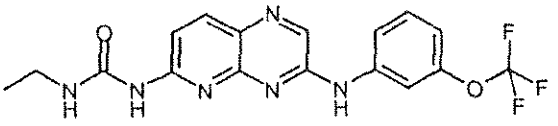
Compound 262 1-Ethyl-3-[3-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



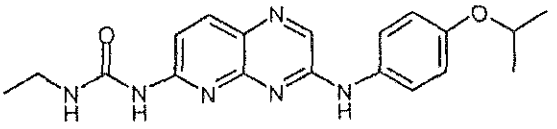
Compound 263 1-Ethyl-3-[3-(quinoxalin-6-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



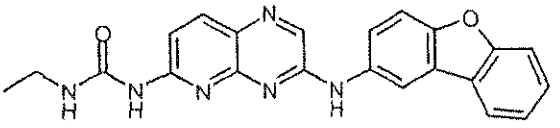
Compound 264 1-Ethyl-3-[3-(3-trifluoromethoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



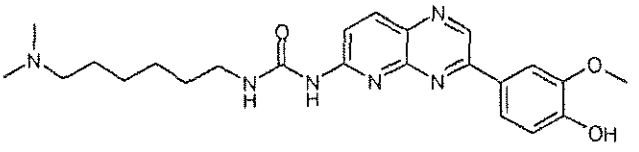
Compound 265 1-Ethyl-3-[3-(4-isopropoxy-phenylamino)-pyrido[2,3-b]pyrazin-6-yl]-urea



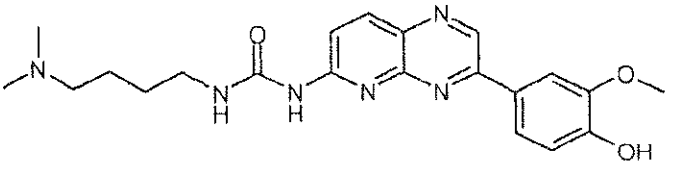
Compound 266 1-[3-(Dibenzofuran-2-ylamino)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



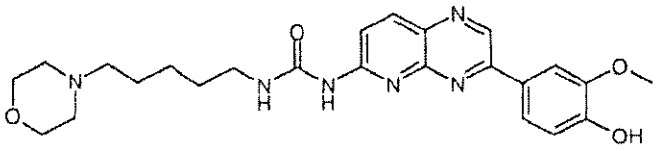
Compound 267 1-(6-Dimethylamino-hexyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



Compound 268 1-(4-Dimethylamino-butyl)-3-[3-(4-hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-urea



Compound 269 1-[3-(4-Hydroxy-3-methoxy-phenyl)-pyrido[2,3-b]pyrazin-6-yl]-3-(5-morpholin-4-yl-pentyl)-urea



for the production of a medicinal product for the treatment or prevention of physiological and/or pathophysiological states in a mammal mediated by modulation of ras-Raf-Mek-Erk signal transduction pathway, PI3K-Akt signal transduction pathway and the SAPK signal transduction pathway,

wherein the physiological and/or pathophysiological state is selected from the group consisting of inflammatory diseases, inflammations, pain, rheumatic diseases, arthritic diseases, HIV infections, neurological or neurodegenerative diseases, rheumatism, arthritis, AIDS, AIDS related complex, dementia, Alzheimer's disease, hyperproliferative diseases, psoriasis, endometriosis, scarring, benign prostatahyperplasia, diseases of the immune system, autoimmune diseases, immunodeficiency diseases, diabetes, diabetic nephropathy, fibrotic diseases, cystic fibrosis, thrombotic microangiopathy syndrome, organ transplant rejection, glomerulopathy, metabolic diseases, solid/fixed tumours, rheumatic arthritis, diabetic retinopathy, asthma, allergies, allergic diseases, chronic obstructive pulmonary diseases, inflammatory bowel disease, fibrosis, atherosclerosis, heart diseases, cardiovascular diseases, diseases of the myocardium, vascular diseases, angiogenetic diseases, kidney diseases, rhinitis, Grave's disease, focal ischemia, cardiac failure, ischemia, cardiac hypertrophia, renal failure, cardiac myocytic malfunction, high blood pressure, vasoconstriction, stroke, anaphylactic shock, platelet agglutination, skeletomuscular atrophy, obesity, overweight, glucosis homeostasis, congestive cardiac insufficiency, angina, heart attack, cardiac infarction, hyperglycaemia, hypoglycaemia, and hypertension.

2. The use according to claim 1, wherein the medicinal product comprises at least one further pharmacologically active substance.

3. The use according to claim 2, wherein the further pharmacologically active substance is selected from the group consisting of DNA topoisomerase I and/or II inhibitors, DNA intercalators, alkylating agents, microtubuli destabilisers, hormone and/or growth factor receptor agonists and/or antagonists, antibodies against growth factors and their receptors, kinase inhibitors, and antimetabolites.

4. The use according to claim 2 or 3, wherein the further pharmacologically active substance is selected from the group consisting of asparaginase, bleomycin, carboplatin, carmustin, chlorambucil, cisplatin, colaspase, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, daunorubicin, doxorubicin, epirubicin, etoposide, 5-fluorouracil, hexamethylmelamine, hydroxurea, ifosfamide, irinotecan, leucovorin, lomustine, mechlorethamine, 6-mercaptopurine, mesna, methotrexate, mitomycin C, mitoxantrone, prednisolone, prednisone, procarbazine, raloxifene, streptozocin, tamoxifen, thioguanine, topotecan, vinblastine, vincristine, vindesine, aminoglutethimide, L-asparaginase, azathioprine, 5-azacytidine cladribine, busulfan, diethylstilbestrol, 2',2'-difluorodeoxycytidine, docetaxel, erythrohydroxynonyladenine, ethinylestradiol, 5-fluorodeoxyuridin, 5-fluorodeoxyuridin monophosphate, fludarabine phosphate, fluoxymesterone, flutamide, hydroxyprogesterone caproate, idarubicin, interferon, medroxyprogesterone acetate, megestrol acetate, melphalan, mitotane, paclitaxel, oxaliplatin, pentostatin, N-phosphonoacetyl-L-aspartate, plicamycin, semustine, teniposide, testosterone propionate, thiotepa, trimethylmelamine, uridine, vinorelbin, epothilone, gemcitabine, Taxotere, BCNU, CCNU, DTIC, 5-fluorouarcil, Herceptin, Avastin, Erbitux, Sorafenib, Gleevec, Iressa, Tarceva, rapamycin, and actinomycin D.

5. A pyridopyrazine selected from the group consisting ofcompounds 38 to 136 and 138 to 269 according to claim 1.

6. A pharmaceutical composition comprising a pharmacologically active quantity of at least one compound according to claim 5, and at least one pharmaceutically compatible excipient.

7. The pharmaceutical composition according to claim 6, wherein the active substance is present in a unit dose of 0.001 mg to 100 mg per kg body weight of a patient.

8. The pharmaceutical composition according to claim 6 or 7, wherein the composition contains at least one further pharmacologically active substance.

9. The pharmaceutical composition according to claim 8, wherein the further pharmacologically active substance is selected from the group consisting of DNA topoisomerase I and/or II inhibitors, DNA intercalators, alkylating agents, microtubuli destabilisers, hormone and/or growth factor receptor agonists and/or antagonists, antibodies against growth factors and their receptors, kinase inhibitors, and antimetabolites.

10. The pharmaceutical composition according to claim 8 or 9, wherein the further pharmacologically active substance is selected from the group consisting of asparaginase, bleomycin, carboplatin, carmustin, chlorambucil, cisplatin, colaspase, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, daunorubicin, doxorubicin, epirubicin, etoposide, 5-fluorouracil, hexamethylmelamine, hydroxurea, ifosfamide, irinotecan, leucovorin, lomustine, mechlorethamine, 6-mercaptopurine, mesna, methotrexate, mitomycin C, mitoxantrone, prednisolone, prednisone, procarbazine, raloxifene, streptozocin, tamoxifen, thioguanine, topotecan, vinblastine, vincristine, vindesine, aminoglutethimide, L-asparaginase, azathioprine, 5-azacytidine cladribine, busulfan, diethylstilbestrol, 2',2'-difluorodeoxycytidine, docetaxel, erythrohydroxynonyladenine, ethinylestradiol, 5-fluorodeoxyuridin, 5-fluorodeoxyuridin monophosphate, fludarabine phosphate, fluoxymesterone, flutamide, hydroxyprogesterone caproate, idarubicin, interferon, medroxyprogesterone acetate, megestrol acetate, melphalan, mitotane, paclitaxel, oxaliplatin, pentostatin, N-phosphonoacetyl-L-aspartate, plicamycin, semustine, teniposide, testosterone propionate, thiotepa, trimethylmelamine, uridine, vinorelbin, epothilone, gemcitabine, Taxotere, BCNU, CCNU, DTIC, 5-fluorouarcil, Herceptin, Avastin, Erbitux, Sorafenib, Gleevec, Iressa, Tarceva, rapamycin, and actinomycin D.

11. A kit comprising a pharmacologically active quantity of at least one compound according to claim 5 and a pharmacologically active quantity of at least one further pharmacologically active substance according to claim 9 or 10.

PYRIDOPYRAZINE DERIVATIVES AND USE THEREOF AS MODULATORS OF THE SIGNAL TRANSDUCTION PATHS

Abstract

The invention relates to novel pyridopyrazine compounds which are suited for the treatment or prevention of physiological and/or pathophysiological conditions in mammals, especially humans, transmitted and/or modulated by signal transduction paths and/or enzymes.

No Suitable Figure