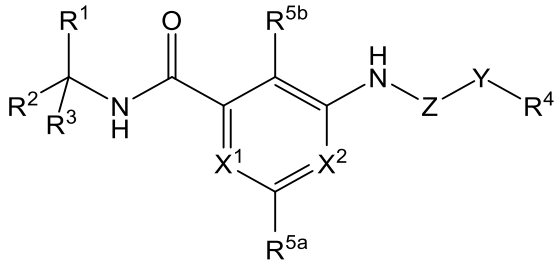
CLAIMS

1. A compound of general formula (I) including all tautomeric forms all enantiomers and isotopic variants and salts and solvates thereof:



(I)

wherein:

R^1 is H, CN, $C(O)OR^{12}$, C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl, any of which alkyl, alkenyl or alkynyl groups are optionally substituted with one or more substituents, suitably one substituent, selected from fluoro, OR^{12}, $N(R^{12})_2$, $C(O)OR^{12}$, $C(O)N(R^{12})_2$, $C(O)R^{12}$ and $N(R^{13})C(O)R^{12}$;

wherein each R^{12} and R^{13} is independently selected from H, C_{1-6} alkyl and C_{1-6} fluoroalkyl

R^2 is H or C_{1-6} alkyl optionally substituted with OR^{12};

R^3 is:

C_{1-10} alkyl, C_{2-10} alkenyl or C_{2-10} alkynyl, any of which is optionally substituted with one or more substituents, suitably one substituent, selected from fluoro, CN, R^{14} OR^{14}, OR^{15}, $N(R^{15})_2$, $C(O)OR^{15}$, $C(O)N(R^{15})_2$, $N(R^{16})C(O)R^{15}$, $N(R^{15})S(O)_2R^{14}$, $N(R^{15})S(O)_2R^{16}$ and $N(R^{15})C(O)OR^{16}$; or a 3- to 7-membered carbocyclic or heterocyclic ring system or a 6- to 10 membered aryl or 5- to 10-membered heteroaryl ring system, either of which is optionally substituted with one or more substituents selected from halo, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, OR^{17} and $N(R^{17})_2$;

wherein R^{14} is a 6- to 10-membered aryl or 5- to 10-membered heteroaryl ring system or a 3- to 7-membered carbocyclic or heterocyclic ring system, any of which is optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} haloalkyl, OR^{17} and $N(R^{17})_2$; wherein each R^{17} is independently H, C_{1-4} alkyl or C_{1-4} haloalkyl;

each R^{15} and R^{16} is independently H, C_{1-6} alkyl or C_{1-6} haloalkyl; or

R^2 and R^3 together with the carbon atom to which they are attached combine to form a 3- to 10-membered carbocyclic or heterocyclic ring system optionally substituted with one or more substituents selected from halo, CN, OR^9, $N(R^9)_2$, $C(O)OR^9$, $C(O)N(R^9)_2$, $C(O)R^9$, $N(R^9)C(O)R^9$ and C_{1-4} alkyl optionally substituted with halo, OR^9 or $N(R^9)_2$; or

R^1, R^2 and R^3 together with the carbon atom to which they are attached combine to form a bridged 5- to 10-membered carbocyclic or heterocyclic ring system or phenyl, any of which is optionally substituted with one or more substituents selected from halo, CN, OR^9, $N(R^9)_2$, $C(O)OR^9$, $C(O)N(R^9)_2$, $C(O)R^9$, $N(R^9)C(O)R^9$ and C_{1-4} alkyl optionally substituted with halo, OR^9 or $N(R^9)_2$;

each R^9 is independently selected from H, C_{1-6} alkyl or C_{1-6} haloalkyl;

X^1 is N;

X^2 is CR^8;

R^8 is H, halo, OH, $O(C_{1-4}$ alkyl), CN or NH_2;

Y is a bond or a straight C_{1-6} alkylene chain which is optionally substituted with one or more substituents R^{18}, wherein two substituents R^{18} may be attached to the same or to different carbon atoms;

wherein each R^{18} is independently C_{1-3} alkyl or C_{1-3} haloalkyl in which a $-CH_2-$ is optionally replaced with -NH- or -O- and wherein two R^{18} groups may combine with the atom or atoms to which they are attached to form a 3- to 6-membered carbocyclic or heterocyclic ring system;

Z is -C(O)- or -C(O)NH-;

R^4 is a 6- to 14-membered aryl, 5- to 14-membered heteroaryl or a 5- to 10-membered carbocyclic ring system, any of which is optionally substituted with one or more substituents selected from:
halo, CN, nitro, R^{19}, OR^{19}, OR^6, SR^6, NR^6R^7, $C(O)R^6$, $C(O)R^{19}$, $C(O)OR^6$, $C(O)N(R^6)(R^7)$, $N(R^7)C(O)R^6$;
C_{1-6} alkyl or $O(C_{1-6}$ alkyl), either of which is optionally substituted with one or more substituents selected from halo, CN, nitro, R^{19}, OR^6, SR^6, NR^6R^7, $C(O)R^6$ $C(O)OR^6$, $C(O)N(R^6)(R^7)$ and $N(R^7)C(O)R^6$; and
when R^4 is not fully aromatic in character, oxo;

wherein R^{19} is 5- or 6-membered aryl or heteroaryl ring system or a 3- to 7-membered carbocyclic or heterocyclic ring system, any of which is optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} haloalkyl, OH, $O(C_{1-4}$ alkyl), $O(C_{1-4}$ haloalkyl);

R^6 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, benzyl, 3- to 7-membered carbocyclyl or 3- to 7-membered heterocyclyl;

R^7 is H, C_{1-6} alkyl or C_{1-6} haloalkyl; or

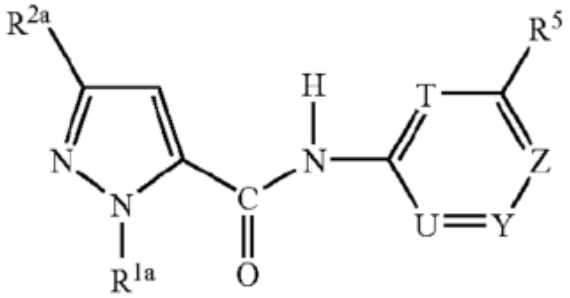
R^6 and R^7 together with the nitrogen atom to which they are attached may form a 4 to 7-membered heterocyclic ring optionally containing one or more further heteroatoms and optionally substituted with one or more substituents selected from oxo and halo; and

each of R^{5a} and R^{5b} is independently H, C_{1-4} alkyl or halo;

provided that:

when X^2 is CH, Z is -C(O)- and Y is a bond, R^4 is not a 5- to 10-membered heteroaryl ring linked to Y via a nitrogen atom, and

wherein the compounds of formula (A):

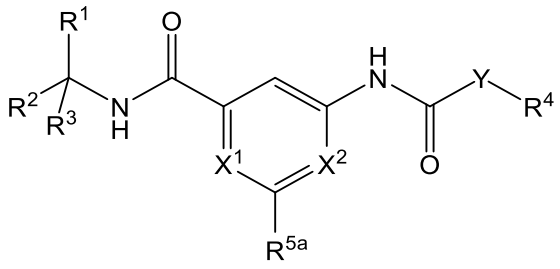


(A)

wherein R^{1a} is ethyl; R^{2a} is *tert*-butyl; T, U and Y are CH and Z is N; and R^5 is C(O)NHEt, $C(O)NH(CH_2)_2CH_3$, $C(O)NH(CH_2)_2CH_2F$, $C(O)NH(CH_2)_3CH_3$, $C(O)NH(CH_2)_3CH_2F$, $C(O)NHCH_2C{\equiv}CH$ or $C(O)NHCH_2CH{=}CH_2$ are disclaimed and any tautomeric forms, enantiomers and isotopic variants and salts and solvates of the compounds of Formula (A) are not disclaimed.

2. A compound according to claim 1, wherein:

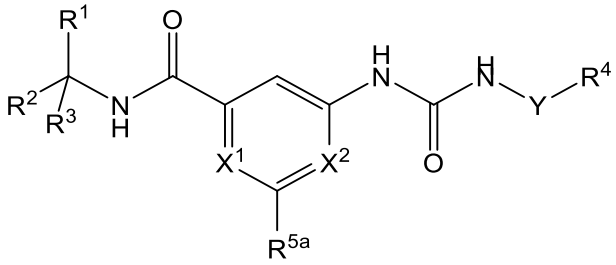
Z is -C(O)- and R^{5b} is H, such that the compound is of formula (Iz):



(Iz)

wherein R^1, R^2, R^3, R^4, R^{5a}, X^1, X^2 and Y are as defined in claim 1; or

Z is -C(O)NH-, and R^{5b} is H such that the compound is of general formula (Iy):



(Iy)

wherein R^1, R^2, R^3, R^4, R^{5a}, X^1, X^2 and Y are as defined in claim 1.

3. A compound according to claim 2, wherein the compound is a compound according to Formula (Iz) and Y is not a bond.

4. A compound according to any one of claims 1 to 3, wherein R^1 is H, CN, ethynyl or methyl, either of which is unsubstituted or is substituted with OH.

5. A compound according to any one of claims 1 to 4, wherein:

R^2 is methyl or ethyl; and

R^3 is $C_{1\text{-}4}$ alkyl optionally substituted with one or more substituents selected from hydroxyl, methoxy, ethoxy, -C(O)O-($C_{1\text{-}4}$ alkyl) and -N(H)C(O)O-($C_{1\text{-}4}$ alkyl); or

wherein

R^3 is $C_{1\text{-}10}$ alkyl or $C_{2\text{-}3}$ alkynyl either of which is unsubstituted or substituted with a single substituent selected from fluoro, R^{14} OR^{14}, OR^{15}, $C(O)OR^{15}$, $N(R^{16})S(O)_2R^{15}$ and $N(R^{16})C(O)OR^{15}$; wherein

R^{14} is selected from phenyl, pyridyl and a 5- or 6-membered heterocyclic ring;

R^{15} is selected from H, or $C_{1\text{-}4}$ alkyl; and

R^{16} is H; or

R^3 is a 3- to 7-membered carbocyclic or heterocyclic ring system, which is unsubstituted or substituted as defined in claim 1; or

R^3 is phenyl or pyridyl, either or which is unsubstituted or substituted with one or more substituents selected from OR^{17} and $N(R^{17})_2$, wherein each R^{17} is H or methyl.

6. A compound according to claim 5 wherein:
R^1 is methyl or CN and R^2 and R^3 are both methyl; or
R^2 and R^3 combine with the carbon atom to which they are attached to form a carbocyclic or heterocyclic ring system and R^1 is H, methyl, methyl substituted with OH, CN, ethynyl or $C(O)OR^{12}$, wherein R^{12} is as defined in claim 1.

7. A compound according to any one of claims 1 to 6 wherein Y is $-CH_2-$, $-CH_2CH_2-$, $-CH(CH_3)CH_2-$, $-CH_2CH(CH_3)-$ or $-CH_2CH_2CH_2-$,
wherein:
R^{5a} and R^{5b} are both H and/or
X^2 is CH and/or

wherein:
R^4 is a 6- to 11-membered aryl group selected from phenyl, naphthyl, indanyl, 1,2,3,4-tetrahydronaphthyl and benzocycloheptanyl, any of which is optionally substituted as defined in claim 1; or

R^4 is a 5- to 10-membered heteroaryl group selected from pyridyl, quinolinyl, quinoxalinyl, indazolyl, indolyl, benzoxazolyl, dihydrobenzofuranyl, furyl and thienyl, any of which is optionally substituted as defined in claim 1;

R^4 is a carbocyclyl group selected from cyclohexyl and adamantyl, any of which is optionally substituted as defined in claim 1; or

R^4 is phenyl optionally substituted with one or more substituents as defined in claim 1; or

R^4 is 5-10-membered heteroaryl selected from pyridyl, pyrrolyl, thienyl, furyl, benzoxazolyl, imidazolyl, indolyl or indazolyl any of which is optionally substituted as defined in claim 1.

8. A compound according to claim 7, wherein R^4 is phenyl which is substituted with an OH group at either the 2- or the 3-position and optionally with one or more further substituents selected from:

halo, CN, R^{19}, OR^{19};

OR^6, $C(O)OR^6$;

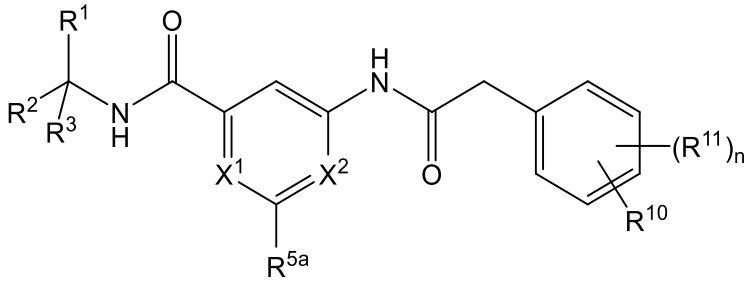
C_{1-4} alkyl or $O(C_{1-4}$ alkyl) either of which is optionally substituted with one or more substituents selected from halo, CN, R^{19}, OR^{19}, OR^6 and NR^6R^7;

wherein R^6 is H, C_{1-4} alkyl or C_{1-4} haloalkyl or, for a moiety NR^6R^7, R^6 and R^7 combine with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocyclic ring, optionally containing one or more further heteroatoms and optionally substituted with one or more halo substituents;

R^7 is as defined in claim 1; and

R^{19} is a 3- to 6- membered carbocyclyl group or phenyl, either or which is optionally substituted with one or more substituents selected from halo, methyl and methoxy.

9. A compound according to any one of claims 1 to 8 wherein Y is-CH_2-, R^4 is phenyl and the compound is a compound of general formula (Ia):



(Ia)

wherein

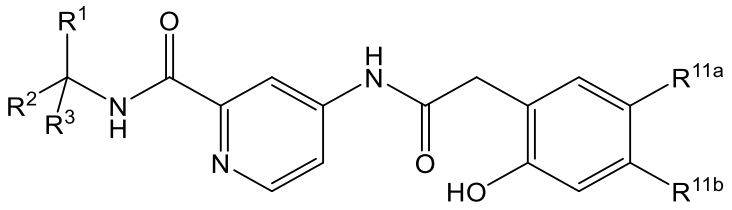
R^1, R^2, R^3, R^{5a}, X^1 and X^2 are as defined in claim 1;

R^{10} is H, OH, halo, C_{1-6} alkyl, -$O(C_{1-6}$ alkyl);

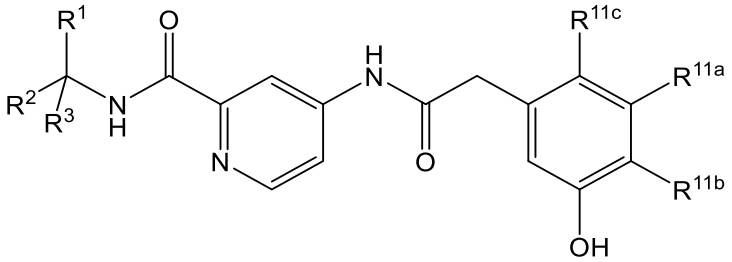
each R^{11} is independently H, halo, OH, CN, C_{1-6} alkyl, C_{1-6} haloalkyl, -$O(C_{1-6}$ alkyl) or $C(O)O$-(C_{1-6} alkyl); and

n is 1 or 2; or

a compound of general formula (Id) or (Ie):



(Id)



(Ie)

wherein

R^1, R^2 and R^3, are as defined in claim 1;

R^{11a} is H, halo, C_{1-4} alkyl, C_{1-4} haloalkyl or C(O)O(C_{1-4} alkyl);

R^{11b} is H, halo, C_{1-4} alkyl or C_{1-4} haloalkyl; and

R^{11c} is H, halo, CN, C_{1-4} alkyl or C_{1-4} haloalkyl.

10. A compound of claim 1, wherein Y is a straight C_{1-3} alkylene unsubstituted or substituted with one or more substituents R^{18}, wherein R^{18} is as defined above and wherein two substituents R^{18} may be attached to the same or to different carbon atoms.

11. A compound of claim 1, wherein R^4 is a 6- to 11-membered aryl group selected from phenyl, naphthyl, indanyl, 1,2,3,4-tetrahydronaphthyl and benzocycloheptanyl, any of which is unsubstituted or substituted as defined in claim 1.

12. A compound according to claim 1 selected from:

N-tert-Butyl-4-[[2-(2-hydroxyphenyl)acetyl]amino]pyridine-2-carboxamide (Compound 1);

N-(1-Adamantyl)-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide(Compound 1.3);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(3-methoxy-1,1-dimethyl-propyl)pyridine-2-carboxamide (Compound 1.4);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-methylcyclobutyl)pyridine-2-carboxamide (Compound 1.6);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-methylcyclohexyl)pyridine-2-carboxamide (Compound 1.7);
tert-Butyl N-[3-[[4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carbonyl]amino]-3-methyl-butyl]carbamate (Compound 1.8);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-cyclohexyl-pyridine-2-carboxamide (Compound 1.10);
N-tert-Butyl-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3);
N-(1,1-Dimethylpropyl)-4-[[2-(4-fluoro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.1a);
N-tert-Butyl-4-[[2-(4-fluoro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.2a);
N-tert-Butyl-4-[[2-(2-chloro-6-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.3a);
4-[[2-(4-Bromo-5-chloro-2-hydroxy-phenyl)acetyl]amino]-N-tert-butyl-pyridine-2-carboxamide (Compound 3.4a);
4-[[2-(5-tert-Butyl-2-hydroxy-phenyl)acetyl]amino]-N-(1-cyanocyclobutyl)pyridine-2-carboxamide (Compound 3.5a);
4-[[2-(5-tert-Butyl-2-hydroxy-phenyl)acetyl]amino]-N-(1-methyl cyclobutyl)pyridine-2-carboxamide (Compound 3.6a);
N-tert-butyl-4-[2-(2,5-dibromo-3-fluoro-6-hydroxyphenyl)acetamido]pyridine-2-carboxamide (Compound 3.7a);
N-tert-Butyl-4-[[2-[2-hydroxy-5-(trifluoromethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 3.5b);
N-tert-Butyl-4-[[2-(4-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.6b);
N-tert-Butyl-4-[[2-[2-hydroxy-4-(trifluoro methyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 3.7b);
N-tert-Butyl-4-[[2-(2-hydroxy-5-methoxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.8b);

N-tert-Butyl-4-[(6-hydroxyindane-1-carbonyl)amino]pyridine-2-carboxamide (Compound 3.9b);
N-tert-Butyl-4-[(7-hydroxyindane-1-carbonyl)amino]pyridine-2-carboxamide (Compound 3.10b);
N-tert-Butyl-4-[[2-(2,5-dibromo-3-chloro-6-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.11b);
N-tert-Butyl-4-[[2-(3-hydroxyphenyl) acetyl]amino]pyridine-2-carboxamide (Compound 3.12b);
N-tert-Butyl-4-[[2-(2-fluoro-5-hydroxy-phenyl) acetyl]amino]pyridine-2-carboxamide (Compound 3.13b);
N-tert-Butyl-4-[[2-(4-chloro-3-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.14b);
N-tert-Butyl-4-[[2-(2-chloro-3-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.15b);
N-tert-Butyl-4-[[2-(2-chloro-5-hydroxy-phenyl) acetyl]amino]pyridine-2-carboxamide (Compound 3.16b);
N-tert-Butyl-4-[[2-(3-chloro-5-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3.17b);
N-tert-Butyl-4-[[2-(2-thienyl)acetyl]amino]pyridine-2-carboxamide (Compound 5);
4-[[2-(2-Adamantyl)acetyl]amino]-N-tert-butyl-pyridine-2-carboxamide (Compound 5.1);
N-tert-Butyl-4-[[2-(4-fluoro-2-methoxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 5.2);
N-tert-Butyl-4-[[2-(5-chloro-2-fluoro-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 5.3);
N-tert-Butyl-4-[[2-(2-furyl)acetyl]amino] pyridine-2-carboxamide (Compound 5.4);
N-tert-Butyl-4-[[2-(3-chlorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.5);
N-tert-Butyl-4-[[2-(1H-indol-3-yl)acetyl] amino]pyridine-2-carboxamide (Compound 5.6);
N-tert-Butyl-4-[[2-(o-tolyl)acetyl] amino]pyridine-2-carboxamide (Compound 5.7);
N-tert-Butyl-4-[[2-(3,4-dichlorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.8);
N-tert-Butyl-4-[[2-(3-fluorophenyl)acetyl] amino]pyridine-2-carboxamide (Compound 5.9);
N-tert-Butyl-4-[[2-(5-chloro-2-methoxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 5.10);
N-tert-Butyl-4-[[2-(p-tolyl)acetyl] amino]pyridine-2-carboxamide (Compound 5.11);
N-tert-Butyl-4-[[2-(2-fluorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.12);
N-tert-Butyl-4-[[2-(4-fluorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.13);
N-tert-Butyl-4-[[2-(m-tolyl)acetyl] amino]pyridine-2-carboxamide (Compound 5.14);
4-[[2-(1,3-Benzoxazol-6-yl)acetyl] amino]-N-tert-butyl-pyridine-2-carboxamide (Compound 5.15);

N-tert-Butyl-4-[[2-(2-chloro-3-pyridyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.16);
N-tert-Butyl-4-[[2-(2,6-dichlorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.17);
N-tert-Butyl-4-[[2-(4-chloro-3-fluoro-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 5.18);
N-tert-Butyl-4-[[2-(3,5-dichloro phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 5.19);
N-tert-Butyl-4-[[2-(2-chlorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.20);
N-tert-Butyl-4-[[2-(3-chloro-4-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 5.21);
N-tert-Butyl-4-(indane-1-carbonyl amino)pyridine-2-carboxamide (Compound 5.22);
N-tert-Butyl-4-[(2-quinoxalin-6-ylacetyl) amino]pyridine-2-carboxamide (Compound 5.23);
N-tert-Butyl-4-[[2-(2-naphthyl) acetyl]amino]pyridine-2-carboxamide (Compound 5.24);
N-tert-Butyl-4-(2,3-dihydrobenzofuran-3-carbonylamino)pyridine-2-carboxamide (Compound 5.25);
N-tert-Butyl-4-(6,7,8,9-tetrahydro-5H-benzo[7]annulene-5-carbonylamino) pyridine-2-carboxamide (Compound 5.26);
N-tert-Butyl-4-(tetralin-1-carbonylamino) pyridine-2-carboxamide (Compound 5.27);
N-tert-Butyl-4-[[2-(6-quinolyl)acetyl] amino]pyridine-2-carboxamide (Compound 5.29);
N-tert-butyl-4-[[1-(3-chlorophenyl) cyclopropanecarbonyl]amino]pyridine-2-carboxamide (Compound 5.31);
N-tert-Butyl-4-[[2-(2,3-dihydro-1,4-benzodioxin-6-yl)acetyl]amino]pyridine-2-carboxamide (Compound 5.32);
N-(1,1-Dimethylprop-2-ynyl)-4-[(2-isochroman-1-ylacetyl)amino]pyridine-2-carboxamide (Compound 5.33);
4-[[2-(4,4-Difluorocyclohexyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 5.34);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[4-(trifluoromethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 5.35);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[3-(trifluoromethyl)-1H-pyrazol-4-yl]acetyl] amino] pyridine-2-carboxamide (Compound 5.36);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[3-(trifluoromethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 5.37);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[2-(trifluoromethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 5.38);

4-[[2-(2,3-Dihydro-1,4-benzoxazin-4-yl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 5.39);

N-tert-Butyl-4-[[2-(5-cyano-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 6);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(1,1-dimethylbutyl)pyridine-2-carboxamide (Compound 7.2);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(1,1,2-trimethylpropyl)pyridine-2-carboxamide (Compound 7.6);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-isopropyl-pyridine-2-carboxamide (Compound 7.7);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(4-methyltetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 7.9);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-tetrahydropyran-4-yl-pyridine-2-carboxamide (Compound 7.11);

4-[2-(5-Chloro-2-hydroxyphenyl)acetamido]-N-[(1s,4s)-4-hydroxycyclohexyl]pyridine-2-carboxamide (Compound 7.12);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-sec-butyl-pyridine-2-carboxamide (Compound 7.13);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(2-hydroxy-1,1,2-trimethyl-propyl)pyridine-2-carboxamide (Compound 7.14);

N-(3-Bicyclo[1.1.1]pentanyl)-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 7.15);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(1-cyanocyclobutyl)pyridine-2-carboxamide (Compound 7.16);

tert-Butyl-3-[[4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carbonyl]amino]piperidine-1-carboxylate (Compound 8.1);

tert-Butyl (1r,5s,6s)-6-{4-[2-(5-chloro-2-hydroxyphenyl)acetamido]pyridine-2-amido}-3-azabicyclo[3.1.0]hexane-3-carboxylate (Compound 8.3);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylpropyl)pyridine-2-carboxamide (Compound 9.2);

N-tert-Butyl-4-[[2-(5-tert-butyl-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 10);

Methyl 3-[2-[[2-(tert-butylcarbamoyl)-4-pyridyl]amino]-2-oxo-ethyl]-4-hydroxy-benzoate (Compound 13);

N-tert-Butyl-4-[[2-(2-hydroxy-5-methyl-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 15);
N-tert-Butyl-4-[[2-(3-hydroxy-2-pyridyl)acetyl]amino]pyridine-2-carboxamide (Compound 19);
N-tert-Butyl-4-[[2-(5-fluoro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 20);
N-tert-Butyl-4-[[(1R) or (1S)-indane-1-carbonyl]amino]pyridine-2-carboxamide (Compound 21a);
N-tert-Butyl-4-[[(1R) or (1S)-indane-1-carbonyl]amino]pyridine-2-carboxamide (Compound 21b);
N-tert-Butyl-4-[(2-phenylacetyl)amino]pyridine-2-carboxamide (Compound 22);
4-(3,3-Dimethylbutanoylamino)-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 22.1);
4-[(2-Cyclopentylacetyl)amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 22.2);
4-[[2-(3-Chloro-4-pyridyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 22.3);
4-[[2-(4-Chlorophenyl)acetyl]amino]-N-(1-cyanocyclopropyl)pyridine-2-carboxamide (Compound 23);
4-[[2-(3-Chlorophenyl)acetyl] amino]-N-(1-cyanocyclo propyl)pyridine-2-carboxamide (Compound 23.1);
4-[[2-(2-Chloro-5-fluoro-phenyl) acetyl] amino]-N-(1-cyanocyclo propyl)pyridine-2-carboxamide (Compound 23.2);
N-tert-Butyl-4-(indane-2-carbonyl amino)pyridine-2-carboxamide (Compound 23.3);
N-tert-Butyl-4-[[2-[2-(difluoromethoxy) phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 23.4);
N-tert-Butyl-4-[[2-[2-(difluoromethyl) phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 23.5);
N-tert-Butyl-4-[[2-(3,4-difluorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 23.6);
N-tert-Butyl-4-[[2-(3,5-difluorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 23.7);
N-tert-Butyl-4-[[2-(2,3-difluorophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 23.8);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-tetrahydropyran-4-yl-pyridine-2-carboxamide (Compound 23.9);
N-(1-Cyanocyclobutyl)-4-[[2-(6-quinolyl) acetyl]amino]pyridine-2-carboxamide (Compound 23.11);
N-tert-Butyl-4-[[2-[2-(trifluoromethyl) phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 23.12);

4-[[2-(2-Bromophenyl)acetyl]amino]-N-tert-butyl-pyridine-2-carboxamide (Compound 23.13);
N-tert-Butyl-4-[[2-(2-cyanophenyl) acetyl]amino]pyridine-2-carboxamide (Compound 23.14);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(4-cyanotetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 23.15);
N-(4-Cyanotetrahydropyran-4-yl)-4-[[2-(6-quinolyl)acetyl]amino]pyridine-2-carboxamide (Compound 23.16);
4-[[2-(2-Chloro-5-methoxy-phenyl)acetyl] amino]-N-(1-cyanocyclopropyl)pyridine-2-carboxamide (Compound 24);
N-(3-Bicyclo[1.1.1]pentanyl)-4-[[2-(5-tert-butyl-2-hydroxy-phenyl)acetyl]amino] pyridine-2-carboxamide (Compound 25);
4-[[2-(5-tert-Butyl-2-hydroxy-phenyl)acetyl]amino]-N-(4-cyanotetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 25.1);
N-tert-Butyl-4-[[2-(2-hydroxy-5-phenyl-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 26);
N-tert-Butyl-4-[[2-[5-chloro-2-hydroxy-4-(pyrrolidin-1-ylmethyl)phenyl]acetyl] amino]pyridine-2-carboxamide (Compound 27);
N-tert-Butyl-4-[[2-[4-[(tert-butylamino)methyl]-5-chloro-2-hydroxy-phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 27.1);
N-tert-Butyl-4-[[2-[5-chloro-2-hydroxy-4-(morpholinomethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 27.2);
N-tert-Butyl-4-[[2-[5-chloro-4-[(3,3-difluoropyrrolidin-1-yl)methyl]-2-hydroxy-phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 27.3);
N-tert-butyl-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]-5-fluoro-pyridine-2-carboxamide (Compound 28);
N-tert-Butyl-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]-3-fluoro-pyridine-2-carboxamide (Compound 28.1);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1-cyanocyclobutyl)pyridine-2-carboxamide (Compound 30);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 30.1);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(4-fluoro-1-bicyclo[2.1.1]hexanyl)pyridine-2-carboxamide (Compound 30.2);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1-cyclopropyl-1-methyl-ethyl)pyridine-2-carboxamide (Compound 30.3);

4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 30.3a);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1-methyl-3-bicyclo[1.1.1] pentanyl)pyridine-2-carboxamide (Compound 30.4);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1-cyano-3-bicyclo[1.1.1]pentanyl) pyridine-2-carboxamide (Compound 30.5);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(2,2-difluorocyclopropyl)pyridine-2-carboxamide (Compound 30.6);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1-cyanocyclopropyl)pyridine-2-carboxamide (Compound 30.7);
4-[[2-(2-Clorophenyl)acetyl]amino]-N-(1-methylcyclopropyl)pyridine-2-carboxamide (Compound 30.8);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(3-fluoro-1-bicyclo[1.1.1]pentanyl)pyridine-2-carboxamide (Compound 30.9);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(2-fluoro-1,1-dimethyl-ethyl)pyridine-2-carboxamide (Compound 30.10);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(4-ethynyltetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 30.11);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(1-cyanocyclopentyl)pyridine-2-carboxamide (Compound 30.12);
4-[[2-(2-Chlorophenyl)acetyl]amino]-N-(2,2-difluoro-1,1-dimethyl-ethyl)pyridine-2-carboxamide (Compound 30.13);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(4-cyanotetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 31);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-ethynylcyclopentyl)pyridine-2-carboxamide (Compound 31.2);
4-[2-(5-Chloro-2-hydroxyphenyl)acetamido]-N-[(1s,2s)-2-hydroxycyclohexyl] pyridine-2-carboxamide (Compound 31.3);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1S,2S)-2-hydroxycyclo hexyl]pyridine-2-carboxamide or 4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1R,2R)-2-hydroxycyclohexyl]pyridine-2-carboxamide (Compound 31.3a);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(4-ethynyltetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 31.4);

N-[(6-Amino-2-pyridyl)methyl]-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl] amino]pyridine-2-carboxamide (Compound 32);

12-[[4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carbonyl] amino]dodecanoic acid (Compound 32.1);

4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-(3-pyridylmethyl)pyridine-2-carboxamide (Compound 32.2);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(2-pyridylmethyl)pyridine-2-carboxamide (Compound 32.3);

4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-(4-pyridylmethyl)pyridine-2-carboxamide (Compound 32.4);

4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-[(2-hydroxyphenyl) methyl]pyridine-2-carboxamide (Compound 32.5);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(1,1-dimethyl-2-morpholino-ethyl)pyridine-2-carboxamide (Compound 32.6);

4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-(2-hydroxy-1,1-dimethyl-ethyl)pyridine-2-carboxamide (Compound 32.7);

4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl] amino]-N-(3,3-difluoro-4-piperidyl)pyridine-2-carboxamide (Compound 32.8);

4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-(1H-imidazol-2-yl)pyridine-2-carboxamide (Compound 32.9);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1R,2R)-2-hydroxycyclopentyl] pyridine-2-carboxamide (Compound 33);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 34);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[3-(hydroxymethyl) tetrahydrofuran-3-yl]pyridine-2-carboxamide (Compound 35);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(3R)-3-(hydroxymethyl)tetrahydro furan-3-yl]pyridine-2-carboxamide or 4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(3S)-3-(hydroxymethyl)tetrahydrofuran-3-yl]pyridine-2-carboxamide (Compound 35a);

-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(3R)-3-(hydroxymethyl)tetrahydro furan-3-yl]pyridine-2-carboxamide or 4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(3S)-3-(hydroxymethyl)tetrahydrofuran-3-yl]pyridine-2-carboxamide (Compound 35b);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(4-hydroxy-4-methyl-cyclohexyl) pyridine-2-carboxamide as a 6:4 mixture of stereoisomers (Compound 35.1);

4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-[(1s,2r)-2-(hydroxy methyl)cyclohexyl]pyridine-2-carboxamide (Compound 35.2);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-[(1s,3r)-3-hydroxycyclopentyl] pyridine-2-carboxamide (Compound 35.3);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-[2-hydroxy-1-(hydroxy methyl)-1-methyl-ethyl]pyridine-2-carboxamide (Compound 35.4);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(3-hydroxycyclohexyl)pyridine-2-carboxamide as a mixture of stereoisomers (Compound 35.6);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(3-phenoxypropyl)pyridine-2-carboxamide (Compound 35.7);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(1-methylcyclo propyl)pyridine-2-carboxamide (Compound 35.8);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-[1-methyl-1-(2-pyridyl) ethyl]pyridine-2-carboxamide (Compound 35.9);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(3-phenylpropyl)pyridine-2-carboxamide (Compound 35.10);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-[2-hydroxy-1-(2-pyridyl)ethyl] pyridine-2-carboxamide (Compound 35.11);
4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-[(5-methoxy-2-pyridyl)methyl]pyridine-2-carboxamide (Compound 35.12);
Ethyl 3-[[4-[[2-(5-chloro-2-hydroxy-phenyl) acetyl]amino]pyridine-2-carbonyl]amino]-3-methyl-butanoate (Compound 35.13);
4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-(3-hydroxy-1,1-dimethyl-propyl)pyridine-2-carboxamide (Compound 35.14);
N-Benzyl-4-[[2-(5-chloro-2-hydroxy-phenyl) acetyl]amino]pyridine-2-carboxamide (Compound 35.15);
4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-phenyl-pyridine-2-carboxamide (Compound 35.16);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-[(1S,2S)-2-hydroxycyclopentyl]pyridine-2-carboxamide (Compound 35.17);
4-[[2-(5-Chloro-2-hydroxy-phenyl) acetyl]amino]-N-[(1R,2S)-2-hydroxy cyclopentyl]pyridine-2-carboxamide (Compound 35.18);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-[(1S,2R)-2-hydroxy cyclopentyl]pyridine-2-carboxamide (Compound 35.19);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-ethynylcyclohexyl)pyridine-2-carboxamide (Compound 35.24);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[1-(hydroxymethyl)cyclobutyl]pyridine-2-carboxamide (Compound 35.25);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[3-(hydroxymethyl)oxetan-3-yl]pyridine-2-carboxamide (Compound 35.26);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-2-methoxy-1-methyl-ethyl)pyridine-2-carboxamide (Compound 35.27);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1-hydroxycyclobutyl)methyl]pyridine-2-carboxamide (Compound 35.28);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 36);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-1,2-dimethyl-propyl)pyridine-2-carboxamide (Compound 37);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-methylcyclopentyl)pyridine-2-carboxamide (Compound 38);
N-(4-tert-Butylcyclohexyl)-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 39);
N-tert-Butyl-4-[[2-(2-chloro-3-fluoro-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 40);
N-tert-Butyl-4-[[2-(2-chloro-5-fluoro-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 40.1);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[4-(2-hydroxyethyl) tetrahydropyran-4-yl]pyridine-2-carboxamide (Compound 42);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[1,1-dimethyl-3-(2,2,2-trifluoro ethylamino)propyl]pyridine-2-carboxamide (Compound 43);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(4-fluoro-1-bicyclo[2.1.1] hexanyl)pyridine-2-carboxamide (Compound 44);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[3-(2,2-dimethylpropanoyl amino)-1,1-dimethyl-propyl]pyridine-2-carboxamide (Compound 45);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-2-hydroxy-1-methyl-ethyl)pyridine-2-carboxamide (Compound 46);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1S)-1-cyano-2-hydroxy-1-methyl-ethyl]pyridine-2-carboxamide or 4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1R)-1-cyano-2-hydroxy-1-methyl-ethyl]pyridine-2-carboxamide (Compound 46a);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1S)-1-cyano-2-hydroxy-1-methyl-ethyl]pyridine-2-carboxamide or 4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(1R)-1-cyano-2-hydroxy-1-methyl-ethyl]pyridine-2-carboxamide (Compound 46b);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(3-cyanotetrahydrofuran-3-yl)pyridine-2-carboxamide (Compound 47);

Methyl2-[4-[[4-[[2-(5-chloro-2-hydroxy-phenyl) acetyl]amino]pyridine-2-carbonyl]amino]tetrahydropyran-4-yl]acetate (Compound 47.1);

Methyl 4-[[4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carbonyl] amino]tetrahydropyran-4-carboxylate (Compound 47.2);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl] amino]-N-(3-cyanooxetan-3-yl)pyridine-2-carboxamide (Compound 47.3);

4-[[2-(5-Fluoro-2-hydroxy-phenyl)acetyl]amino]-N-(1-methylcyclobutyl)pyridine-2-carboxamide (Compound 48);

N-(4-Cyanotetrahydropyran-4-yl)-4-[[2-(5-fluoro-2-hydroxy-phenyl)acetyl]amino] pyridine-2-carboxamide (Compound 48.1);

N-[3-(tert-Butylamino)-1,1-dimethyl-3-oxo-propyl]-4-[[2-(5-chloro-2-hydroxy-phenyl) acetyl]amino]pyridine-2-carboxamide (Compound 49);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[3-(methanesulfonamido)-1,1-dimethyl -propyl]pyridine-2-carboxamide (Compound 50);

N-(3-Acetamido-1,1-dimethyl-propyl)-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl] amino]pyridine-2-carboxamide (Compound 51);

4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[4-(hydroxymethyl)tetrahydro pyran-4-yl]pyridine-2-carboxamide (Compound 53);

N-tert-Butyl-4-[[2-[3-(1-hydroxyethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 54);

N-tert-Butyl-5-chloro-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 55);

N-tert-Butyl-4-[[2-[5-chloro-2-[(4-methoxyphenyl)methoxy]phenyl]acetyl] amino]pyridine-2-carboxamide (Compound 56);

N-tert-butyl-4-[[(1S) or (1R)-4-chloro-7-hydroxy-indane-1-carbonyl]amino]pyridine-2-carboxamide (Compound 57a);

N-tert-butyl-4-[[(1S) or (1R)-4-chloro-7-hydroxy-indane-1-carbonyl]amino]pyridine-2-carboxamide (Compound 57b);
N-tert-Butyl-4-[[2-(2-cyclopropylphenyl)acetyl]amino]pyridine-2-carboxamide (Compound 58);
4-[[2-(3-Bromo-5-chloro-2-hydroxy-phenyl)acetyl]amino]-N-tert-butyl-pyridine-2-carboxamide (Compound 59);
N-(4-Fluoro-1-bicyclo[2.1.1]hexanyl)-4-[[2-(2-fluorophenyl)acetyl]amino]pyridine-2-carboxamide (Compound 60);
N-(1-Cyano-2-hydroxy-1-methyl-ethyl)-4-[[2-(2-fluorophenyl)acetyl]amino]pyridine-2-carboxamide (Compound 60.1);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-(2-fluorophenyl)acetyl]amino]pyridine-2-carboxamide (Compound 60.2);
N-tert-Butyl-4-[[2-(5-chloro-2-hydroxy-3-isopropyl-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 61);
N-tert-Butyl-4-[[2-[5-chloro-2-hydroxy-3-(1-methoxyethyl)phenyl]acetyl]amino] pyridine-2-carboxamide (Compound 62);
4-[[2-(6-Quinolyl)acetyl]amino]-N-tetrahydropyran-4-yl-pyridine-2-carboxamide (Compound 63);
4-(Benzylcarbamoylamino)-N-tert-butyl-pyridine-2-carboxamide (Compound 64);
N-tert-Butyl-4-(cyclohexylmethylcarbamoyl amino)pyridine-2-carboxamide (Compound 64.1);
N-tert-Butyl-4-(2-phenylethylcarbamoyl amino)pyridine-2-carboxamide (Compound 64.2);
N-tert-Butyl-4-[[(1R)-1-phenylethyl]carbamoyl amino]pyridine-2-carboxamide (Compound 64.3);
N-tert-Butyl-4-[[(1S)-1-phenylethyl] carbamoylamino]pyridine-2-carboxamide (Compound 64.4);
N-tert-Butyl-4-[(2-chlorophenyl) methylcarbamoylamino]pyridine-2-carboxamide (Compound 64.5);
N-tert-Butyl-4-[(3-chlorophenyl)methyl carbamoylamino]pyridine-2-carboxamide (Compound 64.7);
N-tert-butyl-4-[(4-chlorophenyl)methyl carbamoylamino]pyridine-2-carboxamide (Compound 64.8);
N-tert-Butyl-4-[(2-hydroxyphenyl)carbamoylamino]pyridine-2-carboxamide (Compound 65);
N-tert-Butyl-4-[(2-methoxyphenyl)methylcarbamoylamino]pyridine-2-carboxamide (Compound 65.1);
N-tert-Butyl-4-[(2-hydroxyphenyl)methylcarbamoylamino]pyridine-2-carboxamide (Compound 65.2);
N-tert-Butyl-4-[(3-hydroxyphenyl)methylcarbamoylamino]pyridine-2-carboxamide (Compound 65.3);

N-tert-Butyl-4-[(4-hydroxyphenyl)methylcarbamoylamino]pyridine-2-carboxamide (Compound 65.4);
N-tert-Butyl-4-[[2-[2-hydroxy-5-(1-hydroxyethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 66);
N-tert-Butyl-4-[[2-[2-hydroxy-5-[1-(2,2,2-trifluoroethylamino)ethyl]phenyl] acetyl]amino]pyridine-2-carboxamide (Compound 67);
N-tert-Butyl-4-[[2-[3-(cyanomethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 68);
N-tert-Butyl-4-[[2-[3-(methoxymethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 69);
N-tert-Butyl-4-[[2-[2-hydroxy-5-(morpholinomethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 70);
4-[[2-(5-Fluoro-2-hydroxy-phenyl)acetyl]amino]-N-[3-(hydroxymethyl)tetrahydro furan-3-yl]pyridine-2-carboxamide (Compound 72);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[1-(hydroxymethyl)-2-methoxy-1-methyl-ethyl]pyridine-2-carboxamide (Compound 73);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylbut-2-ynyl) pyridine-2-carboxamide (Compound 73.1);
N-tert-Butyl-4-[[2-[2-hydroxy-5-(3-hydroxypropyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 75);
4-[[2-(5-Chloro-4-fluoro-2-hydroxy-phenyl)acetyl]amino]-N-(1-methylcyclo butyl)pyridine-2-carboxamide (Compound 76);
4-[[2-(2,5-Difluorophenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 77);
4-[[2-(2,5-Difluorophenyl)acetyl]amino]-N-(4-fluoro-1-bicyclo[2.1.1]hexanyl) pyridine-2-carboxamide (Compound 77.1);
4-[[2-(4-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 78);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[2-hydroxy-4-(trifluoromethyl)phenyl]acetyl] amino]pyridine-2-carboxamide (Compound 78.1);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[2-hydroxy-5-(trifluoromethyl)phenyl]acetyl] amino]pyridine-2-carboxamide (Compound 78.2);
4-[(2-Chroman-4-ylacetyl)amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 79);

N-(1,1-Dimethylprop-2-ynyl)-4-[[2-(1-isopropyl-3,5-dimethyl-pyrazol-4-yl)acetyl] amino]pyridine-2-carboxamide (Compound 79.1);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-(1H-indazol-4-yl)acetyl]amino]pyridine-2-carboxamide (Compound 79.2);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-(1H-indol-7-yl)acetyl]amino]pyridine-2-carboxamide (Compound 79.3);
N-(1-Cyano-1-methyl-ethyl)-4-[[2-(5-fluoro-2-hydroxy-phenyl)acetyl]amino] pyridine-2-carboxamide (Compound 81);
N-(1-Cyano-2-hydroxy-1-methyl-ethyl)-4-[[2-(5-fluoro-2-hydroxy-phenyl)acetyl]amino] pyridine-2-carboxamide (Compound 81.1);
4-[[2-(5-Fluoro-2-hydroxy-phenyl)acetyl]amino]-N-isopropyl-pyridine-2-carboxamide (Compound 81.2);
N-(1,1-Dimethylprop-2-ynyl)-4-[[2-(5-fluoro-2-hydroxy-phenyl)acetyl]amino] pyridine-2-carboxamide (Compound 81.3);
N-(4-Fluoro-1-bicyclo[2.1.1]hexanyl)-4-[[2-(5-fluoro-2-hydroxy-phenyl)acetyl]amino] pyridine-2-carboxamide (Compound 81.4);
4-[[2-(5-Fluoro-2-hydroxy-phenyl)acetyl]amino]-N-[1-(hydroxymethyl)cyclobutyl] pyridine-2-carboxamide (Compound 81.5);
N-(1-Cyano-1-methyl-ethyl)-4-(thiophene-3-carbonylamino)pyridine-2-carboxamide (Compound 83);
N-(1-Cyano-1-methyl-ethyl)-4-[(2-cyclohexylacetyl) amino]pyridine-2-carboxamide (Compound 83.1);
N-(1-Cyano-1-methyl-ethyl)-4-(cyclohexane carbonylamino)pyridine-2-carboxamide (Compound 83.2);
N-(1-Cyano-1-methyl-ethyl)-4-[(3,3-difluorocyclo pentanecarbonyl)amino]pyridine-2-carboxamide (Compound 83.3);
N-(1-Cyano-1-methyl-ethyl)-4-[(1-methylcyclo pentanecarbonyl)amino]pyridine-2-carboxamide (Compound 83.4);
N-(1-Cyano-1-methyl-ethyl)-4-(3-cyclohexyl propanoylamino)pyridine-2-carboxamide (Compound 83.5);
4-(2-{Bicyclo[2.2.1]heptan-2-yl}acetamido)-N-(1-cyano-1-methylethyl)pyridine-2-carboxamide (Compound 83.6);
N-(1-Cyano-1-methyl-ethyl)-4-[[2-(1-methylcyclo hexyl)acetyl]amino]pyridine-2-carboxamide (Compound 83.7);

N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-2-cyclopropyl-pyrimidine-5-carboxamide (Compound 83.8);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-3-isobutyl-isoxazole-5-carboxamide (Compound 83.9);
N-(1-Cyano-1-methyl-ethyl)-4-[[2-(4,4-difluorocyclo hexyl)acetyl]amino]pyridine-2-carboxamide (Compound 83.10);
4-[(1-Benzylcyclopropanecarbonyl)amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 83.11);
N-(1-Cyano-1-methyl-ethyl)-4-[3-(2-methoxy-4-pyridyl)propanoylamino]pyridine-2-carboxamide (Compound 83.13);
4-[(5-tert-Butyl-2-methyl-pyrazole-3-carbonyl)amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 83.14);
N-(1-Cyano-1-methyl-ethyl)-4-[(2-pyrazol-1-ylbenzoyl)amino]pyridine-2-carboxamide (Compound 83.15);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-6-(trifluoromethyl)pyridine-2-carboxamide (Compound 83.16);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-3-oxo-4H-1,4-benzoxazine-7-carboxamide (Compound 83.17);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-1-ethyl-indole-2-carboxamide (Compound 83.18);
N-(1-Cyano-1-methyl-ethyl)-4-[[2-(2,2,2-trifluoroethyl)pyrazole-3-carbonyl]amino]pyridine-2-carboxamide (Compound 83.19);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-3-phenyl-isoxazole-4-carboxamide (Compound 83.20);
4-[(1-Benzylpyrazole-4-carbonyl)amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 83.21);
N-(1-Cyano-1-methyl-ethyl)-4-[(2-methyl-5-phenyl-pyrazole-3-carbonyl)amino]pyridine-2-carboxamide (Compound 83.22);
N-(1-Cyano-1-methyl-ethyl)-4-[[2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoyl]amino]pyridine-2-carboxamide (Compound 83.23);
N-(1-Cyano-1-methyl-ethyl)-4-[(3-methyl-1-phenyl-pyrazole-4-carbonyl)amino]pyridine-2-carboxamide (Compound 83.24);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-2-phenoxy-pyridine-3-carboxamide (Compound 83.25);

N-(1-Cyano-1-methyl-ethyl)-4-[[2,5-dimethyl-1-(2-thienylmethyl)pyrrole-3-carbonyl]amino]pyridine-2-carboxamide (Compound 83.26);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-5-(2-methoxyphenyl)isoxazole-3-carboxamide (Compound 83.27);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-4-methyl-2-phenyl-thiazole-5-carboxamide (Compound 83.28);
4-[(4-Acetamidobenzoyl)amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 83.29);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-1,3-benzothiazole-7-carboxamide (Compound 83.30);
N-(1-Cyano-1-methyl-ethyl)-4-[3-(4-fluorophenyl) butanoylamino]pyridine-2-carboxamide (Compound 83.31);
N-[2-[(1-Cyano-1-methyl-ethyl)carbamoyl]-4-pyridyl]-1-methyl-2-oxo-quinoline-3-carboxamide (Compound 83.32);
N-tert-Butyl-3-[[2-(2-hydroxycyclohexyl)acetyl]amino]benzamide (Compound 84);
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[1-cyano-2-methoxy-1-(methoxy methyl)ethyl]pyridine-2-carboxamide (Compound 86);
4-[[2-(3-Amino-4-tert-butyl-phenyl)acetyl]amino]-N-tert-butyl-pyridine-2-carboxamide (Compound 87);
4-[[2-(2-Amino-4-tert-butyl-phenyl)acetyl]amino]-N-tert-butyl-pyridine-2-carboxamide (Compound 88);
N-tert-Butyl-4-[[2-(4-tert-butyl-3-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 89);
N-tert-Butyl-4-[[2-(4-tert-butyl-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 90);
N-tert-Butyl-4-[[2-(4-tert-butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 91);
4-[[2-(4-Chloro-3-hydroxy-phenyl)acetyl]amino]-N-(4-cyanotetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 92);
4-[[2-(4-Chloro-3-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 92.1);
4-[[2-(4-Chloro-3-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 92.2);

4-[[2-(4-Chloro-3-hydroxy-phenyl)acetyl]amino]-N-[(1s,2s)-2-hydroxycyclopentyl]pyridine-2-carboxamide (Compound 92.3);
4-[[2-(4-tert-Butyl-3-hydroxy-phenyl)acetyl]amino]-N-[3-(hydroxymethyl) tetrahydrofuran-3-yl]pyridine-2-carboxamide (Compound 93);
4-[[2-(4-tert-Butyl-3-hydroxy-phenyl)acetyl]amino]-N-[(2S)-2-hydroxycyclohexyl]pyridine-2-carboxamide (Compound 93.1);
4-[[2-(4-tert-Butyl-3-hydroxy-phenyl)acetyl]amino]-N-[(2S)-2-hydroxycyclopentyl]pyridine-2-carboxamide (Compound 93.2);
4-[[2-(4-tert-Butyl-3-hydroxy-phenyl)acetyl]amino]-N-(4-cyanotetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 93.3);
4-[[2-(4-tert-Butyl-3-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 93.4);
4-[[2-(4-tert-Butyl-3-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 93.5); and
4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1-methyl-1-phenyl-ethyl) pyridine-2-carboxamide (Compound 94);
and salts and solvates of any of the above.

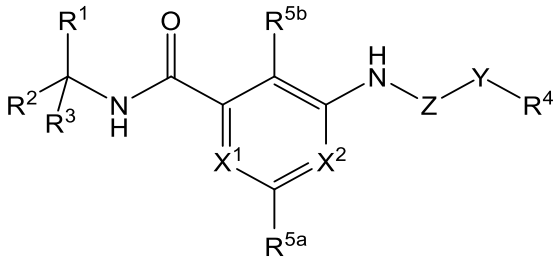
13. A compound according to claim 1 which is N-tert-Butyl-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 3) or a salt or solvate thereof.

14. A compound according to claim 1 which is 4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(3R)-3-(hydroxymethyl)tetrahydro furan-3-yl]pyridine-2-carboxamide or 4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]-N-[(3S)-3-(hydroxymethyl)tetrahydrofuran-3-yl]pyridine-2-carboxamide (Compound 35a) or a salt or solvate thereof.

15. A compound according to claim 1 which is 4-[[2-(5-Chloro-2-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 36) or a salt or solvate thereof.

16. A compound according to claim 1 which is N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[3-(trifluoromethyl)-1H-pyrazol-4-yl]acetyl] amino] pyridine-2-carboxamide (Compound 5.36) or a salt or solvate thereof.

17. A compound of general formula (I):



(I),

or a salt or solvate thereof wherein:

R^1 is H, CN, $C(O)OR^{12}$, C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl, any of which alkyl, alkenyl or alkynyl groups are unsubstituted or substituted with one or more substituents selected from fluoro, OR^{12}, $N(R^{12})_2$, $C(O)OR^{12}$, $C(O)N(R^{12})_2$, $C(O)R^{12}$ and $N(R^{13})C(O)R^{12}$;

wherein each R^{12} and R^{13} is independently selected from H, C_{1-6} alkyl and C_{1-6} fluoroalkyl

R^2 is H or C_{1-6} alkyl unsubstituted or substituted with OR^{12};

R^3 is:

C_{1-10} alkyl, C_{2-10} alkenyl or C_{2-10} alkynyl, any of which is unsubstituted or substituted with one or more substituents selected from fluoro, CN, R^{14} OR^{14}, OR^{15}, $N(R^{15})_2$, $C(O)OR^{15}$, $C(O)N(R^{15})_2$, $N(R^{16})C(O)R^{15}$, $N(R^{15})S(O)_2R^{14}$, $N(R^{15})S(O)_2R^{16}$ and $N(R^{15})C(O)OR^{16}$; or

a 3- to 7-membered carbocyclic or heterocyclic ring system or a 6- to 10 membered aryl or 5- to 10-membered heteroaryl ring system, either of which is unsubstituted or substituted with one or more substituents selected from halo, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, OR^{17} and $N(R^{17})_2$;

wherein R^{14} is a 6- to 10-membered aryl or 5- to 10-membered heteroaryl ring system or a 3- to 7-membered carbocyclic or heterocyclic ring system, any of which is unsubstituted or substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} haloalkyl, OR^{17} and $N(R^{17})_2$; wherein each R^{17} is independently H, C_{1-4} alkyl or C_{1-4} haloalkyl;

each R^{15} and R^{16} is independently H, C_{1-6} alkyl or C_{1-6} haloalkyl; or

R^2 and R^3 together with the carbon atom to which they are attached combine to form a 3- to 10-membered carbocyclic or heterocyclic ring system unsubstituted or substituted with one or more

substituents selected from halo, CN, OR^9, $N(R^9)_2$, $C(O)OR^9$, $C(O)N(R^9)_2$, $C(O)R^9$, $N(R^9)C(O)R^9$ and C_{1-4} alkyl unsubstituted or substituted with halo, OR^9 or $N(R^9)_2$; or

R^1, R^2 and R^3 together with the carbon atom to which they are attached combine to form a bridged 5- to 10-membered carbocyclic or heterocyclic ring system or phenyl, any of which is unsubstituted or substituted with one or more substituents selected from halo, CN, OR^9, $N(R^9)_2$, $C(O)OR^9$, $C(O)N(R^9)_2$, $C(O)R^9$, $N(R^9)C(O)R^9$ and C_{1-4} alkyl unsubstituted or substituted with halo, OR^9 or $N(R^9)_2$;

each R^9 is independently selected from H, C_{1-6} alkyl or C_{1-6} haloalkyl;

X^1 is N;

X^2 is CR^8

R^8 is H, halo, OH, $O(C_{1-4}$ alkyl), CN or NH_2;

Y is a bond or a straight C_{1-6} alkylene chain which is unsubstituted or substituted with one or more substituents R^{18}, wherein two substituents R^{18} may be attached to the same or to different carbon atoms;

wherein each R^{18} is independently C_{1-3} alkyl or C_{1-3} haloalkyl in which a $-CH_2-$ may be replaced with -NH- or -O- and wherein two R^{18} groups may combine with the atom or atoms to which they are attached to form a 3- to 6-membered carbocyclic or heterocyclic ring system;

Z is -C(O)- or -C(O)NH-;

R^4 is a 6- to 14-membered aryl, 5- to 14-membered heteroaryl or a 5- to 10-membered carbocyclic ring system, any of which is unsubstituted or substituted with one or more substituents selected from:

halo, CN, nitro, R^{19}, OR^{19}, OR^6, SR^6, NR^6R^7, $C(O)R^6$, $C(O)R^{19}$, $C(O)OR^6$, $C(O)N(R^6)(R^7)$, $N(R^7)C(O)R^6$;

C_{1-6} alkyl or $O(C_{1-6}$ alkyl), either of which is unsubstituted or substituted with one or more substituents selected from halo, CN, nitro, R^{19}, OR^6, SR^6, NR^6R^7, $C(O)R^6$ $C(O)OR^6$, $C(O)N(R^6)(R^7)$ and $N(R^7)C(O)R^6$; and

when R^4 is not fully aromatic in character, oxo;

wherein R^{19} is 5- or 6-membered aryl or heteroaryl ring system or a 3- to 7-membered carbocyclic or heterocyclic ring system, any of which is unsubstituted or substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} haloalkyl, OH, O(C_{1-4} alkyl), O(C_{1-4} haloalkyl);

R^6 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, benzyl, 3- to 7-membered carbocyclyl or 3- to 7-membered heterocyclyl;

R^7 is H, C_{1-6} alkyl or C_{1-6} haloalkyl; or

R^6 and R^7 together with the nitrogen atom to which they are attached may form a 4 to 7-membered heterocyclic ring which may further contain one or more further heteroatoms and which may be substituted with one or more substituents selected from oxo and halo; and

each of R^{5a} and R^{5b} is independently H, C_{1-4} alkyl or halo; or

a compound according to any one of claims 1 to 16;

for use in the treatment or prevention of diseases and conditions affected by modulation of TMEM16A selected from respiratory disease and conditions, dry mouth, intestinal hypermobility, cholestasis and ocular conditions.

18. The compound for use according to claim 17, wherein the compound is used in combination with an additional active agent useful in the treatment or prevention of respiratory conditions.

19. The compound for use according to claim 17 or 18, wherein the respiratory diseases and conditions are selected from cystic fibrosis, chronic obstructive pulmonary disease, chronic bronchitis, emphysema, bronchiectasis, including non-cystic fibrosis bronchiectasis, asthma and primary ciliary dyskinesia;

wherein the dry mouth results from Sjorgens syndrome, radiotherapy treatment or xerogenic drugs;

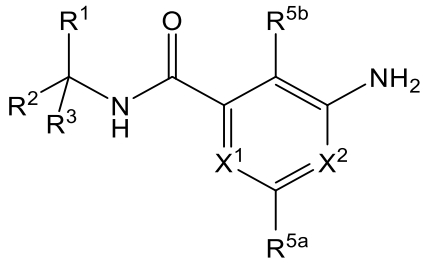
wherein the intestinal hypermobility is associated with gastric dyspepsia, gastroparesis, chronic constipation or irritable bowel syndrome; and,

wherein the ocular disease is dry eye disease.

20. A process for the preparation of a compound according to any one of claims 1 to 16, the process comprising:

A. for a compound of general formula (I) in which Z is -C(O)-:

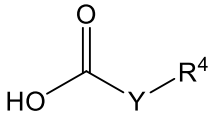
reacting a compound of general formula (II):



(II)

wherein R^1, R^2, R^3, R^{5a}, R^{5b}, X^1 and X^2 are as defined in claim 1;

with a compound of general formula (III):

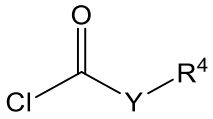


(III)

wherein R^4 and Y are as defined in claim 1;

in the presence of a coupling agent; or

reacting a compound of general formula (II) with an acid chloride of general formula (IV):



(IV)

wherein R^4 and Y are as defined in claim 1; or

B. for compounds of general formula (I) in which Z is C(O)NH and Y is -C_{1-2} alkylene-:

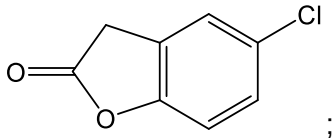
reacting a compound of general formula (II) with a compound of general formula (XIV):

$$O=C=N\text{-}Y^1\text{-}R^4 \qquad \text{(XIV)}$$

wherein R^4 is as defined in claim 1 and Y^1 is -CH_2- or -CH_2CH_2-.

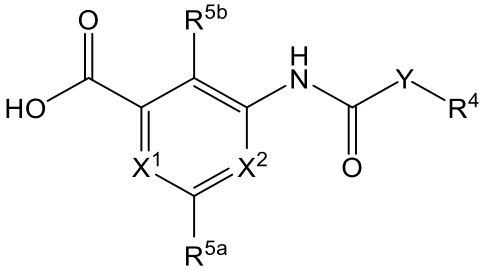
C. for compounds of general formula (Id) as defined in claim 11 in which R^{11a} is Cl and R^{11b} is H:

reacting a compound of general formula (II) with 5-chloro-2(*3H*)-benzofuranone, which has the structure:



; or

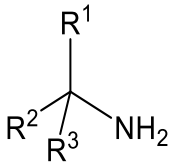
D. reacting a compound of general formula (X):



(X)

wherein X^1, X^2, Y, R^4, R^{5a} and R^{5b} are as defined in claim 1;

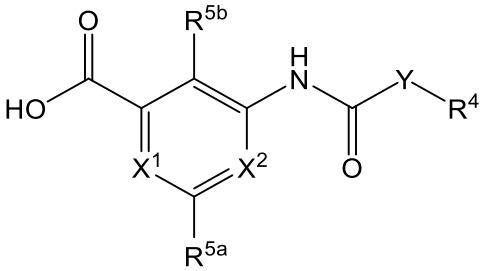
with a compound of general formula (VII):



(VII)

wherein R^1, R^2 and R^3 are as defined in claim 1; or

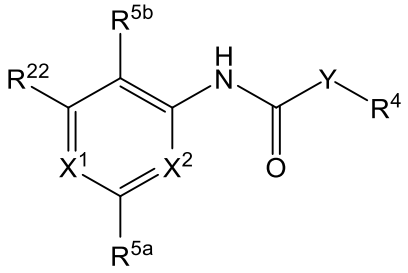
E. reacting a compound of general formula (X):



(X)

wherein X^1, X^2, Y, R^4, R^{5a} and R^{5b} are as defined in claim 1
with a compound of general formula (VII) as defined above; or

F. reacting a compound of general formula (XV):



(XV)

wherein X^1, X^2, Y, R^4, R^{5a} and R^{5b} are as defined in claim 1 and R^{22} is halo;
with an amine of general formula (VII) as defined above and carbon monoxide in the presence of a phosphorus ligand and a palladium catalyst; or

G. converting a compound of general formula (I) to another compound of general formula (I).

21. A pharmaceutical composition comprising a compound according to any one of claims 1 to 16 and a pharmaceutically acceptable excipient.

22. A pharmaceutical composition according to claim 21 further comprising an additional active agent useful in the treatment or prevention of respiratory conditions.

23. A pharmaceutical composition comprising a compound according to any one of claims 1 to 16 and an additional agent useful in the treatment or prevention of respiratory conditions as a combined preparation for simultaneous, sequential or separate use in the treatment of a disease or condition affected by modulation of TMEM16A selected from respiratory disease and conditions, dry mouth, intestinal hypermobility, cholestasis and ocular conditions.

24. A compound according to any one of claims 1 to 16 or a pharmaceutical composition according to claim 22 or 23, wherein the additional agent useful in the treatment or prevention of respiratory conditions is selected from:

β2 adrenoreceptor agonists selected from metaproterenol, isoproterenol, isoprenaline, albuterol, salbutamol, formoterol, salmeterol, indacaterol, terbutaline, orciprenaline, bitolterol mesylate, pirbuterol, olodaterol, vilanterol and abediterol;

antihistamines, histamine H_1 receptor antagonists selected from loratadine, cetirizine, desloratadine, levocetirizine, fexofenadine, astemizole, azelastine and chlorpheniramine or H_4 receptor antagonists;

dornase alpha;

corticosteroids selected from prednisone, prednisolone, flunisolide, triamcinolone acetonide, beclomethasone dipropionate, budesonide, fluticasone propionate mometasone furoate and fluticasone furoate;

Leukotriene antagonists selected from montelukast and zafirlukast;

anticholinergic compounds, muscarinic antagonists selected from ipratropium, tiotropium, glycopyrrolate, aclidinium and umeclidinium;

CFTR repair therapies (e.g. CFTR potentiators, correctors or amplifiers) Ivacaftor, QBW251, VX659, VX445, VX561/CPT-656, VX152, VX440, GLP2737, GLP2222, GLP2451, PTI438, PTI801, PTI808, FDL-169 and FDL-176and CFTR correctors selected from Lumacaftor and Tezacaftor;

ENaC modulators, particularly ENaC inhibitors selected from:

amiloride, VX-371, AZD5634, QBW276, SPX-101, BI443651, ETD001 and compounds having a cation selected from:

2-[({3-amino-5*H*-pyrrolo[2,3-b]pyrazin-2-yl}formamido) ethyl]-6-(4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}piperidine-1-carbonyl)-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;

2-[({3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl}formamido) methyl]-6-{[2-(4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}piperidin-1-yl)ethyl]carbamoyl}-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;

2-[({3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl}formamido)methyl]-5-[4-({bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}methyl)piperidine-1-carbonyl]-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;

2-[({3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl}formamido)methyl]-6-[(3*R*)-3-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}pyrrolidine-1-carbonyl]-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;

2-[({3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl}formamido)methyl]-6-[(3*S*)-3-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}pyrrolidine-1-carbonyl]-

1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;

2-[({3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl}formamido)methyl]-1,3-diethyl-6-{[(1*r*,4*r*)-4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}cyclohexyl]carbamoyl}-1*H*-1,3-benzodiazol-3-ium;

2-[({3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl}formamido)methyl]-1,3-diethyl-6-{[(1*s*,4*s*)-4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}cyclohexyl]carbamoyl}-1*H*-1,3-benzodiazol-3-ium;

and a suitable anion, selected from halide, sulfate, nitrate, phosphate, formate, acetate, trifluoroacetate, fumarate, citrate, tartrate, oxalate, succinate, mandelate, methane sulfonate or p-toluene sulfonate;

antibiotics;

airway hydrating agents (osmoloytes) selected from hypertonic saline and mannitol (Bronchitol®); and

mucolytic agents eg. N-acetyl cysteine.