Pyrazolo[3,4-b]pyridine compounds, and their use as phosphodiesterase inhibitors

The present invention relates to pyrazolopyridine compounds, processes for their preparation, intermediates usable in these processes, and pharmaceutical compositions containing the compounds. The invention also relates to the use of the pyrazolopyridine compounds in therapy, for example as inhibitors of phosphodiesterases and/or for the treatment and/or prophylaxis of inflammatory and/or allergic diseases such as chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis or allergic rhinitis.

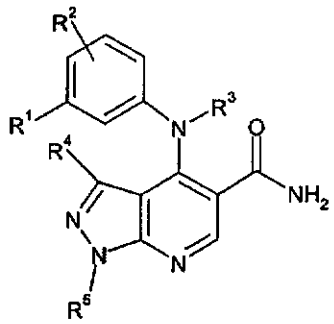
US 3,979,399, US 3,840,546, and US 3,966,746 (E.R.Squibb & Sons) disclose 4-amino derivatives of pyrazolo[3,4-b]pyridine-5-carboxamides wherein the 4-amino group NR_3R_4 can be an acyclic amino group wherein R_3 and R_4 may each be hydrogen, lower alkyl (e.g. butyl), phenyl, etc.; NR_3R_4 can alternatively be a 3-6-membered heterocyclic group such as pyrrolidino, piperidino and piperazino. The compounds are disclosed as central nervous system depressants useful as ataractic, analgesic and hypotensive agents.

US 3,925,388, US 3,856,799, US 3,833,594 and US 3,755,340 (E.R.Squibb & Sons) disclose 4-amino derivatives of pyrazolo[3,4-b]pyridine-5-carboxylic acids and esters. The 4-amino group NR_3R_4 can be an acyclic amino group wherein R_3 and R_4 may each be hydrogen, lower alkyl (e.g. butyl), phenyl, etc.; NR_3R_4 can alternatively be a 5-6-membered heterocyclic group in which an additional nitrogen is present such as pyrrolidino, piperidino, pyrazolyl, pyrimidinyl, pyridazinyl or piperazinyl. The compounds are mentioned as being central nervous system depressants useful as ataractic agents or tranquilisers, as having antiinflammatory and analgesic properties. The compounds are mentioned as increasing the intracellular concentration of adenosine-3',5'-cyclic monophosphate and for alleviating the symptoms of asthma.

H. Hoehn et al., *J. Heterocycl. Chem.*, 1972, 9(2), 235-253 discloses a series of 1*H*-pyrazolo[3,4-b]pyridine-5-carboxylic acid derivatives with 4-hydroxy, 4-chloro, 4-alkoxy, 4-hydrazino, and 4-amino substituents.

CA 1003419, CH 553 799 and T.Denzel, *Archiv der Pharmazie*, 1974, 307(3), 177-186 disclose 4,5-disubstituted 1*H*-pyrazolo[3,4-b]pyridines unsubstituted at the 1-position.

Japanese laid-open patent application JP-2002-20386-A (Ono Yakuhin Kogyo KK) published on 23 January 2002 discloses pyrazolopyridine compounds of the following formula:



JP-2002-20386-A
(Ono)

wherein R^1 denotes 1) a group $-OR^6$, 2) a group $-SR^7$, 3) a C2-8 alkynyl group, 4) a nitro group, 5) a cyano group, 6) a C1-8 alkyl group substituted by a hydroxy group or a C1-8 alkoxy group, 7) a phenyl group, 8) a group $-C(O)R^8$, 9) a group $-SO_2NR^9R^{10}$, 10) a group $-NR^{11}SO_2R^{12}$, 11) a group $-NR^{13}C(O)R^{14}$ or 12) a group $-CH=NR^{15}$. R^6 and R^7 denote i) a hydrogen atom, ii) a C1-8 alkyl group, iii) a C1-8 alkyl group substituted by a C1-8 alkoxy group, iv) a trihalomethyl group, v) a C3-7 cycloalkyl group, vi) a C1-8 alkyl group substituted by a phenyl group or vii) a 3-15 membered mono-, di- or tricyclic hetero ring containing 1-4 nitrogen atoms, 1-3 oxygen atoms and/or 1-3 sulphur atoms. R^2 denotes 1) a hydrogen atom or 2) a C1-8 alkoxy group. R^3 denotes 1) a hydrogen atom or 2) a C1-8 alkyl group. R^4 denotes 1) a hydrogen atom, 2) a C1-8 alkyl group, 3) a C3-7 cycloalkyl group, 4) a C1-8 alkyl group substituted by a C3-7 cycloalkyl group, 5) a phenyl group which may be substituted by 1-3 halogen atoms or 6) a 3-15 membered mono-, di- or tricyclic hetero ring containing 1-4 nitrogen atoms, 1-3 oxygen atoms and/or 1-3 sulphur atoms. R^5 denotes 1) a hydrogen atom, 2) a C1-8 alkyl group, 3) a C3-7 cycloalkyl group, 4) a C1-8 alkyl group substituted by a C3-7 cycloalkyl group or 5) a phenyl group which may be substituted by 1-3 substituents. In group R^3, a hydrogen atom is preferred. In group R^4, methyl, ethyl, cyclopropyl, cyclobutyl or cyclopentyl are preferred. The compounds of JP-2002-20386-A are stated as having PDE4 inhibitory activity and as being useful in the prevention and/or treatment of inflammatory diseases and many other diseases.

EP 0 076 035 A1 (ICI Americas) discloses pyrazolo[3,4-b]pyridine derivatives as central nervous system depressants useful as tranquilisers or ataractic agents for the relief of anxiety and tension states.

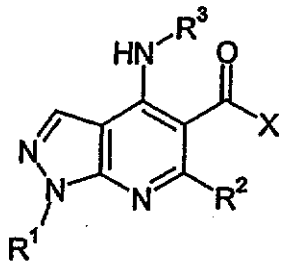
The compound cartazolate, ethyl 4-(n-butylamino)-1-ethyl-1H-pyrazolo[3,4-b]-pyridine-5-carboxylate, is known. J.W. Daly et al., *Med. Chem. Res.*, 1994, 4, 293-306 and D. Shi et al., *Drug Development Research*, 1997, 42, 41-56 disclose a series of 4-(amino)substituted 1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid derivatives, including ethyl 4-cyclopentylamino-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, and their affinities and antagonist activities at A_1- and A_{2A}-adenosine receptors, and the latter paper discloses their affinities at various binding sites of the $GABA_A$-receptor channel. S. Schenone et al., *Bioorg. Med. Chem. Lett.*, 2001, 11, 2529-2531 and F. Bondavalli et

al., *J. Med. Chem.*, 2002, vol. 45 (Issue 22, 24 October 2002, allegedly published on Web 09/24/2002), pp. 4875-4887 disclose a series of 4-amino-1-(2-chloro-2-phenylethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid ethyl esters as A_1-adenosine receptor ligands.

WO 02/060900 A2 appears to disclose, as MCP-1 antagonists for treatment of allergic, inflammatory or autoimmune disorders or diseases, a series of bicyclic heterocyclic compounds with a -C(O)-NR^4-C(O)-NR^5R^6 substituent, including isoxazolo[5,4-b]pyridines and 1*H*-pyrazolo[3,4-b]pyridines (named as pyrazolo[5,4-b]pyridines) with the -C(O)-NR^4-C(O)-NR^5R^6 group as the 5-substituent and optionally substituted at the 1-, 3-, 4-, and/or 6-positions. Bicyclic heterocyclic compounds with a $-C(O)NH_2$ substituent instead of the -C(O)-NR^4-C(O)-NR^5R^6 substituent are alleged to be disclosed in WO 02/060900 as intermediates in the synthesis of the -C(O)-NR^4-C(O)-NR^5R^6 substituted compounds.

It is desirable to find new compounds which bind to, and preferably inhibit, phosphodiesterase type IV (PDE4).

The present invention provides a compound of formula (I) or a salt thereof (in particular, a pharmaceutically acceptable salt thereof):



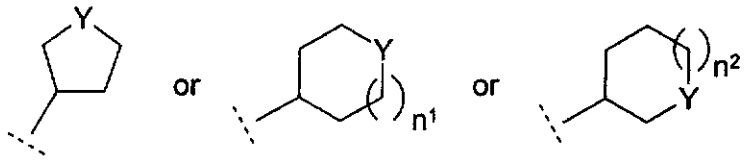
(I)

wherein:

R^1 is C_{1-3}alkyl, C_{1-2}fluoroalkyl or $-CH_2CH_2OH$;

R^2 is a hydrogen atom (H), methyl or C_1 fluoroalkyl;

R^3 is substituted C_{3-8}cycloalkyl or an optionally substituted heterocyclic group of sub-formula (aa), (bb) or (cc);



(aa) (bb) (cc)

in which n^1 and n^2 independently are 1 or 2; and in which Y is O, S, SO_2, or NR^{10}; where R^{10} is a hydrogen atom (H), methyl, ethyl, $C(O)NH_2$, C(O)methyl or $C(O)-CF_3$;

and wherein, when R^3 is substituted C_{3-8}cycloalkyl, then R^3 is cyclohexyl substituted by one substituent being oxo (=O), OH, NHR^{21} wherein R^{21} is a hydrogen atom (H) or C_{1-5} straight-chain alkyl, $-CH_2OH$, $-C(O)OR^{23}$ wherein R^{23} is H or methyl, $-C(O)NHR^{24}$ wherein R^{24} is H or methyl, $-C(O)R^{25}$ wherein R^{25} is C_{1-2}alkyl, hydroxyimino (=N-OH), or (C_{1-4}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-4}alkyl); and wherein any OH or NHR^{21} substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (I);

and wherein the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc) is optionally substituted with one or two substituents being oxo (=O);

and X is NR^4R^5 or OR^{5a}, in which:

R^4 is a hydrogen atom (H); and

R^5 is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl optionally substituted by a C_{1-2}alkyl group; or $-(CH_2)_n{}^4-C_{3-8}$cycloalkyl optionally substituted, in the $-(CH_2)_n{}^4-$ moiety or in the C_{3-8}cycloalkyl moiety, by a C_{1-2}alkyl group, wherein n^4 is 1, 2 or 3;

or R^5 is C_{2-6}alkyl substituted by one or two independent substituents R^{11};

wherein each substituent R^{11}, independently of any other R^{11} substituent present, is: hydroxy (OH); C_{1-6}alkoxy; phenyloxy; benzyloxy; $-NR^{12}R^{13}$; $-NR^{15}-C(O)R^{16}$; $-NR^{15}-C(O)-O-R^{16}$; $-NR^{15}-C(O)-NH-R^{15}$; or $-NR^{15}-SO_2R^{16}$; and wherein any R^{11} substituent which is OH, alkoxy or $-NR^{12}R^{13}$ is not substituted at any carbon atom, of any R^4 or R^5 substituted alkyl, which is bonded to the nitrogen of NR^4R^5;

or R^5 is $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{12}-C(O)NR^{12}R^{13}$; $-CHR^{19}-C(O)NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-C(O)OR^{16}$; $-(CH_2)_n{}^{12}-C(O)OH$; $-CHR^{19}-C(O)OR^{16}$; $-CHR^{19}-C(O)OH$; $-(CH_2)_n{}^{12}-SO_2-NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-SO_2R^{16}$; or $-(CH_2)_n{}^{12}-CN$; wherein n^{11} is 0, 1, 2, 3 or 4 and n^{12} is 1, 2, 3 or 4;

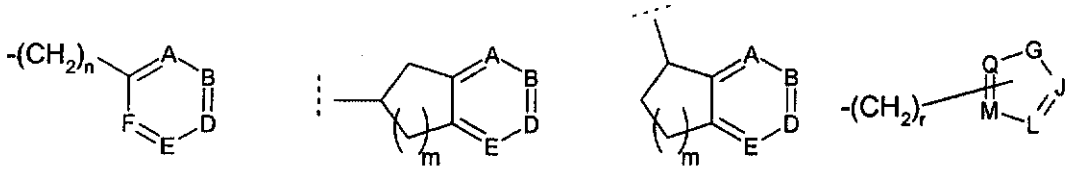
or R^5 is $-(CH_2)_n{}^{13}$-Het wherein n^{13} is 0, 1, 2, 3 or 4 and Het is a 4-, 5-, 6- or 7-membered saturated or partly-saturated heterocyclic ring containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-hetero-atoms present are not bound to the $-(CH_2)_n{}^{13}-$ moiety when n^{13} is 1 and are not bound to the nitrogen of NR^4R^5 when n^{13} is 0; wherein any ring-nitrogens which are present and which are not unsaturated (i.e. which do not partake in a double bond) are present as NR^{17} where R^{17} is as defined herein; and wherein one or two of the carbon ring-atoms independently are optionally substituted by C_{1-2}alkyl;

or R^5 is phenyl optionally substituted with, independently, one, two or three of: a halogen atom; C_{1-6}alkyl; C_{1-2}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{3-6}cycloalkyloxy; $-C(O)R^{16a}$; $-C(O)OR^{30}$; $-S(O)_2-R^{16a}$; $R^{16a}-S(O)_2-NR^{15a}-$; $R^7R^8N-S(O)_2-$; C_{1-2}alkyl-C(O)-$R^{15a}N-S(O)_2-$; C_{1-4}alkyl-S(O)-; Ph-S(O)-; R^7R^8N-CO-; $-NR^{15}-C(O)R^{16}$; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-$S(O)_2-CH_2-$; $R^7R^8N-S(O)_2-CH_2-$; C_{1-2}alkyl-$S(O)_2-NR^{15a}-CH_2-$; $-CH_2-OH$; $-CH_2CH_2-OH$; $-CH_2-NR^7R^8$; $-CH_2-CH_2-NR^7R^8$; $-CH_2-C(O)OR^{30}$; $-CH_2-C(O)-NR^7R^8$; $-CH_2-NR^{15a}-C(O)-C_{1-3}$alkyl; $-(CH_2)_n{}^{14}-Het^1$ where n^{14} is 0 or 1; cyano (CN); Ar^{5a}; or phenyl, pyridinyl or pyrimidinyl wherein the phenyl, pyridinyl or pyrimidinyl independently are optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or where two adjacent substituents, on the R^5 optionally substituted phenyl, taken together are $-O-(CMe_2)-O-$ or $-O-(CH_2)_n{}^{14a}-O-$ where n^{14a} is 1 or 2;

wherein R^7 and R^8 are independently a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or R^7 and R^8 together are $-(CH_2)_n{}^6-$ or $-C(O)-(CH_2)_n{}^7-$ or $-C(O)-(CH_2)_n{}^7-C(O)-$ or $-(CH_2)_n{}^8-X^7-(CH_2)_n{}^9-$ or $-C(O)-X^7-(CH_2)_n{}^{10}-$ in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3 , and X^7 is O or NR^{14} wherein R^{14} is H, C_{1-2}alkyl or C(O)Me;

or R^5 has the sub-formula (x), (y), (y1) or (z):



(x) (y) (y1) (z)

wherein in sub-formula (x), n = 0, 1 or 2; in sub-formula (y) and (y1), m = 1 or 2; and in sub-formula (z), r = 0, 1 or 2;

wherein in sub-formula (x) and (y) and (y1), none, one or two of A, B, D, E and F are independently nitrogen or nitrogen-oxide (N^+-O^-) provided that no more than one of A, B, D, E and F is nitrogen-oxide; and the remaining of A, B, D, E and F are independently CH or CR^6;

provided that when n is 0 in sub-formula (x) then one or two of A, B, D, E and F are independently nitrogen or nitrogen-oxide (N^+-O^-) and no more than one of A, B, D, E and F is nitrogen-oxide;

wherein, each R^6, independently of any other R^6 present, is: a halogen atom; C_{1-6}alkyl; C_{1-4}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{3-6}cycloalkyloxy; -C(O)R^{16a}; -C(O)OR^{30}; -S(O)$_2$-R^{16a}; R^{16a}-S(O)$_2$-NR^{15a}-; R^7R^8N-S(O)$_2$-; C_{1-2}alkyl-C(O)-R^{15a}N-S(O)$_2$-; C_{1-4}alkyl-S(O)-; Ph-S(O)-; R^7R^8N-CO-; -NR^{15}-C(O)R^{16}; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-S(O)$_2$-CH_2-; R^7R^8N-S(O)$_2$-CH_2-; C_{1-2}alkyl-S(O)$_2$-NR^{15a}-CH_2-; -CH_2-OH; -CH_2CH_2-OH; -CH_2-NR^7R^8; -CH_2-CH_2-NR^7R^8; -CH_2-C(O)OR^{30}; -CH_2-C(O)-NR^7R^8; -CH_2-NR^{15a}-C(O)-C_{1-3}alkyl; -$(CH_2)_n{}^{14}$-Het^1 where n^{14} is 0 or 1; cyano (CN); Ar^{5b}; or phenyl, pyridinyl or pyrimidinyl wherein the phenyl, pyridinyl or pyrimidinyl independently are optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or where two adjacent R^6 taken together are –O–(CMe_2)–O– or –O–$(CH_2)_n{}^{14a}$–O– where n^{14a} is 1 or 2;

wherein R^7 and R^8 are as herein defined;

wherein sub-formula (y) and (y1), independently, are optionally substituted by oxo (=O) at a ring carbon adjacent the 6-membered aromatic ring;

wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is a hydrogen atom (H), C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one, two or three of J, L, M and Q are nitrogen; and

the remaining of J, L, M and Q are independently CH or CR^6 where R^6, independently of any other R^6 present, is as defined herein; and

R^{5a} is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl; $-(CH_2)_{n^{4a}}-C_{3-6}$cycloalkyl wherein n^{4a} is 1 or 2; phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^{5a} has the sub-formula (x), (y), (y1) or (z) as defined herein;

and wherein:

R^{12} and R^{13} independently are H; C_{1-5}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or R^{12} and R^{13} together are $-(CH_2)_{n^6}-$ or $-C(O)-(CH_2)_{n^7}-$ or $-C(O)-(CH_2)_{n^7}-C(O)-$ or $-(CH_2)_{n^8}-X^{12}-(CH_2)_{n^9}-$ or $-C(O)-X^{12}-(CH_2)_{n^{10}}-$ in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3 and X^{12} is O or NR^{14a} wherein R^{14a} is H, C_{1-2}alkyl or C(O)Me;

R^{15} is a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

R^{15a}, independent of other R^{15a}, is a hydrogen atom (H) or C_{1-4}alkyl;

R^{16} and R^{16a} independently are:

C_{1-6}alkyl;

C_{3-6}cycloalkyl optionally substituted by one oxo (=O), OH or C_{1-2}alkyl substituent;

C_{3-6}cycloalkyl-CH_2-;

pyridinyl optionally substituted on a ring carbon atom by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

Ar^{5c};

phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

benzyl optionally substituted at an aromatic carbon atom by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or

a 4-, 5-, 6- or 7-membered saturated heterocyclic ring connected at a ring-carbon and containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-nitrogens which are present are present as NR^{27} where R^{27} is H, C_{1-2}alkyl or -C(O)Me; and wherein the ring is optionally substituted at carbon by one

C_{1-2}alkyl or oxo (=O) substituent, provided that any oxo (=O) substituent is substituted at a ring-carbon atom bonded to a ring-nitrogen;

wherein Ar^{5a}, Ar^{5b} and Ar^{5c} independently is/are a 5-membered aromatic heterocyclic ring containing one O, S or NR^{15a} in the 5-membered ring, wherein the 5-membered ring can optionally additionally contain one or two N atoms, and wherein the heterocyclic ring is optionally substituted on a ring carbon atom by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, $-CH_2OH$, $-CH_2-OC_{1-2}$alkyl, OH (including the keto tautomer thereof) or $-CH_2-NR^{28}R^{29}$ wherein R^{28} and R^{29} independently are H or methyl;

and R^{17} is a hydrogen atom (H); C_{1-4}alkyl; C_{1-2}fluoroalkyl; C_{3-6}cycloalkyl; $-(CH_2)_p{}^6-C(O)R^{16}$ wherein p^6 is 0, 1, 2 or 3; $-(CH_2)_p{}^6-C(O)NR^{12}R^{13}$; $-(CH_2)_p{}^6-C(O)OR^{16}$; $-(CH_2)_p{}^6-C(O)OH$; $-SO_2R^{16}$; $-C(O)-CH_2-NR^{12}R^{13}$; $-C(O)-CH_2-NR^{15a}-C(O)-C_{1-3}$alkyl; $-C(O)-CH_2-O-C_{1-3}$alkyl; or phenyl or benzyl wherein the phenyl or benzyl is optionally substituted at an aromatic carbon atom by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

R^{19} is C_{1-4}alkyl; $-(CH_2)_n{}^{20}-OR^{20}$ wherein n^{20} is 1, 2, 3 or 4 and R^{20} is a hydrogen atom (H) or C_{1-4}alkyl; $-CH(Me)-OH$; $-CH_2-SH$; $-CH_2-CH_2-S-Me$; benzyl; or (4-hydroxyphenyl)methyl (i.e. 4-hydroxy-benzyl); and

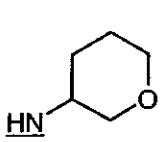
R^{30}, independent of other R^{30}, is a hydrogen atom (H), C_{1-4}alkyl or C_{3-6}cycloalkyl; and

Het^1, independent of other Het^1, is a 4-, 5-, 6- or 7-membered saturated heterocyclic ring connected at a ring-carbon and containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-nitrogens which are present are present as NR^{31} where R^{31} is H, C_{1-2}alkyl or -C(O)Me; and wherein the ring is optionally substituted at carbon by one C_{1-2}alkyl or oxo (=O) substituent, provided that any oxo (=O) substituent is substituted at a ring-carbon atom bonded to a ring-nitrogen;

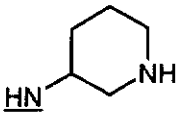
provided that: when R^3 is the heterocyclic group of sub-formula (aa) and Y is NR^{10}, then R^{10} is not $C(O)NH_2$, C(O)methyl or $C(O)-CF_3$;

provided that:
when R^3 is the heterocyclic group of sub-formula (bb), n^1 is 1, and Y is NR^{10}, then:
either (a) R^{10} is not methyl or ethyl;
or (b) R^{10} is methyl and the compound is: 1-ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide or 1-ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide;

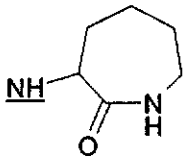
provided that: when R^3 is the heterocyclic group of sub-formula (cc), then NHR^3 is of sub-formula (L), (m), (m1) or (m2), wherein the -NH- connection point of the NHR^3 group to the 4-position of the pyrazolopyridine of formula (I) is underlined:



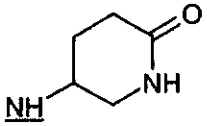
(L)



(m)



(m1)



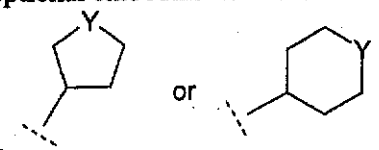
(m2) ;

and provided that: where R^3 is substituted C_{3-8}cycloalkyl, then any OH, $-CH_2OH$, $-C(O)OR^{23}$, $-C(O)NHR^{24}$ or $-C(O)R^{25}$ substituent is at the 3-, 4- or 5- position of the R^3 cyclohexyl ring (wherein, in this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (I)).

In one optional embodiment of the invention, R^1 C_{1-4}alkyl or C_{1-2}fluorolkyl.

Alternatively or additionally, in one optional embodimenbt of the invention, R^2 is a hydrogen atom (H).

Alternatively or additionally, in one optional embodiment of the invention, R^3 is

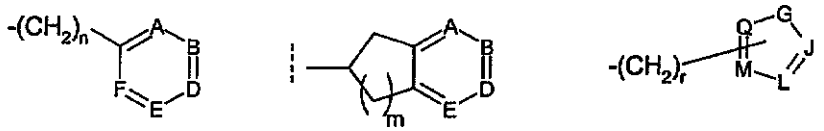


C_{3-8}cycloalkyl or a heterocyclic group being in which Y is O, S, SO_2, or NR^{10}; where R^{10} is hydrogen, C_{1-4}alkyl, C_{1-2}fluoroalkyl, C(O)-C_{1-2}alkyl, or C(O)-CF_3;

and wherein in R^3 the C_{3-8}cycloalkyl or heterocyclic group is optionally substituted with one or two substituents being OH, C_{1-2}alkoxy, trimethoxy, or C_{1-2}alkyl; and wherein any OH, alkoxy or trimethoxy substituent is not substituted at the (R^3) ring carbon attached (bonded) to the -NH- group of formula (I) and is not substituted at either (R^3) ring carbon bonded to the Y group of the heterocyclic group.

Alternatively or additionally, in one optional embodiment of the invention, R^4 is hydrogen, C_{1-2}alkyl or C_{1-2}fluoroalkyl.

Alternatively or additionally, in one optional embodiment of the invention, R^5 is hydrogen, C_{1-8}alkyl, C_{1-8} fluoroalkyl, or C_{3-8}cycloalkyl; or phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^5 has the sub-formula (x), (y) or (z):



(x) (y) (z)

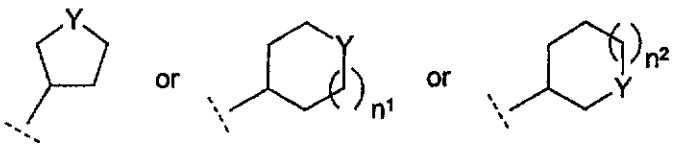
wherein in sub-formula (x), n = 1 or 2; in sub-formula (y), m = 1 or 2; and in sub-formula (z), r = 1 or 2;

wherein in sub-formula (x) and (y), none, one or two of A, B, D, E and F are nitrogen; and the remaining of A, B, D, E and F are CH or CR^6 where R^6 is a halogen atom, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{1-2}alkoxy, C_{1-2}fluoroalkoxy, C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-), C_{1-2}alkyl-SO_2-NH-, R^7R^8N-SO_2-, R^7R^8N-CO-, R^7R^8N, OH, C_{1-4}alkoxymethyl, or C_{1-2}alkyl-SO_2-CH_2-, wherein R^7 and R^8 are independently hydrogen or C_{1-2}alkyl;

wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one or two of J, L, M and Q are nitrogen; and the remaining of J, L, M and Q are CH or CR^6 where R^6 is as defined herein.

In the alternative to the above R^4 and/or R^5 optional embodiments, in one optional embodiment of the invention, R^4 and R^5 taken together can be $-(CH_2)_{p^1}-$ where $p^1 = 3$, 4 or 5 (preferably $p^1 = 4$ or 5).

In one optional embodiment of the invention, R^3 is optionally substituted C_{3-8}cycloalkyl or an optionally substituted heterocyclic group of sub-formula (aa), (bb) or (cc);



(aa) (bb) (cc)

in which n^1 and n^2 independently are 1 or 2; and in which Y is O, S, SO_2, or NR^{10}; where R^{10} is a hydrogen atom (H), C_{1-4}alkyl (e.g. methyl or ethyl), C_{1-2}fluoroalkyl, $CH_2C(O)NH_2$, $C(O)NH_2$, $C(O)$-C_{1-2}alkyl, or $C(O)$-C_1fluoroalkyl;

and wherein in R^3 the C_{3-8}cycloalkyl or the heterocyclic group of sub-formula (aa), (bb) or (cc) is optionally substituted with one or two substituents being oxo (=O), OH, C_{1-2}alkoxy, C_{1-2}fluoroalkoxy (e.g. trifluoromethoxy), or C_{1-2}alkyl; and wherein any OH, alkoxy or fluoroalkoxy substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (I) and is not substituted at either R^3 ring carbon bonded to the Y group of the heterocyclic group (aa), (bb) or (cc).

Alternatively or additionally to the above optional R^3 definition, in one optional embodiment of the invention, X is NR^4R^5 or OR^{5a}, in which:

R^4 is a hydrogen atom (H); C_{1-6}alkyl; C_{1-3}fluoroalkyl; or C_{2-6}alkyl substituted by one substituent R^{11}; and

R^5 is a hydrogen atom (H); C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl optionally substituted by a C_{1-2}alkyl group; or $-(CH_2)_n{}^4$-C_{3-8}cycloalkyl optionally substituted, in the $-(CH_2)_n{}^4$- moiety or in the C_{3-8}cycloalkyl moiety, by a C_{1-2}alkyl group, wherein n^4 is 1, 2 or 3;

or R^5 is C_{2-6}alkyl substituted by one or two independent substituents R^{11};

wherein each substituent R^{11}, independently of any other R^{11} substituent present, is: hydroxy (OH); C_{1-6}alkoxy; phenyloxy; benzyloxy; $-NR^{12}R^{13}$; $-NR^{15}$-$C(O)R^{16}$; $-NR^{15}$-$C(O)$-O-R^{16}; $-NR^{15}$-$C(O)$-NH-R^{15}; or $-NR^{15}$-SO_2R^{16}; and wherein any R^{11} substituent which is OH, alkoxy or $-NR^{12}R^{13}$ is not substituted at any carbon atom, of any R^4 or R^5 substituted alkyl, which is bonded to the nitrogen of NR^4R^5;

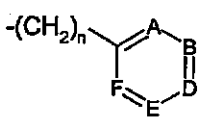
or R^5 is $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{12}-C(O)NR^{12}R^{13}$; $-CHR^{19}-C(O)NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-C(O)OR^{16}$; $-CHR^{19}-C(O)OR^{16}$; $-(CH_2)_n{}^{12}-SO_2-NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-SO_2R^{16}$; or $-(CH_2)_n{}^{12}-CN$; wherein n^{11} is 0, 1, 2, 3 or 4 and n^{12} is 1, 2, 3 or 4;

or R^5 is $-(CH_2)_n{}^{13}$-Het wherein n^{13} is 0, 1, 2, 3 or 4 and Het is a 4-, 5-, 6- or 7-membered saturated or partly-saturated heterocyclic ring containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-hetero-atoms present are not bound to the $-(CH_2)_n{}^{13}-$ moiety when n^{13} is 1 and are not bound to the nitrogen of NR^4R^5 when n^{13} is 0; wherein any ring-nitrogens which are present and which are not unsaturated (i.e. which do not partake in a double bond) are present as NR^{17} where R^{17} is as defined herein; and wherein one or two of the carbon ring-atoms independently are optionally substituted by C_{1-2}alkyl;

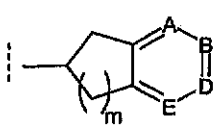
or R^5 is phenyl optionally substituted with one or two of: a halogen atom; C_{1-4}alkyl (e.g. C_{1-2}alkyl); C_{1-2}fluoroalkyl (e.g. trifluoromethyl); C_{1-4}alkoxy (e.g. C_{1-2}alkoxy); C_{1-2}fluoroalkoxy (e.g. trifluoromethoxy); C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-; $-NR^{15}-C(O)R^{16}$; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

wherein R^7 and R^8 are independently a hydrogen atom (H); C_{1-4}alkyl (e.g. C_{1-2}alkyl such as methyl); C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or R^7 and R^8 together are $-(CH_2)_n{}^6-$ or $-C(O)-(CH_2)_n{}^7-$ or $-C(O)-(CH_2)_n{}^7-C(O)-$ or $-(CH_2)_n{}^8-X^7-(CH_2)_n{}^9-$ or $-C(O)-X^7-(CH_2)_n{}^{10}-$ in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5 (preferably n^7 is 2, 3 or 4), n^8 and n^9 and n^{10} independently are 2 or 3, and X^7 is O or NR^{14} wherein R^{14} is H or C_{1-2}alkyl;

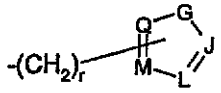
or R^5 has the sub-formula (x), (y) or (z):



(x)



(y)



(z)

wherein in sub-formula (x), n = 1 or 2; in sub-formula (y), m = 1 or 2; and in sub-formula (z), r = 0, 1 or 2;

wherein in sub-formula (x) and (y), none, one or two of A, B, D, E and F are nitrogen; and the remaining of A, B, D, E and F are independently CH or CR^6;

where R^6 is a halogen atom; C_{1-4}alkyl (e.g. C_{1-2}alkyl); C_{1-4}fluoroalkyl (e.g. C_{1-2}fluoroalkyl); C_{1-4}alkoxy (e.g. C_{1-2}alkoxy); C_{1-2}fluoroalkoxy; C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-; -NR^{15}-C(O)R^{16}; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; wherein R^7 and R^8 are as herein defined;

wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is a hydrogen atom (H), C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one, two or three of J, L, M and Q are nitrogen; and the remaining of J, L, M and Q are independently CH or CR^6 where R^6 is as defined herein;

or R^4 and R^5 taken together are –$(CH_2)_p{}^1$– or -C(O)-$(CH_2)_p{}^2$- or -$(CH_2)_p{}^3$-X^5-$(CH_2)_p{}^4$- or -C(O)-X^5-$(CH_2)_p{}^5$-, in which: p^1 = 3, 4, 5 or 6 (preferably p = 4 or 5), p^2 is 2, 3, 4, or 5 (preferably p^2 is 2, 3 or 4), and p^3 and p^4 and p^5 independently are 2 or 3 (independently preferably 2) and X^5 is O or NR^{17};

wherein R^{17} is a hydrogen atom (H); C_{1-4}alkyl (e.g. C_{1-2}alkyl); C_{1-2}fluoroalkyl; C_{3-6}cycloalkyl; -$(CH_2)_p{}^6$-C(O)R^{16} wherein p^6 is 0, 1, 2 or 3 (preferably p^6 is 0); -$(CH_2)_p{}^6$-C(O)$NR^{12}R^{13}$; -$(CH_2)_p{}^6$-C(O)OR^{16}; -SO_2R^{16}; or phenyl or benzyl wherein the phenyl or benzyl is optionally substituted at an aromatic carbon atom by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

and wherein, when R^4 and R^5 taken together are –$(CH_2)_p{}^1$– or -C(O)-$(CH_2)_p{}^2$-, the NR^4R^5 heterocycle is optionally substituted by one R^{18} substituent wherein R^{18} is: C_{1-4}alkyl (e.g. C_{1-2}alkyl); C_{1-2}fluoroalkyl; C_{3-6}cycloalkyl; C_{1-2}alkoxy (not substituted at a ring-carbon bonded to the NR^4R^5 ring-nitrogen); C_1fluoroalkoxy (not substituted at a ring-carbon bonded to the NR^4R^5 ring-nitrogen); OH (not substituted at a ring-carbon bonded to the NR^4R^5 ring-nitrogen); -$(CH_2)_p{}^7$-C(O)R^{16} wherein p^7 is 0, 1, 2 or 3 (preferably p^7 is 0 or 1); -$(CH_2)_p{}^7$-C(O)OR^{16}; -$(CH_2)_p{}^7$-OC(O)R^{16}; -$(CH_2)_p{}^7$-C(O)$NR^{12}R^{13}$; -$(CH_2)_p{}^7$-NR^{15}C(O)R^{16}; -$(CH_2)_p{}^7$-NR^{15}C(O)$NR^{12}R^{13}$; -$(CH_2)_p{}^7$-NR^{15}C(O)OR^{16}; -$(CH_2)_p{}^7$-SO_2R^{16}; -$(CH_2)_p{}^7$-SO_2 $NR^{12}R^{13}$; -$(CH_2)_p{}^7$-$NR^{15}SO_2R^{16}$; -$(CH_2)_p{}^7$-OH; -$(CH_2)_p{}^7$-OR^{16}; or phenyl optionally

substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or R^4 and R^5 taken together are $-(CH_2)_p{}^1-$ or $-C(O)-(CH_2)_p{}^2-$ or $-(CH_2)_p{}^3-X^5-(CH_2)_p{}^4-$ or $-C(O)-X^5-(CH_2)_p{}^5-$ as defined herein, and wherein the NR^4R^5 heterocycle is fused to a phenyl ring optionally substituted on the phenyl by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; and

R^{5a} is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl; phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^{5a} has the sub-formula (x), (y) or (z) as defined herein

and wherein:

R^{12} and R^{13} independently are H; C_{1-5}alkyl (e.g. C_{1-3}alkyl); C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or R^{12} and R^{13} together are $-(CH_2)_n{}^6-$ or $-C(O)-(CH_2)_n{}^7-$ or $-C(O)-(CH_2)_n{}^7-C(O)-$ or $-(CH_2)_n{}^8-X^{12}-(CH_2)_n{}^9-$ or $-C(O)-X^{12}-(CH_2)_n{}^{10}-$ in which: n^6 is 3, 4, 5 or 6 (preferably n^6 is 4 or 5), n^7 is 2, 3, 4, or 5 (preferably n^7 is 2, 3 or 4), n^8 and n^9 and n^{10} independently are 2 or 3 (independently preferably 2) and X^{12} is O or NR^{14} wherein R^{14} is H or C_{1-2}alkyl;

R^{15} is a hydrogen atom (H); C_{1-4}alkyl (e.g. ^{t}Bu or C_{1-2}alkyl e.g. methyl); C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

R^{16} is C_{1-4}alkyl (e.g. C_{1-2}alkyl); C_{3-6}cycloalkyl; pyridinyl (e.g. pyridin-2-yl); or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; and

$R^{19}$is C_{1-4}alkyl; $-(CH_2)_n{}^{20}-OR^{20}$ wherein n^{20} is 1, 2, 3 or 4 and R^{20} is a hydrogen atom (H) or C_{1-4}alkyl; -CH(Me)-OH; $-CH_2-SH$; $-CH_2-CH_2-S-Me$; benzyl; or (4-hydroxyphenyl)methyl (i.e. 4-hydroxy-benzyl).

In compounds, for example in the compounds of formula (I) (or formula (IA) or formula (IB), see later), an "alkyl" group or moiety may be straight-chain or branched. Alkyl groups, for example C_{1-8}alkyl or C_{1-6}alkyl or C_{1-4}alkyl or C_{1-3}alkyl or C_{1-2}alkyl, which may be employed include C_{1-6}alkyl or C_{1-4}alkyl or C_{1-3}alkyl or C_{1-2}alkyl such as methyl, ethyl, n-propyl, n-butyl, n-pentyl, or n-hexyl or any branched isomers thereof such as isopropyl, t-butyl, sec-butyl, isobutyl, 3-methylbutan-2-yl, 2-ethylbutan-1-yl, or the like.

A corresponding meaning is intended for "alkoxy", "alkylene", and like terms derived from alkyl. For example, "alkoxy" such as C_{1-6}alkoxy or C_{1-4}alkoxy or C_{1-2}alkoxy includes methoxy, ethoxy, propyloxy, and oxy derivatives of the alkyls listed above. "Alkylsulfonyl" such as C_{1-4}alkylsulfonyl includes methylsulfonyl (methanesulfonyl), ethylsulfonyl, and others derived from the alkyls listed above. "Alkylsulfonyloxy" such as C_{1-4}alkylsulfonyloxy includes methanesulfonyloxy (methylsulfonyloxy), ethanesulfonyloxy, *et al.*

"Cycloalkyl", for example C_{3-8}cycloalkyl, includes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, and the like. Preferably, a C_{3-8}cycloalkyl group is C_{3-6}cycloalkyl or C_{5-6}cycloalkyl , that is contains a 3-6 membered or 5-6 membered carbocyclic ring.

"Fluoroalkyl" includes alkyl groups with one, two, three, four, five or more fluorine substituents, for example C_{1-4}fluoroalkyl or C_{1-3}fluoroalkyl or C_{1-2}fluoroalkyl such as monofluoromethyl, difluoromethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl (CF_3CH_2-), 2,2-difluoroethyl (CHF_2CH_2-), 2-fluoroethyl (CH_2FCH_2-), etc. "Fluoroalkoxy" includes C_{1-4}fluoroalkoxy or C_{1-2}fluoroalkoxy such as trifluoromethoxy, pentafluoroethoxy, monofluoromethoxy, difluoromethoxy, etc. "Fluoroalkylsulfonyl" such as C_{1-4}fluoroalkylsulfonyl includes trifluoromethanesulfonyl, pentafluoroethylsulfonyl, etc.

A halogen atom ("halo") present in compounds, for example in the compounds of formula (I), can be a fluorine, chlorine, bromine or iodine atom ("fluoro", "chloro", "bromo" or "iodo").

When the specification states that atom or moiety A is "bonded" or "attached" to atom or moiety B, it means that atom/moiety A is directly bonded to atom/moiety B usually by means of one or more covalent bonds, and excludes A being indirectly attached to B via one or more intermediate atoms/moieties (e.g. excludes A-C-B); unless it is clear from the context that another meaning is intended.

Preferably, R^1 is C_{1-4}alkyl (e.g. methyl, ethyl, n-propyl, isopropyl or n-butyl), C_{1-3}fluoroalkyl or -CH_2CH_2OH; R^1 is more preferably C_{1-3}alkyl (e.g. methyl, ethyl or n-propyl), C_{1-2}fluoroalkyl, or -CH_2CH_2OH; still more preferably C_{1-3}alkyl, C_2fluoroalkyl or -CH_2CH_2OH such as methyl, ethyl, n-propyl or -CH_2CH_2OH. Yet more preferably, R^1 is C_{2-3}alkyl (e.g. ethyl or n-propyl), C_2fluoroalkyl (e.g.

C_1fluoroalkyl-CH_2- such as CF_3-CH_2-) or -CH_2CH_2OH; in particular ethyl, n-propyl or -CH_2CH_2OH. R^1 is most preferably ethyl.

Preferably, R^2 is a hydrogen atom (H) or methyl, more preferably a hydrogen atom (H).

Preferably, in R^3 there is one substituent or no substituent.

In one optional embodiment, R^3 is the optionally substituted C_{3-8}cycloalkyl or the optionally substituted heterocyclic group of sub-formula (aa), (bb) or (cc). In this embodiment, optionally, in R^3, the C_{3-8}cycloalkyl or the heterocyclic group of sub-formula (aa), (bb) or (cc) is optionally substituted with one or two substituents independently being (e.g. being) oxo (=O), OH, C_{1-2}alkoxy, C_{1-2}fluoroalkoxy (e.g. trifluoromethoxy), or C_{1-2}alkyl; and wherein any OH, alkoxy or fluoroalkoxy substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (I) and is not substituted at either R^3 ring carbon bonded to the Y group of the heterocyclic group (aa), (bb) or (cc).

In one optional embodiment, where R^3 is optionally substituted C_{3-8}cycloalkyl, it is not optionally substituted C_5cycloalkyl, i.e. not optionally substituted cyclopentyl. In this case, more preferably, R^3 is optionally substituted C_{6-8}cycloalkyl.

Where R^3 is optionally substituted C_{3-8}cycloalkyl, it is more preferably optionally substituted C_6cycloalkyl (i.e. cyclohexyl); for example C_6cycloalkyl optionally substituted with one or two substituents independently being (e.g. being) oxo (=O), OH, C_{1-2}alkoxy, C_{1-2}fluoroalkoxy (e.g. trifluoromethoxy), or C_{1-2}alkyl, and wherein any OH, alkoxy or fluoroalkoxy substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (I).

Where R^3 is optionally substituted C_{3-8}cycloalkyl, the one or two optional substituents preferably comprise (e.g. is or independently are (e.g. is or are)) oxo (=O); OH; C_1alkoxy; C_1fluoroalkoxy (e.g. trifluoromethoxy); NHR^{21} wherein R^{21} is a hydrogen atom (H) or C_{1-2} straight-chain alkyl; C_{1-2}alkyl such as methyl; C_1fluoroalkyl such as -CH_2F or -CHF_2; -CH_2OH; -CH_2NHR^{22} wherein R^{22} is H; -$C(O)OR^{23}$ wherein R^{23} is H or methyl; -$C(O)NHR^{24}$ wherein R^{24} is H or methyl; -$C(O)R^{25}$ wherein R^{25} is methyl; fluoro; hydroxyimino (=N-OH); or (C_{1-2}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-2}alkyl); and wherein any OH, alkoxy, fluoroalkoxy or NHR^{21} substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (I) and is not substituted at either R^3 ring carbon bonded to the Y group of the heterocyclic group (aa), (bb) or (cc).

More preferably, where R^3 is optionally substituted C_{3-8}cycloalkyl, the one or two optional substituents comprise (e.g. is or independently are (e.g. is or are)) oxo (=O); OH; NHR^{21} wherein R^{21} is a hydrogen atom (H); C_{1-2}alkyl such as methyl; C_1fluoroalkyl such as $-CH_2F$ or $-CHF_2$; $-C(O)OR^{23}$ wherein R^{23} is H or methyl; $-C(O)NHR^{24}$ wherein R^{24} is H or methyl; fluoro; hydroxyimino (=N-OH); or (C_{1-2}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-2}alkyl).

Still more preferably, where R^3 is optionally substituted C_{3-8}cycloalkyl, the one or two optional substituents comprise (e.g. is or independently are (e.g. is or are)) oxo (=O); OH; NHR^{21} wherein R^{21} is a hydrogen atom (H); methyl; $-CH_2F$; $-CHF_2$; $-C(O)OR^{23}$ wherein R^{23} is H; fluoro; hydroxyimino (=N-OH); or (C_{1-2}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-2}alkyl). Yet more preferably, where R^3 is optionally substituted C_{3-8}cycloalkyl, the one or two optional substituents comprise (e.g. is or independently are (e.g. is or are)) oxo (=O); OH; methyl; fluoro; hydroxyimino (=N-OH); or (C_{1-2}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-2}alkyl).

Most preferably, where R^3 is optionally substituted C_{3-8}cycloalkyl, the one or two optional substituents comprise (e.g. is or independently are (e.g. is or are)) OH, oxo (=O) or oximo (=N-OH). For example, the one or two optional substituents can comprise (e.g. is or are) OH and/or oxo (=O).

Optionally, in R^3, the C_{3-8}cycloalkyl can be unsubstituted.

Where R^3 is optionally substituted C_{3-8}cycloalkyl, e.g. optionally substituted C_{5-8}cycloalkyl such as optionally substituted C_6cycloalkyl (optionally substituted cyclohexyl), the one or two optional substituents if present preferably comprise a substituent (for example is or are substituent(s)) at the 3-, 4- or 5- position(s) of the R^3 cycloalkyl ring. (In this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (I)).

Where R^3 is optionally substituted C_{3-8}cycloalkyl, any OH, alkoxy, fluoroalkoxy, $-CH_2OH$, $-CH_2CH_2OH$, $-CH_2NHR^{22}$, $-C(O)OR^{23}$, $-C(O)NHR^{24}$, $-C(O)R^{25}$ or fluoro substituent (particularly any OH substituent) is more preferably at the the 3-, 4- or 5-position, e.g. 3- or 5-position, of the R^3 cycloalkyl (e.g. C_{6-8}cycloalkyl) ring. For example, any OH, alkoxy, fluoroalkoxy, $-CH_2OH$, $-CH_2CH_2OH$, $-CH_2NHR^{22}$, $-C(O)OR^{23}$, $-C(O)NHR^{24}$, $-C(O)R^{25}$ or fluoro substituent (particularly any OH substituent) can be at the 3-position of a R^3 C_5cycloalkyl (cyclopentyl) ring or at the 3-,

4- or 5- position, e.g. 3- or 5-position, of a R^3 C_6cycloalkyl (cyclohexyl) ring. (In this connection, and also below, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (I)).

Where R^3 is optionally substituted C_{3-8}cycloalkyl, any NHR^{21} substituent is preferably at the 2-, 3-, 4- or 5- position, preferably the 2- or 3-position or more preferably the 3-position, of the R^3 cycloalkyl (e.g. C_{6-8}cycloalkyl e.g. cyclohexyl) ring.

Where R^3 is optionally substituted C_{3-8}cycloalkyl, any alkyl or fluoroalkyl substituent is preferably at the 1-, 2-, 3-, 4- or 5- position, more preferably the 1-, 2-, 3- or 5-position, still more preferably the 1- or 3-position, of the R^3 cycloalkyl (e.g. C_{6-8}cycloalkyl e.g. cyclohexyl) ring.

Where R^3 is optionally substituted C_{3-8}cycloalkyl, any oxo (=O), hydroxyimino (=N-OH); or (C_{1-4}alkoxy)imino (=N-OR^{26}) substituent is preferably at the 3- or 4-position, preferably at the 4-position, of the R^3 cycloalkyl (e.g. C_{6-8}cycloalkyl e.g. cyclohexyl) ring.

Where R^3 is optionally substituted C_{3-8}cycloalkyl, R^3 is preferably cyclohexyl (i.e. unsubstituted), or cyclohexyl substituted by one oxo (=O), OH, NHR^{21}, C_{1-2}alkyl, C_{1-2}fluoroalkyl, -CH_2OH, -C(O)OR^{23}, -C(O)NHR^{24}, -C(O)R^{25}, fluoro, hydroxyimino (=N-OH), (C_{1-4}alkoxy)imino (=N-OR^{26}) substituent, or cyclohexyl substituted by two fluoro substituents. More preferably, R^3 is cyclohexyl (i.e. unsubstituted), or cyclohexyl substituted by one oxo (=O), OH, NHR^{21}, C_{1-2}alkyl, C_{1-2}fluoroalkyl, -C(O)OR^{23}, fluoro, hydroxyimino (=N-OH) or (C_{1-4}alkoxy)imino (=N-OR^{26}) substituent, or cyclohexyl substituted by two fluoro substituents. Still more preferably R^3 is cyclohexyl (i.e. unsubstituted) or cyclohexyl substituted by one oxo (=O), hydroxyimino (=N-OH), C_{1-2}alkyl or OH substituent. The optional substituent can be at the 3- or 4- position, e.g. 3-position, of the R^3 cyclohexyl ring; more preferably any OH substituent is preferably at the 3-position of the R^3 cyclohexyl ring, and/or any oxo (=O), hydroxyimino (=N-OH) or (C_{1-4}alkoxy)imino (=N-OR^{26}) substituent is preferably at the 4-position of the R^3 cyclohexyl ring.

Where R^3 is optionally substituted C_6cycloalkyl, R^3 can for example be 4-hydroxy-cyclohexyl (i.e. 4-hydroxycyclohexan-1-yl), but R^3 is more preferably cyclohexyl (i.e. unsubstituted), 3-hydroxy-cyclohexyl (i.e. 3-hydroxycyclohexan-1-yl), 4-oxo-cyclohexyl (i.e. 4-oxocyclohexan-1-yl), 4-(hydroxyimino)cyclohexyl (i.e. 4-(hydroxyimino)cyclohexan-1-yl), 4-(C_{1-2}alkoxyimino)cyclohexyl, 1-methylcyclohexyl

or 3-methylcyclohexyl. Where R^3 is optionally substituted C_6cycloalkyl, R^3 is most preferably cyclohexyl (i.e. unsubstituted), 4-oxo-cyclohexyl (i.e. 4-oxocyclohexan-1-yl) or 4-(hydroxyimino)cyclohexyl (i.e. 4-(hydroxyimino)cyclohexan-1-yl).

Where R^3 is optionally substituted C_5cycloalkyl (optionally substituted cyclopentyl), R^3 can for example be cyclopentyl (i.e. unsubstituted) or 3-hydroxy-cyclopentyl.

Where R^3 is optionally substituted mono-unsaturated-C_{5-7}cycloalkenyl, preferably it is optionally substituted mono-unsaturated-C_{5-6}cycloalkenyl, more preferably optionally substituted mono-unsaturated-C_6cycloalkenyl (i.e. optionally substituted mono-unsaturated-cyclohexenyl = optionally substituted cyclohexenyl). Still more preferably, the R^3 cyclohexenyl is optionally substituted cyclohex-3-en-1-yl.

Where R^3 is optionally substituted mono-unsaturated-C_{5-7}cycloalkenyl, preferably the R^3 cycloalkenyl is optionally substituted with one or two substituents being fluoro or methyl provided that if there are two substituents then they are not both methyl. Preferably, the R^3 cycloalkenyl is optionally substituted with one substituent being fluoro or C_{1-2}alkyl (e.g. methyl); more preferably the R^3 cycloalkenyl is substituted with one fluoro substituent or is unsubstituted. For R^3 cycloalkenyl, the optional substituent(s) can be at the 1-, 2-, 3-, 4- or 5- position(s) of the cycloalkenyl ring.

Where R^3 is the heterocyclic group of sub-formula (aa), (bb) or (cc), then Y is preferably O, S, SO_2, NH or N-C(O)methyl, more preferably O, NH or N-C(O)methyl, still more preferably O or N-C(O)methyl, most preferably O. (When Y is NH or N-C(O)methyl, then R^{10} is H or C(O)methyl).

Preferably, R^{10} is a hydrogen atom (H), methyl, ethyl, $C(O)NH_2$, C(O)methyl or $C(O)\text{-}CF_3$. Optionally, R^{10} can be a hydrogen atom (H), methyl, ethyl, C(O)methyl or $C(O)\text{-}CF_3$, more preferably H, C(O)methyl or $C(O)\text{-}CF_3$, still more preferably H or C(O)methyl.

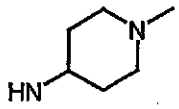
Where R^3 is the heterocyclic group of sub-formula (aa), (bb) or (cc), then it is preferable that R^3 is the heterocyclic group of sub-formula (aa) or (bb), more preferably of sub-formula (bb).

In sub-formula (bb), n^1 is preferably 1. In sub-formula (cc), n^2 is preferably 1. That is, six-membered rings are preferred in the R^3 heterocyclic group.

Suitably, in R^3, the heterocyclic group of sub-formula (aa), (bb) or (cc) is unsubstituted (In this connection, where Y is NR^{10}, R^{10} is not classified as a substituent).

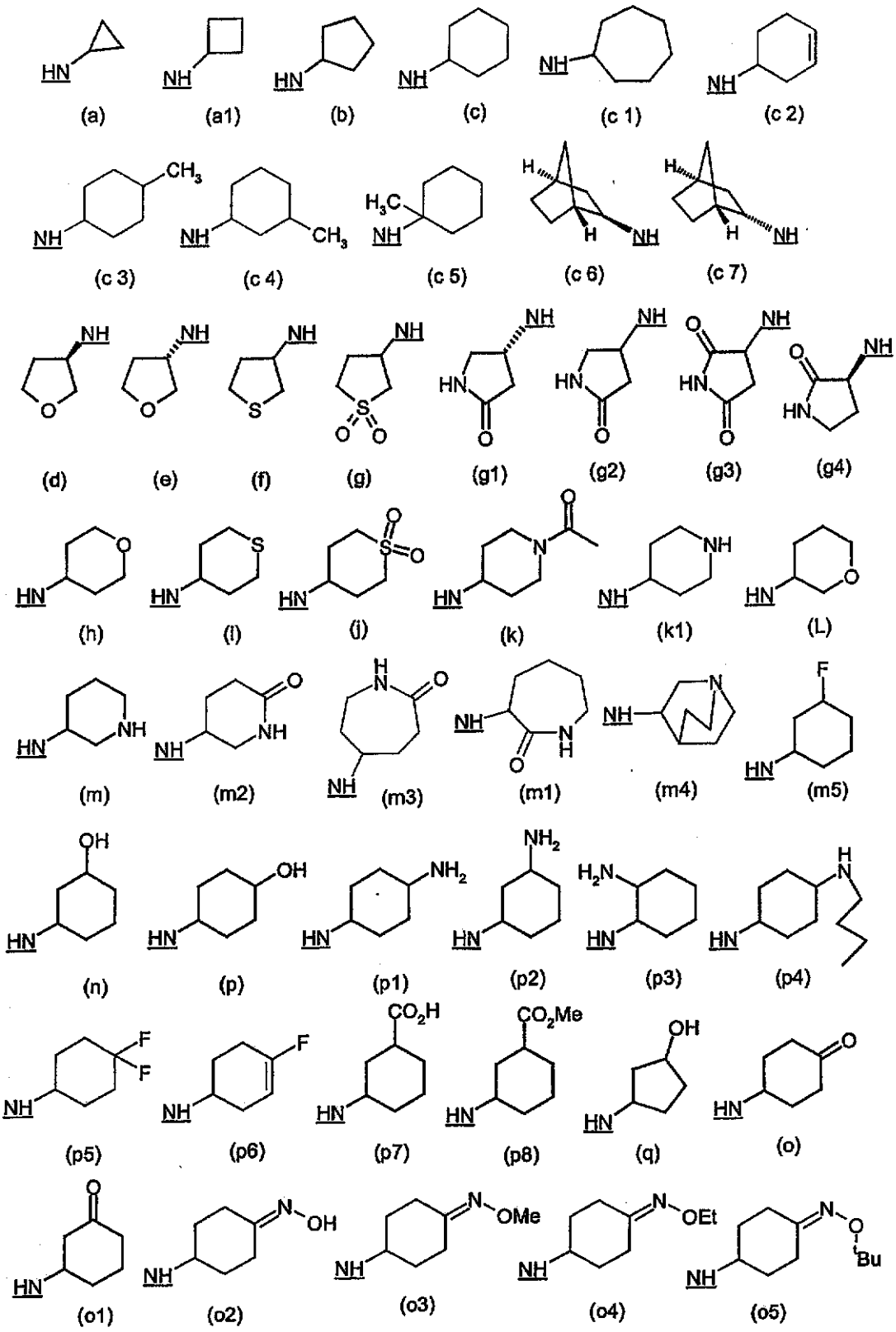
In the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc), the one or two optional substituents preferably comprise (e.g. is or independently are ((e.g. is or are)) OH; oxo (=O); C_{1-2}alkyl (e.g. methyl) or C_{1-2}fluoroalkyl (e.g. C_1fluoroalkyl such as $-CH_2F$ or $-CHF_2$). More preferably, in the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc), the one or two optional substituents comprise (e.g. is or independently are ((e.g. is or are)) OH and/or oxo; most preferably the one or two optional substituents comprise (e.g. is or are) oxo (=O). In the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc), any oxo (=O) substituents are preferably on a carbon atom bonded (adjacent) to X, and/or can be at the 2-, 3-, 4- or 5- position(s) of the R^3 heterocyclic ring. (In this connection, the 1-position of the R^3 heterocyclic ring is deemed to be the connection point to the -NH- in formula (I)). Preferably, only C_{1-2}alkyl, C_{1-2}fluoroalkyl, fluoro or oxo (=O) substitution or no substitution is allowed at each of the 2- and 6-positions of the R^3 heterocyclic ring.

When R^3 is the heterocyclic group of sub-formula (aa) and Y is NR^{10}, then preferably R^{10} is not C(O)-Me. More preferably, when R^3 is the heterocyclic group of sub-formula (aa) and Y is NR^{10}, then R^{10} is preferably not C(O)R, i.e. or e.g. R^{10} is preferably not $C(O)NH_2$, C(O)-C_{1-2}alkyl or C(O)-C_1fluoroalkyl. In one embodiment, Y is O, S, SO_2 or NH when R^3 is the heterocyclic group of sub-formula (aa).

Optionally, according to one embodiment of the invention, NHR^3 is not . More preferably, when R^3 is the heterocyclic group of sub-formula (bb) and Y is NR^{10}, and optionally when n^1 is 1, then preferably R^{10} is not methyl. More preferably, when R^3 is the heterocyclic group of sub-formula (bb) and Y is NR^{10}, and optionally when n^1 is 1, then R^{10} is preferably not alkyl or substituted alkyl, i.e. or e.g. R^{10} is preferably not C_{1-4}alkyl (e.g. methyl or ethyl), C_{1-2}fluoroalkyl or $CH_2C(O)NH_2$. In one embodiment, when R^3 is the heterocyclic group of sub-formula (bb), Y is preferably O, S, SO_2 or NR^{10}, wherein R^{10} is H, $C(O)NH_2$, C(O)-C_{1-2}alkyl or C(O)-C_1fluoroalkyl, or more preferably Y is H or C(O)Me. More preferably, for sub-formula (bb), Y is O or NR^{10}.

Where R^3 is a bicyclic group of sub-formula (dd) or (ee), preferably it is of sub-formula (ee). In sub-formula (ee), preferably Y^1, Y^2 and Y^3 are all CH_2.

Preferably, NHR^3 is of sub-formula (a), (a1), (b), (c), (c 1), (c 2), (c 3), (c 4), (c 5), (c 6), (c 7), (d), (e), (f), (g), (g1), (g2), (g3), (g4), (h), (i), (j), (k), (k1), (L), (m), (m1), (m2), (m3), (m4), (m5), (n), (o), (o1), (o2), (o3), (o4), (o5), (p), (p1), (p2), (p3), (p4), (p5), (p6), (p7), (p8) or (q):


(a)
(a1)
(b)
(c)
(c 1)
(c 2)
(c 3)
(c 4)
(c 5)
(c 6)
(c 7)
(d)
(e)
(f)
(g)
(g1)
(g2)
(g3)
(g4)
(h)
(i)
(j)
(k)
(k1)
(L)
(m)
(m2)
(m3)
(m1)
(m4)
(m5)
(n)
(p)
(p1)
(p2)
(p3)
(p4)
(p5)
(p6)
(p7)
(p8)
(q)
(o)
(o1)
(o2)
(o3)
(o4)
(o5)

In the sub-formulae (a) to (q) etc above, the -NH- connection point of the NHR^3 group to the 4-position of the pyrazolopyridine of formula (I) is underlined.

Preferably, NHR^3 is of sub-formula (c), (c1), (c 2), (c 3), (c 4), (c 5), (c 6), (c 7), (d), (e), (f), (g1), (g4), (h), (i), (j), (k), (k1), (L), (m), (m1), (m2), (m3), (m5), (n), (o), (o1), (o2), (o3), (o4), (o5), (p), (p2), (p3), (p5), (p6), (p7) or (q). More preferably, NHR^3 is of sub-formula (c), (c1), (c 4), (c 5), (h), (i), (j), (k), (m1), (m2), (n), (o), (o2), (o3), (p2), (p5), (p6) or (q). Still more preferably, NHR^3 is of sub-formula (c), (h), (k), (n), (o) or (o2); for example (c), (h), (o) or (o2). Most preferably, R^3 is tetrahydro-2H-pyran-4-yl; that is NHR^3 is most preferably of sub-formula (h), as shown above.

According to one embodiment, NHR^3 is of sub-formula (a), (b), (c), (d), (e), (f), (g), (g1), (g2), (g3), (h), (i), (j), (k), (L), (m), (m1), (n), (o), (o1), (p) or (q). In this embodiment, preferably, NHR^3 is of sub-formula (c), (d), (e), (f), (g1), (h), (i), (j), (k), (m), (m1), (n), (o), (o1), (p), or (q); and more preferably in this embodiment, NHR^3 is of sub-formula (c), (h), (i), (j), (k), (m1), (n), (o) or (q). Still more preferably in this embodiment, NHR^3 is of sub-formula (c), (h), (k), (n) or (o). Most preferably, R^3 is tetrahydro-2H-pyran-4-yl; that is NHR^3 is most preferably of sub-formula (h), as shown above.

According to another embodiment, NHR^3 is of sub-formula (a), (b), (c), (d), (e), (f), (g), (h), (i), (j) or (k). In this embodiment, preferably, NHR^3 is of sub-formula (c), (d), (e), (f), (h), (i), (j) or (k); and more preferably in this embodiment, NHR^3 is of sub-formula (c), (h), (i), (j) or (k). Most preferably, R^3 is tetrahydro-2H-pyran-4-yl; that is NHR^3 is most preferably of sub-formula (h), as shown above.

When NHR^3 is of sub-formula (n), then preferably it is a *cis*-(3-hydroxycyclohex-1-yl)amino group, eg in any enantiomeric form or mixture of forms but preferably racemic.

Preferably, X is NR^4R^5.

Where R^4 is C_{1-6}alkyl, then preferably it is C_{1-4}alkyl or C_{1-2}alkyl. Where R^4 is C_{1-3}fluoroalkyl then preferably it is C_{1-2}fluoroalkyl.

Most preferably, R^4 is a hydrogen atom (H).

Where R^4 is C_{2-6}alkyl substituted by one substituent R^{11}, then preferably R^4 is C_{2-4}alkyl (e.g. C_{2-3}alkyl) substituted by one substituent R^{11}. More preferably, R^4 is

$-(CH_2)_{n^3}-R^{11}$ wherein n^3 is 2, 3 or 4. Still more preferably, n^3 is 2 and/or R^4 is $-(CH_2)_{n^3}-OH$.

When R^5 is C_{2-6}alkyl substituted by one or two independent substituents R^{11}, it is preferable that R^5 is C_{2-4}alkyl (e.g. C_{2-3}alkyl) substituted by one or two independent substituents R^{11}. When R^5 is C_{2-6}alkyl (e.g. C_{2-4}alkyl or C_{2-3}alkyl) substituted by one or two independent substituents R^{11}, it is preferable that R^5 is C_{2-6}alkyl (e.g. C_{2-4}alkyl or C_{2-3}alkyl) substituted by one substituent R^{11}. It is more preferable that R^5 is $-(CH_2)_{n^5}-R^{11}$ wherein n^5 is 2, 3 or 4. Preferably n^5 is 2 or 3, more preferably 2.

Preferably, each substituent R^{11}, independently of any other R^{11} substituent present, is: hydroxy (OH); C_{1-6}alkoxy (e.g. C_{1-4}alkoxy such as t-butyloxy, ethoxy or methoxy); phenyloxy; benzyloxy; $-NR^{12}R^{13}$; $-NR^{15}-C(O)R^{16}$; $-NR^{15}-C(O)-NH-R^{15}$; or $-NR^{15}-SO_2R^{16}$ (more preferably C_{1-6}alkoxy, $-NR^{15}-C(O)-NH-R^{15}$, or $-NR^{15}-SO_2R^{16}$; most preferably $-NR^{15}-SO_2R^{16}$). In all cases, any R^{11} substituent which is OH, alkoxy or $-NR^{12}R^{13}$ is not substituted at any carbon atom, of any R^4 or R^5 substituted alkyl, which is bonded to the nitrogen of NR^4R^5.

Where R^5 is C_{1-8}alkyl, then preferably it is C_{1-5}alkyl or C_{1-3}alkyl. Where R^5 is C_{1-8}fluoroalkyl then preferably it is C_{1-3}fluoroalkyl or C_{1-2}fluoroalkyl. Where R^5 is C_{3-8}cycloalkyl optionally substituted by a C_{1-2}alkyl group, then preferably the C_{3-8}cycloalkyl is not substituted at the ring-carbon bonded to the nitrogen of NR^4R^5. Where R^5 is optionally substituted C_{3-8}cycloalkyl, then more preferably it is C_{3-8}cycloalkyl (i.e. unsubstituted).

When R^5 is optionally substituted $-(CH_2)_{n^4}-C_{3-8}$cycloalkyl wherein n^4 is 1, 2 or 3, then n^4 is preferably 1 or 2 or more preferably 1, and/or preferably R^5 is optionally substituted $-(CH_2)_{n^4}-C_{5-6}$cycloalkyl or optionally substituted $-(CH_2)_{n^4}-C_6$cycloalkyl. When R^5 is optionally substituted $-(CH_2)_{n^4}-C_{3-8}$cycloalkyl, preferably it is not substituted. Most preferably R^5 is (cyclohexyl)methyl-, that is $-CH_2$-cyclohexyl.

When R^{19} is C_{1-4}alkyl, then preferably it is isobutyl, sec-butyl, or C_{1-3}alkyl such as methyl or isopropyl. When R^{19} is $-(CH_2)_{n^{20}}-OR^{20}$, then preferably n^{20} is 1 and/or preferably R^{20} is a hydrogen atom (H).

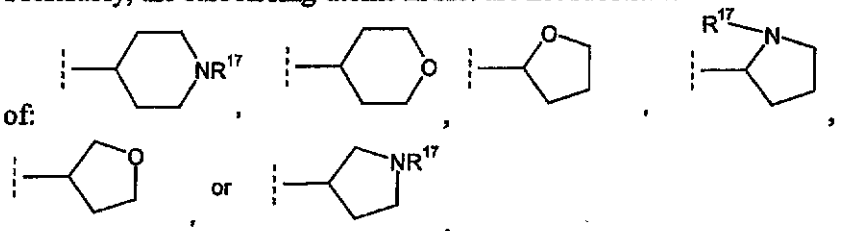
When R^5 is $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{12}-C(O)NR^{12}R^{13}$; $-CHR^{19}-C(O)NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-C(O)OR^{16}$; $-CHR^{19}-C(O)OR^{16}$; $-(CH_2)_n{}^{12}-SO_2-NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-SO_2R^{16}$; or $-(CH_2)_n{}^{12}-CN$; then in one embodiment of the invention R^5 can be: $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{12}-C(O)NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-C(O)OR^{16}$; $-(CH_2)_n{}^{12}-SO_2-NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-SO_2R^{16}$; or $-(CH_2)_n{}^{12}-CN$.

When R^5 is $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{12}-C(O)NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-C(O)OR^{16}$; $-(CH_2)_n{}^{12}-SO_2-NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-SO_2R^{16}$; or $-(CH_2)_n{}^{12}-CN$; then R^5 can for example be $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{12}-C(O)NR^{12}R^{13}$; or $-(CH_2)_n{}^{12}-CN$; preferably $-(CH_2)_n{}^{11}-C(O)R^{16}$.

Preferably, n^{11} is 1, 2, 3 or 4; more preferably n^{11} is 1 or 2. Advantageously, n^{12} is 1 or 2.

When R^5 is $-(CH_2)_n{}^{13}$-Het, it is preferable that n^{13} is 0, 1 or 2, more preferably 0 or 1.

Preferably, Het is a 5- or 6-membered saturated or partly-saturated heterocyclic ring and/or preferably is a 4-, 5-, 6- or 7-membered saturated heterocyclic ring. Preferably, the heterocyclic ring Het contains one ring-hetero-atom selected from O, S and N. Preferably, the carbon ring-atoms in Het are not substituted. Het is most preferably one of:



When R^5 is optionally substituted phenyl, then preferably it is phenyl optionally substituted with one or two of the substituents defined herein.

When R^5 is optionally substituted phenyl, then preferably R^5 is phenyl optionally substituted with, independently, one, two or three (preferably one or two; or one) of: a halogen atom (preferably fluoro and/or chloro); C_{1-2}alkyl; C_{1-2}fluoroalkyl (e.g. trifluoromethyl); C_{1-2}alkoxy (e.g. methoxy); trifluoromethoxy; C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-; $-NR^{15}-C(O)R^{16}$; R^7R^8N; OH; C_{1-2}alkoxymethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one of fluoro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy. More preferably R^5 is phenyl optionally substituted with one or two (preferably one) of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy,

trifluoromethoxy, R^7R^8N-SO_2-, R^7R^8N-CO-, or C_{1-2}alkyl-SO_2-CH_2-. When R^5 is optionally substituted phenyl, then preferably one or all of the one or two optional substituents are substituted at the *meta*- (3- and/or 5-) and/or *para*- (4-) position(s) of the phenyl ring with respect to the phenyl ring-carbon bonded to the nitrogen of NR^4R^5.

Preferably, R^7 and/or R^8 are independently a hydrogen atom (H); C_{1-2}alkyl such as methyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one of: fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or R^7 and R^8 together are $-(CH_2)_n{}^6-$ or $-(CH_2)_n{}^8-X^7-(CH_2)_n{}^9-$ wherein X^7 is NR^{14} or preferably O.

When R^7 is cycloalkyl or optionally substituted phenyl, then preferably R^8 is neither cycloalkyl nor optionally substituted phenyl.

Most preferably, R^7 and/or R^8 independently are a hydrogen atom (H) or C_{1-2}alkyl. It is preferable that R^7 is a hydrogen atom (H).

Preferably n^6 is 4 or 5. Preferably n^7 is 2, 3 or 4. Preferably, n^8, n^9 and/or n^{10} is/are independently 2.

In general, it is preferable that R^5 has the sub-formula (x) or (y) or (y1) or (z).

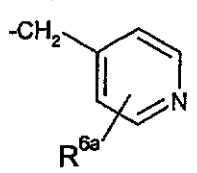
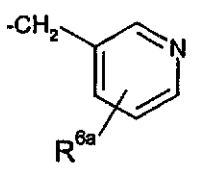
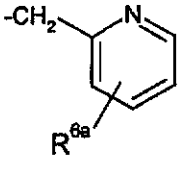
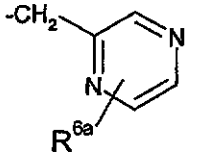
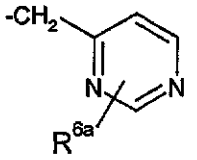
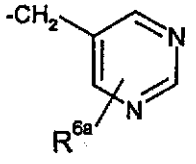
When R^5 has the sub-formula (x) or (y) or (y1) or (z), then preferably R^5 has the sub-formula (x) or (y) or (y1) or has the sub-formula (x) or (y) or (z). More preferably R^5 has the sub-formula (x) or (y), most preferably (x). In one embodiment, R^5 has the sub-formula (z).

Preferably, n is 1 or 2. More preferably, n = 1. Preferably, m = 1. Preferably, r = 1 or 2, more preferably 1.

In sub-formula (x), (y) and/or (y1), it is preferred that none, one or two of A, B, D, E and F are nitrogen; none, one, two or three of A, B, D, E and F are CR^6; and the remaining of A, B, D, E and F are CH. More preferably, none, one or two of A, B, D, E and F are nitrogen; none, one or two of A, B, D, E and F are CR^6; and the remaining of A, B, D, E and F are CH.

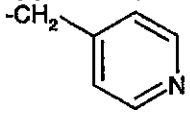
In sub-formula (x), (y) and/or (y1), preferably, none or one of A, B, D, E and F are nitrogen, and/or preferably none, one or two of A, B, D, E and F are CR^6.

Preferably, sub-formula (x) is: benzyl; phenethyl (Ph-C_2H_4-); benzyl substituted on the phenyl ring with one or two R^6 substituents; phenethyl (Ph-C_2H_4-) substituted on the phenyl ring with one or two R^6 substituents; or one of the following:

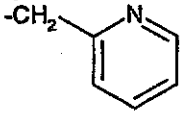







, wherein R^{6a} is either R^6 as defined herein or (preferably) hydrogen.

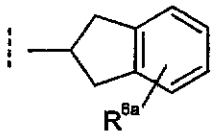
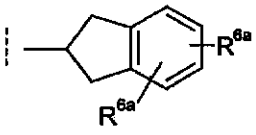
Most preferably, sub-formula (x) is benzyl or pyridinylmethyl

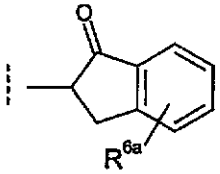


[e.g. pyridin-4-ylmethyl (i.e.), pyridin-3-ylmethyl, or preferably

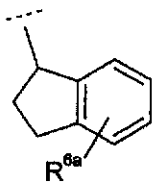
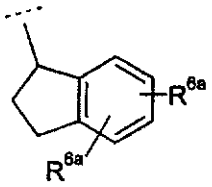
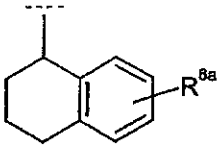


pyridin-2-ylmethyl (i.e.)].

Preferably, sub-formula (y) is:  or  or



, wherein R^{6a} is or independently are either R^6 as defined herein or preferably hydrogen. Preferably, sub-formula (y) is not substituted by oxo (=O) at the carbon between the 6-membered aromatic ring and the carbon bonded to the nitrogen of NR^4R^5.

Preferably, sub-formula (y1) is:  or  or , wherein R^{6a} is or independently are either R^6 as defined herein or preferably hydrogen.

Preferably, in sub-formula (z), none, one or two of J, L, M and Q are nitrogen.

In sub-formula (x), (y) and/or (z), preferably, each R^6, independently of any other R^6 present, is a fluorine, chlorine, bromine or iodine atom, methyl, ethyl, n-propyl, isopropyl, C_4alkyl, trifluoromethyl, -CH_2OH, methoxy, ethoxy, C_1fluoroalkoxy (e.g. trifluoromethoxy or difluoromethoxy), OH, C_{1-3}alkylS(O)$_2$- (such as methylsulphonyl which is MeS(O)$_2$-), C_{1-3}alkylS(O)$_2$-NH- such as methyl-SO_2-NH-, Me_2N-S(O)$_2$-, H_2N-S(O)$_2$-, -$CONH_2$, -CONHMe, -CO_2H, cyano (CN), NMe_2, t-butoxymethyl, or C_{1-3}alkylS(O)$_2$-CH_2- such as methyl-SO_2-CH_2-. More preferably, each R^6, independently of any other R^6 present, is a fluorine, chlorine, bromine or iodine atom, methyl, ethyl, n-propyl, isopropyl, isobutyl, trifluoromethyl, -CH_2OH, methoxy, ethoxy, C_1fluoroalkoxy (e.g. trifluoromethoxy or difluoromethoxy), C_{1-3}alkylS(O)$_2$- such as methylsulphonyl, C_{1-3}alkylS(O)$_2$-NH- such as methyl-SO_2-NH-, Me_2N-S(O)$_2$-, H_2N-S(O)$_2$-, -$CONH_2$, or C_{1-3}alkylS(O)$_2$-CH_2- such as methyl-SO_2-CH_2. Still more preferably, each R^6, independently of any other R^6 present, is a fluorine, chlorine or bromine atom, methyl, ethyl, n-propyl, isopropyl, trifluoromethyl, -CH_2OH, methoxy, difluoromethoxy, methylsulphonyl, methyl-SO_2-NH- or methyl-SO_2-CH_2-.

The above preferred R^6 substituents are also, independently, the preferred phenyl optional and independent substituents for where R^5 is optionally substituted phenyl.

In sub-formula (x) and/or (y), preferably, one, two or three R^6 substituents are present in B, D and/or E; so that for example in sub-formula (x), one, two or three R^6 substituents are present in the meta- (3- and/or 5-) and/or para- (4-) positions with respect to the –$(CH_2)_n$– side-chain.

Preferably, R^5 has the sub-formula (x), n is 1 and none of A, B, D, E and F are nitrogen or nitrogen-oxide (N^+-O^-); and all of A, B, D, E and F are independently CH or CR^6; that

is R^5 has the sub-formula (x) and is optionally substituted benzyl. In this embodiment, preferably, a R^6 substituent is present at the 4-position with respect to the $-(CH_2)_n-$ side-chain (that is D is CR^6: i.e. a R^6 substituent is present in D); and/or preferably a R^6 substituent is present at the 3- and/or 5- position with respect to the $-(CH_2)_n-$ side-chain (that is B and/or E is CR^6: i.e. one or two R^6 substituents are present in B and/or E). For monosubstitution, i.e. where one of A, B, D, E and F is CR^6, then the one R^6 substituent is preferably present at the 4-position with respect to the $-(CH_2)_n-$ side-chain (i.e. D is CR^6). Where there is disubstitution, that is where two of A, B, D, E and F are independently CR^6, then 3,4-disubstitution (B+D or D+E are independently CR^6), 2,4-disubstitution (A+D or D+F are independently CR^6) or 2,3-disubstitution (A+B or E+F are independently CR^6) is preferred.

In sub-formula (x) and/or (y), any optional R^6 substituent can optionally be present only in B, D and/or E, so that in sub-formula (x) any optional R^6 substituent is present only in the meta- (3- and/or 5-) and/or para- (4-) positions with respect to the $-(CH_2)_n-$ side-chain. Alternatively, in sub-formula (x), any optional R^6 substituent can be present in the ortho- (2- and/or 6-) position with respect to the $-(CH_2)_n-$ side-chain, either alone or in combination with one or more other optional R^6 substituents.

Overall for R^5, it is preferable that R^5 is a hydrogen atom (H); C_{1-6}alkyl (e.g. $C_{1,2or3}$alkyl or C_{3-6}alkyl); C_{1-4}fluoroalkyl, C_{3-6}cycloalkyl (e.g. C_{5-6}cycloalkyl), (C_{5-6}cycloalkyl)methyl-, phenyl optionally substituted with one or two of: a fluorine or chlorine atom, methyl, trifluoromethyl, methoxy or trifluoromethoxy; or R^5 has the sub-formula (x), (y) or (z), for example as described above.

Still more preferably, R^5 is a hydrogen atom (H), methyl, ethyl, n-propyl, iso-propyl, 2-ethylbutan-1-yl, cyclopentyl, cyclohexyl, (cyclohexyl)methyl-, optionally substituted phenyl e.g. fluorophenyl e.g. 4-fluorophenyl, optionally substituted benzyl, or optionally substituted pyridinylmethyl, or R^5 has the sub-formula (z).

Optionally, R^5 can be benzyl, pyridinylmethyl (e.g. pyridin-4-ylmethyl, pyridin-3-ylmethyl, or preferably pyridin-2-ylmethyl), or 4-fluorophenyl.

In one preferable embodiment, R^5 has the sub-formula (x) and is: benzyl, (monoalkyl-phenyl)methyl, [mono(fluoroalkyl)-phenyl]methyl, (monohalo-phenyl)methyl, (monoalkoxy-phenyl)methyl, [mono(fluoroalkoxy)-phenyl]methyl, [mono(N,N-dimethylamino)-phenyl]methyl, [mono(methyl-SO_2-NH-)-phenyl]methyl, [mono(methyl-SO_2-)-phenyl]methyl, (dialkyl-phenyl)methyl, (monoalkyl-monohalo-phenyl)methyl, [mono(fluoroalkyl)-monohalo-phenyl]methyl, (dihalo-phenyl)methyl, (dihalo-monoalkyl-phenyl)methyl, [dihalo-mono(hydroxymethyl)-phenyl]methyl, or

(dialkoxy-phenyl)methyl such as (3,4-dimethoxy-phenyl)methyl. The substituents can preferably be further defined, as defined in preferable embodiments herein.

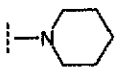
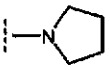
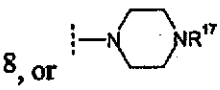
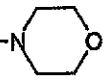
In one preferable embodiment, R^5 is of sub-formula (x) and is: (monoalkyl-phenyl)methyl, [mono(fluoroalkyl)-phenyl]methyl, (monohalo-phenyl)methyl, (monoalkoxy-phenyl)methyl, [mono(fluoroalkoxy)-phenyl]methyl, [mono(N,N-dimethylamino)-phenyl]methyl, (dialkyl-phenyl)methyl, (monoalkyl-monohalo-phenyl)methyl, (dihalo-phenyl)methyl or (dihalo-monoalkyl-phenyl)methyl or [dihalo-mono(hydroxymethyl)-phenyl]methyl. More preferably, in this embodiment, R^5 is:
- (monoC_{1-3}alkyl-phenyl)methyl such as (4-C_{1-3}alkyl-phenyl)methyl;
- (monoC_1fluoroalkyl-phenyl)methyl such as (4-C_1fluoroalkyl-phenyl)methyl;
- (monoC_{1-2}alkoxy-phenyl)methyl such as (4-C_{1-2}alkoxy-phenyl)methyl;
- [mono(C_1fluoroalkoxy)-phenyl]methyl such as (4-C_1fluoroalkoxy-phenyl)methyl;
- (diC_{1-2}alkyl-phenyl)methyl or (dimethyl-phenyl)methyl such as (3,4-dimethyl-phenyl)methyl, (2,4-dimethyl-phenyl)methyl, (3,5-dimethyl-phenyl)methyl, (2,3-dimethyl-phenyl)methyl or (2,5-dimethyl-phenyl)methyl; more preferably (3,4-dimethyl-phenyl)methyl or (2,4-dimethyl-phenyl)methyl;
- (monoC_{1-2}alkyl-monohalo-phenyl)methyl or (monoC_{1-2}alkyl-monochloro-phenyl)methyl such as (4-methyl-3-chloro-phenyl)methyl, (3-methyl-4-chloro-phenyl)methyl, (2-methyl-4-chloro-phenyl)methyl;
- (dihalo-phenyl)methyl such as (2-chloro-4-fluorophenyl)methyl or (2,4-difluoro-phenyl)methyl or (4-bromo-2-fluorophenyl)methyl or preferably (4-chloro-2-fluorophenyl)methyl; for example (dichloro-phenyl)methyl such as (3,4-dichloro-phenyl)methyl or (2,4-dichloro-phenyl)methyl or (2,6-dichloro-phenyl)methyl or preferably (2,3-dichloro-phenyl)methyl;
- (dihalo-monoC_{1-2}alkyl-phenyl)methyl e.g. (2,4-dichloro-6-methyl-phenyl)methyl; or
- [dihalo-mono(hydroxymethyl)-phenyl]methyl such as [2,3-dichloro-6-(hydroxymethyl)-phenyl]methyl.

In an alternative preferable embodiment, R^5 has the sub-formula (z), and one or preferably none of J, L, M or Q is CR^6, and/or R^9 is a hydrogen atom (H) or methyl. Preferably r is 1. Preferably, for (z), R^6 is independently OH (including any keto tautomer thereof), or more preferably C_{1-2}alkyl (e.g. methyl) or C_1fluoroalkyl.

Preferably NR^4R^5 is not NH_2. R^5 is preferably not a hydrogen atom (H).

When R^4 and R^5 taken together are optionally substituted $-(CH_2)_p{}^1-$ or optionally substituted $-C(O)-(CH_2)_p{}^2-$ or $-(CH_2)_p{}^3-X^5-(CH_2)_p{}^4-$ or $-C(O)-X^5-(CH_2)_p{}^5-$ or a partially unsaturated derivative of any of the foregoing, preferably R^4 and R^5 taken together are optionally substituted $-(CH_2)_p{}^1-$ or optionally substituted $-C(O)-(CH_2)_p{}^2-$

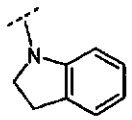
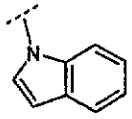
or -$(CH_2)_p{}^3$-X^5-$(CH_2)_p{}^4$- or -C(O)-X^5-$(CH_2)_p{}^5$- (i.e. not a partially unsaturated derivative of any of these).

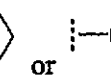
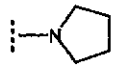
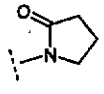
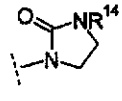
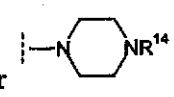
When R^4 and R^5 taken together are –$(CH_2)_p{}^1$– optionally substituted by R^{18}, or -C(O)-$(CH_2)_p{}^2$- optionally substituted by R^{18}, or -$(CH_2)_p{}^3$-X^5-$(CH_2)_p{}^4$-, NR^4R^5 can for example be  optionally substituted by R^{18}, or  optionally substituted by R^{18}, or  optionally substituted by R^{18}, or  (i.e. R^4 and R^5 taken together are -$(CH_2)_2$-N(R^{17})-$(CH_2)_2$-), or  (i.e. R^4 and R^5 taken together are -$(CH_2)_2$-O-$(CH_2)_2$-).

Preferably, R^{17} is a hydrogen atom (H); C_{1-4}alkyl (e.g. C_{1-2}alkyl); C_{3-6}cycloalkyl; -$(CH_2)_p{}^6$-C(O)R^{16}, or the optionally substituted phenyl or benzyl. More preferably, R^{17} is H; C_{1-2}alkyl; -$(CH_2)_p{}^6$-C(O)R^{16} or the optionally substituted phenyl.

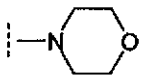
When R^4 and R^5 taken together are –$(CH_2)_p{}^1$– or -C(O)-$(CH_2)_p{}^2$-, the NR^4R^5 heterocycle is preferably not substituted by R^{18}.

When R^4 and R^5 taken together are -$(CH_2)_p{}^1$- or -C(O)-$(CH_2)_p{}^2$-, and if the NR^4R^5 heterocycle is substituted by R^{18}, then optionally R^{18} is not substituted at a ring-carbon bonded to the NR^4R^5 ring-nitrogen.

When R^4 and R^5 taken together are –$(CH_2)_p{}^1$– or -C(O)-$(CH_2)_p{}^2$- or -$(CH_2)_p{}^3$-X^5-$(CH_2)_p{}^4$- or -C(O)-X^5-$(CH_2)_p{}^5$- or a partially unsaturated derivative of any of these, and wherein the NR^4R^5 heterocycle is fused to a phenyl ring optionally substituted on the phenyl by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; then in one embodiment of the invention NR^4R^5 is  or  wherein the phenyl is optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy.

In one embodiment of the invention, NR^7R^8 and/or $NR^{12}R^{13}$ can for example independently be  or  or  or  , or 

(i.e. R^{12} and R^{13} together or R^7 and R^8 together are $-(CH_2)_2-N(R^{14})-(CH_2)_2-$), or



(i.e. R^{12} and R^{13} together or R^7 and R^8 together are $-(CH_2)_2-O-(CH_2)_2-$), or NMe_2.

Preferably, R^{15} is a hydrogen atom (H) or C_{1-4}alkyl (e.g. ^{t}Bu or C_{1-2}alkyl e.g. methyl); more preferably, R^{15} is a hydrogen atom (H).

Preferably, however, R^4 and R^5 are not taken together , i.e. are not taken together to form the NR^4R^5 ring systems described herein.

(Similar preferances apply for R^{5a} as for R^5, except that R^{5a} cannot be a hydrogen atom. Most preferably, R^{5a} is ethyl.)

In an especially preferable embodiment, NR^4R^5 is the NR^4R^5 group as defined in any one of: Examples 21-98, 100-182, 187-188, 191-200, 201-203, 210-353, 355-651, 653-658, 660-664 and 665-686.

It is particularly preferred that the compound of formula (I) or the salt thereof is:

Ethyl 4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(1-acetylpiperidin-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-(cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate (not this compound per se, and for the use or method of treatment preferably not this compound),
Ethyl 1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-(cyclopropylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
N-Benzyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Cyclopentyl-4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

4-(Cyclohexylamino)-N-cyclopentyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Cyclopentyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-N-cyclopentyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Cyclopentyl-1-ethyl-5-(pyrrolidin-1-ylcarbonyl)-1H-pyrazolo[3,4-b]pyridin-4-amine,
N-Cyclohexyl-1-ethyl-5-(pyrrolidin-1-ylcarbonyl)-1H-pyrazolo[3,4-b]pyridin-4-amine,
1-Ethyl-5-(pyrrolidin-1-ylcarbonyl)-N-tetrahydro-2H-pyran-4-yl-1H-pyrazolo[3,4-b]pyridin-4-amine,
4-(Cyclopentylamino)-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(pyridin-4-ylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-N-benzyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopentylamino)-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-ethylbutyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopentylamino)-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopentylamino)-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-n-propyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-(cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-(cyclohexylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopentylamino)-N-(2-ethylbutyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-N-(2-ethylbutyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(2-Ethylbutyl)-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopentylamino)-N-(4-fluorophenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-N-(4-fluorophenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(4-Fluorophenyl)-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-N-benzyl-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N,N-dimethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-isopropyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-(cyclopropylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-(Cyclopropylamino)-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1,1-Dioxidotetrahydrothien-3-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide, or
4-[(1,1-Dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide;

or a salt thereof, e.g. a pharmaceutically acceptable salt thereof.

The structures of these specific compounds are given in Examples 1-98 hereinafter.

Alternatively, it is particularly preferred that the compound of formula (I) or the salt thereof is:

1-Ethyl-*N*-[4-(methylsulfonyl)benzyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[3-(methylsulfonyl)benzyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-5-{[5-methoxy-6-(trifluoromethyl)-2,3-dihydro-1*H*-indol-1-yl]carbonyl}-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine,
N-[(5-Chloropyridin-2-yl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(4-Chlorobenzyl)-1-ethyl-*N*-isopropyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3-Chlorobenzyl)-1-ethyl-*N*-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(5-methyl-3-phenylisoxazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2-*tert*-Butoxyethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3-thiazol-2-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(pyrimidin-4-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(2-methyl-1,3-thiazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(*tert*-Butoxymethyl)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

1-Ethyl-*N*-{2-[methyl(methylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(pyrazin-2-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-5-{[4-(pyridin-2-ylcarbonyl)piperazin-1-yl]carbonyl}-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine,
N-(2-Chloro-6-fluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(6-oxo-1,6-dihydropyridin-3-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(Aminocarbonyl)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{4-[(methylamino)carbonyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(1-methyl-1*H*-imidazol-4-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-{2-[(Anilinocarbonyl)amino]ethyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(1*H*-tetraazol-5-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[2-(1*H*-1,2,4-triazol-1-yl)ethyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
tert-Butyl 4-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)piperidine-1-carboxylate,
1-Ethyl-*N*-{3-[(methylsulfonyl)amino]propyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[2-(Dimethylamino)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(1-ethylpyrrolidin-2-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(tetrahydrofuran-2-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-*N*-tetrahydro-2*H*-pyran-4-yl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-{4-[(Dimethylamino)sulfonyl]benzyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{3-[(methylsulfonyl)amino]benzyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(4-methoxyphenyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

1-Ethyl-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(pyridin-3-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(1-methylpiperidin-4-yl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(1-ethylpropyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(2-piperidin-1-ylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(3-morpholin-4-ylpropyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3-Ethoxypropyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(Cyclohexylmethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(Dimethylamino)propyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-neopentyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-*N*-(4-methoxybenzyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{2-[(phenylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[2-(Acetylamino)ethyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{2-[(methylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{2-[(2-methoxyphenyl)(methyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(2-oxo-2-phenylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1H-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2,5-Difluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[4-(trifluoromethyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N,1-Diethyl-*N*-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Cyclopropyl-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

N-(2-amino-2-oxoethyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-*N*-(3-methoxyphenyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3,4-Difluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
Ethyl 3-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)propanoate,
N-(1-Benzylpiperidin-4-yl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Butyl-4-{[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}piperazine-1-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3,4-thiadiazol-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2,3-Dihydro-1*H*-inden-2-yl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(2-oxoimidazolidin-1-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3,4-Dimethoxybenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3-Chlorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-5-[(4-methylpiperazin-1-yl)carbonyl]-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine,
1-Ethyl-*N*-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-5-{[4-(4-methoxyphenyl)piperazin-1-yl]carbonyl}-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine,
1-Ethyl-*N*-{4-[(methylsulfonyl)methyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(dimethylamino)-3-oxopropyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-*N*-[(1-methyl-1*H*-imidazol-5-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{4-[(methylamino)sulfonyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2-Cyanoethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-methyl-*N*-[(1-methyl-1*H*-imidazol-2-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(2-thien-2-ylethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[2-(4-Chlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(2-methoxyphenyl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
Ethyl 4-(cyclohexylamino)-1-(3-ethoxy-3-oxopropyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
Ethyl 1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
Ethyl 1-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
N-[4-(Methylsulfonyl)benzyl]-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(4-Fluorophenyl)-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
Ethyl 1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
Ethyl 4-(cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
4-(Cyclohexylamino)-1-ethyl-6-methyl-*N*-[4-(methylsulfonyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-4-(cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-ethyl-*N*-(4-fluorophenyl)-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
4-(Cyclohexylamino)-1-ethyl-6-methyl-*N*-[4-(trifluoromethyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
4-(Cyclohexylamino)-*N*-(2,3-dihydro-1*H*-inden-2-yl)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(2-oxoazepan-3-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(3-hydroxycyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(4-hydroxycyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(3-hydroxycyclopentyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide, **or**
N-Benzyl-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide;

or a salt thereof, e.g. a pharmaceutically acceptable salt thereof.

The structures of these specific compounds are given in Examples 100-201 hereinafter.

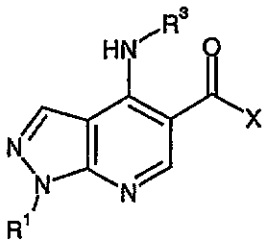
Alternatively, the compound of formula (I) or the salt thereof can be:
1-Ethyl-*N*-(2-hydroxy-1-methylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide, or
Methyl (2*S*)-2-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)-3-hydroxypropanoate;
or a salt thereof, e.g. a pharmaceutically acceptable salt thereof. (See for example Examples 202-203).

Alternatively, it is particularly preferred that the compound of formula (I) or the salt thereof is one of Examples 204 to 664 or one of Examples 665 to 686, as a compound or a salt thereof, e.g. a pharmaceutically acceptable salt thereof. The structures of these specific compounds are given in Examples 204 to 664 and Examples 665 to 686 hereinafter, and their names are given in the Examples section.

In one embodiment, is still further preferred that the compound of formula (I) or the salt thereof is a compound of Example 260, 261, 263, 266, 431, 493, 494, 518, 528, 584, 626, 643, 653, 679, 680, 681, 682, 683, 684, 685 or 686 (more preferably Example 260, 518, 653, 679, 680, 681 or 684), as defined by the structures and/or names described herein, or a salt thereof, e.g. a pharmaceutically acceptable salt thereof. The structures and names of these Examples are described in the Examples section. These Examples are thought to be suitable for inhaled administration.

In another embodiment, is still further preferred that the compound of formula (I) or the salt thereof is a compound of Example 21, 22, 83, 100, 109, 167, 172, 178 or 600, as defined by the structures and/or names described herein, or a salt thereof, e.g. a pharmaceutically acceptable salt thereof. The structures and names of these Examples are described in the Examples section. These Examples are thought to be suitable for oral administration.

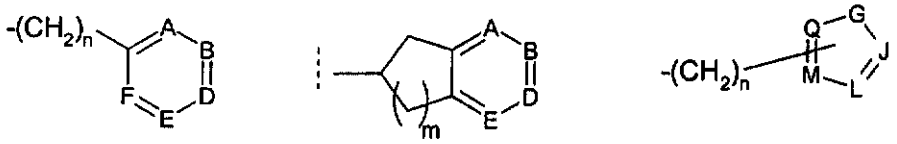
A second aspect of the present invention provides a compound of formula (IA) or a salt thereof (in particular, a pharmaceutically acceptable salt thereof):



(IA)

R^4 is hydrogen, and

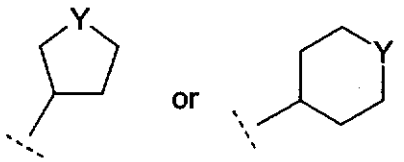
R^5 is C_{1-8}alkyl, C_{1-8} fluoroalkyl, or C_{3-8}cycloalkyl, phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^5 has the sub-formula (x), (y) or (z):



(x) (y) (z)

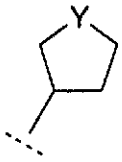
wherein in sub-formula (x) and (z), n = 1 or 2; and in sub-formula (y), m = 1 or 2;
wherein in sub-formula (x) and (y), none, one or two of A, B, D, E and F are nitrogen; and the remaining of A, B, D, E and F are CH or CR^6 where R^6 is a halogen atom, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{1-2}alkoxy, C_{1-2}fluoroalkoxy, C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-), C_{1-2}alkyl-SO_2-NH-, R^7R^8N-SO_2-, R^7R^8N-CO-, R^7R^8N, OH, C_{1-4}alkoxymethyl, or C_{1-2}alkyl-SO_2-CH_2-, wherein R^7 and R^8 are independently hydrogen or C_{1-2}alkyl;
wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one or two of J, L, M and Q are nitrogen; and the remaining of J, L, M and Q are CH or CR^6 where R^6 is as defined herein;

R^{5a} is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl; phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^{5a} has the sub-formula (x), (y) or (z) as defined herein;

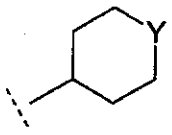
R^3 is C_{3-8}cycloalkyl or a heterocyclic group being  in which Y is O, S, SO_2, or NR^{10}; where R^{10} is hydrogen, methyl, ethyl, C(O)methyl or C(O)-CF_3;

and wherein in R^3 the C_{3-8}cycloalkyl is cyclohexyl substituted with one substituent being OH; wherein the OH substituent is not substituted at the ring carbon attached to the -NH- group of formula (IA); and

R^1 = C_{1-3}alkyl or C_{1-2}fluoroalkyl;

provided that: when R^3 is the heterocyclic group being  and Y is NR^{10}, then R^{10} is not C(O)methyl or C(O)-CF_3;

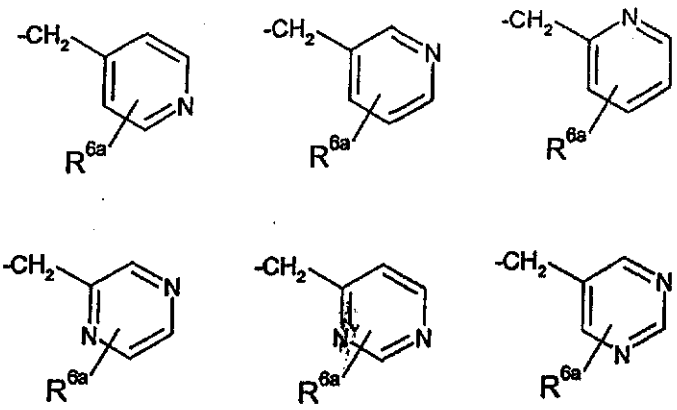
provided that:

when R^3 is the heterocyclic group being  and Y is NR^{10}, then:
either (a) R^{10} is hydrogen, C(O)methyl or C(O)-CF_3;
or (b) R^{10} is methyl and the compound is: 1-ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide or 1-ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide;

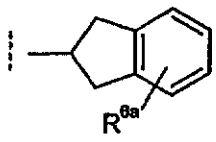
and provided that: where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is a substituent at the 3-, 4- or 5- position of the R^3 cycloalkyl ring (wherein, in this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (IA)).

In formula (IA), in sub-formula (x) and/or (y), it is preferred that none, one or two of A, B, D, E and F are nitrogen; none, one, two or three of A, B, D, E and F are CR^6; and the remaining of A, B, D, E and F are CH. More preferably, none, one or two of A, B, D, E and F are nitrogen; none or one or two of A, B, D, E and F are CR^6; and the remaining of A, B, D, E and F are CH. In formula (IA), in sub-formula (x) and/or (y), preferably, none or one of A, B, D, E and F are nitrogen.

In formula (IA), preferably, sub-formula (x) is: benzyl; phenethyl (Ph-C_2H_4-); benzyl or phenethyl being substituted on the phenyl ring with a single R^6 substituent, or one of the following:

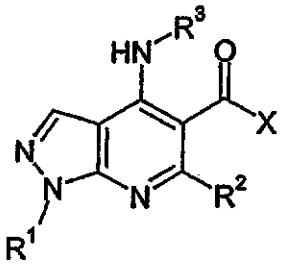


, wherein R^{6a} is either R^6 as defined herein or (preferably) hydrogen.

In formula (IA), preferably, sub-formula (y) is:  , wherein R^{6a} is either R^6 as defined herein or preferably hydrogen.

Examples 1-99 are examples of compounds or salts of the second aspect of the invention (Formula (IA)).

A third aspect of the present invention provides a compound of formula (IB) or a salt thereof (in particular, a pharmaceutically acceptable salt thereof):



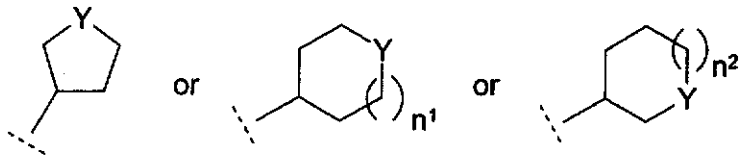
(IB)

wherein:

R^1 is C_{1-3}alkyl, C_{1-2}fluoroalkyl or $-CH_2CH_2OH$;

R^2 is a hydrogen atom (H), methyl or C_1fluoroalkyl;

R^3 is substituted C_{3-8}cycloalkyl or an optionally substituted heterocyclic group of sub-formula (aa), (bb) or (cc);



(aa) (bb) (cc)

in which n^1 and n^2 independently are 1 or 2; and in which Y is O, S, SO_2, or NR^{10}; where R^{10} is a hydrogen atom (H), methyl, ethyl, $C(O)NH_2$, C(O)methyl or $C(O)-CF_3$;

and wherein, when R^3 is substituted C_{3-8}cycloalkyl, then R^3 is cyclohexyl substituted by one substituent being oxo (=O) or OH; and wherein any OH substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (IB);

and wherein the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc) is optionally substituted with one or two substituents being oxo (=O);

and X is NR^4R^5 or OR^{5a}, in which:

R^4 is a hydrogen atom (H); and

R^5 is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl optionally substituted by a C_{1-2}alkyl group; or $-(CH_2)_n{}^4-C_{3-8}$cycloalkyl optionally substituted, in the $-(CH_2)_n{}^4-$ moiety or in the C_{3-8}cycloalkyl moiety, by a C_{1-2}alkyl group, wherein n^4 is 1, 2 or 3;

or R^5 is C_{2-6}alkyl substituted by one or two independent substituents R^{11};

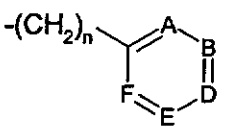
wherein each substituent R^{11}, independently of any other R^{11} substituent present, is: hydroxy (OH); C_{1-6}alkoxy; phenyloxy; benzyloxy; $-NR^{12}R^{13}$; $-NR^{15}-C(O)R^{16}$; $-NR^{15}-C(O)-O-R^{16}$; $-NR^{15}-C(O)-NH-R^{15}$; or $-NR^{15}-SO_2R^{16}$; and wherein any R^{11} substituent which is OH, alkoxy or $-NR^{12}R^{13}$ is not substituted at any carbon atom, of any R^4 or R^5 substituted alkyl, which is bonded to the nitrogen of NR^4R^5;

or R^5 is $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{11}-C(O)NR^{12}R^{13}$; $-CHR^{19}-C(O)NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-C(O)OR^{16}$; $-CHR^{19}-C(O)OR^{16}$; $-(CH_2)_n{}^{12}-SO_2-NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-SO_2R^{16}$; or $-(CH_2)_n{}^{12}-CN$; wherein n^{11} is 0, 1, 2, 3 or 4 and n^{12} is 1, 2, 3 or 4;

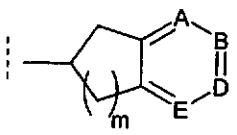
or R^5 is $-(CH_2)_n{}^{13}$-Het wherein n^{13} is 0, 1, 2, 3 or 4 and Het is a 4-, 5-, 6- or 7-membered saturated or partly-saturated heterocyclic ring containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-hetero-atoms present are not bound to the $-(CH_2)_n{}^{13}-$ moiety when n^{13} is 1 and are not bound to the nitrogen of NR^4R^5 when n^{13} is 0; wherein any ring-nitrogens which are present and which are not unsaturated (i.e. which do not partake in a double bond) are present as NR^{17} where R^{17} is as defined herein; and wherein one or two of the carbon ring-atoms independently are optionally substituted by C_{1-2}alkyl;

or R^5 is phenyl optionally substituted with one or two of: a halogen atom; C_{1-4}alkyl; C_{1-2}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-; $-NR^{15}-C(O)R^{16}$; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;
wherein R^7 and R^8 are independently a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or R^7 and R^8 together are $-(CH_2)_n{}^6-$ or $-C(O)-(CH_2)_n{}^7-$ or $-C(O)-(CH_2)_n{}^7-C(O)-$ or $-(CH_2)_n{}^8-X^7-(CH_2)_n{}^9-$ or $-C(O)-X^7-(CH_2)_n{}^{10}-$ in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3, and X^7 is O or NR^{14} wherein R^{14} is H or C_{1-2}alkyl;

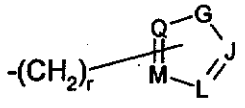
or R^5 has the sub-formula (x), (y) or (z):



(x)



(y)



(z)

wherein in sub-formula (x), n = 1 or 2; in sub-formula (y), m = 1 or 2; and in sub-formula (z), r = 0, 1 or 2;

wherein in sub-formula (x) and (y), none, one or two of A, B, D, E and F are nitrogen; and the remaining of A, B, D, E and F are independently CH or CR^6;

where R^6 is a halogen atom; C_{1-4}alkyl; C_{1-4}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-; -NR^{15}-C(O)R^{16}; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; wherein R^7 and R^8 are as herein defined;

wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is a hydrogen atom (H), C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one, two or three of J, L, M and Q are nitrogen; and the remaining of J, L, M and Q are independently CH or CR^6 where R^6 is as defined herein; and

R^{5a} is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl; phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^{5a} has the sub-formula (x), (y) or (z) as defined herein

and wherein:

R^{12} and R^{13} independently are H; C_{1-5}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or R^{12} and R^{13} together are -$(CH_2)_n{}^6$- or -C(O)-$(CH_2)_n{}^7$- or -C(O)-$(CH_2)_n{}^7$-C(O)- or -$(CH_2)_n{}^8$-X^{12}-$(CH_2)_n{}^9$- or -C(O)-X^{12}-$(CH_2)_n{}^{10}$- in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3 and X^{12} is O or NR^{14} wherein R^{14} is H or C_{1-2}alkyl;

R^{15} is a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

R^{16} is C_{1-4}alkyl; C_{3-6}cycloalkyl; pyridinyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

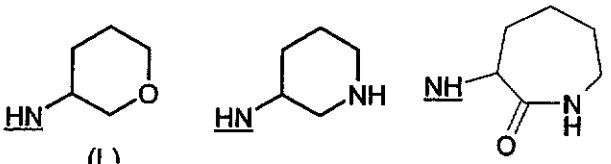
R^{17} is a hydrogen atom (H); C_{1-4}alkyl; C_{1-2}fluoroalkyl; C_{3-6}cycloalkyl; -$(CH_2)_p{}^6$-C(O)R^{16} wherein p^6 is 0, 1, 2 or 3; -$(CH_2)_p{}^6$-C(O)$NR^{12}R^{13}$; -$(CH_2)_p{}^6$-C(O)OR^{16}; -SO_2R^{16}; or phenyl or benzyl wherein the phenyl or benzyl is optionally substituted at an aromatic carbon atom by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; and

R^{19} is C_{1-4}alkyl; -$(CH_2)_n{}^{20}$-OR^{20} wherein n^{20} is 1, 2, 3 or 4 and R^{20} is a hydrogen atom (H) or C_{1-4}alkyl; -CH(Me)-OH; -CH_2-SH; -CH_2-CH_2-S-Me; benzyl; or (4-hydroxyphenyl)methyl (i.e. 4-hydroxy-benzyl);

provided that: when R^3 is the heterocyclic group of sub-formula (aa) and Y is NR^{10}, then R^{10} is not $C(O)NH_2$, C(O)methyl or $C(O)$-CF_3;

provided that:
when R^3 is the heterocyclic group of sub-formula (bb), n^1 is 1, and Y is NR^{10}, then:
either (a) R^{10} is not methyl or ethyl;
or (b) R^{10} is methyl and the compound is: 1-ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide or 1-ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide;

provided that: when R^3 is the heterocyclic group of sub-formula (cc), then NHR^3 is of sub-formula (L), (m) or (m1), wherein the -NH- connection point of the NHR^3 group to the 4-position of the pyrazolopyridine of formula (IB) is underlined:



(L) (m) (m1) ;

and provided that: where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is a substituent at the 3-, 4- or 5- position of the R^3 cycloalkyl ring (wherein, in this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (IB)).

In formula (IB), where R^3 is optionally substituted C_{3-8}cycloalkyl, the one or two optional substituents preferably comprise (e.g. is or are) OH and/or oxo (=O). In formula (IB), in the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc), the one or two optional substituents preferably comprise (e.g. is or are) OH and/or oxo.

Examples 1-203 are examples of compounds or salts of the third aspect of the invention (Formula (IB)).

The preferred or optional features for the compound or salt of formula (IA) and for the compound or salt of formula (IB) are the same as or similar to the preferred or optional features for the compound or salt of formula (I), with all necessary changes (for example to the formula, to the R groups and/or to substituents) having been made. Generally, whenever formula (I) is mentioned herein, then in alternative embodiments the statement mentioning formula (I) applies to formula (IA) or formula (IB), with all necessary changes having been made.

Salts, solvates, isomers, tautomeric forms, molecular weights, etc.

Because of their potential use in medicine, the salts of the compounds of formula (I) are preferably pharmaceutically acceptable. Suitable pharmaceutically acceptable salts can include acid or base addition salts. A pharmaceutically acceptable acid addition salt can be formed by reaction of a compound of formula (I) with a suitable inorganic or organic acid (such as hydrobromic, hydrochloric, sulfuric, nitric, phosphoric, succinic, maleic, acetic, fumaric, citric, tartaric, benzoic, p-toluenesulfonic, methanesulfonic or naphthalenesulfonic acid), optionally in a suitable solvent such as an organic solvent, to give the salt which is usually isolated for example by crystallisation and filtration. A pharmaceutically acceptable acid addition salt of a compound of formula (I) can be for example a hydrobromide, hydrochloride, sulfate, nitrate, phosphate, succinate, maleate, acetate, fumarate, citrate, tartrate, benzoate, p-toluenesulfonate, methanesulfonate or naphthalenesulfonate salt. A pharmaceutically acceptable base addition salt can be

formed by reaction of a compound of formula (I) with a suitable inorganic or organic base, optionally in a suitable solvent such as an organic solvent, to give the base addition salt which is usually isolated for example by crystallisation and filtration. Other suitable pharmaceutically acceptable salts include pharmaceutically acceptable metal salts, for example pharmaceutically acceptable alkali-metal or alkaline-earth-metal salts such as sodium, potassium, calcium or magnesium salts; in particular pharmaceutically acceptable metal salts of one or more carboxylic acid moieties that may be present in the the compound of formula (I).

Other non-pharmaceutically acceptable salts, eg. oxalates, may be used, for example in the isolation of compounds of the invention, and are included within the scope of this invention.

The invention includes within its scope all possible stoichiometric and non-stoichiometric forms of the salts of the compounds of formula (I).

Also included within the scope of the invention are all solvates, hydrates and complexes of compounds and salts of the invention.

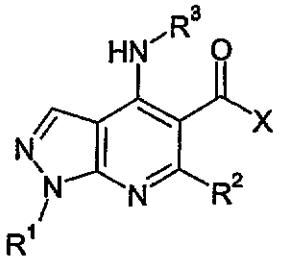
Certain groups, substituents, compounds or salts included in the present invention may be present as isomers. The present invention includes within its scope all such isomers, including racemates, enantiomers and mixtures thereof.

Certain of the groups, e.g. heteroaromatic ring systems, included in compounds of formula (I) or their salts may exist in one or more tautomeric forms. The present invention includes within its scope all such tautomeric forms, including mixtures.

Especially when intended for oral medicinal use, the compound of formula (I) can optionally have a molecular weight of 1000 or less, for example 800 or less, in particular 650 or less or 600 or less. Molecular weight here refers to that of the unsolvated "free base" compound, that is excluding any molecular weight contributed by any addition salts, solvent (e.g. water) molecules, etc.

Synthetic Process Routes

The following processes can be used to make the compounds of the invention:



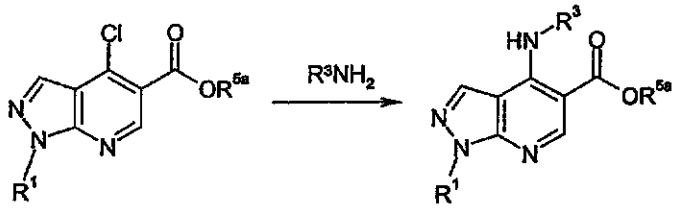
(I)

Most of the following synthetic processes following are exemplified for compounds of Formula (I) wherein R^2 is a hydrogen atom (H). However, some or all of these processes

can also be used with appropriate modification, e.g. of starting materials and reagents, for making compounds of Formula (I) wherein R^2 is other than H.

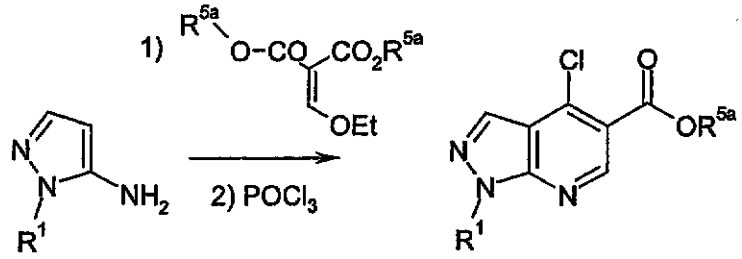
Process A

Compounds of formula (I) where X = OR^{5a}, can be prepared according to a method, for example as described by Yu et. al. in *J. Med Chem.*, 2001, 44, 1025-1027, by reaction of a compound of formula (II) with an amine of formula R^3NH_2. The reaction is preferably carried out in the presence of a base such as triethylamine or N,N-diisopropylethylamine, and/or in an organic solvent such as ethanol, dioxane or acetonitrile. The reaction may require heating e.g. to ca. 60-100 °C , for example ca. 80-90 °C:



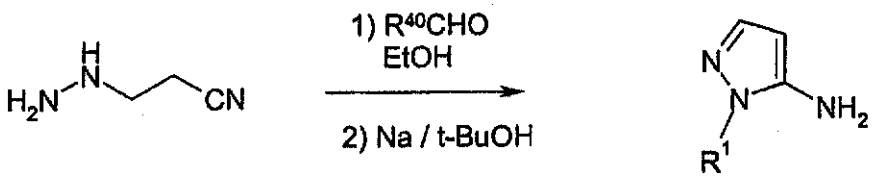
(II) (I)

Compounds of formula (II) are also described in the above reference and can be prepared by reaction of a compound of formula (III) with, for example, diethylethoxymethylene malonate (where R^{5a} = Et) with heating, followed by reaction with phosphorous oxychloride, again with heating:



Formula III Formula II

Where the desired amino pyrazole of formula (III) is not commercially available, preparation can be achieved using methods described by Dorgan et. al. in J. Chem. Soc., Perkin Trans. 1, (4), 938-42; 1980, by reaction of cyanoethylhydrazine with a suitable aldehyde of formula $R^{40}CHO$ in a solvent such as ethanol, with heating, followed by reduction with, for example sodium in a solvent such as t-butanol. R^{40} should be chosen so as to contain one less carbon atom than R^1, for example R^{40} = methyl will afford R^1 = ethyl.

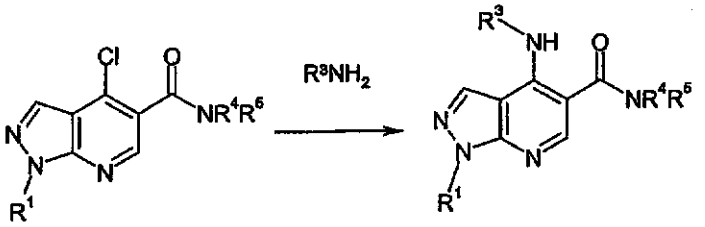


Formula III

In an alternative embodiment of Process A, the 4-chloro substituent in the compound of formula (II) can be replaced by a halogen atom, such as a bromine atom or preferably a chlorine atom, in a compound of formula (IIA) as defined below. In this embodiment of Process A, the compound of formula (IIA) is reacted with the amine of formula R^3NH_2.

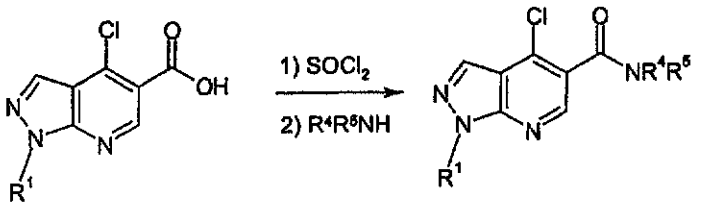
Process B

Compounds of formula (I) where $X = NR^4R^5$, can be prepared by reaction of a compound of formula (IV) with an amine of formula R^3NH_2. The reaction is preferably carried out in the presence of a base, such as triethylamine or N,N-diisopropylethylamine, and/or in an organic solvent such as ethanol, THF, dioxane or acetonitrile. The reaction may require heating, e.g. to ca. 60-100 °C or ca. 80-90 °C, for example for 8-48 or 12-24 hours:



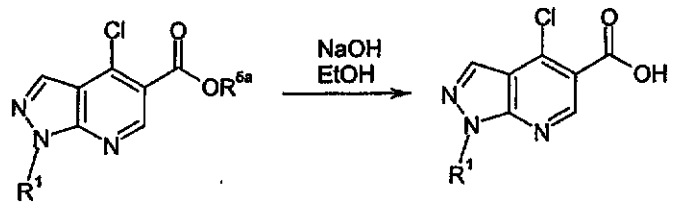
Formula IV Formula I

Compounds of formula (IV) can be prepared in a two step procedure as described by Bare et. al. in *J. Med. Chem.* 1989, 32, 2561-2573. This process involves, first, reaction of a compound of formula (V) with thionyl chloride (or another agent suitable for forming an acid chloride from a carboxylic acid), either in an organic solvent such as chloroform or THF, or as a neat solution. This reaction may require heating and the thus-formed intermediate may or may not be isolated. Step two involves reaction with an amine of formula R^4R^5NH, in an organic solvent such as THF or chloroform and may also involve the use of a base such as triethylamine or diisopropylethyl amine:



Formula V Formula IV

Compounds of formula (V) can be prepared by hydrolysis of an ester of formula (II) according to the method described by Yu et. al. in *J. Med Chem.*, 2001, 44, 1025-1027. This procedure preferably involves reaction with a base such as sodium hydroxide or potassium hydroxide in a solvent e.g. an aqueous solvent such as aqueous ethanol or aqueous dioxane:

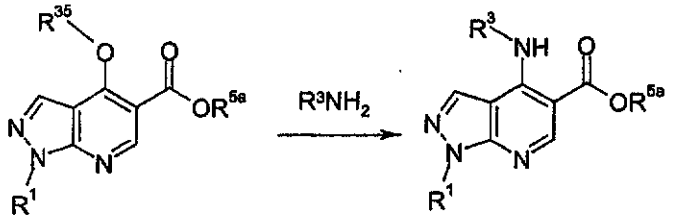


Formula II Formula V

In an alternative embodiment of Process B, the 4-chloro substituent in the compound of formula (IV) can be replaced by a halogen atom, such as a bromine atom or preferably a chlorine atom, in a compound of formula (IVA) as defined below. In this embodiment of Process B, the compound of formula (IVA) is reacted with the amine of formula R^3NH_2.

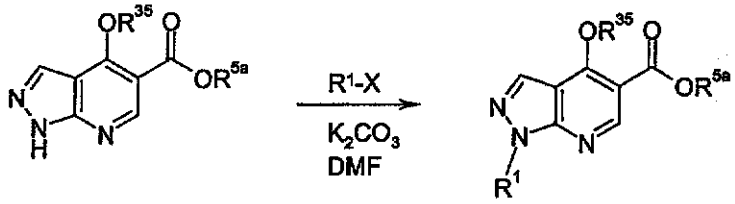
Process C

Compounds of formula (I) can also be prepared according to a method, for example as described by Bare et. al. in *J. Med. Chem.* 1989, 32, 2561-2573, which involves reaction of a compound of formula (VI), in which -O-R^{35} is a leaving group displaceable by an amine, with an amine of formula R^3NH_2. The -O-R^{35} leaving group can be -O-C_{1-4}alkyl (in particular -O-Et) or –O-S(O)$_2$-R^{37}, wherein R^{37} is C_{1-8}alkyl (e.g. C_{1-4}alkyl or C_{1-2}alkyl such as methyl), C_{1-6}fluoroalkyl (e.g. C_{1-4}fluoroalkyl or C_{1-2}fluoroalkyl such as CF_3 or C_4F_9), or phenyl wherein the phenyl is optionally substituted by one or two of independently C_{1-2}alkyl, halogen or C_{1-2}alkoxy (such as phenyl or 4-methyl-phenyl). The reaction may be carried out with or without solvent and may require heating:



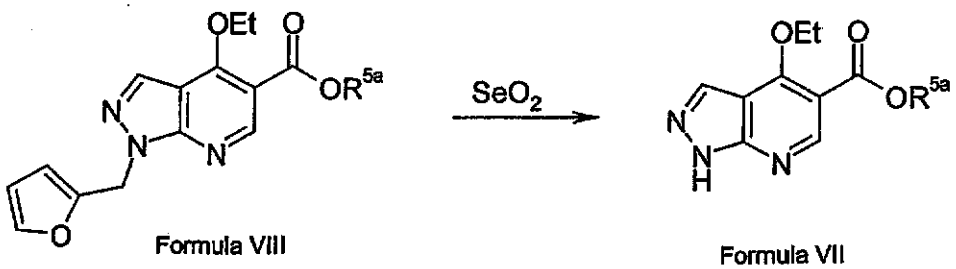
Formula VI Formula I

Compounds of formula (VI) (also described in the above reference) can be prepared by reaction of a compound of formula (VII) with a suitable alkylating agent of formula R^1-X, where X is a leaving group such as halogen. The reaction is preferably carried out in the presence of a base such as potassium carbonate, in an anhydrous solvent such as DMF:



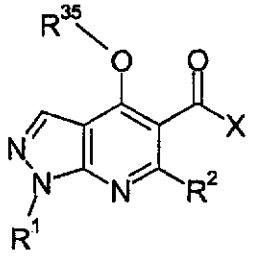
Formula VII Formula VI

The preparation of compounds of formula VII, e.g. where OR^{35} is OEt, by oxidative cleavage of compounds of formula VIII is described by Bare et. al. in *J. Med. Chem.* 1989, 32, 2561-2573 (further referred to Zuleski et. al. in *J. Drug. Metab. Dispos.*, 1985, 13,139).



Formula VIII Formula VII

In another embodiment of Process C, the compound of formula (VI) can be replaced by a compound of formula (VIA), wherein X is NR^4R^5 or OR^{5a} as defined herein:

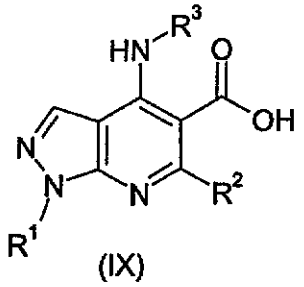


(VIA)

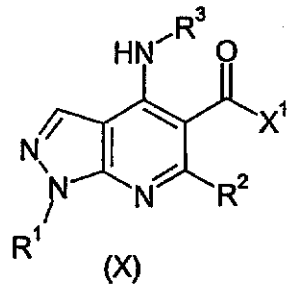
In this embodiment of Process C, the compound of formula (VIA) is reacted with the amine of formula R^3NH_2.

Process D:

To form a compound of formula (I) wherein X = NR^4R^5, a compound of formula (I) but wherein X = OH (a carboxylic acid, the compound of formula (IX) as defined below) can be converted into an activated compound of formula (I) but wherein X = a leaving group X^1 substitutable by an amine (a compound of formula (X) as defined below, wherein X^1 is a leaving group substitutable by an amine); and subsequently the activated compound can be reacted with an amine of formula R^4R^5NH:

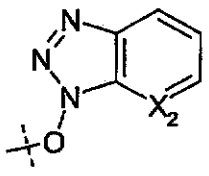


(IX)



(X)

For example, the activated compound (the compound of formula (X)) can be the acid chloride i.e. an activated compound of formula (I) but wherein the leaving group X^1 = Cl. This can be formed from the carboxylic acid (X = OH, the compound of formula (IX)) e.g. by reaction with thionyl chloride, either in an organic solvent such as chloroform or without solvent. See for example Examples 81-85. Alternatively, the activated compound (the compound of formula (X)) can be an activated ester wherein the leaving group X^1 is



X_2 = CH or N

The latter activated compound of formula (X) can be formed from the carboxylic acid (X = OH, the compound of formula (IX))

either:

(a) by reaction of the carboxylic acid with a carbodiimide such as EDC, which is 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide and is also 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide, or a salt thereof e.g. hydrochloride salt,
preferably followed by reaction of the resulting product with 1-hydroxybenzotriazole (HOBT); reaction (a) usually being carried out in the presence of a solvent (preferably anhydrous) such as dimethyl formamide (DMF) or acetonitrile and/or preferably under anhydrous conditions and/or usually at room temperature (e.g. about 20 to about 25 °C); or
(b) by reaction with 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU) or O-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU) ,in the presence of a base such as diisopropylethylamine ($^iPr_2NEt$ = DIPEA), and usually in the presence of a solvent such as dimethyl formamide (DMF) or acetonitrile and/or preferably under anhydrous conditions and/or usually at room temperature (e.g. about 20 to about 25 °C).

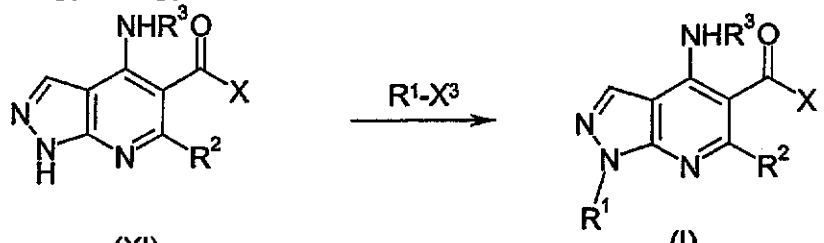
The carboxylic acid wherein X = OH (the compound of formula (IX) below) is usually prepared by hydrolysis of the corresponding ester of formula (I) wherein X is OR^{5a}. This ester can itself be prepared by any of Processes A, C, E or F as described herein.

Process D1

This is the same as Process D, but involves reaction of the activated compound of formula (X), wherein X^1 = a leaving group substitutable by an amine (for example a leaving group as defined herein), with an amine of formula R^4R^5NH.

Process E

Compounds of formula (I) can be prepared by reaction of a compound of formula (XI) with an alkylating agent of formula R^1-X^3, where X^3 is a leaving group displaceable by the 1-position pyrazolopyridine nitrogen atom of the compound of formula (XI):



(XI) (I)

A suitable alkylating agent of formula R^1-X^3 can be used. For example, X^3 can be a halogen atom such as a chlorine atom or more preferably a bromine or iodine atom, or X^3 can be $-O\text{-}S(O)_2\text{-}R^{36}$ wherein R^{36} is C_{1-8}alkyl (e.g. C_{1-4}alkyl or C_{1-2}alkyl such as methyl), C_{1-6}fluoroalkyl (e.g. C_{1-4}fluoroalkyl or C_{1-2}fluoroalkyl such as CF_3 or C_4F_9), or phenyl wherein the phenyl is optionally substituted by one or two of independently C_{1-2}alkyl, halogen or C_{1-2}alkoxy (such as phenyl or 4-methyl-phenyl). The reaction is

preferably carried out in the presence of a base; the base can for example comprise or be potassium carbonate, sodium carbonate, sodium hydride, potassium hydride, or a basic resin or polymer such as polymer-bound 2-tert-butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosphorine. The reaction is preferably carried out in the presence of a solvent, e.g. an organic solvent such as DMF; the solvent is preferably anhydrous. Examples of alkylation Process E include Examples 183, 185, 186 and 354.

For preferable methods of making compounds of formula (XI), see for example (Reference) Examples 19-20, and Intermediates 48 and 54A.

Process F: *Conversion of one compound of formula (I) or salt thereof into another compound of formula (I) or salt thereof*

One compound of formula (I) or salt thereof can be converted into another compound of formula (I) or salt thereof. This conversion preferably comprises or is one or more of the following processes F1 to F10:

F1. An oxidation process. For example, the oxidation process can comprise or be oxidation of an alcohol to a ketone (e.g. using Jones reagent, e.g. see Example 205) or oxidation of an alcohol or a ketone to a carboxylic acid. The oxidation process can e.g. comprise or be conversion of a nitrogen-containing compound of formula (I) or salt thereof to the corresponding N-oxide (e.g. using *meta*-chloroperoxybenzoic acid), for example conversion of a pyridine-containing compound to the corresponding pyridine N-oxide (e.g. Examples 210-212).

F2. A reduction process, for example reduction of a ketone or a carboxylic acid to an alcohol.

F3. Acylation, for example acylation of an amine (e.g. Examples 329-349, Example 353) or hydroxy group.

F4. Alkylation, for example alkylation of an amine or of a hydroxy group.

F5. Hydrolysis, e.g. hydrolysis of an ester to the corresponding carboxylic acid or salt thereof (e.g. Examples 351, 488, 489, 650, 651).

F6. Deprotection, e.g. deprotection (e.g. deacylation or t-butyloxycarbonyl (BOC) removal) of an amine group (e.g. Examples 320, (321), and (352)).

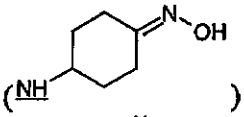
F7. Formation of an ester or amide, for example from the corresponding carboxylic acid.

F8. Conversion of a ketone into the corresponding oxime (e.g. Examples 652, 653, 654 and 680-686).

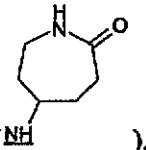
F9. Sulfonylation, e.g. sulfonamide formation by reaction of an amine with a sulfonyl halide e.g. a sulfonyl chloride (e.g. Examples 322-328).

and/or

F10. Beckmann rearrangement of one compound of formula (I) into another compound of formula (I), preferably using cyanuric chloride (2,4,6-trichloro-1,3,5-triazine) together with a formamide such as DMF, e.g. at room temperature (see L.D. Luca, *J. Org. Chem.*, 2002, 67, 6272-6274). The Beckmann rearrangement can for example comprise conversion of a compound of formula (I) wherein NHR^3 is of sub-formula (o2)

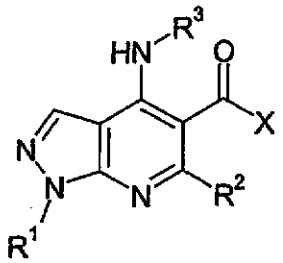


) into a compound of formula (I) wherein NHR^3 is of sub-formula



(m3) ( ), e.g. as illustrated in Examples 658 and 659.

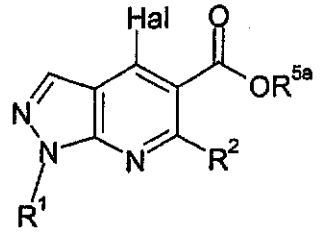
The present invention therefore also provides a method of preparing a compound of formula (I) or a salt thereof:



(I)

wherein R^1, R^2 and R^3 are as defined herein and X is NR^4R^5 or OR^{5a} as defined herein, the method comprising :

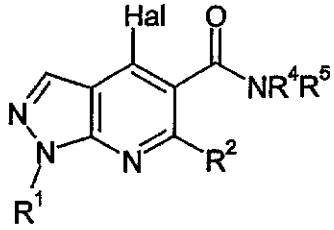
(a) for a compound of formula (I) wherein X = OR^{5a}, reaction of a compound of formula (IIA):



(IIA)

wherein Hal is a halogen atom (such as a bromine atom or preferably a chlorine atom), with an amine of formula R^3NH_2, or

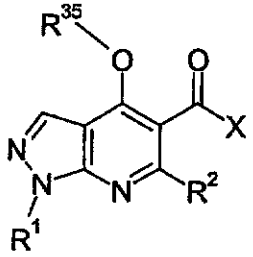
(b) for a compound of formula (I) wherein X = NR^4R^5, reaction of a compound of formula (IVA) :



(IVA)

wherein Hal is a halogen atom (such as a bromine atom or preferably a chlorine atom), with an amine of formula R^3NH_2, or

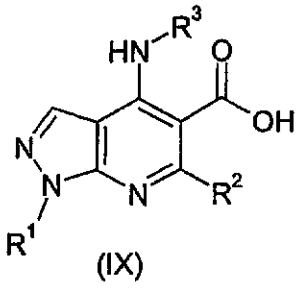
(c) reaction of a compound of formula (VIA):



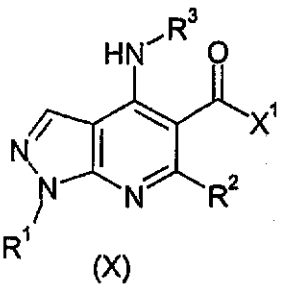
(VIA)

, in which -O-R^{35} is a leaving group displaceable by an amine (such as -O-C_{1-4}alkyl or –O-S(O)$_2$-R^{37}),
with an amine of formula R^3NH_2; or

(d) to form a compound of formula (I) wherein X = NR^4R^5, conversion of a compound of formula (IX) into an activated compound of formula (X) wherein X^1 = a leaving group substitutable by an amine:



(IX)

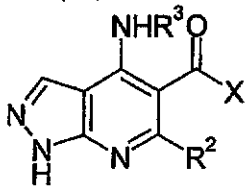


(X)

, and subsequent reaction of the activated compound of formula (X) with an amine of formula R^4R^5NH; or

(d1) to form a compound of formula (I) wherein $X = NR^4R^5$, reaction of an activated compound of formula (X) as defined above with an amine of formula R^4R^5NH; or

(e) reaction of a compound of formula (XI):



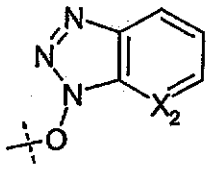
(XI)

with an alkylating agent of formula R^1-X^2, where X^2 is a leaving group displaceable by the 1-position pyrazolopyridine nitrogen atom of the compound of formula (XI); or

(f) conversion of one compound of formula (I) or salt thereof into another compound of formula (I) or salt thereof;

and optionally converting the compound of formula (I) into a salt thereof e.g. a pharmaceutically acceptable salt thereof.

In methods (d) and/or (d1), the activated compound of formula (X) wherein X^1 = a leaving group substitutable by an amine can be the acid chloride i.e. an activated compound of formula (X) wherein X^1 = Cl. Alternatively, the activated compound of formula (X) can be an activated ester wherein the leaving group X^1 is



X_2 = CH or N

Preferred features of methods (a), (b), (c), (d), (d1) and (e), independently of each other, are as described above for Processes A, B, C, D, D1 and E, with all necessary changes being made.

The present invention also provides: (g) a method of preparing a pharmaceutically acceptable salt of a compound of formula (I) comprising conversion of the compound of formula (I) or a salt thereof into the desired pharmaceutically acceptable salt thereof. (See for example Examples 490, 491, 518A, 593).

The present invention also provides a compound of formula (I) or a salt thereof, prepared by a method as defined herein.

Medical uses

The present invention also provides a compound of formula (I) or a pharmaceutically acceptable salt thereof for use as an active therapeutic substance in a mammal such as a human. The compound or salt can be for use in the treatment and/or prophylaxis of any of the diseases / conditions described herein (e.g. for use in the treatment and/or prophylaxis of an inflammatory and/or allergic disease in a mammal) and/or for use as a phosphodiesterase inhibitor e.g. for use as a phosphodiesterase 4 (PDE4) inhibitor. "Therapy" may include treatment and/or prophylaxis.

Also provided is the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament (e.g. pharmaceutical composition) for the treatment and/or prophylaxis of any of the diseases / conditions described herein in a mammal such as a human, e.g. for the treatment and/or prophylaxis of an inflammatory and/or allergic disease in a mammal such as a human.

Also provided is a method of treatment and/or prophylaxis of any of the diseases / conditions described herein in a mammal (e.g. human) in need thereof, e.g. a method of treatment and/or prophylaxis of an inflammatory and/or allergic disease in a mammal (e.g. human) in need thereof, which method comprises administering to the mammal (e.g. human) a therapeutically effective amount of a compound of formula (I) as herein defined or a pharmaceutically acceptable salt thereof.

Phosphodiesterase 4 inhibitors are thought to be useful in the treatment and/or prophylaxis of a variety of diseases / conditions, especially inflammatory and/or allergic diseases, in mammals such as humans, for example: asthma, chronic obstructive pulmonary disease (COPD) (e.g. chronic bronchitis and/or emphysema), atopic

dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxic shock, adult respiratory distress syndrome, multiple sclerosis, cognitive impairment (e.g. in a neurological disorder such as Alzheimer's disease), depression, or pain. Ulcerative colitis and/or Crohn's disease are collectively often referred to as inflammatory bowel disease.

In the treatment and/or prophylaxis, the inflammatory and/or allergic disease is preferably chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis or allergic rhinitis in a mammal (e.g. human). More preferably, the treatment and/or prophylaxis is of COPD or asthma in a mammal (e.g. human).

PDE4 inhibitors are thought to be effective in the treatment of asthma (e.g. see M.A.Giembycz, *Drugs*, Feb. 2000, 59(2), 193-212; Z. Huang et al., *Current Opinion in Chemical Biology*, 2001, 5: 432-438; H.J.Dyke et al., *Expert Opinion on Investigational Drugs*, January 2002, 11(1), 1-13; C.Burnouf et al., *Current Pharmaceutical Design*, 2002, 8(14), 1255-1296; A.M.Doherty, *Current Opinion Chem. Biol.*, 1999, 3(4), 466-473; and refs cited therein).

PDE4 inhibitors are thought to be effective in the treatment of COPD (e.g. see S.L. Wolda, *Emerging Drugs*, 2000, 5(3), 309-319; Z. Huang et al., *Current Opinion in Chemical Biology*, 2001, 5: 432-438; H.J.Dyke et al., *Expert Opinion on Investigational Drugs*, January 2002, 11(1), 1-13; C.Burnouf et al., *Current Pharmaceutical Design*, 2002, 8(14), 1255-1296; A.M.Doherty, *Current Opinion Chem. Biol.*, 1999, 3(4), 466-473; and refs cited therein). COPD is often characterised by the presence of airflow obstruction due to chronic bronchitis and/or emphysema (S.L. Wolda, *Emerging Drugs*, 2000, 5(3), 309-319).

PDE4 inhibitors are thought to be effective in the treatment of allergic rhinitis (e.g. see B.M. Schmidt et al., *J. Allergy & Clinical Immunology*, 108(4), 2001, 530-536).

PDE4 inhibitors are thought to be effective in the treatment of rheumatoid arthritis and multiple sclerosis (e.g. see H.J.Dyke et al., *Expert Opinion on Investigational Drugs*, January 2002, 11(1), 1-13; C.Burnouf et al., *Current Pharmaceutical Design*, 2002, 8(14), 1255-1296; and A.M.Doherty, *Current Opinion Chem. Biol.*, 1999, 3(4), 466-473; and refs cited therein). See e.g. A.M.Doherty, *Current Opinion Chem. Biol.*, 1999, 3(4), 466-473 and refs cited therein for atopic dermatitis use.

PDE4 inhibitors have been suggested as having analgesic properties and thus being effective in the treatment of pain (A.Kumar et al., *Indian J. Exp. Biol.*, 2000, 38(1), 26-30).

In the invention, the treatment and/or prophylaxis can be of cognitive impairment e.g. cognitive impairment in a neurological disorder such as Alzheimer's disease. For example, the treatment and/or prophylaxis can comprise cognitive enhancement e.g. in a neurological disorder. See for example: H.T.Zhang et al. in: *Psychopharmacology*, June 2000, 150(3), 311-316 and *Neuropsychopharmacology*, 2000, 23(2), 198-204; and T. Egawa et al., *Japanese J. Pharmacol.*, 1997, 75(3), 275-81.

PDE4 inhibitors such as rolipram have been suggested as having antidepressant properties (e.g. J. Zhu et al., *CNS Drug Reviews*, 2001, 7(4), 387-398; O'Donnell, *Expert Opinion on Investigational Drugs*, 2000, 9(3), 621-625; and H.T. Zhang et al., *Neuropsychopharmacology*, October 2002, 27(4), 587-595).

Pharmaceutical compositions and dosing

For use in medicine, the compounds of the present invention are usually administered as a pharmaceutical composition.

The present invention therefore provides in a further aspect a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers and/or excipients.

The pharmaceutical composition can be for use in the treatment and/or prophylaxis of any of the conditions described herein.

The invention also provides a method of preparing a pharmaceutical composition comprising a compound of formula (I), as herein defined, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers and/or excipients,

the method comprising mixing the compound or salt with the one or more pharmaceutically acceptable carriers and/or excipients.

The invention also provides a pharmaceutical composition prepared by said method.

The compounds of formula (I) and/or the pharmaceutical composition may be administered, for example, by oral, parenteral (e.g. intravenous, subcutaneous, or intramuscular), inhaled or nasal administration. Accordingly , the pharmaceutical composition is preferably suitable for oral, parenteral (e.g. intravenous, subcutaneous, or intramuscular), inhaled or nasal administration. More preferably, the pharmaceutical composition is suitable for inhaled or oral administration, e.g. to a mammal such as a human. Inhaled administration involves topical administration to the lung e.g. by aerosol or dry powder composition. Oral administration to a human is most preferred.

A pharmaceutical composition suitable for oral administration can be liquid or solid; for example it can be a syrup, suspension or emulsion, a tablet, a capsule or a lozenge.

A liquid formulation will generally consist of a suspension or solution of the compound or pharmaceutically acceptable salt in a suitable pharmaceutically acceptable liquid carrier(s), for example an aqueous solvent such as water, ethanol or glycerine, or a non-aqueous solvent, such as polyethylene glycol or an oil. The formulation may also contain a suspending agent, preservative, flavouring and/or colouring agent.

A pharmaceutical composition suitable for oral administration being a tablet can comprise one or more pharmaceutically acceptable carriers and/or excipients suitable for preparing tablet formulations. Examples of such carriers include lactose and cellulose. The tablet can also or instead contain one or more pharmaceutically acceptable excipients, for example binding agents, lubricants such as magnesium stearate, and/or tablet disintegrants.

A pharmaceutical composition suitable for oral administration being a capsule can be prepared using encapsulation procedures. For example, pellets containing the active ingredient can be prepared using a suitable pharmaceutically acceptable carrier and then filled into a hard gelatin capsule. Alternatively, a dispersion or suspension can be prepared using any suitable pharmaceutically acceptable carrier, for example an aqueous gum or an oil and the dispersion or suspension then filled into a soft gelatin capsule.

Preferably the composition is in unit dose form such as a tablet or capsule for oral administration, e.g. for oral administration to a human.

A parenteral composition can comprise a solution or suspension of the compound or pharmaceutically acceptable salt in a sterile aqueous carrier or parenterally acceptable oil. Alternatively, the solution can be lyophilised; the lyophilised parenteral pharmaceutical composition can be reconstituted with a suitable solvent just prior to administration.

Compositions for nasal or inhaled administration may conveniently be formulated as aerosols, drops, gels or dry powders.

Aerosol formulations, e.g. for inhaled administration, can comprise a solution or fine suspension of the active substance in a pharmaceutically acceptable aqueous or non-aqueous solvent. Aerosol formulations can be presented in single or multidose quantities in sterile form in a sealed container, which can take the form of a cartridge or refill for use with an atomising device or inhaler. Alternatively the sealed container may be a unitary dispensing device such as a single dose nasal inhaler or an aerosol dispenser fitted with a metering valve (metered dose inhaler) which is intended for disposal once the contents of the container have been exhausted.

Where the dosage form comprises an aerosol dispenser, it preferably contains a suitable propellant under pressure such as compressed air, carbon dioxide, or an organic propellant such as a chlorofluorocarbon (CFC) or hydrofluorocarbon (HFC). Suitable CFC propellants include dichlorodifluoromethane, trichlorofluoromethane and dichlorotetrafluoroethane. Suitable HFC propellants include 1,1,1,2,3,3,3-

heptafluoropropane and 1,1,1,2-tetrafluoroethane. The aerosol dosage forms can also take the form of a pump-atomiser.

For pharmaceutical compositions suitable and/or adapted for inhaled administration, it is preferred that the compound or salt of formula (I) is in a particle-size-reduced form, and more preferably the size-reduced form is obtained or obtainable by micronisation. Micronisation usually involves subjecting the compound/salt to collisional and abrasional forces in a fast-flowing circular or spiral/vortex-shaped airstream often including a cyclone component. The preferable particle size (e.g. D50 value) of the size-reduced (e.g. micronised) compound or salt is about 0.5 to about 10 microns, e.g. about 1 to about 5 microns (e.g. as measured using laser diffraction). For example, it is preferable for the compound or salt of formula (I) to have a particle size defined by: a D10 of about 0.3 to about 3 microns (e.g. about 1 micron), and/or a D50 of about 1 to about 5 microns (e.g. about 2-5 or about 2-3 microns), and/or a D90 of about 2 to about 20 microns or about 3 to about 10 microns (e.g. about 5-8 or about 5-6 microns); for example as measured using laser diffraction. The laser diffraction measurement can use a dry method (suspension of compound/salt in airflow crosses laser beam) or a wet method [suspension of compound/salt in liquid dispersing medium, such as isooctane or (e.g. if compound soluble in isooctane) 0.1% Tween 80 in water, crosses laser beam]. With laser diffraction, particle size is preferably calculated using the Fraunhofer calculation; and/or preferably a Malvern Mastersizer or Sympatec apparatus is used for measurement.

An illustrative non-limiting example of a small-scale micronisation process is now given:

Micronisation Example: Micronisation of Example 518 or 518A

- Purpose: To micronize approximately 600-1000 mg of Example 518 or 518A (described hereinafter) using a Jetpharma MC1 micronizer.
- The parent (unmicronised) and micronised materials are analyzed for particle size by laser diffraction and crystallinity by PXRD.

Equipment and material

Equipment/material	Description and specification
Jetpharma MC1 Micronizer	Nitrogen supply: Air tank with 275psi rate tubing
Analytical balance	Sartorius Analytical
Top loader balance	Mettler PM400
Digital Caliper	VWR Electronic caliper
Vibrational spatula	Auto-spat Dispenser
Materials to be micronised	Example 518 or 518A

The Jetpharma MC1 Micronizer comprises a horizontal disc-shaped milling housing having: a tubular compound inlet (e.g. angled at ca. 30degrees to the horizontal) for entry of a suspension of unmicronised compound of formula (I) or salt in an gasflow, a separate gas inlet for entry of gases, a gas outlet for exit of gases, and a collection vessel for collecting micronised material. The milling housing has two chambers: an outer annular chamber in gaseous connection with the gas inlet the chamber being for receiving pressurised gas (e.g. air or nitrogen), an disc-shaped inner milling chamber within and coaxial with the outer chamber for micronising the input compound / salt, the two chambers being separated by an annular wall. The annular wall (ring R) has a plurality of narrow-bored holes connecting the inner and outer chambers and circumferentially-spaced-apart around the annular wall. The holes open into the inner chamber directed at an angle (directed part-way between radially and tangentially), and in use act as nozzles directing pressurised gas at high velocity from the outer chamber into the inner chamber and in an inwardly-spiral path (vortex) around the inner chamber (cyclone). The compound inlet is is gaseous communication with the inner chamber via a nozzle directed tangentially to the inner chamber, within and near to the annular wall. Upper and lower broad-diameter exit vents in the central axis of the the inner milling chamber connect to (a) (lower exit) the collection vessel which has no air outlet, and (b) (upper exit) the gas outlet which leads to a collection bag, filter and a gas exhaust. Inside the tubular compound inlet and longitudinally-movable within it is positioned a venturi inlet (V) for entry of gases. The compound inlet also has a bifurcation connecting to an upwardly-directed material inlet port for inputting material.

In use, the narrow head of the venturi inlet (V) is preferably positioned below and slightly forward of the material inlet port so that when the venturi delivers pressurised gas (eg air or nitrogen) the feed material is sucked into the gasstream thorough the compound inlet and accelerates it into the inner milling chamber tangentially at a subsonic speed. Inside the milling chamber the material is further accelerated to a supersonic speed by the hole/nozzle system around the ring (R) (annular wall) of the milling chamber. The nozzles are slightly angled so that the acceleration pattern of the material is in the form of an inwardly-directed vortex or cyclone. The material inside the milling chamber circulates rapidly and particle collisions occur during the process, causing larger particles to fracture into smaller ones. "Centrifugal" acceleration in the vortex causes the larger particles to remain at the periphery of the inner chamber while progressively smaller particles move closer to the center until they exit the milling chamber, generally through the lower exit, at low pressure and low velocity. The particles that exit the milling chamber are heavier than air and settle downward thorugh the lower exit into the collection vessel, while the exhaust gas rises (together with a miinority of small particles of micronised material) and escapes into the atmosphere at low pressure and low velocity.

Procedure:

The micronizer is assembled. The venturi protrusion distance from input port is adjusted to 1.0cm respectively (e.g. so that the narrow head of the venturi inlet is

positioned below and slightly forward of the material inlet port) and is measured with a micro-caliper to make sure that it is inserted correctly. The ring (R) and venturi (V) pressures are adjusted according to the values specified in the experimental design (refer to experimental section below) by adjusting the valves on the pressure gauges on the micronizer. The setup is checked for leakage by observing if there is any fluctuation in the reading of the pressure gauges.

Note that the venturi (V) pressure is kept at least 2 bars greater than the ring (R) pressure to prevent regurgitation of material, e.g. outwardly from the material inlet port.

Balance performance is checked with calibration weights. Specified amount of the parent material (see section on experimental run) is weighed into a plastic weigh boat. The material is then fed into the micronizer using a vibrational spatula (e.g. V-shaped in cross-section) at a specified feed rate. The material feeding time and equipment pressures are monitored during the micronization process.

Upon completion of the micronising run, the nitrogen supply is shut off and the collection bag is tapped to allow particles to settle into the recovery / collection vessel at the bottom of the micronizer. The collection bag is removed and set aside. The micronised powder in the recovery vessel (collection vessel) and the cyclone (above the recovery vessel) are collected separately into different weighed+labelled collection vials. The weight of the micronised material is recorded. The micronizer is disassembled and residual PDE4 compound on the micronizer inner surface is rinsed with 70/30 isopropyl alcohol / water and collected into a flask. The micronizer is then thoroughly cleaned by rinsing and wiping with suitable solvent and dried before subsequent runs are performed.

Preferred Experimental Parameters

Parent (unmicronised) material (Procedure 1): Example 518 or 518A
Parent (unmicronised) material (Procedure 2): Example 518
Balance(s) Used: Sartorius analytical
Venturi outlet insertion depth: 10.0 mm

Procedure no.	Material input amount (g)	Venturi (V) / ring (R) Pressure (bar)	Intended feed-rate	Time needed to feed material (min+sec)	Actual feed-rate (g/min)
1	0.8795g	V= 10 bar R= 6 bar	200 mg/min	4 min 51 sec	181 mg/min
2	0.9075g	V= 8 bar R= 5.5 bar	200 mg/min	4 min 43 sec	192 mg/min

The above parameters can be varied using the skilled person's knowledge.

Results and/or observations

% yield = [(Material from vessel + Material from cyclone)/Material input amount] x100

In general, very approximately 50-75% yields are achievable using this method. Procedure 1 has not been completed.
In Procedure 2, a 70.8% yield (0.6427g) of Example 518 micronised material was obtained, including material from collection vessel and material from inside walls of cyclone.
Particle size analysis of Example 518 micronised material from Procedure 2, using laser diffraction measurement with Malvern Mastersizer longbed version, dispersing medium 0.1% Tween 80 in water, stir rate 1500 rpm, 3 mins sonification prior to final dispersion and analysis, 300 RF (Reverse Fourier) lens, Fraunhofer calculation with Malvern software:
- material from collection vessel: D10 = 0.97 microns, D50 = 3.86 microns, D90 = 12.64 microns.
- material from inside walls of cyclone: D10 = 0.95 microns, D50 = 3.42 microns, D90 = 9.42 microns.

Alternative embodiment: Examples of the compounds/salts of the invention other than Examples 518 or 518A can be micronised.

For pharmaceutical compositions suitable and/or adapted for inhaled administration, it is preferred that the pharmaceutical composition is a dry powder inhalable composition. Such a composition can comprise a powder base such as lactose or starch, the compound of formula (I) or salt thereof (preferably in particle-size-reduced form, e.g. in micronised form), and optionally a performance modifier such as L-leucine, mannitol, trehalose and/or magnesium stearate. Preferably, the dry powder inhalable composition comprises a dry powder blend of lactose and the compound of formula (I) or salt thereof. The lactose is preferably lactose hydrate e.g. lactose monohydrate and/or is preferably inhalation-grade and/or fine-grade lactose. Preferably, the particle size of the lactose is defined by 90% or more (by weight or by volume) of the lactose particles being less than 1000 microns (micrometres) (e.g. 10-1000 microns e.g. 30-1000 microns) in diameter, and/or 50% or more of the lactose particles being less than 500 microns (e.g. 10-500 microns) in diameter. More preferably, the particle size of the lactose is defined by 90% or more of the lactose particles being less than 300 microns (e.g. 10-300 microns e.g. 50-300 microns) in diameter, and/or 50% or more of the lactose particles being less than 100 microns in diameter. Optionally, the particle size of the lactose is defined by 90% or more of the lactose particles being less than 100-200 microns in diameter, and/or 50% or more of the lactose particles being less than 40-70 microns in diameter. Most importantly, it is preferable that about 3 to about 30% (e.g. about 10%) (by weight or by volume) of the particles are less than 50 microns or less than 20 microns in diameter. For example, without limitation, a suitable inhalation-grade lactose is E9334 lactose (10% fines) (Borculo Domo Ingredients, Hanzeplein 25, 8017 JD Zwolle, Netherlands).

In the dry powder inhalable composition, preferably, the compound of formula (I) or salt thereof is present in about 0.1% to about 70% (e.g. about 1% to about 50%, e.g. about 5% to about 40%, e.g. about 20 to about 30%) by weight of the composition.

An illustrative non-limiting example of a dry powder inhalable composition follows:

Dry Powder Formulation Example - Dry powder Lactose Blend Preparation

Using a size-reduced e.g. micronised form of the compound of formula (I) or salt thereof (e.g. as prepared in the Micronisation Example above), the dry powder blend is prepared by mixing the required amount of the compound/salt (e.g. 10 mg, 1% w/w) with inhalation-grade lactose containing 10% fines (e.g. 990 mg, 99% w/w) in a Teflon™ (polytetrafluoroethene) pot in a Mikro-dismembrator ball-mill (but without a ball bearing) at ¾ speed (ca. 2000-2500 rpm) for about 4 hours at each blend concentration. The Mikro-dismembrator (available from B. Braun Biotech International, Schwarzenberger Weg 73-79, D-34212 Melsungen, Germany; www.bbraunbiotech.com) comprises a base with an upwardly-projecting and sidewardly-vibratable arm to which is attached the Teflon ™ pot. The vibration of the arm achieves blending.

Other blends: 10% w/w compound/salt (50 mg) + 90% w/w lactose (450 mg, inhalation-grade lactose containing 10% fines).

Serial dilution of the 1% w/w blend can achieve e.g. 0.1% and 0.3% w/w blends.

Optionally, in particular for dry powder inhalable compositions, a pharmaceutical composition for inhaled administration can be incorporated into a plurality of sealed dose containers (e.g. containing the dry powder composition) mounted longitudinally in a strip or ribbon inside a suitable inhalation device. The container is rupturable or peel-openable on demand and the dose, e.g. of the dry powder composition, can be administered by inhalation via a device such as the DISKUS ™ device, marketed by GlaxoSmithKline. The DISKUS ™ inhalation device is usually substantially as described in GB 2,242,134 A. In such device at least one container for the pharmaceutical composition in powder form (the at least one container preferably being a plurality of sealed dose containers mounted longitudinally in a strip or ribbon) is defined between two members peelably secured to one another; the device comprises: means defining an opening station for the said at least one container; means for peeling the members apart at the opening station to open the container; and an outlet, communicating with the opened container, through which a user can inhale the pharmaceutical composition in powder form from the opened container.

In the pharmaceutical composition, a or each dosage unit for oral or parenteral administration preferably contains from 0.01 to 3000 mg, more preferably 0.5 to 1000 mg, of a compound of the formula (I) or a pharmaceutically acceptable salt thereof, calculated as the free base. A or each dosage unit for nasal or inhaled administration

preferably contains from 0.001 to 50 mg, more preferably 0.01 to 5 mg, of a compound of the formula (I) or a pharmaceutically acceptable salt thereof, calculated as the free base.

A pharmaceutically acceptable compound or salt of the invention is preferably administered to a mammal (e.g. human) in a daily oral or parenteral dose of 0.001 mg to 50 mg per kg body weight per day (mg/kg/day), for example 0.01 to 20 mg/kg/day or 0.03 to 10 mg/kg/day or 0.1 to 2 mg/kg/day, of the compound of the formula (I) or a pharmaceutically acceptable salt thereof, calculated as the free base.

A pharmaceutically acceptable compound or salt of the invention is preferably administered to a mammal (e.g. human) in a daily nasal or inhaled dose of: 0.0001 to 5 mg/kg/day or 0.0001 to 1 mg/kg/day, e.g. 0.001 to 1 mg/kg/day or 0.001 to 0.3 mg/kg/day or 0.001 to 0.1 mg/kg/day or 0.005 to 0.3 mg/kg/day, of the compound of the formula (I) or a pharmaceutically acceptable salt thereof, calculated as the free base.

The pharmaceutically acceptable compounds or salts of the invention is preferably administered in a daily dose (for an adult patient) of, for example, an oral or parenteral dose of 0.01 mg to 3000 mg per day or 0.5 to 1000 mg per day e.g. 2 to 500 mg per day, or a nasal or inhaled dose of 0.001 to 300 mg per day or 0.001 to 50 mg per day or 0.01 to 30 mg per day or 0.01 to 5 mg per day or 0.02 to 2 mg per day, of the compound of the formula (I) or a pharmaceutically acceptable salt thereof, calculated as the free base.

Combinations

The compounds, salts and/or pharmaceutical compositions according to the invention may also be used in combination with another therapeutically active agent, for example, a β_2 adrenoreceptor agonist, an anti-histamine, an anti-allergic or an anti-inflammatory agent.

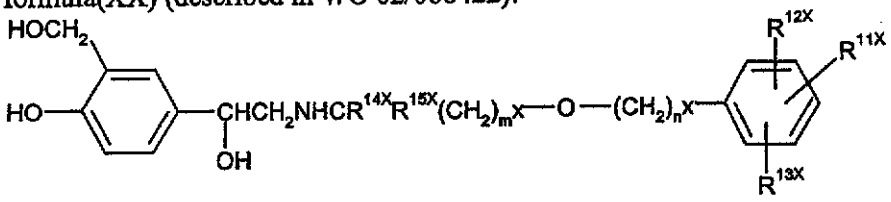
The invention thus provides, in a further aspect, a combination comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof together with another therapeutically active agent, for example, a β_2-adrenoreceptor agonist, an anti-histamine, an anti-allergic, an anti-inflammatory agent or an antiinfective agent.

Preferably, the β_2-adrenoreceptor agonist is salmeterol (e.g. as racemate or a single enantiomer such as the R-enantiomer), salbutamol, formoterol, salmefamol, fenoterol or terbutaline, or a salt thereof (e.g. pharmaceutically acceptable salt thereof), for example the xinafoate salt of salmeterol, the sulphate salt or free base of salbutamol or the fumarate salt of formoterol. Long-acting β_2-adrenoreceptor agonists are preferred, especially those having a therapeutic effect over a 12-24 hour period such as salmeterol or formoterol. Preferably, the β_2-adrenoreceptor agonist is for inhaled administration, e.g. once per day and/or for simultaneous inhaled administration; and more preferably the β_2-adrenoreceptor agonist is in particle-size-reduced form e.g. as defined herein. Preferably, the β_2-adrenoreceptor agonist combination is for treatment and/or

prophylaxis of COPD or asthma. Salmeterol or a pharmaceutically acceptable salt thereof, e.g. salmeterol xinofoate, is preferably administered to humans at an inhaled dose of 25 to 50 micrograms twice per day (measured as the free base). The combination with a β_2-adrenoreceptor agonist can be as described in WO 00/12078.

Preferred long acting β_2-adrenoreceptor agonists include those described in WO 02/066422A, WO 03/024439, WO 02/070490 and WO 02/076933.

Especially preferred long-acting β_2-adrenoreceptor agonists include compounds of formula(XX) (described in WO 02/066422):



(XX)

or a salt or solvate thereof, wherein in formula (XX):
m^X is an integer of from 2 to 8;
n^X is an integer of from 3 to 11,
with the proviso that $m^X + n^X$ is 5 to 19,
R^{11X} is $-XSO_2NR^{16X}R^{17X}$ wherein X is $-(CH_2)_{p^X}-$ or C_{2-6} alkenylene;
R^{16X} and R^{17X} are independently selected from hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl, $C(O)NR^{18X}R^{19X}$, phenyl, and phenyl (C_{1-4}alkyl)-,
or R^{16X} and R^{17X}, together with the nitrogen to which they are bonded, form a 5-, 6-, or 7-membered nitrogen containing ring, and R^{16X} and R^{17X} are each optionally substituted by one or two groups selected from halo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, hydroxy-substituted C_{1-6}alkoxy, $-CO_2R^{18X}$, $-SO_2NR^{18X}R^{19X}$, $-CONR^{18X}R^{19X}$, $-NR^{18X}C(O)R^{19X}$, or a 5-, 6- or 7-membered heterocylic ring;
R^{18X} and R^{19X} are independently selected from hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, phenyl, and phenyl (C_{1-4}alkyl)-; and
p^X is an integer of from 0 to 6, preferably from 0 to 4;
R^{12X} and R^{13X} are independently selected from hydrogen, C_{1-6}alkyl, C_{1-6}alkoxy, halo, phenyl, and C_{1-6}haloalkyl; and
R^{14X} and R^{15X} are independently selected from hydrogen and C_{1-4}alkyl with the proviso that the total number of carbon atoms in R^{14X} and R^{15X} is not more than 4.

Preferred β_2-adrenoreceptor agonists disclosed in WO 02/066422 include:
3-(4-{[6-({(2R)-2-hydroxy-2-[4-hydroxy-3-(hydroxymethyl)-phenyl]ethyl}amino)hexyl]oxy}butyl)benzenesulfonamide and
3-(3-{[7-({(2R)-2-hydroxy-2-[4-hydroxy-3-hydroxymethyl)phenyl]ethyl}-amino)heptyl]oxy}propyl)benzenesulfonamide.

A preferred β_2-adrenoreceptor agonist disclosed in WO 03/024439 is:
4-{(1*R*)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol.

A combination of a compound of formula (I) or salt together with an anti-histamine is preferably for oral administration (e.g. as a combined composition such as a combined tablet), and can be for treatment and/or prophylaxis of allergic rhinitis. Examples of anti-histamines include methapyrilene, or H1 antagonists such as cetirizine, loratadine (e.g. Clarityn TM), desloratadine (e.g. Clarinex TM) or fexofenadine (e.g. Allegra TM).

The invention also provides, in a further aspect, a combination comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof together with an anticholinergic compound, e.g. a muscarinic (M) receptor antagonist in particular an M_1, M_2, M_1/M_2, or M_3 receptor antagonist, more preferably a M_3 receptor antagonist, still more preferably a M_3 receptor antagonist which selectively antagonises (e.g. antagonises 10 times or more strongly) the M_3 receptor over the M_1 and/or M_2 receptor. For combinations of anticholinergic compounds / muscarinic (M) receptor antagonist with PDE4 inhibitors, see for example WO 03/011274 A2 and WO 02/069945 A2 / US 2002/0193393 A1 and US 2002/052312 A1, and some or all of these publications give examples of anticholinergic compounds / muscarinic (M) receptor antagonists which may be used with the compounds of formula (I) or salts, and/or suitable pharmaceutical compositions. For example, the muscarinic receptor antagonist can comprise or be an ipratropium salt (e.g. ipratropium bromide), an oxitropium salt (e.g. oxitropium bromide), or more preferably a tiotropium salt (e.g. tiotropium bromide); see e.g. EP 418 716 A1 for tiotropium.

The anticholinergic compound or muscarinic (M) receptor antagonist, e.g. M_3 receptor antagonist, is preferably for inhaled administration, more preferably in particle-size-reduced form e.g. as defined herein. More preferably, both the muscarinic (M) receptor antagonist and the compound of formula (I) or the pharmaceutically acceptable salt thereof are for inhaled administration. Preferably, the anticholinergic compound or muscarinic receptor antagonist and the compound of formula (I) or salt are for simultaneous administration. The muscarinic receptor antagonist combination is preferably for treatment and/or prophylaxis of COPD.

Other suitable combinations include, for example, a combination comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof together with another anti-inflammatory agent such as an anti-inflammatory corticosteroid; or a non-steroidal anti-inflammatory drug (NSAID) such as a leukotriene antagonist (e.g. montelukast), an iNOS inhibitor, a tryptase inhibitor, a elastase inhibitor, a beta-2 integrin antagonist, a adenosine 2a agonist, a CCR3 antagonist, or a 5-lipoxogenase inhibitor); or an

antiinfective agent (e.g. an antibiotic or antiviral). An iNOS inhibitor is preferably for oral administration. Suitable iNOS inhibitors (inducible nitric oxide synthase inhibitors) include those disclosed in WO 93/13055, WO 98/30537, WO 02/50021, WO 95/34534 and WO 99/62875. Suitable CCR3 inhibitors include those disclosed in WO 02/26722.

In a combination comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof together with an anti-inflammatory corticosteroid (which is preferably for treatment and/or prophylaxis of asthma, COPD or allergic rhinitis), then preferably the anti-inflammatory corticosteroid is fluticasone, fluticasone propionate (e.g. see US patent 4,335,121), beclomethasone, beclomethasone 17-propionate ester, beclomethasone 17,21-dipropionate ester, dexamethasone or an ester thereof, mometasone or an ester thereof, ciclesonide, budesonide, flunisolide, or a compound as described in WO 02/12266 A1 (e.g. as claimed in any of claims 1 to 22 therein), or a pharmaceutically acceptable salt of any of the above. If the anti-inflammatory corticosteroid is a compound as described in WO 02/12266 A1, then preferably it is Example 1 therein {which is 6α,9α-difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester} or Example 41 therein {which is 6α,9α-difluoro-11β-hydroxy-16α-methyl-17α-[(4-methyl-1,3-thiazole-5-carbonyl)oxy]-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester}, or a pharmaceutically acceptable salt thereof. The anti-inflammatory corticosteroid is preferably for intranasal or inhaled administration. Fluticasone propionate is preferred and is preferably for inhaled administration to a human either (a) at a dose of 250 micrograms once per day or (b) at a dose of 50 to 250 micrograms twice per day.

Also provided is a combination comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof together with β_2-adrenoreceptor agonist and an anti-inflammatory corticosteroid, for example as described in WO 03/030939 A1. Preferably this combination is for treatment and/or prophylaxis of asthma, COPD or allergic rhinitis. The β_2-adrenoreceptor agonist and/or the anti-inflammatory corticosteroid can be as described above and/or as described in WO 03/030939 A1. Most preferably, in this "triple" combination, the β_2-adrenoreceptor agonist is salmeterol or a pharmaceutically acceptable salt thereof (e.g. salmeterol xinafoate) and the anti-inflammatory corticosteroid is fluticasone propionate.

The combinations referred to above may conveniently be presented for use in the form of a pharmaceutical composition and thus a pharmaceutical composition comprising a combination as defined above together with one or more pharmaceutically acceptable carriers and/or excipients represent a further aspect of the invention.

The individual compounds of such combinations may be administered either sequentially or simultaneously in separate or combined pharmaceutical composition.

In one embodiment, the combination as defined herein can be for simultaneous inhaled administration and is disposed in a combination inhalation device. Such a combination inhalation device is another aspect of the invention. Such a combination inhalation device can comprise a combined pharmaceutical composition for simultaneous inhaled administration (e.g. dry powder composition), the composition comprising all the individual compounds of the combination, and the composition being incorporated into a plurality of sealed dose containers mounted longitudinally in a strip or ribbon inside the inhalation device, the containers being rupturable or peel-openable on demand; for example such inhalation device can be substantially as described in GB 2,242,134 A (DISKUS ™) and/or as described above. Alternatively, the combination inhalation device can be such that the individual compounds of the combination are administrable simultaneously but are stored separately (or wholly or partly stored separately for triple combinations), e.g. in separate pharmaceutical compositions, for example as described in PCT/EP03/00598 filed on 22 January 2003 (e.g. as described in the claims thereof e.g. claim 1).

The invention also provides a method of preparing a combination as defined herein, the method comprising either

(a) preparing a separate pharmaceutical composition for administration of the individual compounds of the combination either sequentially or simultaneously, or

(b) preparing a combined pharmaceutical composition for administration of the individual compounds of the combination simultaneously,

wherein the pharmaceutical composition comprises the combination together with one or more pharmaceutically acceptable carriers and/or excipients.

The invention also provides a combination as defined herein, prepared by a method as defined herein.

BIOLOGICAL TEST METHODS

PDE 3, PDE 4B, PDE 4D, PDE 5, PDE 6 Primary assay methods

The activity of the compounds can be measured in the assay methods shown below. Preferred compounds of the invention are selective PDE4 inhibitors, i.e. they inhibit PDE4 (e.g. PDE4B and/or PDE4D, preferably PDE4B) more strongly than they inhibit PDE3 and/or more strongly than they inhibit PDE5 and/or more strongly than they inhibit PDE6.

PDE enzyme sources and literature references

Human recombinant PDE4B, in particular the 2B splice variant thereof (HSPDE4B2B), is disclosed in WO 94/20079 and also M.M. McLaughlin et al., "A low *Km*, rolipram-sensitive, cAMP-specific phosphodiesterase from human brain: cloning and expression of cDNA, biochemical characterisation of recombinant protein, and tissue distribution of mRNA", *J. Biol. Chem.*, 1993, **268**, 6470-6476. For example, in Example 1 of WO 94/20079, human recombinant PDE4B is described as being expressed in the PDE-deficient yeast *Saccharomyces cerevisiae* strain GL62, e.g. after induction by addition of 150 uM $CuSO_4$, and 100,000 x *g* supernatant fractions of yeast cell lysates are described for use in the harvesting of PDE4B enzyme.

Human recombinant PDE4D (HSPDE4D3A) is disclosed in P. A. Baecker et al., "Isolation of a cDNA encoding a human rolipram-sensitive cyclic AMP phoshodiesterase (PDE IV_D)", *Gene*, 1994, **138**, 253-256.

Human recombinant PDE5 is disclosed in K. Loughney et al., "Isolation and characterisation of cDNAs encoding PDE5A, a human cGMP-binding, cGMP-specific 3',5'-cyclic nucleotide phosphodiesterase", *Gene*, 1998, **216**, 139-147.

PDE3 was purified from bovine aorta as described by H. Coste and P. Grondin, "Characterisation of a novel potent and specific inhibitor of type V phosphodiesterase", *Biochem. Pharmacol.*, 1995, **50**, 1577-1585.

PDE6 was purified from bovine retina as described by: P. Catty and P. Deterre, "Activation and solubilization of the retinal cGMP-specific phosphodiesterase by limited proteolysis", *Eur. J. Biochem.*, 1991, **199**, 263-269; A. Tar et al. "Purification of bovine retinal cGMP phosphodiesterase", *Methods in Enzymology*, 1994, **238**, 3-12; and/or D. Srivastava et al. "Effects of magnesium on cyclic GMP hydrolysis by the bovine retinal rod cyclic GMP phosphodiesterase", *Biochem. J.*, 1995, **308**, 653-658.

Inhibition of PDE 3, PDE 4B, PDE 4D, PDE 5 or PDE 6 activity: radioactive Scintillation Proximity Assay (SPA)

The ability of compounds to inhibit catalytic activity at PDE4B or 4D (human recombinant), PDE3 (from bovine aorta), PDE5 (human recombinant) or PDE6 (from bovine retina) was determined by Scintillation Proximity Assay (SPA) in 96-well format. Test compounds (preferably as a solution in DMSO, e.g. 0.5 to 1 microlitre (ul) volume) were preincubated at ambient temperature (room temperature, e.g. 19-23°C) in Wallac Isoplates (code 1450-514) with PDE enzyme in 50mM Tris-HCl buffer pH 7.5 , 8.3mM $MgCl_2$, 1.7mM EGTA, 0.05% (w/v) bovine serum albumin for 10-30 minutes (usually 30 minutes). The enzyme concentration was adjusted so that no more than 20% hydrolysis of the substrate defined below occurred in control wells without compound, during the incubation. For the PDE3, PDE4B and PDE4D assays, [5',8-^{3}H]Adenosine 3',5'-cyclic phosphate (Amersham Pharmacia Biotech, code TRK.559; or Amersham Biosciences UK Ltd, Pollards Wood, Chalfont St Giles, Buckinghamshire HP8 4SP, UK) was added to give 0.05uCi per well and ~ 10nM final concentration. For the PDE5 and PDE6 assays, [8-^{3}H]Guanosine 3',5'-cyclic phosphate (Amersham Pharmacia Biotech, code TRK.392) was added to give 0.05uCi per well and ~ 36nM final concentration. Plates, e.g. containing approx. 100 ul volume of assay mixture, were mixed on an orbital shaker for 5 minutes and incubated at ambient temperature for 1 hour. Phosphodiesterase SPA beads (Amersham Pharmacia Biotech, code RPNQ 0150) were added (~1mg per well) to terminate the assay. Plates were sealed and shaken and allowed to stand at ambient temperature for 35 minutes to 1hour (preferably 35 minutes) to allow the beads to settle. Bound radioactive product was measured using a WALLAC TRILUX 1450 Microbeta scintillation counter. For inhibition curves, 10 concentrations (1.5nM - 30uM) of each compound were assayed. Curves were analysed using ActivityBase and XLfit (ID Business Solutions Limited, 2 Ocean Court, Surrey Research Park, Guildford, Surrey GU2 7QB, United Kindgom) Results were expressed as pIC_{50} values.

In an alternative to the above radioactive SPA assay, PDE4B or PDE4D inhibition can be measured in the following Fluorescence Polarisation (FP) assay:

Inhibition of PDE4B or PDE4D activity: Fluorescence Polarisation (FP) assay

The ability of compounds to inhibit catalytic activity at PDE4B (human recombinant) or PDE4D (human recombinant) was determined by IMAP Fluorescence Polarisation (FP) assay (IMAP Explorer kit, available from Molecular Devices Corporation, Sunnydale, CA, USA; Molecular Devices code: R8062) in 384-well format. The IMAP FP assay is able to measure PDE activity in an homogenous, non-radioactive assay format. The FP assay uses the ability of immobilised trivalent metal cations, coated onto nanoparticles (tiny beads), to bind the phosphate group of Fl-AMP that is produced on the hydrolysis of fluorescein-labelled (Fl) cyclic adenosine mono-phosphate (Fl-cAMP) to the non-cyclic Fl-AMP form. Fl-cAMP does not bind. Binding of Fl-AMP product to the beads (coated with the immobilised trivalent cations) slows the rotation of

the bound Fl-AMP and leads to an increase in the fluorescence polarisation ratio of parallel to perpendicular light. Inhibition of the PDE reduces/inhibits this signal increase.

Test compounds (small volume, e.g. 0.5 to 1 ul, of solution in DMSO) were preincubated at ambient temperature (room temperature, e.g. 19-23°C) in black 384-well microtitre plates (supplier: NUNC, code 262260) with PDE enzyme in 10mM Tris-HCl buffer pH 7.2, 10mM $MgCl_2$, 0.1% (w/v) bovine serum albumin, and 0.05% NaN_3 for 10-30 minutes. The enzyme level was set by experimentation so that reaction was linear throughout the incubation. Fluorescein adenosine 3',5'-cyclic phosphate (from Molecular Devices Corporation, Molecular Devices code: R7091) was added to give about 40nM final concentration (final assay volume usually ca. 25-40 ul). Plates were mixed on an orbital shaker for 10 seconds and incubated at ambient temperature for 40 minutes. IMAP binding reagent (as described above, from Molecular Devices Corporation, Molecular Devices code: R7207) was added (60ul of a 1 in 400 dilution in binding buffer of the kit stock solution) to terminate the assay. Plates were allowed to stand at ambient temperature for 1 hour. The Fluorescence Polarisation (FP) ratio of parallel to perpendicular light was measured using an Analyst^{TM} plate reader (from Molecular Devices Corporation). For inhibition curves, 10 concentrations (1.5nM - 30uM) of each compound were assayed. Curves were analysed using ActivityBase and XLfit (ID Businesss Solutions Limited, 2 Ocean Court, Surrey Research Park, Guildford, Surrey GU2 7QB, United Kindgom). Results were expressed as pIC_{50} values.

In the FP assay, all reagents were dispensed using Multidrop^{TM} (available from Thermo Labsystems Oy, Ratastie 2, PO Box 100, Vantaa 01620, Finland).

For a given PDE4 inhibitor, the PDE4B (or PDE4D) inhibition values measured using the SPA and FP assays can differ slightly. However, in a regression analysis of 100 test compounds, the pIC_{50} inhibition values measured using SPA and FP assays have been found generally to agree within 0.5 log units, for PDE4B and PDE4D (linear regression coefficient 0.966 for PDE4B and 0.971 for PDE4D; David R.Mobbs et al., "Comparison of the IMAP Fluorescence Polarisation Assay with the Scintillation Proximity Assay for Phosphodiesterase Activity", poster to be presented at 2003 Molecular Devices UK & Europe User Meeting, 2nd October 2003, Down Hall, Harlow, Essex, United Kingdom).

Biological Data obtained for some of the Examples (PDE4B inhibitory activity, either as one reading or as an average of ca. 2-6 readings) are as follows, based on current measurements only. In each of the SPA and FP assays, absolute accuracy of measurement is not possible, and the readings given are accurate only up to about ± 0.5 of a log unit, depending on the number of readings made and averaged:

Example number	**PDE4B pIC_{50}** (± about 0.5)
2	8.0
3	7.8
6	6.6
11	7.4

21	8.5
22	7.9
32	7.7
40	8.3
63	6.9
1, 36, 39, 41, 42, 43, 44, 47, 48, 63, 83, 109, 178, 187 and 600	7.0 to 7.9
100, 155, 165, 167, 201, 260, 261, 263, 265, 266, 267, 271, 431, 493, 494, 495, 498, 518, 518A, 528, 551, 575, 581, 584, 619, 622, 624-626, 628, 630, 636, 638, 643-645, 653, and 677 to 686	8.2 to 10.0
196	7.9
198	8.5

Examples 1-201 were generally tested for PDE4B inhibition using the radioactive SPA assay. Of Examples 207-665, and 677-686, all or almost all (except perhaps for Examples 451, 631-632, 635, 652) were tested for PDE4B inhibition; and of these some were tested by the radioactive SPA assay, some were tested by the FP assay. Examples 1-201, 207-450, 452-630, 633-634, 636-651, 653-665, and 677-686, but excluding reference examples 19-20, have PDE4B inhibitory activities in the range of pIC_{50} = about 6 (± about 0.5) to about 10.0 (± about 0.5). Examples 666-676 are predicted to have PDE4B inhibitory activities in the range of pIC_{50} = about 6 (± about 0.5) to about 10.0 (± about 0.5).

The Examples wherein R^3 = cyclohexyl (NHR^3 = sub-formula (c)), tetrahydro-2H-pyran-4-yl (NHR^3 = group (h)), 4-oxocyclohexyl (NHR^3 = sub-formula (o)), or certain other types of substituted cyclohexyl or certain heterocycles, usually or often (especially with R^1 = ethyl) have a higher level of selectivity for PDE4B over PDE5, as measured in the above enzyme inhibition assays, compared to the selectivities of comparable Examples wherein R^3 = cyclopropyl (NHR^3 = sub-formula (b)). For example, based on current measurements only, and subject to cumulative assay inaccuracies:

- Examples 21, 40, 90, 198 and 201 (wherein NHR^3 = sub-formula (h), (c), (j), (n) and (o) respectively, R^1 = ethyl) have selectivities for PDE4B over PDE5 in the range of about 3 to 20 or more times greater than the selectivity achieved for the equivalent Example 39 wherein R^3 = cyclopropyl (NHR^3 = sub-formula (b));

- Examples 43 and 44 (wherein NHR^3 = sub-formula (c) and (h) respectively) have selectivities for PDE4B over PDE5 in the range of about 4 to 8 or more times greater than the selectivity achieved for the equivalent R^3 = cyclopropyl Example 42;
- Examples 22 and 48 (wherein NHR^3 = sub-formula (h) and (c) respectively) have selectivities for PDE4B over PDE5 in the range of about 2.5 to 10 or more times greater than the selectivity achieved for the equivalent R^3 = cyclopropyl Example 47; and
- Examples 2 and 3 (wherein NHR^3 = sub-formula (c) and (h) respectively) have selectivities for PDE4B over PDE5 in the range of about 2 to 5 or more times greater than the selectivity achieved for the equivalent R^3 = cyclopropyl Example 1.

Emesis: Some known PDE4 inhibitors can cause emesis and/or nausea to greater or lesser extents (e.g. see Z. Huang et al., *Current Opinion in Chemical Biology*, 2001, 5: 432-438, see especially pages 433-434 and refs cited therein). Therefore, it would be preferable, but not essential, if a PDE4 inhibitory compound or salt of the invention were to cause only limited or manageable emetic side-effects. Emetic side-effects can for example be measured by the emetogenic potential of the compound or salt when administered to ferrets; for example one can measure the time to onset, extent, frequency and/or duration of vomiting, retching and/or writhing in ferrets after oral or parenteral administration of the compound or salt. See for example In vivo Assay 4 hereinafter for a measurement method for anti-inflammatory effect, emetic side-effects and therapeutic index (TI) in the ferret. See also for example A. Robichaud et al., "Emesis induced by inhibitors of [PDE IV] in the ferret", *Neuropharmacology*, 1999, 38, 289-297, erratum *Neuropharmacology*, 2001, 40, 465-465. However, optionally, emetic side-effects and therapeutic index (TI) in rats can be conveniently measured by monitoring the pica feeding behaviour of rats after administration of the compound or salt of the invention (see In Vivo Assay 2 below).

Other side effects: Some known PDE4 inhibitors can cause other side effects such as headache and other central nervous sytem (CNS-) mediated side effects; and/or gastrointestinal (GI) tract disturbances. Therefore, it would be preferable but not essential if a particular PDE4 inhibitory compound or salt of the invention were to cause only limited or manageable side-effects in one or more of these side-effect categories.

***In Vivo* Biological Assays**

The *in vitro* enzymatic PDE4B inhibition assay described above should be regarded as being the primary test of biological activity. However, additional *in vivo* biological tests, which are optional and which are not an essential measure of efficacy or side-effects, are described below.

In Vivo Assay 1. LPS-induced pulmonary neutrophilia in rats: effect of orally administered PDE4 inhibitors

Pulmonary neutrophil influx has been shown to be a significant component to the family of pulmonary diseases like chronic obstructive pulmonary disease (COPD) which can involve chronic bronchitis and/or emphysema (G.F. Filley, *Chest.* 2000; 117(5); 251s-260s). The purpose of this neutrophilia model is to study the potentially anti-inflammatory effects *in vivo* of orally administered PDE4 inhibitors on neutrophilia induced by inhalation of aerosolized lipopolysaccharide (LPS), modelling the neutrophil inflammatory component(s) of COPD. See the literature section below for scientific background.

Male Lewis rats (Charles River, Raleigh, NC, USA) weighing approximately 300-400 grams are pretreated with either (a) test compound suspended in 0.5% methylcellulose (obtainable from Sigma-Aldrich, St Louis, MO, USA) in water or (b) vehicle only, delivered orally in a dose volume of 10 ml/kg. Generally, dose response curves are generated using the following doses of PDE4 inhibitors: 10.0, 2.0, 0.4, 0.08 and 0.016 mg/kg. Thirty minutes following pretreatment, the rats are exposed to aerosolized LPS (Serotype E. Coli 026:B6 prepared by trichloroacetic acid extraction, obtainable from Sigma-Aldrich, St Louis, MO, USA), generated from a nebulizer containing a 100 μg/ml LPS solution. Rats are exposed to the LPS aerosol at a rate of 4 L/min for 20 minutes. LPS exposure is carried out in a closed chamber with internal dimensions of 45 cm length x 24 cm width x 20 cm height. The nebulizer and exposure chamber are contained in a certified fume hood. At 4 hours-post LPS exposure the rats are euthanized by overdose with pentobarbital at 90 mg/kg, administered intraperitoneally. Bronchoalveolar lavage (BAL) is preformed through a 14 gauge blunt needle into the exposed trachea. Five, 5 ml washes are performed to collect a total of 25 ml of BAL fluid. Total cell counts and leukocyte differentials are performed on BAL fluid in order to calculate neutrophil influx into the lung. Percent neutrophil inhibition at each dose (cf. vehicle) is calculated and a variable slope, sigmoidal dose-response curve is generated, usually using Prism Graph-Pad. The dose-response curve is used to calculate an ED50 value (in mg per kg of body weight) for inhibition by the PDE4 inhibitor of the LPS-induced neutrophilia.

Results: Based on current measurements, the compounds of Examples 22, 83 and 155, administered orally in the above procedure, exhibited neutrophilia-inhibition ED50 values in the range of about 0.5 mg/kg to about 2 mg/kg.

Alternative method and results: In an alternative embodiment of the procedure, single oral doses of 10 mg/kg or 1.0 mg/kg of the PDE4 inhibitor (or vehicle) is administered to the rats, and percent neutrophil inhibition is calculated and reported for that specific dose. In this embodiment, based on current measurements, the compounds of Examples 21, 100, 109, 167, 172 and 600, administered orally in the above procedure at a single dose of 1.0 mg/kg, exhibited percent neutrophilia-inhibition in the range of about 19% to about 69% (or in the range of about 32% to about 69% for Examples 21, 100, 109, 167 and 600).

Literature:

Filley G.F. Comparison of the structural and inflammatory features of COPD and asthma. *Chest.* 2000; 117(5) 251s-260s.

Howell RE, Jenkins LP, Fielding LE, and Grimes D. Inhibition of antigen-induced pulmonary eosinophilia and neutrophilia by selective inhibitors of

phosphodiesterase types 3 and 4 in brown Norway rats. *Pulmonary Pharmacology.* 1995; 8: 83-89.

Spond J, Chapman R, Fine J, Jones H, Kreutner W, Kung TT, Minnicozzi M. Comparison of PDE 4 inhibitors, Rolipram and SB 207499 (Ariflo™), in a rat model of pulmonary neutrophilia. *Pulmonary Pharmacology and Therapeutics.* 2001; 14: 157-164.

Underwood DC, Osborn RR, Bochnowicz S, Webb EF, Rieman DJ, Lee JC, Romanic AM, Adams JL, Hay DWP, and Griswold DE. SB 239063, a p38 MAPK inhibitor, reduces neutrophilia, inflammatory cytokines, MMP-9, and fibrosis in lung. *Am J Physiol Lung Cell Mol Physiol.* 2000; 279: L895-L902.

In Vivo Assay 2. Rat Pica Model of emesis

Background: Selective PDE4 inhibitors have been shown to inhibit inflammation in various *in vitro* and *in vivo* models by increasing intracellular levels of cAMP of many immune cells (e.g. lymphocytes, monocytes). However, a side effect of some PDE4 inhibitors in many species is emesis. Because many rat models of inflammation are well characterized, they have been used in procedures (see e.g. In Vivo Assay 1 above) to show beneficial anti-inflammatory effects of PDE 4 inhibitors. However rats have no emetic response (they have no vomit reflex), so that the relationship between beneficial anti-inflammatory effects of PDE 4 inhibitors and emesis is difficult to study directly in rats.

However, in 1991, Takeda *et al.* (see Literature section below) demonstrated that the pica feeding response is analogous to emesis in rats. Pica feeding is a behavioural response to illness in rats wherein rats eat non-nutritive substances such as earth or in particular clay (e.g. kaolin) which may help to absorb toxins. Pica feeding can be induced by motion and chemicals (especially chemicals which are emetic in humans), and can be inhibited pharmacologically with drugs that inhibit emesis in humans. The Rat Pica Model, In Vivo Assay 2, can determine the level of pica response of rats to PDE 4 inhibition at pharmacologically relevant doses in parallel to *in vivo* anti-inflammatory Assays in (a separate set of) rats (e.g. In Vivo Assay 1 above). Anti-inflammatory and pica assays in the same species together can provide data on the "therapeutic index" (TI) in the rat of the compounds/salts of the invention. The Rat TI can for example be calculated as the ratio of a) the potentially-emetic Pica Response ED50 dose from Assay 2 to b) the rat anti-inflammatory ED50 dose (e.g. measured by rat neutrophilia-inhibition in eg In Vivo Assay 1), with larger TI ratios possibly indicating lower emesis at many anti-inflammatory doses. This might allow a choice of a non-emetic or minimal-emetic pharmaceutical dose of the compounds or salts of the invention which has an anti-inflammatory effect. It is recognised however that achieving a low-emetic PDE4 inhibitory compound is not essential.

Procedure: On the first day of the experiment, the rats are housed individually in cages without bedding or "enrichment". The rats are kept off of the cage floor by a wire screen. Pre-weighed food cups containing standard rat chow and clay pellets are placed in the cage. The clay pellets, obtainable from Languna Clay Co, City of Industry, CA, USA, are the same size and shape as the food pellets. The rats are acclimated to the clay for 72 hours, during which time the cups and food and clay debris from the cage are weighed daily on an electronic balance capable of measuring to the nearest 0.1 grams. By

the end of the 72 hour acclimation period the rats generally show no interest in the clay pellets.

At the end of 72 hours the rats are placed in clean cages and the food cups weighed. Rats that are still consuming clay regularly are removed from the study. Immediately prior to the dark cycle (the time when the animals are active and should be eating) the animals are split into treatment groups and dosed orally with a dose of the compound/salt of the invention (different doses for different treatment groups) or with vehicle alone, at a dose volume of 2 ml/kg. In this oral dosing, the compound/salt is in the form of a suspension in 0.5% methylcellulose (obtainable Sigma-Aldrich, St. Louis, MO, USA) in water. The food and clay cups and cage debris are weighed the following day and the total clay and food consumed that night by each individual animal is calculated.

A dose response is calculated by first converting the data into quantal response, where animals are either positive or negative for the pica response. A rat is "pica positive" if it consumes greater than or equal to 0.3 grams of clay over the mean of is usually calculated using logistic regression performed by the Statistica software statistical package. A Pica Response ED50 value in mg per kg of body weight can then be calculated.

Results: Using the above procedure, and according to current measurements, the compounds of Examples 22, 83 and 155 exhibited a Pica Response ED50 in the range of about 4.8 mg/kg to greater than or equal to about 40 mg/kg. It can be seen that these Pica Response ED50 doses are higher than the neutrophilia-inhibition ED50 values for these three Examples (see In Vivo Assay 1 above), so that a Therapeutic Index (TI) in rats of >2, as measured by Assays 1+2 and according to current measurements, appears at first sight to have been achieved for these three Examples.

The Therapeutic Index (TI) calculated this way is often significantly different to, and often higher than, the TI calculated in the ferret (see In vivo Assay 4 below).

Literature:

Beavo JA, Contini, M., Heaslip, R.J. Multiple cyclic nucleotide phosphodiesterases. *Mol Pharmacol.* 1994; 46:399-405.

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Takeda N, Hasegawa S, Morita M, and Matsunaga T. Pica in rats is analogous to emesis: an animal model in emesis research. *Pharmacology, Biochemistry and Behavior.* 1991; 45:817-821.

Takeda N, Hasegawa S, Morita M, Horii A, Uno A, Yamatodani A and Matsunaga T. Neuropharmacological mechanisms of emesis. I. Effects of antiemetic drugs on motion- and apomorphine-induced pica in rats. *Meth Find Exp Clin Pharmacol.* 1995; 17(9) 589-596.

Takeda N, Hasegawa S, Morita M, Horii A, Uno A, Yamatodani A and Matsunaga T. Neuropharmacological mechanisms of emesis. II. Effects of antiemetic drugs on cisplatin-induced pica in rats. *Meth Find Exp Clin Pharmacol.* 1995; 17(9) 647-652.

In Vivo Assay 3. LPS induced pulmonary neutrophilia in rats: effect of intratracheally administered PDE4 inhibitors

This assay is an animal model of inflammation in the lung – specifically neutrophilia induced by lipopolysaccharide (LPS) – and allows the study of putative inhibition of such neutrophilia (anti-inflammatory effect) by intratracheally (i.t.) administered PDE4 inhibitors. The PDE4 inhibitors are preferably in dry powder or wet suspension form. I.t. administration is one model of inhaled administration, allowing topical delivery to the lung.

Animals: Male CD (Sprague Dawley Derived) rats supplied by Charles River, Raleigh, NC, USA were housed in groups of 5 rats per cage, acclimatised after delivery for at least 7 days with bedding/nesting material regularly changed, fed on SDS diet R1 pelleted food given *ad lib,* and supplied with daily-changed pasteurised animal grade drinking water.

Device for dry powder administration: Disposable 3-way tap between dosing needle and syringe. A 3-way sterile tap (Vycon Ref 876.00) was weighed, the drug blend or inhalation grade lactose (vehicle control) was then added to the tap, the tap closed to prevent loss of drug, and the tap was re-weighed to determine the weight of drug in the tap. After dosing, the tap was weighed again to determine the weight of drug that had left the tap. The needle, a Sigma Z21934-7 syringe needle 19-gauge 152 mm (6 inches) long with luer hub, was cut by engineering to approximately 132 mm (5.2 inches), a blunt end was made to prevent them damaging the rat's trachea, and the needle weighed prior to and after drug delivery to confirm that no drug was retained in the needles after dosing.

Device for wet suspension administration: This is the similar to the above but a blunt dosing needle, whose forward end was slightly angled to the needle axis, was used, with a flexible plastic portex canula inserted into the needle.

Drugs and Materials: Lipopolysaccharide (LPS) (Serotype:0127:B8) (L3129 Lot 61K4075) was dissolved in phosphate-buffered saline (PBS). PDE4 inhibitors are used in size-reduced (e.g. micronised) form, for example according to the Micronisation Example given above. For dry powder administration of the drug, the Dry Powder Formulation Example given above, comprising drug and inhalation-grade lactose, can be used. The inhalation-grade lactose usually used (Lot E98L4675 Batch 845120) has 10% fines (10% of material under 15um particle size measured by Malvern particle size).

Wet suspensions of the drug can be prepared by adding the required volume of vehicle to the drug; the vehicle used being a mixture of saline/tween (0.2% tween 80). The wet suspension was sonicated for 10 minutes prior to use.

Preparation, and dosing with PDE 4 inhibitor: Rats were anaesthetised by placing the animals in a sealed Perspex chamber and exposing them to a gaseous mixture of isoflourane (4.5 %), nitrous oxide (3 litres.minute^{-1}) and oxygen (1 litre.minute^{-1}). Once anaesthetised, the animals were placed onto a stainless steel i.t. dosing support table. They were positioned on their back at approximately a 35° angle. A light was angled against the outside of the throat to highlight the trachea. The mouth was opened and the opening of the upper airway visualised. The procedure varies for wet suspension and dry powder administration of PDE4 inhibitors as follows:

Dosing with a Wet suspension: A portex cannula was introduced via a blunt metal dosing needle that had been carefully inserted into the rat trachea. The animals were intratracheally dosed with vehicle or PDE4 inhibitor via the dosing needle with a new internal canula used for each different drug group. The formulation was slowly (10 seconds) dosed into the trachea using a syringe attached to the dosing needle.

Dosing with a Dry Powder: The three-way tap device and needle were inserted into the rat trachea up to a pre-determined point established to be located approximately 1 cm above the primary bifurcation. Another operator holds the needle at the specified position whilst 2x 4ml of air is delivered through the three-way tap by depressing the syringes (ideally coinciding with the animal inspiring), aiming to expel the entire drug quantity from the tap. After dosing, the needle and tap are removed from the airway and the tap closed off to prevent any retained drug leaving the tap.

After dosing with either wet suspension or dry powder, the animals are then removed from the table and observed constantly until they have recovered from the effects of anaesthesia. The animals are returned to the holding cages and given free access to food and water; they are observed and any unusual behavioural changes noted.

Exposure to LPS: About 2 hours after i.t. dosing with vehicle control or the PDE4 inhibitor, the rats were placed into sealed Perspex containers and exposed to an aerosol of LPS (nebuliser concentration 150 μg.ml^{-1}) for 15 minutes. Aerosols of LPS were generated by a nebuliser (DeVilbiss, USA) and this was directed into the Perspex exposure chamber. Following the 15-minute LPS-exposure period, the animals were returned to the holding cages and allowed free access to both food and water.

[In an alternative embodiment, the rats can exposed to LPS less than 2 hours after i.t. dosing. In another alternative embodiment, the rats can exposed to LPS more than 2 hours (e.g. ca. 4 or ca. 6 hours) after i.t. dosing by vehicle or PDE4 inhibitor, to test whether or not the PDE4 inhibitor has a long duration of action (which is not essential).]

Bronchoalveolar lavage: 4 hours after LPS exposure the animals were killed by overdose of sodium pentobarbitone (i.p.). The trachea was cannulated with polypropylene tubing and the lungs lavaged (washed out) with 3 x 5 mls of heparinised (25 units.ml^{-1}) phosphate buffered saline (PBS).

Neutrophil cell counts: The Bronchoalveolar lavage (BAL) samples were centrifuged at 1300 rpm for 7 minutes. The supernatant was removed and the resulting cell pellet resuspended in 1 ml PBS. A cell slide of the resuspension fluid was prepared by placing 100μl of resuspended BAL fluid into cytospin holders and then spun at 5000

rpm for 5 minutes. The slides were allowed to air dry and then stained with Leishmans stain (20 minutes) to allow differential cell counting. The total cells were also counted from the resuspension. From these two counts, the total numbers of neutrophils in the BAL were determined. For a measure of PDE4-inhibitor-induced inhibition of neutrophilia, a comparison of the neutrophil count in rats treated with vehicle and rats treated with PDE4 inhibitors is conducted.

By varying the dose of the PDE4 inhibitor used in the dosing step (e.g. 0.2 or 0.1 mg of PDE4 inhibitor per kg of body weight, down to e.g. 0.01 mg/kg), a dose-response curve can be generated.

In Vivo Assay 4. Evaluation of Therapeutic Index of PDE 4 inhibitors in the conscious ferret

1.1 Materials

The following materials are used for these studies:

PDE4 inhibitors are prepared for oral (p.o.) administration by dissolving in a fixed volume (1 ml) of acetone and then adding cremophor to 20% of the final volume. Acetone is evaporated by directing a flow of nitrogen gas onto the solution. Once the acetone is removed, the solution is made up to final volume with distilled water.
LPS is dissolved in phosphate buffered saline.

1.2 Animals

Male ferrets (Mustela Pulorius Furo, weighing 1 – 2 kg) are transported and allowed to acclimatise for not less than 7 days. The diet comprises SDS diet C pelleted food given *ad lib* with Whiskers^{TM} cat food given 3 times per week. The animals are supplied with pasteurised animal grade drinking water changed daily.

1.3 Experimental Protocol(s)

1.3.1 Dosing with PDE4 inhibitors

PDE4 inhibitors are administered orally (p.o.), using a dose volume of 1ml/kg.
Ferrets are fasted overnight but allowed free access to water. The animals are orally dosed with vehicle or PDE 4 inhibitor using a 15cm dosing needle that is passed down the back of the throat into the oesophagus. After dosing, the animals are returned to holding cages fitted with perspex doors to allow observation, and given free access to water. The animals are constantly observed and any emetic episodes (retching and vomiting) or behavioural changes are recorded. The animals are allowed access to food 60 – 90 minutes after p.o. dosing.

1.3.2 Exposure to LPS

Thirty minutes after oral dosing with compound or vehicle control, the ferrets are placed into sealed perspex containers and exposed to an aerosol of LPS (30 μg/ml) for 10 minutes. Aerosols of LPS are generated by a nebuliser (DeVilbiss, USA) and this is directed into the perspex exposure chamber. Following a 10-minute exposure period, the animals are returned to the holding cages and allowed free access to water, and at a later stage, food. General observation of the animals continues for a period of at least 2.5 hours post oral dosing. All emetic episodes and behavioural changes are recorded.

1.3.3 Bronchoalveolar lavage and cell counts

Six hours after LPS exposure the animals are killed by overdose of sodium pentobarbitone administered intraperitoneally. The trachea is then cannulated with polypropylene tubing and the lungs lavaged twice with 20 ml heparinised (10 units/ml) phosphate buffered saline (PBS). The bronchoalveolar lavage (BAL) samples are centrifuged at 1300 rpm for 7 minutes. The supernatant is removed and the resulting cell pellet re-suspended in 1 ml PBS. A cell smear of re-suspended fluid is prepared and stained with Leishmans stain to allow differential cell counting. A total cell count is made using the remaining re-suspended sample. From this, the total number of neutrophils in the BAL sample is determined.

1.3.4 Pharmacodynamic readouts

The following parameters are recorded:

a) % inhibition of LPS-induced pulmonary neutrophilia to determine the dose of PDE4 inhibitor which gives 50% inhibition (D50).

b) Emetic episodes – the number of vomits and retches are counted to determine the dose of PDE4 inhibitor that gives a 20% incidence of emesis (D20).

c) A therapeutic index (TI), using this assay, is then calculated for each PDE4 inhibitor using the following equation:

$$\text{Therapeutic index (TI)} = \frac{\text{D20 incidence of emesis}}{\text{D50 inhibition of neutrophilia}}$$

It is noted that the Therapeutic index (TI) calculated using this in vivo Assay 4 is often significantly different to, and often lower than, that calculated using the rat oral inflammation and pica feeding Assays 1+2.

The calculation of TI using the PDE4 inhibitor roflumilast in this Assay 4 is:

D20 for emesis = 0.5mg/kg p.o., D50 for neutroplilia = 0.49mg/kg p.o., TI = 1.02

All publications, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference herein as though fully set forth.

EXAMPLES

The various aspects of the invention will now be described by reference to the following examples. These examples are merely illustrative and are not to be construed as a limitation of the scope of the present invention. In this section, "Intermediates" represent syntheses of intermediate compounds intended for use in the synthesis of the "Examples".

Abbreviations used herein:

DMSO	dimethyl sulfoxide
DCM	dichloromethane
EtOAc	ethyl acetate
Et_2O	diethyl ether
DMF	dimethyl formamide
MeOH	methanol
HPLC	high pressure liquid chromatography
SPE	solid phase extraction
NMR	nuclear magnetic resonance (in which: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet, H = no. of protons)
LCMS	liquid chromatography/mass spectroscopy
TLC	thin layer chromatography
BEMP	2-t-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphazine
EDC	1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
HATU	O-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
HBTU	O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
HOBT	hydroxybenzotriazole = 1-hydroxybenzotriazole
h	hours
DIPEA	diisopropylethyl amine ($^iPr_2NEt$)
T_{RET}	retention time
THF	Tetrahydrofuran
Lawesson's reagent	2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulphide
Room temperature	this is usually in the range of about 20 to about 25 °C.

Machine Methods used herein:

LCMS (liquid chromatography/mass spectroscopy)

Waters ZQ mass spectrometer operating in positive ion electrospray mode, mass range 100-1000 amu.
UV wavelength : 215-330nM
Column : 3.3cm x 4.6mm ID, 3µm ABZ+PLUS

Flow Rate : 3ml/min
Injection Volume : 5µl
Solvent A : 95% acetonitrile + 0.05% formic acid
Solvent B : 0.1% formic acid + 10mMolar ammonium acetate
Gradient : 0% A/0.7min, 0-100% A/3.5min, 100% A/1.1min, 100-0% A/0.2min

Mass directed autoprep HPLC
The prep column used was a Supelcosil ABZplus (10cm x 2.12cm)
(usually 10cm x 2.12cm x 5 µm).
UV wavelength : 200-320nM
Flow : 20ml/min
Injection Volume: 1ml; or more preferably 0.5 ml
Solvent A : 0.1% formic acid
Solvent B : 95% acetonitrile + 5% formic acid; or more usually 99.95% acetonitrile + 0.05% formic acid
Gradient : 100% A/1min, 100-80% A/9min, 80-1% A/3.5min, 1% A/1.4min, 1-100%A/0.1min

Intermediates and Examples

All reagents not detailed in the text below are commercially available from established suppliers such as Sigma-Aldrich. The addresses of the suppliers for some of the starting materials mentioned in the Intermediates and Examples below or the Assays above are as follows:

- ABCR GmbH & CO. KG, P.O. Box 21 01 35, 76151 Karlsruhe, Germany
- Aceto Color Intermediates (catalogue name), Aceto Corporation, One Hollow Lane, Lake Success, NY, 11042-1215, USA
- Acros Organics, A Division of Fisher Scientific Company, 500 American Road, Morris Plains, NJ 07950, USA
- Apin Chemicals Ltd., 82 C Milton Park, Abingdon, Oxon OX14 4RY, United Kingdom
- Apollo Scientific Ltd., Unit 1A, Bingswood Industrial Estate, Whaley Bridge, Derbyshire SK23 7LY, United Kingdom
- Aldrich (catalogue name), Sigma-Aldrich Company Ltd., Dorset, United Kingdom, telephone: +44 1202 733114; Fax: +44 1202 715460; ukcustsv@eurnotes.sial.com; or
- Aldrich (catalogue name), Sigma-Aldrich Corp., P.O. Box 14508, St. Louis, MO 63178-9916, USA; telephone: 314-771-5765; fax: 314-771-5757; custserv@sial.com; or
- Aldrich (catalogue name), Sigma-Aldrich Chemie Gmbh, Munich, Germany; telephone: +49 89 6513 0; Fax: +49 89 6513 1169; deorders@eurnotes.sial.com.
- Alfa Aesar, A Johnson Matthey Company, 30 Bond Street, Ward Hill, MA 01835-8099, USA
- Amersham Biosciences UK Ltd, Pollards Wood, Chalfont St Giles, Buckinghamshire HP8 4SP, United Kingdom
- Array Biopharma Inc., 1885 33rd Street, Boulder, CO 80301, USA

- AstaTech, Inc., 8301 Torresdale Ave., 19C, Philadelphia, PA 19136, USA
- Austin Chemical Company, Inc., 1565 Barclay Blvd., Buffalo Grove, IL 60089, USA
- Avocado Research, Shore Road, Port of Heysham Industrial Park, Heysham Lancashire LA3 2XY, United Kingdom
- Bayer AG, Business Group Basic and Fine Chemicals, D-51368 Leverkusen, Germany
- Berk Univar plc, Berk House, P.O.Box 56, Basing View, Basingstoke, Hants RG21 2E6, United Kingdom
- Butt Park Ltd., Braysdown Works, Peasedown St. John, Bath BA2 8LL, United Kingdom
- Chemical Building Blocks (catalogue name), Ambinter, 46 quai Louis Bleriot, Paris, F-75016, France
- ChemBridge Europe, 4 Clark's Hill Rise, Hampton Wood, Evesham, Worcestershire WR11 6FW, United Kingdom
- ChemService Inc., P.O.Box 3108, West Chester, PA 19381, USA
- Combi-Blocks Inc., 7949 Silverton Avenue, Suite 915, San Diego, CA 92126, USA
- Dynamit Nobel GmbH, Germany; also available from: Saville Whittle Ltd (UK agents of Dynamit Nobel), Vickers Street, Manchester M40 8EF, United Kingdom
- E. Merck, Germany; or E. Merck (Merck Ltd), Hunter Boulevard, Magna Park, Lutterworth, Leicestershire LE17 4XN, United Kingdom
- Esprit Chemical Company, Esprit Plaza, 7680 Matoaka Road, Sarasota, FL 34243, USA
- Exploratory Library (catalogue name), Ambinter, 46 quai Louis Bleriot, Paris, F-75016, France
- Fluka Chemie AG, Industriestrasse 25, P.O. Box 260, CH-9471 Buchs, Switzerland
- Fluorochem Ltd., Wesley Street, Old Glossop, Derbyshire SK13 7RY, United Kingdom
- ICN Biomedicals, Inc., 3300 Hyland Avenue, Costa Mesa, CA 92626, USA
- Interchim Intermediates (catalogue name), Interchim, 213 Avenue Kennedy, BP 1140, Montlucon, Cedex, 03103, France
- Key Organics Ltd., 3, Highfield Indusrial Estate, Camelford, Cornwall PL32 9QZ, United Kingdom
- Lancaster Synthesis Ltd., Newgate, White Lund, Morecambe, Lancashire LA3 3DY, United Kingdom
- Manchester Organics Ltd., Unit 2, Ashville Industrial Estate, Sutton Weaver, Runcorn, Cheshire WA7 3PF, United Kingdom
- Matrix Scientific, P.O. Box 25067, Columbia, SC 29224-5067, USA
- Maybridge Chemical Company Ltd., Trevillett, Tintagel, Cornwall PL34 0HW, United Kingdom
- Maybridge Reactive Intermediates (catalogue name), Maybridge Chemical Company Ltd., Trevillett, Tintagel, Cornwall PL34 0HW, United Kingdom
- MicroChemistry Building Blocks (catalogue name), MicroChemistry-RadaPharma, Shosse Entusiastov 56, Moscow, 111123, Russia
- Miteni S.p.A., Via Mecenate 90, Milano, 20138, Italy
- Molecular Devices Corporation, Sunnydale, CA, USA
- N.D. Zelinsky Institute, Organic Chemistry, Leninsky prospect 47, 117913 Moscow B-334, Russia
- Optimer Building Block (catalogue name), Array BioPharma, 3200 Walnut Street, Boulder, CO 80301, USA

- Peakdale Molecular Ltd., Peakdale Science Park, Sheffield Road, Chapel-en-le-Frith, High Peak SK23 0PG, United Kingdom
- Pfaltz & Bauer, Inc., 172 East Aurora Street, Waterbury, CT 06708, USA
- Rare Chemicals (catalogue name), Rare Chemicals GmbH, Schulstrasse 6, 24214 Gettorf, Germany
- SALOR (catalogue name) (Sigma Aldrich Library of Rare Chemicals), Aldrich Chemical Company Inc, 1001 West Saint Paul Avenue, Milwaukee, WI 53233, USA
- Sigma (catalogue name), Sigma-Aldrich Corp., P.O. Box 14508, St. Louis, MO 63178-9916, USA; see "Aldrich" above for other non-US addresses and other contact details
- SIGMA-RBI, One Strathmore Road, Natick, MA 01760-1312, USA
- Synchem OHG Heinrich-Plett-Strasse 40, Kassel, D-34132, Germany
- Syngene International Pvt Ltd, Hebbagodi, Hosur Road, Bangalore, India.
- TCI America, 9211 North Harborgate Street, Portland, OR 97203, USA
- TimTec Building Blocks A, TimTec, Inc., P O Box 8941, Newark, DE 19714-8941, USA
- Trans World Chemicals, Inc., 14674 Southlawn Lane, Rockville, MD 20850, USA
- Ubichem PLC, Mayflower Close, Chandlers Ford Industrial Estate, Eastleigh, Hampshire SO53 4AR, United Kingdom
- Ultrafine (UFC Ltd.), Synergy House, Guildhall Close, Manchester Science Park, Manchester M15 6SY, United Kingdom

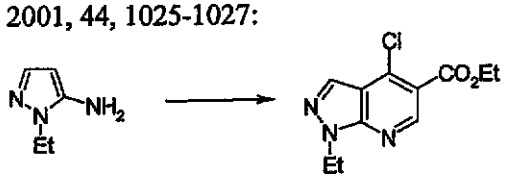
Table of Intermediates

Inter-mediate Number	Name
1	Ethyl 4-chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
2	Ethyl 4-ethoxy-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
3	Ethyl 1-methyl-4-ethoxy-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
4	Ethyl 1-benzyl-4-ethoxy-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
5	Ethyl 4-chloro-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
6	1-Acetyl-4-aminopiperidine
7	1-Methyl-4-aminopiperidine
8	4-Aminotetrahydropyran
8A	Tetrahydro-2H-pyran-4-amine hydrochloride = 4-Aminotetrahydropyran hydrochloride
9	(R)-(+)-3-Amino tetrahydrofuran 4-toluene sulphonate
10	(S)-(-)-3-Amino tetrahydrofuran 4-toluene sulphonate
11	Tetrahydro-2H-thiopyran-4-amine
12	Tetrahydro-3-thiopheneamine
13	Tetrahydro-3-thiopheneamine 1,1-dioxide hydrochloride
14	Tetrahydro-2H-thiopyran-4-amine-1,1-dioxide hydrochloride

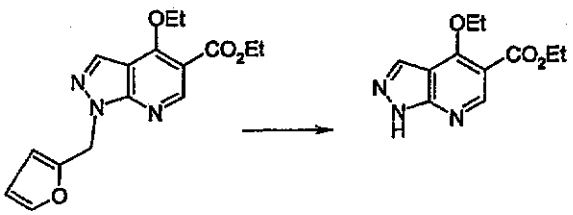
15	4-Chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
16	4-Chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carbonyl chloride
17	N-Benzyl-4-chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
18	4-Chloro-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
19	4-Chloro-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
20	4-Chloro-N-cyclopentyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
21	4-Chloro-1-ethyl-5-(pyrrolidin-1-ylcarbonyl)-1H-pyrazolo[3,4-b]pyridine
22	4-Chloro-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
23	4-Chloro-1-ethyl-N-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
24	4-Chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
25	Ethyl 4-chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
26	4-Chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
27	4-Chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carbonyl chloride
28	N-Benzyl-4-chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
29	4-Chloro-1-methyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
30	4-Chloro-1-methyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
31	4-Chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
32	Ethyl 1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
33	1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
34	Ethyl 1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
35	Ethyl 1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
36	Ethyl 1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
37	Ethyl 1-ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
38	Ethyl 4-(cyclopropylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
39	Ethyl 4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
40	Ethyl 4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
41	1-Ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
42	Ethyl 1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
43	1-Ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid

44	1-Ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
45	4-(Cyclopropylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
46	4-[(1,1-Dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
47	4-[(1,1-Dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
48	Ethyl 4-(cyclohexylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
49	4-(Cyclohexylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
50	1-n-Propyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid
51	Ethyl 4-chloro-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
52	4-(Cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid
53	1-Ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid
54	4-Aminocyclohexanone hydrochloride
76	1-Ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid

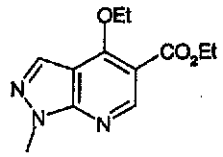
Intermediate 1: Ethyl 4-chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
Prepared from commercially available 5-amino-1-ethyl pyrazole as described by G. Yu et. al. in *J. Med Chem.*, 2001, 44, 1025-1027:



Intermediate 2: Ethyl 4-ethoxy-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
Can be prepared by oxidative cleavage (SeO_2) of 1-furanylmethyl derivative, as described by T. M. Bare *et. al.* In *J. Med. Chem.*, 1989, 32, 2561-2573, (further referenced to Zuleski, F. R., Kirkland, K. R., Melgar, M. D.; Malbica, *J. Drug. Metab. Dispos.*, 1985, 13, 139)

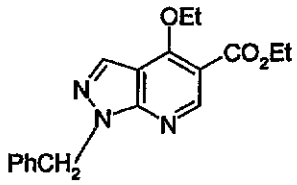


Intermediate 3: Ethyl 1-methyl-4-ethoxy-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



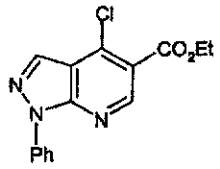
A mixture of Intermediate 2 (0.47g) and anhydrous potassium carbonate (0.83g) (previously dried by heating at 100°C) in anhydrous dimethylformamide (DMF) (4ml) was treated with iodomethane (0.26ml) and stirred vigorously for 3h. The mixture was then filtered and the filtrate concentrated in vacuo to afford a residual oil, which was partitioned between dichloromethane (DCM) (25ml) and water (25ml). The layers were separated and the aqueous phase was extracted with further DCM (2x25ml). The combined organic extracts were dried over anhydrous sodium sulphate and evaporated to an orange solid which was applied to an SPE cartridge (silica, 20g). The cartridge was eluted sequentially with EtOAc : petrol (1:4, 1:2 and 1:1), then chloroform : methanol (49:1, 19:1 and 9:1). Fractions containing desired material were combined and concentrated in vacuo to afford Intermediate 3 (0.165g). LCMS showed MH^+= 250; T_{RET} = 2.59 min.

Intermediate 4: Ethyl 1-benzyl-4-ethoxy-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



A mixture of Intermediate 2 (0.47g) and anhydrous potassium carbonate (0.83g) (previously dried by heating at 100°C) in anhydrous DMF (4ml) was treated with benzyl bromide (0.72g) then stirred vigorously and heated at 55°C for 4.5h. The mixture was allowed to cool, then filtered and the filtrate concentrated in vacuo to afford a residual oil, which was partitioned between DCM (25ml) and water (25ml). The layers were separated and the aqueous phase was extracted with further DCM (2x25ml). The combined organic extracts were dried over anhydrous sodium sulphate and evaporated to a yellow oily solid which was dissolved in DCM and applied to an SPE cartridge (silica, 20g). The cartridge was eluted with a gradient of EtOAc : petrol (1:4, 1:2 and 1:1) then chloroform : methanol (49:1, 19:1 and 9:1). Fractions containing desired material were combined and concentrated in vacuo to afford Intermediate 4 (0.33g). LCMS showed MH^+= 326; T_{RET} = 3.24 min.

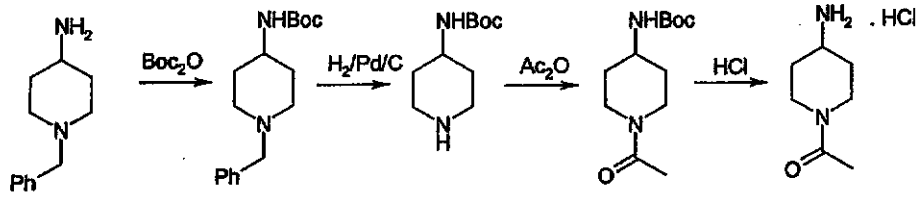
Intermediate 5: Ethyl 4-chloro-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



A mixture of 5-amino-1-phenyl pyrazole (2.0g) and diethylethoxymethylene malonate (2.54ml) was heated under Dean Stark conditions at 120°C for 16h. The solution was cooled, phosphorus oxychloride (16ml) was then added and the mixture heated under reflux for a further 20h. Excess phosphorus oxychloride was removed in vacuo and the residue partitioned between diethyl ether and water, proceeding with extreme caution on addition of water. The ethereal layer was washed with further water, then dried over magnesium sulphate and concentrated in vacuo to afford ethyl 4-chloro-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate (2.09g). LCMS showed MH^+= 302; T_{RET} = 3.80 min.

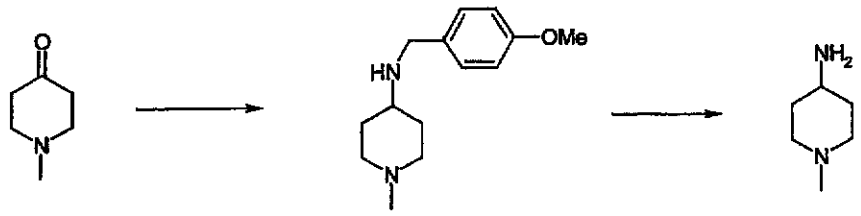
Intermediate 6: 1-Acetyl-4-aminopiperidine

Prepared from commercially available N1-benzyl-4-aminopiperidine as described by Yamada *et. al.* In WO 00/42011:



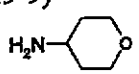
Intermediate 7: 1-Methyl-4-aminopiperidine

Prepared from commercially available N-methyl-4-piperidone as described by C. M. Andersson *et. al.* in WO01/66521:

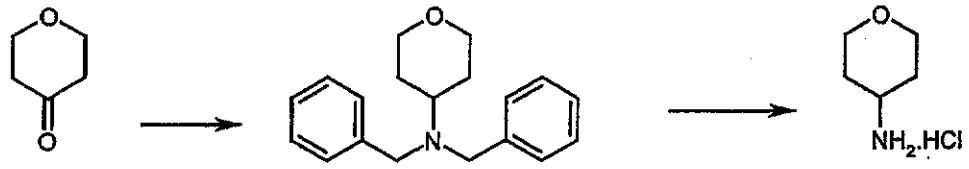


Intermediate 8: 4-Aminotetrahydropyran

Commercially available from Combi-Blocks Inc., 7949 Silverton Avenue, Suite 915, San Diego, CA 92126, USA (CAS 38041-19-9)



Intermediate 8A: Tetrahydro-2H-pyran-4-amine hydrochloride = 4-Aminotetrahydropyran hydrochloride



Step1: N,N-dibenzyltetrahydro-2H-pyran-4-amine

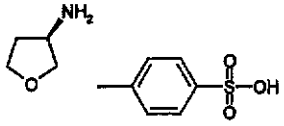
Dibenzylamine (34.5g) and acetic acid (6.7ml) were added to a stirred solution of tetrahydro-4H-pyran-4-one (16.4g, commercially available from e.g. Aldrich) in dichloromethane (260ml) at 0 °C to 5 °C. After 2.5h at 0 °C to 5 °C, sodium triacetoxyborohydride (38.9g) was added portionwise, and the mixture was allowed to warm to room temperature. After stirring at room temperature overnight, the reaction mixture was washed successively with 2M-sodium hydroxide (200ml and 50ml), water (2 x 50ml) and brine (50ml), then dried and evaporated to give a yellow oil (45g). This oil was stirred with methanol (50ml) at 4 °C for 30min to give the product as a white solid (21.5g). LCMS showed $MH^+ = 282$; $T_{RET} = 1.98$ min.

Step 2: Tetrahydro-2H-pyran-4-amine hydrochloride

N,N-dibenzyltetrahydro-2*H*-pyran-4-amine (20.5g) was dissolved in ethanol (210ml) and hydrogenated over 10% palladium on carbon catalyst (4g) at 100 psi for 72h at room temperature. The reaction mixture was filtered and the filtrate was adjusted to pH 1 with 2M-hydrogen chloride in diethyl ether. Evaporation of solvents gave a solid which was triturated with diethyl ether to give the product as a white solid (9.23g). ^{1}H NMR (400MHz in d_6-DMSO, 27°C, δppm) 8.24 (br. s, 3H), 3.86 (dd, 12, 4Hz, 2H), 3.31 (dt, 2, 12Hz, 2H), 3.20 (m, 1H), 1.84 (m, 2H), 1.55 (dq, 4, 12Hz, 2H).

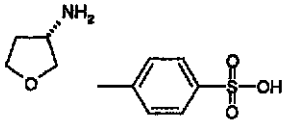
Intermediate 9: (R)-(+)-3-Amino tetrahydrofuran 4-toluenesulphonate

Commercially available from Fluka Chemie AG, Germany (CAS 111769-27-8)



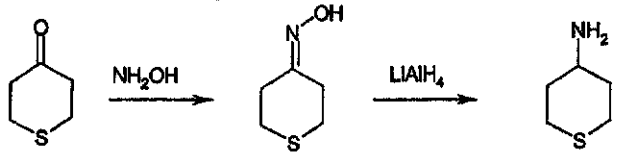
Intermediate 10: (S)-(-)-3-Amino tetrahydrofuran 4-toluenesulphonate

Commercially available from E. Merck, Germany; or from E. Merck (Merck Ltd), Hunter Boulevard, Magna Park, Lutterworth, Leicestershire LE17 4XN, United Kingdom (CAS 104530-80-5)



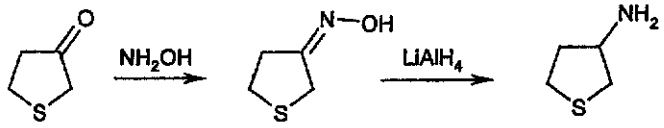
Intermediate 11: Tetrahydro-2H-thiopyran-4-amine

Prepared from commercially available tetrahydrothiopyran-4-one as described by Subramanian et. al., *J. Org. Chem.*, 1981, 46, 4376-4383. Subsequent preparation of the hydrochloride salt can be achieved by conventional means.



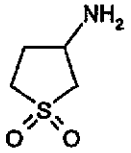
Intermediate 12: Tetrahydro-3-thiopheneamine

Prepared in an analogous manner to Intermediate 11 from commercially available tetrahydrothiophene-4-one. The oxime formation is described by Grigg et.al., *Tetrahedron*, 1991, 47, 4477-4494 and the oxime reduction by Unterhalt et. al., *Arch. Pharm.*, 1990, 317-318.



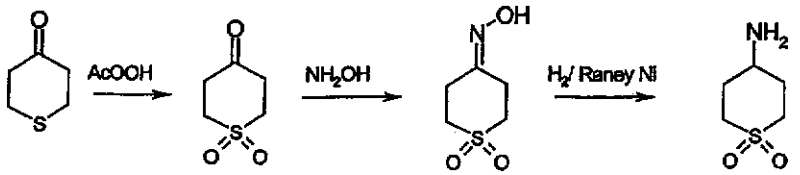
Intermediate 13: Tetrahydro-3-thiopheneamine 1,1-dioxide hydrochloride

Commercially available from Sigma Aldrich Library of Rare Chemicals (SALOR) (CAS-6338-70-1). Preparation of the hydrochloride salt of the amine can be achieved by conventional means.

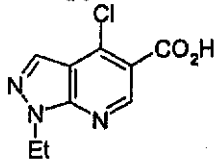


Intermediate 14: Tetrahydro-2H-thiopyran-4-amine-1,1-dioxide hydrochloride

Prepared in an analogous manner to Intermediate 11 from commercially available tetrahydrothiophene-4-one. Oxidation to 1,1-dioxo-tetrahydro-1λ^6-thiopyran-4-one is described by Rule et. al., in *J. Org. Chem.*, 1995, 60, 1665-1673. Oxime formation is described by Truce et.al., in *J. Org. Chem.*, 1957, 617, 620 and oxime reduction by Barkenbus et. al., *J. Am. Chem. Soc.*, 1955, 77, 3866. Subsequent preparation of the hydrochloride salt of the amine can be achieved by conventional means.

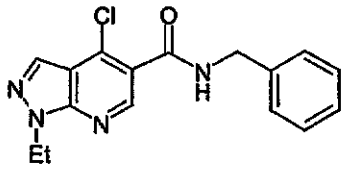


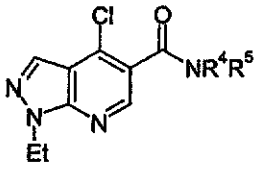
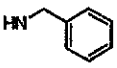
Intermediate 15: 4-Chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid



A solution of Intermediate 1 (3.5g) in dioxane (28ml) was treated with potassium hydroxide (6.3g) as a solution in water (20ml). The mixture was stirred for 2h, then concentrated in vacuo, acidified to pH 3 with 2M aqueous hydrochloric acid and extracted with ethyl acetate. The layers were separated, the organic layer dried over sodium sulphate, then concentrated in vacuo to afford Intermediate 15 as a white solid (2.4g). LCMS showed $MH^+ = 226$; $T_{RET} = 2.62$min.

Intermediate 17: N-Benzyl-4-chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

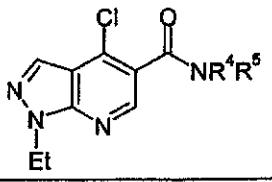


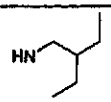
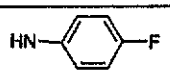
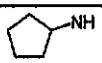
That is, Intermediate 17 is:  wherein NR^4R^5 = 

Intermediate 15 (3.5g) was dried over phosphorus pentoxide for 1h, then treated with thionyl chloride (47g). The mixture was stirred and heated at 75°C for 1.3h. Excess thionyl chloride was removed in vacuo and the residual oil azeotroped with dichloromethane (DCM) to afford **Intermediate 16**, presumed to be the acid chloride derivative of Intermediate 15, as a white solid (3.3g).

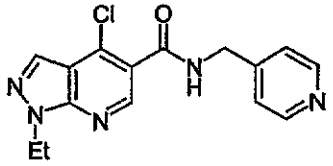
Intermediate 16 (0.473g) was dissolved in tetrahydrofuran (THF) (4ml) and treated with N,N-diisopropylethylamine (DIPEA) (0.509ml), then with benzylamine (0.209g) and the mixture stirred under nitrogen for 0.5h. The mixture was concentrated in vacuo, then partitioned between dichloromethane and water. The layers were separated and the organics concentrated in vacuo to afford **Intermediate 17** (0.574g). LCMS showed $MH^+ = 315$; $T_{RET} = 2.90$min.

Similarly prepared were the following:



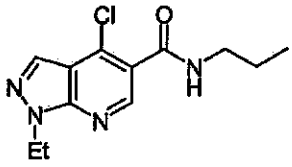
	NR^4R^5	Amine reagent	MH^+ ion	T_{RET} (min)
Intermediate 18		2-Ethyl-N-butylamine	309	3.07
Intermediate 19		4-Fluoroaniline	319	3.08
Intermediate 20		Cyclopentylamine	293	2.76
Intermediate 21		Pyrrolidine	279	2.46

Intermediate 22: 4-Chloro-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



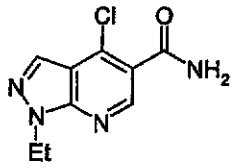
Acid chloride Intermediate 16 was synthesised from Intermediate 15 using the method shown above for Intermediate 17. Intermediate 16 (0.473g) was dissolved in THF (4ml) and treated with diisopropylethylamine (DIPEA) (0.509ml), then with 4-(aminomethyl)pyridine (0.211g) and the mixture stirred under nitrogen for 0.5h. The mixture was concentrated in vacuo, then partitioned between DCM and water. The layers were separated and the organics concentrated in vacuo, then applied to an SPE cartridge (silica, 10g) which was eluted with a gradient of cyclohexane : EtOAc (2:1 increasing stepwise up to 0:1), followed by MeOH : EtOAc (5:95, then 10:90). Fractions containing desired material were combined and concentrated in vacuo to afford Intermediate 22 (0.086g). LCMS showed $MH^+ = 316$; $T_{RET} = 1.84$min.

Intermediate 23: 4-Chloro-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



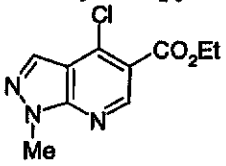
Acid chloride Intermediate 16 was synthesised from Intermediate 15 using the method shown above for Intermediate 17. Intermediate 16 (0.473g) was dissolved in THF (4ml) and treated with DIPEA (0.509ml), then with n-propyl amine (0.115g) and the mixture stirred under nitrogen for 0.5h. A further portion of n-propyl amine (0.023g) was then added and stirring continued for 18h. The mixture was concentrated in vacuo, then partitioned between DCM and water. The layers were separated and the organics concentrated in vacuo to afford Intermediate 23 (0.405g). LCMS showed $MH^+ = 267$; $T_{RET} = 2.54$min.

Intermediate 24: 4-Chloro-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



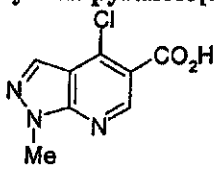
Acid chloride Intermediate 16 was synthesised from Intermediate 15 using the method shown above for Intermediate 17. Intermediate 16 (0.30g) was dissolved in THF (3ml) and treated with a 0.5M solution of ammonia in dioxane (4.92ml). The mixture was stirred under nitrogen for 18h. A further portion of 0.5M ammonia in dioxane (4.92ml) was added and stirring continued for 72h. The mixture was concentrated in vacuo and the residue partitioned between DCM and 2M sodium hydroxide solution. The layers were separated and the organics concentrated to afford Intermediate 24 (0.278g). LCMS showed $MH^+ = 225$; $T_{RET} = 2.10$min.

Intermediate 25: Ethyl 4-chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



A mixture of 5-amino-1-methyl pyrazole (4.0g) and diethylethoxymethylene malonate (9.16ml) was heated at 150°C under Dean Stark conditions for 5h. Phosphorous oxychloride (55ml) was carefully added to the mixture and the resulting solution heated at 130°C under reflux for 18h. The mixture was concentrated in vacuo, then the residual oil cooled in an ice bath and treated carefully with water (100ml)(caution: exotherm). The resulting mixture was extracted with DCM (3x100ml) and the combined organic extracts were dried over anhydrous sodium sulphate and concentrated in vacuo. The residual solid was purified by Biotage chromatography (silica, 90g), eluting with Et_20 : petrol (1:3). Fractions containing desired material were combined and concentrated in vacuo to afford Intermediate 25 (4.82g). LCMS showed $MH^+ = 240$; $T_{RET} = 2.98$min

Intermediate 26: 4-Chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid



A solution of Intermediate 25 (4.0g) in dioxane (30ml) was treated with potassium hydroxide (7.54g) as a solution in water (20ml). The mixture was stirred for 16h, then diluted with water (150ml) and acidified to pH 3 with 5M aqueous hydrochloric acid. The mixture was stirred in an ice bath for 15min, then collected by filtration, washed with ice-cold water and dried in vacuo over phosphorous pentoxide to afford Intermediate 26 as a white solid (2.83g). LCMS showed $MH^+ = 212$; $T_{RET} = 2.26$min.

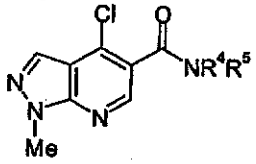
Intermediate 28: N-Benzyl-4-chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

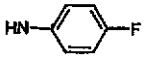


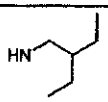
Intermediate 26 (2.5g) (previously dried over phosphorus pentoxide) was treated with thionyl chloride (25ml) and the mixture heated under reflux for 1h. Excess thionyl chloride was removed in vacuo to afford **Intermediate 27**, presumed to be the acid chloride derivative of Intermediate 26, as a white solid (2.7g).

Intermediate 27 (0.68g) was dissolved in THF (10ml) and treated with DIPEA (0.77ml), then with benzyl amine (0.339g) and the mixture stirred under nitrogen for 3h. The mixture was concentrated in vacuo, then partitioned between DCM (20ml) and water (10ml). The layers were separated and the organics concentrated in vacuo to afford **Intermediate 28** (0.90g). LCMS showed $MH^+ = 301$; $T_{RET} = 2.72$min.

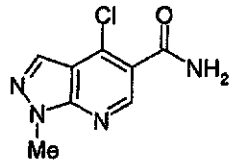
Similarly prepared were the following:



	NR^4R^5	Amine reagent	MH^+ ion	T_{RET} (min)
Intermediate 29		4-Fluoroaniline	305	2.91

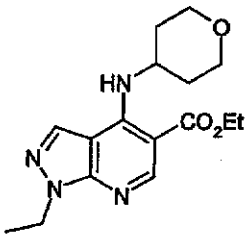
Intermediate 30		2-Ethyl-N-butylamine	295	2.97

Intermediate 31: 4-Chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



Acid chloride Intermediate 27 was synthesised from Intermediate 26 using the method shown above for Intermediate 28. Intermediate 27 (0.68g) was then treated with a 0.5M solution of ammonia in dioxane (17.7ml). Diisopropylethylamine (0.51ml) was then added and the mixture stirred for 21h. The mixture was then partitioned between DCM (100ml) and water (30ml). An insoluble solid was removed by filtration, washed with water (20ml) and dried in vacuo over phosphorous pentoxide to afford Intermediate 31 (0.544g). LCMS showed $MH^+ = 211$; $T_{RET} = 1.84$min.

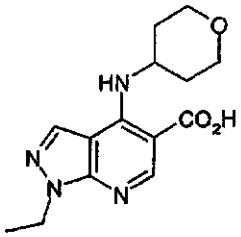
Intermediate 32 (= Example 3): Ethyl 1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



Intermediate 1 (0.20g) and triethylamine (0.55ml) were suspended in ethanol (8ml) and 4-aminotetrahydropyran (0.088g) was added. The mixture was stirred under nitrogen, heated at 80°C for 16h, then concentrated in vacuo. The residue was partitioned between DCM and water. The layers were separated and the organic layer was loaded directly onto an SPE cartridge (silica, 5g) which was eluted sequentially with; (i) DCM, (ii) DCM : Et_2O (2:1), (iii) DCM : Et_2O (1:1), (iv) Et_2O and (v) EtOAc. Fractions containing desired material were combined and concentrated in vacuo to afford Intermediate 32 (0.21g). LCMS showed $MH^+ = 319$; $T_{RET} = 2.93$min.

In an alternative embodiment, Intermediate 32 (= Example 3) can be made as described below under "Example 3", in particular according to "Example 3, Method B" below.

Intermediate 33: 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid

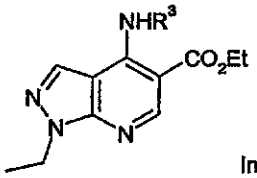


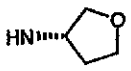
A solution of Intermediate 32 (Example 3) (0.21g) in ethanol : water (95:5, 10ml) was treated with sodium hydroxide (0.12g). The mixture was heated at 50°C for 8h, then concentrated in vacuo, dissolved in water and acidified to pH 4 with acetic acid. The resultant white solid was removed by filtration and dried under vacuum to afford Intermediate 33 as an off-white solid (0.156g). LCMS showed MH^+ = 291; T_{RET} = 2.11min.

An alternative preparation of Intermediate 33 is as follows:

A solution of Intermediate 32 (Example 3) (37.8g) in ethanol : water (4:1, 375ml) was treated with sodium hydroxide (18.9g). The mixture was heated at 50 °C for 5 hours, then concentrated in vacuo, dissolved in water and acidified to pH 2 with aqueous hydrochloric acid (2M). The resultant white solid was removed by filtration and dried under vacuum to afford Intermediate 33 as an off-white solid (29.65g). LCMS showed MH^+ = 291; T_{RET} = 2.17 min.

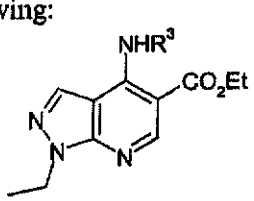
Intermediate 34 (= Example 8): Ethyl 1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

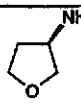
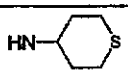
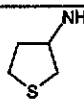
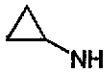


Intermediate 34 NHR^3 = 

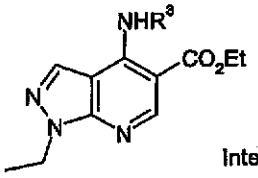
Intermediate 1 (0.05g) and (S)-(-)-3-aminotetrahydrofuran 4-toluenesulphonate (0.052g) were suspended in ethanol (1ml) and triethylamine (0.14ml) was added. The mixture was stirred under nitrogen and heated at 80°C for 24h. After cooling to room temperature, ethanol was removed by evaporation under a stream of nitrogen and the residue partitioned between DCM (2ml) and water (1.5ml). The layers were separated and the organic layer concentrated to dryness. Purification was carried out using an SPE cartridge (silica, 5g), eluting with a gradient of EtOAc : cyclohexane; (1:16 then, 1:8, 1:4, 1:2, 1:1 and 1:0). Fractions containing desired material were combined and concentrated in vacuo to afford Intermediate 34 (= Example 8) (0.052g). LCMS showed MH^+ = 305; T_{RET} = 2.70min.

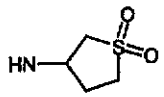
Similarly prepared were the following:



	NHR^3	Amine Reagent	MH^+ ion	T_{RET}(min)
Intermediate 35 (= Example 9)		(R)-(+)-3-Aminotetrahydrofuran 4-toluenesulphonate	305	2.73
Intermediate 36 (= Example 10)		Intermediate 11	335	3.21
Intermediate 37 (= Example 11)		Intermediate 12	321	3.10
Intermediate 38 (= Example 12)		Cyclopropylamine	275	2.98

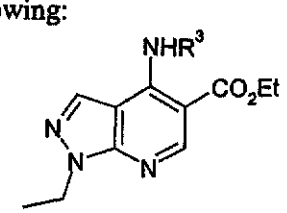
Intermediate 39 (= Example 13): Ethyl 4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

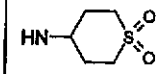


Intermediate 39 NHR^3 = 

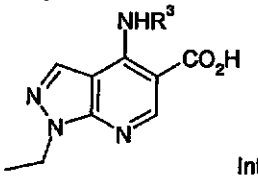
Intermediate 1 (0.05g) and Intermediate 13 (0.027g) were suspended in ethanol (1ml) and triethylamine (0.14ml) was added. The mixture was stirred under nitrogen and heated at 80°C for 24h. After cooling to room temperature, ethanol was removed by evaporation under a stream of nitrogen and the residue partitioned between DCM (2ml) and water (1.5ml). The layers were separated and the organic layer concentrated to dryness. Purification was carried out using an SPE cartridge (silica, 5g), eluting with a gradient of EtOAc : cyclohexane; (1:8 then 1:4, 1:2, 1:1 and 1:0). Fractions containing desired material were combined and concentrated in vacuo to afford Intermediate 39 (= Example 13) (0.045g) as a mixture of enantiomers. LCMS showed $MH^+ = 353$; $T_{RET} = 2.60$min.

Similarly prepared was the following:



	NHR^3	Amine Reagent	MH$^+$ ion	T_{RET}(min)
Intermediate 40 (= Example 14)		Intermediate 14	367	2.64

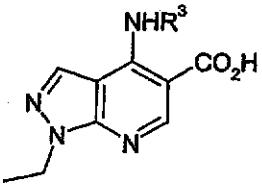
Intermediate 41: 1-Ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid



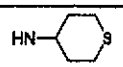
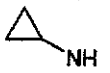
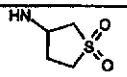
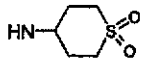
Intermediate 41 NHR^3 = 

A solution of Intermediate 34 (0.037g) in ethanol : water (95:5, 3ml) was treated with sodium hydroxide (0.019g). The mixture was heated at 50°C for 16h, then concentrated in vacuo. The residue was dissolved in water (1.5ml) and acidified to pH 4 with acetic acid. The resultant white solid precipitate was removed by filtration and dried under vacuum. The filtrate was extracted with ethyl acetate and the organic layer collected and concentrated in vacuo to afford a further portion of white solid. The two solids were combined to afford Intermediate 41 (0.033g). LCMS showed MH$^+$ = 277; T_{RET} = 2.05 min.

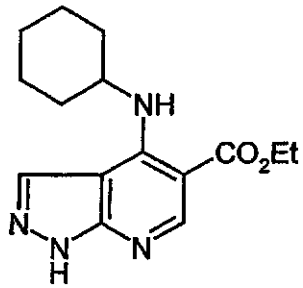
Similarly prepared were the following:



	NHR^3	Starting material	MH$^+$ ion	T_{RET}(min)
Intermediate 42		Intermediate 35	277	2.05

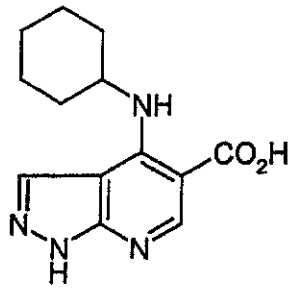
Intermediate 43		Intermediate 36	307	2.40
Intermediate 44		Intermediate 37	293	2.59
Intermediate 45		Intermediate 38	247	2.24
Intermediate 46		Intermediate 39	325	2.05
Intermediate 47		Intermediate 40	339	2.05

<u>Intermediate 48</u>: Ethyl 4-(cyclohexylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



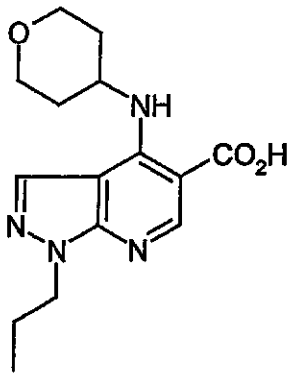
Intermediate 2 (0.69g) was suspended in cyclohexylamine (1.01ml), and the mixture was heated at 90 °C for 3h. The residual mixture was allowed to cool to room temperature and partitioned between chloroform (25ml) and water (25ml). The phases were separated and the organic phase was evaporated to dryness. The residue was triturated with Et_2O (25ml) and the insoluble solid was collected and dried to afford Intermediate 48 as a beige solid (0.58g). LCMS showed MH^+=289; T_{RET} = 2.91min.

Intermediate 49: **4-(Cyclohexylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid**



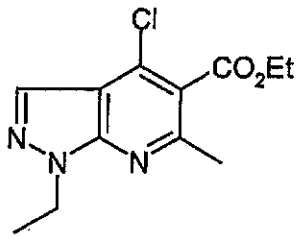
2M-Sodium hydroxide solution (0.5ml) was added to a stirred suspension of Intermediate 48 (0.2g) in dioxan (4ml) and water (0.5ml). After stirring overnight at room temperature, the reaction mixture was heated at 40 °C for 8h. A further quantity of 2M-sodium hydroxide solution (1.5ml) was added, and the reaction mixture was heated at 40 °C for 48h. The reaction solution was concentrated, diluted with water (10ml) and acidified with glacial acetic acid. The resulting precipitate was collected by filtration, washed with water and dried to give Intermediate 49 (0.18g). LCMS showed $MH^+ = 261$; $T_{RET} =$ 2.09min.

Intermediate 50: **1-n-Propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid**



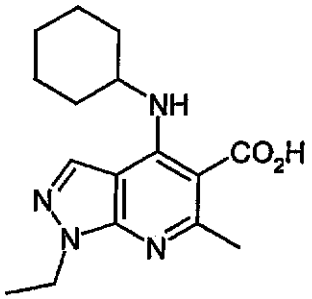
2M-Sodium hydroxide solution (0.7ml) was added to a stirred suspension of Example 185 (0.23g, described hereinafter) in ethanol (5ml) and water (1.5ml). After stirring overnight at room temperature, a further quantity of 2M-sodium hydroxide solution (0.7ml) was added, and the reaction mixture was heated at 43 °C for 2.5h. The reaction solution was concentrated, diluted with water (5ml) and acidified with 2M-hydrochloric acid. The resulting precipitate was collected by filtration, washed with water and dried to give Intermediate 50 as a white solid (0.14g). LCMS showed $MH^+ = 305$; $T_{RET} =$ 2.42min.

Intermediate 51: **Ethyl 4-chloro-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate**



A mixture of 5-amino-1-ethylpyrazole (1.614g, 14.5mmol) and diethyl 2-(1-ethoxyethylidene)malonate (3.68g, 16.0mmol, as described by P.P.T. Sah, *J. Amer. Chem. Soc.*, 1931, 53, 1836) was heated at 150 °C under Dean Stark conditions for 5 hours. Phosphorous oxychloride (25ml) was carefully added to the mixture and the resulting solution was heated at 130 °C under reflux for 18 hours. The mixture was concentrated *in vacuo*, then the residual oil was carefully added, with cooling, to water (100ml). The resulting mixture was extracted with DCM (3x100ml) and the combined organic extracts were dried over anhydrous sodium sulphate and concentrated *in vacuo*. The residual oil was purified by Biotage chromatography (silica, 90g) eluting with ethyl acetate-petrol (1:19). Fractions containing the desired product were combined and concentrated in vacuo to afford Intermediate 51 (1.15g). LCMS showed $MH^+ = 268$; $T_{RET} = 3.18$min.

Intermediate 52: **4-(Cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid**

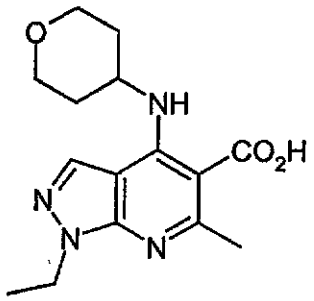


2M-Sodium hydroxide solution (0.39ml, 0.78mmol) was added to Example 190 (0.128g, 0.39mmol, described hereinafter) in ethanol (1.5ml), and the mixture was heated at 50 °C for 16 hours. The reaction mixture was concentrated, and the resulting aqueous solution was neutralised with 2M-hydrochloric acid to precipitate a solid which was collected by filtration. The filtrate was applied to an OASIS ® hydrophilic-lipophilic balance (HLB) Extraction cartridge * (1g) which was eluted with water followed by methanol. Evaporation of the methanol fraction gave a solid which was combined with the initial precipitated solid to afford Intermediate 52 (0.083g) as a white solid, presumed to be the carboxylic acid.

* OASIS ® HLB Extraction cartridges are available from Waters Corporation, 34 Maple Street, Milford, MA 01757, USA. The cartridges include a column containing a

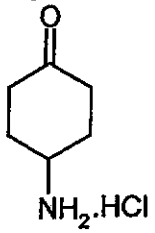
copolymer sorbent having a HLB such that when an aqueous solution is eluted through the column, the solute is absorbed or adsorbed into or onto the sorbent, and such that when organic solvent (e.g. methanol) is eluted the solute is released as an organic (e.g. methanol) solution. This is a way to separate the solute from aqueous solvent.

Intermediate 53: **1-Ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid**



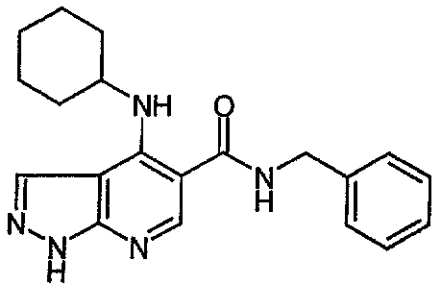
2M-Sodium hydroxide solution (0.75ml, 1.5mmol) was added to Example 189 (0.248g, 0.75mmol, described hereinafter) in ethanol (2ml), and the mixture was heated at reflux for 16 hours. The reaction mixture was concentrated, diluted with water (1ml) and acidified with 2M-hydrochloric acid (0.75ml) to precipitate a solid which was collected by filtration to afford Intermediate 53 (0.168g). LCMS showed $MH^+ = 305$; $T_{RET} =$ 1.86min.

Intermediate 54: **4-Aminocyclohexanone hydrochloride**



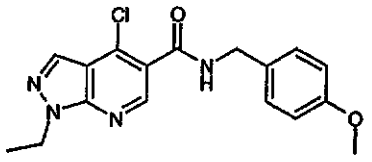
A solution of hydrogen chloride in dioxan (0.5ml, 2.0mmol, 4M) was added to a stirred solution of *tert*-butyl 4-oxocyclohexylcarbamate (0.043g, 0.20mmol, commercially available from Astatech Inc., Philadelphia, USA) in dioxan (0.5ml) and the mixture was stirred at room temperature. After 1h, the reaction mixture was evaporated to give Intermediate 54 as a cream solid (34mg). ^{1}H NMR (400MHz in d_6-DMSO, 27°C, δppm) 8.09 (br. s, 3H), 3.51 (tt, 11, 3.5Hz, 1H), 2.45 (m, 2H, partially obscured), 2.29 (m, 2H), 2.16 (m, 2H), 1.76 (m, 2H).

Intermediate 54A: ***N*-Benzyl-4-(cyclohexylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**

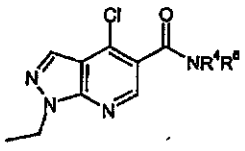


Benzylamine (0.16ml) was added to a stirred mixture of Intermediate 49 (0.13g), DIPEA (0.26ml) and HATU (0.285g) in DMF (3ml). The resultant mixture was heated with stirring at 85 °C for 16 hours. Further portions of HATU (0.14g), DIPEA (0.13ml) and benzylamine (0.082ml) were added and the mixture heated for 16 hours at 88 °C. The resultant solution was concentrated, diluted with dichloromethane (20ml) and washed with saturated sodium bicarbonate solution (20ml), separated by hydrophobic frit and the organic layer concentrated. The residue was purified on a SPE cartridge (silica, 20g) eluting with 60-80% ethyl acetate in cyclohexane. The residue was purified further on a SPE cartridge (Isolute SCX sulphonic acid cartridge, 5g x2), eluting with methanol (2x20ml) and 10% ammonia in methanol (4x20ml); the basic fractions were combined and concentrated to give Intermediate 54A as a white solid (0.07g). LCMS showed MH^+ = 350; T_{RET} = 2.99min.

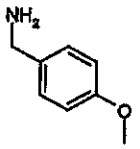
Intermediate 55: **4-Chloro-1-ethyl-N- {[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide**



That is, Intermediate 55 is:



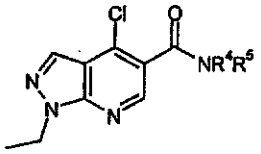
Where NR^4R^5 =

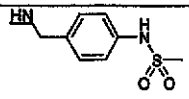
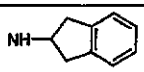


Intermediate 15 (1.04g) was treated with thionyl chloride (13.22g). The mixture was stirred and heated at 75 °C for 2h. Excess thionyl chloride was removed *in vacuo* and the residual oil azeotroped with toluene to afford Intermediate 16, presumed to be the acid chloride derivative of intermediate 15, as a cream solid (1.12g).

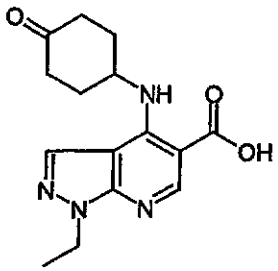
Intermediate 16 (0.997g) was dissolved in tetrahydrofuran (THF) (25ml) and treated with N,N-diisopropylethylamine (1.07ml) then with 1-[4-(methyloxy)phenyl]methanamine = 4-methoxybenzylamine (0.54ml) (obtainable from e.g. Aldrich, Acros, or *Tetrahedron Lett.*, 2002, 43(48), 8735; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Organic Letters*, 2002, 4(12), 2055) and the mixture was stirred for 3h. The solution was concentrated *in vacuo*, then partitioned between DCM and water. The layers were separated and the organics concentrated *in vacuo*. The solid was then triturated in 1:1 ethyl acetate: cyclohexane to give Intermediate 55 (1.27g). LCMS showed MH^+= 345, T_{RET}= 2.86 min.

Similarly prepared were the following:



	NR^4R^5	Source of HNR^4R^5	MH^+ ion	T_{RET} (min)
Intermediate 56		Lis et al., *J. Med. Chem.*, 1990, 33(10), 2883, see Scheme III and ref. 24	408	2.60
Intermediate 57		Maybridge-Int; or Aldrich; or TCI-America	341	3.08

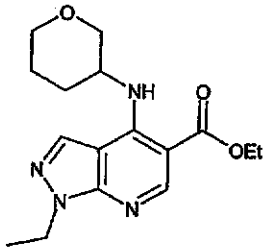
<u>Intermediate 58</u>: 1-Ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid



A solution of sodium hydroxide (0.053g, 1.32mmol) in water (0.41ml) was added to a stirred solution of Example 205 (0.1g, 0.303mmol) in ethanol (1ml), and the resulting mixture was heated at 50°C. After 1h, the cooled reaction mixture was adjusted to pH3 with 2M hydrochloric acid, and extracted with EtOAc (2 x 6ml). The combined organic extracts were dried (Na_2SO_4) and evaporated to give Intermediate 58 (0.072g) as a white solid. LCMS showed $MH^+ = 303$; $T_{RET} = 2.13$min.

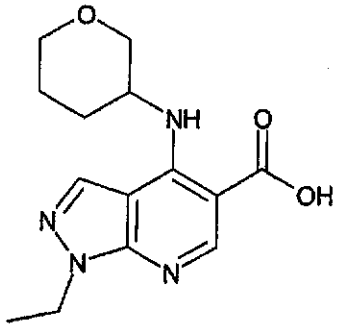
An alternative preparation of Intermediate 58 is as follows:
A solution of sodium hydroxide (0.792g, 19.8mmol) in water (6ml) was added to a stirred solution of Example 205 (1.487g, 4.5mmol) in ethanol (15ml), and the resulting mixture was heated at 50°C. After 1 hour, the cooled reaction mixture was adjusted to pH4 with 2M hydrochloric acid, and extracted with EtOAc (3 x 30ml). The combined organic extracts were dried (Na_2SO_4) and evaporated to give Intermediate 58 (1.188g) as a white solid. LCMS showed $MH^+ = 303$; $T_{RET} = 2.12$min.

Intermediate 58A: Ethyl 1-ethyl-4-(tetrahydro-2*H*-pyran-3-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



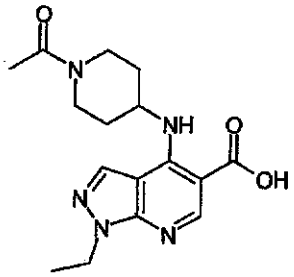
Intermediate 1 (0.76g, 3.0mmol)) was dissolved in acetonitrile (10ml). Tetrahydro-2*H*-pyran-3-amine hydrochloride (0.5g, 3.6mmol, *Anales De Quimica*, 1988, 84, 148) and *N,N*-diisopropylethylamine (3.14ml, 18.0mmol) were added and the mixture was stirred at 85°C for 24h. After 24h a further portion of tetrahydro-2*H*-pyran-3-amine hydrochloride (0.14g, 1.02mmol) was added and stirring was continued at 85°C. After a further 8h, the mixture was concentrated *in vacuo*. The residue was partitioned between DCM (20ml) and water (12ml). The layers were separated and the aqueous layer was extracted with further DCM (12ml). The combined organic extracts were dried (Na_2SO_4), and concentrated *in vacuo* to give a brown solid which was purified on a SPE cartridge (silica, 20g) eluting with a gradient of ethyl acetate:cyclohexane (1:16, 1:8, 1:4, 1:2, 1:1, 1:0). Fractions containing the desired material were combined and evaporated to afford Intermediate 58A (0.89g). LCMS showed $MH^+ = 319$; $T_{RET} = 2.92$ min.

Intermediate 59: 1-Ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid



A solution of Intermediate 58A (0.89g, 2.79mmol) in ethanol (16.7ml) was treated with sodium hydroxide (0.47g, 11.7mmol) as a solution in water (3.1ml). The mixture was stirred at 50 °C. After 12h, the reaction mixture was concentrated *in vacuo* to give a residual oil which was dissolved in water (16ml), then cooled and acidified to pH 3 with 2M hydrochloric acid. After stirring at 0°C for 30min, the resulting precipitate was collected by filtration, washed with cooled water (2ml) and dried in vacuo to afford Intermediate 59 as a white solid (0.73g). LCMS showed $MH^+ = 291$; $T_{RET} = 2.19$min.

Intermediate 60: 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid

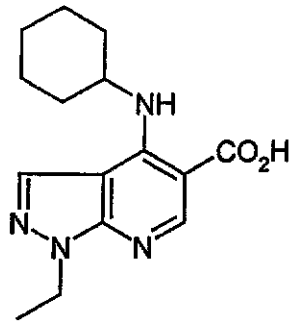


Aqueous sodium hydroxide solution (8.55ml, 2M) was added to a solution of Example 207 (1.55g) in EtOH (13ml). The mixture was heated at 50 °C for 18h then neutralised using aqueous hydrochloric acid and evaporated in vacuo to afford a mixture of 1-ethyl-4-(4-piperidinylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid and 4-[(1-acetyl-4-piperidinyl)amino]-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid

Acetic acid (0.36ml) was added to a stirred mixture of HATU (2.41g) and N,N-diisopropylethylamine (2.21ml) in N,N-dimethylformamide (65ml). After stirring for 15 min the mixture was added to the mixture of 1-ethyl-4-(4-piperidinylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid and 4-[(1-acetyl-4-piperidinyl)amino]-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid and the reaction stirred for 15h. The reaction mixture was evaporated in vacuo and the residue purified by chromatography

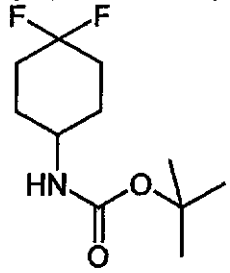
using Biotage (silica 90g) eluting with DCM : MeOH (0% - 5% MeOH) to afford Intermediate 60 (1.36g) as a white solid. LCMS showed MH^+ 334; T_{RET} = 2.06 min.

Intermediate 61: 4-(Cyclohexylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid



A solution of Example 2 (5.37g, 17mmol) in ethanol (30ml) was treated with a solution of sodium hydroxide (2.72g, 68mmol) in water (20ml), and the resulting mixture was stirred at 50°C for 3h. The reaction mixture was concentrated in vacuo, dissolved in water (250ml) and the cooled solution was acidified to pH 1 with 5M-hydrochloric acid. The resultant solid was collected by filtration and dried in vacuo to afford Intermediate 61 as a white solid (4.7g). LCMS showed MH^+ = 289; T_{RET} = 2.83min.

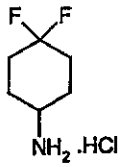
Intermediate 62: 1,1-Dimethylethyl (4,4-difluorocyclohexyl)carbamate



(Diethylamino)sulphur trifluoride (DAST), (0.06ml, 0.47mmol), was added to a stirred solution of 1,1-dimethylethyl(4-oxocyclohexyl)carbamate, (250mg, 1.17mmol, commercially available from AstaTech Inc., Philadelphia, USA) in anhydrous dichloromethane (5ml) and the mixture was stirred under nitrogen at 20°C. After 22h, the reaction mixture was cooled to 0°C, treated with saturated sodium hydrogen carbonate solution (4ml), and then allowed to warm to ambient temperature. The phases were separated by passage through a hydrophobic frit and the aqueous phase was further extracted with DCM (5ml). The combined organic phases were concentrated in vacuo to give an orange solid (369mg) which was further purified by chromatography using a SPE cartridge (silica, 10g), eluting with DCM to afford Intermediate 62 (140mg) containing

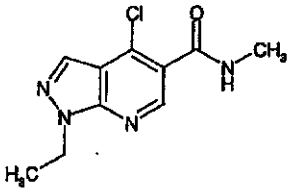
20% of **1,1-dimethylethyl (4-fluoro-3-cyclohexen-1-yl)carbamate.** ^{1}H NMR (400MHz in $CDCl_3$, 27°C, δppm)
Minor component: δ5.11 (dm, 16Hz, 1H), 4.56 (br, 1H), 3.80 (br, 1H) 2.45-1.45 (m's, 6H excess), 1.43 (s, 9H). Major component: δ4.43 (br, 1H), 3.58 (br, 1H), 2.45-1.45 (m's, 8H excess), 1.45 (s, 9H).

Intermediate 63: (4,4-Difluorocyclohexyl)amine hydrochloride



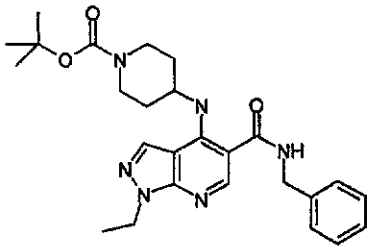
A solution of hydrogen chloride in dioxane (4M, 1.6ml) was added at 20°C to a stirred solution of Intermediate 62 (140mg, 0.6mmol), in dioxane (1.6ml). After 3h, the reaction mixture was concentrated in vacuo to afford intermediate 63 (96.5mg) containing **4-fluoro-3-cyclohexen-1-amine.** ^{1}H NMR (400MHz in d_6-DMSO, 27°C, δppm) Minor component: δ8.22 (br, 3H excess), 5.18 (dm, 16Hz, 1H), 3.28-3.13 (m, 1H excess), 2.41-1.53 (m's, 6H excess). Major component: δ8.22 (br, 3H excess), 3.28-3.13 (m, 1H excess), 2.41-1.53 (m's, 8H excess). Impurities are also present.

Intermediate 64: 4-Chloro-1-ethyl-*N*-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



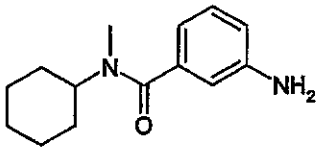
Intermediate 15 (0.06g, 0.266mmol) was treated with thionyl chloride (0.48ml). The mixture was stirred and heated at 75°C for 2h. Excess thionyl chloride was removed in vacuo and the residual oil azeotroped with dichloromethane (DCM) to afford **Intermediate 16**, presumed to be the acid chloride derivative of Intermediate 15, as a white solid. Intermediate 16 was dissolved in anhydrous tetrahydrofuran (THF) (2ml) and treated with N,N-diisopropylethylamine (DIPEA) (0.069ml), then with methylamine (2M in tetrahydrofuran, 0.15ml) and the mixture stirred under nitrogen for 16h. A further 0.05ml of methylamine (2M in THF) was added and the solution stirred for 2h. The mixture was concentrated in vacuo, then partitioned between dichloromethane (2ml) and aqueous sodium hydroxide solution (2M, 2ml), then the organic layer washed with water (2ml). The layers were separated and the organics concentrated in vacuo to afford Intermediate 64 (0.052g). LCMS showed $MH^+ = 239$; $T_{RET} = 2.17$min.

Intermediate 65: Ethyl 4-[(1-{[(1,1-dimethylethyl)oxy]carbonyl}-4-piperidinyl)amino]-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



A mixture of Intermediate 17 (2.0g, 6.37mmol), 1,1-dimethylethyl 4-amino-1-piperidinecarboxylate (2.04g, 10.2mmol) and N,N,-diisopropylethylamine (5.54ml, 31.9mmol) in MeCN (40ml) was heated at 85 °C for 42h. The reaction was evaporated and the residues partitioned between DCM and water. The organic phase was dried ($MgSO_4$) then evaporated in vacuo. The residue was chromatographed on silica (Biotage, 90g) eluting with cyclohexane : EtOAc (1:1) to give Intermediate 65 as a white solid (2.70g). LCMS showed $MH^+ = 479$; $T_{RET} = 3.37$min.

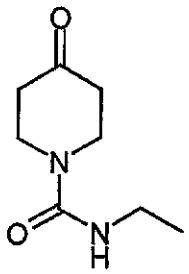
Intermediate 67: 3-Amino-*N*-cyclohexyl-*N*-methylbenzamide



A solution of 3-nitrobenzoyl chloride (2.0g, 10.78mmol) in DCM (20ml) was added dropwise to a stirred mixture of N-methylcyclohexylamine (1.83ml, 14.01mmol), N,N,-diisopropylethylamine (3.76ml, 21.56mmol) and N,N-dimethylaminopyridine (0.01g) in DCM at 20 °C. The reaction mixture was stirred for 56h then evaporated in vacuo. The residue was partitioned between ethyl acetate and water. The organic phase was washed with aqueous HCl then dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by chromatography on silica eluting with cyclohexane : EtOAc (9:1 followed by 2:1) to afford *N*-cyclohexyl-*N*-methyl-3-nitrobenzamide (1.40g). MS showed MH^+ 263.

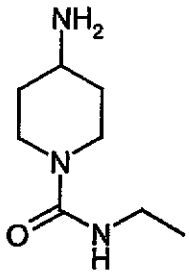
A mixture of *N*-Cyclohexyl-*N*-methyl-3-nitrobenzamide (1.40g, 5.35mmol) and palladium on carbon (5%, 0.140g) in ethanol (10ml) was stirred under an atmosphere of hydrogen for1 hour. The reaction mixture was filtered through Celite and the filtrate evaporated to afford Intermediate 67 as a brown solid (0.107g). LCMS showed $MH^+ = 233$; $T_{RET} = 2.56$min.

Intermediate 68: ***N*-Ethyl-4-oxo-1-piperidinecarboxamide**



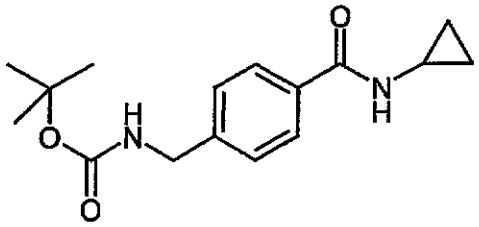
A solution of ethyl isocyanate (2.31g, 32.5mmol) in DCM (40ml) was added, dropwise over 15min, to a vigorously stirred solution of 4-piperidone monohydrate hydrochloride (5.0g, 32.5mmol, commercially available from Aldrich) and sodium hydrogen carbonate (8.2g, 97.5mmol) in water (60ml) at 0°C. The reaction mixture was stirred at room temperature for 20h. Sodium chloride (7.0g) was added to the reaction mixture and the organic phase was separated. The aqueous phase was extracted with further DCM (3 x 75ml). The combined organic extracts were dried (Na_2SO_4) and evaporated in vacuo to give a white solid (4.0g). Recrystallisation from ethyl acetate: cyclohexane (10:1) afforded Intermediate 68 as a white solid (2.3g).
TLC (silica) gave $R_f = 0.24$ (ethyl acetate). Anal. Found: C, 56.7; H, 8.3; N, 16.35. $C_8H_{14}N_2O_2$ requires C, 56.5; H, 8.3; N, 16.5.

Intermediate 69: **4-Amino-*N*-ethyl-1-piperidinecarboxamide**



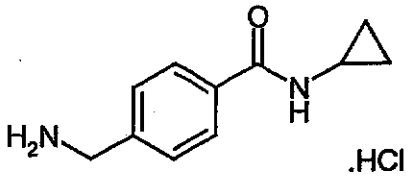
A solution of Intermediate 68 (1.5g, 8.8mmol) and benzylamine (1.04g, 9.7mmol) in absolute ethanol (60ml) was hydrogenated over pre-reduced 10% palladium on charcoal catalyst (0.6g) in ethanol (20ml) until the uptake of hydrogen had ceased (22h). The reaction mixture was filtered through filter agent (Celite), and then through silica gel (100ml) eluting with ethanol:0.88-ammonia (100:1) to give a black oil. The oil was dissolved in ethanol (30ml) and treated with a solution of hydrogen chloride in ethanol (3M) until the solution was acidic. The solvent was evaporated and the residue was triturated with ethanol to afford Intermediate 69 as a white solid (1.09g).
TLC (silica) gave $R_f = 0.73$ (ethyl acetate:methanol, 10:1). Anal. Found: C, 45.9; H, 8.4; N, 19.8. $C_8H_{18}ClN_3O$ requires C, 46.3; H, 8.7; N, 20.2.

Intermediate 70: 1,1-Dimethylethyl ({4-[(cyclopropylamino)carbonyl]phenyl}methyl)carbamate



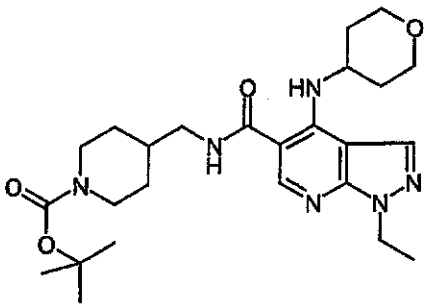
Cyclopropylamine (0.136g, 2.39mmol) and diisopropylethylamine (0.68ml, 3.9mmol) were added to a stirred solution of 4-[({[(1,1-dimethylethyl)oxy]carbonyl}amino)-methyl]benzoic acid (0.501g, 2.0mmol), EDC (0.612g, 3.2mmol) and HOBT (0.35g, 2.6mmol) in DMF (2ml). The resulting mixture was stirred at room temperature overnight. Solvents were removed in vacuo, and the residue was dissolved in ethyl acetate (20ml) and washed with 0.5M-hydrochloric acid (3 x 20ml). The organic phase was dried (Na_2SO_4) and evaporated in vacuo to give the crude product which was purified by Biotage chromatography (silica) eluting with ethyl acetate:cyclohexane (1.3:1) to afford Intermediate 70 as a white solid (0.512g). LCMS showed $MH^+ = 291$; $T_{RET} = 2.75$min.

Intermediate 71: 4-(Aminomethyl)-*N*-cyclopropylbenzamide hydrochloride



Intermediate 70 (0.506g, 1.74mmol) was dissolved in a solution of hydrogen chloride in dioxan (20ml, 4M) under nitrogen. After 1h, methanol (3ml) was added to the mixture and stirring was continued at room temperature overnight. Solvents were removed in vacuo to afford Intermediate 71 as a white solid (0.416g). LCMS showed $MH^+ = 191$; $T_{RET} = 0.82$min.

Intermediate 72

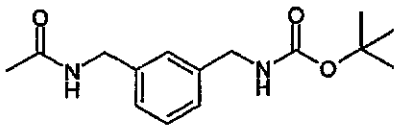


Intermediate 33 (1.36g, 4.7mmol), EDC (1.26g, 6.57mmol) and HOBT (0.76g, 5.62mmol) were suspended in DMF (50ml) and stirred vigorously at room temperature for 0.5h, before adding 1,1-dimethylethyl 4-(aminomethyl)-1-piperidinecarboxylate (1.3g, 6.07mmol, commercially available from Maybridge Chemical Co. Ltd.,). After stirring at room temperature overnight, a further quantity of 1,1-dimethylethyl 4-(aminomethyl)-1-piperidinecarboxylate (1.01g, 4.7mmol) was added to the reaction mixture which was then heated at 50°C. After 6h, diisopropylethylamine (0.25ml, 1.44mmol) was added, and the mixture was maintained at 50°C for a further 6h. Solvents were removed in vacuo and the residue was partitioned between DCM (100ml) and water (100ml). The phases were separated by passage through a hydrophobic frit, and the organic phase was evaporated in vacuo to give the crude product. Further purification using SPE cartridges (aminopropyl followed by silica) afford Intermediate 72 as a cream solid (1.24g). LCMS showed $MH^+ = 487$; $T_{RET} = 2.97$min.

Intermediate 73

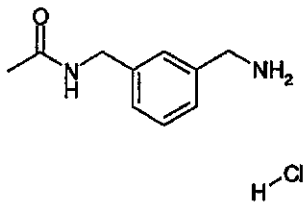
Intermediate 73 is used *in situ* in the general procedure for Examples 360-414.

Intermediate 74: 1,1-Dimethylethyl ({3-[(acetylamino)methyl]phenyl}methyl)carbamate



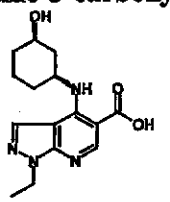
Acetic anhydride (0.52ml, 5.5mmol) was added to a mixture of *tert*-butyl *N*-[3-aminomethyl)benzyl] carbamate (1.1g, 4.65mmol commercially available from Astatech) and triethylamine (0.7ml, 5mmol) in THF (20ml). The reaction mixture was stirred at 20 °C from 16h then concentrated *in vacuo*. The residue was partitioned between EtOAc and water. The organic phase was dried (MgSO4) and evaporated *in* vacuo. The residue was chromatographed over silica eluting with hexanes : EtOAc (1:1) followed by EtOAc to afford Intermediate 74 (1.2g) as a colourless oil. Anal. Found: C, 64.79; H, 7.93; N, 10.10. $C_{15}H_{22}N_2O_3$ requires C, 64.73; H, 7.97; N, 10.06. MS $(M+Na)^+$ 301.

Intermediate 75: ***N*-{[3-(Aminomethyl)phenyl]methyl}acetamide hydrochloride**



Hydrogen chloride in dioxane (4ml, 4M) was added to a solution of Intermediate 74 (1.0g, 3.6mmol) in dioxane (10ml) and the resultant mixture stirred for 6 hours at 20 °C. The reaction was diluted with Et_2O (20ml) and filtered to afford Intermediate 75 (0.7g) as a white solid. MS MH^+ 179. ^1H NMR (300MHz in d6-DMSO, 27°C, δppm) δ 8.6 - 8.4 (br m, 3H), 7.38 - 7.26 (m, 3H), 7.22 (bm, 1H), 4.24 (d, J = 5.7Hz, 2H), 3.95 (dd, J = 11.6, 5.7Hz, 2H), 1.87 (s, 3H).

Intermediate 76 1-Ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid



(*cis*-3-hydroxycyclohex-1-ylamino group, racemic)

A solution of Example 665 (0.681g, 2.05mmol) in ethanol (7ml) was treated with a solution of sodium hydroxide (0.362g, 9.05mmol) in water (2.9ml). The resulting mixture was stirred at 50°C. After 3h, the reaction mixture was concentrated in vacuo to give a residual oil which was dissolved in water (3ml), then cooled and acidified to pH 3 with 2M-hydrochloric acid. After stirring at 0°C for 1h, the resulting precipitate was collected by filtration, washed with cooled water (0.5ml) and dried in vacuo to afford Intermediate 76 as a white solid (0.491g). LCMS showed $MH^+ = 305$; $T_{RET} = 2.14$min.

Table of Examples

Example Number	Name
1	Ethyl 4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
2	Ethyl 4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
3	Ethyl 1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
5	Ethyl 4-[(1-acetylpiperidin-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
6	Ethyl 4-(cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
7	Ethyl 1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
8	Ethyl 1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
9	Ethyl 1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
10	Ethyl 1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
11	Ethyl 1-ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
12	Ethyl 4-(cyclopropylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
13	Ethyl 4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
14	Ethyl 4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
21	N-Benzyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
22	1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
23	N-Cyclopentyl-4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
24	4-(Cyclohexylamino)-N-cyclopentyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
25	N-Cyclopentyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
27	4-[(1-Acetylpiperidin-4-yl)amino]-N-cyclopentyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
28	N-Cyclopentyl-1-ethyl-5-(pyrrolidin-1-ylcarbonyl)-1H-pyrazolo[3,4-b]pyridin-4-amine
29	N-Cyclohexyl-1-ethyl-5-(pyrrolidin-1-ylcarbonyl)-1H-pyrazolo[3,4-b]pyridin-4-

	amine
30	1-Ethyl-5-(pyrrolidin-1-ylcarbonyl)-N-tetrahydro-2H-pyran-4-yl-1H-pyrazolo[3,4-b]pyridin-4-amine
31	4-(Cyclopentylamino)-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
32	4-(Cyclohexylamino)-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
33	1-Ethyl-N-(pyridin-4-ylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
34	4-(Cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
35	4-(Cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
36	1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
39	N-Benzyl-4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
40	N-Benzyl-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
41	4-[(1-Acetylpiperidin-4-yl)amino]-N-benzyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
42	4-(Cyclopentylamino)-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
43	4-(Cyclohexylamino)-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
44	1-Ethyl-N-(2-ethylbutyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
45	1-Ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
46	4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
47	4-(Cyclopentylamino)-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
48	4-(Cyclohexylamino)-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
49	1-Ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
50	4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
51	4-(Cyclopentylamino)-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
52	4-(Cyclohexylamino)-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

53	1-Ethyl-N-n-propyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
55	4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
57	4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
61	N-Benzyl-4-(cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
62	N-Benzyl-4-(cyclohexylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
63	N-Benzyl-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
64	4-(Cyclopentylamino)-N-(2-ethylbutyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
65	4-(Cyclohexylamino)-N-(2-ethylbutyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
66	N-(2-Ethylbutyl)-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
67	4-(Cyclopentylamino)-N-(4-fluorophenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
68	4-(Cyclohexylamino)-N-(4-fluorophenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
69	N-(4-Fluorophenyl)-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
70	4-(Cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
71	4-(Cyclohexylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
74	4-[(1-Acetylpiperidin-4-yl)amino]-N-benzyl-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
81	1-Ethyl-N-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
82	1-Ethyl-N,N-dimethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
83	1-Ethyl-N-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
84	1-Ethyl-N-isopropyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
85	N-Benzyl-1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
86	N-Benzyl-1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
87	N-Benzyl-1-ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-

	carboxamide
88	N-Benzyl-4-(cyclopropylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
89	N-Benzyl-4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
90	N-Benzyl-4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
91	N-Benzyl-1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
92	1-Ethyl-N-(4-fluorophenyl)-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
93	1-Ethyl-N-(4-fluorophenyl)-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
94	1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
95	1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
96	4-(Cyclopropylamino)-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
97	4-[(1,1-Dioxidotetrahydrothien-3-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
98	4-[(1,1-Dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

Example No.	Name
100	1-Ethyl-*N*-[4-(methylsulfonyl)benzyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
102	1-Ethyl-*N*-[3-(methylsulfonyl)benzyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
103	1-Ethyl-5-{[5-methoxy-6-(trifluoromethyl)-2,3-dihydro-1*H*-indol-1-yl]carbonyl}-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine
104	*N*-[(5-Chloropyridin-2-yl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
105	*N*-(4-Chlorobenzyl)-1-ethyl-*N*-isopropyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
106	*N*-(3-Chlorobenzyl)-1-ethyl-*N*-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
107	1-Ethyl-*N*-[(5-methyl-3-phenylisoxazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

108	*N*-(2-*tert*-Butoxyethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
109	1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3-thiazol-2-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
110	1-Ethyl-*N*-(pyrimidin-4-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
111	1-Ethyl-*N*-[(2-methyl-1,3-thiazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
112	*N*-[3-(*tert*-Butoxymethyl)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
113	1-Ethyl-*N*-{2-[methyl(methylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
114	1-Ethyl-*N*-(pyrazin-2-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
115	1-Ethyl-5-{[4-(pyridin-2-ylcarbonyl)piperazin-1-yl]carbonyl}-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine
116	*N*-(2-Chloro-6-fluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
117	1-Ethyl-*N*-[(6-oxo-1,6-dihydropyridin-3-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
118	*N*-[3-(Aminocarbonyl)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
119	1-Ethyl-*N*-{4-[(methylamino)carbonyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
120	1-Ethyl-*N*-[2-(1-methyl-1*H*-imidazol-4-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
121	*N*-{2-[(Anilinocarbonyl)amino]ethyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
122	1-Ethyl-*N*-(1*H*-tetraazol-5-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide hydrochloride
123	1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[2-(1*H*-1,2,4-triazol-1-yl)ethyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
125	1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
126	*tert*-Butyl 4-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)piperidine-1-carboxylate
127	1-Ethyl-*N*-{3-[(methylsulfonyl)amino]propyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
128	*N*-[2-(Dimethylamino)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
129	1-Ethyl-*N*-[(1-ethylpyrrolidin-2-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

130	1-Ethyl-*N*-(tetrahydrofuran-2-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
131	1-ethyl-*N*-tetrahydro-2*H*-pyran-4-yl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
132	*N*-{4-[(Dimethylamino)sulfonyl]benzyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
133	1-Ethyl-*N*-{3-[(methylsulfonyl)amino]benzyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
135	1-Ethyl-*N*-(4-methoxyphenyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
136	1-Ethyl-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
137	1-Ethyl-*N*-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
138	1-Ethyl-*N*-(pyridin-3-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
139	1-Ethyl-*N*-(1-methylpiperidin-4-yl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
140	1-Ethyl-*N*-(1-ethylpropyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
141	1-Ethyl-*N*-(2-piperidin-1-ylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
142	1-Ethyl-*N*-(3-morpholin-4-ylpropyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
143	*N*-(3-Ethoxypropyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
144	*N*-(Cyclohexylmethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
145	*N*-[3-(Dimethylamino)propyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
146	1-Ethyl-*N*-neopentyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
147	1-ethyl-*N*-(4-methoxybenzyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
148	1-Ethyl-*N*-{2-[(phenylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
149	*N*-[2-(Acetylamino)ethyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
150	1-Ethyl-*N*-{2-[(methylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
152	1-Ethyl-*N*-{2-[(2-methoxyphenyl)(methyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

153	1-Ethyl-*N*-(2-oxo-2-phenylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1H-pyrazolo[3,4-*b*]pyridine-5-carboxamide
154	*N*-(2,5-Difluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
155	1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[4-(trifluoromethyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
156	*N*,1-Diethyl-*N*-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
157	*N*-Cyclopropyl-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
158	N-(2-amino-2-oxoethyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
159	1-Ethyl-*N*-(3-methoxyphenyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
160	*N*-(3,4-Difluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
161	Ethyl 3-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)propanoate
162	*N*-(1-Benzylpiperidin-4-yl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
163	*N*-Butyl-4-{[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}piperazine-1-carboxamide
164	1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3,4-thiadiazol-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
165	*N*-(2,3-Dihydro-1*H*-inden-2-yl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
166	1-Ethyl-*N*-[2-(2-oxoimidazolidin-1-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
167	*N*-(3,4-Dimethoxybenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
168	*N*-(3-Chlorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
169	1-Ethyl-5-[(4-methylpiperazin-1-yl)carbonyl]-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine
170	1-Ethyl-*N*-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
171	1-Ethyl-5-{[4-(4-methoxyphenyl)piperazin-1-yl]carbonyl}-*N*-tetrahydro-2*H*-pyran-4-yl-1*H*-pyrazolo[3,4-*b*]pyridin-4-amine
172	1-Ethyl-*N*-{4-[(methylsulfonyl)methyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
173	N-[3-(dimethylamino)-3-oxopropyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

174	1-Ethyl-*N*-[(1-methyl-1*H*-imidazol-5-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
175	1-Ethyl-*N*-{4-[(methylamino)sulfonyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
176	*N*-(2-Cyanoethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
178	1-Ethyl-*N*-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
179	1-Ethyl-*N*-methyl-*N*-[(1-methyl-1*H*-imidazol-2-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
180	1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(2-thien-2-ylethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
181	*N*-[2-(4-Chlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
182	1-Ethyl-*N*-[2-(2-methoxyphenyl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
183	Ethyl 4-(cyclohexylamino)-1-(3-ethoxy-3-oxopropyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
185	Ethyl 1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
186	Ethyl 1-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
187	N-[4-(Methylsulfonyl)benzyl]-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-b]pyridine-5-carboxamide
188	N-(4-Fluorophenyl)-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
189	Ethyl 1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
190	Ethyl 4-(cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
191	4-(Cyclohexylamino)-1-ethyl-6-methyl-*N*-[4-(methylsulfonyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
192	*N*-Benzyl-4-(cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
193	4-(Cyclohexylamino)-1-ethyl-*N*-(4-fluorophenyl)-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
194	4-(Cyclohexylamino)-1-ethyl-6-methyl-*N*-[4-(trifluoromethyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
195	4-(Cyclohexylamino)-*N*-(2,3-dihydro-1*H*-inden-2-yl)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
196	*N*-Benzyl-1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-

	pyrazolo[3,4-*b*]pyridine-5-carboxamide
197	*N*-Benzyl-1-ethyl-4-[(2-oxoazepan-3-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
198	*N*-Benzyl-1-ethyl-4-[(3-hydroxycyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide; also called *N*-benzyl-1-ethyl-4-[(3-hydroxycyclohexan-1-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
199	*N*-Benzyl-1-ethyl-4-[(4-hydroxycyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide; also called *N*-benzyl-1-ethyl-4-[(4-hydroxycyclohexan-1-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
200	*N*-Benzyl-1-ethyl-4-[(3-hydroxycyclopentyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide; also called *N*-benzyl-1-ethyl-4-[(3-hydroxycyclopentan-1-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
201	*N*-Benzyl-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide; also called *N*-Benzyl-1-ethyl-4-[(4-oxocyclohexan-1-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
202	1-Ethyl-*N*-(2-hydroxy-1-methylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
203	Methyl (2*S*)-2-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)-3-hydroxypropanoate

Example no.	**Name**
204	Ethyl 1-ethyl-4-[(4-hydroxycyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
205	Ethyl 1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
207	Ethyl 4-[(1-acetyl-4-piperidinyl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
209	Ethyl 4-[(4-aminocyclohexyl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate
210	Ethyl-N-[(1-oxido-3-pyridinyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
211	1-Ethyl-N-[(1-oxido-2-pyridinyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
212	1-Ethyl-N-[(1-oxido-4-pyridinyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
214	4-[(cis-4-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
221	4-(Cyclobutylamino)-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
222	4-(Cycloheptylamino)-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
223	1-Ethyl-4-[(4-methylcyclohexyl)amino]-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-

carboxamide

224 1-Ethyl-4-[(3-methylcyclohexyl)amino]-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

225 1-Ethyl-4-[(1-methylcyclohexyl)amino]-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

226 4-[(1R,2R,4S)-Bicyclo[2.2.1]hept-2-ylamino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

227 4-[(1R,2S,4S)-Bicyclo[2.2.1]hept-2-ylamino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

228 1-Ethyl-4-{[(3S)-2-oxo-3-pyrrolidinyl]amino}-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

229 4-[(2,5-Dioxo-3-pyrrolidinyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

230 4-(1-Azabicyclo[2.2.2]oct-3-ylamino)-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

231 1-Ethyl-4-[(1-methylcyclohexyl)amino]-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

233 4-(Cyclobutylamino)-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

234 4-(Cycloheptylamino)-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

235 4-[(1R,2R,4S)-Bicyclo[2.2.1]hept-2-ylamino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

236 1-Ethyl-4-[(4-methylcyclohexyl)amino]-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

237 1-Ethyl-4-[(3-methylcyclohexyl)amino]-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

238 4-[(1R,2S,4S)-Bicyclo[2.2.1]hept-2-ylamino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

239 4-[(cis-4-Aminocyclohexyl)amino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

240 4-(Cycloheptylamino)-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

241 4-(Cyclobutylamino)-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

242 4-[(1R,2R,4S)-Bicyclo[2.2.1]hept-2-ylamino]-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

243 4-[(1R,2S,4S)-Bicyclo[2.2.1]hept-2-ylamino]-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

244 1-Ethyl-4-[(4-methylcyclohexyl)amino]-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

245 1-Ethyl-4-[(3-methylcyclohexyl)amino]-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

247 1-Ethyl-4-[(1-methylcyclohexyl)amino]-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

248 4-[(cis-4-Aminocyclohexyl)amino]-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

249 4-(Cyclohexylamino)-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

250 4-(Cycloheptylamino)-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

251 4-(Cyclobutylamino)-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

253 N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-4-[(3-methylcyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

254 N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-4-[(4-methylcyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

255 4-[(1R,2R,4S)-Bicyclo[2.2.1]hept-2-ylamino]-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

256 4-[(1R,2S,4S)-Bicyclo[2.2.1]hept-2-ylamino]-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

257 N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-4-[(1-methylcyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

258 4-[(cis-4-Aminocyclohexyl)amino]-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

259 1-Ethyl-N-{4-[(methylsulfonyl)methyl]phenyl}-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

260 N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

261 N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

262 N-[(3,4-Dichlorophenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

263 1-Ethyl-N-{[4-(methyloxy)phenyl]methyl}-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

264 1-Ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

265 N-{[4-(Dimethylamino)phenyl]methyl}-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

266 N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

267 1-Ethyl-4-[(4-oxocyclohexyl)amino]-N-{[4-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

268 1-Ethyl-N-{[4-(methylsulfonyl)phenyl]methyl}-4-[(4-oxocyclohexyl)amino]-1H-

pyrazolo[3,4-b]pyridine-5-carboxamide

269 1-Ethyl-N-(4-fluorophenyl)-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

270 1-Ethyl-4-[(4-oxocyclohexyl)amino]-N-(2-pyridinylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

271 N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

272 N-(1-Acetyl-4-piperidinyl)-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

273 1-Ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

274 N,1-Diethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

275 1-Ethyl-4-[(4-oxocyclohexyl)amino]-N-(1,3-thiazol-2-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

276 1-Ethyl-N-(phenylmethyl)-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

277 N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

278 1-Ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-N-{[4-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

279 1-Ethyl-N-{[4-(methylsulfonyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

280 1-Ethyl-N-{4-[(methylsulfonyl)methyl]phenyl}-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

281 1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

282 1-Ethyl-N-(2-pyridinylmethyl)-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

283 N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

284 N-(1-Acetyl-4-piperidinyl)-1-ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

285 1-Ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

286 N,1-Diethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

287 1-Ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-N-(1,3-thiazol-2-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

288 4-[(4,4-Difluorocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

289 1-Ethyl-4-[(4-fluoro-3-cyclohexen-1-yl)amino]-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide.

290 4-[(1-Acetyl-4-piperidinyl)amino]-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

291 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(3,4-dichlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

292 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-[(3-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

293 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(3,4-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

294 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2,5-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

295 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[3-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

296 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[4-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

297 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2,6-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

298 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(3-chlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

299 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

300 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-[4-(methyloxy)phenyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

301 4-[(1-Acetyl-4-piperidinyl)amino]-N-({4-[(dimethylamino)sulfonyl]phenyl}methyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

302 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

303 4-[(1-Acetyl-4-piperidinyl)amino]-N-{[2-(dimethylamino)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

304 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2,4-dichlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

305 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

306 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2-chloro-6-fluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

307 4-[(1-Acetyl-4-piperidinyl)amino]-N-({4-[(difluoromethyl)oxy]phenyl}methyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

308 4-[(1-Acetyl-4-piperidinyl)amino]-N-{[3-chloro-4-(methyloxy)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

309 4-[(1-Acetyl-4-piperidinyl)amino]-N-[(5-chloro-2-pyridinyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

310 4-[(1-Acetyl-4-piperidinyl)amino]-N-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

311 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-(1,3-thiazol-2-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

312 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[4-(methylsulfonyl)phenyl]methyl}-1H-

pyrazolo[3,4-b]pyridine-5-carboxamide

313 4-[(1-Acetyl-4-piperidinyl)amino]-N-(2,2-diphenylethyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

314 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

315 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-({4-[(methylamino)carbonyl]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

316 4-[(1-Acetyl-4-piperidinyl)amino]-N-{[4-(aminosulfonyl)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

317 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-({3-[(methylamino)carbonyl]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

318 4-[(1-Acetyl-4-piperidinyl)amino]-N-{[4-(aminocarbonyl)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

319 4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[6-(methyloxy)-3-pyridinyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

320 1-Ethyl-N-4-piperidinyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

321 1-Ethyl-N-(4-piperidinylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

322 1-Ethyl-N-[1-(ethylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

323 1-Ethyl-N-{1-[(1-methylethyl)sulfonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

324 N-[1-(Cyclopentylsulfonyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

325 1-Ethyl-N-[1-(methylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

326 1-Ethyl-N-{1-[(phenylmethyl)sulfonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

327 1-Ethyl-N-[1-(phenylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

328 1-Ethyl-N-[1-(propylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

329 N-[1-(Cyclopropylcarbonyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

330 1-Ethyl-N-[1-(3-furanylcarbonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

331 N-[1-(3,3-Dimethylbutanoyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

332 1-Ethyl-N-[1-(2-ethylbutanoyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

333 N-[1-(Cyclopentylacetyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

334 1-Ethyl-N-[1-(2-methylpropanoyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

335 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)-4-piperidinyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

336 1-Ethyl-N-(1-propanoyl-4-piperidinyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

337 N-[1-(N-Acetylglycyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

338 1-Ethyl-N-[1-(4-morpholinylacetyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

339 1-Ethyl-N-{1-[(4-oxocyclohexyl)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

340 1-Ethyl-N-[1-(1-piperidinylacetyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

341 1-Ethyl-N-{1-[(1-methyl-5-oxo-3-pyrrolidinyl)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

342 1-Ethyl-N-{1-[(3-methyl-3-oxetanyl)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

343 1-Ethyl-N-{1-[(4-fluorophenyl)acetyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

344 N-{[1-(3,3-Dimethylbutanoyl)-4-piperidinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

345 N-{[1-(Cyclopentylacetyl)-4-piperidinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

346 N-{[1-(Cyclopropylcarbonyl)-4-piperidinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

347 1-Ethyl-N-({1-[(4-oxocyclohexyl)carbonyl]-4-piperidinyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

348 1-Ethyl-N-({1-[(4-fluorophenyl)acetyl]-4-piperidinyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

349 1-Ethyl-N-({1-[(1-methyl-5-oxo-3-pyrrolidinyl)carbonyl]-4-piperidinyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

350 Methyl 3-[(1-ethyl-5-{[(phenylmethyl)amino]carbonyl}-1H-pyrazolo[3,4-b]pyridin-4-yl)amino]cyclohexanecarboxylate

351 3-[(1-Ethyl-5-{[(phenylmethyl)amino]carbonyl}-1H-pyrazolo[3,4-b]pyridin-4-yl)amino]cyclohexanecarboxylic acid

352 1-Ethyl-N-(phenylmethyl)-4-(4-piperidinylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

353 Ethyl 1-ethyl-4-({1-[(methyloxy)acetyl]-4-piperidinyl}amino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

354 Ethyl 1-(1-methylethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

355 4-(Cyclohexylamino)-1-ethyl-N-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

356 1-Ethyl-N-(4-fluorophenyl)-6-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

357 1-Ethyl-6-methyl-N-{[4-(methylsulfonyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

358 N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-6-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

360 1-Ethyl-N-[3-(1-piperidinylcarbonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

361 1-Ethyl-N-[4-(1-methylethyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

362 1-Ethyl-N-(2-fluorophenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

363 N-{3-[(Dimethylamino)carbonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

364 N-{4-[(Difluoromethyl)oxy]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

365 N-{4-[Acetyl(methyl)amino]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

366 1-Ethyl-N-(4-hydroxyphenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

367 1-Ethyl-N-[4-(4-morpholinyl)-2-(trifluoromethyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

368 1-Ethyl-N-4-pyridinyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

369 1-Ethyl-N-{4-[(4-methyl-1-piperazinyl)carbonyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

370 1-Ethyl-N-[2-(2-oxo-1-pyrrolidinyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

371 1-Ethyl-N-[3-(methylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

372 N-{3-[Acetyl(methyl)amino]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

373 1-Ethyl-N-{3-[(methylsulfonyl)amino]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

374 1-Ethyl-N-(4-fluoro-2-hydroxyphenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

375 N-(4-Chlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

376 N-(3-Chloro-2-cyanophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

377 1-Ethyl-N-[3-(1-piperidinylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

379 1-Ethyl-N-[2-(methylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-

b]pyridine-5-carboxamide

380 N-{2-[Acetyl(methyl)amino]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

381 1-Ethyl-N-[3-(4-morpholinylcarbonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

382 N-(4-Chloro-3-cyanophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

383 1-Ethyl-N-(3-hydroxyphenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

384 N-(3-Chlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

386 N-[3-[(Acetylamino)methyl]-4-(methyloxy)phenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

387 1-Ethyl-N-[4-(1-piperidinylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

388 N-(3-{[Cyclohexyl(methyl)amino]carbonyl}phenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

389 1-Ethyl-N-[2-(4-morpholinyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

390 N-{3-[(Acetylamino)sulfonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

391 N-(3-Chloro-4-hydroxyphenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

392 1-Ethyl-N-{4-[(methylsulfonyl)amino]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

393 1-Ethyl-N-{3-[(methylamino)carbonyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

394 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[3-(trifluoromethyl)phenyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

395 1-Ethyl-N-3-pyridinyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

396 N-(3,4-Dichlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

397 N-[3-(Aminosulfonyl)-4-chlorophenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

398 1-Ethyl-N-[3-(4-morpholinyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

399 1-Ethyl-N-[4-(4-morpholinylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

400 1-Ethyl-N-{2-[(4-methyl-1-piperazinyl)carbonyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

401 N-{2-[(Dimethylamino)carbonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

402 N-[2-Chloro-4-(trifluoromethyl)phenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

403 N-{2-[(Acetylamino)methyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

404 N-(2-Chlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

405 N-(3-Chloro-2-fluorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

406 1-Ethyl-N-(3-fluorophenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

407 N-(2-Cyano-3-fluorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

408 1-Ethyl-N-[4-(propylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

409 N-{4-[(Dimethylamino)carbonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

411 1-Ethyl-N-[4-(methylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

413 N-{4-[(Acetylamino)methyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

414 1-Ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

415 N-[2-(Aminosulfonyl)ethyl]-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

416 N-(2-Amino-2-oxoethyl)-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide (non-preferred name)

417 4-(Cyclohexylamino)-1-ethyl-N-{2-[(methylsulfonyl)amino]ethyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

418 4-(Cyclohexylamino)-1-ethyl-N-(tetrahydro-2H-pyran-4-yl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

419 4-(Cyclohexylamino)-1-ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

420 4-(Cyclohexylamino)-1-ethyl-N-{[3-(methylsulfonyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

421 N-{[3-(Aminocarbonyl)phenyl]methyl}-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

422 4-(Cyclohexylamino)-1-ethyl-N-(tetrahydro-2-furanylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

423 4-(Cyclohexylamino)-N-({4-[(dimethylamino)sulfonyl]phenyl}methyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

424 N-[(5-Chloro-2-pyridinyl)methyl]-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

425 4-(Cyclohexylamino)-1-ethyl-N-{[4-(methylsulfonyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

426 4-(Cyclohexylamino)-1-ethyl-N-{[6-(methyloxy)-3-pyridinyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

427 4-(Cyclohexylamino)-1-ethyl-N-{4-[(methylamino)carbonyl]phenyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

428 4-(Cyclohexylamino)-1-ethyl-N-({3-[(methylamino)carbonyl]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

429 N-{[4-(Aminocarbonyl)phenyl]methyl}-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

430 4-(Cyclohexylamino)-1-ethyl-N-[(4-hydroxyphenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

431 4-(Cyclohexylamino)-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

432 4-(Cyclohexylamino)-N-[(3,4-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

433 4-(Cyclohexylamino)-1-ethyl-N-{[4-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

434 4-(Cyclohexylamino)-1-ethyl-N-({3-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

435 4-(Cyclohexylamino)-N-[(2,5-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

436 4-(Cyclohexylamino)-1-ethyl-N-[(4-methylphenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

438 4-(Cyclohexylamino)-1-ethyl-N-(2-{4-[(methylsulfonyl)amino]phenyl}ethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

439 4-(Cyclohexylamino)-1-ethyl-N-[(2-hydroxyphenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

440 4-(Cyclohexylamino)-N-[(3,4-dichlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

441 4-(Cyclohexylamino)-N-[(3,5-dichlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

442 4-(Cyclohexylamino)-1-ethyl-N-(2-phenylethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

443 4-(Cyclohexylamino)-1-ethyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

444 4-(Cyclohexylamino)-1-ethyl-N-{[2-(methylsulfinyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

445 4-(Cyclohexylamino)-1-ethyl-N-[2-(4-hydroxyphenyl)ethyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

446 N-{2-[4-(Aminosulfonyl)phenyl]ethyl}-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

447 4-(Cyclohexylamino)-1-ethyl-N-({2-[(methylamino)carbonyl]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

448 4-(Cyclohexylamino)-1-ethyl-N-{[2-(methylsulfonyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

449 Methyl 2-[({[4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate

450 4-(Cyclohexylamino)-1-ethyl-N-{2-[4-(methylsulfonyl)phenyl]ethyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

451 N-[4,5-Bis(methyloxy)-2,3-dihydro-1H-inden-2-yl]-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

452 4-(Cyclohexylamino)-1-ethyl-N-{[2-fluoro-3-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

453 4-(Cyclohexylamino)-N-[(3,4-dimethylphenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

454 4-(Cyclohexylamino)-1-ethyl-N-[2-(4-fluorophenyl)ethyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

455 4-(Cyclohexylamino)-1-ethyl-N-[2-(4-methylphenyl)ethyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

456 4-(Cyclohexylamino)-1-ethyl-N-{2-[4-(methyloxy)phenyl]ethyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

457 4-(Cyclohexylamino)-1-ethyl-N-(2-pyridinylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

458 4-(Cyclohexylamino)-N-[(3,5-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

459 4-(Cyclohexylamino)-N-(2,3-dihydro-1H-inden-1-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

460 4-(Cyclohexylamino)-N-{[4-(dimethylamino)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

461 4-(Cyclohexylamino)-1-ethyl-N-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

462 N-{[2,4-Bis(methyloxy)phenyl]methyl}-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

463 N-[(6-Chloro-2-pyridinyl)methyl]-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

464 N-({2-[Acetyl(methyl)amino]phenyl}methyl)-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

465 4-(Cyclohexylamino)-1-ethyl-N-{[4-fluoro-3-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

466 4-(Cyclohexylamino)-N-[(1R)-2,3-dihydro-1H-inden-1-yl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

467 4-(Cyclohexylamino)-N-[(2,6-dichlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

468 Methyl 3-[({[4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate

469 4-(Cyclohexylamino)-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

470 Methyl 4-[({[4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-

yl]carbonyl}amino)methyl]benzoate

471 4-(Cyclohexylamino)-1-ethyl-N-(1H-tetrazol-5-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

472 4-(Cyclohexylamino)-N-({4-[(difluoromethyl)oxy]phenyl}methyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

473 4-(Cyclohexylamino)-1-ethyl-N-[(2-methyl-1,3-thiazol-4-yl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

474 N-[(2-Chloro-6-fluorophenyl)methyl]-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

475 N-{[2-(Aminocarbonyl)phenyl]methyl}-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

477 4-(Cyclohexylamino)-N-{[2-(dimethylamino)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

478 4-(Cyclohexylamino)-1-ethyl-N-[(4-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

479 4-(Cyclohexylamino)-1-ethyl-N-{[3-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

480 4-(Cyclohexylamino)-N-[(2,6-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

481 4-(Cyclohexylamino)-1-ethyl-N-[(3-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

482 4-(Cyclohexylamino)-1-ethyl-N-{[2-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

483 N-(5-Chloro-2,3-dihydro-1H-inden-2-yl)-4-(cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

484 4-(Cyclohexylamino)-1-ethyl-N-({4-[(methylamino)carbonyl]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

485 4-(Cyclohexylamino)-1-ethyl-N-[4-(methyloxy)phenyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

486 4-(cyclohexylamino)-1-ethyl-N-[(6-oxo-1,6-dihydro-3-pyridinyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

487 4-(Cyclohexylamino)-1-ethyl-N-(3-pyridinylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

488 4-[({[4-(Cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid

489 3-[({[4-(Cyclohexylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid

490 4-(Cyclohexylamino)-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide hydrochloride

491 4-(Cyclohexylamino)-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide methanesulphonate

492 N-({2-[(1,1-Dimethylethyl)oxy]-3-pyridinyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

493 N-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

494 N-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

495 N-({2-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

496 1-Ethyl-N-({2-[(1-methylethyl)oxy]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

497 1-Ethyl-N-({3-[(1-methylethyl)oxy]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

498 N-({3-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

499 1-Ethyl-N-{[4-hydroxy-3-(methyloxy)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

500 N-[(5-Acetyl-2-hydroxyphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

501 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-{2-[3-(trifluoromethyl)phenyl]ethyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

502 N-{[4-(Acetylamino)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

503 1-Ethyl-N-[2-(3-hydroxyphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

504 N-[2-(3-Chlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

505 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-(2-{4-[(trifluoromethyl)oxy]phenyl}ethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

506 1-Ethyl-N-{2-[3-(methyloxy)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

507 N-[2-(4-Acetylphenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

508 N-[2-(3,4-Dichlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

509 N-{2-[3-(Aminosulfonyl)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

510 N-{2-[3,4-Bis(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

512 N-[2-(2,3-Dichlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

513 N-{2-[3,5-Bis(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

514 1-Ethyl-N-{2-[3-methyl-4-(methyloxy)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

515 N-[2-(2,6-Difluorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-

pyrazolo[3,4-b]pyridine-5-carboxamide

516 N-{2-[2,6-Bis(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

517 1-Ethyl-N-[2-(2-methylphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

518 N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

519 N-[4,5-Bis(methyloxy)-2,3-dihydro-1H-inden-2-yl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

521 N-{2-[4-(Aminosulfonyl)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

522 1-Ethyl-N-{[2-(methylsulfinyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

523 1-Ethyl-N-(2-phenylethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

524 N-{[4-(Dimethylamino)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

525 1-Ethyl-N-[2-(4-fluorophenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

526 1-Ethyl-N-[2-(4-methylphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

527 N-{[3-(Aminosulfonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

528 1-Ethyl-N-[(4-methylphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

530 1-Ethyl-N-{[4-fluoro-3-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

531 Methyl 2-[({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate

532 N-[(6-Chloro-2-pyridinyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

533 N-(2,3-Dihydro-1H-inden-1-yl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

534 N-({2-[Acetyl(methyl)amino]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

535 N-[(1S)-2,3-Dihydro-1H-inden-1-yl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

536 N-[(1R)-2,3-Dihydro-1H-inden-1-yl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

537 1-Ethyl-N-({3-[(methylsulfonyl)amino]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

538 1-Ethyl-N-(phenylmethyl)-N-propyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

540 N-[2-(Dimethylamino)ethyl]-1-ethyl-N-(phenylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

541 N-Butyl-1-ethyl-N-(phenylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

542 N,1-Diethyl-N-(phenylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

544 1-Ethyl-N-(1-phenyl-4-piperidinyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

545 1-ethyl-N-{1-[(ethylamino)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

546 Formic acid - 1-ethyl-N-[1-methyl-2-(4-methyl-1-piperazinyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide (1:1)

547 Methyl [4-({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)-1-piperidinyl]acetate

548 1-Ethyl-N-{[4-(4-morpholinylmethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

549 1-Ethyl-N-({3-[(4-methyl-1-piperazinyl)methyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

550 N-{[5-(Aminocarbonyl)-3-pyridinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

551 1-Ethyl-N-{[4-(1-methylethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

552 N-{[3-(Cyclopentyloxy)-4-(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

553 1-Ethyl-N-({4-[(4-methyl-1-piperazinyl)methyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

554 N-[(2,4-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

555 N-[(2,4-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

556 N-[(2-Chloro-4-fluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

557 N-{2-[2-Chloro-3-(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

558 Methyl 3-[({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate

559 1-Ethyl-N-{[3-(1-pyrrolidinylmethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate

560 1-Ethyl-N-(2-{4-[(methylsulfonyl)amino]phenyl}ethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

561 N-{[2,5-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

562 N-{[2,6-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-

pyrazolo[3,4-b]pyridine-5-carboxamide

563 1-Ethyl-N-[(2-fluorophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

564 N-[(3,5-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

565 N-[(4-Chlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

567 N-Cyclohexyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

568 1-Ethyl-N-{2-[4-(methylsulfonyl)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

569 1-Ethyl-N-{[2-fluoro-3-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

570 N-({4-[(Cyclopropylamino)carbonyl]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

571 1-Ethyl-N-{[4-(4-methyl-1-piperazinyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

572 1-Ethyl-N-{[4-(1-pyrrolidinylmethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

573 1-Ethyl-N-[6-(methyloxy)-1-oxo-2,3-dihydro-1H-inden-2-yl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

574 N-[(2,5-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

575 N-[(3,5-Diethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

576 N-[(2,3-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

577 1-Ethyl-N-{[2-(methylsulfonyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

578 1-Ethyl-N-[(3-hydroxyphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

579 N-{[3,5-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

580 1-Ethyl-N-[2-(4-hydroxyphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

581 N-[(3,5-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

582 N-{[2,4-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

583 1-Ethyl-N-{[2-(methyloxy)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

584 N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

585 1-Ethyl-N-({2-[(methylamino)carbonyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

586 1-Ethyl-N-{2-[4-(methyloxy)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

587 N-[(2-Chlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

588 1-Ethyl-N-[(2-hydroxyphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

589 N-(1,3-Benzodioxol-5-ylmethyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

590 1-Ethyl-N-[3-(methyloxy)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

591 N-(Cyclohexylmethyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

592 1-Ethyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

593 Methyl 4-[({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate

594 N-[(3,4-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

595 N-{[4-(Aminocarbonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

596 N-[(2,6-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

597 N-{[3-(Aminocarbonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

598 1-Ethyl-N-[(4-hydroxyphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

599 1-Ethyl-N-{[6-(methyloxy)-3-pyridinyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

600 1-Ethyl-N-(2-pyridinylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

601 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-{[3-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

602 N-[4-(2-Amino-2-oxoethyl)phenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

603 1-Ethyl-N-({4-[(methylamino)carbonyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

604 1-Ethyl-N-{4-[2-(methylamino)-2-oxoethyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

605 1-Ethyl-N-[(3-fluorophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

606 1-Ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-

1H-pyrazolo[3,4-b]pyridine-5-carboxamide

607 N-{[4-(Aminosulfonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

608 N-{[2-(Aminocarbonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

609 N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

610 N-({3-[(Dimethylamino)methyl]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

611 N-{[3-Chloro-4-(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

612 N-(1-Acetyl-4-piperidinyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

613 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-{[2-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

615 N-(5-Chloro-2,3-dihydro-1H-inden-2-yl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

616 N-({3-[(Acetylamino)methyl]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

617 1-Ethyl-N-[(4-fluorophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

618 1-Ethyl-N-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

619 1-Ethyl-N-[(2-ethylphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

620 1-Ethyl-N-{[2-fluoro-5-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

621 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[(2,3,4-trifluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

622 N-[(4-Chloro-2-fluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

623 N-[(4-Bromo-2-fluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

624 N-[(3,5-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

625 N-[(2,3-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

626 N-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

627 N-[(4-Cyanophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

628 N-[(4-Bromophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

629 1-Ethyl-N-{[5-fluoro-2-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

630 1-Ethyl-N-[(4-iodophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

631 N-{[4-(1,1-Dimethylethyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

632 N-[(3-Cyanophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

633 N-[(2,6-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

634 N-[(5-Chloro-2-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

635 N-[(3,5-Dibromophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

636 1-Ethyl-N-[(4-ethylphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

637 1-Ethyl-N-{[3-fluoro-4-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

638 1-Ethyl-N-[(2-iodophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

639 N-[(2-Bromophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

640 1-Ethyl-N-{[4-(hydroxymethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

641 1-Ethyl-N-{[3-(hydroxymethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

642 1-Ethyl-N-{[3-(hydroxymethyl)-2-methylphenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

643 N-{[2,3-Dichloro-6-(hydroxymethyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

644 N-[(2,4-Dichloro-6-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

645 1-Ethyl-N-{[4-(2-methylpropyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

646 N-[(2,5-dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

647 1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[(2,4,5-trifluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

648 1-Ethyl-N-{[2-fluoro-4-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

649 N-[(2-Chloro-6-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

650 4-[({[1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-

yl]carbonyl}amino)methyl]benzoic acid sodium salt

651 3-[({[1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid

652 Ethyl 1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

653 1-Ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

654 N-{[4-(Dimethylamino)phenyl]methyl}-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

655 1-Ethyl-4-({4-[(ethyloxy)imino]cyclohexyl}amino)-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

656 1-Ethyl-4-({4-[(methyloxy)imino]cyclohexyl}amino)-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

657 4-[(4-{[(1,1-Dimethylethyl)oxy]imino}cyclohexyl)amino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

658 1-Ethyl-N-{[4-(methyloxy)phenyl]methyl}-4-[(7-oxohexahydro-1H-azepin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

659 Ethyl 1-ethyl-4-[(7-oxohexahydro-1H-azepin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

660 4-{[cis-4-(Butylamino)cyclohexyl]amino}-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

661 4-[(trans-4-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

662 4-[(trans-2-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

663 4-[(cis-2-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

664 4-[(3-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

Example No.	Name
665	Ethyl 1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
666	*N*,1-Diethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
667	1-Ethyl-*N*-(4-fluorophenyl)-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
668	1-Ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-(1,3-thiazol-2-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide
669	1-ethyl-*N*-[(4-fluorophenyl)methyl]-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

670 1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-{[4-(methylsulfonyl)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

671 *N*-{[3,4-bis(methyloxy)phenyl]methyl}-1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

672 1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-(2-pyridinylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

673 1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

674 *N*-[(3,4-dimethylphenyl)methyl]-1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

675 1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-{[4-(methyloxy)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

676 *N*-[(2,4-dimethylphenyl)methyl]-1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

667 *N*-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

678 *N*-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

679 *N*-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

680 *N*-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

681 *N*-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

682 *N*-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

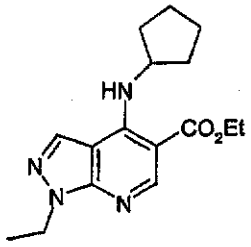
683 *N*-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

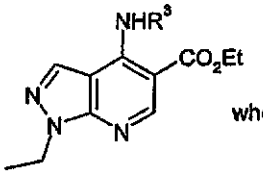
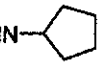
684 *N*-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

685 *N*-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

686 1-Ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-*N*-{[4-(trifluoromethyl)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

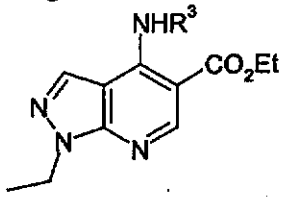
Example 1: Ethyl 4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



That is, Example 1 is  where NHR^3 = 

Intermediate 1 (0.051g) and cyclopentyl amine (0.019g) were suspended in ethanol (2ml) and triethylamine (0.14ml) was added. The mixture was stirred under nitrogen and heated at 80°C for 16h. After cooling to room temperature, ethanol was removed by evaporation under a stream of nitrogen and the residue partitioned between dichloromethane (DCM) and water. The layers were separated and the organic layer was loaded directly onto an solid phase extraction (SPE) cartridge (silica, 5g) which was eluted sequentially with; (i) DCM, (ii) DCM : Et_2O (2:1), (iii) DCM : Et_2O (1:1), (iv) Et_2O, (v) EtOAc, (vi) MeOH. Fractions containing desired material were combined and concentrated in vacuo to afford Example 1 (0.074g). LCMS showed $MH^+ = 303$; $T_{RET} = 3.45$min.

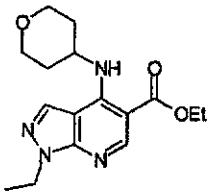
Similarly prepared were the following:



	NHR^3	Amine reagent	MH^+ ion	T_{RET} (min)
Example 2		Cyclohexyl amine	317	3.65
Example 3 (= Intermediate 32)		4-Amino tetrahydropyran	319	2.93
Example 5 (= Example 207*)		Intermediate 6	360	3.20

* For alternative synthesis of Example 5, see Example 207 hereinafter

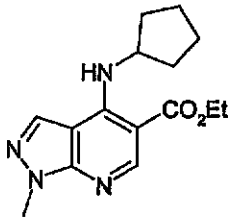
Example 3 (=Intermediate 32): Ethyl 1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



Instead of the method shown above for Examples 1-5 (called Method A), the compound of Example 3 can also be made: either using the minor variation of Method A described in detail under "Intermediate 32" hereinabove, or using the following Method B:

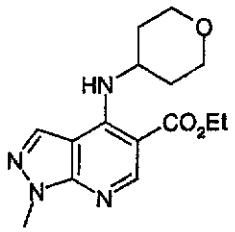
Example 3, Method B: Intermediate 1 (2.5g) was dissolved in acetonitrile (15ml). 4-Aminotetrahydropyran hydrochloride (1.1g) and N,N-diisopropylethylamine (9.4ml) were added and the mixture stirred under nitrogen at 85°C for 16h. A trace of starting material remained, so an additional portion of 4-aminotetrahydropyran hydrochloride (0.11g) was added and stirring continued at 85°C for a further 16h. The mixture was then concentrated in vacuo. The residue was partitioned between DCM and water. The layers were separated and the organic layer was washed with further water (2x20ml) then dried (Na_2SO_4) and concentrated in vacuo. The residue was further purified by chromatography using Biotage (silica, 90g), eluting with cyclohexane : ethyl acetate to afford Example 3 (2.45g). LCMS showed $MH^+ = 319$; $T_{RET} = 2.90$min.

Example 6: Ethyl 4-(cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



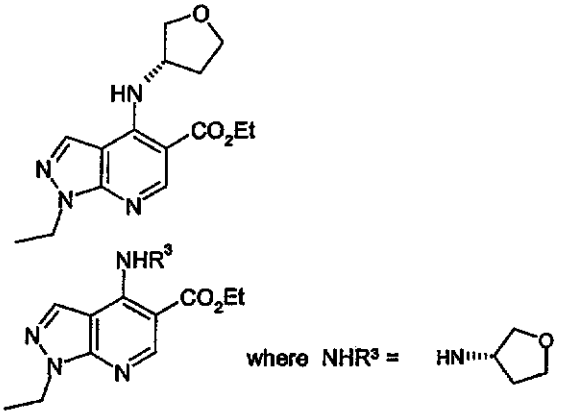
Intermediate 3 (0.045g) was placed in a Reactivial™ and treated with cyclopentyl amine (0.07ml). The mixture was heated at 90°C for 2h, then allowed to cool to room temperature and partitioned between chloroform (2ml) and water (1ml). The layers were separated and the organic phase was evaporated to a brown solid, which was purified by mass directed autoprep HPLC, to afford Example 6 as a white solid (0.008g). LCMS showed $MH^+ = 289$; $T_{RET} = 3.22$ min.

Example 7: Ethyl 1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



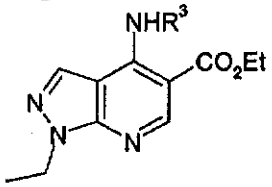
Intermediate 3 (0.035g) was placed in a Reactivial™ and treated with 4-amino tetrahydropyran (0.06ml). The mixture was heated at 90°C for 2h, then allowed to cool to room temperature and partitioned between chloroform (2ml) and water (1ml). The layers were separated and the organic phase was concentrated, then applied to a preparative TLC plate (silica, 20cm x 20cm x 1mm) which was eluted with ethyl acetate. The required band was removed from the plate and the silica washed with ethyl acetate (2 x 15ml). Concentration of the ethyl acetate solution *in vacuo* afforded Example 7 as a white solid (0.008g). LCMS showed $MH^+ = 305$; $T_{RET} = 2.67$ min.

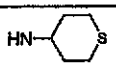
Example 8: Ethyl 1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



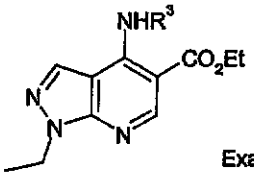
Intermediate 1 (0.05g) and (S)-(-)-3-aminotetrahydrofuran 4-toluene sulphonate (0.052g) were suspended in ethanol (1ml) and triethylamine (0.14ml) was added. The mixture was stirred under nitrogen and heated at 80°C for 24h. After cooling to room temperature, ethanol was removed by evaporation under a stream of nitrogen and the residue partitioned between DCM (2ml) and water (1.5ml). The layers were separated and the organic layer concentrated to dryness. Purification was carried out using an SPE cartridge (silica, 5g), eluting with a gradient of EtOAc : cyclohexane; (1:16 then, 1:8, 1:4, 1:2, 1:1 and 1:0). Fractions containing desired material were combined and concentrated in vacuo to afford Example 8 (0.052g). LCMS showed $MH^+ = 305$; $T_{RET} = 2.70$min.

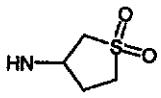
Similarly prepared were the following:



	NHR^3	Amine Reagent	MH^+ ion	T_{RET}(min)
Example 9		(R)-(+)-3-Aminotetrahydrofuran 4-toluene sulphonate	305	2.73
Example 10		Intermediate 11	335	3.21
Example 11 (mixture of enantiomers)		Intermediate 12	321	3.10
Example 12		Cyclopropyl amine	275	2.98

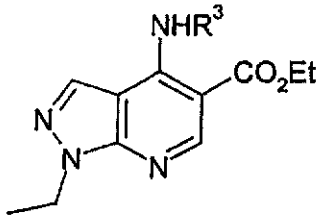
Example 13: Ethyl 4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

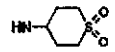


Example 13 NHR^3 = 

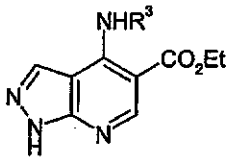
Intermediate 1 (0.05g) and Intermediate 13 (0.027g) were suspended in ethanol (1ml) and triethylamine (0.14ml) was added. The mixture was stirred under nitrogen and heated at 80°C for 24h. After cooling to room temperature, ethanol was removed by evaporation under a stream of nitrogen and the residue partitioned between DCM (2ml) and water (1.5ml). The layers were separated and the organic layer concentrated to dryness. Purification was carried out using an SPE cartridge (silica, 5g), eluting with a gradient of EtOAc : cyclohexane; (1:8 then 1:4, 1:2, 1:1 and 1:0). Fractions containing desired material were combined and concentrated in vacuo to afford Example 13 (0.045g) as a mixture of enantiomers. LCMS showed $MH^+ = 353$; $T_{RET} = 2.60$min.

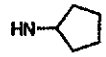
Similarly prepared was the following:



	NHR3	Amine Reagent	MH+ ion	T_{RET}(min)
Example 14		Intermediate 14	367	2.64

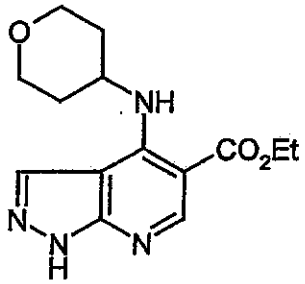
Example 19 (reference example, as an intermediate): Ethyl 4-(cyclopentylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

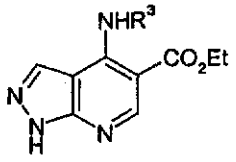
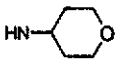


Example 19 NHR³ = 

Intermediate 2 (0.035g) was placed in a Reactivial™ and treated with cyclopentyl amine (0.05ml). The mixture was heated at 90°C for 1.5h, then allowed to cool to room temperature and partitioned between chloroform (2ml) and water (1ml). The layers were separated and the organic phase was concentrated. The residual solid was triturated with Et_2O and the insoluble off-white solid collected and air-dried to afford Example 19 (0.016g). LCMS showed $MH^+ = 275$; $T_{RET} = 2.58$ min.

Example 20 (reference example, as an intermediate): Ethyl 4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate



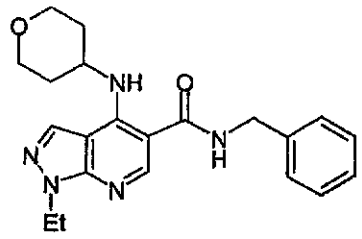
that is:  Example 20 NHR^3 = 

Intermediate 2 (0.035g) was placed in a Reactivial™ and treated with 4-aminotetrahydropyran (0.05ml). The mixture was heated at 90°C for 1.5h, then allowed to cool to room temperature and partitioned between chloroform (2ml) and water (1ml). The layers were separated and the organic phase was concentrated. The crude product was purified by mass directed autoprep HPLC to afford Example 20 as an off-white solid (0.011g). LCMS showed MH^+= 291; T_{RET} = 2.08 min.

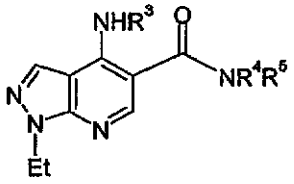
Alternative synthetic method for Example 20:

Intermediate 2 (2g) was suspended in 4-aminotetrahydropyran (2g), and the mixture was heated at 90 °C for 6h. The residual mixture was allowed to cool to room temperature and partitioned between chloroform (50ml) and water (50ml). The phases were separated and the organic phase was evaporated to dryness. The residue was triturated with Et_2O (30ml) and the insoluble solid was collected and dried to afford Example 20 as a cream solid (2.24g). LCMS showed MH^+= 291; T_{RET} = 2.19min.

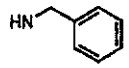
Example 21: N-benzyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



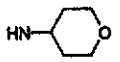
that is, Example 21 is:



wherein NR^4R^5 =



NHR^3 =



Three alternative methods, A, B and C, have been used to make Example 21, as follows:

Example 21, Method A:

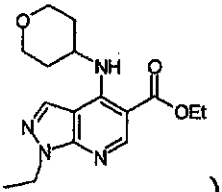
A solution of the 4-chloro Intermediate 17 (0.031g, 0.1 mmol) in ethanol (1.9ml) was treated with triethylamine (0.07ml, 0.5 mmol), followed by a 0.1M ethanolic solution of 4-aminotetrahydropyran (Intermediate 8, 1.1ml of the 0.1M ethanolic solution = 0.11 mmol). The mixture was heated at reflux (80°C) for 18h. A further portion of 4-amino-tetrahydropyran (0.01ml of undiluted amine, not a solution thereof) was then added and heating continued for a further 24h. Volatiles were removed in vacuo and the residue dissolved in dichloromethane (DCM), then applied to an solid phase extraction (SPE) cartridge (aminopropyl, 1g) which was eluted first with DCM, then with methanol. Fractions containing desired material were concentrated in vacuo to afford Example 21 (0.004g). LCMS showed $MH^+ = 380$; $T_{RET} = 2.92$min.

Example 21 , Method B:

Intermediate 17 (0.031g, 0.1 mmol) was dissolved in acetonitrile (1ml). 4-Aminotetrahydropyran hydrochloride (Intermediate 8A, 0.015g, 0.11 mmol) and N,N-diisopropylethylamine (0.08ml, 0.5 mmol) were added and the mixture stirred under nitrogen at 85°C for 16h, then concentrated in vacuo. The residue was partitioned between dichloromethane (DCM) and water. The layers were separated and the organic layer was concentrated in vacuo to afford Example 21 (0.027g). LCMS showed $MH^+ = 380$; $T_{RET} = 2.92$ min.

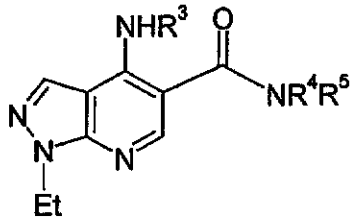
Example 21 , Method C:

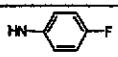
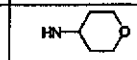
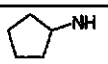
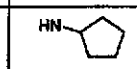
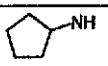
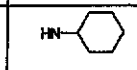
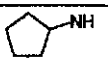
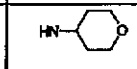
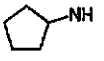
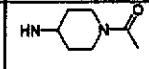
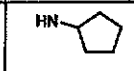
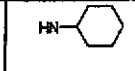
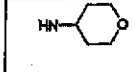
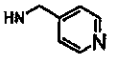
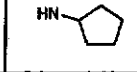
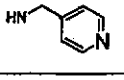
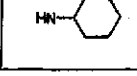
This alternative route C to Example 21 involves formation of the ester of Example 3 =

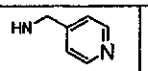
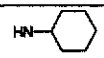
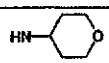


Intermediate 32 ( ) using one of the methods described above, conversion of the ester of Example 3 / Intermediate 32 into the carboxylic acid (Intermediate 33) using the method given above for Intermediate 33, and then amide bond formation to form Example 21 using the method of Examples 81-84 below.

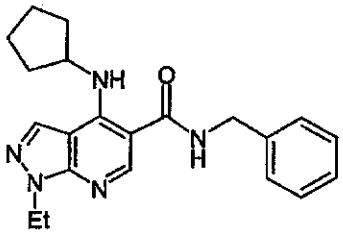
The following compounds can be similarly prepared using one or more of Methods A, B or C above, preferably Method A or B:



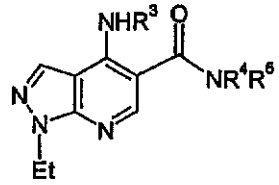
	NR^4R^5	NHR^3	Starting Material (for Method A or B)	Amine Reagent	MH^+ ion	T_{RET} (min)
Example 22			Intermediate 19	4-amino tetrahydropyran	384	3.09
Example 23			Intermediate 20	Cyclopentyl amine	342	3.29
Example 24			Intermediate 20	Cyclohexyl amine	356	3.47
Example 25			Intermediate 20	4-amino tetrahydropyran	358	2.79
Example 27			Intermediate 20	Intermediate 6	400	2.64
Example 28			Intermediate 21	Cyclopentyl amine	328	2.69
Example 29			Intermediate 21	Cyclohexyl amine	342	2.87
Example 30			Intermediate 21	4-amino tetrahydropyran	344	2.33
Example 31			Intermediate 22	Cyclopentyl amine	365	2.38
Example 32			Intermediate 22	Cyclohexyl amine	379	2.54

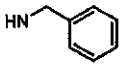
Example 33			Intermediate 22	4-amino tetrahydropyran	381	2.09
Example 34	NH_2		Intermediate 24	Cyclopentyl amine	274	2.59
Example 35	NH_2		Intermediate 24	Cyclohexyl amine	288	2.79
Example 36	NH_2		Intermediate 24	4-amino tetrahydropyran	290	2.22

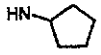
<u>Example 39:</u> N-Benzyl-4-(cyclopentylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



that is, Example 39 is:

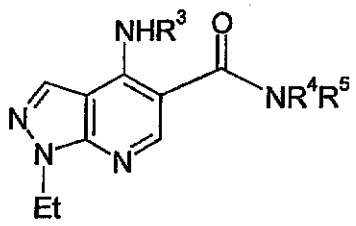


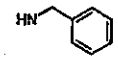
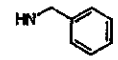
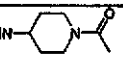
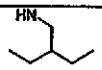
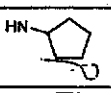
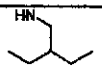
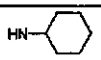
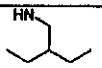
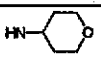
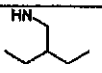
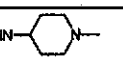
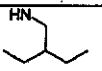
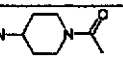
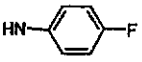
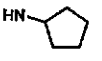
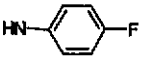
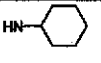
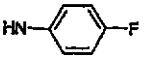
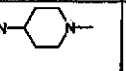
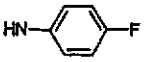
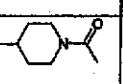
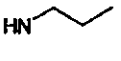
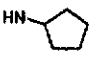
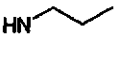
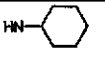
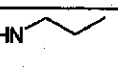
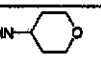
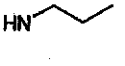
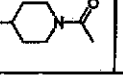
wherein NR^4R^5 = 

NHR^3 = 

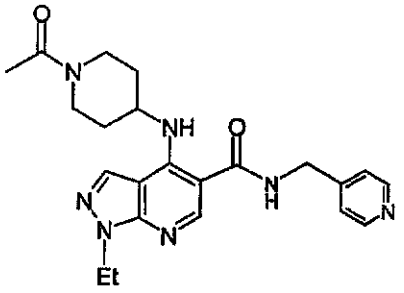
A solution of Intermediate 17 (0.031g, 0.1 mmol) in ethanol (1ml) was treated with triethylamine (0.07ml, 0.5 mmol), followed by a 0.1M ethanolic solution of cyclopentyl amine (1.1ml of the 0.1M ethanolic solution = 0.11 mmol). The mixture was heated at reflux (80°C) for 18h. A further portion of cyclopentyl amine (0.009ml of undiluted amine, not a solution thereof) was then added and heating continued for a further 24h. Volatiles were removed in vacuo and the residue dissolved in DCM, then applied to an SPE cartridge (aminopropyl, 1g) which was eluted first with DCM, then with methanol. The DCM fraction was concentrated in vacuo, then applied to an SPE cartridge (silica, 0.5g) which was eluted sequentially with (i) DCM, (ii) Et_2O, (iii) EtOAc and (iv) MeOH. Fractions containing desired material were combined to afford Example 39 (0.007g). LCMS showed $MH^+ = 364$; $T_{RET} = 3.38$min.

Similarly prepared were the following:

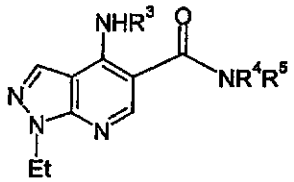


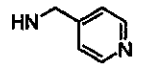
	NR^4R^5	NHR^3	Starting Material	Amine reagent	MH^+ ion	T_{RET} (min)
Example 40			Intermediate 17	Cyclohexyl amine	378	3.43
Example 41			Intermediate 17	Intermediate 6	421	2.75
Example 42			Intermediate 18	Cyclopentyl amine	358	3.63
Example 43			Intermediate 18	Cyclohexyl amine	372	3.79
Example 44			Intermediate 18	4-amino tetrahydro-pyran	374	3.13
Example 45			Intermediate 18	Intermediate 7	387	2.37
Example 46			Intermediate 18	Intermediate 6	415	2.92
Example 47			Intermediate 19	Cyclopentyl amine	368	3.61
Example 48			Intermediate 19	Cyclohexyl amine	382	3.76
Example 49			Intermediate 19	Intermediate 7	397	2.29
Example 50			Intermediate 19	Intermediate 6	425	2.88
Example 51			Intermediate 23	Cyclopentyl amine	316	3.05
Example 52			Intermediate 23	Cyclohexyl amine	330	3.26
Example 53			Intermediate 23	4-amino tetrahydro-pyran	332	2.58
Example 55			Intermediate 23	Intermediate 6	373	2.46

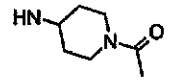
Example 57: 4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



that is, Example 57 is:



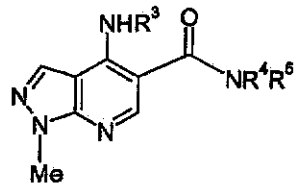
wherein NR^4R^5 = 

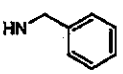
NHR^3 = 

A solution of Intermediate 22 (0.03g, *ca.* 0.1 mmol) in ethanol (1ml) was treated with triethylamine (0.07ml, 0.5 mmol), followed by a 0.1M ethanolic solution of Intermediate 6 (1.1ml of the solution = 0.11 mmol). The mixture was heated at reflux (80°C) for 18h. A further portion of Intermediate 6 (0.01ml, undiluted) was then added and heating continued for a further 24h. Volatiles were removed in vacuo and the residue dissolved in DCM, then applied to an SPE cartridge (aminopropyl, 1g) which was eluted first with DCM, then with methanol.

The DCM fraction was concentrated in vacuo, then applied to an SPE cartridge (silica, 0.5g) eluting with (I) DCM, (ii) EtOAc and (iii) a stepwise gradient of chloroform : methanol (from 99:1 up to 4:1). Fractions containing desired material were combined to afford Example 57 (0.003g). LCMS showed $MH^+ = 422$; $T_{RET} = 2.1$min.

Example 61: N-Benzyl-4-(cyclopentylamino)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



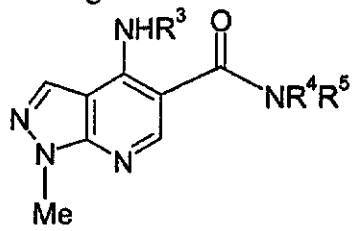
Example 61 NR^4R^5 = 

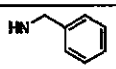
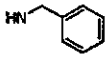
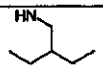
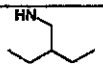
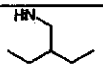
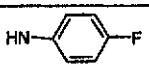
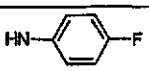
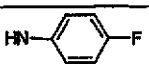
NHR^3 = 

A solution of Intermediate 28 (0.03g, 0.1 mmol) in ethanol (1ml) was treated with a 0.1M ethanolic solution of cyclopentyl amine (1.1ml of solution = 0.11 mmol). Triethylamine (0.07ml, 0.5 mmol) was then added and the mixture heated at reflux (85°C), under

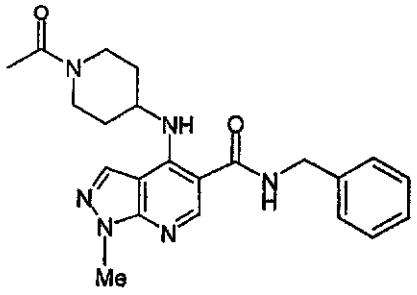
nitrogen for 12h. A further portion of cyclopentyl amine (0.009ml, undiluted) was then added and heating continued for a further 36h. The mixtures were concentrated in vacuo and the residue treated with chloroform. A small amount of insoluble material was collected by filtration, then the filtrate applied to an SPE cartridge (aminopropyl, 1g) which was eluted first with DCM, then with methanol. Fractions containing desired material were combined to afford Example 61 (0.039g). LCMS showed $MH^+ = 350$; $T_{RET} = 2.88$min.

Similarly prepared were the following:

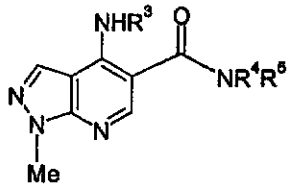


	NR^4R^5	NHR^3	Starting Material	Amine Reagent	MH^+ ion	T_{RET} (min)
Example 62			Intermediate 28	Cyclohexyl amine	364	3.05
Example 63			Intermediate 28	4-amino tetrahydropyran	366	2.52
Example 64			Intermediate 30	Cyclopentyl amine	344	3.06
Example 65			Intermediate 30	Cyclohexyl amine	358	3.23
Example 66			Intermediate 30	4-amino tetrahydropyran	360	2.69
Example 67			Intermediate 29	Cyclopentyl amine	354	3.17
Example 68			Intermediate 29	Cyclohexyl amine	368	3.33
Example 69			Intermediate 29	4-amino tetrahydropyran	370	2.72
Example 70	NH_2		Intermediate 31	Cyclopentyl amine	260	2.10
Example 71	NH_2		Intermediate 31	Cyclohexyl amine	274	2.29

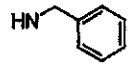
Example 74: 4-[(1-Acetylpiperidin-4-yl)amino]-N-benzyl-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



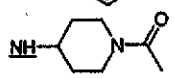
that is, Example 74 is:



wherein NR^4R^5 =

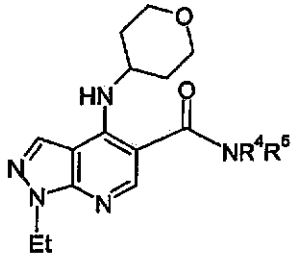


NHR^3 =



A solution of Intermediate 28 (0.03g, 0.1 mmol) in ethanol (1ml) was treated with a 0.1M ethanolic solution of Intermediate 6 (1.1ml of solution = 0.11 mmol). Triethylamine (0.07ml, 0.5 mmol) was then added and the mixture heated at reflux (85°C), under nitrogen for 12h. A further portion of Intermediate 6 (0.1 mmol) was then added and heating continued for a further 36h. The mixtures were concentrated in vacuo and the residue treated with chloroform. A small amount of insoluble material was collected by filtration, then the filtrate applied to an SPE cartridge (aminopropyl, 1g) which was eluted first with DCM, then with methanol. Fractions containing desired material were combined and concentrated in vacuo. The residue was further purified by SPE (silica, 0.5g) eluting with (i) DCM, (ii) chloroform, (iii) EtOAc and (iv) a stepwise gradient of chloroform : methanol (from 99:1 up to 4:1). Fractions containing desired material were combined to afford Example 74 (0.029g). LCMS showed $MH^+ = 407$; $T_{RET} = 2.57$ min.

Example 81: 1-Ethyl-N-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

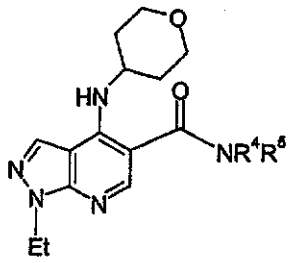


Example 81 NR^4R^5 = NHMe

To a stirred suspension of Intermediate 33 (0.025g, ca. 0.08 to 0.09 mmol) in chloroform (2ml) was added thionyl chloride (0.025ml) and the mixture stirred at room temperature

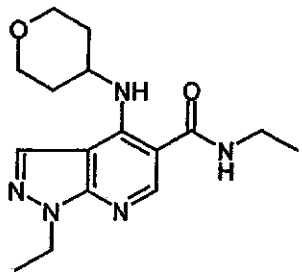
for 1h. The mixture was cooled to 0°C and methylamine added (2M solution in THF, 0.69ml = 1.38 mmol). After returning to room temperature the mixture was stirred for a further 1h, then quenched by addition of water (4ml) and the layers separated. The organic layer was concentrated then applied to an SPE cartridge (silica, 1g) which was eluted with (i) DCM, (ii) Et_2O (2:1), (iii) EtOAc, (iv) MeOH: EtOAc (1:9). Fractions containing desired material were combined to afford Example 81 (0.019g). LCMS showed $MH^+ = 304$; $T_{RET} = 2.19$min.

Similarly prepared:



	NR^4R^5	Amine reagent	MH^+ ion	T_{RET} (min)
Example 82	NMe_2	Dimethylamine (2M in THF)	318	2.06
Example 83	NHEt	Ethylamine (2M in THF)	318	2.31
Example 84	NH^iPr	Isopropylamine (2M in THF)	332	2.44

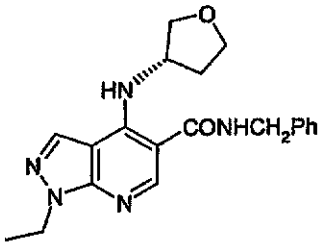
Example 83: *N*,1-Diethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide; also named 1-ethyl-*N*-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



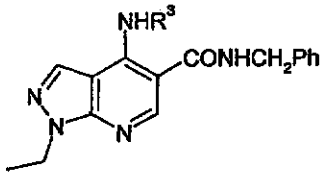
In an alternative embodiment to the process described for Examples 81-84 above, Example 83 can be made according to the following method:
A mixture of Intermediate 33 (3.0g, 10.33mmol), EDC (2.25g, 11.7mmol), and HOBT (1.68g, 12.4mmol) was stirred at room temperature for 1 hour. Ethylamine (6.2ml,

12.4mmol, 2M-solution in THF) was added, and stirring was continued at room temperature for 22 hours. The solvents were removed in vacuo, and the residual solid was dissolved in chloroform (250ml) and washed successively with water (70ml) and 5%-sodium hydrogen carbonate solution (70ml). After drying over anhydrous sodium sulphate, the organic solution was evaporated in vacuo to give a pale orange solid (4.15g). This solid was dissolved in a mixture of dichloromethane (15ml) and chloroform (5ml) and purified by-column chromatography (Biotage, silica, 100g), eluting initially with EtOAc-cyclohexane (2:1) and finally with neat EtOAc. The product containing fractions were combined and evaporated to give Example 83 as a pale yellow solid (3.05g). LCMS showed $MH^+ = 318$; $T_{RET} = 2.33$min. ^1H NMR (400MHz in d_6-DMSO, 27°C, δppm) 9.76 (d, 1H) 8.35 (s, 1H) 7.94 (s, 1H) 5.99 (br m, 1H) 4.47 (q, 2H) 4.16-4.01 (m's, 3H) 3.62 (m, 2H) 3.48 (m, 2H) 2.13 (m, 2H) 1.77 (m, 2H) 1.49 (t, 3H) 1.28 (t, 3H).

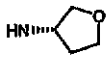
Example 85: N-Benzyl-1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



That is, Example 85 is:

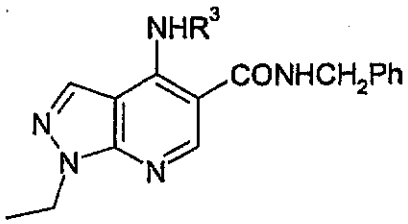


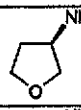
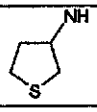
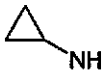
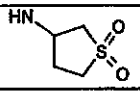
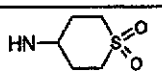
wherein NHR^3 =



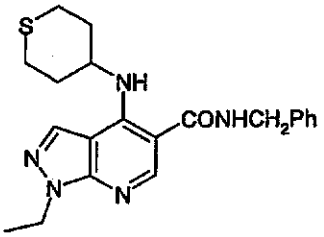
Intermediate 41 (0.017g, 0.062 mmol) was dissolved in DMF (2ml), then treated with HATU (0.023g) followed by diisopropylethyl amine (0.021ml) and the mixture stirred for 10 min. Benzylamine (0.007ml) was then added and stirring continued for a further 64h. The mixture was concentrated in vacuo and the residue dissolved in DCM (1.5ml) then treated with saturated aqueous sodium bicarbonate solution (1.5ml). This mixture was stirred for 30 min, then the layers were separated and the organic layer was applied to an SPE cartridge (silica, 1g) which was eluted sequentially with a gradient of ethyl acetate: cyclohexane (1:4, then 1:2, 1:1, 2:1 and 1:0). Fractions containing desired material were concentrated in vacuo to afford Example 85 (0.017g). LCMS showed $MH^+ = 366$; $T_{RET} = 2.80$min.

Similarly prepared were the following:



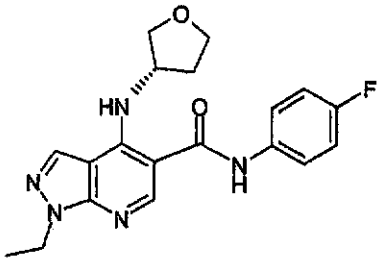
	NHR^3	Starting material	MH$^+$ ion	T_{RET} (min)
Example 86		Intermediate 42	366	2.80
Example 87		Intermediate 44	382	3.11
Example 88		Intermediate 45	336	3.00
Example 89		Intermediate 46	414	2.69
Example 90		Intermediate 47	428	2.75

Example 91: N-Benzyl-1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide

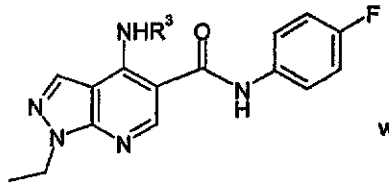


Intermediate 43 (0.019g) was dissolved in DMF (2ml), then treated with HATU (0.024g) followed by diisopropylethyl amine (0.022ml) and the mixture stirred for 10 min. Benzylamine (0.007ml) was then added and stirring continued for a further 64h. The mixture was concentrated in vacuo and the residue dissolved in DCM (1.5ml) then treated with saturated aqueous sodium bicarbonate solution (1.5ml). This mixture was stirred for 30 min, then the layers were separated and the organic layer applied to an SPE cartridge (silica, 1g) which was eluted sequentially with a gradient of ethyl acetate: cyclohexane (1:4, then 1:2, 1:1 and 1:0). Fractions containing desired material were concentrated in vacuo to afford Example 91 (0.023g). LCMS showed MH$^+$ = 396; T_{RET} = 3.26min.

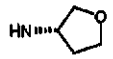
Example 92: 1-Ethyl-N-(4-fluorophenyl)-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide



that is, Example 92 is:

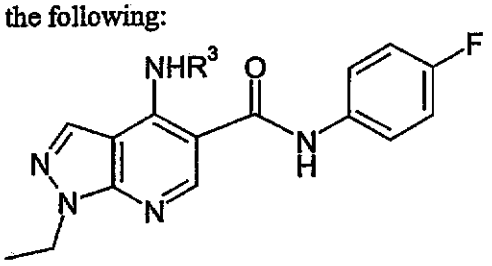


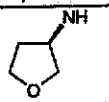
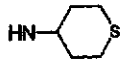
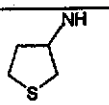
wherein NHR^3 =

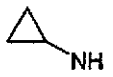
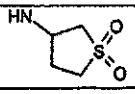
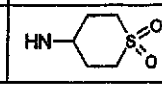


Intermediate 41 (0.017g) was dissolved in DMF (2ml), then treated with HATU (0.023g) followed by diisopropylethyl amine (0.021ml) and the mixture stirred for 10 min. 4-Fluoroaniline (0.006ml) was then added and stirring continued for a further 64h. The mixture was concentrated in vacuo and the residue dissolved in DCM (1.5ml) then treated with saturated aqueous sodium bicarbonate solution (1.5ml). This mixture was stirred for 30 min, then the layers were separated and the organic layer concentrated in vacuo. The crude mixture was purified by mass directed autoprep HPLC to afford Example 92 (0.013g). LCMS showed $MH^+ = 370$; $T_{RET} = 2.91$min.

Similarly prepared were the following:

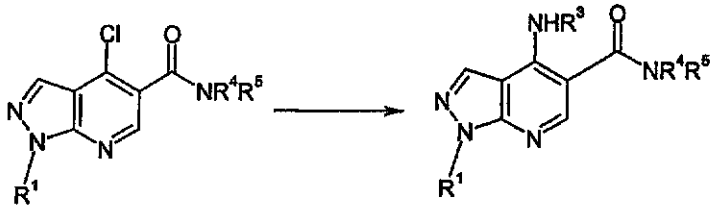


	NHR^3	Starting material	MH^+ ion	T_{RET} (min)
Example 93		Intermediate 42	370	2.91
Example 94		Intermediate 43	400	3.37
Example 95		Intermediate 44	386	3.27

Example 96		Intermediate 45	340	3.21
Example 97		Intermediate 46	418	2.80
Example 98		Intermediate 47	432	2.84

Example 99

In all of Examples 22 to 98, where a 4-amino 5-carboxamide Example of the following Formula I has been synthesised from the 4-chloro derivative, then an alternative final-step synthesis is as follows:

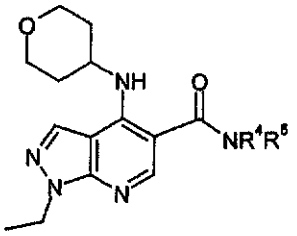


Formula IV

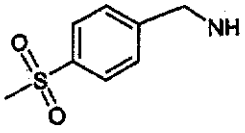
Formula I

An intermediate of Formula IV above (0.1mmol) was dissolved in acetonitrile (1ml). An amine of formula R^3NH_2 (0.11mmol, 1.1 mole equivalents) and N,N-diisopropylethylamine (0.5mmol, 5 mole equivalents) were added and the mixture stirred under nitrogen at 85°C for 16h. After concentration in vacuo, the residue was partitioned between dichloromethane (DCM) and water. The layers were separated and the organic layer was concentrated in vacuo to afford an Example of Formula I.

Example 100

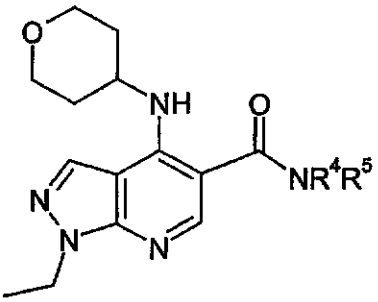


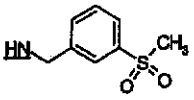
Example 100 NR^4R^5 =

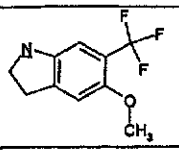
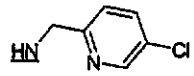
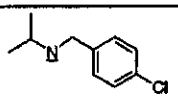
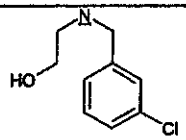
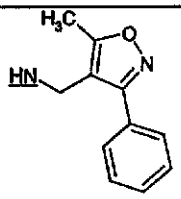
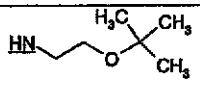
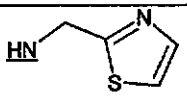
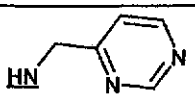
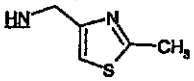


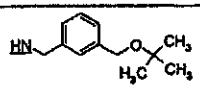
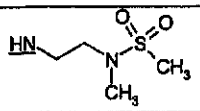
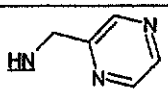
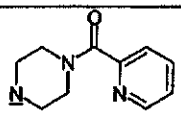
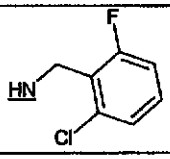
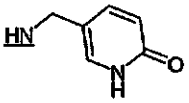
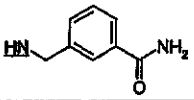
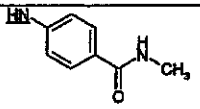
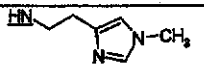
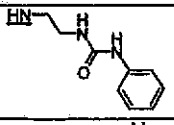
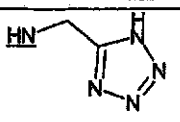
Intermediate 33 (0.048mmol) was dissolved in DMF (0.5ml), then treated with HATU (0.048mmol) followed by diisopropylethyl amine (0.096mmol) and the mixture stirred for 10 min. 4-Methylsulfonylbenzylamine (0.052mmol, available from Acros Organics) was then added and stirring continued for a further 16 hours. The mixture was concentrated *in vacuo*. The crude mixture was purified by mass directed autoprep HPLC to afford Example 100 (0.013g). LCMS showed $MH^+ = 458$; $T_{RET} = 2.22$min.

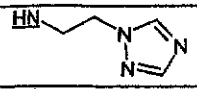
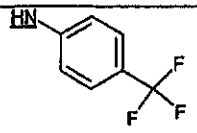
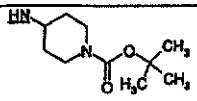
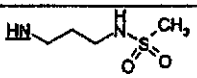
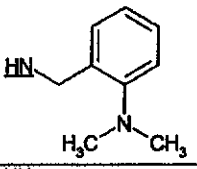
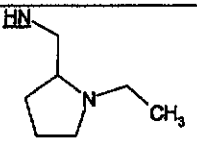
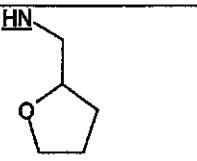
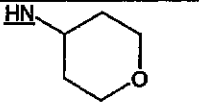
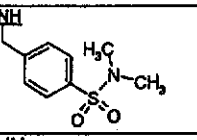
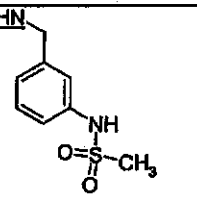
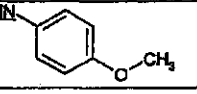
Similarly prepared, but replacing the 4-methylsulfonylbenzylamine with the same or similar number of moles of another amine R^4R^5NH, were the following compounds **(Examples 102 to 182)**:

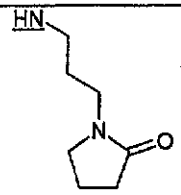
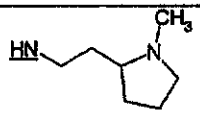
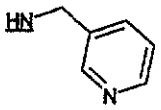
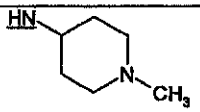
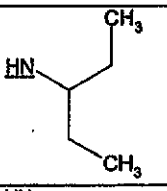
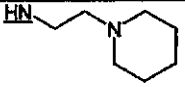
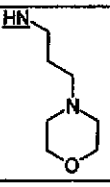
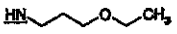
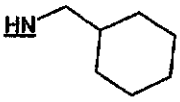
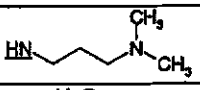
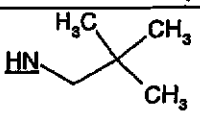


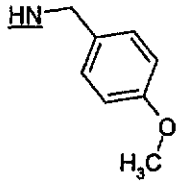
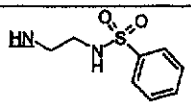
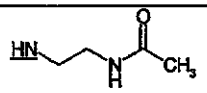
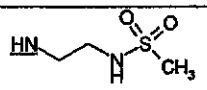
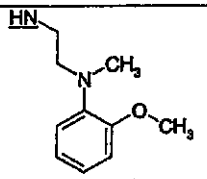
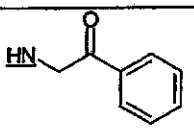
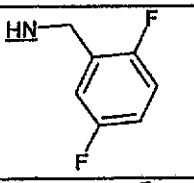
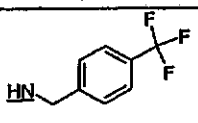
	NR^4R^5 (the N atom linking R^4 and R^5 to the –CO-pyrazolo-pyridine moiety is underlined)	**Source of R^4R^5NH**	**Starting Material**	**MH^+ ion**	**T_{RET} (min)**
Example 102		*J. Chem. Soc.*, 1945, 633	Intermediate 33	458	2.2

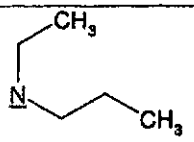
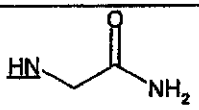
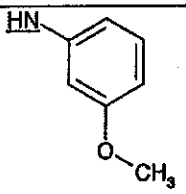
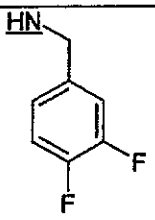
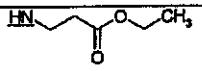
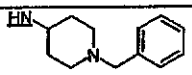
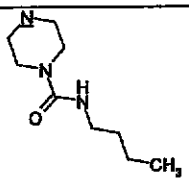
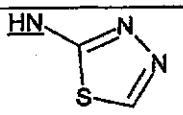
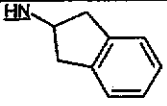
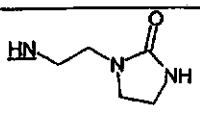
Example 103		WO 98/52943	Intermediate 33	490	2.66
Example 104		*J. Org. Chem.*, 1979, 44(3), 396	Intermediate 33	415	2.28
Example 105		*Seriya Khimicheskaya*, 1989, (7), 1694	Intermediate 33	456	2.65
Example 106		SALOR (Aldrich)	Intermediate 33	458	2.32
Example 107		Maybridge Chemical Company Ltd. Trevillett Tintagel Cornwall PL34 0HW United Kingdom	Intermediate 33	461	2.5
Example 108		MicroChemistry-RadaPharma Shosse Entusiastov 56 Moscow, 111123 Russia	Intermediate 33	390	2.28
Example 109		MicroChemistry-RadaPharma Shosse Entusiastov 56 Moscow, 111123 Russia. Alternatively, available from: Matrix Scientific (USA), or *Synthesis* 1998, 641, or *Tetrahedron* 1995, 51, 12731	Intermediate 33	387	2.13
Example 110		*Bulletin des Societes Chimiques Belges*, (1982), 91(2), 153	Intermediate 33	382	1.98
Example 111		MicroChemistry-RadaPharma Shosse Entusiastov 56 Moscow, 111123 Russia	Intermediate 33	401	2.14

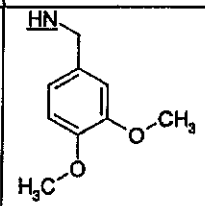
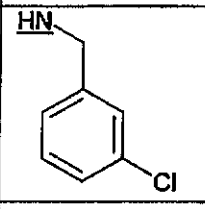
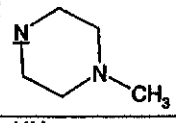
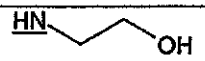
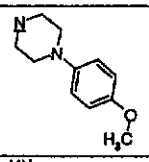
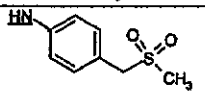
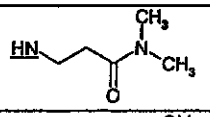
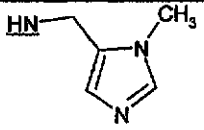
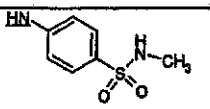
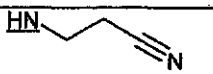
Example 112			Intermediate 33	466	2.67
Example 113		Ultrafine (UFC Ltd.), see above for address	Intermediate 33	425	2
Example 114		Austin Chemical Company, Inc. 1565 Barclay Blvd. Buffalo Grove, IL, 60089 USA	Intermediate 33	382	2
Example 115		WO 02/83624	Intermediate 33	464	1.97
Example 116		Fluka Chemie AG	Intermediate 33	432	2.52
Example 117		MicroChemistry-RadaPharma Shosse Entusiastov 56 Moscow, 111123 Russia	Intermediate 33	397	1.96
Example 118		WO 02/85860	Intermediate 33	423	2.09
Example 119		Butt Park Ltd. Braysdown Works Peasedown St. John Bath, BA2 8LL, United Kingdom	Intermediate 33	423	2.19
Example 120		Sigma	Intermediate 33	398	1.77
Example 121		US 4562184	Intermediate 33	452	2.21
Example 122		Dynamit Nobel GmbH, Germany; or Saville Whittle Ltd (UK agents of Dynamit Nobel), Vickers Street, Manchester M40 8EF, United Kingdom	Intermediate 33	372	1.93

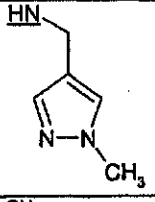
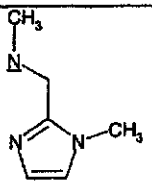
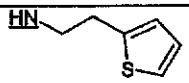
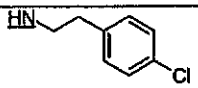
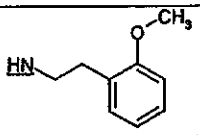
Example 123		WO 02/66470	Intermediate 33	385	1.93
Example 125		Aldrich	Intermediate 33	434	2.84
Example 126		AstaTech, Inc. 8301 Torresdale Ave. 19C, Philadelphia, PA, 19136, USA	Intermediate 33	473	2.5
Example 127			Intermediate 33	425	1.99
Example 128		*J. Org. Chem.*, 2001, 66(6), 1999	Intermediate 33	423	1.97
Example 129		Acros Organics	Intermediate 33	401	1.82
Example 130		Aldrich	Intermediate 33	374	2.08
Example 131		Combi-Blocks Inc., 7949 Silverton Av., Suite 915, San Diego, CA 92126, USA (see also Intermediate 8A)	Intermediate 33	374	2.04
Example 132		*J. Org. Chem.*, 1955, 20, 1657	Intermediate 33	487	2.39
Example 133		*J. Med. Chem.*, 1999, 42(14), 2504; or variation of: Lis et al., *J. Med. Chem.*, 1990, 33(10), 2883, see Scheme III and ref. 24	Intermediate 33	473	2.24
Example 135		Aldrich	Intermediate 33	396	2.42

Example 136		Aldrich	Intermediate 33	415	2.03
Example 137		Aldrich	Intermediate 33	401	1.78
Example 138		Aldrich	Intermediate 33	381	1.81
Example 139		MicroChemistry-RadaPharma Shosse Entusiastov 56 Moscow, 111123 Russia	Intermediate 33	387	1.74
Example 140		Aldrich	Intermediate 33	360	2.16
Example 141		Aldrich	Intermediate 33	401	1.81
Example 142		Aldrich	Intermediate 33	417	1.75
Example 143		Aldrich	Intermediate 33	376	2.16
Example 144		Aldrich; or Baruah et al., *Synlett*, 1999, 4, 409	Intermediate 33	386	2.59
Example 145		Aldrich	Intermediate 33	375	1.73
Example 146		Fluorochem Ltd. Wesley Street Old Glossop Derbyshire SK13 7RY United Kingdom	Intermediate 33	360	2.16

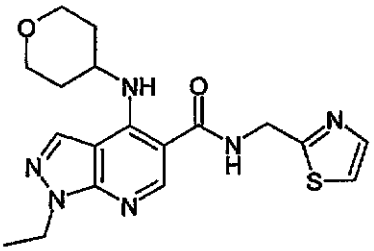
Example 147		Aldrich; or Acros; or Jung et al., *Tetrahedron Lett.*, 2002, 43(48), 8735; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Organic Lett.*, 2002, 4(12), 2055	Intermediate 33	410	2.4
Example 148		Berk Univar plc Berk House P.O.Box 56 Basing View Basingstoke Hants RG21 2E6, United Kingdom	Intermediate 33	473	2.26
Example 149		Aldrich	Intermediate 33	375	1.9
Example 150		MicroChemistry-RadaPharma Shosse Entusiastov 56 Moscow, 111123 Russia	Intermediate 33	411	1.95
Example 152		*Nippon Kagaku Zasshi.*, 1960, 81 p.962.	Intermediate 33	453	1.96
Example 153		Aldrich	Intermediate 33	408	2.35
Example 154		Aldrich	Intermediate 33	416	2.5
Example 155		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Organic Letters*, 2002, 4(12), 2055	Intermediate 33	448	2.68

Example 156		Alfa Aesar, A Johnson Matthey Company 30 Bond Street Ward Hill, MA 01835-8099 USA	Intermediate 33	360	2.16
Example 157		Aldrich	Intermediate 33	330	2.04
Example 158		Aldrich	Intermediate 33	347	1.83
Example 159		Aldrich	Intermediate 33	396	2.49
Example 160		Aldrich	Intermediate 33	416	2.53
Example 161		Aldrich	Intermediate 33	390	2.18
Example 162		Aldrich	Intermediate 33	463	1.96
Example 163		US 4987132	Intermediate 33	458	2.13
Example 164		Aldrich	Intermediate 33	374	2.22
Example 165		Aldrich; or TCI-America; or Maybridge-Int.	Intermediate 33	406	2.53
Example 166		Maybridge Chemical Company Ltd. Trevillett Tintagel	Intermediate 33	402	1.93

		Cornwall PL34 0HW United Kingdom			
Example 167		Aldrich; or Baruah et al., *Synlett*, 1999, 4, 409	Intermediate 33	440	2.3
Example 168		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Organic Letters*, 2002, 4(12), 2055	Intermediate 33	414	2.58
Example 169		Aldrich	Intermediate 33	373	1.64
Example 170		Aldrich	Intermediate 33	334	1.85
Example 171		Aldrich	Intermediate 33	465	2.29
Example 172		EP 666258	Intermediate 33	458	2.25
Example 173		*J. Chem. Soc.*, 1954, 1171	Intermediate 33	389	1.98
Example 174		Peakdale Molecular Ltd, Peakdale Science Park, Sheffield Road, Chapel-en-le-Frith, High Peak SK23 0PG, United Kingdom	Intermediate 33	384	1.76
Example 175		Fluorochem Ltd. Wesley Street Old Glossop Derbyshire SK13 7RY United Kingdom	Intermediate 33	459	2.36
Example 176		Lancaster Synthesis Ltd, Newgate, White Lund, Morecambe, Lancashire LA3 3DY,	Intermediate 33	343	2.01

		United Kingdom			
Example 178		TimTec, Inc. P O Box 8941 Newark, DE, 19714-8941 USA	Intermediate 33	384	2.03
Example 179		ChemBridge Europe, 4 Clark's Hill Rise, Hampton Wood, Evesham, Worcestershire WR11 6FW, United Kingdom	Intermediate 33	398	1.70
Example 180		Aldrich	Intermediate 33	400	2.41
Example 181		Aldrich	Intermediate 33.	428	2.61
Example 182		Aldrich	Intermediate 33	424	2.49

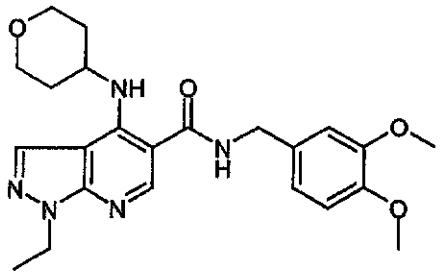
Example 109: 1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3-thiazol-2-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



An alternative process for preparing Example 109 is given below:
1-Hydroxybenzotriazole (0.215g, 1.59mmol) and 1-[3-(dimethylamino)propyl]-3-ethyl-carbodiimide hydrochloride (0.357g, 1.86mmol) were added to a suspension of Intermediate 33 (0.384g, 1.32mmol) in DMF (10ml). After stirring at room temperature for 30 minutes, (1,3-thiazol-2-ylmethyl)amine (0.182g, 1.59mmol) (commercially available from MicroChemistry Building Blocks (Russia) or Matrix Scientific (USA), or preparable as disclosed in *Synthesis* 1998, 641, or *Tetrahedron* 1995, 51, 12731) was added. The reaction was stirred for 18 hours and then partitioned between ether and water. The organic phase was washed with brine, dried ($MgSO_4$) and evaporated *in*

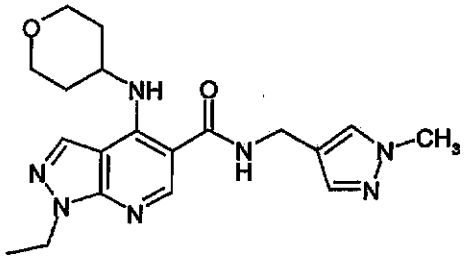
vacuo. The residue was purified by chromatography (Biotage, silica90g) eluting with cyclohexane: EtOAc followed by EtOAc. The material was triturated with cyclohexane and filtered to afford Example 109 (0.244g) as a pale yellow solid. LCMS showed MH^+ 387; T_{RET} = 2.49min. 1H NMR (400MHz in $CDCl_3$, δppm) δ 9.74 (d, 1H) 8.50 (s, 1H) 7.94 (s, 1H) 7.74 (d, 1H), 7.33 (d, 1H), 7.17 (m, 1H), 4.94 (d, 2H) 4.45 (q, 2H) 4.15 - 4.00 (m, 3H), 3.63 (m, 2H). 2.15 (m, 2H) 1.85 - 1.73 (m, 3H) 1.48 (t, 3H).

Example 167: ***N*-{[3,4-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



In an alternative embodiment to the process described above for Examples 100-182, Example 167 can be made according to the following method:
A mixture of Intermediate 33 (0.498g, 1.72mmol), EDC (0.46g, 2.41mmol), and HOBT (0.278g, 1.68mmol) was stirred at room temperature for 0.25 hours. Veratrylamine (3,4-dimethoxybenzylamine, 0.31ml, 2.05mmol, obtainable from Aldrich or *Synlett*, 1999, 4, 409) was added, and stirring was continued at room temperature for 22 hours. The reaction mixture was partitioned between Et_2O and water. The aqueous phase was extracted with Et_2O and the combined organic phases washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. The residue was purified by chromatography (Biotage, silica 40g) eluting with EtOAc : cyclohexane (2:1). The material was further purified by SPE (SCX-2, 10g) eluting with methanol then ammonia in methanol (0.5M). The ammonia methanol fractions were combined and evaporated *in vacuo* to afford Example 167 as a white foam (0.633g). LCMS showed $MH^+ = 440$; $T_{RET} = 2.65$min. ^{1}H NMR (400MHz in $CDCl_3$, 27°C, δppm) 9.78 (d, 1H) 8.37 (s, 1H) 7.94 (s, 1H) 6.94 - 6.82 (m, 3H) 6.29 (br m, 1H) 4.56 (d, 2H) 4.46 (q, 2H) 4.15-4.01 (m's, 3H) 3.89 (s, 6H) 3.63 (m, 2H) 2.15 (m, 2H) 1.78 (m, 2H) 1.49 (t, 3H).

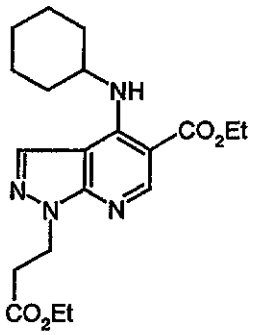
Example 178 1-Ethyl-*N*-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



The ^{1}H NMR data for Example 178 (as prepared by the process described in Examples 100-182 above) was as follows:

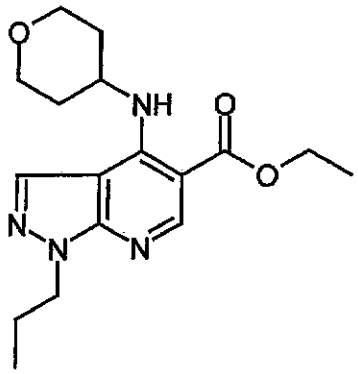
^{1}H NMR (400MHz in $CDCl_3$, δppm) δ 9.90 (m, 1H) 8.37 (s, 1H) 7.94 (s, 1H) 7.49 (s, 1H), 7.40 (s, 1H) 6.39 (m, 1H) 4.50 - 4 .42 (m, 4H) 4.15 - 4.00 (m, 3H) 3.89 (s, 3H), 3.63 (m, 2H) 2.52 (m, 2H) 2.20-2.10 (m, 2H) 1.85 - 1.73 (m, 3H) 1.48 (t, 3H).

Example 183: **Ethyl 4-(cyclohexylamino)-1-(3-ethoxy-3-oxopropyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate**



A vigorously stirred mixture of Intermediate 48 (40mg), anhydrous potassium carbonate (57mg) and ethyl 3-bromopropanoate (0.027ml) in anhydrous DMF (1ml) was heated at 65 °C overnight. The reaction mixture was concentrated, and the residue was partitioned between dichloromethane (5ml) and water (5ml). The phases were separated and the organic phase was evaporated to a residual oil which was purified by mass directed autoprep HPLC to afford Example 183 (5mg). LCMS showed $MH^+ = 389$; T_{RET} = 3.65min.

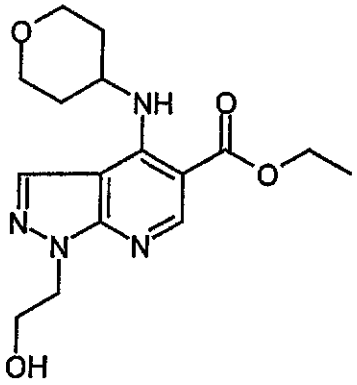
Example 185: **Ethyl 1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate**



Sodium hydride (0.067g, 60% dispersion in oil) was added to a stirred solution of Example 20 (0.47g) in DMF (19ml), followed by n-propyl iodide (0.17ml). The mixture was stirred at 23 °C for 16 hours, then concentrated, diluted with chloroform (30ml) and washed with 1:1 water:brine solution (30ml), separated and the organic layer concentrated. The residue was purified on a SPE catridge (silica, 10g) eluting with 10ml volumes of dichloromethane, 1:1 diethyl ether:cyclohexane, and diethyl ether. The

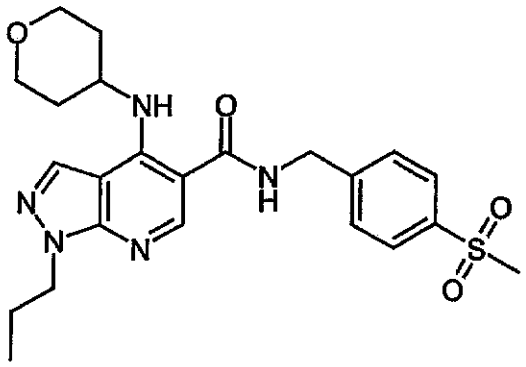
combined 1:1 diethyl ether: cyclohexane, and diethyl ether, fractions were concentrated to give Example 185 as a clear gum (0.23g). LCMS showed MH^+ = 333; T_{RET} = 3.14min.

Example 186: **Ethyl 1-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate**



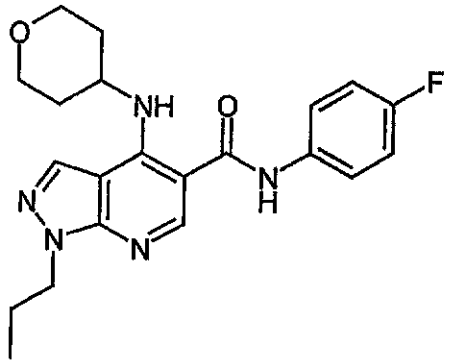
2-Bromoethanol (0.008ml) was added to a solution of Example 20 (0.03g) in anhydrous DMF (1.5ml), with 2-tert-butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosphorine (polymer bound, 2.3mmol/g loading, 0.045g). The mixture was shaken at 23 °C for 16 hours, then the solution drained from the resin, and the resin was washed with DMF. The combined organics were concentrated, and the residue purified on a SPE cartridge (silica, 1g) eluting with 70-100% ethyl acetate in cyclohexane. The combined fractions were concentrated to give Example 186 as a white solid (0.011g). LCMS showed MH^+ =335; T_{RET} = 2.47min.

Example 187: ***N*-[4-(Methylsulfonyl)benzyl]-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



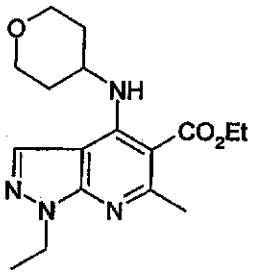
Intermediate 50 (0.03g) was stirred in DMF (1ml) with DIPEA (0.035ml) and HATU (0.038g) for 20 min. 4-(Methylsulfonyl)benzylamine hydrochloride (0.024g) was added to the mixture and the solution was stirred for 8 hours at 23 °C. The solution was concentrated and the residue dissolved in dichloromethane (6ml) then washed with saturated sodium bicarbonate solution (6ml) and 1:1 brine:water (6ml), separated by hydrophobic frit. The organic layer was concentrated to give Example 187 as a white solid (0.039g). LCMS showed MH^+ = 472; T_{RET} = 2.67min.

Example 188: ***N*-(4-Fluorophenyl)-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



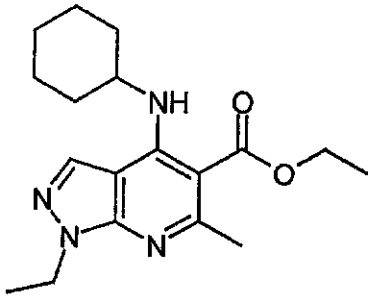
The synthetic method is as described in Example 187, except that in place of 4-(methylsulfonyl)benzylamine hydrochloride, 4-fluoroaniline (0.01ml) was added to the mixture. The resultant product required further purification, which was performed by mass directed autoprep HPLC, giving Example 188 as a clear gum (0.03g). LCMS showed $MH^+ = 398$; $T_{RET} = 3.13$min.

Example 189: **Ethyl 1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate**



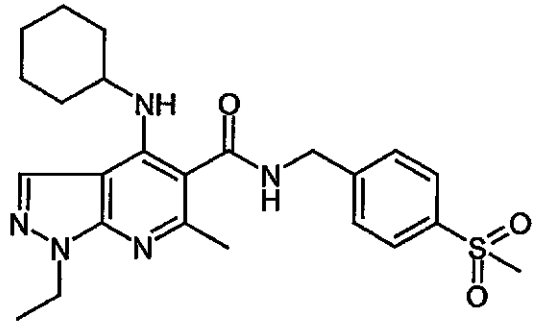
4-Aminotetrahydropyran hydrochloride (Intermediate 8A, 0.413g, 3.0mmol) was added to a mixture of Intermediate 51 (0.268g, 1.0mmol) and N,N-diisopropylethylamine (0.87ml, 5.0mmol) in acetonitrile (3ml). The resulting mixture was heated at 85 °C for 24 hours. Volatiles were removed *in vacuo* and the residue was dissolved in chloroform (1.5ml) and applied to a SPE cartridge (silica, 5g). The cartridge was eluted successively with Et_2O, EtOAc and EtOAc-MeOH (9/1). Fractions containing the desired product were combined and concentrated *in vacuo* to give the desired product contaminated with starting material (Intermediate 51). Further purification using a SPE cartridge (silica, 5g) eluting with ethyl acetate-cyclohexane (1/3) afforded Example 189 (0.248g). LCMS showed $MH^+ = 333$; $T_{RET} = 2.75$min.

Example 190: **Ethyl 4-(cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate**



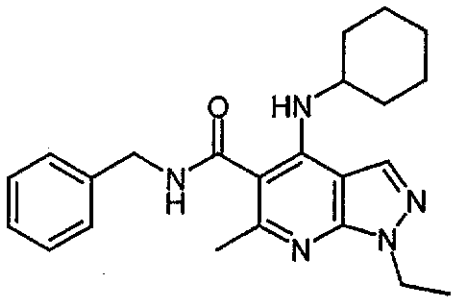
Cyclohexylamine (0.149g, 1.5mmol) was added to a mixture of Intermediate 51 (0.201g, 0.75mmol) and N,N-diisopropylethylamine (0.65ml, 3.73mmol) in acetonitrile (3ml). The resulting mixture was heated at 85 °C for 40 hours. Volatiles were removed *in vacuo* and the residue was dissolved in chloroform (1.5ml) and applied to a SPE cartridge (silica, 5g). The cartridge was eluted successively with Et_2O, EtOAc and MeOH. Fractions containing the desired product were combined and concentrated *in vacuo* to afford Example 190 (0.128g). LCMS showed $MH^+ = 331$; $T_{RET} = 3.64$min.

Example 191: **4-(Cyclohexylamino)-1-ethyl-6-methyl-*N*-[4-(methylsulfonyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



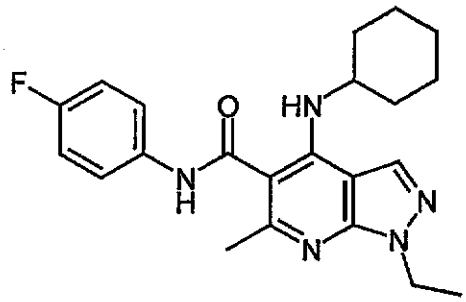
A mixture of Intermediate 52 (0.014g, 0.046mmol), HATU (0.018g, 0.048mmol) and DIPEA (0.022ml, 0.125mmol) in DMF (1ml) was shaken at room temperature for 10min. 1-[4-(Methylsulfonyl)phenyl]methanamine (0.009g, 0.046mmol) was then added, and the mixture was shaken for several minutes to give a solution. This solution was stored at room temperature for 16 hours. The solution was concentrated *in vacuo*, and the residue was dissolved in chloroform (0.5ml) and applied to a SPE cartridge (aminopropyl, 0.5g). The cartridge was eluted successively with chloroform (1.5ml), EtOAc (1.5ml) and EtOAc-MeOH (9:1, 1.5ml). Fractions containing the desired product were concentrated *in vacuo* to afford Example 191 (0.005g). LCMS showed $MH^+ = 470$; $T_{RET} = 2.54$min.

Example 192: ***N*-Benzyl-4-(cyclohexylamino)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



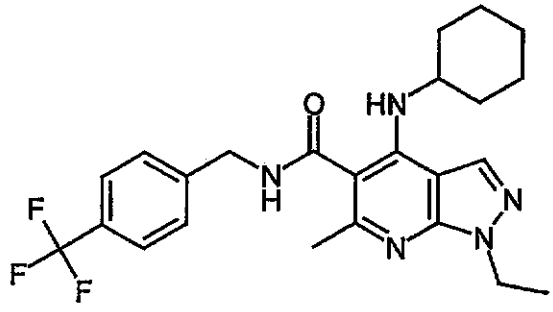
Example 192 was prepared from Intermediate 52 using a method analagous to Example 191. LCMS showed $MH^+ = 392$: $T_{RET} = 2.43$.

Example 193: **4-(Cyclohexylamino)-1-ethyl-*N*-(4-fluorophenyl)-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



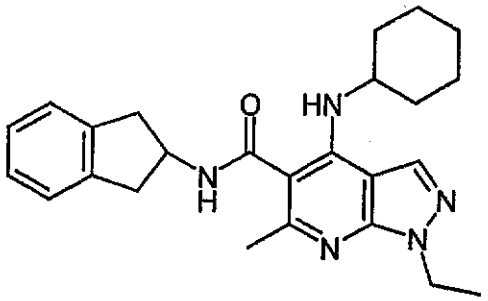
Example 193 was prepared from Intermediate 52 using an analagous method to Example 191. LCMS showed $MH^+ = 396$; $T_{RET} = 2.6$min.

Example 194: **4-(Cyclohexylamino)-1-ethyl-6-methyl-*N*-[4-(trifluoromethyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



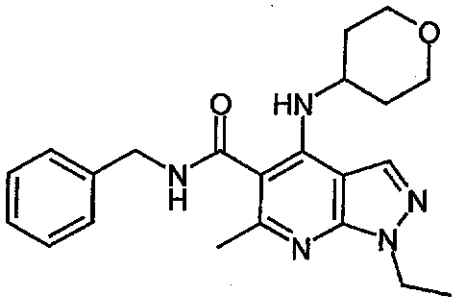
Example 194 was prepared from Intermediate 52 using an analagous method to Example 191. LCMS showed $MH^+ = 460$; $T_{RET} = 2.74$min.

Example 195: **4-(Cyclohexylamino)-*N*-(2,3-dihydro-1*H*-inden-2-yl)-1-ethyl-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



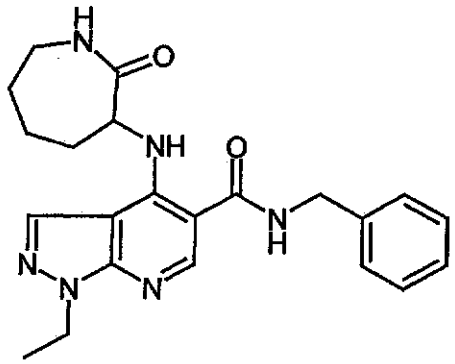
Example 195 was prepared from Intermediate 52 using an analagous method to Example 191. LCMS showed $MH^+ = 418$; $T_{RET} = 2.55$min.

Example 196: ***N*-Benzyl-1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



Example 196 was prepared from Intermediate 53 using an analagous method to Example 191. LCMS showed $MH^+ = 394$; $T_{RET} = 2.02$min.

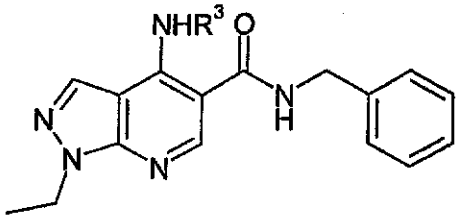
Example 197: ***N*-Benzyl-1-ethyl-4-[(2-oxoazepan-3-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**

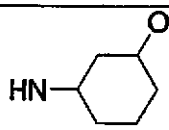
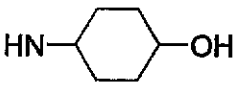
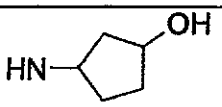


3-Aminoazepan-2-one (0.043g, 0.335mmol, commercially available from Sigma-Aldrich Company Ltd) was added to a mixture of Intermediate 17 (0.021g, 0.067mmol) and DIPEA (0.058ml, 0.335mmol) in acetonitrile (0.5ml). The resulting mixture was heated at

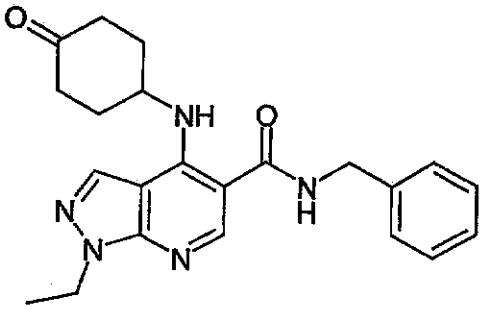
85 °C for 48 hours. Volatiles were removed in vacuo, and the residue was dissolved in chloroform (0.5ml) and applied to a SPE cartridge (silica, 0.5g) which was eluted successively with diethyl ether (1.5ml), ethyl acetate (1.5ml) and ethyl acetate-methanol (9/1, 1.5ml). Fractions containing the desired material were concentrated in vacuo to afford Example 197 (0.009g). LCMS showed $MH^+ = 407$; $T_{RET} = 2.81$min.

Similarly prepared, but replacing the 3-aminoazepan-2-one with the same or similar number of moles of another amine R^3NH_2 were the following compounds:



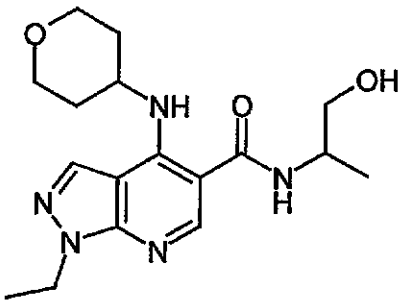
Example Number	NHR^3	Source of R^3NH_2	Starting Material	MH^+ ion	T_{RET} (min)
Example 198		*J. Chem. Soc., Perkin Trans. 1*, 1994, 537	Intermediate 17	394	2.75
Example 199		Aldrich; or TCI-America	Intermediate 17	394	2.82
Example 200		US 4219660	Intermediate 17	380	2.70

Example 201: *N*-Benzyl-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



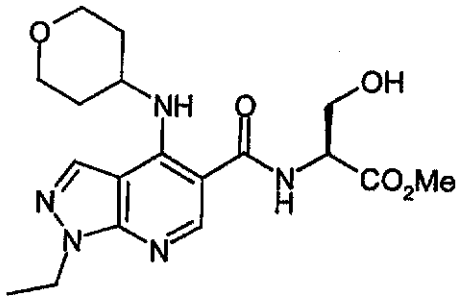
Intermediate 54 (0.048g, 0.32mmol) was added to a mixture of Intermediate 17 (0.050g, 0.16mmol) and DIPEA (0.17ml, 0.98mmol) in acetonitrile (3ml). The resulting mixture was heated under reflux. After 12 hours, further quantities of Intermediate 54 (0.044g, 0.29mmol), DIPEA (0.17ml, 0.98mmol) and acetonitrile (1ml) were added to reaction mixture which was maintained under reflux. After 36 hours, the reaction mixture was concentated in vacuo, and the residual oil was dissolved in dichloromethane (8ml) and washed with 5% sodium bicarbonate solution (2ml). Evaporation of the organic solution gave a viscous oil which was dissolved in dichloromethane (2ml) and applied to a SPE cartridge (silica, 5g). The cartridge was eluted successively with a gradient of ethyl acetate-cyclohexane (1:16, then 1:8, 1:4, 1:2, 1:1 and 1:0). Fractions containing the desired material were concentrated in vacuo to afford Example 201 (0.018g). LCMS showed $MH^+ = 392$; $T_{RET} = 2.95$min.

Example 202: 1-Ethyl-*N*-(2-hydroxy-1-methylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

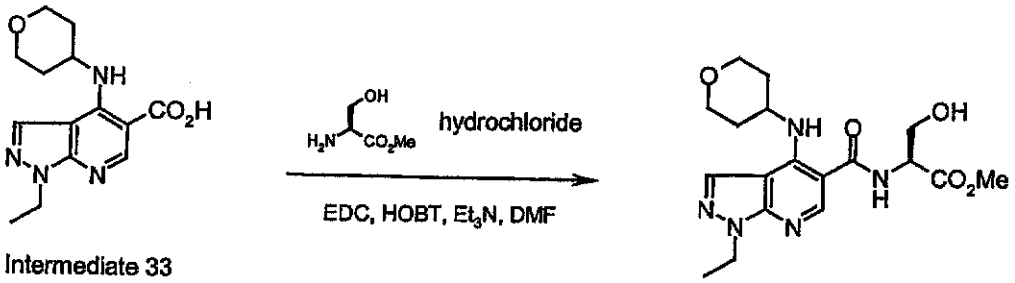


Intermediate 33 (0.1g, 0.34mmol), EDC (0.066g, 0.34mmol) and HOBT (0.05g, 0.37mmol) were suspended in DMF (2ml) and stirred at room temperature under nitrogen for 15 min. 2-aminopropan-1-ol (0.026g, 0.34mmol) and triethylamine (0.036g, 0.36mmol) were added and the mixture was stirred at room temperature under nitrogen for 6 hours. Solvents were removed in vacuo and the residue partitioned between DCM and water. The organic layer was concentrated and applied to an SPE cartridge (aminopropyl, 5g), which was eluted with methanol. Concentration in vacuo afforded Example 202 (0.095g). LCMS showed $MH^+ = 348$, $T_{RET} = 2.15$min.

Example 203: **Methyl (2*S*)-2-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)-3-hydroxypropanoate**



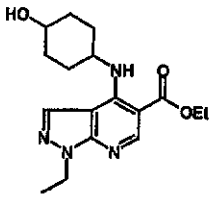
Reaction scheme:



Intermediate 33

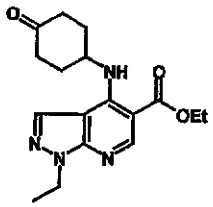
Intermediate 33 (0.1g, 0.34mmol), EDC (0.066g, 0.34mmol) and HOBT (0.05g, 0.37mmol) were suspended in DMF (2ml) and stirred at room temperature under nitrogen for 15 mins. L-Serine methyl ester hydrochloride (0.054g, 0.34mmol) and triethylamine (0.036g, 0.36mmol) were added and the mixture stirred at room temperature under nitrogen for 18 hours. Solvents were removed in vacuo and the residue was partitioned between DCM and water. The organic layer was concentrated in vacuo and applied to an SPE cartridge (aminopropyl, 5g), which was eluted with methanol. Concentration in vacuo afforded an impure residue which was further purified by SPE cartridge (silica, 5g), eluting with ethyl acetate followed by 5% methanol/ethyl acetate. The desired fractions were concentrated in vacuo to afford Example 203 (0.055g). LCMS showed $MH^+ = 393$; $T_{RET} = 2.22$min.

Example 204 Ethyl 1-ethyl-4-[(4-hydroxycyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



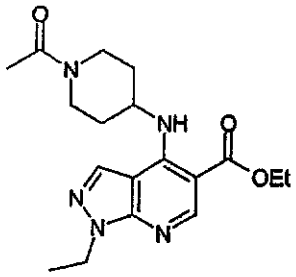
Intermediate 1 (1.5g, 5.9mmol) was dissolved in acetonitrile (80ml). Trans-4-aminocyclohexanol (0.817g, 7.1mmol, commercially available from TCI-America; alternatively (e.g. as the HCl salt) from Aldrich) and diisopropylethylamine (6.18ml, 35.5mmol) were added and the mixture was stirred at 85°C for 16h. The mixture was concentrated *in vacuo*, and the residue was partitioned between DCM (120ml) and water (30ml). The phases were separated and the organic phase was dried (Na_2SO_4) and evaporated to give a pale yellow solid. The solid was dissolved in a mixture of DCM (10ml) and chloroform (3ml), and applied in equal portions to two SPE cartridges (silica, 20g) which were eluted sequentially with a gradient of EtOAc:cyclohexane (1:16, then 1:8, 1:4, 1:2, 1:1 and 1:0). Fractions containing the desired material were combined and evaporated *in vacuo* to give Example 204 (1.893g) as a white solid. LCMS showed $MH^+ = 333$; $T_{RBT} = 2.79$min.

Example 205: Ethyl 1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



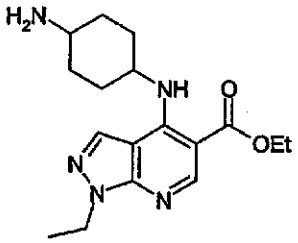
Example 204 (1.893g, 5.7mmol) was suspended in acetone (12ml) and the stirred suspension was treated at 0°C with Jones reagent (1.81ml). After 30min, a further quantity of Jones reagent (1.81ml) was added to the reaction mixture which was maintained at 0°C. After a further 2h, a final portion of Jones reagent (1.44ml) was added to the reaction mixture, and stirring at 0°C was continued for 1h. Isopropanol (3.8ml) was added to the reaction mixture, followed by water (15ml). The resulting mixture was extracted with ethyl acetate (2 x 40ml). The combined organic extracts were washed with water (8ml), dried (Na_2SO_4) and evaporated to a grey solid. The solid was dissolved in DCM (10ml) and applied in equal portions to two SPE cartridges (silica, 20g) which were eluted sequentially with a gradient of ethyl acetate:cyclohexane (1:16, then 1:8, 1:4, 1:2, and 1:1). Fractions containing the desired material were combined and evaporated *in vacuo* to give Example 205 (1.893g) as a white solid. LCMS showed $MH^+ = 331$; $T_{RBT} = 2.84$min.

Example 207 (= Example 5): Ethyl 4-[(1-acetyl-4-piperidinyl)amino]-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



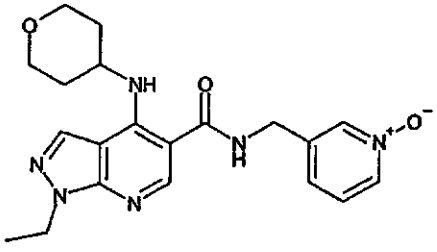
Intermediate 1 (2.58g), Intermediate 6 (2.0g) and N,N-diisopropylethylamine (8.9ml) were dissolved in acetonitrile (98ml). The reaction mixture was heated at 85 °C for 24h then an additional portion of Intermediate 6 (0.18g) was added and heating continued for a further 10h. The reaction was concentrated in vacuo and the residues partitioned between DCM and water. The phases were separated and the organic phase evaporated in vacuo. The residue was purified by chromatography using Biotage (silica 90g) eluting with DCM : MeOH (5%) to afford Example 207 (1.55g) as a white solid. LCMS showed MH^+ 360; T_{RET} = 2.71 min.

Example 209: Ethyl 4-[(4-aminocyclohexyl)amino]-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



Example 209 was prepared from Intermediate 1 and (4-aminocyclohexyl)amine using an analogous method to that used for the preparation of Example 207. LCMS showed MH^+ = 332; T_{RET} = 2.18min

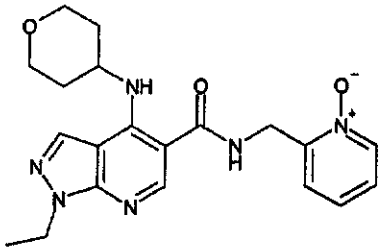
Example 210: 1-Ethyl-*N*-[(1-oxido-3-pyridinyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide.



A solution of *meta*-chloroperoxybenzoic acid (45mg, 0.26mmol) in chloroform (1ml) was added dropwise at 0°C to a stirred solution of Example 138 (0.1g, 0.26mmol) in chloroform (1.5ml). After 1.5h at 0°C, a further quantity of *meta*-chloroperoxybenzoic acid (45mg, 0.26mmol) in chloroform (1ml) was added, and stirring was continued at

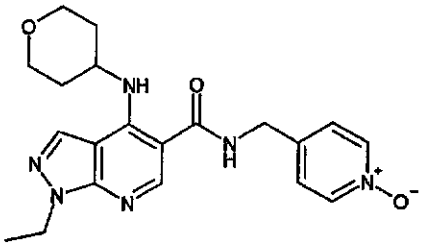
0°C for 1.5h. A trace of starting material remained, so an additional quantity of *meta*-chloroperoxybenzoic acid (22mg, 0.13mmol) in chloroform (0.6ml) was added. After 3.5h at 0°C, 2M sodium carbonate solution (1ml), was added to the reaction mixture. The phases were separated by passage through a hydrophobic frit and the aqueous phase was extracted with more chloroform (2ml). The combined organic extracts were evaporated to a residual foam which was purified by mass directed autoprep HPLC to afford Example **210** (44mg). LCMS showed $MH^+ = 397$; $T_{RET} = 2.13$min.

Example 211: 1-Ethyl-*N*-[(1-oxido-2-pyridinyl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



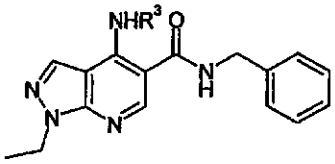
Example 211 was prepared from Example 600 using an analogous method to that used for the preparation of Example 210. LCMS showed $MH^+ = 397$; $T_{RET} = 2.20$min

Example 212: 1-Ethyl-*N*-[(1-oxido-4-pyridinyl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



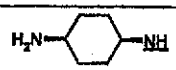
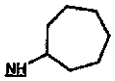
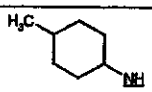
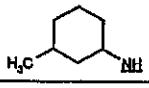
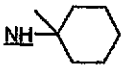
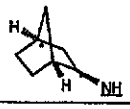
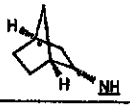
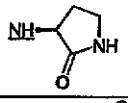
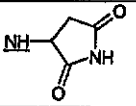
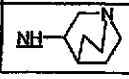
Example 212 was prepared from Example 33 using an analogous method to that used for the preparation of Example 210. LCMS showed $MH^+ = 397$; $T_{RET} = 2.13$min

Examples 214 to 230

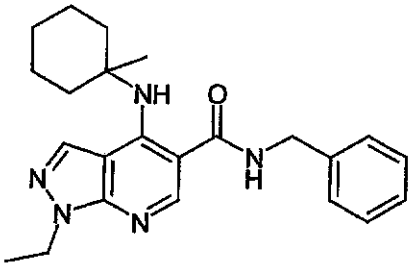


General Procedure

Intermediate 17 (0.15mmol) was treated with an aliquot of the amine (0.95ml, equivalent to 0.19mmol) from a stock solution in acetonitrile (0.2M) and N,N-diisopropylethylamine (0.24mmol). The mixture was heated at reflux for 20h then concentrated in vacuo. The residue was purified by SPE (silica) to give the desired product.

Example no.	NHR^3	Source of R^3NH_2	Starting Material	MH + ion	LC-MC Retention time
214		*J. Med. Chem.*, 1994, 37(17), 2360	Intermediate 17	393	2.16
221		Aldrich	Intermediate 17	350	3.18
222		Aldrich	Intermediate 17	392	3.62
223		Aldrich	Intermediate 17	392	3.63,3.68
224		Pfaltz-Bauer	Intermediate 17	392	3.61,3.66
225		*J. Org. Chem.*, 1985, 50(11), 1859	Intermediate 17	392	3.54
226		Aldrich	Intermediate 17	390	3.56
227		Aldrich	Intermediate 17	390	3.52
228		WO 99/12933	Intermediate 17	379	2.66
229		EP 1188744	Intermediate 17	393	2.58
230		Aldrich	Intermediate 17	405	2.19

Example 225: 1-ethyl-4-[(1-methylcyclohexyl)amino]-*N*-(phenylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

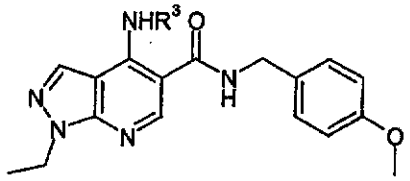


A preferred method for the preparation of Example 225 involving 1-methylcyclohexylamine and a longer reaction time is as follows:

A solution of Intermediate 17 (46mg), 1-methylcyclohexylamine (26mg) and diisopropylethylamine (94mg) in acetonitrile (1ml) was stirred and heated at reflux for 77h. More 1-methylcyclohexylamine (102mg), diisopropylethylamine (93mg) and acetonitrile (1ml) were added and the reaction mixture was heated at reflux for a further 68h. The solution was cooled and concentrated *in vacuo*. The residue was triturated in ethyl acetate and filtered. The filtrate was purified by mass directed autoprep. HPLC to give Example 225 (19mg). LCMS showed $MH^+ = 392$; $T_{RET} =$ 3.46min.

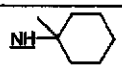
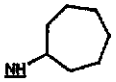
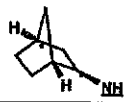
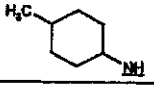
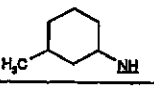
Examples 231, 247 and 257, shown below and also involving 1-methylcyclohexylamine, can also preferably be prepared in a similar manner.

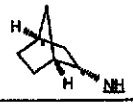
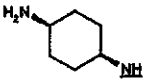
Examples 231 - 239



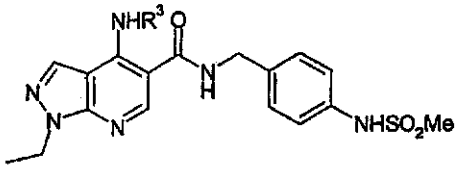
General Procedure

Intermediate 55 (0.15mmol) was treated with an aliquot of the amine (0.95ml, equivalent to 0.19mmol) from a stock solution in acetonitrile (0.2M) and N, N-diisopropylethylamine (0.24mmol). The mixture was heated at reflux for 20h then concentrated in vacuo. The residue was purified by SPE (silica) to give the desire product.

Example no.	NHR^3	Source of R^3NH_2	Starting Material	MH + ion	LC-MC Retention time
231		*J. Org. Chem.*, 1985, 50(11), 1859	Intermediate 55	422	3.43
233		Aldrich	Intermediate 55	380	3.20
234		Aldrich	Intermediate 55	422	3.58
235		Aldrich	Intermediate 55	420	3.52
236		Aldrich	Intermediate 55	422	3.57,3.64
237		Pfaltz-Bauer	Intermediate 55	422	3.56,3.62

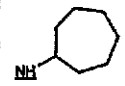
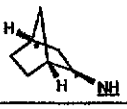
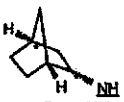
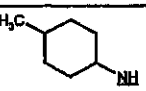
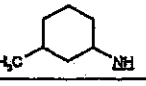
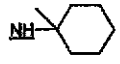
238		Aldrich	Intermediate 55	420	3.48
239		*J. Med. Chem.*, 1994, 37(17), 2360	Intermediate 55	423	2.16

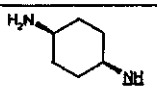
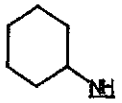
Examples 240 - 249



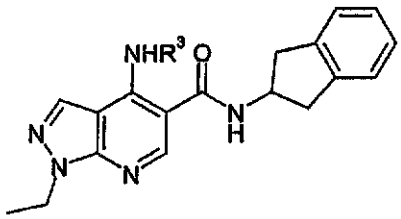
General Procedure

Intermediate 56 (0.15mmol) was treated with an aliquot of the amine (0.95ml, equivalent to 0.19mmol) from a stock solution in acetonitrile (0.2M) and N,N-diisopropylethylamine (0.24mmol). The mixture was heated at reflux for 20h then concentrated in vacuo. The residue was purified by SPE (silica) to give the desire product.

Example no.	NHR^3	Source of NH_2R^3	Starting Material	MH + ion	LC-MC Retention time
240		Aldrich	Intermediate 56	485	3.26
241		Aldrich	Intermediate 56	443	2.94
242		Aldrich	Intermediate 56	483	3.20
243		Aldrich	Intermediate 56	483	3.14
244		Aldrich	Intermediate 56	485	3.25,3.33
245		Pfatlz-Bauer	Intermediate 56	485	3.24,3.31
247		*J. Org. Chem.*, 1985, 50(11), 1859	Intermediate 56	483	3.10

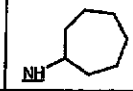
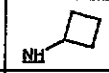
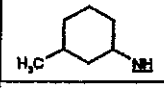
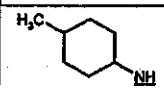
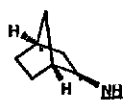
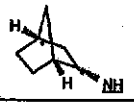
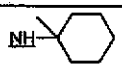
248		*J. Med. Chem.*, 1994, 37(17), 2360	Intermediate 56	486	2.05
249		Aldrich	Intermediate 56	471	3.21

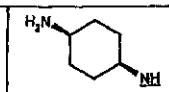
Examples 250 - 258



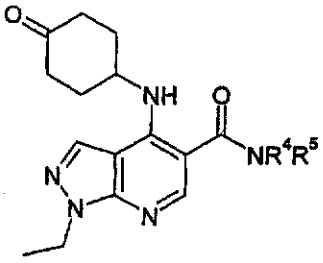
General Procedure

Intermediate 57 (0.15mmol) was treated with an aliquot of the amine (0.95ml, equivalent to 0.19mmol) from a stock solution in acetonitrile (0.2M) and N, N-diisopropylethylamine (0.24mmol). The mixture was heated at reflux for 20h then concentrated in vacuo. The residue was purified by SPE (silica) to give the desire product.

Example no.	NHR^3	Source of NH_2R^3	Starting Material	MH + ion	LC-MC Retention time
250		Aldrich	Intermediate 57	418	3.78
251		Aldrich	Intermediate 57	376	3.42
253		Pfaltz-Bauer	Intermediate 57	418	3.78,3.84
254		Aldrich	Intermediate 57	418	3.82,3.86
255		Aldrich	Intermediate 57	416	3.66
256		Aldrich	Intermediate 57	416	3.77
257		*J. Org. Chem.*, 1985, 50(11), 1859	Intermediate 57	418	3.74

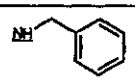
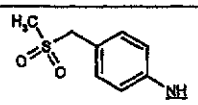
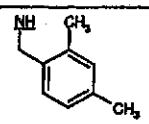
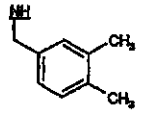
258		*J. Med. Chem.*, 1994, 37(17), 2360	Intermediate 57	419	2.38

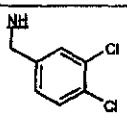
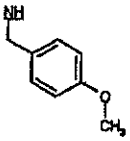
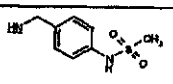
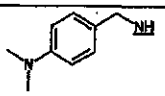
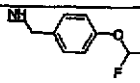
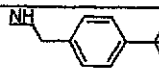
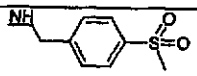
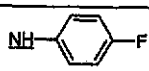
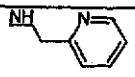
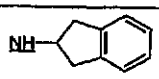
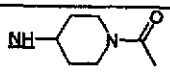
Examples 259 - 275

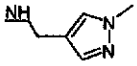
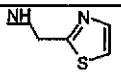


General Procedure

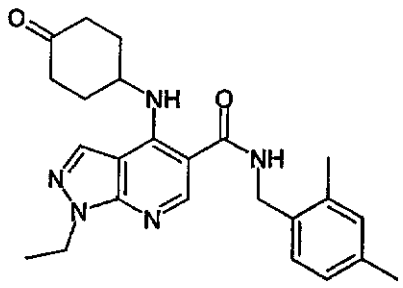
A mixture of Intermediate 58 (0.1mmol), HATU (0.1mmol) and DIPEA (0.4mmol) in DMF (0.4ml) was shaken at room temperature for 10 min. A solution of the amine (0.1mmol) in DMF (0.2ml) was then added and the mixture agitated for several minutes to give a solution. The solution was stored at room temperature for 16 hours then concentrated *in vacuo*. The residue was dissolved in chloroform (0.5ml) and applied to a SPE cartridge (aminopropyl, 0.5g). The cartridge was eluted successively with chloroform (1.5ml), EtOAc (1.5ml) and EtOAc:MeOH (9:1, 1.5ml). Fractions containing the desired product were concentrated *in vacuo* and the residue purified by mass directed autoprep HPLC.

Example no.	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
201		Aldrich	Intermediate 58	392	2.60
259		EP 666258	Intermediate 58	470	2.44
260		Salor; or ICN Biomedicals, Inc.; or *Synthesis*, 1982, 12, 1036	Intermediate 58	420	3.09
261		CHMSRV-AS; or Matrix Scientific; or *Chem. Ber.*, 1969, 102, 2770	Intermediate 58	420	3.09

262		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 58	454	3.20
263		Acros; or Aldrich; *Tetrahedron Lett.*, 2002, 43(48), 8735; or *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 58	422	2.86
264		Lis et al., *J. Med. Chem.*, 1990, 33(10), 2883; see Scheme III and ref. 24	Intermediate 58	485	2.64
265		Aldrich	Intermediate 58	435	2.54
266		Fluorochem; or WO 98/45268	Intermediate 58	458	2.81
267		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 58	460	2.96
268		Peakdale	Intermediate 58	470	2.39
269		Aldrich	Intermediate 58	396	2.80
270 (as CF_3CO_2H salt)		Aldrich	Intermediate 58	393	1.89
271		TCI-America; or Aldrich; or Maybridge-Int	Intermediate 58	418	2.77
272		WO 99/38877	Intermediate 58	427	2.13

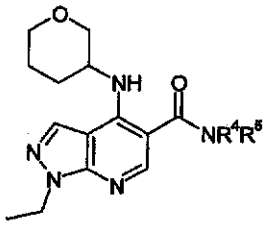
273		N.D. Zelinsky Institute	Intermediate 58	396	2.15
274		Aldrich	Intermediate 58	330	2.10
275		Matrix Scientific	Intermediate 58	399	2.29

Example 260 (Alternative Procedure)
***N*-[(2,4-dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



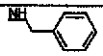
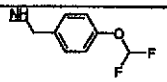
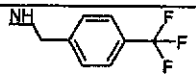
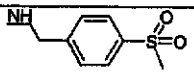
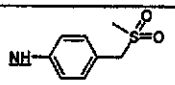
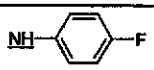
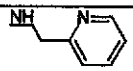
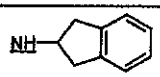
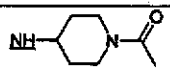
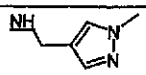
Alternative procedure for preparing Example 260:
A solution of Intermediate 58 (45mg), HATU (63mg) and DIPEA (39mg) in acetonitrile (5ml) was stirred for 10min. A solution of 2,4-dimethylbenzylamine (24mg) (available from Salor; or ICN Biomedicals, Inc.; or *Synthesis*, 1982, 12, 1036) in acetonitrile (1ml) was added. The reaction mixture was stirred for 18h. The solution was concentrated and the residue partitioned between ethyl acetate (25ml) and 0.5M sodium bicarbonate (20ml). The organic phase was separated, washed with water (20ml), dried over Na_2SO_4 and concentrated to leave a gum which was applied to an SPE cartridge (5g). The cartridge was eluted with ethyl acetate. Fractions containing the desired compound were combined and concentrated *in vacuo* to give **Example 260** (32mg). LC-MS showed $MH^+ = 420$; $T_{RET} = 3.16$min. δ_H ($CDCl_3$): 1.49 (3H, t), 2.11 (2H, m), 2.33 (3H, s), 2.35 (3H, s), 2.40 (2H, m), 2.52 (2H, m), 2.61 (2H, m), 4.36 (1H, m), 4.47 (2H, q), 4.55 (2H, d), 6.14 (1H, t), 7.01 + 7.18 (2H, AA'BB'), 7.04 (1H, s), 8.01 (1H, s), 8.36 (1H, s), 9.96 (1H, d).

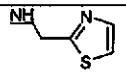
Example 276 - 287



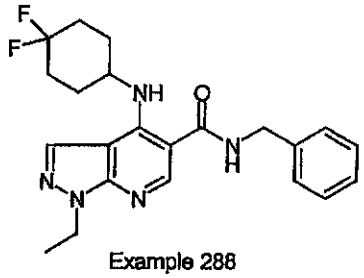
General Procedure

A mixture of Intermediate 59 (0.1mmol), HATU (0.1mmol) and DIPEA (0.4mmol) in DMF (0.4ml) was shaken at room temperature for 10 min. A solution of the amine (0.1mmol) in DMF (0.2ml) was then added and the mixture agitated for several minutes to give a solution. The solution was stored at room temperature for 16 hours then concentrated *in vacuo*. The residue was dissolved in chloroform (0.5ml) and applied to a SPE cartridge (aminopropyl, 0.5g). The cartridge was eluted successively with chloroform (1.5ml), EtOAc (1.5ml) and EtOAc:MeOH (9:1, 1.5ml). Fractions containing the desired product were concentrated *in vacuo* and the residue purified by mass directed autoprep HPLC.

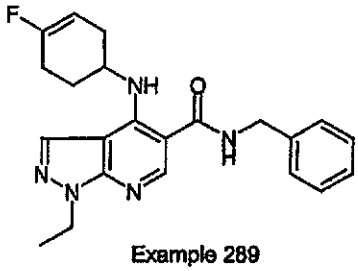
Example no.	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
276		Aldrich	Intermediate 59	392	2.60
277		Fluorochem; or WO 98/45268	Intermediate 59	446	2.84
278		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 59	448	3.0
279		Acros	Intermediate 59	458	2.40
280		EP 382570	Intermediate 59	458	2.47
281		Aldrich	Intermediate 59	384	2.85
282 (as CF_3CO_2H salt)		Aldrich	Intermediate 59	381	1.89
283		TCI-America; or Aldrich; or Maybridge-Int	Intermediate 59	406	2.80
284		WO 99/38877	Intermediate 59	415	2.14
285		N.D. Zelinsky Institute	Intermediate 59	384	2.16
286		Aldrich	Intermediate 59	318	2.11

287		Matrix Scientific	Intermediate 59	399	2.29

Example 288: 4-[(4,4-Difluorocyclohexyl)amino]-1-ethyl-*N*-(phenylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide and Example 289: 1-Ethyl-4-[(4-fluoro-3-cyclohexen-1-yl)amino]-*N*-(phenylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide.



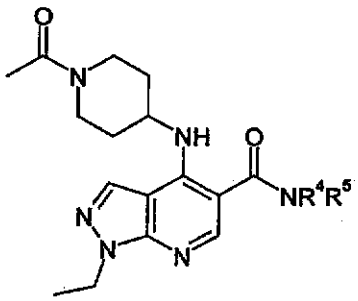
Example 288



Example 289

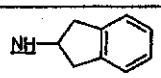
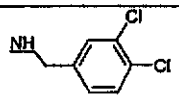
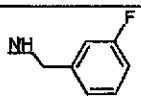
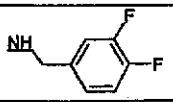
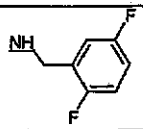
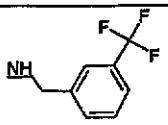
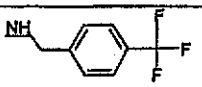
Diisopropylethylamine (0.113ml, 0.65mmol) was added to a stirred mixture of Intermediate 17 (40mg, 0.13mmol) and Intermediate 63 (45mg, 0.26mmol) in acetonitrile (2ml). The mixture was stirred at 85°C. After 18h, a further portion of Intermediate 63 (22.5mg, 0.13mmol) and diisopropylethylamine (0.113ml, 0.65mmol) was added to the reaction mixture and stirring was continued at 90°C for 24h. The mixture was then concentrated in vacuo and the residue was partitioned between DCM (20ml) and water (5ml). The phases were separated and the aqueous phase was extracted with further DCM (10ml). The combined organic extracts were dried (Na_2SO_4) and evaporated in vacuo to give a brown oil (65mg) which was partially purified on a SPE cartridge (silica, 10g), eluting with ethyl acetate : petroleum ether (1:8; 1:4; 1:2; 1:1 and 1:0). The resulting two-component pale-brown oil (34mg) was separated by mass directed auto prep HPLC to give Example 288 (19mg) as a white foam (LCMS showed $MH^+ = 414$; $T_{RET} = 3.24$min) and Example 289 (9mg) as a white solid (LCMS showed $MH^+ = 394$; $T_{RET} = 3.21$min).

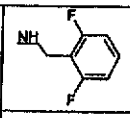
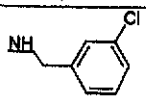
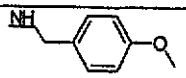
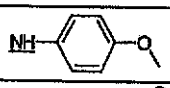
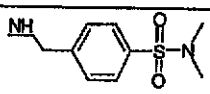
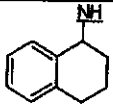
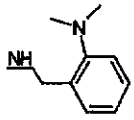
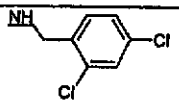
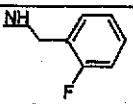
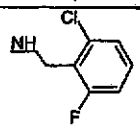
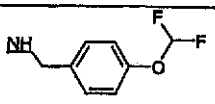
Examples 290 - 319

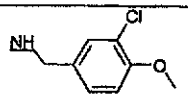
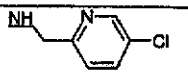
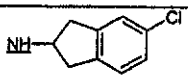
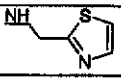
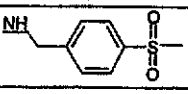
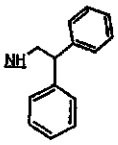
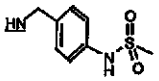
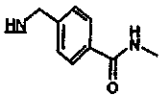
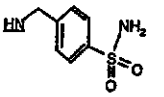
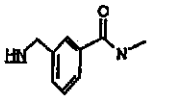
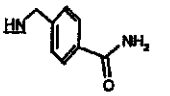
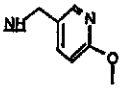


General Procedure

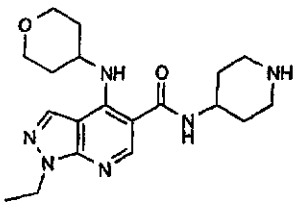
A mixture of Intermediate 60 (0.1mmol), HATU (0.1mmol) and DIPEA (0.4mmol) in DMF (0.4ml) was shaken at room temperature for 10 min. A solution of the amine (0.1mmol) in DMF (0.2ml) was then added and the mixture agitated for several minutes to give a solution. The solution was stored at room temperature for 16 hours then concentrated *in vacuo*. The residue was dissolved in chloroform (0.5ml) and applied to a SPE cartridge (aminopropyl, 0.5g). The cartridge was eluted successively with chloroform (1.5ml), EtOAc (1.5ml) and EtOAc:MeOH (9:1, 1.5ml). Fractions containing the desired product were concentrated *in vacuo* and the residue purified by mass directed autoprep HPLC.

Example no.	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
290		Aldrich; or TCI-America; or Maybridge-Int	Intermediate 60	447	2.96
291		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 60	488/ 490	3.16
292		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 60	439	2.84
293		Aldrich	Intermediate 60	457	2.92
294		Aldrich	Intermediate 60	457	2.87
295		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 60	489	3.06
296		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 60	489	3.08

297		Aldrich	Intermediate 60	457	2.82
298		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 60	455	2.98
299		Aldrich; or Acros; or Jung et al., *Tetrahedron Lett.*, 2002, 43(48), 8735; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 60	451	2.79
300		Aldrich	Intermediate 60	437	2.82
301		Peakdale Molecular Ltd	Intermediate 60	528	2.76
302		Aldrich	Intermediate 60	461	3.00
303		Peakdale Molecular Ltd	Intermediate 60	464	2.31
304		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 60	489	3.16
305		Aldrich; or *Org. Lett.*, 2002, 4(12), 2055	Intermediate 60	439	2.84
306		Fluka	Intermediate 60	473	2.92
307		Fluorochem Ltd; or WO 98/45268	Intermediate 60	487	2.95

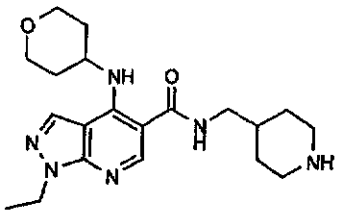
308		Apin	Intermediate 60	485	2.94
309		Key Organics Ltd	Intermediate 60	456	2.65
310		*J. Med. Chem.*, 2001, 44(26), 4628	Intermediate 60	481	3.16
311		Manchester Organics Ltd	Intermediate 60	428	2.28
312		Acros Chimica	Intermediate 60	499	2.37
313		Aldrich	Intermediate 60	511	3.18
314		Lis et al., *J. Med. Chem.*, 1990, 33(10), 2883, see Scheme III and ref. 24	Intermediate 60	514	2.60
315		WO 94/17035	Intermediate 60	478	2.47
316		Sigma	Intermediate 60	500	2.50
317		Peakdale Molecular Ltd	Intermediate 60	478	2.49
318		WO 02/85860	Intermediate 60	464	2.42
319		Syngene	Intermediate 60	452	2.45

Example 320 1-Ethyl-*N*-4-piperidinyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



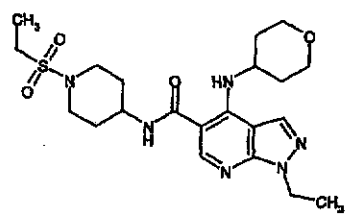
A solution of hydrogen chloride in dioxan (30ml, 4M, 0.12mol) was added to a suspension of Example 126 (1.3g, 2.75mmol), in dioxan (10ml) and the mixture was stirred at room temperature for 6h. The reaction mixture was left to stand for 14h, then the solution was evaporated, azeotroping with DCM to give a white solid the hydrochloride salt. The solid was suspended in ethyl acetate (50ml) and washed with sodium hydroxide solution (2N, 50ml). The organic layer was dried over Na_2SO_4 and concentrated in vacuo to give Example 318 as a white solid (995mg). LCMS showed $MH^+ = 373$; $T_{RET} = 1.89$min.

Example 321 1-Ethyl-*N*-(4-piperidinylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



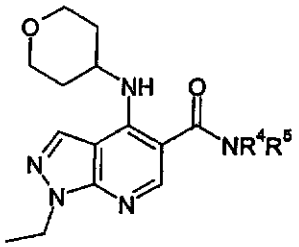
A solution of hydrogen chloride in dioxan (30ml, 4M, 0.12mol) was added to a suspension of Intermediate 72 (1.2g, 2.5mmol), in dioxan (10ml) and the mixture was stirred at room temperature for 6h. The reaction mixture was left to stand for 14h, then the solution was evaporated, azeotroping with DCM to give a white solid (1.24g). A portion of the solid (68mg) was suspended in ethyl acetate and washed with 2M-sodium hydroxide solution. The organic layer was dried over Na_2SO_4 and concentrated in vacuo to afford Example 321 as a white solid (60mg). LCMS showed $MH^+ = 387$; $T_{RET} = 1.92$min.

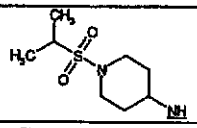
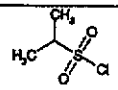
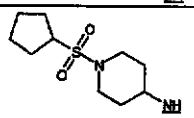
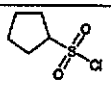
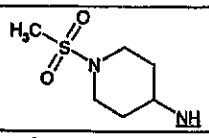
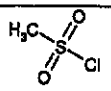
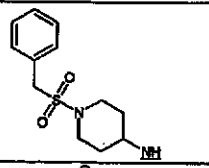
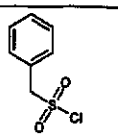
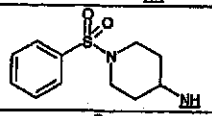
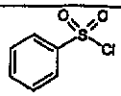
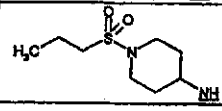
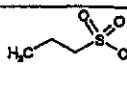
Example 322 1-Ethyl-*N*-[1-(ethylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



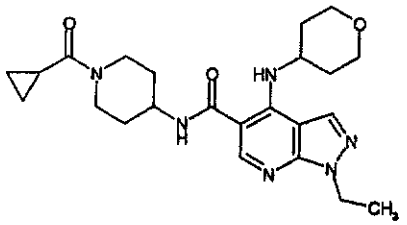
Triethylamine (0.023ml, 0.16mmol) was added to a solution of Example 320 (0.043g, 0.115mol) in DCM (1ml). The mixture was cooled (ice/water bath for 10min) and ethane sulfonyl chloride (0.014ml, 0.138mmol) was added. The resultant solution was stirred at room temperature for 18h, then the solvent was removed with a steam of nitrogen. The residue was dissolved in dichloromethane (1.5ml) and stirred with water (1.5ml). The organic layer was separated and blown down with nitrogen, and applied to a SPE cartridge (silica, 2g) eluting with 60%-100% ethyl acetate in cyclohexane. The desired fractions were concentrated in vacuo to afford Example 322 as a white solid (32mg). LCMS showed $MH^+ = 465$; $T_{RET} = 2.52$min

Similarly prepared were the following, using the same or a similar number of moles of reagents and the same or similar volumes of solvents:



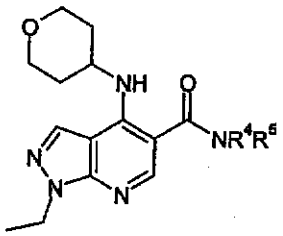
Example no.	NR^4R^5	Sulfonyl chloride	Source of sulfonyl chloride	MH + ion	LC-MC Retention time
323			Aldrich	479	2.58
324			*J. Org. Chem.*, 1952, 17, 1529	505	2.75
325			Aldrich	451	2.41
326			Aldrich	527	2.90
327			Aldrich	513	2.66
328			Aldrich	479	2.42

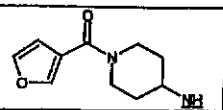
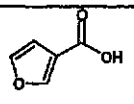
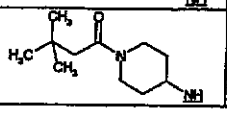
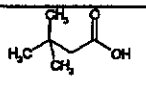
Example 329 ***N*-[1-(Cyclopropylcarbonyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**

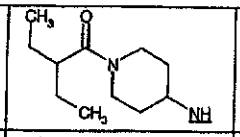
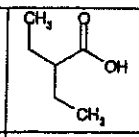
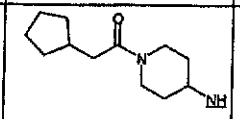
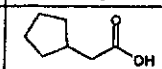
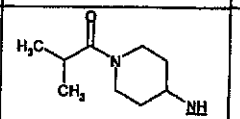
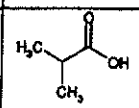
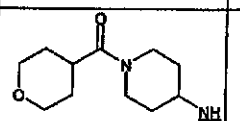
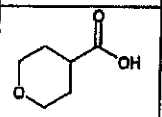
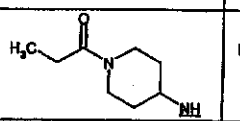
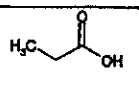
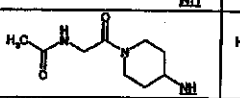
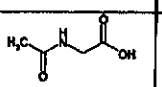
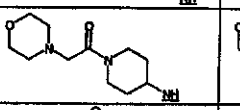
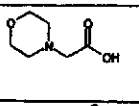
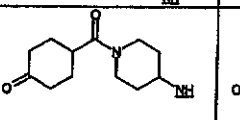
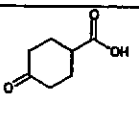
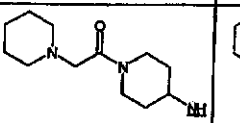
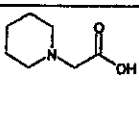
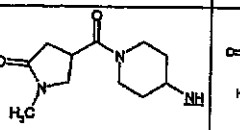
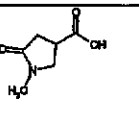
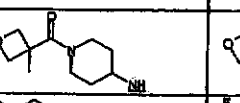
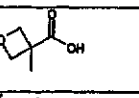
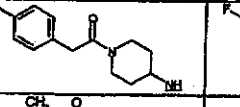
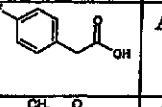
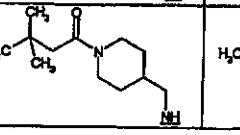
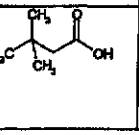


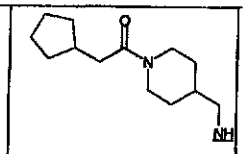
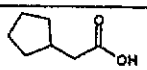
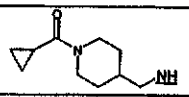
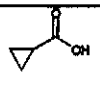
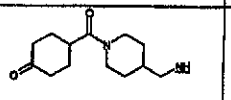
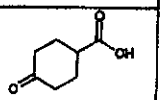
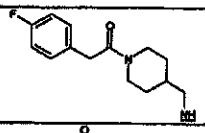
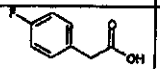
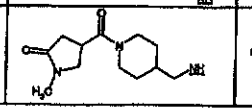
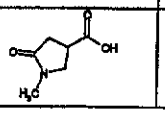
Cyclopropane carboxylic acid (0.011ml, 0.138mmol), EDC (0.031g, 0.161mmol) and HOBT (0.019g, 0.138mmol) were suspended in DMF (2ml) and stirred at room temperature for 1h. Example 320 (0.043g, 0.115mmol) was added and the mixture was stirred at room temperature for 16 hours. Most of the solvent was removed using a stream of nitrogen and the residue was partitioned between DCM (3ml) and water (3ml). The organic layer was blown down with nitrogen and applied to a SPE cartridge (aminopropyl, 1g), which was eluted with methanol. Concentration by blowing down with nitrogen afforded an impure residue which was further purified by SPE cartridge (silica, 1g), eluting with 50-100% EtOAc in cyclohexane followed by 5% methanol inEtOAc. The desired fractions were concentrated *in vacuo* to afford Example 329 as a white solid (49mg). LCMS showed $MH^+ = 441$; $T_{RBT} = 2.23$min

Similarly prepared, using the same or similar numbers of moles of reagents and volumes of solvents, and using Example 320 as the starting material to make Examples 330 to 343, but using Example 321 (similar number of moles) instead of Example 320 as the starting material to make Examples 344 to 349, were the following:

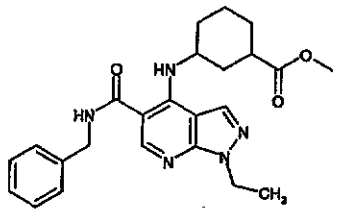


Example no.	NR^4R^5	Carboxylic acid	Source of Carboxylic acid	MH+ ion	LC-MC Retention time
330			Aldrich	467	2.50
331			Aldrich	471	2.73

332			Aldrich	471	2.72
333			Aldrich	483	2.81
334			Aldrich	443	2.27
335			Combi-Blocks	485	2.17
336			Aldrich	429	2.38
337			Aldrich	472	2.20
338			Synchem OHG	500	1.91
339			*J. Med. Chem.*, 1998, 41(5), 760	497	2.17
340			Micro-Chemistry Building Blocks	498	1.94
341			Interchim Intermediates	498	2.07
342			DE 3618135	471	2.33
343			Aldrich	509	2.75
344			Aldrich	485	2.78

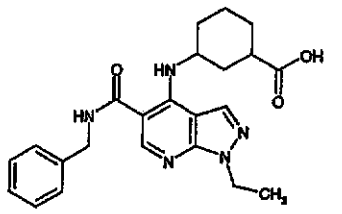
345			Aldrich	497	2.85
346			Aldrich	455	2.50
347			*J. Med. Chem.*, 1998, 41(5), 760	511	2.42
348			Aldrich	523	2.78
349			Interchim Intermediates	512	2.29

Example 350 Methyl 3-[(1-ethyl-5-{[(phenylmethyl)amino]carbonyl}-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)amino]cyclohexanecarboxylate



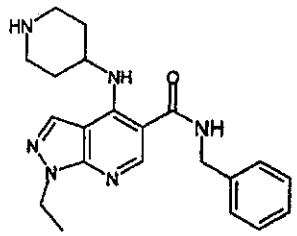
Example 350 was prepared from Intermediate 17 and using an analogous method to that used for the preparation of Example 207. LCMS showed $MH^+ = 436$; $T_{RET} = 3.20$.

Example 351 3-[(1-Ethyl-5-{[(phenylmethyl)amino]carbonyl}-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)amino]cyclohexanecarboxylic acid



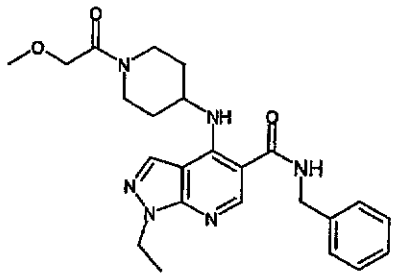
2M-Sodium hydroxide solution (0.5ml) was added to a stirred suspension of Example 350 (0.12g, 0.275mmol) in methanol (3.5ml) and water (0.8ml). After stirring overnight at room temperature, the reaction solution was concentrated, diluted with water (3ml) and acidified with 2M-hydrochloric acid. The resulting precipitate was collected by filtration, washed with water and dried to give Example 351, as a white solid (0.105g). LCMS showed $MH^+ = 422$; $T_{RET} = 2.95$min.

Example 352: 1-Ethyl-*N*-(phenylmethyl)-4-(4-piperidinylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



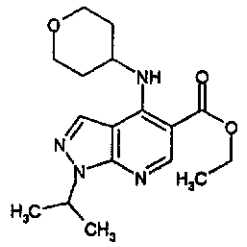
Aqueous hydrochloric acid (20ml, 5M) was added to a solution of Intermediate 65 (2.58g, 5.40mmol) in tetrahydrofuran (10ml). The reaction mixture was stirred at 20 °C for 22h then evaporated in vacuo. The residue was partitoned between DCM and water. The aqueous phase was basified with aqueous sodium hydroxide solution (2M) and extracted with diethyl ether. The organic phases was evaporated in vacuo to give Example 352 as a white solid (2.04g). LCMS showed $MH^+ = 379$; $T_{RET} =$ 2.10min.

Example 353: Ethyl 1-ethyl-4-({1-[(methyloxy)acetyl]-4-piperidinyl}amino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



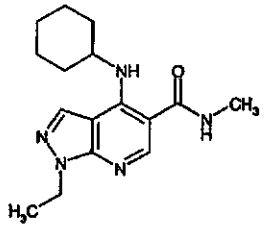
Methoxyacetyl chloride (0.016mg, 0.144mmol) and triethylamine (0.02mol, 0.144mmol) were added to a solution of Example 352 (0.046g, 0.122mmol) in DCM in a Reactivial. The reaction was stirred for 22h at 20 °C then diluted with DCM and washed with aqueous sodium hydrogen carbonate solution. The organic phase was separated and applied directly to a SPE cartridge (silica 2g). The cartridge was eluted with DCM : MeOH (1% followed by 3%) to give Example 353 as a white solid (0.05g). LCMS showed $MH^+ = 451$; $T_{RET} = 2.66$min.

Example 354: Ethyl 1-(1-methylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



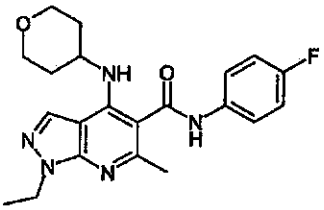
Prepared in a similar manner to example 186 using Example 20 (0.03g, 0.1mmol), with isopropylbromide (10uL, 0.11mmol), a further 0.11mmol of alkylating agent was added after 16 hours. The final compound was formed as a clear gum (16mg). LCMS showed $MH^+ = 333$; $T_{RET} = 3.16$min.

Example 355: 4-(Cyclohexylamino)-1-ethyl-*N*-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



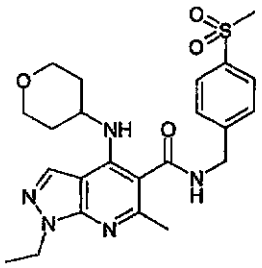
Intermediate 64 (0.02g, 0.084mmol) and diisopropylethylamine (0.044ml, 0.252mmol) were suspended in N-methyl pyrrolidinone (1ml) and cyclohexylamine (0.012ml, 0.1mmol) was added. The mixture was heated at 85°C with stirring in a Reactivial™ for 8h, then concentrated in vacuo. The residue was partitioned between DCM (2ml) and water (2ml). The layers were separated and the organic layer was concentrated in vacuo, then purified by mass directed autoprep HPLC to afford Example 355 (0.012g). LCMS showed $MH^+ = 302$; $T_{RET} = 2.85$min.

Example 356: 1-Ethyl-*N*-(4-fluorophenyl)-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



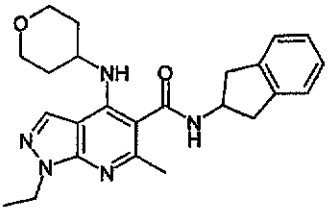
Example 356 was prepared from Intermediate 53 using an analogous method to Example 191. LCMS showed $MH^+ = 398$; $T_{RET} = 2.18$min.

Example 357: 1-Ethyl-6-methyl-*N*-{[4-(methylsulfonyl)phenyl]methyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



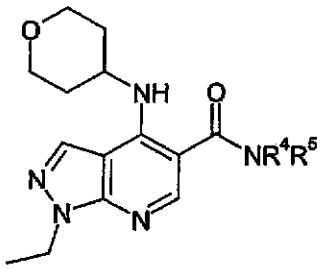
Example 357 was prepared from Intermediate 53 using an analogous method to Example 191. LCMS showed $MH^+ = 472$; $T_{RET} = 2.15$min.

Example 358: *N*-(2,3-Dihydro-1*H*-inden-2-yl)-1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



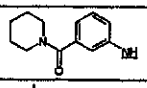
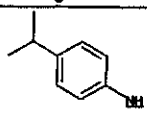
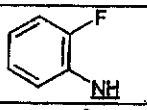
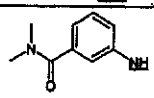
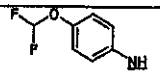
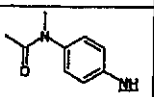
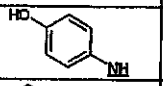
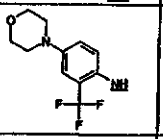
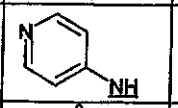
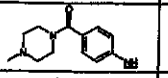
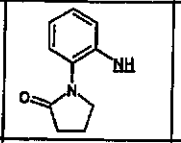
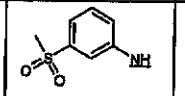
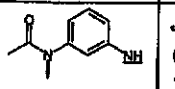
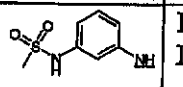
Example 358 was prepared from Intermediate 53 using an analogous method to Example 191. LCMS showed $MH^+ = 394$; $T_{RET} = 2.04$min.

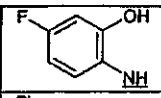
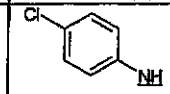
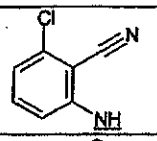
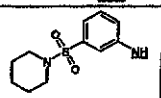
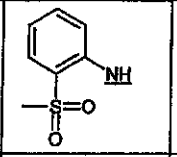
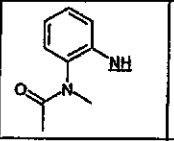
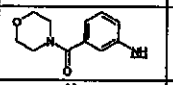
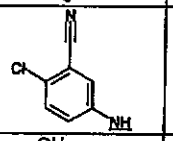
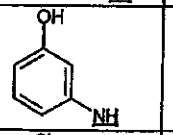
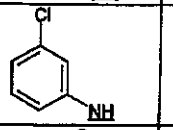
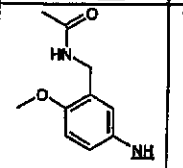
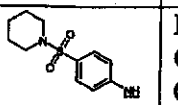
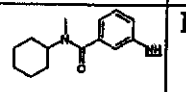
Examples 360 - 414

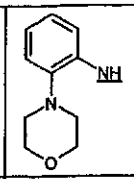
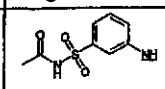
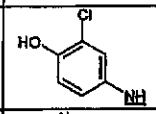
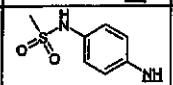
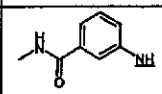
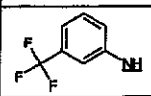
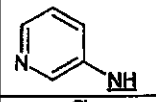
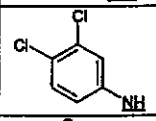
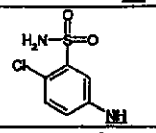
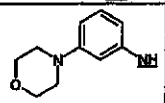
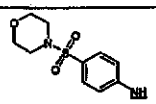
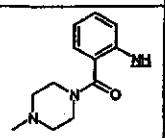
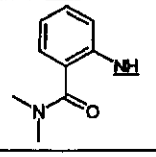


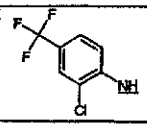
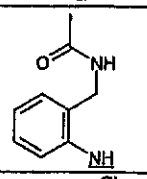
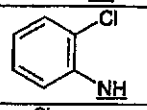
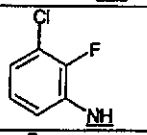
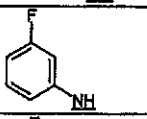
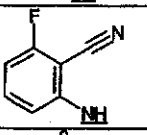
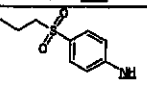
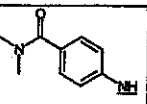
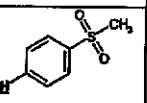
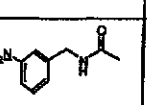
General Procedure

Intermediate 33 (1.89g) was treated with thionyl chloride (10ml) and the mixture heated under reflux for 2h. Excess thionyl chloride was removed in vacuo to afford Intermediate 73, presumed to be the acid chloride of Intermediate 33 as a cream solid. The solid was suspended in tetrahydrofuran (32.5ml) and an aliquot of the suspension added to a mixture of the amine (0.11mmol) and N,N-diisopropylethylamine (0.165 - 0.22mmol) in THF (0.5ml). The reaction mixture was agitated for 24h and the solvent removed in vacuo. The residue was purified by mass directed autoprep HPLC.

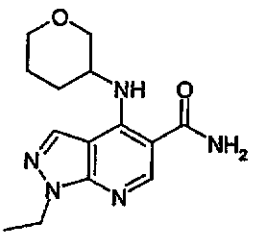
Example Number	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
360		Interchim Intermediates	Intermediate 33	477	2.98
361		Aldrich	Intermediate 33	408	3.45
362		Aldrich	Intermediate 33	384	3.09
363		Butt Park Ltd.	Intermediate 33	437	2.69
364		Aldrich	Intermediate 33	432	3.21
365		Maybridge Chemical Company Ltd.	Intermediate 33	437	2.72
366		Aldrich	Intermediate 33	382	2.67
367		Interchim Intermediates	Intermediate 33	519	3.01
368		Aldrich	Intermediate 33	367	2.19
369		Butt Park Ltd.	Intermediate 33	492	2.21
370		*J. Chem. Soc. C*, 1969, 1444	Intermediate 33	449	2.72
371		Peakdale Technologies Limited M	Intermediate 33	444	2.81
372		*J. Heterocycl. Chem.*, 1975, 12(2), 225	Intermediate 33	437	2.74
373		Interchim Intermediates	Intermediate 33	459	2.79

374		Apollo Scientific Ltd.	Intermediate 33	400	2.99
375		Aldrich	Intermediate 33	400	3.35
376		Lancaster	Intermediate 33	425	3.07
377		Maybridge CombiChem	Intermediate 33	513	3.33
379		Peakdale Technologies Limited	Intermediate 33	444	2.99
380		J. Heterocycl. Chem., 1975, 12(2), 225	Intermediate 33	437	2.64
381		Interchim Intermediates	Intermediate 33	479	2.68
382		Aceto Corporation	Intermediate 33	425	3.38
383		Aldrich	Intermediate 33	382	2.78
384		Aldrich	Intermediate 33	400	3.38
386		WO 03/32986	Intermediate 33	467	2.65
387		Maybridge Chemical Company Ltd.	Intermediate 33	513	3.35
388		Intermediate 67	Intermediate 33	505	3.23

389		Lancaster	Intermediate 33	451	3.17
390		EP 538945	Intermediate 33	487	2.80
391		Aldrich	Intermediate 33	416	2.99
392		Interchim Intermediates	Intermediate 33	459	2.74
393		Butt Park Ltd.	Intermediate 33	423	2.66
394		Aldrich	Intermediate 33	434	3.43
395		Aldrich	Intermediate 33	367	2.40
396		Aldrich; or Reetz, *Synthesis*, 1999, 9, 1555	Intermediate 33	434	3.67
397		Bayer AG	Intermediate 33	479	2.89
398		Exploratory Library	Intermediate 33	451	2.91
399		Maybridge Chemical Company Ltd.	Intermediate 33	515	3.02
400		TimTec	Intermediate 33	492	2.20
401		Exploratory Library	Intermediate 33	437	2.68

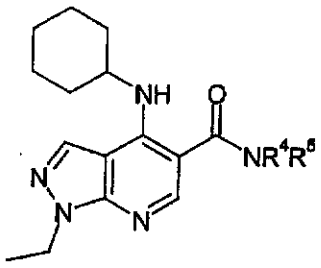
402		Lancaster	Intermediate 33	468	3.53
403		*Heterocycles*, 1983 20(3), 445	Intermediate 33	437	2.70
404		Aldrich	Intermediate 33	400	3.09
405		Aldrich	Intermediate 33	418	3.21
406		Aldrich	Intermediate 33	384	3.19
407		Aldrich	Intermediate 33	409	2.95
408		*Helv. Chim. Acta*, 1983 66(4), 1046	Intermediate 33	472	3.07
409		Butt Park Ltd.	Intermediate 33	437	2.68
411		Salor	Intermediate 33	444	2.69
413		Peakdale Molecular Limited	Intermediate 33	437	2.35

Example 414: 1-Ethyl-4-(tetrahydro-2*H*-pyran-3-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



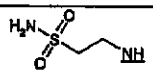
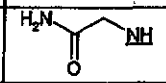
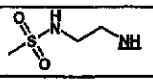
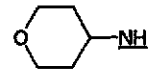
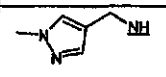
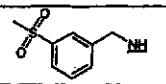
Example 414 was prepared from Intermediate 59 using the general method described for examples 360 - 413 method. LCMS showed $MH^+ = 398$; $T_{RET} = 2.90$min.

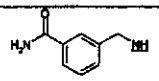
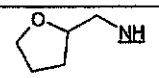
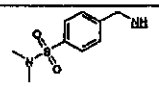
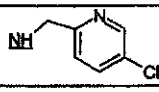
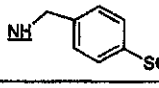
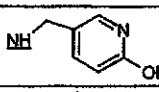
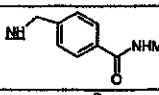
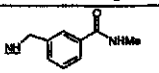
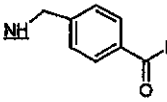
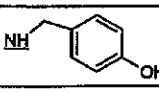
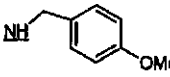
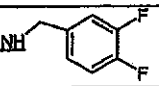
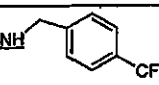
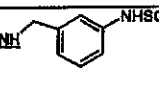
Examples 415 - 487

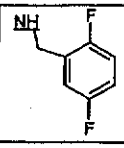
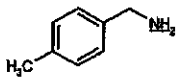
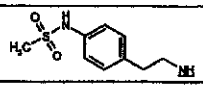
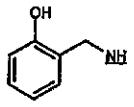
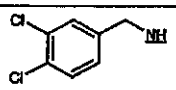
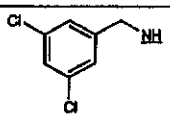
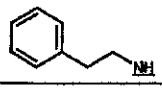
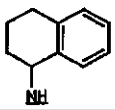
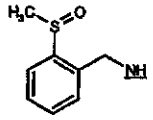
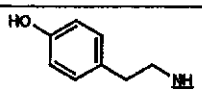
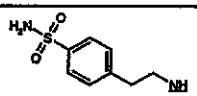
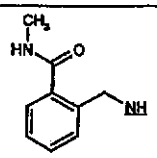
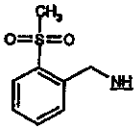


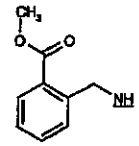
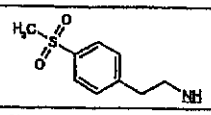
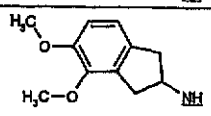
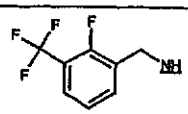
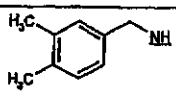
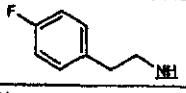
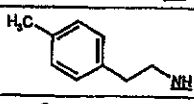
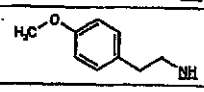
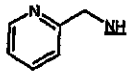
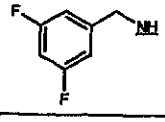
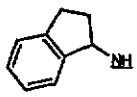
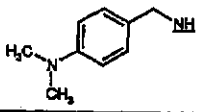
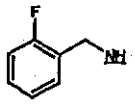
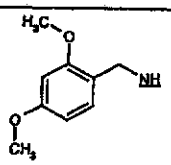
General Procedure

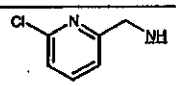
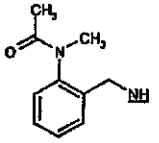
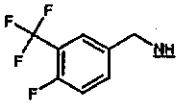
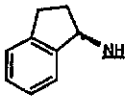
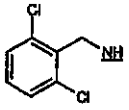
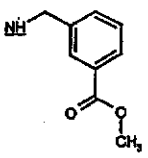
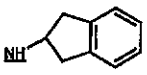
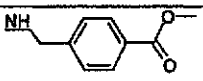
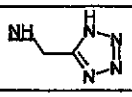
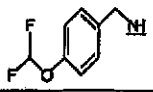
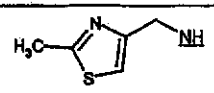
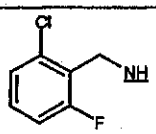
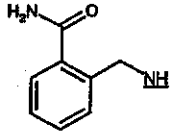
A mixture of Intermediate 61 (0.1mmol), HATU (0.1mmol) and DIPEA (0.4mmol) in DMF (0.4ml) was shaken at room temperature for 10 min. A solution of the amine (0.1mmol) in DMF (0.2ml) was then added and the mixture agitated for several minutes to give a solution. The solution was stored at room temperature for 16 hours then concentrated *in vacuo*. The residue was dissolved in chloroform (0.5ml) and applied to a SPE cartridge (aminopropyl, 0.5g). The cartridge was eluted successively with chloroform (1.5ml), EtOAc (1.5ml) and EtOAc:MeOH (9:1, 1.5ml). Fractions containing the desired product were concentrated *in vacuo* and the residue purified by mass directed autoprep HPLC.

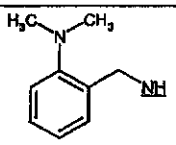
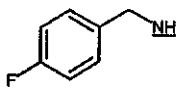
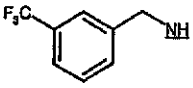
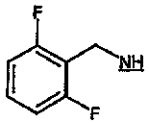
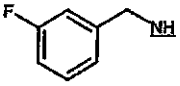
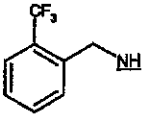
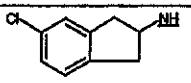
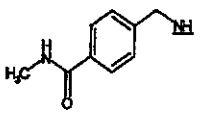
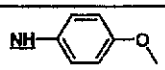
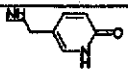
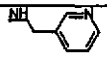
Example number	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
415		Rare Chemicals GmbH	Intermediate 61	395	2.80
416		Aldrich	Intermediate 61	345	2.64
417		Ultrafine (UFC Ltd)	Intermediate 61	409	2.84
418		Intermediate 8A; or Intermediate 8 (Combi-Blocks)	Intermediate 61	372	3.03
419		N.D. Zelinsky Institute Organic Chemistry	Intermediate 61	382	2.96
420		Peakdale Molecular	Intermediate 61	456	3.22

		Ltd.			
421		Peakdale Molecular Ltd.	Intermediate 61	421	3.03
422		Aldrich	Intermediate 61	372	3.09
423		*J. Org. Chem.*, 1955, 20, 1657	Intermediate 61	485	3.44
424		Key Organics Ltd	Intermediate 61	413	3.39
425		Acros	Intermediate 61	456	3.19
426		WO 00/17163	Intermediate 61	409	3.3
427		Peakdale Molecular Ltd	Intermediate 61	421	3.23
428		Peakdale Molecular Ltd	Intermediate 61	435	3.07
429		Peakdale Molecular Ltd	Intermediate 61	421	2.97
430		Apin	Intermediate 61	394	3.25
431		Acros; or Aldrich; or Jung et al., *Tetrahedron Lett.*, 2002, 43(48), 8735; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002, 4, 2055	Intermediate 61	408	3.51
432		Aldrich	Intermediate 61	414	3.68
433		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 61	446	3.81
434		*J. Med. Chem.*, 1999, 42(14), 2504	Intermediate 61	471	3.23

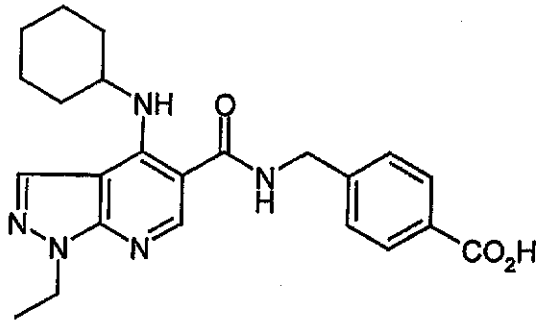
435		Aldrich	Intermediate 61	414	3.66
436		Aldrich; or *Organic Letters*, 2002, 4(12), 2055	Intermediate 61	392	3.69
438		Key Organics Ltd	Intermediate 61	485	3.25
439		Buttpark	Intermediate 61	394	3.52
440		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 61	446	4
441		Lancaster; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 61	446	4.08
442		Aldrich	Intermediate 61	392	3.62
443		Aldrich	Intermediate 61	418	3.83
444		WO 01/38323	Intermediate 61	440	3.07
445		Aldrich	Intermediate 49	408	3.31
446		Acros	Intermediate 61	471	3.13
447		Peakdale Molecular Ltd	Intermediate 61	435	3.13
448		Peakdale Molecular Ltd	Intermediate 61	456	3.32

449		Peakdale Molecular Ltd	Intermediate 61	436	3.56
450		Aldrich	Intermediate 61	471	2.79
451		*J. Med. Chem.*, 1982, 25(12), 1442	Intermediate 61	465	3.11
452		ABCR	Intermediate 61	464	3.47
453		Matrix Scientific; or *Chem. Ber.*, 1969, 102, 2770	Intermediate 61	407	3.35
454		Aldrich	Intermediate 61	411	3.18
455		Aldrich	Intermediate 61	407	3.3
456		Aldrich	Intermediate 61	423	3.09
457 (as $CF_3C(O)OH$ salt)		Aldrich	Intermediate 61	379	2.92
458		Aldrich	Intermediate 61	414	3.68
459		Aldrich	Intermediate 61	404	3.72
460 (as $CF_3C(O)OH$ salt)		Aldrich	Intermediate 61	421	3.29
461		Aldrich	Intermediate 61	396	3.58
462		Aldrich	Intermediate 61	438	3.53

463 (as $CF_3C(O)OH$ salt)		*Inorganic Chemistry*, 1997, 36(9), 1967	Intermediate 61	413	3.4
464 (as $CF_3C(O)OH$ salt)		Peakdale Molecular Ltd	Intermediate 61	449	3.18
465		ABCR	Intermediate 61	422	3.77
466		Aldrich	Intermediate 61	404	3.72
467		Pfaltz-Bauer; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 61	446	3.85
468		Peakdale Molecular Ltd	Intermediate 61	436	3.53
469		Aldrich	Intermediate 61	404	3.66
470		Aldrich	Intermediate 61	435	3.52
471		Esprit	Intermediate 61	370	2.82
472		Apollo	Intermediate 61	444	3.63
473		MicroChemistry-RadaPharma	Intermediate 61	399	3.16
474		Fluka	Intermediate 61	430	3.72
475		*J. Am. Chem. Soc.*, 1977, 99, 3075	Intermediate 61	421	3.04

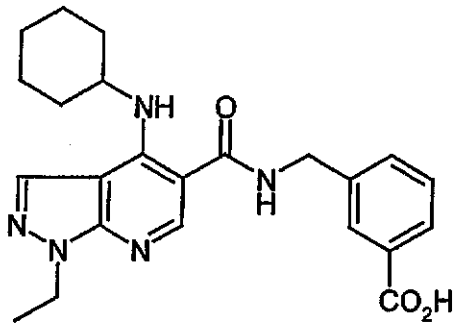
477		*J. Org. Chem.*, 2001, 66(6), 1999	Intermediate 61	421	2.89
478		Aldrich	Intermediate 61	396	3.59
479		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 61	446	3.80
480		Aldrich	Intermediate 61	414	3.57
481		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 61	396	3.62
482		Aldrich	Intermediate 61	446	3.82
483		*J. Med. Chem.*, 2001, 44(26), 4628	Intermediate 61	438	3.95
484		WO 9417035	Intermediate 61		
485		Aldrich	Intermediate 61	394	3.61
486		MicroChemistry-RadaPharma	Intermediate 61	395	2.78
487		Aldrich	Intermediate 61	379	2.71

Example 488: 4-[({[4-(Cyclohexylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid



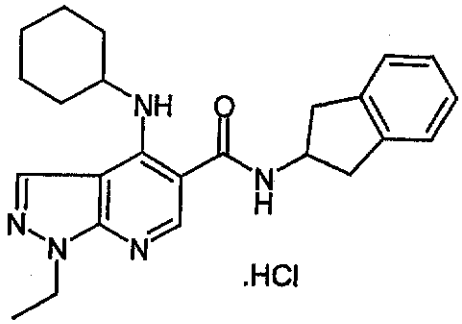
2M-Sodium hydroxide solution (29μL, 0.058mmol) was added to a stirred solution of Example 470 (6mg, 0.014mmol) in methanol (28μL) and water (2μL). The resulting solution was stirred at 50°C under nitrogen. After 16h, the mixture was diluted with water (0.5ml) and adjusted to pH 4 with acetic acid. The precipitated solid was collected by filtration and dried in vacuo to afford Example 488 as a white solid (4.5mg). LCMS showed $MH^+ = 422$; $T_{RET} = 3.26$min.

Example 489: 3-[({[4-(Cyclohexylamino)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid



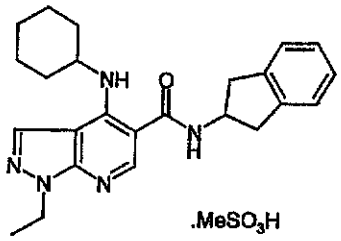
2M-Sodium hydroxide solution (83μL, 0.166mmol) was added to a stirred solution of Example 468 (18mg, 0.042mmol) in methanol (88μL) and water (5μL). The resulting solution was stirred at 50°C under nitrogen. After 16h, a further quantity of 2M-sodium hydroxide solution (29μL, 0.058mmol) was added to the reaction mixture. After 24h, the reaction mixture was diluted with water (0.5ml) and adjusted to pH 4 with acetic acid. The mixture was extracted with ethyl acetate (2 x 0.5ml), and the combined extracts were dried (Na_2SO_4) and evaporated in vacuo to give a solid (21mg). This solid was purified on an SPE cartridge (silica, 1g) eluting with ethyl acetate:cyclohexane (1:1) followed by methanol. Fractions containing the desired product were combined and concentrated to afford Example 489 as a white solid (4.6mg). LCMS showed $MH^+ = 422$; $T_{RET} = 3.22$min.

Example 490: 4-(Cyclohexylamino)-*N*-(2,3-dihydro-1*H*-inden-2-yl)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide hydrochloride



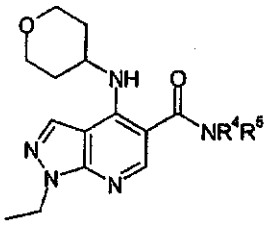
A solution of Example 469 (71mg, 0.17mmol) in anhydrous THF (2ml) was treated with hydrogen chloride in dioxane (4M, 0.3ml). After standing at ambient temperature for 16 hours the resulting solid was collected by filtration and dried under vacuum to give Example 490 as rod like crystals (36mg). LCMS showed MH^+= 404; T_{RET} = 3.60min.

Example 491: 4-(Cyclohexylamino)-*N*-(2,3-dihydro-1*H*-inden-2-yl)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide methanesulphonate



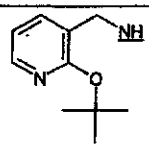
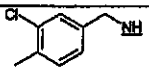
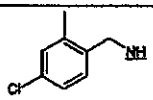
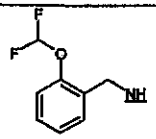
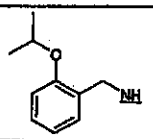
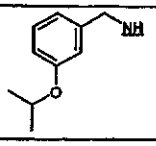
A solution of Example 469 (71mg, 0.17mmol) in anhydrous THF (2ml) was treated with anhydrous methane sulphonic acid (11.4μL, 0.17mmol). After standing at ambient temperature for 16 hours the resulting solid was collected by filtration and dried under vacuum to give Example 491 as rod like crystals (23mg). LCMS showed MH^+= 404; T_{RET} = 3.59min.

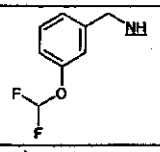
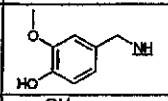
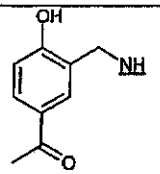
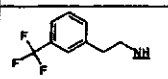
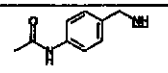
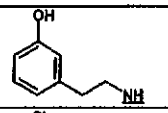
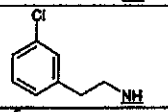
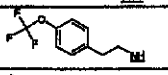
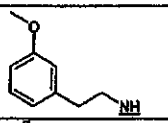
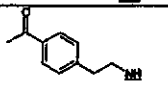
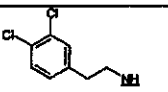
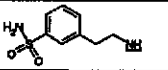
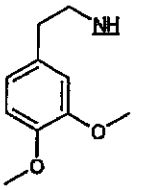
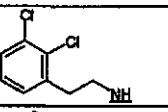
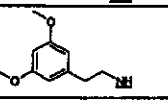
Examples 492 - 649

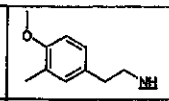
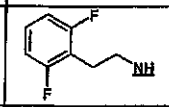
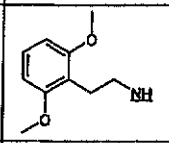
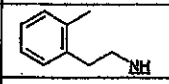
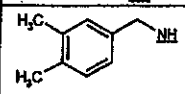
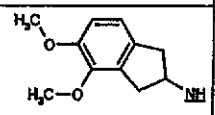
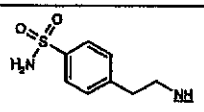
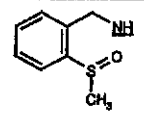
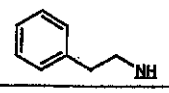
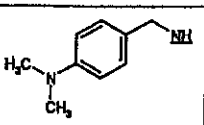
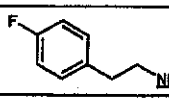
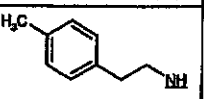
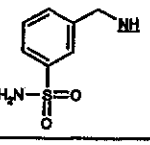
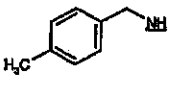


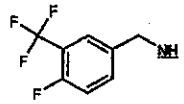
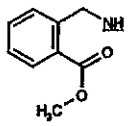
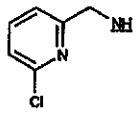
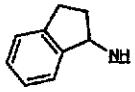
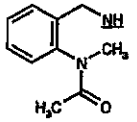
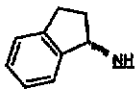
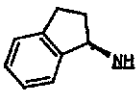
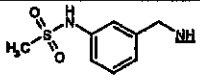
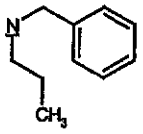
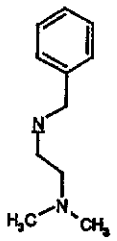
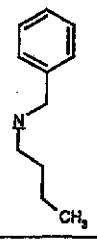
General Procedure

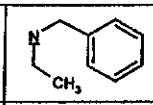
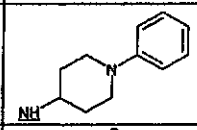
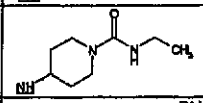
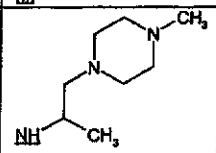
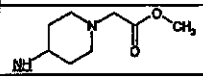
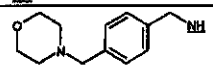
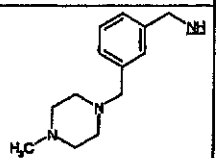
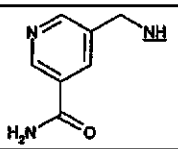
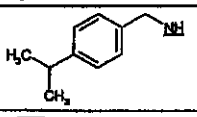
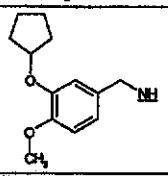
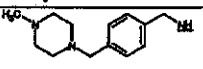
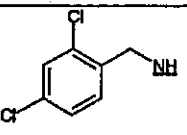
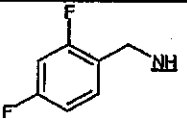
A mixture of Intermediate 33 (0.1mmol), HATU (0.1mmol) and DIPEA (0.4mmol) in DMF (0.4ml) was shaken at room temperature for 10 min. A solution of the amine (0.1mmol) in DMF (0.2ml) was then added and the mixture agitated for several minutes to give a solution. The solution was stored at room temperature for 16 hours then concentrated *in vacuo*. The residue was dissolved in chloroform (0.5ml) and applied to a SPE cartridge (aminopropyl, 0.5g). The cartridge was eluted successively with chloroform (1.5ml), EtOAc (1.5ml) and EtOAc:MeOH (9:1, 1.5ml). Fractions containing the desired product were concentrated *in vacuo* and the residue purified by mass directed autoprep HPLC.

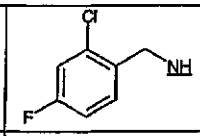
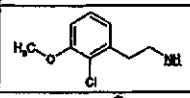
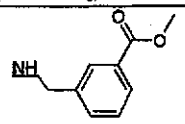
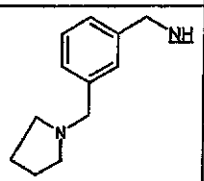
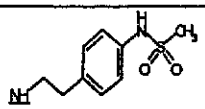
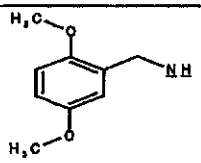
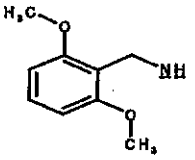
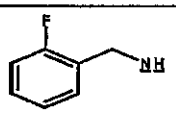
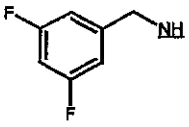
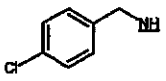
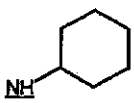
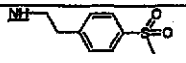
Example number	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
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493		Maybridge Chemical Company Ltd.; or WO 01/30745	Intermediate 33	428	2.92
494		Trans World Chemicals, Inc.; or DE 1953059	Intermediate 33	428	2.91
495		Fluorochem Ltd.	Intermediate 33	446	2.70
496		Peakdale Molecular Ltd.	Intermediate 33	438	2.83
497		Peakdale Molecular Ltd.	Intermediate 33	438	2.79

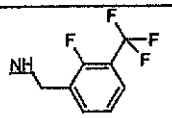
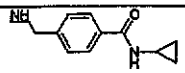
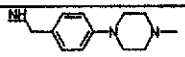
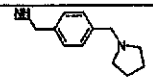
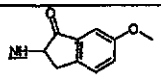
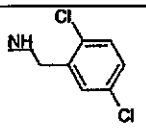
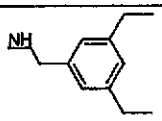
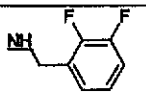
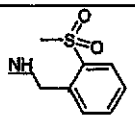
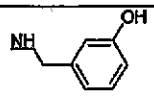
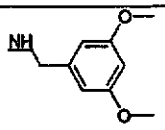
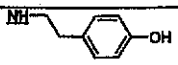
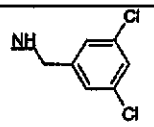
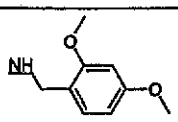
498		Fluorochem Ltd.	Intermediate 33	446	2.73
499		Aldrich	Intermediate 33	426	2.50
500		*Nippon Kagaku Zasshi*; 1952, 73; 393	Intermediate 33	438	2.62
501		Apollo Scientific Ltd.	Intermediate 33	462	2.88
502		Apin Chemicals Ltd.	Intermediate 33	437	2.19
503		Sigma	Intermediate 33	410	2.60
504		Aldrich	Intermediate 33	428	2.80
505		Miteni S.p.A.	Intermediate 33	478	2.97
506		Aldrich	Intermediate 33	424	2.58
507		*J. Med. Chem.*, 1997, 20(9), 1210	Intermediate 33	436	2.44
508		Fluorochem Ltd.	Intermediate 33	462	2.99
509		JP 11080156	Intermediate 33	473	2.2
510		Aldrich	Intermediate 33	454	2.41
512		Synchem OHG	Intermediate 33	462	2.96
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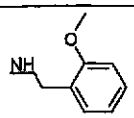
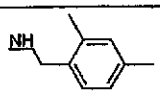
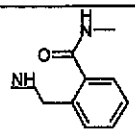
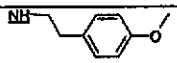
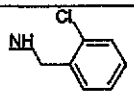
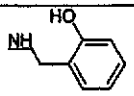
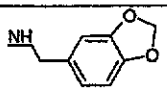
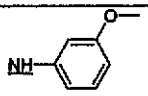
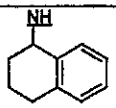
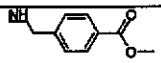
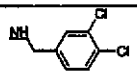
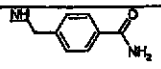
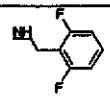
514		*J. Chem. Soc. Perkin Trans. 1*, 1977, 386	Intermediate 33	438	2.75
515		SIGMA-RBI	Intermediate 33	430	2.65
516		WO 9303022	Intermediate 33	454	2.67
517		SIGMA-RBI	Intermediate 33	408	2.73
518		Matrix Scientific; or *Chem. Ber.*, 1969, 102, 2770	Intermediate 33	408	3.2
519		*J. Med. Chem.*, 1982 25(12), 1442	Intermediate 33	466	3
521		Acros	Intermediate 33	473	2.62
522		WO 01/38323	Intermediate 33	445	2.55
523		Aldrich	Intermediate 33	394	3
524		Aldrich	Intermediate 33	423	2.51
525		Aldrich	Intermediate 33	412	3.06
526		Aldrich	Intermediate 33	408	3.16
527		*Yakugaku Zasshi*; 1950 70, 71	Intermediate 33	459	2.6
528		Aldrich; or *Organic Letters*, 2002, 4(12), 2055	Intermediate 33	394	3.08

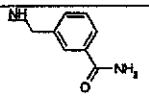
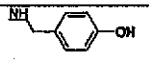
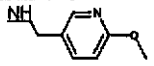
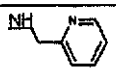
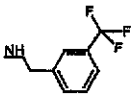
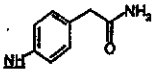
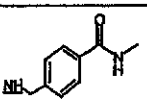
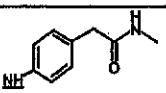
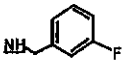
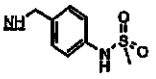
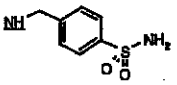
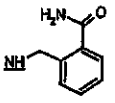
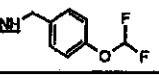
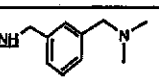
530		Lancaster	Intermediate 33	466	3.31
531		*J. Am. Chem. Soc.*, 1976, 78(22), 6978	Intermediate 33	438	3
532 (as $CF_3C(O)OH$ salt)		*Inorganic Chemistry*, 1997, 36(9), 1967	Intermediate 33	415	2.82
533		Aldrich	Intermediate 33	406	3.14
534		Peakdale Molecular Ltd.	Intermediate 33	451	2.71
535		Aldrich	Intermediate 33	406	3.15
536		Aldrich	Intermediate 33	406	3.15
537		*J. Med. Chem.*, 1999, 42(14), 2504	Intermediate 33	473	2.58
538		Chemical Building Blocks	Intermediate 33	422	2.92
540		Aldrich	Intermediate 33	451	2.13
541		Aldrich	Intermediate 33	436	3.15

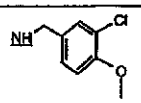
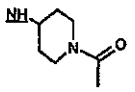
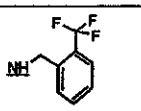
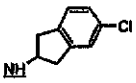
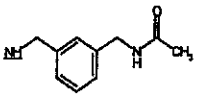
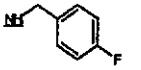
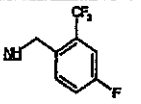
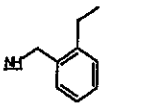
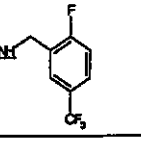
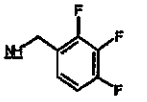
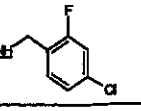
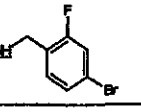
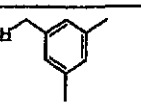
542		Aldrich	Intermediate 33	408	2.85
544		Janssen Pharma-ceuticals	Intermediate 33	449	2.67
545		Intermediate 69	Intermediate 33	444	2.34
546 (as H-C(O)OH salt = formic acid addition salt)		*Arzneimittel Forschung*, 1974, 24(4a), 584	Intermediate 33	430	1.95
547		WO 97/25323	Intermediate 33	445	1.96
548 (as $CF_3C(O)OH$ salt)		WO 03/32980	Intermediate 33	479	2.21
549 (as $CF_3C(O)OH$ salt)		WO 03/32980	Intermediate 33	492	2.24
550 (as $CF_3C(O)OH$ salt)		WO 02/85860	Intermediate 33	424	2.33
551		Salor	Intermediate 33	422	3.36
552		WO 95/00516	Intermediate 33	494	3.22
553 (as $CF_3C(O)OH$ salt)		WO 03/32980	Intermediate 33	492	2.21
554		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 33	448	3.4
555		Aldrich	Intermediate 33	416	3.06

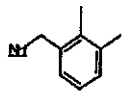
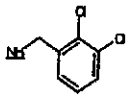
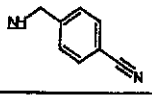
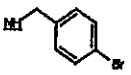
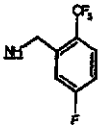
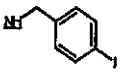
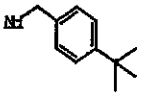
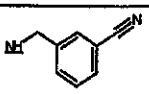
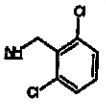
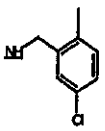
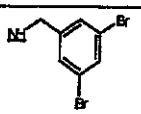
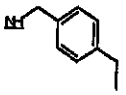
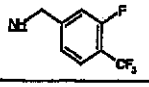
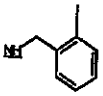
556		Salor	Intermediate 33	432	3.21
557		DE 2300018	Intermediate 33	458	3.12
558		Peakdale Molecular Ltd	Intermediate 33	436	3.41
559 (as $CF_3C(O)OH$ salt)		JP 10045736	Intermediate 33	463	2.28
560		WO 02/16318 EP 338793	Intermediate 33	487	2.74
561		Maybridge Chemical Company Ltd.	Intermediate 33	440	2.99
562		Lancaster	Intermediate 33	440	3.00
563		Aldrich	Intermediate 33	398	3.01
564		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 33	416	3.11
565		Aldrich; or *Organic Letters*, 2002, 4(12), 2055	Intermediate 33	414	3.19
567		Aldrich	Intermediate 33	372	3.01
568		*J. Biol. Chem.*, 1997, 272(3),	Intermediate 33	472	2.69

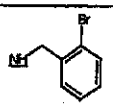
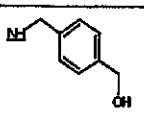
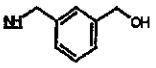
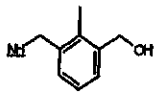
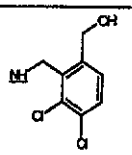
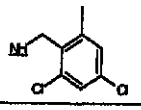
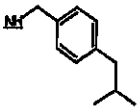
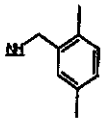
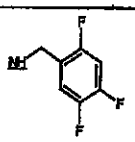
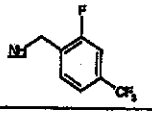
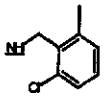
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569		Fluorochem Ltd.	Intermediate 33	466	3.29
570		Intermediate 71	Intermediate 33	463	2.66
571		Maybridge Reactive intermediates	Intermediate 33	478	2.25
572		WO 99/67204	Intermediate 33	463	2.24
573		*Eur. J. Med. Chem.*, 1987, 22(5), 417	Intermediate 33	450	2.90
574		Lancaster	Intermediate 33	446/ 448/ 450	3.35
575		*Eur. J. Med. Chem.*, 1987, 33(5), 363	Intermediate 33	436	3.48
576		Avocado	Intermediate 33	416	3.06
577		WO 02/30930	Intermediate 33	458	2.80
578		Apin	Intermediate 33	458	2.80
579		Aldrich	Intermediate 33	458	2.80
580		Aldrich	Intermediate 33		
581		Lancaster; or *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 33	446/ 448/ 450	2.80
582		Aldrich	Intermediate 33	440	2.96

583		Aldrich	Intermediate 33	410	2.98
584		ICN Biomedicals, Inc.; or Salor; or *Synthesis*, 1982, 12, 1036	Intermediate 33	408	3.18
585		WO 03/32986	Intermediate 33	437	2.62
586		Aldrich	Intermediate 33	424	3.05
587		Aldrich	Intermediate 33	414/ 416	3.13
588		Buttpark	Intermediate 33	396	2.14
589		Aldrich	Intermediate 33	424	2.76
590		Lancaster	Intermediate 33	396	2.95
591		Aldrich; or Synlett, 1999, 4, 409	Intermediate 33	386	3.10
592		Aldrich	Intermediate 33		
593		Apin	Intermediate 33	438	2.82
594		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 33	448/ 450/ 452	3.26
595		WO 02/85860	Intermediate 33	423	2.29
596		Aldrich	Intermediate 33	416	3.0

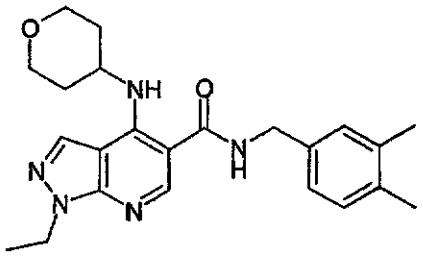
597		Aldrich	Intermediate 33	423	2.56
598		Apin	Intermediate 33	396	2.54
599		WO 00/17163	Intermediate 33	411	2.72
600		Aldrich; or *J. Med. Chem.*, 2003, 46(4), 461.	Intermediate 33	381	1.89
601		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 33	448	2.96
602		Peakdale Molecular Limited	Intermediate 33	423	2.28
603		WO 94/17035	Intermediate 33	437	2.28
604		*J.Pharm Sci.*, 1987, 76(1), 18-20	Intermediate 33	437	2.34
605		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Organic Letters*, 2002, 4(12), 2055	Intermediate 33	398	2.71
606		Lis et al., *J. Med. Chem.*, 1990, 33(10), 2883, see Scheme III and ref. 24	Intermediate 33	473	2.40
607		Sigma	Intermediate 33	459	2.31
608		Peakdale Molecular Ltd.	Intermediate 33	423	2.55
609		Fluorochem Ltd.	Intermediate 33	446	2.82
610		DE 19937494	Intermediate 33	437	1.86

611		FluorochemL	Intermediate 33	444	2.80
612		WO00/72834	Intermediate 33	415	2.12
613		Aldrich	Intermediate 33	448	2.96
615		*J. Med. Chem.*, 2001, 44(26), 4628	Intermediate 33	440	3.03
616		Intermediate 75 (as HCl salt)	Intermediate 33	451	2.62
617		Aldrich; or *Organic Letters*, 2002, 4(12), 2055	Intermediate 33	398	2.90
618		Alfa	Intermediate 33	466	2.98
619		*Energy & Fuels*, (1994), 8(4), 990-1001	Intermediate 33	408	2.86
620		Alfa	Intermediate 33	466	2.94
621		Apollo	Intermediate 33	434	2.82
622		Acros	Intermediate 33	432	2.9
623		Acros	Intermediate 33	476	2.95
624		Apollo; or *Eur. J. Med. Chem.*, 1998, 33(5), 363	Intermediate 33	408	2.88

625		Maybridge	Intermediate 33	408	2.83
626		Lancaster	Intermediate 33	448	3.02
627		Apin	Intermediate 33	405	2.56
628		Ubi-Chem	Intermediate 33	458	2.89
629		ABCR	Intermediate 33	466	2.97
630		Lancaster	Intermediate 33	505.9	2.97
631		Apollo	Intermediate 33	436	3.11
632		WO 98/33767; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111.	Intermediate 33	405	2.55
633		Pfaltz-Bauer; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111	Intermediate 33	448	2.88
634		Transworld	Intermediate 33	428	3.22
635		Apin (HNR^4R^5 used as HCl salt)	Intermediate 33	536	3.47
636		Matrix	Intermediate 33	408	3.18
637		Avocado	Intermediate 33	466	3.25
638		Pfaltz-Bauer	Intermediate 33	505.9	2.92

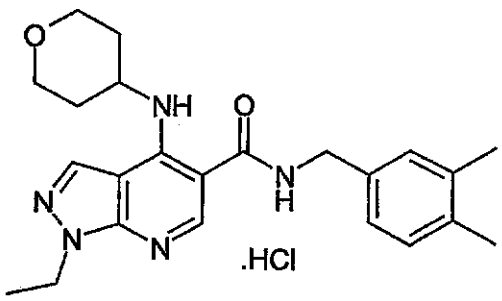
639		Alfa	Intermediate 33	458	3.10
640		WO 03/35621 (HNR^4R^5 used as HCl salt)	Intermediate 33	410	2.49
641		WO 03/35621 (HNR^4R^5 used as HCl salt)	Intermediate 33	410	2.51
642		DE 2136624 (HNR^4R^5 used as HCl salt)	Intermediate 33	424	2.55
643		(HNR^4R^5 used as HCl salt)	Intermediate 33	478	2.96
644		Aldrich	Intermediate 33	462	3.13
645			Intermediate 33	436	3.18
646		Matrix	Intermediate 33	408	2.84
647		Apollo	Intermediate 33	434	2.80
648		ABCR	Intermediate 33	466	2.99
649		Lancaster	Intermediate 33	428	2.87

Example 518: *N*-[(3,4-dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide; also known as: *N*-(3,4-dimethylbenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



An alternative process for preparing Example 518 is given below:
To a solution of Intermediate 33 (3.5g, 12.07mmol) in DMF (500ml) was added HATU (4.5g, 12.07mmol) and the mixture stirred at room temperature for 30 min. 3,4-Dimethylbenzylamine (1.63g, 12.07mmol, obtainable from Matrix Scientific, Columbia, USA or by a process described in *Chem. Ber.*, 1969, 102, 2770) was added followed by DIPEA (4.5ml, 26.55mmol) and the solution stirred at room temperature for 16 hours. The solvent was removed under reduced pressure and the residue partitioned between saturated aqueous $NaHCO_3$ (200ml) and ethyl acetate (250ml), the aqueous phase re-extracted with ethyl acetate (2x200ml), the organic extracts combined, dried (Na_2SO_4) and evaporated. The resultant viscous oil was recrystallised from hot ethyl acetate (ca. 100ml) to give the title compound as a white crystalline solid (3.36g, 80%). LCMS showed $MH^+ = 408$; $T_{ret} =$ 3.06min. δ_H (D_6 DMSO) 1.36 (3H, t), 1.51 (2H, m), 2.00 (2H, m), 2.18 (3H, s), 2.19 (3H, s), 2.50 (2H, m), 3.61 (2H. m), 3.83 (2H, m), 4.17 (1H, m), 4.36 (2H, q), 4.38 (2H, d), 7.02-7.09 (3H, m), 8.17 (1H, s), 8.62 (1H, s), 8.93 (1H, t), 9.96 (1H, d): δ_C (D_6 DMSO) 14.65, 18.91, 19.33, 32.81, 41.06, 41.86, 48.57, 64.94, 101.69, 102.18, 124.44, 128.22, 129.24, 133.28, 134.31, 135.78, 136.91, 149.26, 149.59, 151.36, 168.81

Example 518A: *N*-[(3,4-dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide hydrochloride; also known as: *N*-(3,4-dimethylbenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide hydrochloride

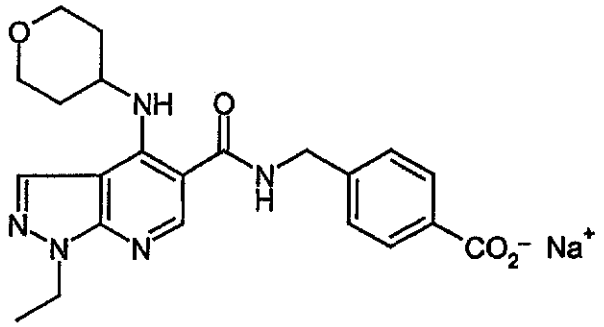


A solution of Example 518 (1.3g, 3.19mmol) in anhydrous tetrahydrofuran (200ml) was treated with a solution of hydrogen chloride in dioxane (4M, 8ml) and the

mixture stirred at ambient temperature for 16 hours. The resultant white precipitate was collected by filtration and recrystallised from hot methanol (100ml) to give the title compound Example 518A as a white crystalline solid (1.12g, 79%).

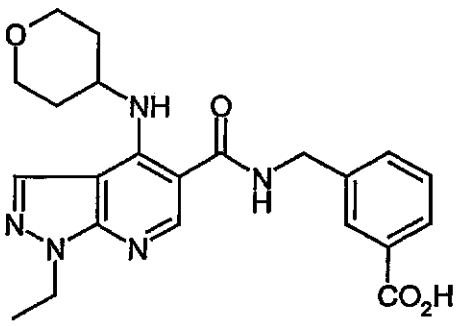
LCMS showed MH^+= 408; T_{ret} = 3.21min. δ_H (D_6 DMSO) 1.39 (3H, t), 1.59 (2H, m), 2.01 (2H, m), 2.19 (3H, s), 2.20 (3H, s), 3.64 (2H, t), 3.83 (2H, m), 4.28 (1H, m), 4.40 (2H, d), 4.50 (2H, q), 7.04-7.11 (3H, m), 9.40 (1H, s (br)), 10.72 (1H, s (br)).

Example 650: 4-[({[1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid sodium salt.



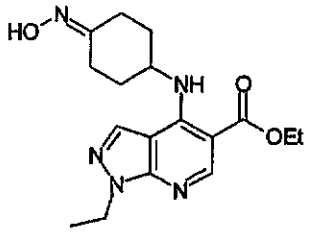
2M-Sodium hydroxide solution (98µL, 0.196mmol) was added to a stirred solution of Example 593 (22mg, 0.049mmol) in methanol (104µL) and water (6µL). The resulting solution was stirred at 50°C under nitrogen. After 16h, the reaction mixture was diluted with water (0.5ml) and adjusted to pH 4 with acetic acid. The mixture was extracted with ethyl acetate (2 x 0.5ml), and the combined extracts were dried (Na_2SO_4) and evaporated in vacuo to give a solid (15mg). This solid was suspended in water (0.5ml) and treated with 2M-sodium hydroxide solution (15µL). Evaporation of solvent *in vacuo* afforded Example 650 as a white solid (11mg). LCMS showed MH^+ = 425; T_{RET} = 2.69min.

Example 651: 3-[({[1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid



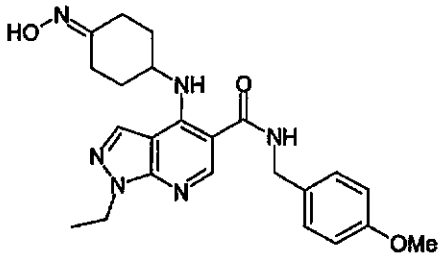
2M-Sodium hydroxide solution (98μL, 0.196mmol) was added to a stirred solution of Example 558 (22mg, 0.049mmol) in methanol (104μL) and water (6μL). The resulting solution was stirred at 50°C under nitrogen. After 16h, the reaction mixture was diluted with water (0.5ml) and adjusted to pH 4 with acetic acid. The precipitated solid was collected by filtration and dried *in vacuo* to afford Example 651 as a white solid (15mg). LCMS showed $MH^+ = 425$; $T_{RET} = 2.72$min.

Example 652: Ethyl 1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



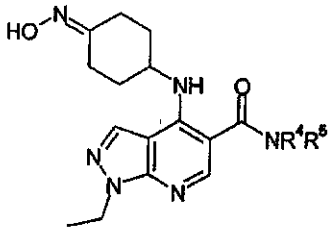
A mixture of Example 205 (200mg), hydroxylamine hydrochloride (50mg) and anhydrous potassium carbonate (420mg) in acetonitrile (10 ml) was stirred and heated at reflux for 17 hours. The solution was cooled and concentrated *in vacuo*. The residue was partitioned between EtOAc and water. The organic phase was separated, dried over Na_2SO_4 and concentrated *in vacuo* to give Example 652 as a white powder (203mg). LCMS showed $MH^+ = 346$; $T_{RET} = 2.84$min.

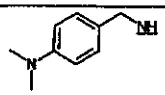
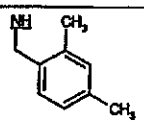
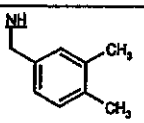
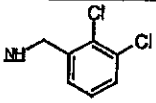
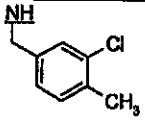
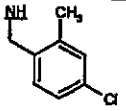
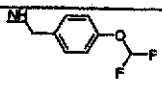
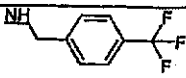
Example 653: 1-Ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-*N*-{[4-(methyloxy)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



A mixture of Example 263 (217mg), hydroxylamine hydrochloride (43mg) and anhydrous potassium carbonate (355mg) in acetonitrile (10 ml) was stirred and heated at reflux for 17 hours. The solution was cooled and concentrated *in vacuo*. The residue was partitioned between EtOAc and water. The organic phase was separated, dried over Na_2SO_4 and concentrated *in vacuo* to give Example 653 as a yellow solid (186mg). LCMS showed $MH^+ = 437$; $T_{RET} = 2.82$min. δ_H ($CDCl_3$) 1.49 (3H, t), 1.80 (2H, m), 2.2-2.4 (4H, m), 2.54 (1H, m), 3.13 (1H, dt), 3.81 (3H, s), 4.13 (1H, m), 4.46 (2H, q), 4.54 (2H, d), 6.28 (1H, t), 6.90 + 7.28 (4H, AA'BB'), 7.98 (1H, s), 8.36 (1H, s), 9.84 (1H, d). Hydroxyl proton not visible.

The following examples were prepared by a similar procedure, e.g. using the same or a similar number of moles of reagents and the same or similar volumes of solvents:

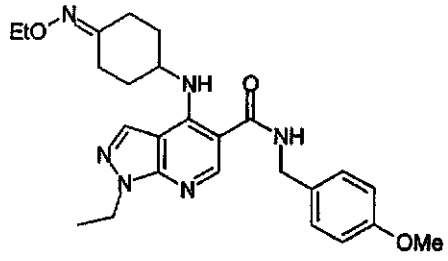


Example No.	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
654		Aldrich	Example 265	450	2.35
680		Salor; or ICN Biomedicals, Inc.; or *Synthesis*, 1982, 12, 1036	Example 260	435	3.10
681		CHMSRV-AS; or Matrix Scientific; or *Chem. Ber.*, 1969, 102, 2770	Example 261	435	3.08
682		Lancaster	Example 677	475	3.20
683		Maybridge Chemical Company Ltd.; or WO 01/30745	Example 678	455	3.17
684		Trans World Chemicals, Inc.; or DE 1953059	Example 679	455	3.17
685		Fluorochem; or WO 98/45268	Example 266	473	3.00
686		Aldrich; or Meindl et al., *J. Med. Chem.*, 1984, 27(9), 1111; or *Org. Lett.*, 2002,	Example 267	475	3.13

		4(12), 2055			

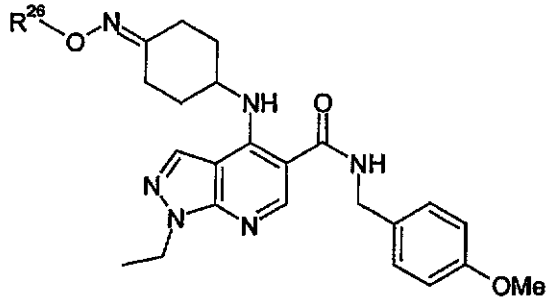
See later for alternative preparation of Example 681.

Example 655: 1-Ethyl-4-({4-[(ethyloxy)imino]cyclohexyl}amino)-*N*-{[4-(methyloxy)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



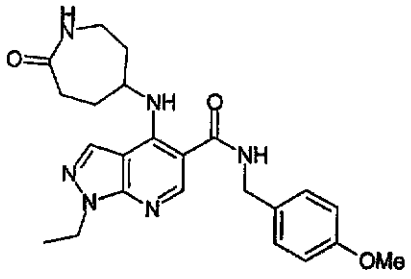
A mixture of Example 263 (25mg), ethoxyamine hydrochloride ($R^{26}ONH_2$ where R^{26} = Et, 20mg) and diisopropylethylamine (30mg) in acetonitrile (3 ml) was stirred and heated at reflux for 3.25 hours. The solution was cooled and concentrated *in vacuo*. The residue was applied to an SPE cartridge (5g). The cartridge was eluted with EtOAc. Fractions containing the desired product were concentrated in vacuo to give Example 655 as a colourless gum (20mg). LCMS showed MH^+ = 465; T_{RET} = 3.28min.

The following examples were prepared by a similar procedure, e.g. using the same or a similar number of moles of reagents and the same or similar volumes of solvents:



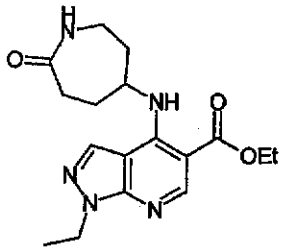
Example No.	R^{26}	Source of $R^{26}ONH_2$	Starting Material	MH + ion	LC-MC Retention time
656	Me	Aldrich	Example 263	451	2.52
657	^tBu	Aldrich	Example 263	493	3.66

Example 658: 1-Ethyl-*N*-{[4-(methyloxy)phenyl]methyl}-4-[(7-oxohexahydro-1*H*-azepin-4-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide



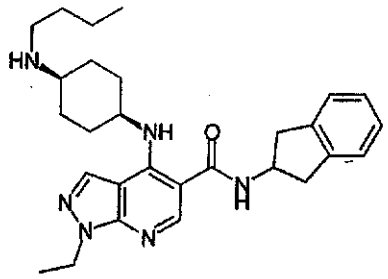
A suspension of cyanuric chloride (2,4,6-trichloro-1,3,5-triazine) (150mg) in DMF (0.2 ml) was stirred for 30 minutes at room temperature. The suspension was diluted to 7ml with DMF, with stirring. A 1.0ml portion of the resultant suspension was removed and added to Example 653 (52mg). The resultant solution was stirred for 90 hours at room temperature, then concentrated *in vacuo*. The residue was partitioned between EtOAc and water. The organic phase was separated and washed consecutively with saturated sodium carbonate, 10% w/v citric acid and saturated brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was applied to an SPE cartridge (2g). The cartridge was eluted successively with EtOAc:cyclohexane (1:1), EtOAc and then a (100:8:1) mixture of dichloromethane, ethanol and ammonia. Fractions containing the desired product (eluted in the ammoniacal solution) were concentrated *in vacuo* to give Example 658 as a colourless oil (11mg). LCMS showed $MH^+ = 437$; $T_{RET} = 2.50$min.

Example 659: Ethyl 1-ethyl-4-[(7-oxohexahydro-1*H*-azepin-4-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



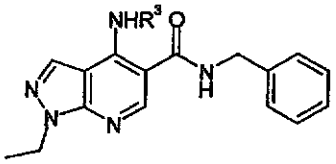
Example 659 was prepared from Example 652, using an identical procedure to that used for Example 658. LCMS showed $MH^+ = 346$; $T_{RET} = 2.56$min.

Example 660: 4-{[*cis*-4-(Butylamino)cyclohexyl]amino}-*N*-(2,3-dihydro-1*H*-inden-2-yl)-1-ethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

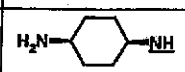


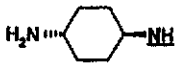
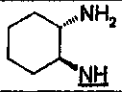
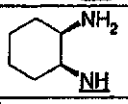
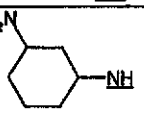
A solution of Example 258 (25mg), butyraldehyde (5mg) and glacial acetic acid (30mg) in DCM (3ml) was stirred for 10min. Sodium triacetoxyborohydride (21mg) was added. The reaction mixture was stirred for 1.5 hours. Sodium bicarbonate (1.0Molar, 3ml) was added dropwise, with stirring. After stirring for 5 min. the phases were separated. The organic phase was dried over Na_2SO_4 and applied to an SPE cartridge (5g). The cartridge was eluted with a (100:8:1) mixture of dichloromethane, ethanol and ammonia. Fractions containing the desired product were concentrated *in vacuo* to give Example 660 as an amorphous, cream solid (19mg). LCMS showed $MH^+ = 346$; $T_{RET} = 2.56$min.

Examples 661 to 664



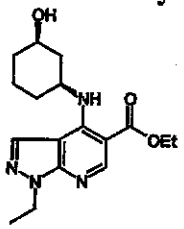
General Procedure:
Intermediate 17 (0.16mmol) in acetonitrile (1ml) was treated with the R^3NH_2 amine (0.8mmol) in acetonitrile (1ml) and N,N-diisopropylethylamine (0.8mmol). The mixture was heated at 50°C for 18h then concentrated in vacuo. The residue was diluted with water (3ml) and extracted with dichloromethane (2 x 5ml). The combined organic extracts were evaporated, and the residue was purified by mass directed autoprep HPLC to give the desired product containing formic acid. This material was dissolved in chloroform-methanol (10/1, 5.5ml) and washed with 5% sodium hydrogen carbonate solution (1ml) to give after evaporation of solvents the pure product.

Example no.	NHR^3 **	Source of R^3NH_2	Starting Material	MH + ion	LC-MC Retention time
214		*J. Med. Chem.*, 1994, 37(17), 2360	Intermediate 17	393	2.16

661		Aldrich	Intermediate 17	393	2.16
662		Aldrich	Intermediate 17	393	2.29
663		Aldrich	Intermediate 17	393	2.30
664		Peakdale Molecular Ltd	Intermediate 17	393	2.21

** For NHR^3 in Examples 214 and 661-663, NHR^3 is the *cis* or *trans* isomer as shown. For Examples 662-664, NHR^3 is the 3-amino- or 2-amino- cyclohex-1-ylamino group in a racemic form.

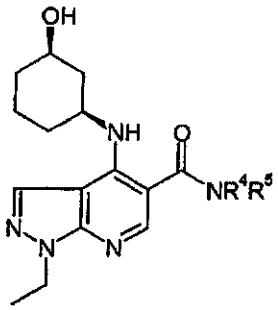
Example 665 Ethyl 1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate



[*cis*-(3-hydroxycyclohex-1-yl)amino group, racemic]

3-Aminocyclohexanol (0.677g, 5.9mmol, as described in *J. Chem. Soc., Perkin Trans 1*, 1994, 537) in acetonitrile (10ml) and ethanol (1ml) was added at room temperature to a stirred solution of Intermediate 1 (1.24g, 4.9mmol) and diisopropylethylamine (4.26ml, 24.5mmol) in acetonitrile (25ml). The resulting mixture was stirred at 85°C for 17h. The mixture was concentrated *in vacuo*, and the residue was partitioned between DCM (50ml) and water (10ml). The phases were separated and the organic phase was dried (Na_2SO_4) and evaporated to give an orange-brown oil. The oil was purified by Biotage chromatography (silica 100g) eluting with 30-50% EtOAc in cyclohexane to give Example 665 as a white foam (0.681g). LCMS showed MH^+ = 333; T_{RET} = 2.76min.

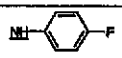
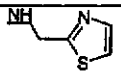
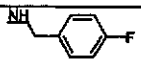
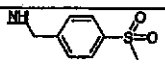
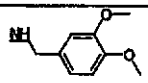
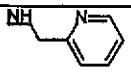
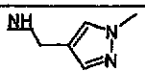
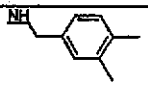
Examples 666 – 676

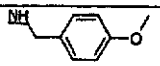
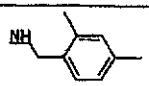


[*cis*-(3-hydroxycyclohex-1-yl)amino group, racemic]

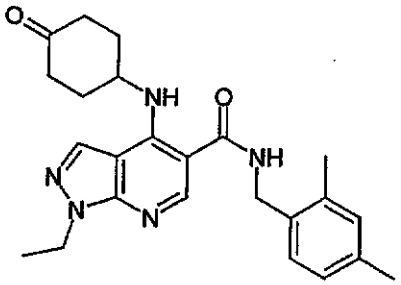
General Procedure:

A mixture of Intermediate 76 (0.1mmol), HATU (0.1mmol) and DIPEA (0.4mmol) in DMF (0.5ml) was shaken at room temperature for 10min. A solution of the amine HNR^4R^5 (0.12mmol) in DMF (0.5ml) was then added and the mixture agitated for several minutes to give a solution. The solution was stored at room temperature for 16h, then concentrated in vacuo. The residue was purified by mass directed autoprep HPLC.

Example no.	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
666		Aldrich	Intermediate 76	332	2.35
667		Aldrich	Intermediate 76	398	2.96
668		Manchester Organics Ltd	Intermediate 76	401	2.48
669		Aldrich	Intermediate 76	412	2.88
670		Acros	Intermediate 76	472	2.57
671		Aldrich	Intermediate 76	454	2.67
672		Aldrich	Intermediate 76	395	2.15
673		N.D. Zelinsky Institute	Intermediate 76	398	2.35
674		Matrix Scientific; or *Chem. Ber.*, 1969, 102, 2770	Intermediate 76	422	3.08

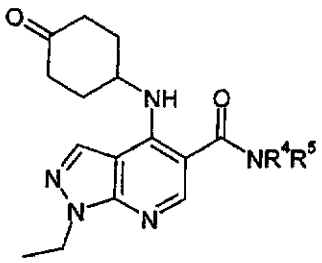
675		Aldrich	Intermediate 76	424	2.81
676		ICN Biomedicals, Inc.; or Salor; or *Synthesis*, 1982, 12, 1036	Intermediate 76	422	3.08

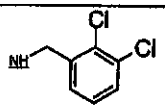
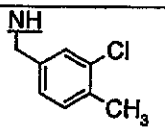
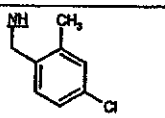
Example 260 (Alternative Procedure)
***N*-[(2,4-dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide**



Alternative procedure for preparing Example 260:
A solution of Intermediate 58 (45mg), HATU (63mg) and DIPEA (39mg) in acetonitrile (5ml) was stirred for 10min. A solution of 2,4-dimethylbenzylamine (24mg) (available from Salor; or ICN Biomedicals, Inc.; or *Synthesis*, 1982, 12, 1036) in acetonitrile (1ml) was added. The reaction mixture was stirred for 18h. The solution was concentrated and the residue partitioned between ethyl acetate (25ml) and 0.5M sodium bicarbonate (20ml). The organic phase was separated, washed with water (20ml), dried over Na_2SO_4 and concentrated to leave a gum which was applied to an SPE cartridge (5g). The cartridge was eluted with ethyl acetate. Fractions containing the desired compound were combined and concentrated *in vacuo* to give **Example 260** (32mg). LC-MS showed $MH^+ = 420$; $T_{RET} = 3.16$min. δ_H ($CDCl_3$): 1.49 (3H, t), 2.11 (2H, m), 2.33 (3H, s), 2.35 (3H, s), 2.40 (2H, m), 2.52 (2H, m), 2.61 (2H, m), 4.36 (1H, m), 4.47 (2H, q), 4.55 (2H, d), 6.14 (1H, t), 7.01 + 7.18 (2H, AA'BB'), 7.04 (1H, s), 8.01 (1H, s), 8.36 (1H, s), 9.96 (1H, d).

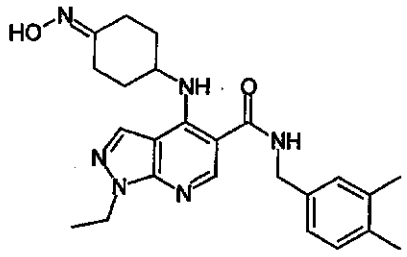
The following **Examples 677-679** were prepared in a similar manner to Example 260 (alternative procedure above), for example using the same or a similar number of moles of reagents and the same or similar volumes of solvents:



Example no.	NR^4R^5	Source of HNR^4R^5	Starting Material	MH + ion	LC-MC Retention time
677		Lancaster	Intermediate 58	460	3.28
678		Maybridge Chemical Company Ltd.; or WO 01/30745	Intermediate 58	440	3.25
679		Trans World Chemicals, Inc.; or DE 1953059	Intermediate 58	440	3.24

Examples 680-686 and their preparation are shown above together with Example 653.

Alternative Preparation of Example 681: *N*-[(3,4-dimethylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide

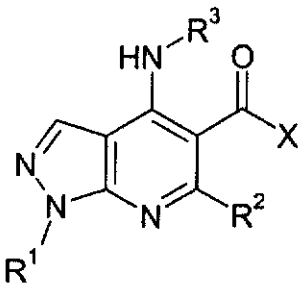


A mixture of Example 261 (35mg), hydroxylamine hydrochloride (10mg) and diisopropylethylamine (26mg) in acetonitrile (4 ml) was stirred and heated at reflux for 2.5 hours. The solution was cooled and concentrated *in vacuo*. The residue was partitioned between EtOAc and water. The organic phase was separated, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was applied to an SPE cartridge (10g). The cartridge was eluted with EtOAc:cyclohexane (1:1) and then EtOAc. Fractions containing the desired compound were combined and concentrated *in vacuo* to give Example 681 as a white, amorphous solid (18mg). LCMS showed $MH^+ = 435$; $T_{RET} = 3.08$min. δ_H ($CDCl_3$) 1.49 (3H, t), 1.79 (2H, m), 2.24 (6H, s), 2.19-2.38 (4H,

m), 2.56 (2H, dt), 4.13 (1H, m), 4.46 (2H, q), 4.53 (2H, d), 6.36 (1H, t), 7.09 (2H, t), 7.12 (1H, s), 7.98 (1H, s), 8.38 (1H, s), 9.79 (1H, d). Hydroxyl proton not visible.

CLAIMS

1. A compound of formula (I) or a salt thereof:



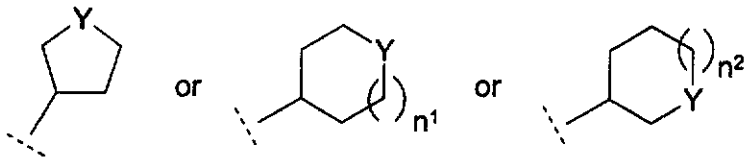
(I)

wherein:

R^1 is C_{1-3}alkyl, C_{1-2}fluoroalkyl or $-CH_2CH_2OH$;

R^2 is a hydrogen atom (H), methyl or C_1fluoroalkyl;

R^3 is substituted C_{3-8}cycloalkyl or an optionally substituted heterocyclic group of sub-formula (aa), (bb) or (cc);



(aa) (bb) (cc)

in which n^1 and n^2 independently are 1 or 2; and in which Y is O, S, SO_2, or NR^{10}; where R^{10} is a hydrogen atom (H), methyl, ethyl, $C(O)NH_2$, C(O)methyl or $C(O)-CF_3$;

and wherein, when R^3 is substituted C_{3-8}cycloalkyl, then R^3 is cyclohexyl substituted by one substituent being oxo (=O), OH, NHR^{21} wherein R^{21} is a hydrogen atom (H) or C_{1-5} straight-chain alkyl, $-CH_2OH$, $-C(O)OR^{23}$ wherein R^{23} is H or methyl, $-C(O)NHR^{24}$ wherein R^{24} is H or methyl, $-C(O)R^{25}$ wherein R^{25} is C_{1-2}alkyl, hydroxyimino (=N-OH), or (C_{1-4}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-4}alkyl); and wherein any OH or NHR^{21} substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (I);

and wherein the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc) is optionally substituted with one or two substituents being oxo (=O);

and X is NR^4R^5 or OR^{5a}, in which:

R^4 is a hydrogen atom (H); and

R^5 is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl optionally substituted by a C_{1-2}alkyl group; or $-(CH_2)_n{}^4$-C_{3-8}cycloalkyl optionally substituted, in the $-(CH_2)_n{}^4$- moiety or in the C_{3-8}cycloalkyl moiety, by a C_{1-2}alkyl group, wherein n^4 is 1, 2 or 3;

or R^5 is C_{2-6}alkyl substituted by one or two independent substituents R^{11};

wherein each substituent R^{11}, independently of any other R^{11} substituent present, is: hydroxy (OH); C_{1-6}alkoxy; phenyloxy; benzyloxy; $-NR^{12}R^{13}$; $-NR^{15}$-C(O)R^{16}; $-NR^{15}$-C(O)-O-R^{16}; $-NR^{15}$-C(O)-NH-R^{15}; or $-NR^{15}$-SO_2R^{16}; and wherein any R^{11} substituent which is OH, alkoxy or $-NR^{12}R^{13}$ is not substituted at any carbon atom, of any R^4 or R^5 substituted alkyl, which is bonded to the nitrogen of NR^4R^5;

or R^5 is $-(CH_2)_n{}^{11}$-C(O)R^{16}; $-(CH_2)_n{}^{12}$-C(O)$NR^{12}R^{13}$; $-CHR^{19}$-C(O)$NR^{12}R^{13}$; $-(CH_2)_n{}^{12}$-C(O)OR^{16}; $-(CH_2)_n{}^{12}$-C(O)OH; $-CHR^{19}$-C(O)OR^{16}; $-CHR^{19}$-C(O)OH; $-(CH_2)_n{}^{12}$-SO_2-$NR^{12}R^{13}$; $-(CH_2)_n{}^{12}$-SO_2R^{16}; or $-(CH_2)_n{}^{12}$-CN; wherein n^{11} is 0, 1, 2, 3 or 4 and n^{12} is 1, 2, 3 or 4;

or R^5 is $-(CH_2)_n{}^{13}$-Het wherein n^{13} is 0, 1, 2, 3 or 4 and Het is a 4-, 5-, 6- or 7-membered saturated or partly-saturated heterocyclic ring containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-hetero-atoms present are not bound to the $-(CH_2)_n{}^{13}$- moiety when n^{13} is 1 and are not bound to the nitrogen of NR^4R^5 when n^{13} is 0; wherein any ring-nitrogens which are present and which are not unsaturated (i.e. which do not partake in a double bond) are present as NR^{17} where R^{17} is as defined herein; and wherein one or two of the carbon ring-atoms independently are optionally substituted by C_{1-2}alkyl;

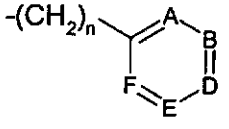
or R^5 is phenyl optionally substituted with, independently, one, two or three of: a halogen atom; C_{1-6}alkyl; C_{1-2}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{3-6}cycloalkyloxy; $-C(O)R^{16a}$; $-C(O)OR^{30}$; $-S(O)_2$-R^{16a}; R^{16a}-$S(O)_2$-NR^{15a}-; R^7R^8N-$S(O)_2$-; C_{1-2}alkyl-C(O)-$R^{15a}N$-$S(O)_2$-; C_{1-4}alkyl-S(O)-; Ph-S(O)-;

R^7R^8N-CO-; -NR^{15}-C(O)R^{16}; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-$S(O)_2$-CH_2-; R^7R^8N-$S(O)_2$-CH_2-; C_{1-2}alkyl-$S(O)_2$-NR^{15a}-CH_2-; -CH_2-OH; -CH_2CH_2-OH; -CH_2-NR^7R^8; -CH_2-CH_2-NR^7R^8; -CH_2-C(O)OR^{30}; -CH_2-C(O)-NR^7R^8; -CH_2-NR^{15a}-C(O)-C_{1-3}alkyl; -$(CH_2)_n{}^{14}$-Het^1 where n^{14} is 0 or 1; cyano (CN); Ar^{5a}; or phenyl, pyridinyl or pyrimidinyl wherein the phenyl, pyridinyl or pyrimidinyl independently are optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

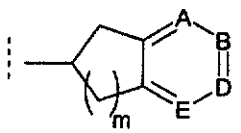
or where two adjacent substituents, on the R^5 optionally substituted phenyl, taken together are –O–(CMe_2)–O– or –O–$(CH_2)_n{}^{14a}$–O– where n^{14a} is 1 or 2;

wherein R^7 and R^8 are independently a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or R^7 and R^8 together are -$(CH_2)_n{}^6$- or -C(O)-$(CH_2)_n{}^7$- or -C(O)-$(CH_2)_n{}^7$-C(O)- or -$(CH_2)_n{}^8$-X^7-$(CH_2)_n{}^9$- or -C(O)-X^7-$(CH_2)_n{}^{10}$- in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3 , and X^7 is O or NR^{14} wherein R^{14} is H, C_{1-2}alkyl or C(O)Me;

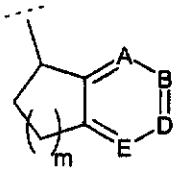
or R^5 has the sub-formula (x), (y), (y1) or (z):



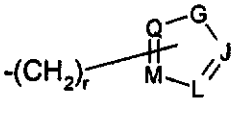
(x)



(y)



(y1)



(z)

wherein in sub-formula (x), n = 0, 1 or 2; in sub-formula (y) and (y1), m = 1 or 2; and in sub-formula (z), r = 0, 1 or 2;

wherein in sub-formula (x) and (y) and (y1), none, one or two of A, B, D, E and F are independently nitrogen or nitrogen-oxide (N^+-O^-) provided that no more than one of A, B, D, E and F is nitrogen-oxide; and the remaining of A, B, D, E and F are independently CH or CR^6;

provided that when n is 0 in sub-formula (x) then one or two of A, B, D, E and F are independently nitrogen or nitrogen-oxide (N^+-O^-) and no more than one of A, B, D, E and F is nitrogen-oxide;

wherein, each R^6, independently of any other R^6 present, is: a halogen atom; C_{1-6}alkyl; C_{1-4}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{3-6}cycloalkyloxy;

-C(O)R^{16a}; -C(O)OR^{30}; -$S(O)_2$-R^{16a}; R^{16a}-$S(O)_2$-NR^{15a}-; R^7R^8N-$S(O)_2$-; C_{1-2}alkyl-C(O)-$R^{15a}N$-$S(O)_2$-; C_{1-4}alkyl-S(O)-; Ph-S(O)-; R^7R^8N-CO-; -NR^{15}-C(O)R^{16}; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-$S(O)_2$-CH_2-; R^7R^8N-$S(O)_2$-CH_2-; C_{1-2}alkyl-$S(O)_2$-NR^{15a}-CH_2-; -CH_2-OH; -CH_2CH_2-OH; -CH_2-NR^7R^8; -CH_2-CH_2-NR^7R^8; -CH_2-C(O)OR^{30}; -CH_2-C(O)-NR^7R^8; -CH_2-NR^{15a}-C(O)-C_{1-3}alkyl; -$(CH_2)_n{}^{14}$-Het^1 where n^{14} is 0 or 1; cyano (CN); Ar^{5b}; or phenyl, pyridinyl or pyrimidinyl wherein the phenyl, pyridinyl or pyrimidinyl independently are optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or where two adjacent R^6 taken together are –O–(CMe_2)–O– or –O–$(CH_2)_n{}^{14a}$–O– where n^{14a} is 1 or 2;

wherein R^7 and R^8 are as herein defined;

wherein sub-formula (y) and (y1), independently, are optionally substituted by oxo (=O) at a ring carbon adjacent the 6-membered aromatic ring;

wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is a hydrogen atom (H), C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one, two or three of J, L, M and Q are nitrogen; and the remaining of J, L, M and Q are independently CH or CR^6 where R^6, independently of any other R^6 present, is as defined herein; and

R^{5a} is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl; -$(CH_2)_n{}^{4a}$-C_{3-6}cycloalkyl wherein n^{4a} is 1 or 2; phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^{5a} has the sub-formula (x), (y), (y1) or (z) as defined herein;

and wherein:

R^{12} and R^{13} independently are H; C_{1-5}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or R^{12} and R^{13} together are -$(CH_2)_n{}^6$- or -C(O)-$(CH_2)_n{}^7$- or -C(O)-$(CH_2)_n{}^7$-C(O)- or -$(CH_2)_n{}^8$-X^{12}-$(CH_2)_n{}^9$- or -C(O)-X^{12}-$(CH_2)_n{}^{10}$- in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3 and X^{12} is O or NR^{14a} wherein R^{14a} is H, C_{1-2}alkyl or C(O)Me;

R^{15} is a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

R^{15a}, independent of other R^{15a}, is a hydrogen atom (H) or C_{1-4}alkyl;

R^{16} and R^{16a} independently are:

C_{1-6}alkyl;

C_{3-6}cycloalkyl optionally substituted by one oxo (=O), OH or C_{1-2}alkyl substituent;

C_{3-6}cycloalkyl-CH_2-;

pyridinyl optionally substituted on a ring carbon atom by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

Ar^{5c};

phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

benzyl optionally substituted at an aromatic carbon atom by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or

a 4-, 5-, 6- or 7-membered saturated heterocyclic ring connected at a ring-carbon and containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-nitrogens which are present are present as NR^{27} where R^{27} is H, C_{1-2}alkyl or -C(O)Me; and wherein the ring is optionally substituted at carbon by one C_{1-2}alkyl or oxo (=O) substituent, provided that any oxo (=O) substituent is substituted at a ring-carbon atom bonded to a ring-nitrogen;

wherein Ar^{5a}, Ar^{5b} and Ar^{5c} independently is/are a 5-membered aromatic heterocyclic ring containing one O, S or NR^{15a} in the 5-membered ring, wherein the 5-membered ring can optionally additionally contain one or two N atoms, and wherein the heterocyclic ring is optionally substituted on a ring carbon atom by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, -CH_2OH, -CH_2-OC_{1-2}alkyl, OH (including the keto tautomer thereof) or –CH_2-$NR^{28}R^{29}$ wherein R^{28} and R^{29} independently are H or methyl;

and R^{17} is a hydrogen atom (H); C_{1-4}alkyl; C_{1-2}fluoroalkyl; C_{3-6}cycloalkyl; -$(CH_2)_p{}^6$-C(O)R^{16} wherein p^6 is 0, 1, 2 or 3; -$(CH_2)_p{}^6$-C(O)$NR^{12}R^{13}$; -$(CH_2)_p{}^6$-C(O)OR^{16}; -$(CH_2)_p{}^6$-C(O)OH; -SO_2R^{16}; -C(O)-CH_2-$NR^{12}R^{13}$; -C(O)-CH_2-NR^{15a}-C(O)-C_{1-3}alkyl; -C(O)-CH_2-O-C_{1-3}alkyl; or phenyl or benzyl wherein the phenyl or benzyl is optionally substituted at an aromatic carbon atom by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

R^{19} is C_{1-4}alkyl; -$(CH_2)_n{}^{20}$-OR^{20} wherein n^{20} is 1, 2, 3 or 4 and R^{20} is a hydrogen atom (H) or C_{1-4}alkyl; -CH(Me)-OH; -CH_2-SH; -CH_2-CH_2-S-Me; benzyl; or (4-hydroxyphenyl)methyl (i.e. 4-hydroxy-benzyl); and

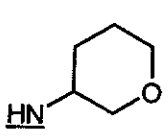
R^{30}, independent of other R^{30}, is a hydrogen atom (H), C_{1-4}alkyl or C_{3-6}cycloalkyl; and

Het^1, independent of other Het^1, is a 4-, 5-, 6- or 7-membered saturated heterocyclic ring connected at a ring-carbon and containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-nitrogens which are present are present as NR^{31} where R^{31} is H, C_{1-2}alkyl or -C(O)Me; and wherein the ring is optionally substituted at carbon by one C_{1-2}alkyl or oxo (=O) substituent, provided that any oxo (=O) substituent is substituted at a ring-carbon atom bonded to a ring-nitrogen;

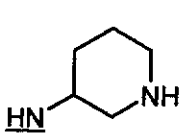
provided that: when R^3 is the heterocyclic group of sub-formula (aa) and Y is NR^{10}, then R^{10} is not $C(O)NH_2$, C(O)methyl or $C(O)-CF_3$;

provided that:
when R^3 is the heterocyclic group of sub-formula (bb), n^1 is 1, and Y is NR^{10}, then:
either (a) R^{10} is not methyl or ethyl;
or (b) R^{10} is methyl and the compound is: 1-ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide or 1-ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide;

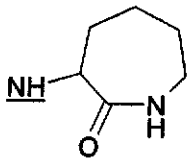
provided that: when R^3 is the heterocyclic group of sub-formula (cc), then NHR^3 is of sub-formula (L), (m), (m1) or (m2), wherein the -NH- connection point of the NHR^3 group to the 4-position of the pyrazolopyridine of formula (I) is underlined:



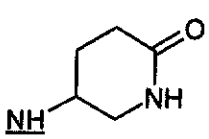
(L)



(m)



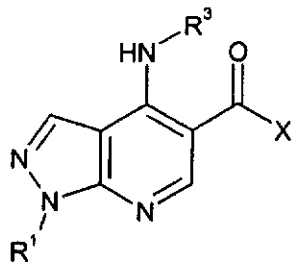
(m1)



(m2) ;

and provided that: where R^3 is substituted C_{3-8}cycloalkyl, then any OH, -CH_2OH, -$C(O)OR^{23}$, -$C(O)NHR^{24}$ or -$C(O)R^{25}$ substituent is at the 3-, 4- or 5- position of the R^3 cyclohexyl ring (wherein, in this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (I)).

2. A compound of formula (IA) or a salt thereof:



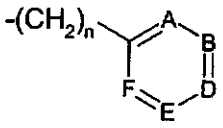
(IA)

wherein:

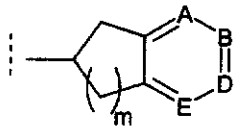
X is NR^4R^5 or OR^{5a}, in which:

R^4 is hydrogen, and

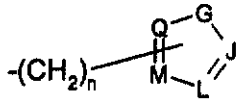
R^5 is C_{1-8}alkyl, C_{1-8} fluoroalkyl, or C_{3-8}cycloalkyl, phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^5 has the sub-formula (x), (y) or (z):



(x)



(y)



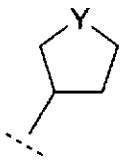
(z)

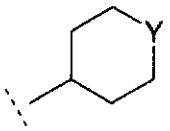
wherein in sub-formula (x) and (z), n = 1 or 2; and in sub-formula (y), m = 1 or 2;

wherein in sub-formula (x) and (y), none, one or two of A, B, D, E and F are nitrogen; and the remaining of A, B, D, E and F are CH or CR^6 where R^6 is a halogen atom, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{1-2}alkoxy, C_{1-2}fluoroalkoxy, C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-), C_{1-2}alkyl-SO_2-NH-, R^7R^8N-SO_2-, R^7R^8N-CO-, R^7R^8N, OH, C_{1-4}alkoxymethyl, or C_{1-2}alkyl-SO_2-CH_2-, wherein R^7 and R^8 are independently hydrogen or C_{1-2}alkyl;

wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one or two of J, L, M and Q are nitrogen; and the remaining of J, L, M and Q are CH or CR^6 where R^6 is as defined herein;

R^{5a} is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl; phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^{5a} has the sub-formula (x), (y) or (z) as defined herein;

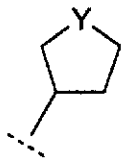


or


R^3 is C_{3-8}cycloalkyl or a heterocyclic group being in which Y is O, S, SO_2, or NR^{10}; where R^{10} is hydrogen, methyl, ethyl, C(O)methyl or C(O)-CF_3;

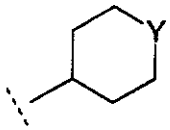
and wherein in R^3 the C_{3-8}cycloalkyl is cyclohexyl substituted with one substituent being OH; wherein the OH substituent is not substituted at the ring carbon attached to the -NH- group of formula (IA); and

R^1 = C_{1-3}alkyl or C_{1-2}fluoroalkyl;

provided that: when R^3 is the heterocyclic group being 

and Y is NR^{10}, then R^{10} is not C(O)methyl or C(O)-CF_3;

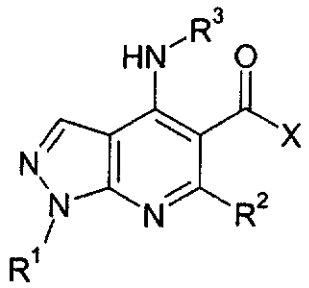
provided that:

when R^3 is the heterocyclic group being 

and Y is NR^{10}, then:
either (a) R^{10} is hydrogen, C(O)methyl or C(O)-CF_3;
or (b) R^{10} is methyl and the compound is: 1-ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide or 1-ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide;

and provided that: where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is a substituent at the 3-, 4- or 5- position of the R^3 cycloalkyl ring (wherein, in this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (IA)).

3. A compound of formula (IB) or a salt thereof:



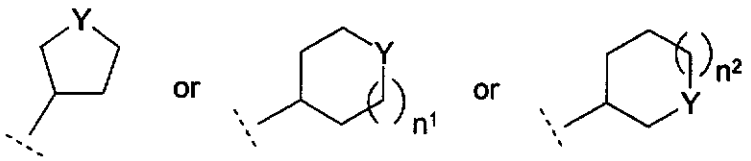
(IB)

wherein:

R^1 is C_{1-3}alkyl, C_{1-2}fluoroalkyl or $-CH_2CH_2OH$;

R^2 is a hydrogen atom (H), methyl or C_1fluoroalkyl;

R^3 is substituted C_{3-8}cycloalkyl or an optionally substituted heterocyclic group of sub-formula (aa), (bb) or (cc);



(aa) (bb) (cc)

in which n^1 and n^2 independently are 1 or 2; and in which Y is O, S, SO_2, or NR^{10}; where R^{10} is a hydrogen atom (H), methyl, ethyl, $C(O)NH_2$, C(O)methyl or $C(O)-CF_3$;

and wherein, when R^3 is substituted C_{3-8}cycloalkyl, then R^3 is cyclohexyl substituted by one substituent being oxo (=O) or OH; and wherein any OH substituent is not substituted at the R^3 ring carbon attached (bonded) to the -NH- group of formula (IB);

and wherein the R^3 heterocyclic group of sub-formula (aa), (bb) or (cc) is optionally substituted with one or two substituents being oxo (=O);

and X is NR^4R^5 or OR^{5a}, in which:

R^4 is a hydrogen atom (H); and

R^5 is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl optionally substituted by a C_{1-2}alkyl group; or $-(CH_2)_n{}^4$-C_{3-8}cycloalkyl optionally substituted, in the

$-(CH_2)_n{}^4-$ moiety or in the C_{3-8}cycloalkyl moiety, by a C_{1-2}alkyl group, wherein n^4 is 1, 2 or 3;

or R^5 is C_{2-6}alkyl substituted by one or two independent substituents R^{11};

wherein each substituent R^{11}, independently of any other R^{11} substituent present, is: hydroxy (OH); C_{1-6}alkoxy; phenyloxy; benzyloxy; $-NR^{12}R^{13}$; $-NR^{15}-C(O)R^{16}$; $-NR^{15}-C(O)-O-R^{16}$; $-NR^{15}-C(O)-NH-R^{15}$; or $-NR^{15}-SO_2R^{16}$; and wherein any R^{11} substituent which is OH, alkoxy or $-NR^{12}R^{13}$ is not substituted at any carbon atom, of any R^4 or R^5 substituted alkyl, which is bonded to the nitrogen of NR^4R^5;

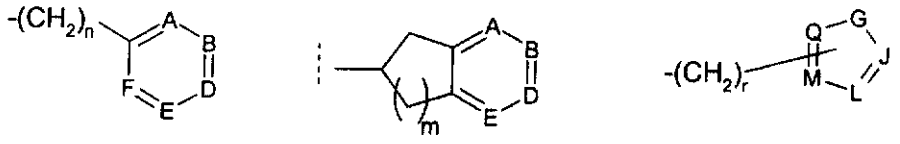
or R^5 is $-(CH_2)_n{}^{11}-C(O)R^{16}$; $-(CH_2)_n{}^{11}-C(O)NR^{12}R^{13}$; $-CHR^{19}-C(O)NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-C(O)OR^{16}$; $-CHR^{19}-C(O)OR^{16}$; $-(CH_2)_n{}^{12}-SO_2-NR^{12}R^{13}$; $-(CH_2)_n{}^{12}-SO_2R^{16}$; or $-(CH_2)_n{}^{12}-CN$; wherein n^{11} is 0, 1, 2, 3 or 4 and n^{12} is 1, 2, 3 or 4;

or R^5 is $-(CH_2)_n{}^{13}$-Het wherein n^{13} is 0, 1, 2, 3 or 4 and Het is a 4-, 5-, 6- or 7-membered saturated or partly-saturated heterocyclic ring containing one or two ring-hetero-atoms independently selected from O, S, and N; wherein any ring-hetero-atoms present are not bound to the $-(CH_2)_n{}^{13}-$ moiety when n^{13} is 1 and are not bound to the nitrogen of NR^4R^5 when n^{13} is 0; wherein any ring-nitrogens which are present and which are not unsaturated (i.e. which do not partake in a double bond) are present as NR^{17} where R^{17} is as defined herein; and wherein one or two of the carbon ring-atoms independently are optionally substituted by C_{1-2}alkyl;

or R^5 is phenyl optionally substituted with one or two of: a halogen atom; C_{1-4}alkyl; C_{1-2}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-; $-NR^{15}-C(O)R^{16}$; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

wherein R^7 and R^8 are independently a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or R^7 and R^8 together are $-(CH_2)_n{}^6-$ or $-C(O)-(CH_2)_n{}^7-$ or $-C(O)-(CH_2)_n{}^7-C(O)-$ or $-(CH_2)_n{}^8-X^7-(CH_2)_n{}^9-$ or $-C(O)-X^7-(CH_2)_n{}^{10}-$ in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3, and X^7 is O or NR^{14} wherein R^{14} is H or C_{1-2}alkyl;

or R^5 has the sub-formula (x), (y) or (z):



(x) (y) (z)

wherein in sub-formula (x), n = 1 or 2; in sub-formula (y), m = 1 or 2; and in sub-formula (z), r = 0, 1 or 2;

wherein in sub-formula (x) and (y), none, one or two of A, B, D, E and F are nitrogen; and the remaining of A, B, D, E and F are independently CH or CR^6;

where R^6 is a halogen atom; C_{1-4}alkyl; C_{1-4}fluoroalkyl; C_{1-4}alkoxy; C_{1-2}fluoroalkoxy; C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-; -NR^{15}-C(O)R^{16}; R^7R^8N; OH; C_{1-4}alkoxymethyl; C_{1-4}alkoxyethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one or two of fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; wherein R^7 and R^8 are as herein defined;

wherein in sub-formula (z), G is O or S or NR^9 wherein R^9 is a hydrogen atom (H), C_{1-4}alkyl or C_{1-4}fluoroalkyl; none, one, two or three of J, L, M and Q are nitrogen; and the remaining of J, L, M and Q are independently CH or CR^6 where R^6 is as defined herein; and

R^{5a} is C_{1-8}alkyl; C_{1-8} fluoroalkyl; C_{3-8}cycloalkyl; phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy or trifluoromethoxy; or R^{5a} has the sub-formula (x), (y) or (z) as defined herein

and wherein:

R^{12} and R^{13} independently are H; C_{1-5}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

or R^{12} and R^{13} together are -$(CH_2)_n{}^6$- or -C(O)-$(CH_2)_n{}^7$- or -C(O)-$(CH_2)_n{}^7$-C(O)- or -$(CH_2)_n{}^8$-X^{12}-$(CH_2)_n{}^9$- or -C(O)-X^{12}-$(CH_2)_n{}^{10}$- in which: n^6 is 3, 4, 5 or 6, n^7 is 2, 3, 4, or 5, n^8 and n^9 and n^{10} independently are 2 or 3 and X^{12} is O or NR^{14} wherein R^{14} is H or C_{1-2}alkyl;

R^{15} is a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

R^{16} is C_{1-4}alkyl; C_{3-6}cycloalkyl; pyridinyl; or phenyl optionally substituted by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

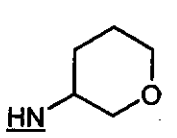
R^{17} is a hydrogen atom (H); C_{1-4}alkyl; C_{1-2}fluoroalkyl; C_{3-6}cycloalkyl; $-(CH_2)_p{}^6$-C(O)R^{16} wherein p^6 is 0, 1, 2 or 3; $-(CH_2)_p{}^6$-C(O)$NR^{12}R^{13}$; $-(CH_2)_p{}^6$-C(O)OR^{16}; $-SO_2R^{16}$; or phenyl or benzyl wherein the phenyl or benzyl is optionally substituted at an aromatic carbon atom by one or two of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; and

R^{19} is C_{1-4}alkyl; $-(CH_2)_n{}^{20}$-OR^{20} wherein n^{20} is 1, 2, 3 or 4 and R^{20} is a hydrogen atom (H) or C_{1-4}alkyl; -CH(Me)-OH; $-CH_2$-SH; $-CH_2-CH_2$-S-Me; benzyl; or (4-hydroxyphenyl)methyl (i.e. 4-hydroxy-benzyl);

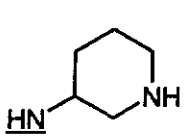
provided that: when R^3 is the heterocyclic group of sub-formula (aa) and Y is NR^{10}, then R^{10} is not $C(O)NH_2$, C(O)methyl or $C(O)-CF_3$;

provided that:
when R^3 is the heterocyclic group of sub-formula (bb), n^1 is 1, and Y is NR^{10}, then:
either (a) R^{10} is not methyl or ethyl;
or (b) R^{10} is methyl and the compound is: 1-ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide or 1-ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide;

provided that: when R^3 is the heterocyclic group of sub-formula (cc), then NHR^3 is of sub-formula (L), (m) or (m1), wherein the -NH- connection point of the NHR^3 group to the 4-position of the pyrazolopyridine of formula (IB) is underlined:



(L)



(m)



(m1) ;

and provided that: where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is a substituent at the 3-, 4- or 5- position of the R^3 cycloalkyl ring (wherein, in this

connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (IB)).

4. A compound or salt as claimed in claim 1 or 3, wherein R^2 is a hydrogen atom (H) or methyl.

5. A compound or salt as claimed in claim 1 or 3, wherein R^2 is a hydrogen atom (H).

6. A compound or salt as claimed in any preceding claim, wherein R^1 is ethyl, n-propyl, C_2fluoroalkyl or $-CH_2CH_2OH$.

7. A compound or salt as claimed in any preceding claim, wherein R^1 is ethyl.

8. A compound or salt as claimed in any preceding claim, wherein in R^3 there is one substituent or no substituent.

9. A compound or salt as claimed in any preceding claim, wherein, where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is oxo (=O); OH; NHR^{21} wherein R^{21} is a hydrogen atom (H); $-C(O)OR^{23}$ wherein R^{23} is H; $-C(O)NHR^{24}$ wherein R^{24} is H; hydroxyimino (=N-OH); or (C_{1-2}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-2}alkyl).

10. A compound or salt as claimed in any preceding claim, wherein, where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is: oxo (=O); OH; NHR^{21} wherein R^{21} is a hydrogen atom (H); $-C(O)OR^{23}$ wherein R^{23} is H; hydroxyimino (=N-OH); or (C_{1-2}alkoxy)imino (=N-OR^{26} where R^{26} is C_{1-2}alkyl).

11. A compound or salt as claimed in any preceding claim, wherein, where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is OH, oxo (=O) or hydroxyimino (=N-OH).

12. A compound or salt as claimed in any preceding claim, wherein, where R^3 is substituted C_{3-8}cycloalkyl, then the one substituent is a substituent at the 3-, 4- or 5-position of the R^3 cycloalkyl ring (wherein, in this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (I) or (IA) or (IB)).

13. A compound or salt as claimed in any preceding claim, wherein, where R^3 is substituted C_{3-8}cycloalkyl, then any NHR^{21} substituent is at the 2-, 3-, 4- or 5-position of the R^3 cycloalkyl ring; and any oxo (=O), hydroxyimino (=N-OH); or

(C_{1-4}alkoxy)imino (=N-OR^{26}) substituent is at the 3- or 4-position of the R^3 cycloalkyl ring (wherein, in this connection, the 1-position of the R^3 cycloalkyl ring is deemed to be the connection point to the -NH- in formula (I) or (IA) or (IB)).

14. A compound or salt as claimed in any preceding claim, wherein, where R^3 is substituted C_6cycloalkyl, then R^3 is 3-hydroxy-cyclohexyl (i.e. 3-hydroxycyclohexan-1-yl), 4-oxo-cyclohexyl (i.e. 4-oxocyclohexan-1-yl), 4-(hydroxyimino)cyclohexyl (i.e. 4-(hydroxyimino)cyclohexan-1-yl), or 4-(C_{1-2}alkoxyimino)cyclohexyl.

15. A compound or salt as claimed in any preceding claim, wherein, where R^3 is the heterocyclic group of sub-formula (aa), (bb) or (cc), then Y is O, NH or N-C(O)methyl.

16. A compound or salt as claimed in any preceding claim, wherein, where R^3 is the heterocyclic group of sub-formula (aa), (bb) or (cc), then Y is O.

17. A compound or salt as claimed in any preceding claim, wherein R^{10} is a hydrogen atom (H) or C(O)methyl.

18. A compound or salt as claimed in any preceding claim, wherein, where R^3 is the heterocyclic group of sub-formula (aa), (bb) or (cc), then R^3 is the heterocyclic group of sub-formula (aa) or (bb).

19. A compound or salt as claimed in claim 18, wherein where R^3 is the heterocyclic group of sub-formula (aa), (bb) or (cc), then R^3 is the heterocyclic group of sub-formula (bb) and n^1 is 1.

20. A compound or salt as claimed in any preceding claim, wherein, in R^3, the heterocyclic group of sub-formula (aa), (bb) or (cc) is unsubstituted (wherein, in this connection, where Y is NR^{10}, R^{10} is not classified as a substituent).

21. A compound or salt as claimed in any preceding claim, wherein

when R^3 is the heterocyclic group of sub-formula (aa) then Y is O, S, SO_2 or NH, and

when R^3 is the heterocyclic group of sub-formula (bb) and Y is NR^{10}, then R^{10} is not methyl or ethyl.

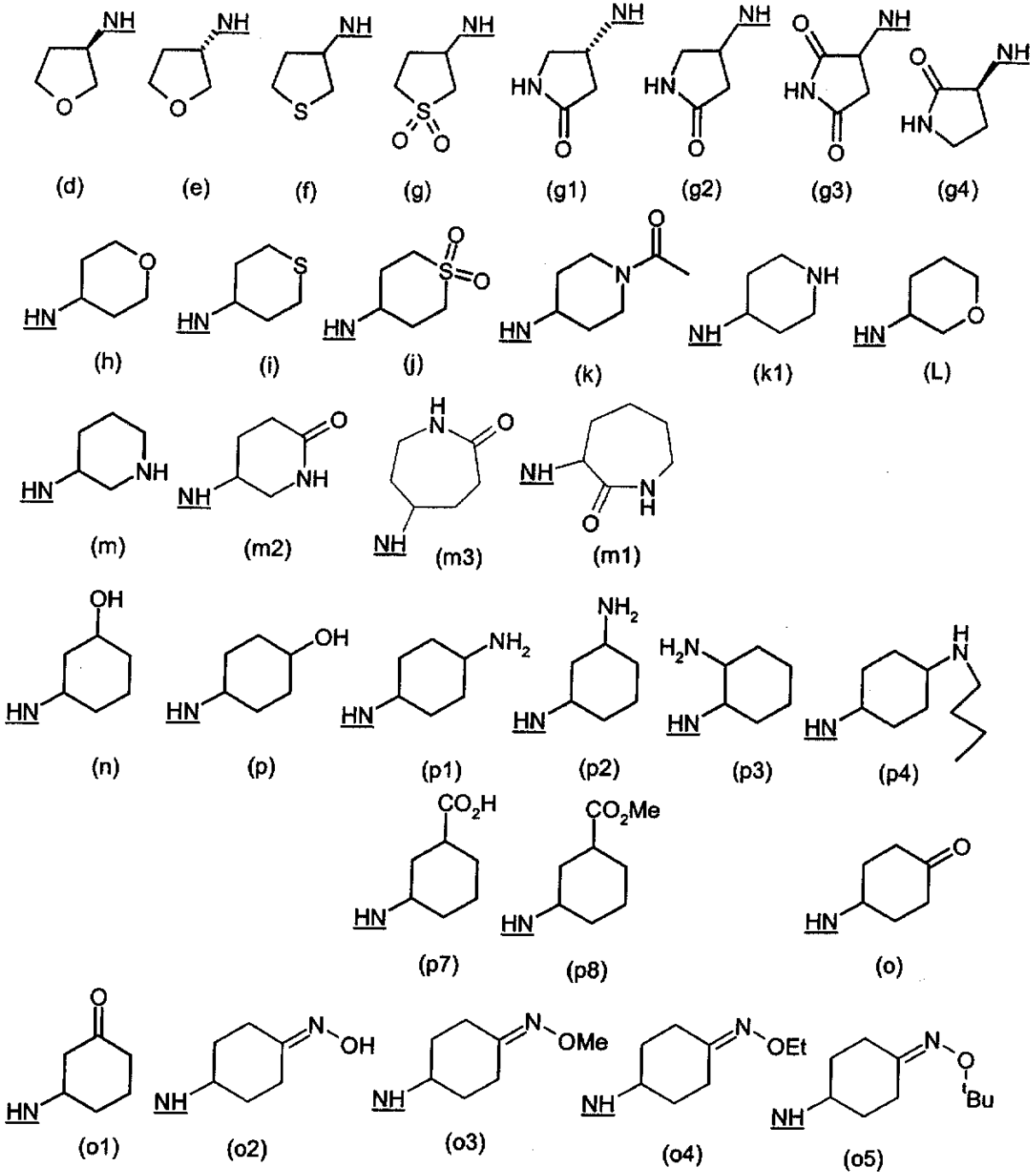
22. A compound or salt as claimed in any preceding claim, wherein, when R^3 is the heterocyclic group of sub-formula (bb), then Y is O, S, SO_2 or NR^{10}, wherein R^{10} is H, $C(O)NH_2$, C(O)methyl or $C(O)\text{-}CF_3$.

23. A compound or salt as claimed in any preceding claim, wherein:

R^3 is the heterocyclic group of sub-formula (bb), n^1 is 1, and Y is O or NR^{10}, wherein R^{10} is H, C(O)NH_2, C(O)methyl or C(O)-CF_3; wherein, in R^3, the heterocyclic group of sub-formula (bb) is unsubstituted (wherein, in this connection, where Y is NR^{10}, R^{10} is not classified as a substituent);

or R^3 is substituted C_6cycloalkyl and is: 3-hydroxy-cyclohexyl (i.e. 3-hydroxycyclohexan-1-yl), 4-oxo-cyclohexyl (i.e. 4-oxocyclohexan-1-yl), 4-(hydroxyimino)cyclohexyl (i.e. 4-(hydroxyimino)cyclohexan-1-yl), or 4-(C_{1-2}alkoxyimino)cyclohexyl.

24. A compound or salt as claimed in any preceding claim, wherein NHR^3 is of sub-formula (d), (e), (f), (g), (g1), (g2), (g3), (g4), (h), (i), (j), (k), (k1), (L), (m), (m1), (m2), (m3), (n), (o), (o1), (o2), (o3), (o4), (o5), (p), (p1), (p2), (p3), (p4), (p7) or (p8), wherein the -NH- connection point of the NHR^3 group to the 4-position of the pyrazolopyridine of formula (I) or (IA) or (IB) is underlined:



25. A compound or salt as claimed in claim 24, wherein NHR^3 is of sub-formula (d), (e), (f), (g4), (h), (i), (j), (k), (k1), (L), (m), (m1), (m2), (m3), (n), (o), (o1), (o2), (o3), (o4), (o5), (p), (p2), (p3) or (p7).

26. A compound or salt as claimed in claim 24, wherein NHR^3 is of sub-formula (d), (e), (f), (h), (i), (j), (k), (m), (m1), (n), (o), (o1) or (p).

27. A compound or salt as claimed in claim 25 or 26, wherein NHR^3 is of sub-formula (h), (i), (j), (k), (m1), (m2), (n), (o), (o2), (o3) or (p2).

28. A compound or salt as claimed in claim 25 or 26, wherein NHR^3 is of sub-formula (h), (k), (n), (o) or (o2).

29. A compound or salt as claimed in claim 24, wherein R^3 is tetrahydro-2H-pyran-4-yl; that is NHR^3 is of sub-formula (h).

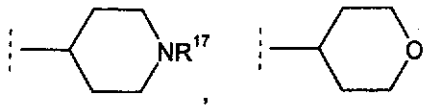
30. A compound or salt as claimed in any of claims 24 to 28, wherein, when NHR^3 is of sub-formula (n), then it is a *cis*-(3-hydroxycyclohex-1-yl)amino group.

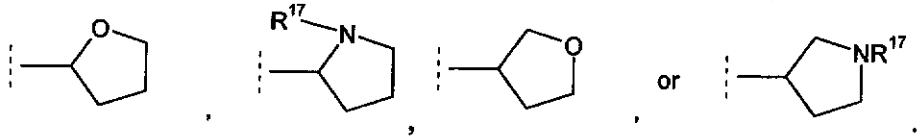
31. A compound or salt as claimed in any preceding claim, wherein X is NR^4R^5.

32. A compound or salt as claimed in any preceding claim, wherein R^5 is:
C_{1-8}alkyl;
C_{1-3}fluoroalkyl;
C_{3-8}cycloalkyl (unsubstituted);
unsubstituted $-(CH_2)_{n^4}-C_{5-6}$cycloalkyl wherein n^4 is 1 or 2;
$-(CH_2)_{n^5}-R^{11}$ wherein n^5 is 2 or 3, and each substituent R^{11}, independently of any other R^{11} substituent present, is C_{1-4}alkoxy, $-NR^{15}-C(O)-NH-R^{15}$, or $-NR^{15}-SO_2R^{16}$;
or
$-(CH_2)_{n^{11}}-C(O)R^{16}$; $-(CH_2)_{n^{12}}-C(O)NR^{12}R^{13}$; $-(CH_2)_{n^{12}}-C(O)OR^{16}$; $-(CH_2)_{n^{12}}-SO_2-NR^{12}R^{13}$; $-(CH_2)_{n^{12}}-SO_2R^{16}$; or $-(CH_2)_{n^{12}}-CN$ wherein n^{11} is 1 or 2 and n^{12} is 1 or 2.

33. A compound or salt as claimed in any of claims 1 to 31, wherein R^5 is $-(CH_2)_{n^{13}}$-Het, n^{13} is 0, 1 or 2, and Het is a 5- or 6-membered saturated heterocyclic ring containing one ring-hetero-atom selected from O, S and N, wherein the carbon ring-atoms in Het are not substituted.

34. A compound or salt as claimed in claim 33, wherein R^5 is $-(CH_2)_{n^{13}}$-Het, n^{13} is 0 or 1, and Het is one of:





35. A compound or salt as claimed in any of claims 1 to 31, wherein R^5 is phenyl optionally substituted with, independently, one or two of: a halogen atom; C_{1-2}alkyl; C_{1-2}fluoroalkyl; C_{1-2}alkoxy; trifluoromethoxy; C_{1-2}alkylsulphonyl (C_{1-2}alkyl-SO_2-); C_{1-2}alkyl-SO_2-NH-; R^7R^8N-SO_2-; R^7R^8N-CO-;

-NR^{15}-C(O)R^{16}; R^7R^8N; OH; C_{1-2}alkoxymethyl; C_{1-2}alkyl-SO_2-CH_2-; cyano (CN); or phenyl optionally substituted by one of fluoro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy.

36. A compound or salt as claimed in claim 35, wherein R^5 is phenyl optionally substituted with one or two of: a halogen atom, C_{1-2}alkyl, trifluoromethyl, C_{1-2}alkoxy, trifluoromethoxy, R^7R^8N-SO_2-, R^7R^8N-CO-, or C_{1-2}alkyl-SO_2-CH_2-.

37. A compound or salt as claimed in any of claims 1 to 31, wherein R^5 has the sub-formula (x) or (y) or (y1) or (z).

38. A compound or salt as claimed in any of claims 1 to 31, wherein R^5 has the sub-formula (x).

39. A compound or salt as claimed in any preceding claim, wherein n = 1, m = 1, and r = 1.

40. A compound or salt as claimed in any preceding claim, wherein, in sub-formula (x), (y) and (y1): none, one or two of A, B, D, E and F are nitrogen; none, one, two or three of A, B, D, E and F are CR^6; and the remaining of A, B, D, E and F are CH.

41. A compound or salt as claimed in claim 40, wherein, in sub-formula (x), (y) and (y1), none or one of A, B, D, E and F are nitrogen.

42. A compound or salt as claimed in any preceding claim, wherein in sub-formula (x), (y), (y1) and (z), each R^6, independently of any other R^6 present, is a fluorine, chlorine, bromine or iodine atom, or methyl, ethyl, n-propyl, isopropyl, C_4alkyl, trifluoromethyl, -CH_2OH, methoxy, ethoxy, C_1fluoroalkoxy, OH, C_{1-3}alkylS(O)$_2$-, C_{1-3}alkylS(O)$_2$-NH-, Me_2N-S(O)$_2$-, H_2N-S(O)$_2$-, -$CONH_2$, -CONHMe, -CO_2H, cyano (CN), NMe_2, t-butoxymethyl, or C_{1-3}alkylS(O)$_2$-CH_2-.

43. A compound or salt as claimed in claim 42, wherein in sub-formula (x), (y), (y1) and (z), each R^6, independently of any other R^6 present, is a fluorine, chlorine or bromine atom, or methyl, ethyl, n-propyl, isopropyl, trifluoromethyl, -CH_2OH, methoxy, difluoromethoxy, methylsulphonyl, methyl-SO_2-NH- or methyl-SO_2-CH_2-.

44. A compound or salt as claimed in any preceding claim, wherein R^5 is of sub-formula (x) and is: benzyl, (monoalkyl-phenyl)methyl, [mono(fluoroalkyl)-phenyl]methyl, (monohalo-phenyl)methyl, (monoalkoxy-phenyl)methyl, [mono(fluoroalkoxy)-phenyl]methyl, [mono(N,N-dimethylamino)-phenyl]methyl, [mono(methyl-SO_2-NH-)-phenyl]methyl, [mono(methyl-SO_2-)-phenyl]methyl, (dialkyl-phenyl)methyl, (monoalkyl-monohalo-phenyl)methyl, [mono(fluoroalkyl)-monohalo-phenyl]methyl, (dihalo-

phenyl)methyl, (dihalo-monoalkyl-phenyl)methyl, [dihalo-mono(hydroxymethyl)-phenyl]methyl, or (dialkoxy-phenyl)methyl.

45. A compound or salt as claimed in claim 44, wherein R^5 is: (monoC_{1-3}alkyl-phenyl)methyl; (monoC_1fluoroalkyl-phenyl)methyl; (monoC_{1-2}alkoxy-phenyl)methyl; [mono(C_1fluoroalkoxy)-phenyl]methyl; (diC_{1-2}alkyl-phenyl)methyl; (monoC_{1-2}alkyl-monohalo-phenyl)methyl; (dihalo-phenyl)methyl; (dihalo-monoC_{1-2}alkyl-phenyl)methyl; or [dihalo-mono(hydroxymethyl)-phenyl]methyl.

46. A compound or salt as claimed in claim 45, wherein R^5 is: (4-C_{1-3}alkyl-phenyl)methyl; (4-C_1fluoroalkyl-phenyl)methyl; (4-C_{1-2}alkoxy-phenyl)methyl; (4-C_1fluoroalkoxy-phenyl)methyl; (3,4-dimethyl-phenyl)methyl; (2,4-dimethyl-phenyl)methyl; (3,5-dimethyl-phenyl)methyl; (2,3-dimethyl-phenyl)methyl; (2,5-dimethyl-phenyl)methyl; (4-methyl-3-chloro-phenyl)methyl; (3-methyl-4-chloro-phenyl)methyl; (2-methyl-4-chloro-phenyl)methyl; (2-chloro-4-fluorophenyl)methyl; (2,4-difluoro-phenyl)methyl, (4-bromo-2-fluorophenyl)methyl; (4-chloro-2-fluorophenyl)methyl; (3,4-dichloro-phenyl)methyl; (2,4-dichloro-phenyl)methyl; (2,6-dichloro-phenyl)methyl; (2,3-dichloro-phenyl)methyl; (2,4-dichloro-6-methyl-phenyl)methyl; or [2,3-dichloro-6-(hydroxymethyl)-phenyl]methyl.

47. A compound or salt as claimed in claim 44, 45 or 46, wherein:
X is NR^4R^5; and
in sub-formula (x), each R^6, independently of any other R^6 present, is a fluorine, chlorine or bromine atom, or methyl, ethyl, n-propyl, isopropyl, trifluoromethyl, -CH_2OH, methoxy, difluoromethoxy, methylsulphonyl, or methyl-SO_2-NH-.

48. A compound or salt as claimed in any of claims 1 to 43, wherein R^5 has the sub-formula (z), r is 1, none or one of J, L, M or Q is CR^6, and if one of J, L, M or Q is CR^6 then R^6 is methyl or C_1fluoroalkyl, and R^9 is a hydrogen atom (H) or methyl.

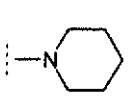
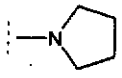
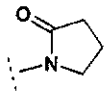
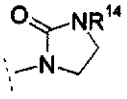
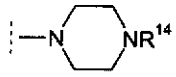
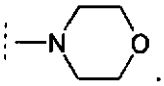
49. A compound or salt as claimed in any preceding claim, wherein:

R^{5a} is ethyl;

R^7 and R^8 are independently a hydrogen atom (H); C_{1-2}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one of: fluoro, chloro, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; and when R^7 is cycloalkyl or optionally substituted phenyl then R^8 is neither cycloalkyl nor optionally substituted phenyl; or R^7 and R^8 together are -$(CH_2)_n{}^6$- or -$(CH_2)_n{}^8$-X^7-$(CH_2)_n{}^9$- wherein X^7 is NR^{14} or O;

n^6 is 4 or 5; n^7 is 2, 3 or 4; and n^8, n^9 and n^{10} are independently 2;

each substituent R^{11}, independently of any other R^{11} substituent present, is: C_{1-4}alkoxy, $-NR^{15}-C(O)-NH-R^{15}$, or $-NR^{15}-SO_2R^{16}$; wherein any R^{11} alkoxy substituent is not substituted at any carbon atom, of any R^5 substituted alkyl, which is bonded to the nitrogen of NR^4R^5;

R^{12} and R^{13} independently are H; C_{1-3}alkyl; C_{3-6}cycloalkyl; or phenyl optionally substituted by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or $NR^{12}R^{13}$ is  or  or  or , or , or ;

R^{15} is a hydrogen atom (H) or C_{1-2}alkyl;

R^{15a}, independent of other R^{15a}, is a hydrogen atom (H) or C_{1-2}alkyl;

R^{16} and R^{16a} independently are:

C_{1-4}alkyl;

C_{5-6}cycloalkyl (unsubstituted);

C_{5-6}cycloalkyl-CH_2-;

pyridin-2-yl optionally substituted on a ring carbon atom by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

Ar^{5c};

phenyl optionally substituted by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy;

benzyl optionally substituted at an aromatic carbon atom by one of: a halogen atom, C_{1-2}alkyl, C_1fluoroalkyl, C_{1-2}alkoxy or C_1fluoroalkoxy; or

a 5- or 6- membered saturated heterocyclic ring connected at a ring-carbon and containing one ring-hetero-atom selected from O, S, and N; wherein any ring-nitrogens which are present are present as NR^{27} where R^{27} is H, C_{1-2}alkyl or -C(O)Me; and wherein the ring is optionally substituted at carbon by one oxo (=O) substituent, provided that any oxo (=O) substituent is substituted at a ring-carbon atom bonded to a ring-nitrogen;

R^{17} is a hydrogen atom (H); C_{1-4}alkyl; C_{3-6}cycloalkyl; $-(CH_2)_p{}^6-C(O)R^{16}$, or the optionally substituted phenyl or benzyl;

and

R^{19} is isobutyl, sec-butyl, methyl, isopropyl; $-(CH_2)_{n^{20}}-OR^{20}$ wherein n^{20} is 1 and R^{20} is a hydrogen atom (H); -CH(Me)-OH; $-CH_2-SH$; $-CH_2-CH_2-S-Me$; benzyl; or (4-hydroxyphenyl)methyl (i.e. 4-hydroxy-benzyl).

50. A compound or salt as claimed in claim 1, which is:

Ethyl 1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(1-acetylpiperidin-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-(cyclopropylamino)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
N-Benzyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Cyclopentyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-N-cyclopentyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(pyridin-4-ylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-N-benzyl-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-ethylbutyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-ethylbutyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(2-ethylbutyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-[(1-methylpiperidin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-n-propyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-n-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-1-ethyl-N-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(2-Ethylbutyl)-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(4-Fluorophenyl)-1-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetylpiperidin-4-yl)amino]-N-benzyl-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-isopropyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-[(1,1-dioxidotetrahydrothien-3-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-[(3S)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-[(3R)-tetrahydrofuran-3-ylamino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-thiopyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydrothien-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1,1-Dioxidotetrahydrothien-3-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

4-[(1,1-Dioxidotetrahydro-2H-thiopyran-4-yl)amino]-1-ethyl-N-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

1-Ethyl-*N*-[4-(methylsulfonyl)benzyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[3-(methylsulfonyl)benzyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(5-Chloropyridin-2-yl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(5-methyl-3-phenylisoxazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2-*tert*-Butoxyethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3-thiazol-2-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(pyrimidin-4-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(2-methyl-1,3-thiazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(*tert*-Butoxymethyl)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{2-[methyl(methylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(pyrazin-2-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2-Chloro-6-fluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(6-oxo-1,6-dihydropyridin-3-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(Aminocarbonyl)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{4-[(methylamino)carbonyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(1-methyl-1*H*-imidazol-4-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-{2-[(Anilinocarbonyl)amino]ethyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(1*H*-tetraazol-5-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[2-(1*H*-1,2,4-triazol-1-yl)ethyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
tert-Butyl 4-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)piperidine-1-carboxylate,
1-Ethyl-*N*-{3-[(methylsulfonyl)amino]propyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[2-(Dimethylamino)benzyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

1-Ethyl-*N*-[(1-ethylpyrrolidin-2-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(tetrahydrofuran-2-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-*N*-tetrahydro-2*H*-pyran-4-yl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-{4-[(Dimethylamino)sulfonyl]benzyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{3-[(methylsulfonyl)amino]benzyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(4-methoxyphenyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(pyridin-3-ylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(1-methylpiperidin-4-yl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(1-ethylpropyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(2-piperidin-1-ylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(3-morpholin-4-ylpropyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3-Ethoxypropyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(Cyclohexylmethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(Dimethylamino)propyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-neopentyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-*N*-(4-methoxybenzyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{2-[(phenylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[2-(Acetylamino)ethyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{2-[(methylsulfonyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{2-[(2-methoxyphenyl)(methyl)amino]ethyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(2-oxo-2-phenylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1H-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2,5-Difluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-[4-(trifluoromethyl)benzyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

N-Cyclopropyl-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2-amino-2-oxoethyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-*N*-(3-methoxyphenyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3,4-Difluorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
Ethyl 3-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)propanoate,
N-(1-Benzylpiperidin-4-yl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3,4-thiadiazol-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2,3-Dihydro-1*H*-inden-2-yl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(2-oxoimidazolidin-1-yl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3,4-Dimethoxybenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3-Chlorobenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{4-[(methylsulfonyl)methyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[3-(dimethylamino)-3-oxopropyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-*N*-[(1-methyl-1*H*-imidazol-5-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{4-[(methylamino)sulfonyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(2-Cyanoethyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(2-thien-2-ylethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[2-(4-Chlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[2-(2-methoxyphenyl)ethyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
Ethyl 1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
Ethyl 1-(2-hydroxyethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
N-[4-(Methylsulfonyl)benzyl]-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(4-Fluorophenyl)-1-n-propyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

Ethyl 1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
N-Benzyl-1-ethyl-6-methyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(2-oxoazepan-3-yl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(3-hydroxycyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(4-hydroxycyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-Benzyl-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

1-Ethyl-*N*-(2-hydroxy-1-methylethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
Methyl (2*S*)-2-({[1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]carbonyl}amino)-3-hydroxypropanoate,

Ethyl 1-ethyl-4-[(4-hydroxycyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(1-acetyl-4-piperidinyl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 4-[(4-aminocyclohexyl)amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl-N-[(1-oxido-3-pyridinyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(1-oxido-2-pyridinyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(1-oxido-4-pyridinyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(cis-4-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-{[(3S)-2-oxo-3-pyrrolidinyl]amino}-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(2,5-Dioxo-3-pyrrolidinyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(cis-4-Aminocyclohexyl)amino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(cis-4-Aminocyclohexyl)amino]-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(cis-4-Aminocyclohexyl)amino]-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{4-[(methylsulfonyl)methyl]phenyl}-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,4-Dichlorophenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(methyloxy)phenyl]methyl}-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

N-{[4-(Dimethylamino)phenyl]methyl}-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-[(4-oxocyclohexyl)amino]-N-{[4-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(methylsulfonyl)phenyl]methyl}-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-[(4-oxocyclohexyl)amino]-N-(2-pyridinylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(1-Acetyl-4-piperidinyl)-1-ethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N,1-Diethyl-4-[(4-oxocyclohexyl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
1-Ethyl-4-[(4-oxocyclohexyl)amino]-N-(1,3-thiazol-2-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(phenylmethyl)-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-N-{[4-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(methylsulfonyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{4-[(methylsulfonyl)methyl]phenyl}-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluorophenyl)-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-pyridinylmethyl)-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(1-Acetyl-4-piperidinyl)-1-ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N,1-Diethyl-4-(tetrahydro-2H-pyran-3-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-3-ylamino)-N-(1,3-thiazol-2-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(3,4-dichlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-[(3-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(3,4-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2,5-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[3-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[4-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2,6-difluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(3-chlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-[4-(methyloxy)phenyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-({4-[(dimethylamino)sulfonyl]phenyl}methyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-{[2-(dimethylamino)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2,4-dichlorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(2-chloro-6-fluorophenyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-({4-[(difluoromethyl)oxy]phenyl}methyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-{[3-chloro-4-(methyloxy)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-[(5-chloro-2-pyridinyl)methyl]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-(1,3-thiazol-2-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[4-(methylsulfonyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-(2,2-diphenylethyl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-({4-[(methylamino)carbonyl]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-{[4-(aminosulfonyl)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-({3-[(methylamino)carbonyl]phenyl}methyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-N-{[4-(aminocarbonyl)phenyl]methyl}-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(1-Acetyl-4-piperidinyl)amino]-1-ethyl-N-{[6-(methyloxy)-3-pyridinyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-4-piperidinyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-piperidinylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

1-Ethyl-N-[1-(ethylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{1-[(1-methylethyl)sulfonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[1-(Cyclopentylsulfonyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(methylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{1-[(phenylmethyl)sulfonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(phenylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(propylsulfonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[1-(Cyclopropylcarbonyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(3-furanylcarbonyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[1-(3,3-Dimethylbutanoyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(2-ethylbutanoyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[1-(Cyclopentylacetyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(2-methylpropanoyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)-4-piperidinyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(1-propanoyl-4-piperidinyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[1-(N-Acetylglycyl)-4-piperidinyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(4-morpholinylacetyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{1-[(4-oxocyclohexyl)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[1-(1-piperidinylacetyl)-4-piperidinyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{1-[(1-methyl-5-oxo-3-pyrrolidinyl)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{1-[(3-methyl-3-oxetanyl)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{1-[(4-fluorophenyl)acetyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[1-(3,3-Dimethylbutanoyl)-4-piperidinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[1-(Cyclopentylacetyl)-4-piperidinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[1-(Cyclopropylcarbonyl)-4-piperidinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({1-[(4-oxocyclohexyl)carbonyl]-4-piperidinyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({1-[(4-fluorophenyl)acetyl]-4-piperidinyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

1-Ethyl-N-({1-[(1-methyl-5-oxo-3-pyrrolidinyl)carbonyl]-4-piperidinyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
Methyl 3-[(1-ethyl-5-{[(phenylmethyl)amino]carbonyl}-1H-pyrazolo[3,4-b]pyridin-4-yl)amino]cyclohexanecarboxylate,
3-[(1-Ethyl-5-{[(phenylmethyl)amino]carbonyl}-1H-pyrazolo[3,4-b]pyridin-4-yl)amino]cyclohexanecarboxylic acid,
1-Ethyl-N-(phenylmethyl)-4-(4-piperidinylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
Ethyl 1-ethyl-4-({1-[(methyloxy)acetyl]-4-piperidinyl}amino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
Ethyl 1-(1-methylethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
1-Ethyl-N-(4-fluorophenyl)-6-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-6-methyl-N-{[4-(methylsulfonyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(2,3-Dihydro-1H-inden-2-yl)-1-ethyl-6-methyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[3-(1-piperidinylcarbonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[4-(1-methylethyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-fluorophenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{3-[(Dimethylamino)carbonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{4-[(Difluoromethyl)oxy]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{4-[Acetyl(methyl)amino]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-hydroxyphenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[4-(4-morpholinyl)-2-(trifluoromethyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-4-pyridinyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{4-[(4-methyl-1-piperazinyl)carbonyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[2-(2-oxo-1-pyrrolidinyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[3-(methylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{3-[Acetyl(methyl)amino]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{3-[(methylsulfonyl)amino]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(4-fluoro-2-hydroxyphenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(4-Chlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(3-Chloro-2-cyanophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[3-(1-piperidinylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

1-Ethyl-N-[2-(methylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[Acetyl(methyl)amino]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[3-(4-morpholinylcarbonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(4-Chloro-3-cyanophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(3-hydroxyphenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(3-Chlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[3-[(Acetylamino)methyl]-4-(methyloxy)phenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[4-(1-piperidinylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(3-{[Cyclohexyl(methyl)amino]carbonyl}phenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[2-(4-morpholinyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{3-[(Acetylamino)sulfonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(3-Chloro-4-hydroxyphenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{4-[(methylsulfonyl)amino]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{3-[(methylamino)carbonyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[3-(trifluoromethyl)phenyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-3-pyridinyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(3,4-Dichlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[3-(Aminosulfonyl)-4-chlorophenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[3-(4-morpholinyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[4-(4-morpholinylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{2-[(4-methyl-1-piperazinyl)carbonyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[(Dimethylamino)carbonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[2-Chloro-4-(trifluoromethyl)phenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[(Acetylamino)methyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(2-Chlorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(3-Chloro-2-fluorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(3-fluorophenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

N-(2-Cyano-3-fluorophenyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[4-(propylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{4-[(Dimethylamino)carbonyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[4-(methylsulfonyl)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{4-[(Acetylamino)methyl]phenyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({2-[(1,1-Dimethylethyl)oxy]-3-pyridinyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
N-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({2-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({2-[(1-methylethyl)oxy]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({3-[(1-methylethyl)oxy]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({3-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-hydroxy-3-(methyloxy)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(5-Acetyl-2-hydroxyphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-{2-[3-(trifluoromethyl)phenyl]ethyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[4-(Acetylamino)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[2-(3-hydroxyphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[2-(3-Chlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-(2-{4-[(trifluoromethyl)oxy]phenyl}ethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{2-[3-(methyloxy)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[2-(4-Acetylphenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[2-(3,4-Dichlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[3-(Aminosulfonyl)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[3,4-Bis(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[2-(2,3-Dichlorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[3,5-Bis(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{2-[3-methyl-4-(methyloxy)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

N-[2-(2,6-Difluorophenyl)ethyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[2,6-Bis(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[2-(2-methylphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[4,5-Bis(methyloxy)-2,3-dihydro-1H-inden-2-yl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[4-(Aminosulfonyl)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[2-(methylsulfinyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-phenylethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[4-(Dimethylamino)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[2-(4-fluorophenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[2-(4-methylphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[3-(Aminosulfonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(4-methylphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-fluoro-3-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
Methyl 2-[({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate,
N-[(6-Chloro-2-pyridinyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
N-(2,3-Dihydro-1H-inden-1-yl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({2-[Acetyl(methyl)amino]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(1S)-2,3-Dihydro-1H-inden-1-yl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(1R)-2,3-Dihydro-1H-inden-1-yl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({3-[(methylsulfonyl)amino]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(1-phenyl-4-piperidinyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-ethyl-N-{1-[(ethylamino)carbonyl]-4-piperidinyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
Formic acid - 1-ethyl-N-[1-methyl-2-(4-methyl-1-piperazinyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide (1:1),
Methyl [4-({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)-1-piperidinyl]acetate,
1-Ethyl-N-{[4-(4-morpholinylmethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
1-Ethyl-N-({3-[(4-methyl-1-piperazinyl)methyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,

N-{[5-(Aminocarbonyl)-3-pyridinyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
1-Ethyl-N-{[4-(1-methylethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[3-(Cyclopentyloxy)-4-(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({4-[(4-methyl-1-piperazinyl)methyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
N-[(2,4-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,4-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2-Chloro-4-fluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{2-[2-Chloro-3-(methyloxy)phenyl]ethyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
Methyl 3-[({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate,
1-Ethyl-N-{[3-(1-pyrrolidinylmethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoroacetate,
1-Ethyl-N-(2-{4-[(methylsulfonyl)amino]phenyl}ethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[2,5-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[2,6-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(2-fluorophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,5-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(4-Chlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-Cyclohexyl-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{2-[4-(methylsulfonyl)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[2-fluoro-3-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({4-[(Cyclopropylamino)carbonyl]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(4-methyl-1-piperazinyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(1-pyrrolidinylmethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[6-(methyloxy)-1-oxo-2,3-dihydro-1H-inden-2-yl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,5-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,5-Diethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,3-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[2-(methylsulfonyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

1-Ethyl-N-[(3-hydroxyphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[3,5-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[2-(4-hydroxyphenyl)ethyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,5-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[2,4-Bis(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[2-(methyloxy)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({2-[(methylamino)carbonyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{2-[4-(methyloxy)phenyl]ethyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2-Chlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(2-hydroxyphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(1,3-Benzodioxol-5-ylmethyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[3-(methyloxy)phenyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(Cyclohexylmethyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
Methyl 4-[({[1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoate,
N-[(3,4-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[4-(Aminocarbonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,6-Difluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[3-(Aminocarbonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(4-hydroxyphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[6-(methyloxy)-3-pyridinyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-(2-pyridinylmethyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-{[3-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[4-(2-Amino-2-oxoethyl)phenyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({4-[(methylamino)carbonyl]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{4-[2-(methylamino)-2-oxoethyl]phenyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

1-Ethyl-N-[(3-fluorophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-({4-[(methylsulfonyl)amino]phenyl}methyl)-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[4-(Aminosulfonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[2-(Aminocarbonyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({3-[(Dimethylamino)methyl]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[3-Chloro-4-(methyloxy)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(1-Acetyl-4-piperidinyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-{[2-(trifluoromethyl)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-(5-Chloro-2,3-dihydro-1H-inden-2-yl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-({3-[(Acetylamino)methyl]phenyl}methyl)-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(4-fluorophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(2-ethylphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[2-fluoro-5-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[(2,3,4-trifluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(4-Chloro-2-fluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(4-Bromo-2-fluorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,5-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,3-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(4-Cyanophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(4-Bromophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[5-fluoro-2-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(4-iodophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[4-(1,1-Dimethylethyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3-Cyanophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

N-[(2,6-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(5-Chloro-2-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(3,5-Dibromophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(4-ethylphenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[3-fluoro-4-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-[(2-iodophenyl)methyl]-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2-Bromophenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(hydroxymethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[3-(hydroxymethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[3-(hydroxymethyl)-2-methylphenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[2,3-Dichloro-6-(hydroxymethyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,4-Dichloro-6-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(2-methylpropyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2,5-dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-N-[(2,4,5-trifluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[2-fluoro-4-(trifluoromethyl)phenyl]methyl}-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-[(2-Chloro-6-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[({[1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid sodium salt,
3-[({[1-Ethyl-4-(tetrahydro-2H-pyran-4-ylamino)-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl}amino)methyl]benzoic acid,
Ethyl 1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,
1-Ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
N-{[4-(Dimethylamino)phenyl]methyl}-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-({4-[(ethyloxy)imino]cyclohexyl}amino)-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-4-({4-[(methyloxy)imino]cyclohexyl}amino)-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(4-{[(1,1-Dimethylethyl)oxy]imino}cyclohexyl)amino]-1-ethyl-N-{[4-(methyloxy)phenyl]methyl}-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
1-Ethyl-N-{[4-(methyloxy)phenyl]methyl}-4-[(7-oxohexahydro-1H-azepin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
Ethyl 1-ethyl-4-[(7-oxohexahydro-1H-azepin-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxylate,

4-{[cis-4-(Butylamino)cyclohexyl]amino}-N-(2,3-dihydro-1H-inden-2-yl)-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(trans-4-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(trans-2-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(cis-2-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,
4-[(3-Aminocyclohexyl)amino]-1-ethyl-N-(phenylmethyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxamide,

Ethyl 1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate,
N,1-Diethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(4-fluorophenyl)-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-(1,3-thiazol-2-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-*N*-[(4-fluorophenyl)methyl]-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-{[4-(methylsulfonyl)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-{[3,4-bis(methyloxy)phenyl]methyl}-1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-(2-pyridinylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3,4-dimethylphenyl)methyl]-1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-*N*-{[4-(methyloxy)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,4-dimethylphenyl)methyl]-1-ethyl-4-{[(1*SR*,3*RS*)-3-hydroxycyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide, or
1-Ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-*N*-{[4-(trifluoromethyl)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide;

or a salt thereof.

51. A compound or salt as claimed in claim 1, which is:

N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{[4-(methyloxy)phenyl]methyl}-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(4-methylphenyl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-{[2,3-Dichloro-6-(hydroxymethyl)phenyl]methyl}-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-*N*-{[4-(methyloxy)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-[(4-oxocyclohexyl)amino]-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,4-Dimethylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3,4-Dimethylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(2,3-Dichlorophenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(3-Chloro-4-methylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-[(4-Chloro-2-methylphenyl)methyl]-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,

N-({4-[(Difluoromethyl)oxy]phenyl}methyl)-1-ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide, or
1-Ethyl-4-{[4-(hydroxyimino)cyclohexyl]amino}-*N*-{[4-(trifluoromethyl)phenyl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide;

or a salt thereof.

52. A compound or salt as claimed in claim 1, which is:

N-Benzyl-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-(4-fluorophenyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[4-(methylsulfonyl)benzyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-*N*-(1,3-thiazol-2-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
N-(3,4-Dimethoxybenzyl)-1-ethyl-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-{4-[(methylsulfonyl)methyl]phenyl}-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide,
1-Ethyl-*N*-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide, or
1-Ethyl-*N*-(2-pyridinylmethyl)-4-(tetrahydro-2*H*-pyran-4-ylamino)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxamide;

or a salt thereof.

53. A compound or salt as claimed any preceding claim, which is the compound or a pharmaceutically acceptable salt thereof.

54. A compound or salt as claimed in any preceding claim, which is in a particle-size-reduced form, wherein the particle size (D50 value) of the size-reduced compound or salt is 0.5 to 10 microns.

55. A compound or a pharmaceutically acceptable salt as claimed in any preceding claim, for use as an active therapeutic substance in a mammal such as a human.

56. A compound or a pharmaceutically acceptable salt as claimed in any preceding claim, for use in the treatment and/or prophylaxis of asthma, chronic

obstructive pulmonary disease (COPD), atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxic shock, adult respiratory distress syndrome, multiple sclerosis, cognitive impairment in a neurological disorder, depression, or pain, in a mammal such as a human.

57. A compound or a pharmaceutically acceptable salt as claimed in claim 56, for use in the treatment and/or prophylaxis of chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, allergic rhinitis or atopic dermatitis in a mammal such as a human.

58. A compound or a pharmaceutically acceptable salt as claimed in claim 56, for use in the treatment and/or prophylaxis of atopic dermatitis in a human.

59. A pharmaceutical composition comprising a compound of formula (I) or (IA) or (IB), as defined in any of claims 1 to 54, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers and/or excipients.

60. A pharmaceutical composition as claimed in claim 59 which is suitable for and/or adapted for inhaled administration, in which the compound or salt is in a particle-size-reduced form, wherein the particle size (D50 value) of the size-reduced compound or salt is 0.5 to 10 microns.

61. A composition as claimed in claim 59, for the treatment and/or prophylaxis of an inflammatory and/or allergic disease, or cognitive impairment in a neurological disorder, in a mammal such as a human.

62. A composition as claimed in claim 59, for use in the treatment and/or prophylaxis of chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, allergic rhinitis or atopic dermatitis in a mammal such as a human.

63. The use of a compound of formula (I) or (IA) or (IB), as defined in any of claims 1 to 54, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment and/or prophylaxis of an inflammatory and/or allergic disease, or cognitive impairment in a neurological disorder, in a mammal such as a human.

64. The use of a compound of formula (I) or (IA) or (IB), as defined in any of claims 1 to 54, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment and/or prophylaxis of asthma, chronic obstructive pulmonary disease (COPD), atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the

myocardium and brain, chronic glomerulonephritis, endotoxic shock, adult respiratory distress syndrome, multiple sclerosis, cognitive impairment in a neurological disorder, depression, or pain, in a mammal such as a human.

65. The use as claimed in claim 63 or 64, wherein the medicament is for the treatment and/or prophylaxis of chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, allergic rhinitis or atopic dermatitis in a mammal such as a human.

66. The use as claimed in claim 63 or 64, wherein the medicament is for the treatment and/or prophylaxis of chronic obstructive pulmonary disease (COPD) in a human.

67. The use as claimed in claim 64, wherein the medicament is for the treatment and/or prophylaxis of atopic dermatitis in a human.

68. The use as claimed in claim 64, wherein the medicament is for the treatment and/or prophylaxis of cognitive impairment in a neurological disorder, or of depression, in a human.

69. The use as claimed in any of claims 63 to 66, wherein the medicament is for oral or inhaled administration and is a pharmaceutical composition as defined in claim 59.

70. A combination comprising a compound of formula (I) or (IA) or (IB), as defined in any of claims 1 to 54, or a pharmaceutically acceptable salt thereof, together with a β_2-adrenoreceptor agonist, an anti-histamine, an anti-allergic, or an anti-inflammatory agent.

71. A combination comprising a compound of formula (I) or (IA) or (IB), as defined in any of claims 1 to 54, or a pharmaceutically acceptable salt thereof, together with a muscarinic (M) receptor antagonist.

72. A combination as claimed in claim 71, wherein the muscarinic (M) receptor antagonist is a M_3 receptor antagonist.

73. A pharmaceutical composition comprising a combination as defined in any of claims 70 to 72, together with one or more pharmaceutically acceptable carriers and/or excipients, the composition being a separate or combined pharmaceutical composition for administration of the individual compounds of the combination either sequentially or simultaneously.

74. A pharmaceutical composition as claimed in claim 73 for inhaled administration, and wherein the combination comprises the compound or salt together with a β_2-adrenoreceptor agonist or a muscarinic (M) receptor antagonist, and wherein

the pharmaceutical composition is for the treatment and/or prophylaxis of chronic obstructive pulmonary disease (COPD) in a human.