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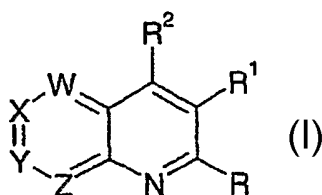
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(54) Title: FUNGICIDES BASED ON NITROGEN-CONTAINING HETEROCYCLES



(57) Abstract: The compound of the general formula (I), wherein W, X, Y, Z, R, R¹ and R²
are defined as set forth in the specification, useful as fungicide.

FUNGICIDES BASED ON NITROGEN-CONTAINING HETEROCYCLES

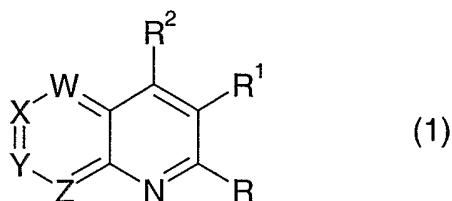
This invention relates to novel pyridine derivatives having a condensed, nitrogen-containing heterocyclic ring, to processes for preparing them, to certain intermediate chemicals used in their manufacture, to compositions containing them and to methods of using them to combat fungi, especially fungal infections of plants.

Derivatives of the nitrogen-containing 5,6 ring system *s*-1,2,4-triazolo[1,5-*a*]pyrimidine are known from the patent literature as being useful for controlling phytopathogenic fungi. Examples of recent patent publications include EP-A-1249452, WO 02/051845, WO 02/083676, WO 02/083677, WO 02/088125, WO 02/088126, WO 02/088127.

Derivatives of pyridopyrazines are known in the chemical literature, for example from *J. Med. Chem.* (1968), 11(6), 1216-18, *J. Med. Chem.* (1970), 13(5), 853-7 and US 3984412, but not for agrochemical purposes.

The present invention is concerned with the provision of novel pyridine derivatives having a condensed, nitrogen-containing heterocyclic ring for combating phytopathogenic diseases on plants and harvested food crops.

Thus, according to the present invention, there is provided a compound of the general formula (1):



wherein

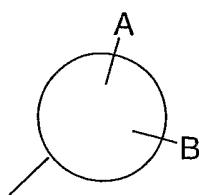
W, X, Y and Z can be N or CR⁸, with at least one and no more than three of W, X, Y and Z being N, but excluding compounds where W, X, Y = N and Z = CR⁸, and X, Y, Z = N and Z = CR⁸;

R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl, CN, C₁₋₄alkylthio, C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, aryl, heteroaryl, halo(C₁₋₆)alkoxy, halo(C₁₋₄)alkylthio, C₂₋₄alkenyl, C₂₋₆alkynyl, C₂₋₆cycloalkyl, or NR³R⁴ ;

R is H, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, cyano, halogen or NR³R⁴;

R² is halo or NR³R⁴;

R¹ is an aryl or heteroaryl ring R²⁰, of the general formula

 R^{20}

where A can be one to four optional substituents independently selected from halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl(C_{1-4})alkyl,

and B is at least one or more substituents independently selected from aryl, heteroaryl, aryloxy (except that phenoxy must be substituted), heteroaryloxy, aryl(C_{1-4})alkoxy (except that benzyloxy must be substituted), heteroaryl(C_{1-4})alkoxy, arylthio, arylsulphinyl, arylsulphonyl, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, aryl(C_{2-4})alkenyl, aryl(C_{2-4})alkynyl, heteroaryl(C_{2-4})alkenyl, heteroaryl(C_{2-4})alkynyl, aryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkyl, with any of the forgoing aryl or heteroaryl substituents being optionally substituted with halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6} alkylthio, halo(C_{1-6})alkylthio, C_{1-4} alkoxy(C_{1-6})alkyl, C_{3-6} cycloalkyl, cyano or nitro;

R^3 and R^4 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl, heteroaryl(C_{1-8})alkyl, NR^5R^6 , usually under the provision that not both R^3 and R^4 are H or NR^5R^6 , or

R^3 and R^4 together form a C_{3-7} alkylene or C_{3-7} alkenylene chain optionally substituted with one or more C_{1-4} alkyl or C_{1-4} alkoxy groups, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine N -(C_{1-4})alkyl (especially N -methyl) ring; and

R^5 and R^6 are independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, aryl(C_{1-8})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-6})alkyl, heteroaryl or heteroaryl(C_{1-8})alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R^8) being optionally substituted with halogen, cyano, C_{1-6} alkoxy, C_{1-6} alkylcarbonyl, C_{1-6} alkoxycarbonyl, C_{1-6} haloalkoxy, C_{1-6} alkylthio, tri(C_{1-4})alkylsilyl, C_{1-6} alkylamino or C_{1-6} dialkylamino,

any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and any of the foregoing aryl or heteroaryl groups or moieties in R³, R⁴, R⁵, R⁶ or R⁸ being optionally substituted with one or more substituents selected from halo, hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR¹³R¹⁴, -NHCOR¹³, -NHCONR¹³R¹⁴, -CONR¹³R¹⁴, -SO₂R¹³, -OSO₂R¹³, -COR¹³, -CR¹³=NR¹⁴ or -N=CR¹³R¹⁴, in which R¹³ and R¹⁴ are independently hydrogen, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.

The invention includes compounds of the general formula (1) as defined immediately above, preferably compounds in which: C₇ alkylene and C₃₋₇ alkenylene are excluded as chains formed by R³ and R⁴; preferably the C₃₋₆ chain that R³ and R⁴ may form may only be optionally substituted with one or more methyl groups; preferably thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R³ and R⁴ may form; preferably tri(C₁₋₄)alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

The compounds of the invention may contain one or more asymmetric carbon atoms and may exist as enantiomers (or as pairs of diastereoisomers) or as mixtures of such. They may also exist as diastereoisomers by virtue of restricted rotation about a bond. However, mixtures of enantiomers or diastereoisomers may be separated into individual isomers or isomer pairs, and this invention embraces such isomers and mixtures thereof in all proportions. It is to be expected that for any given compound, one isomer may be more fungicidally active than another.

Except where otherwise stated, alkyl groups and alkyl moieties of alkoxy, alkylthio, etc., contain from 1 to 8, suitably from 1 to 6 and typically from 1 to 4, carbon atoms in the form of straight or branched chains. Examples are methyl, ethyl, *n*- and *iso*-propyl, *n*-, *sec*-, *iso*- and *tert*-butyl, *n*-pentyl and *n*-hexyl. Cycloalkyl groups contain from 3 to 8, typically

from 3 to 6, carbon atoms and include bicycloalkyl groups such as the bicyclo[2.2.1]heptyl group. Haloalkyl groups or moieties are typically trichloromethyl or trifluoromethyl or contain a trichloromethyl or trifluoromethyl terminal group. The term fluoroalkyl is an alkyl group substituted by one or more fluorine atoms, as for example trifluoromethyl,

5 difluoroethyl or an alkyl comprising a trifluoromethyl terminal group.

Except where otherwise stated, alkenyl and alkynyl moieties also contain from 2 to 8, suitably from 2 to 6 and typically from 2 to 4, carbon atoms in the form of straight or branched chains. Examples are allyl, 2-methylallyl and propargyl. Optional substituents include halo, typically fluoro. An example of halo-substituted alkenyl is 3,4,4-trifluoro-*n*-
10 butenyl.

Halo includes fluoro, chloro, bromo and iodo. Most commonly it is fluoro, chloro or bromo and usually fluoro or chloro.

Aryl is usually phenyl but also includes naphthyl, anthryl and phenanthryl.

Heteroaryl is typically a 5- or 6-membered aromatic ring containing one or more O,
15 N or S heteroatoms, which may be fused to one or more other aromatic or heteroaromatic rings, such as a benzene ring. Examples are thienyl, furyl, pyrrolyl, isoxazolyl, oxazolyl, oxadiazolyl, pyrazolyl, imidazolyl, triazolyl, isothiazolyl, tetrazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, benzofuryl, benzothienyl, dibenzofuryl, benzothiazolyl, benzoxazolyl, benzimidazolyl, indolyl, quinolinyl and quinoxalinyl groups
20 and, where appropriate, N-oxides thereof.

The 6,6-ring systems embraced by the general formula (1) are 1,8-naphthyridines (where W, X and Y are all CR⁸ and Z is N), 1,7-naphthyridines (where W, X and Z are all CR⁸ and Y is N), 1,6-naphthyridines (where W, Y and Z are all CR⁸ and X is N), 1,5-naphthyridines (where X, Y and Z are all CR⁸ and W is N), pyrido[2,3-*c*]pyridazines (where W
25 and X are both CR⁸ and Y and Z are both N), pyrido[2,3-*d*]pyridazines (where W and Z are both CR⁸ and X and Y are both N), pyrido[3,2-*c*]pyridazines (where Y and Z are both CR⁸ and W and X are both N), pyrido[2,3-*b*]pyrazines (where X and Y are both CR⁸ and W and Z are both N), pyrido[2,3-*d*]pyrimidines (where W and Y are both CR⁸ and X and Z are both N), pyrido[3,2-*d*]pyrimidines (where X and Z are both CR⁸ and W and Y are both N),
30 pyrido[2,3-*e*][1,2,4]triazines (where Y is CR⁸ and W, X and Z are all N), and pyrido[3,2-*e*]-[1,2,4]triazines (where X is CR⁸ and W, Y and Z are all N). Of particular interest are pyrido[2,3-*b*]pyrazines and pyrido[3,2-*e*][1,2,4]triazines.

R^8 , which may be the same or different for the CR^8 values of W, X, Y and Z, is H, halo (for example chloro or bromo), C_{1-4} alkyl (for example methyl), C_{1-4} alkoxy (for example methoxy) or halo(C_{1-4})alkyl (for example trifluoromethyl), CN, C_{1-4} alkylthio, C_{1-4} alkylsulphinyl, C_{1-4} alkylsulphonyl, aryl, heteroaryl, halo(C_{1-6})alkoxy, halo(C_{1-4})alkylthio,
 5 C_{2-4} alkenyl, C_{2-6} alkynyl, C_{2-6} cycloalkyl, or NR^3R^4 . Usually R^8 will be H.

One of R and R^2 , preferably R^2 , is NR^3R^4 . The other is typically halo, especially chloro or fluoro. In the case of pyrido[2,3-b]pyrazine ring systems, the more active compounds are those where R^2 is NR^3R^4 and R is chloro or fluoro. R^3 is typically C_{1-8} alkyl (for example ethyl, *n*-propyl, *n*-butyl, *sec*-butyl (the S- or R-isomer or the racemate), isobutyl
 10 and *tert*-butyl), halo(C_{1-8})alkyl (for example 2,2,2-trifluoroethyl, 2,2,2-trifluoro-1-methylethyl (the S- or R-isomer or the racemate), 2,2,2-trifluoro-1-methylpropyl (the S- or R-isomer or the racemate), 3,3,3-trifluoropropyl and 4,4,4-trifluorobutyl), C_{1-4} alkoxy(C_{1-8})alkyl (for example methoxymethyl and methoxy-*iso*-butyl), C_{1-4} alkoxyhalo(C_{1-8})alkyl (for example 2-methoxy-2-trifluoromethylethyl), C_{1-4} alkylcarbonyl(C_{1-8})alkyl (for example 1-
 15 acetyethyl and 1-*tert*-butylcarbonylethyl), C_{1-4} alkylcarbonylhalo(C_{1-8})alkyl (for example 1-acetyl-2,2,2-trifluoroethyl), phenyl(C_{1-4})alkyl (for example benzyl), C_{2-8} alkenyl (for example allyl and methylallyl), halo(C_{2-8})alkenyl (for example 3-methyl-4,4-difluorobut-3-enyl), C_{2-8} alkynyl (for example propargyl), C_{3-8} cycloalkyl (for example cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl) optionally substituted with chloro, fluoro or methyl, C_{3-8} cyclo-
 20 alkyl(C_{1-4})alkyl (for example cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl and cyclohexylmethyl), phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo (typically fluoro, chloro or bromo), C_{1-4} alkyl (typically methyl), halo(C_{1-4})alkyl (typically trifluoromethyl), C_{1-4} alkoxy (typically methoxy) and halo(C_{1-4})alkoxy (typically trifluoromethoxy). R^4 is typically H, C_{1-4} alkyl (for example ethyl and *n*-propyl), halo(C_{1-4})-
 25 alkyl (for example 2,2,2-trifluoroethyl) or amino. Alternatively R^3 and R^4 together form a C_{4-6} alkylene chain optionally substituted with methyl, for example 3-methylpentylene, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or
 30 piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl.

Typically R^1 is an aromatic carbocyclic or heterocyclic ring of formula R^{20} , preferably -an optionally substituted phenyl, pyridyl or thiazole group, and A is from one to four

independent halogen atoms, particularly fluorine and chlorine atoms and especially fluorine atoms, or is from one to three substituents selected from halo (for example fluoro and chloro), C₁₋₄ alkyl (for example methyl), halo(C₁₋₄)alkyl (for example trifluoromethyl), C₁₋₄ alkoxy (for example methoxy) or halo(C₁₋₄)alkoxy (for example trifluoromethoxy), and B is at least one or more of the substituents selected from the group comprising aryl, heteroaryl, aryloxy (except that phenoxy must be substituted), heteroaryloxy, aryl(C₁₋₄)alkoxy (except that benzyloxy must be substituted), heteroaryl(C₁₋₄)alkoxy, arylthio, arylsulphinyl, arylsulphonyl, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, aryl(C₂₋₄)alkenyl, aryl(C₂₋₄)alkynyl, heteroaryl(C₂₋₄)alkenyl, heteroaryl(C₂₋₄)alkynyl, aryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkyl. Examples are 2,6-difluoro-4-phenyl-phenyl, 2-fluoro-4-phenyl-6-chlorophenyl, 2,5,6-trifluoro-4-phenyl phenyl, 2,4,6-trifluoro-4-phenyl-phenyl, 2-chloro-4-phenyl-phenyl, 2-fluoro-4-phenyl-6-methoxyphenyl, and 2-fluoro-6-trifluoromethyl-4-phenyl-phenyl.

Also of particular interest are compounds where R¹ is an aryl or heteroaryl ring R²⁰ being a pyridyl group and A is from one to three halogen atoms or with from one to three substituents selected from halo (for example fluoro and chloro), C₁₋₄ alkyl (for example methyl), halo(C₁₋₄)alkyl (for example trifluoromethyl), C₁₋₄ alkoxy (for example methoxy) or halo(C₁₋₄)alkoxy (for example trifluoromethoxy) and B is at least one or more substituents selected from aryl, heteroaryl, aryloxy (except that phenoxy must be substituted), heteroaryloxy, aryl(C₁₋₄)alkoxy (except that benzyloxy must be substituted), heteroaryl(C₁₋₄)alkoxy, arylthio, arylsulphinyl, arylsulphonyl, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, aryl(C₂₋₄)alkenyl, aryl(C₂₋₄)alkynyl, heteroaryl(C₂₋₄)alkenyl, heteroaryl(C₂₋₄)alkynyl, aryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkyl. Examples are 3-fluoro-5-phenylpyrid-2-yl, 3-chloro-5-phenylpyrid-2-yl and 3,5-difluoro-4-phenylpyrid-2-yl.

In one aspect the invention provides a compound of the general formula (1) wherein W and Z are N and the other two are CR⁸, or W, Y and Z are N and X is CR⁸, or W, X and Z are N and Y is CR⁸;

R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl;

one of R and R² (preferably R²) is NR³R⁴ and the other is halo;

R¹ is an aryl or heteroaryl ring R²⁰, and A is a substituent selected from halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, and B is at least one or more substituents selected from aryl,

heteroaryl, aryloxy (except that phenoxy must be substituted), heteroaryloxy, aryl(C₁₋₄)alkoxy (except that benzyloxy must be substituted), heteroaryl(C₁₋₄)alkoxy, arylthio, arylsulphinyl, arylsulphonyl, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, aryl(C₂₋₄)alkenyl, aryl(C₂₋₄)alkynyl, heteroaryl(C₂₋₄)alkenyl, heteroaryl(C₂₋₄)alkynyl, aryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkyl, with any of the foregoing aryl or heteroaryl substituents being optionally substituted with halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, cyano or nitro;

R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl, NR⁵R⁶, provided that at least one of R³ and R⁴ is NR⁵R⁶, or

R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or,

together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C₁₋₄)alkyl (especially *N*-methyl) ring; and

R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl;

any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl, C₁₋₆ alkoxy carbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino, any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl). Of particular interest are compounds where W and Z are both N and X and Y are both CH.

In a further embodiment, the invention includes a compound of the general formula (1) as defined immediately above except that: C₇ alkylene and C₃₋₇ alkenylene are excluded as chains formed by R³ and R⁴; the C₃₋₆ chain that R³ and R⁴ may form may only be optionally substituted with one or more methyl groups; thiomorpholine, thiomorpholine S-oxide, thiomorpholine S-dioxide and piperazine are excluded as rings that R³ and R⁴ may form; tri(C₁₋₄)alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

In yet a further embodiment of the present invention, the compound of formula 1 the values of the substituents are defined as follows:

R^3 is C_{1-8} alkyl, halo(C_{1-8})alkyl, halo C_{1-4} alkoxy(C_{1-8})alkyl, C_{1-4} alkoxyhalo(C_{1-8})alkyl, C_{1-4} alkoxy carbonyl(C_{1-8})alkyl, C_{1-4} alkoxy carbonylhalo(C_{1-8})alkyl, phenyl(C_{1-4})alkyl, C_{2-8} alkenyl, halo(C_{2-8})alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl optionally substituted with chloro, fluoro or methyl, C_{3-8} cycloalkyl(C_{1-4})alkyl, phenylamino, piperidino or morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-4})alkyl, C_{1-4} alkoxy and halo-
 5 (C_{1-4})alkoxy; and R^4 is H, C_{1-4} alkyl, halo(C_{1-4})alkyl or amino, or R^3 and R^4 together form a
 10 C_{3-7} alkylene or alkenylene chain optionally substituted with methyl, or, together with the nitrogen atom to which they are attached, R^3 and R^4 form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C_{1-4})alkyl (especially *N*-methyl) ring, in which the morpholine or piperazine rings are optionally substituted with methyl. Of particular interest are compounds in which R is halo,
 15 and/or R^2 is NR^3R^4 , where NR^3R^4 are as defined above, and/or W and Z are N and X and Y are CH.

A further embodiment of the invention provides a compound of formula (1) wherein W, X and Z are N and Y is CR^8 ;
 R^8 is H or halo; R is halo and R^2 is NR^3R^4 ; R^1 is an aryl or heteroaryl ring R^{20} and A is a
 20 substituent selected from halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and B is one more substituent selected from aryl, heteroaryl, aryloxy (except that phenoxy must be substituted), heteroaryloxy, arylthio, arylsulphinyl, arylsulphonyl, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, aryl(C_{2-4})alkenyl, aryl(C_{2-4})alkynyl, heteroaryl(C_{2-4})alkenyl, heteroaryl(C_{2-4})alkynyl, aryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkyl, with any of the forgoing aryl
 25 or heteroaryl substituents being optionally substituted with halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, cyano or nitro; R^3 and R^4 are independently H, C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{1-8} perfluoroalkyl C_{2-8} alkenyl, C_{2-8} alkynyl, aryl, C_{3-8} cycloalkyl, heteroaryl. Of particular interest are compounds of the general formula (1) as defined immediately above except that: C_7 alkylene and C_{3-7} alkenylene are excluded as chains
 30 formed by R^3 and R^4 ; tri(C_{1-4})alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and any morpholine, piperidine or pyrrolidine ring is unsubstituted.

In a further embodiment of the invention as defined immediately above, the compounds of formula (1) are compounds in which W, X and Z are N, and the respective other ring members are CH;

R is chloro or fluoro;

5 R² is NR³R⁴;

R¹ is an aryl or heteroaryl ring of formula R²⁰;

R²⁰ is 4-substituted 2,6-difluorophenyl, 4-substituted 2,3,6-trifluorophenyl, 3-substituted 2,4,6-trifluorophenyl, 4-substituted 2-chloro-6-fluorophenyl, 4-substituted 2-chlorophenyl, 5-substituted 3-fluoropyrid-2-yl, 5-substituted 3-chloropyrid-2-yl, 2-substituted 4-chloro-
10 thiazol-5-yl, 2-substituted 4-fluoro-thiazol-5-yl;

R³ is hydrogen, methyl, ethyl, 1,1,1-trifluoroethyl, 2-methylpropen-3-yl;

R⁴ is prop-2-yl, but-2-yl, 2-methylprop-3-yl, 2-methylbut-3-yl, 1,1,1-trifluoroprop-2-yl, 1,1,1-trifluoroethyl, 1,1,1-trifluorobut-2-yl, 1,1,1-trifluoro-3-methyl-but-2-yl; 2-methylpent-4-yl, 1,1,1-trifluoro-4-methylpent-2-yl, 1,1,1-trifluoro-3-methylpent-2-yl, 3-methylpent-2-yl,
15 1,1,-difluorocyclopent-2-yl, heptafluoroprop-1-yl, nonafluorobut-1-yl, 1-carboxyethyl-2-methylprop-1-yl, 1-carboxymethyl-2-methylprop-1-yl, 1,1,1,-trifluoro-2-carboxyethyl-2-ethyl, 1,1,1,-trifluoro-2-carboxymethyl 2-ethyl;

B is phenyl, 4-fluorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-chlorophenyl, 2-chlorophenyl, 3-chlorophenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 5-fluoro-2-pyridyl, 6-fluoro-3-pyridyl, 2-fluoro-4-pyridyl, 2-phenylethenyl, 2-(4-fluorophenyl)ethenyl, phenylethynyl, (4-methylphenyl)ethynyl, (4-fluorophenyl)ethynyl, 4-fluorophenoxy, 2-fluorophenoxy, 3-fluorophenoxy, phenylthio, phenylsulphinyl, phenylsulphonyl;

or, in another embodiment of the invention, W, X and Z are N, and the respective other ring members are CH;

25 R is chloro or fluoro;

R² is NR³R⁴;

R¹ is an aryl or heteroaryl ring of formula R²⁰;

R²⁰ is 4-substituted 2,6-difluorophenyl, 4-substituted 2-chloro-6-fluorophenyl, 4-substituted 2-chlorophenyl, 5-substituted 3-fluoropyrid-2-yl, 5-substituted 3-chloropyrid-2-yl;

30 R³ is hydrogen, ethyl, 2-methylpropen-3-yl;

R⁴ is prop-2-yl, but-2-yl, 2-methylprop-3-yl, 2-methylbut-3-yl, 1,1,1-trifluoroprop-2-yl, 1,1,1-trifluoroethyl, 1,1,1-trifluorobut-2-yl, 1,1,1-trifluoro-3-methyl-but-2-yl; 1,1,1-trifluoro-4-methylpent-2-yl, 1,1,1-trifluoro-3-methylpent-2-yl, 1,1,-difluorocyclopent-2-yl,

heptafluoroprop-1-yl, 1-carboxyethyl-2-methylprop-1-yl, 1,1,1,-trifluoro-2-carboxyethyl-2-ethyl;

B is phenyl, 4-fluorophenyl, 4-chlorophenyl, 5-fluoro-2-pyridyl, 6-fluoro-3-pyridyl, 2-phenylethenyl, 2-(4-fluorophenyl)ethenyl, (4-methylphenyl)ethynyl, (4-fluorophenyl) ethynyl, 4-fluorophenoxy, phenylthio, phenylsulphinyl (or benzenesulphinyl), phenylsulphonyl (or benzenesulphonyl).

Yet another aspect of the invention provides a compound of formula (1) wherein wherein W and Z are N and the other two are CR⁸, or W, Y and Z are N and X is CR⁸,
 10 R⁸ is H or halo; R is halo and R² is NR³R⁴; R¹ is an aryl or heteroaryl ring R²⁰ and A is a substituent selected from halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and B is one more substituent selected from aryl, heteroaryl, aryloxy (except that phenoxy must be substituted), heteroaryloxy, arylthio, arylsulphinyl, arylsulphonyl, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, aryl(C₂₋₄)alkenyl, aryl(C₂₋₄)alkynyl, heteroaryl(C₂₋₄)alkenyl,
 15 heteroaryl(C₂₋₄)alkynyl, aryl(C₁₋₄)alkyl, heteroaryl(C₁₋₄)alkyl, with any of the foregoing aryl or heteroaryl substituents being optionally substituted with halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, cyano or nitro; R³ and R⁴ are independently H, C₁₋₈ alkyl, C₁₋₈ fluoroalkyl, C₁₋₈ perfluoroalkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, C₃₋₈ cycloalkyl, heteroaryl.

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In a further embodiment, the invention includes a compound of the general formula (1) as defined immediately above except that: C₇ alkylene and C₃₋₇ alkenylene are excluded as chains formed by R³ and R⁴; tri(C₁₋₄)alkylsilyl is excluded as a substituent of any alkyl, alkenyl, alkynyl or cycloalkyl group or moiety, and any morpholine, piperidine or
 25 pyrrolidine ring is unsubstituted.

In a further embodiment of the invention, in the compounds of formula (1) are compounds in which W and Z are N, or W, Y and Z are N, and the respective other ring members are CH; R is chloro or fluoro;
 30 R² is NR³R⁴;
 R¹ is an aryl or heteroaryl ring of formula R²⁰;
 R²⁰ is 4-substituted 2,6-difluorophenyl, 4-substituted 2,3,6-trifluorophenyl, 3-substituted 2,4,6-trifluorophenyl, 4-substituted 2-chloro-6-fluorophenyl, 4-substituted 2-chlorophenyl, 5-

substituted 3-fluoropyrid-2-yl, 5-substituted 3-chloropyrid-2-yl, 2-substituted 4-chloro-thiazol-5-yl, 2-substituted 4-fluoro-thiazol-5-yl;

R³ is hydrogen, methyl, ethyl, 1,1,1-trifluoroethyl, 2-methylpropen-3-yl;

R⁴ is prop-2-yl, but-2-yl, 2-methylprop-3-yl, 2-methylbut-3-yl, 1,1,1-trifluoroprop-2-yl,

- 5 1,1,1-trifluoroethyl, 1,1,1-trifluorobut-2-yl, 1,1,1-trifluoro-3-methyl-but-2-yl; 2-methylpent-4-yl, 1,1,1-trifluoro-4-methylpent-2-yl, 1,1,1-trifluoro-3-methylpent-2-yl, 3-methylpent-2-yl, 1,1,-difluorocyclopent-2-yl, heptafluoroprop-1-yl, nonafluorobut-1-yl, 1-carboxyethyl-2-methylprop-1-yl, 1-carboxymethyl-2-methylprop-1-yl, 1,1,1,-trifluoro-2-carboxyethyl-2-ethyl, 1,1,1,-trifluoro-2-carboxymethyl 2-ethyl;

- 10 B is phenyl, 4-fluorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-chlorophenyl, 2-chlorophenyl, 3-chlorophenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 5-fluoro-2-pyridyl, 6-fluoro-3-pyridyl, 2-fluoro-4-pyridyl, 2-phenylethenyl, 2-(4-fluorophenyl)ethenyl, phenylethynyl, (4-methylphenyl)ethynyl, (4-fluorophenyl)ethynyl, 4-fluorophenoxy, 2-fluorophenoxy, 3-fluorophenoxy, phenylthio, phenylsulphinyl, phenylsulphonyl, or
15 benzenesulphonyl;

or, in another embodiment of the invention,

W and Z are N, or W, Y and Z are N, and the respective other ring members are CH;

R is chloro or fluoro;

R² is NR³R⁴;

- 20 R¹ is an aryl or heteroaryl ring of formula R²⁰;

R²⁰ is 4-substituted 2,6-difluorophenyl, 4-substituted 2-chloro-6-fluorophenyl, 4-substituted 2-chlorophenyl, 5-substituted 3-fluoropyrid-2-yl, 5-substituted 3-chloropyrid-2-yl;

R³ is hydrogen, ethyl, 2-methylpropen-3-yl;

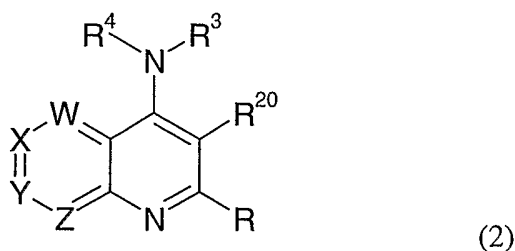
R⁴ is prop-2-yl, but-2-yl, 2-methylprop-3-yl, 2-methylbut-3-yl, 1,1,1-trifluoroprop-2-yl,

- 25 1,1,1-trifluoroethyl, 1,1,1-trifluorobut-2-yl, 1,1,1-trifluoro-3-methyl-but-2-yl; 1,1,1-trifluoro-4-methylpent-2-yl, 1,1,1-trifluoro-3-methylpent-2-yl, 1,1,-difluorocyclopent-2-yl, heptafluoroprop-1-yl, 1-carboxyethyl-2-methylprop-1-yl, 1,1,1,-trifluoro-2-carboxyethyl-2-ethyl;

B is phenyl, 4-fluorophenyl, 4-chlorophenyl, 5-fluoro-2-pyridyl, 6-fluoro-3-pyridyl, 2-

- 30 phenylethenyl, 2-(4-fluorophenyl)ethenyl, (4-methylphenyl)ethynyl, (4-fluorophenyl)ethynyl, 4-fluorophenoxy, phenylthio, phenylsulphinyl (or benzenesulphinyl), phenylsulphonyl (or benzenesulphonyl).

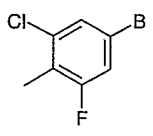
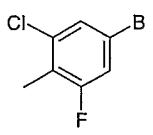
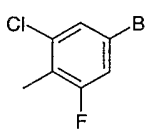
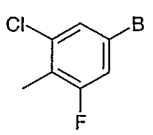
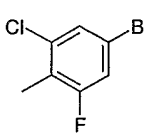
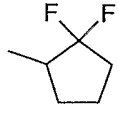
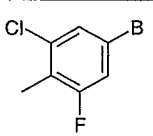
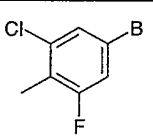
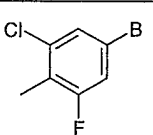
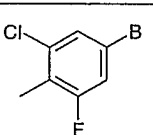
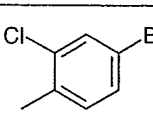
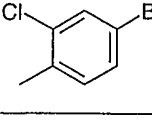
Compounds that form part of the invention are illustrated in Tables 1 to 27 below. Characterising data are given later in the Examples. Single compounds are assigned the number of the table, followed by the number of the combination of substituents as in Table 1. For example, compound 22.005 is the compound as described in Table 22, wherein the substituents defined therein are combined with the substituents as defined in Table 1, position No. 5. In Table 1 to 27 the compounds have the general formula (2) as depicted below.

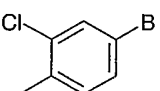
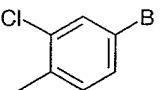
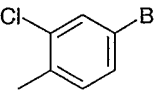
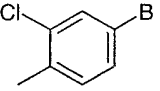
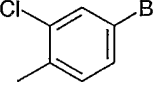
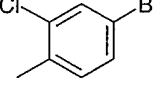
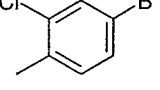
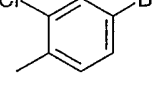
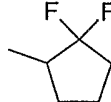
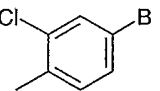
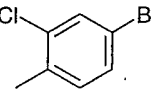
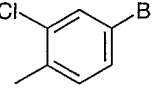
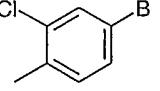


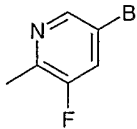
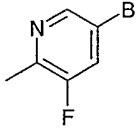
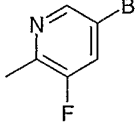
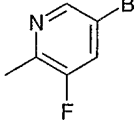
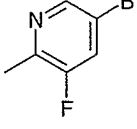
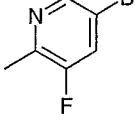
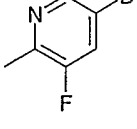
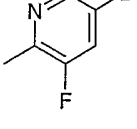
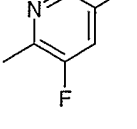
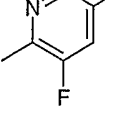
10 Table 1

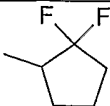
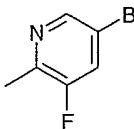
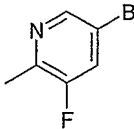
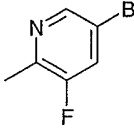
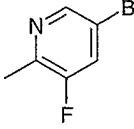
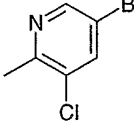
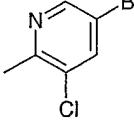
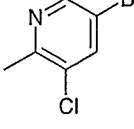
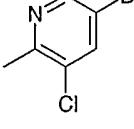
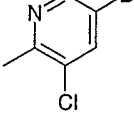
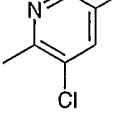
Position No.	R	R ³	R ⁴	R ²⁰
001	Cl	H	-CH(CH ₃) ₂	
002	Cl	H	-CH(CH ₃)CH ₂ CH ₃	
003	Cl	H	-CH ₂ CH(CH ₃) ₂	
004	Cl	H	-CH(CH ₃)CH(CH ₃) ₂	
005	Cl	H	-CH(CH ₃)(CF ₃)	
006	Cl	H	-CH ₂ CF ₃	
007	Cl	H	-CH(CF ₃)CH ₂ CH ₃	

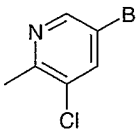
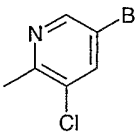
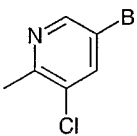
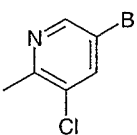
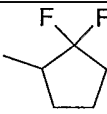
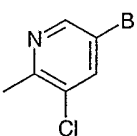
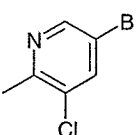
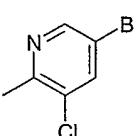
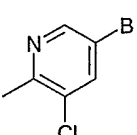
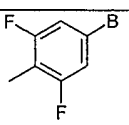
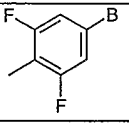
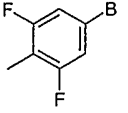
Position No.	R	R ³	R ⁴	R ²⁰
008	Cl	H	$-\text{CH}(\text{CF}_3)\text{CH}(\text{CH}_3)_2$	
009	Cl	H	$-\text{CH}(\text{CF}_3)\text{CH}_2\text{CH}(\text{CH}_3)_2$	
010	Cl	H	$-\text{CH}(\text{CF}_3)\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$	
011	Cl	H		
012	Cl	H	$-\text{CF}_2\text{CF}_2\text{CF}_3$	
013	Cl	H	$-\text{CH}(\text{CH}[\text{CH}_3]_2)\text{COOCH}_2\text{CH}_3$	
014	Cl	H	$-\text{CH}(\text{CF}_3)\text{COOCH}_2\text{CH}_3$	
015	Cl	H	$-\text{CH}(\text{CH}_3)_2$	
016	Cl	H	$-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$	
017	Cl	H	$-\text{CH}_2\text{CH}(\text{CH}_3)_2$	
018	Cl	H	$-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$	
019	Cl	H	$-\text{CH}(\text{CH}_3)(\text{CF}_3)$	

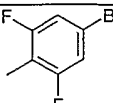
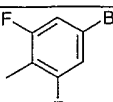
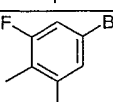
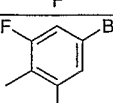
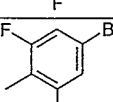
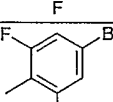
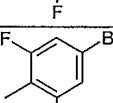
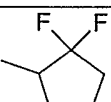
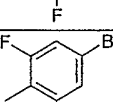
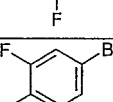
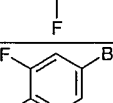
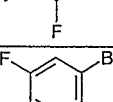
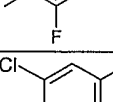
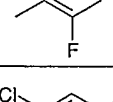
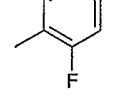
Position No.	R	R ³	R ⁴	R ²⁰
020	Cl	H	-CH ₂ CF ₃	
021	Cl	H	-CH(CF ₃)CH ₂ CH ₃	
022	Cl	H	-CH(CF ₃)CH(CH ₃) ₂	
023	Cl	H	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
024	Cl	H	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
025	Cl	H		
026	Cl	H	-CF ₂ CF ₂ CF ₃	
027	Cl	H	-CH(CH[CH ₃]) ₂ COOCH ₂ CH ₃	
028	Cl	H	-CH(CF ₃)COOCH ₂ CH ₃	
029	Cl	H	-CH(CH ₃) ₂	
030	Cl	H	-CH(CH ₃)CH ₂ CH ₃	

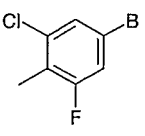
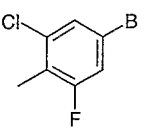
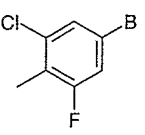
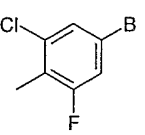
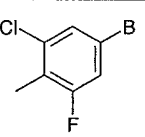
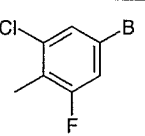
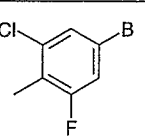
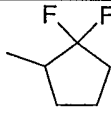
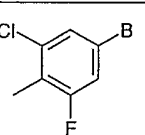
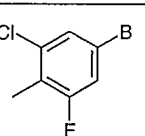
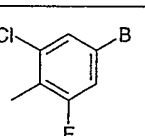
Position No.	R	R ³	R ⁴	R ²⁰
031	Cl	H	-CH ₂ CH(CH ₃) ₂	
032	Cl	H	-CH(CH ₃)CH(CH ₃) ₂	
033	Cl	H	-CH(CH ₃)(CF ₃)	
034	Cl	H	-CH ₂ CF ₃	
035	Cl	H	-CH(CF ₃)CH ₂ CH ₃	
036	Cl	H	-CH(CF ₃)CH(CH ₃) ₂	
037	Cl	H	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
038	Cl	H	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
039	Cl	H		
040	Cl	H	-CF ₂ CF ₂ CF ₃	
041	Cl	H	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
042	Cl	H	-CH(CF ₃)COOCH ₂ CH ₃	

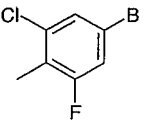
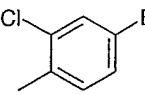
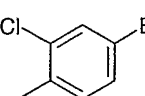
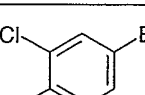
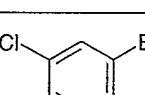
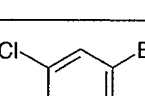
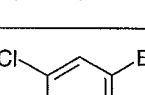
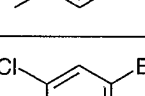
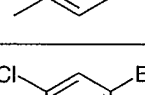
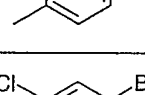
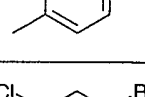
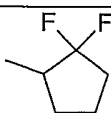
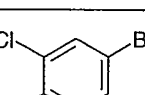
Position No.	R	R ³	R ⁴	R ²⁰
043	Cl	H	-CH(CH ₃) ₂	
044	Cl	H	-CH(CH ₃)CH ₂ CH ₃	
045	Cl	H	-CH ₂ CH(CH ₃) ₂	
046	Cl	H	-CH(CH ₃)CH(CH ₃) ₂	
047	Cl	H	-CH(CH ₃)(CF ₃)	
048	Cl	H	-CH ₂ CF ₃	
049	Cl	H	-CH(CF ₃)CH ₂ CH ₃	
050	Cl	H	-CH(CF ₃)CH(CH ₃) ₂	
051	Cl	H	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
052	Cl	H	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	

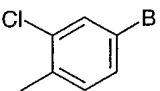
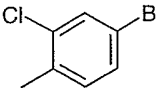
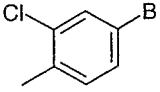
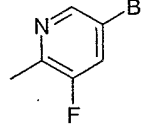
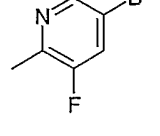
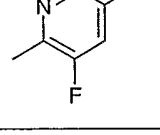
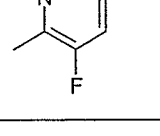
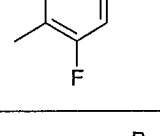
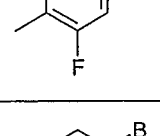
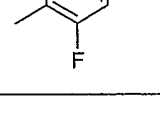
Position No.	R	R ³	R ⁴	R ²⁰
053	Cl	H		
054	Cl	H	-CF ₂ CF ₂ CF ₃	
055	Cl	H	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
056	Cl	H	-CH(CF ₃)COOCH ₂ CH ₃	
057	Cl	H	-CH(CH ₃) ₂	
058	Cl	H	-CH(CH ₃)CH ₂ CH ₃	
059	Cl	H	-CH ₂ CH(CH ₃) ₂	
060	Cl	H	-CH(CH ₃)CH(CH ₃) ₂	
061	Cl	H	-CH(CH ₃)(CF ₃)	
062	Cl	H	-CH ₂ CF ₃	

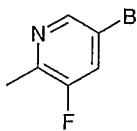
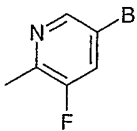
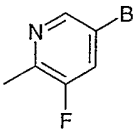
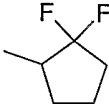
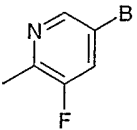
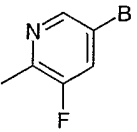
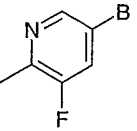
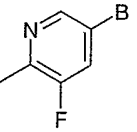
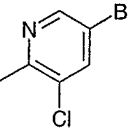
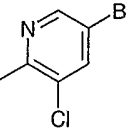
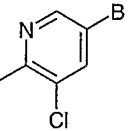
Position No.	R	R ³	R ⁴	R ²⁰
063	Cl	H	-CH(CF ₃)CH ₂ CH ₃	
064	Cl	H	-CH(CF ₃)CH(CH ₃) ₂	
065	Cl	H	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
066	Cl	H	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
067	Cl	H		
068	Cl	H	-CF ₂ CF ₂ CF ₃	
069	Cl	H	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
070	Cl	H	-CH(CF ₃)COOCH ₂ CH ₃	
071	Cl	CH ₂ CH ₃	-CH(CH ₃) ₂	
072	Cl	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
073	Cl	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	

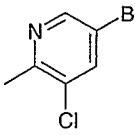
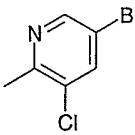
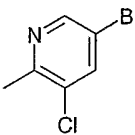
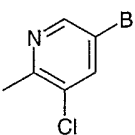
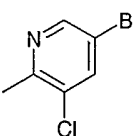
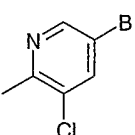
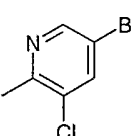
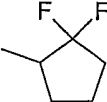
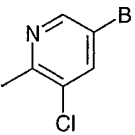
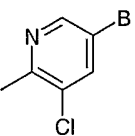
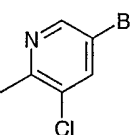
Position No.	R	R ³	R ⁴	R ²⁰
074	Cl	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
075	Cl	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
076	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
077	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
078	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
079	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
080	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
081	Cl	CH ₂ CH ₃		
082	Cl	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
083	Cl	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
084	Cl	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
085	Cl	CH ₂ CH ₃	-CH(CH ₃) ₂	
086	Cl	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
087	Cl	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	

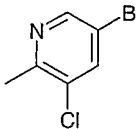
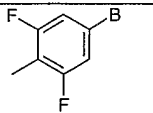
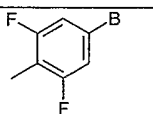
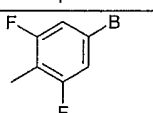
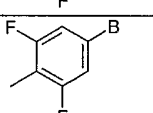
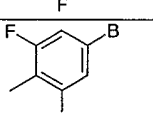
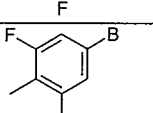
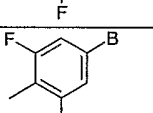
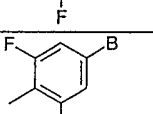
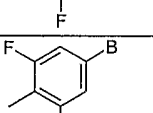
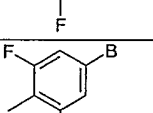
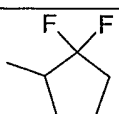
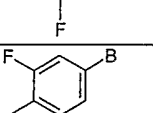
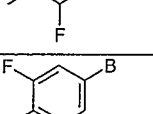
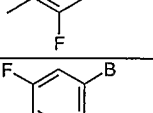
Position No.	R	R ³	R ⁴	R ²⁰
088	Cl	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
089	Cl	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
090	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
091	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
092	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
093	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
094	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
095	Cl	CH ₂ CH ₃		
096	Cl	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
097	Cl	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	

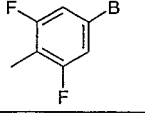
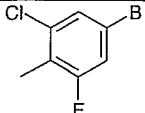
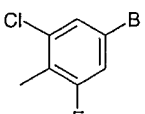
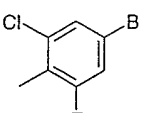
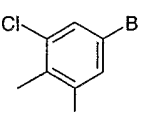
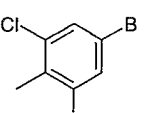
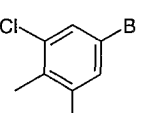
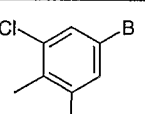
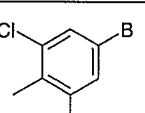
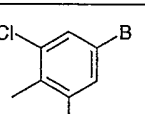
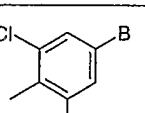
Position No.	R	R ³	R ⁴	R ²⁰
098	Cl	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
099	Cl	CH ₂ CH ₃	-CH(CH ₃) ₂	
100	Cl	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
101	Cl	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	
102	Cl	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
103	Cl	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
104	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
105	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
106	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
107	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
108	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
109	Cl	CH ₂ CH ₃		

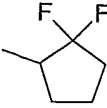
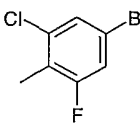
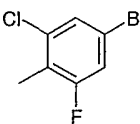
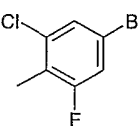
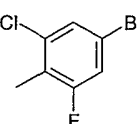
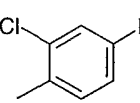
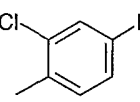
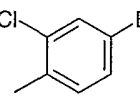
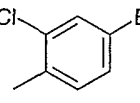
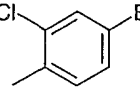
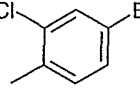
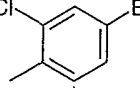
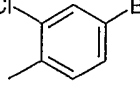
Position No.	R	R ³	R ⁴	R ²⁰
110	Cl	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
111	Cl	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
112	Cl	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
113	Cl	CH ₂ CH ₃	-CH(CH ₃) ₂	
114	Cl	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
115	Cl	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	
116	Cl	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
117	Cl	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
118	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
119	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	

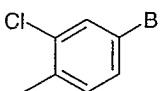
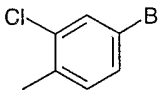
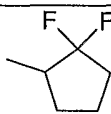
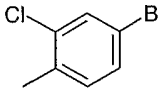
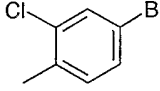
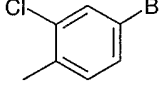
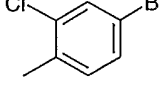
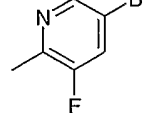
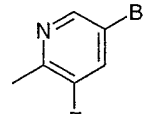
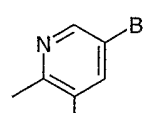
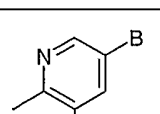
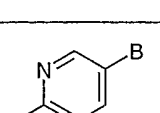
Position No.	R	R ³	R ⁴	R ²⁰
120	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
121	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
122	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
123	Cl	CH ₂ CH ₃		
124	Cl	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
125	Cl	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
126	Cl	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
127	Cl	CH ₂ CH ₃	-CH(CH ₃) ₂	
128	Cl	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
129	Cl	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	

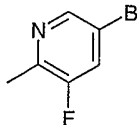
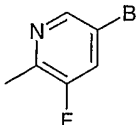
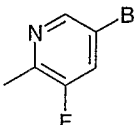
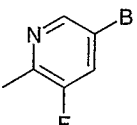
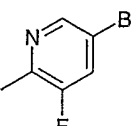
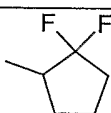
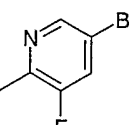
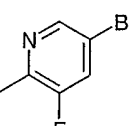
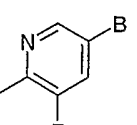
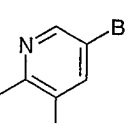
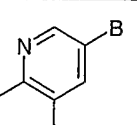
Position No.	R	R ³	R ⁴	R ²⁰
130	Cl	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
131	Cl	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
132	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
133	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
134	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
135	Cl	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
136	Cl	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
137	Cl	CH ₂ CH ₃		
138	Cl	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
139	Cl	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	

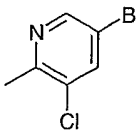
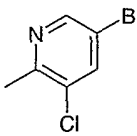
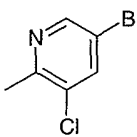
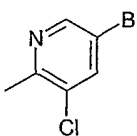
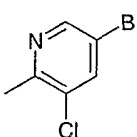
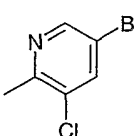
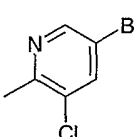
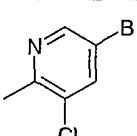
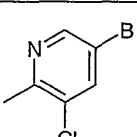
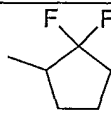
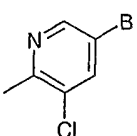
Position No.	R	R ³	R ⁴	R ²⁰
140	Cl	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
141	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
142	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
143	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	
144	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
145	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
146	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
147	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
148	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
149	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
150	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
151	Cl	CH ₂ C(CH ₃)=CH ₂		
152	Cl	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
153	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	

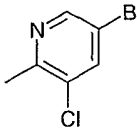
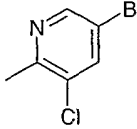
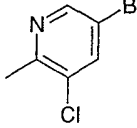
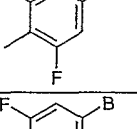
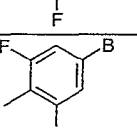
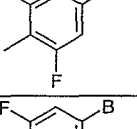
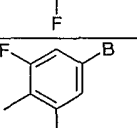
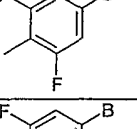
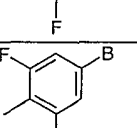
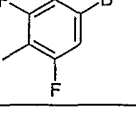

Position No.	R	R ³	R ⁴	R ²⁰
154	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
155	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
156	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
157	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	
158	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
159	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
160	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
161	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
162	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
163	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
164	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	

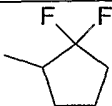
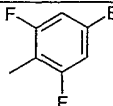
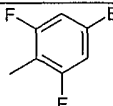
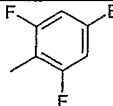
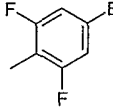
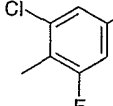
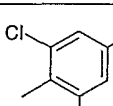
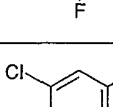
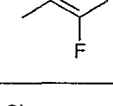
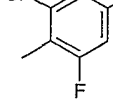
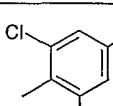
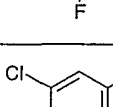
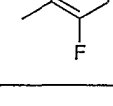
Position No.	R	R ³	R ⁴	R ²⁰
165	Cl	CH ₂ C(CH ₃)=CH ₂		
166	Cl	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
167	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
168	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
169	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
170	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
171	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	
172	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
173	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
174	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
175	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
176	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	

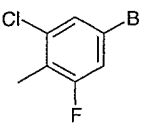
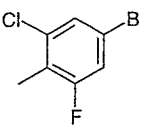
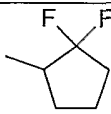
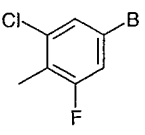
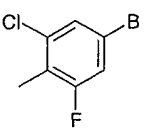
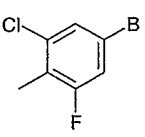
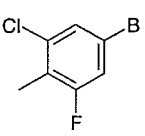
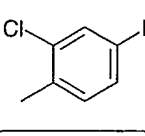
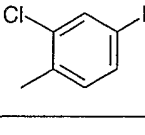
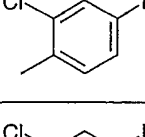
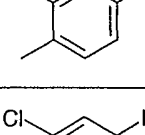
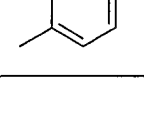
Position No.	R	R ³	R ⁴	R ²⁰
177	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
178	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
179	Cl	CH ₂ C(CH ₃)=CH ₂		
180	Cl	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
181	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
182	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
183	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
184	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
185	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	
186	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
187	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	

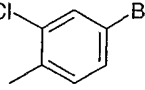
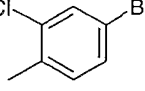
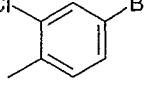
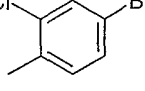
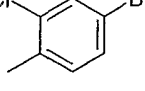
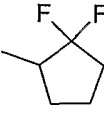
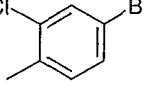
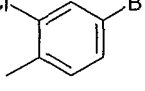
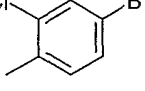
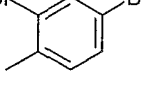
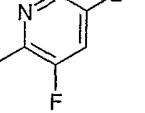
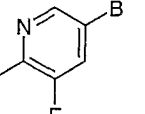
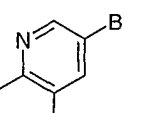
Position No.	R	R ³	R ⁴	R ²⁰
188	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
189	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
190	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
191	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
192	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
193	Cl	CH ₂ C(CH ₃)=CH ₂		
194	Cl	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
195	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
196	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
197	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	

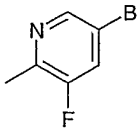
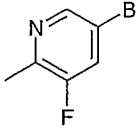
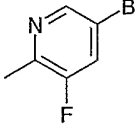
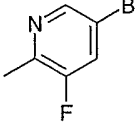
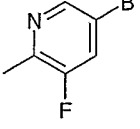
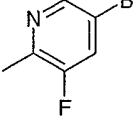
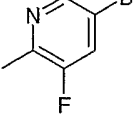
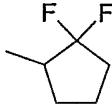
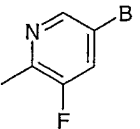
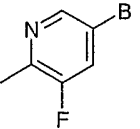
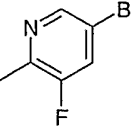
Position No.	R	R ³	R ⁴	R ²⁰
198	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
199	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	
200	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
201	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
202	Cl	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
203	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
204	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
205	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
206	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
207	Cl	CH ₂ C(CH ₃)=CH ₂		

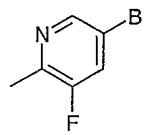
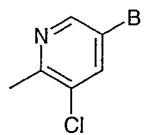
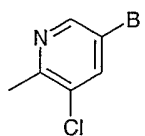
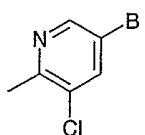
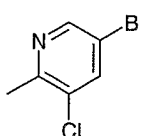
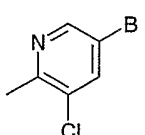
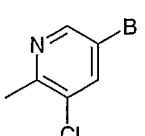
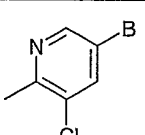
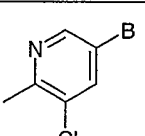
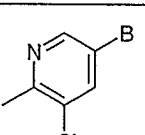
Position No.	R	R ³	R ⁴	R ²⁰
208	Cl	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
209	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
210	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
211	F	H	-CH(CH ₃) ₂	
212	F	H	-CH(CH ₃)CH ₂ CH ₃	
213	F	H	-CH ₂ CH(CH ₃) ₂	
214	F	H	-CH(CH ₃)CH(CH ₃) ₂	
215	F	H	-CH(CH ₃)(CF ₃)	
216	F	H	-CH ₂ CF ₃	
217	F	H	-CH(CF ₃)CH ₂ CH ₃	
218	F	H	-CH(CF ₃)CH(CH ₃) ₂	
219	F	H	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
220	F	H	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	

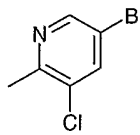
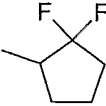
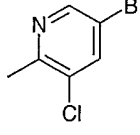
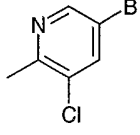
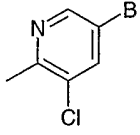
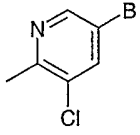
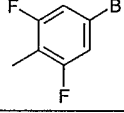

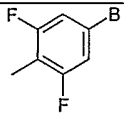
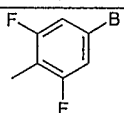
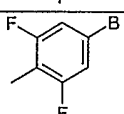
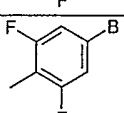
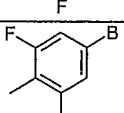
Position No.	R	R ³	R ⁴	R ²⁰
221	F	H		
222	F	H	-CF ₂ CF ₂ CF ₃	
223	F	H	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
224	F	H	-CH(CF ₃)COOCH ₂ CH ₃	
225	F	H	-CH(CH ₃) ₂	
226	F	H	-CH(CH ₃)CH ₂ CH ₃	
227	F	H	-CH ₂ CH(CH ₃) ₂	
228	F	H	-CH(CH ₃)CH(CH ₃) ₂	
229	F	H	-CH(CH ₃)(CF ₃)	
230	F	H	-CH ₂ CF ₃	
231	F	H	-CH(CF ₃)CH ₂ CH ₃	
232	F	H	-CH(CF ₃)CH(CH ₃) ₂	

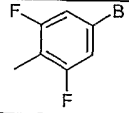
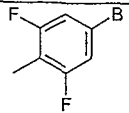
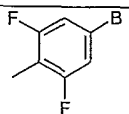
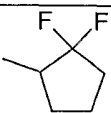
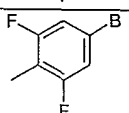
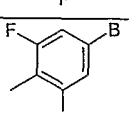
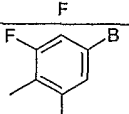
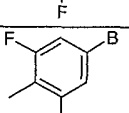
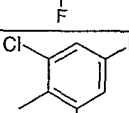
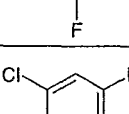
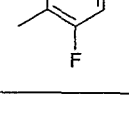
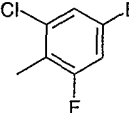
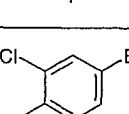
Position No.	R	R ³	R ⁴	R ²⁰
233	F	H	$-\text{CH}(\text{CF}_3)\text{CH}_2\text{CH}(\text{CH}_3)_2$	
234	F	H	$-\text{CH}(\text{CF}_3)\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$	
235	F	H		
236	F	H	$-\text{CF}_2\text{CF}_2\text{CF}_3$	
237	F	H	$-\text{CH}(\text{CH}[\text{CH}_3]_2)\text{COOCH}_2\text{CH}_3$	
238	F	H	$-\text{CH}(\text{CF}_3)\text{COOCH}_2\text{CH}_3$	
239	F	H	$-\text{CH}(\text{CH}_3)_2$	
240	F	H	$-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$	
241	F	H	$-\text{CH}_2\text{CH}(\text{CH}_3)_2$	
242	F	H	$-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$	
243	F	H	$-\text{CH}(\text{CH}_3)(\text{CF}_3)$	

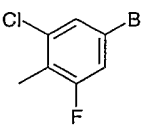
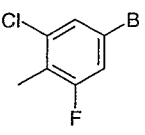
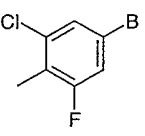
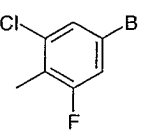
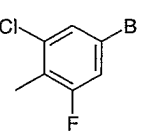
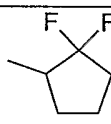
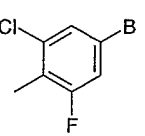
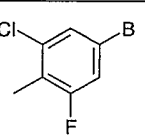
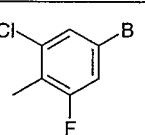
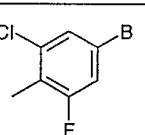
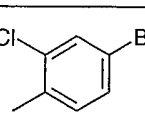
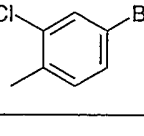
Position No.	R	R ³	R ⁴	R ²⁰
244	F	H	-CH ₂ CF ₃	
245	F	H	-CH(CF ₃)CH ₂ CH ₃	
246	F	H	-CH(CF ₃)CH(CH ₃) ₂	
247	F	H	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
248	F	H	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
249	F	H		
250	F	H	-CF ₂ CF ₂ CF ₃	
251	F	H	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
252	F	H	-CH(CF ₃)COOCH ₂ CH ₃	
253	F	H	-CH(CH ₃) ₂	
254	F	H	-CH(CH ₃)CH ₂ CH ₃	
255	F	H	-CH ₂ CH(CH ₃) ₂	

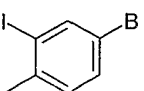
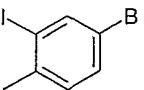
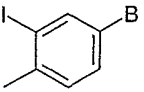
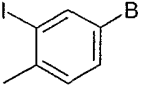
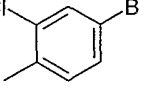
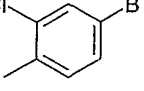
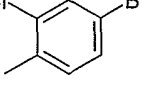
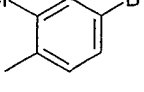
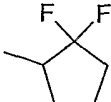
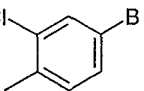
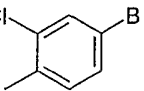
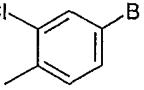
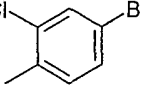
Position No.	R	R ³	R ⁴	R ²⁰
256	F	H	-CH(CH ₃)CH(CH ₃) ₂	
257	F	H	-CH(CH ₃)(CF ₃)	
258	F	H	-CH ₂ CF ₃	
259	F	H	-CH(CF ₃)CH ₂ CH ₃	
260	F	H	-CH(CF ₃)CH(CH ₃) ₂	
261	F	H	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
262	F	H	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
263	F	H		
264	F	H	-CF ₂ CF ₂ CF ₃	
265	F	H	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	

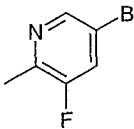
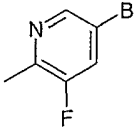
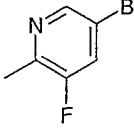
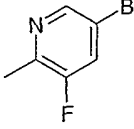
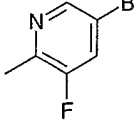
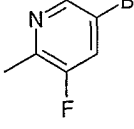
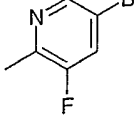
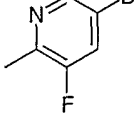
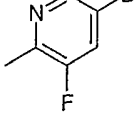
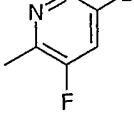
Position No.	R	R ³	R ⁴	R ²⁰
266	F	H	$-\text{CH}(\text{CF}_3)\text{COOCH}_2\text{CH}_3$	
267	F	H	$-\text{CH}(\text{CH}_3)_2$	
268	F	H	$-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$	
269	F	H	$-\text{CH}_2\text{CH}(\text{CH}_3)_2$	
270	F	H	$-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$	
271	F	H	$-\text{CH}(\text{CH}_3)(\text{CF}_3)$	
272	F	H	$-\text{CH}_2\text{CF}_3$	
273	F	H	$-\text{CH}(\text{CF}_3)\text{CH}_2\text{CH}_3$	
274	F	H	$-\text{CH}(\text{CF}_3)\text{CH}(\text{CH}_3)_2$	
275	F	H	$-\text{CH}(\text{CF}_3)\text{CH}_2\text{CH}(\text{CH}_3)_2$	

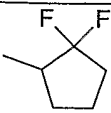
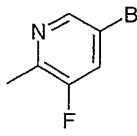
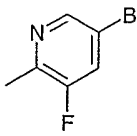
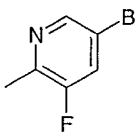
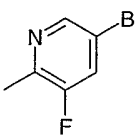
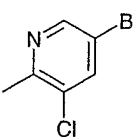
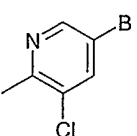
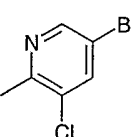
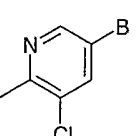
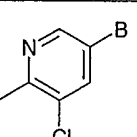
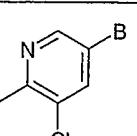
Position No.	R	R ³	R ⁴	R ²⁰
276	F	H	$-\text{CH}(\text{CF}_3)\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$	
277	F	H		
278	F	H	$-\text{CF}_2\text{CF}_2\text{CF}_3$	
279	F	H	$-\text{CH}(\text{CH}[\text{CH}_3]_2)\text{COOCH}_2\text{CH}_3$	
280	F	H	$-\text{CH}(\text{CF}_3)\text{COOCH}_2\text{CH}_3$	
281	F	CH_2CH_3	$-\text{CH}(\text{CH}_3)_2$	
282	F	CH_2CH_3	$-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$	
283	F	CH_2CH_3	$-\text{CH}_2\text{CH}(\text{CH}_3)_2$	
284	F	CH_2CH_3	$-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$	
285	F	CH_2CH_3	$-\text{CH}(\text{CH}_3)(\text{CF}_3)$	
286	F	CH_2CH_3	$-\text{CH}_2\text{CF}_3$	
287	F	CH_2CH_3	$-\text{CH}(\text{CF}_3)\text{CH}_2\text{CH}_3$	

Position No.	R	R ³	R ⁴	R ²⁰
288	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
289	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
290	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
291	F	CH ₂ CH ₃		
292	F	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
293	F	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
294	F	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
295	F	CH ₂ CH ₃	-CH(CH ₃) ₂	
296	F	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
297	F	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	
298	F	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
299	F	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	

Position No.	R	R ³	R ⁴	R ²⁰
300	F	CH ₂ CH ₃	-CH ₂ CF ₃	
301	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
302	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
303	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
304	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
305	F	CH ₂ CH ₃		
306	F	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
307	F	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
308	F	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
309	F	CH ₂ CH ₃	-CH(CH ₃) ₂	
310	F	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	

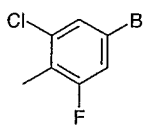
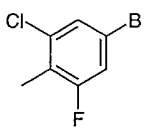
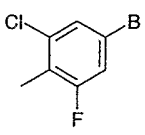
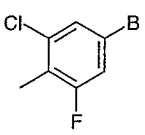
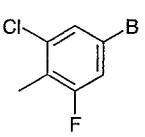
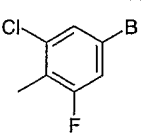
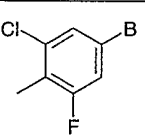
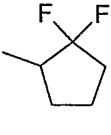
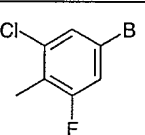
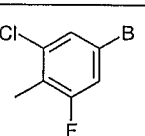
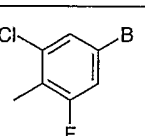
Position No.	R	R ³	R ⁴	R ²⁰
311	F	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	
312	F	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
313	F	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
314	F	CH ₂ CH ₃	-CH ₂ CF ₃	
315	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
316	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
317	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
318	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
319	F	CH ₂ CH ₃		
320	F	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
321	F	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
322	F	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	

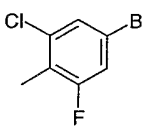
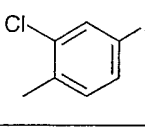
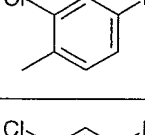
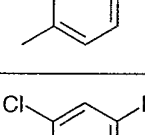
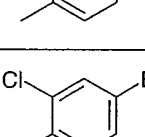
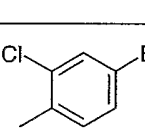
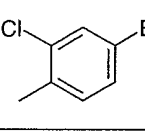
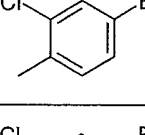
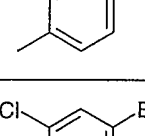
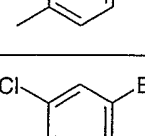
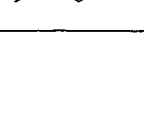
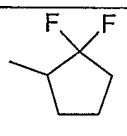
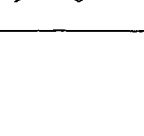
Position No.	R	R ³	R ⁴	R ²⁰
323	F	CH ₂ CH ₃	-CH(CH ₃) ₂	
324	F	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
325	F	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	
326	F	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
327	F	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
328	F	CH ₂ CH ₃	-CH ₂ CF ₃	
329	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
330	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
331	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
332	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	

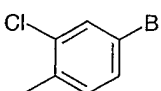
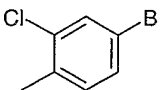
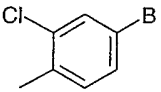
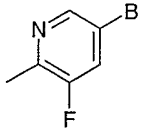
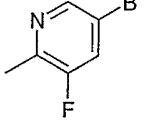
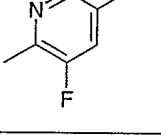
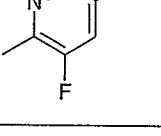
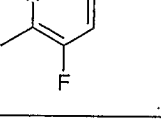
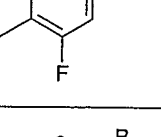
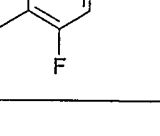
Position No.	R	R ³	R ⁴	R ²⁰
333	F	CH ₂ CH ₃		
334	F	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
335	F	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
336	F	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
337	F	CH ₂ CH ₃	-CH(CH ₃) ₂	
338	F	CH ₂ CH ₃	-CH(CH ₃)CH ₂ CH ₃	
339	F	CH ₂ CH ₃	-CH ₂ CH(CH ₃) ₂	
340	F	CH ₂ CH ₃	-CH(CH ₃)CH(CH ₃) ₂	
341	F	CH ₂ CH ₃	-CH(CH ₃)(CF ₃)	
342	F	CH ₂ CH ₃	-CH ₂ CF ₃	

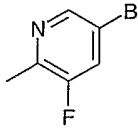
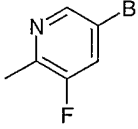
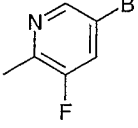
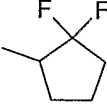
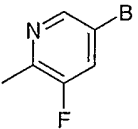
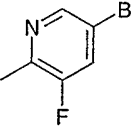
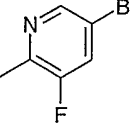
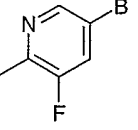
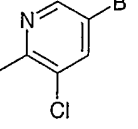
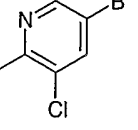
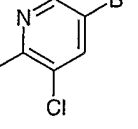
Position No.	R	R ³	R ⁴	R ²⁰
343	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH ₃	
344	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃) ₂	
345	F	CH ₂ CH ₃	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
346	F	CH ₂ CH ₃	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
347	F	CH ₂ CH ₃		
348	F	CH ₂ CH ₃	-CF ₂ CF ₂ CF ₃	
349	F	CH ₂ CH ₃	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
350	F	CH ₂ CH ₃	-CH(CF ₃)COOCH ₂ CH ₃	
351	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
352	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
353	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	

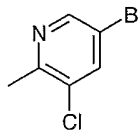
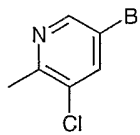
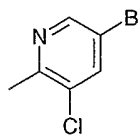
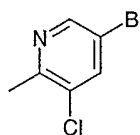
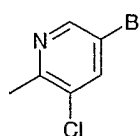
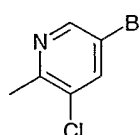
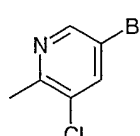
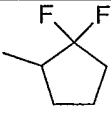
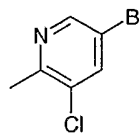
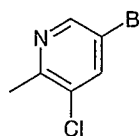
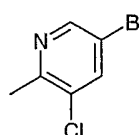
Position No.	R	R ³	R ⁴	R ²⁰
354	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
355	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
356	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
357	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
358	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
359	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
360	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
361	F	CH ₂ C(CH ₃)=CH ₂		
362	F	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
363	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
364	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
365	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
366	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
367	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	

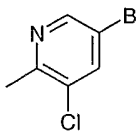
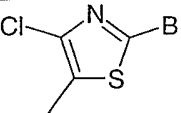
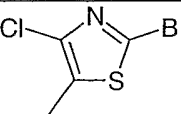
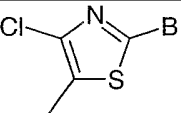
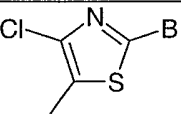
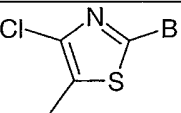
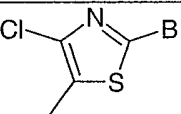
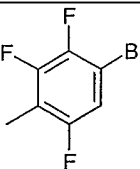
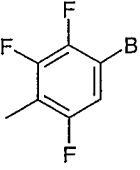
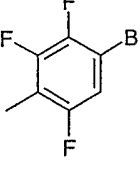
Position No.	R	R ³	R ⁴	R ²⁰
368	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
369	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
370	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
371	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
372	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
373	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
374	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
375	F	CH ₂ C(CH ₃)=CH ₂		
376	F	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
377	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃]) ₂ COOCH ₂ CH ₃	

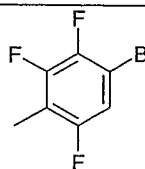
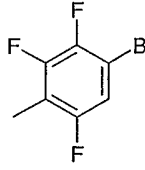
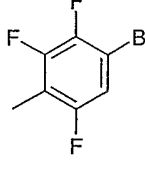
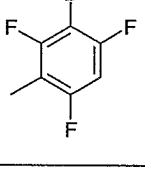
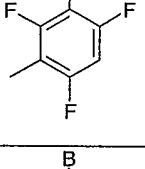
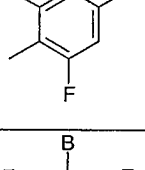
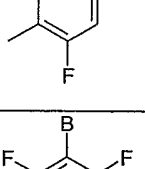
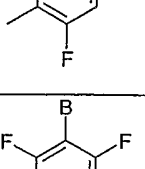
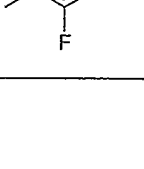
Position No.	R	R ³	R ⁴	R ²⁰
378	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
379	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
380	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
381	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	
382	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
383	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
384	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
385	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
386	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
387	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
388	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
389	F	CH ₂ C(CH ₃)=CH ₂		

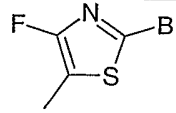
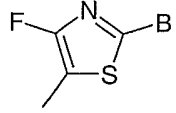
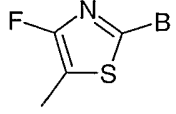
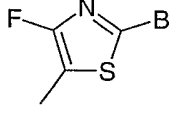
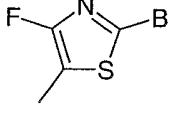
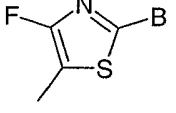
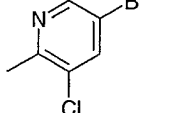
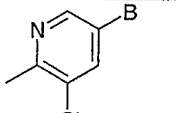
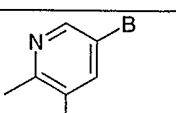
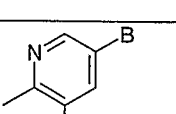
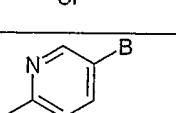
Position No.	R	R ³	R ⁴	R ²⁰
390	F	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
391	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
392	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
393	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
394	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
395	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	
396	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
397	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
398	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
399	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	

Position No.	R	R ³	R ⁴	R ²⁰
400	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
401	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
402	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
403	F	CH ₂ C(CH ₃)=CH ₂		
404	F	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
405	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	
406	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
407	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃) ₂	
408	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH ₂ CH ₃	
409	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CH(CH ₃) ₂	

Position No.	R	R ³	R ⁴	R ²⁰
410	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)CH(CH ₃) ₂	
411	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH ₃)(CF ₃)	
412	F	CH ₂ C(CH ₃)=CH ₂	-CH ₂ CF ₃	
413	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH ₃	
414	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃) ₂	
415	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH ₂ CH(CH ₃) ₂	
416	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
417	F	CH ₂ C(CH ₃)=CH ₂		
418	F	CH ₂ C(CH ₃)=CH ₂	-CF ₂ CF ₂ CF ₃	
419	F	CH ₂ C(CH ₃)=CH ₂	-CH(CH[CH ₃] ₂)COOCH ₂ CH ₃	

Position No.	R	R ³	R ⁴	R ²⁰
420	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)COOCH ₂ CH ₃	
421	Cl	H	CH(CH[CH ₃] ₂)COOCH ₃	
422	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
423	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
424	F	H	CH(CH[CH ₃] ₂)COOCH ₃	
425	F	CH ₂ CH ₃	-CH ₂ CF ₃	
426	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
427	Cl	H	CH(CH[CH ₃] ₂)COOCH ₃	
428	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
429	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	

Position No.	R	R ³	R ⁴	R ²⁰
430	F	H	CH(CH[CH ₃] ₂)COOCH ₃	
431	F	CH ₂ CH ₃	-CH ₂ CF ₃	
432	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
433	Cl	H	CH(CH[CH ₃] ₂)COOCH ₃	
434	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
435	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
436	F	H	CH(CH[CH ₃] ₂)COOCH ₃	
437	F	CH ₂ CH ₃	-CH ₂ CF ₃	
438	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	

Position No.	R	R ³	R ⁴	R ²⁰
439	Cl	H	CH(CH[CH ₃] ₂)COOCH ₃	
440	Cl	CH ₂ CH ₃	-CH ₂ CF ₃	
441	Cl	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
442	F	H	CH(CH[CH ₃] ₂)COOCH ₃	
443	F	CH ₂ CH ₃	-CH ₂ CF ₃	
444	F	CH ₂ C(CH ₃)=CH ₂	-CH(CF ₃)CH(CH ₃)CH ₂ CH ₃	
445	CN	-CH=CH ₂	3-Pyridyl	
446	CF ₃	NH ₂	Phenyl	
447	Br	-NH-Phenyl	cyclohexyl	
448	CN	-CH=CH ₂	Phenyl	
449	CF ₃	NH ₂	3-Pyridyl	

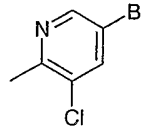
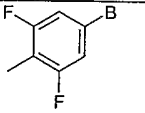
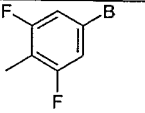
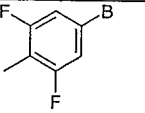
Position No.	R	R ³	R ⁴	R ²⁰
450	Br	-NH-Phenyl	3-Pyridyl	
451	CN	-CH=CH ₂	3-Pyridyl	
452	CF ₃	NH ₂	Phenyl	
453	Br	-NH-Phenyl	cyclohexyl	

Table 2

Table 2 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is phenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

5

Table 3

Table 3 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is 4-fluorophenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

10

Table 4

Table 4 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is 4-chlorophenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

15

Table 5

Table 5 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is 5-fluoro-2-pyridyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

20

Table 6

Table 6 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is 6-fluoro-3-pyridyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

5

Table 7

Table 7 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is 2-phenylethenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

10

Table 8

Table 8 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is 2-(4-fluorophenyl)ethenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

15

Table 9

Table 9 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is (4-methylphenyl)ethynyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

20

Table 10

Table 10 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is (4-fluorophenyl)ethynyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

25

Table 11

Table 11 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is 4-fluorophenoxy, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

30

Table 12

Table 12 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is phenylthio, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

35

Table 13

Table 13 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is phenylsulphinyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

5

Table 14

Table 14 consists of 453 compounds of the general formula (2), where W and Z are N, X and Y are CH, B is phenylsulphonyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

10

Table 15

Table 15 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is phenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

15

Table 16

Table 16 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is 4-fluorophenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

20

Table 17

Table 17 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is 4-chlorophenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

25

Table 18

Table 18 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is 5-fluoro-2-pyridyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

30

Table 19

Table 19 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is 6-fluoro-3-pyridyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

Table 20

Table 20 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is 2-phenylethenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

5

Table 21

Table 21 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is 2-(4-fluorophenyl)ethenyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

10

Table 22

Table 22 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is (4-methylphenyl)ethynyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

15

Table 23

Table 23 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is (4-fluorophenyl)ethynyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

20

Table 24

Table 24 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is 4-fluorophenoxy, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

25

Table 25

Table 25 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is phenylthio, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

30

Table 26

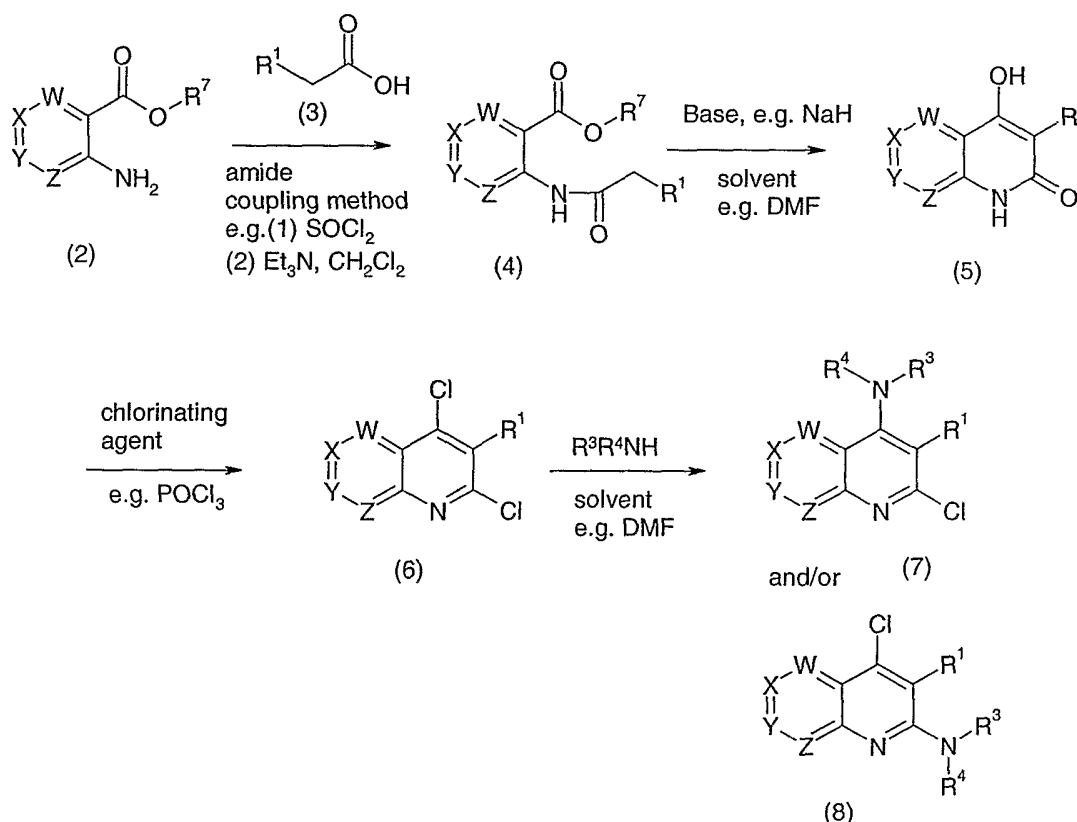
Table 26 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is phenylsulphinyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

Table 27

Table 27 consists of 453 compounds of the general formula (2), where W, Y and Z are N, X is CH, B is phenylsulphonyl, and the values of R, R³, R⁴ and R²⁰ are as listed in Table 1.

5

Compounds of formula (7) or (8), which are examples of compounds of general formula (1) where one of R and R² is NR³R⁴, can be made as shown in Scheme 1, in which W, X, Y, Z, R¹, R³ and R⁴ have the meanings given above and R⁷ is C₁₋₄ alkyl.

Scheme 1

10

Compounds of general formula (4) can be prepared from compounds of general formula (2), which are either commercially available or made by methods known in the literature, by reaction with acids of general formula (3), using standard coupling methods, for example by conversion to the acid chloride using a chlorinating agent such as thionyl chloride, followed by reaction of the resultant acid chloride optionally in the presence of a base such as triethylamine, in a suitable solvent such as dichloromethane or toluene. Compounds of general formula (5) can be prepared by treating compounds of general formula (4) with a base such as sodium hydride, optionally in the presence of a Lewis acid

such as magnesium oxide, in a suitable solvent such as *N,N*-dimethylformamide (DMF) or toluene, at between room temperature and 150°C, but preferably at 60-90°C. Compounds of general formula (6) can be prepared by reaction of compounds of general formula (5) with a chlorination reagent such as phosphorus oxychloride, either neat or in a suitable solvent such as toluene, at between 50 and 150°C, but preferably between 80 and 110°C, or in a microwave reactor at between 150 and 300°C, but preferably between 200 and 250°C. Compounds of formula (7) and (8) can be prepared by reaction of compounds of general formula (6) with an amine R^3R^4NH , either neat, or in a suitable solvent such as DMF, between room temperature and 150°C, but preferably between 50 and 80°C. If compounds (7) and (8) are produced as a mixture they can be separated by suitable means such as crystallisation or chromatography under normal or reverse phase conditions.

Compounds of formula (15) and (16), which are examples of compounds of general formula (1) can be made as shown in Scheme 2, where Hal is a halogen such as bromine or iodine. Compounds of formula (10), can be made by reaction of compounds of formula (9), which are examples of compounds of formula (5) in Scheme 1, by reaction with a compound B-D, where B is a substituent as defined above for R^1 , and D is a metallic group such as a boronic acid $B(OH)_2$, or a tri(C_{1-4}) alkyl tin, in a cross-coupling reaction in the presence of a palladium catalyst for example $PdP(Ph_3)_4$ or $Pd_2(dba)_3$, a ligand for example PPh_3 or $P(t-Bu)_3$, a base for example K_2CO_3 or CsF , in a suitable solvent such as toluene or ethanol, at room temperature to reflux, but preferably at between 50 and 100°C.

Compounds of formula (11) can be formed by reaction of compounds of formula (9) with a chlorination reagent such as phosphorus oxychloride, either neat or in a suitable solvent such as toluene or dichloroethane, at between 50 and 150°C, but preferably between 60 and 110°C.

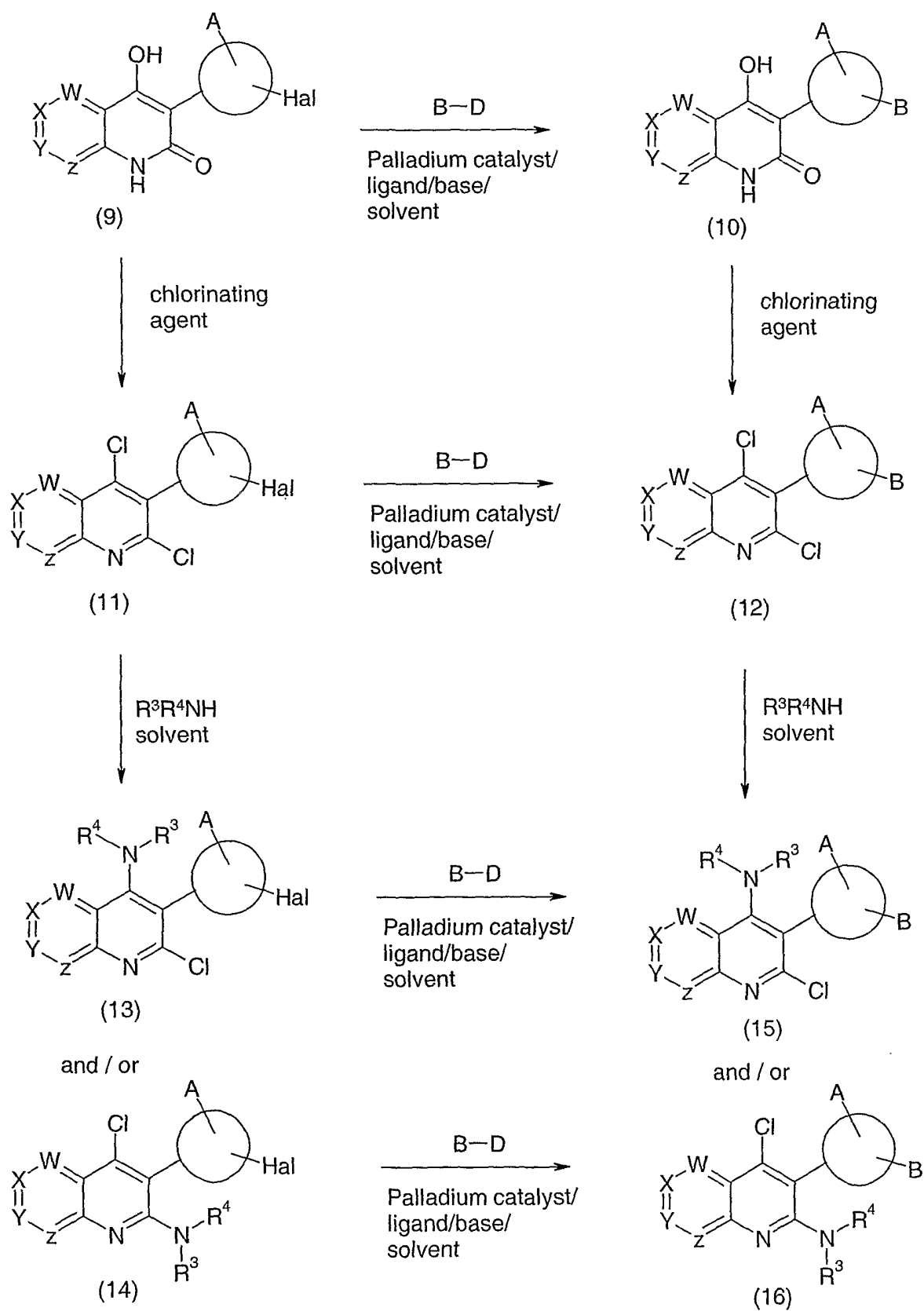
Compounds of formula (12) can be made either by cross-coupling of compounds of formula (11) using conditions for converting (9) to (10), or by chlorination of compounds of formula (10) using conditions for converting (9) to (11).

Compounds of formula (13) and (14) can be prepared by reacting compounds of formula (11) with an amine R^3R^4NH , either neat or in a suitable solvent such as DMF between room temperature, but preferably between 50 and 80°C. If compounds (13) and (14) are produced as a mixture they can be separated by suitable means such as crystallisation or chromatography under normal or reverse phase conditions.

Compounds of formula (15) and (16) can be prepared by reacting compounds of formula (12) with an amine R^3R^4NH , either neat or in a suitable solvent such as DMF between room temperature, but preferably between 50 and 80°C. If compounds (15) and (16) are produced as a mixture they can be separated by suitable means such as

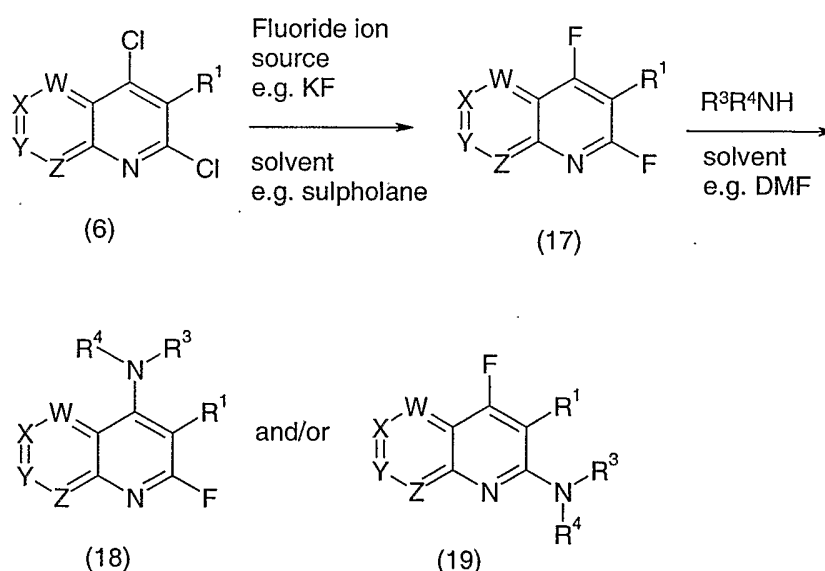
5 crystallisation or chromatography under normal or reverse phase conditions. Compounds of formula (15) and (16) can also be prepared individually from compounds of formula (13) and (14) respectively by cross-coupling using conditions for converting (9) to (10).

Scheme 2



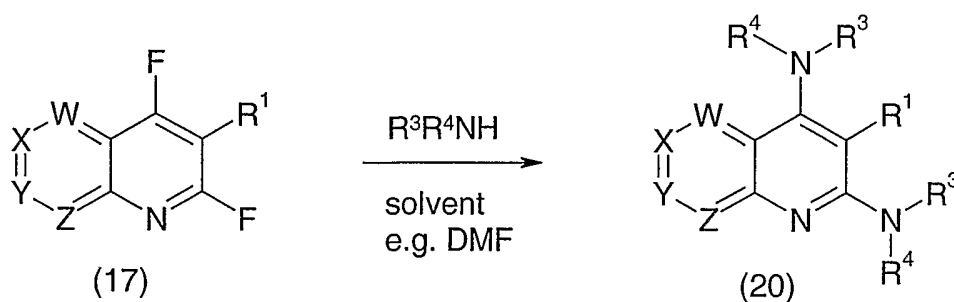
Compounds of formula (17) can be prepared as shown in Scheme 3 from compounds of formula (6) by reaction with a source of fluoride ion, such as potassium fluoride, in a suitable solvent such as sulfolane, at a temperature between 50°C and 200°C, but preferably at 80-150°C. Compounds of formula (18) and/or compounds of formula (19) can be prepared from difluoro compounds of formula (17) by reaction with an amine of formula R^3R^4NH in a suitable solvent such as DMF or CH_2Cl_2 , at a temperature of 0°C-100°C, but preferably at room temperature.

Scheme 3

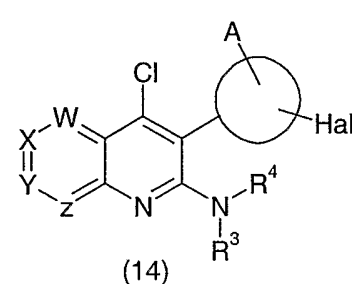
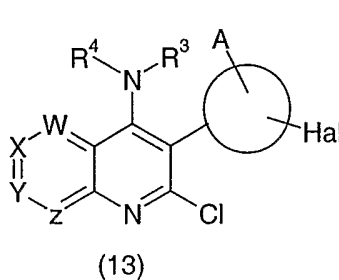
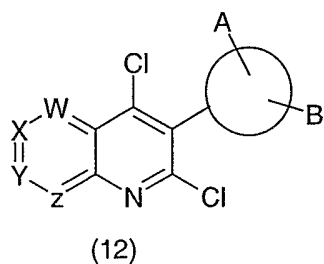
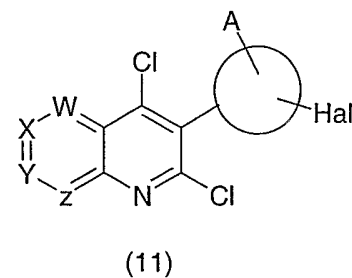
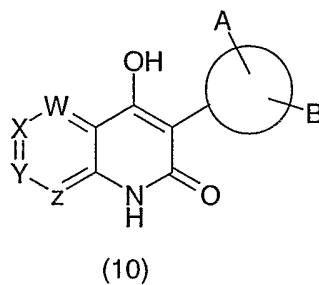
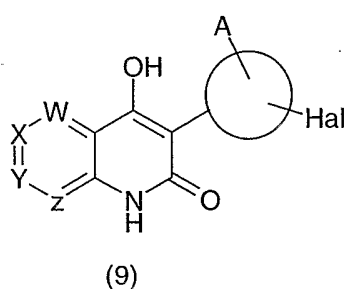
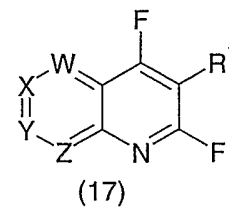
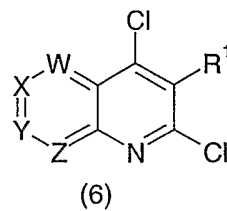
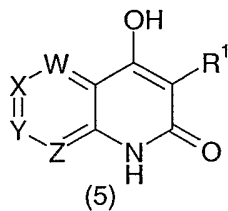
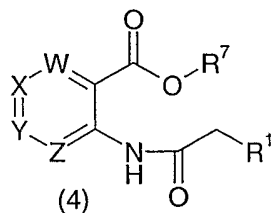


In Scheme 4 compounds of general formula (20), where the two R^3R^4N groups are identical, can be made from compounds of general formula (17) by reaction with a large excess of amine R^3R^4NH in a suitable solvent such as DMF, at a temperature between 0°C and 150°C, but preferably between room temperature and 100°C.

Scheme 4

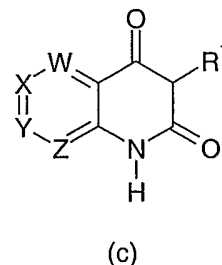
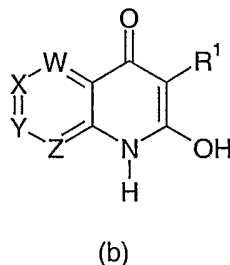
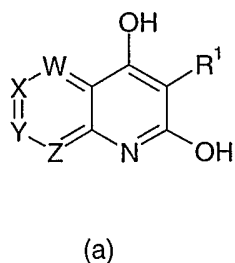


The intermediate chemicals having the general formulae (4), (5), (6), (9), (10), (11), (12), (13) (14) and (17) :



- 5 wherein W, X, Y, Z, R¹, R³, R⁴, R⁷, Hal, A and B are as defined above, are believed to be novel compounds and form a further part of this invention.

It should be noted that the intermediate of general formula (5) may exist in the tautomeric forms (a), (b) and (c) as well as in the form shown in formula (5):



- 10 The invention as defined by the general formula (5) embraces all such tautomers.

Of particular interest are the intermediates listed in Tables below. In Table 28, the compounds have the general formula (4) where R¹ is R²⁰, R⁷ is methyl, W, X, Y, Z and B have the values shown in table 28.

Table 28

Cmpd No.	B	W	X	Y	Z
1	phenyl	N	CH	CH	N
2	4-fluorophenyl	N	CH	CH	N
3	4-chlorophenyl	N	CH	CH	N
4	5-fluoro-2-pyridyl	N	CH	CH	N
5	6-fluoro-3-pyridyl	N	CH	CH	N
6	2-phenylethenyl	N	CH	CH	N
7	2-(4-fluorophenyl)ethenyl	N	CH	CH	N
8	(4-methylphenyl)ethynyl	N	CH	CH	N
9	(4-fluorophenyl)ethynyl	N	CH	CH	N
10	4-fluorophenoxy	N	CH	CH	N
11	phenylthio	N	CH	CH	N
12	phenylsulphinyl	N	CH	CH	N
13	phenylsulphonyl	N	CH	CH	N
14	phenyl	N	CH	N	N
15	4-fluorophenyl	N	CH	N	N
16	4-chlorophenyl	N	CH	N	N
17	5-fluoro-2-pyridyl	N	CH	N	N
18	6-fluoro-3-pyridyl	N	CH	N	N
19	2-phenylethenyl	N	CH	N	N
20	2-(4-fluorophenyl)ethenyl	N	CH	N	N
21	(4-methylphenyl)ethynyl	N	CH	N	N
22	(4-fluorophenyl)ethynyl	N	CH	N	N
23	4-fluorophenoxy	N	CH	N	N
24	phenylthio	N	CH	N	N
25	phenylsulphinyl	N	CH	N	N
26	Phenylsulphonyl	N	CH	N	N

Table 29

Table 29 consists of 26 compounds of the general formula (5), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2,6-difluorophenyl.

5 Table 30

Table 30 consists of 26 compounds of the general formula (5), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2-chloro-6-fluorophenyl.

10 Table 31

Table 31 consists of 26 compounds of the general formula (5), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2-chlorophenyl.

Table 32

15 Table 32 consists of 26 compounds of the general formula (5), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 5-substituted 3-fluoropyrid-2-yl.

Table 33

20 Table 33 consists of 26 compounds of the general formula (5), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 5-substituted 3-chloropyrid-2-yl.

Table 34

25 Table 34 consists of 26 compounds of the general formula (6), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2,6-difluorophenyl.

Table 35

30 Table 35 consists of 26 compounds of the general formula (6), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2-chloro-6-fluorophenyl.

Table 36

Table 36 consists of 26 compounds of the general formula (6), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2-chlorophenyl.

Table 37

Table 37 consists of 26 compounds of the general formula (6), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 5-substituted 3-fluoropyrid-2-yl.

5 Table 38

Table 38 consists of 26 compounds of the general formula (6), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 5-substituted 3-chloropyrid-2-yl.

Table 39

10 Table 39 consists of 26 compounds of the general formula (17), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2,6-difluorophenyl.

Table 40

15 Table 40 consists of 26 compounds of the general formula (17), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2-chloro-6-fluorophenyl.

Table 41

20 Table 41 consists of 26 compounds of the general formula (17), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 4-substituted 2-chlorophenyl.

Table 42

25 Table 42 consists of 26 compounds of the general formula (17), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 5-substituted 3-fluoropyrid-2-yl.

Table 43

Table 43 consists of 26 compounds of the general formula (17), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28 and R^{20} is 5-substituted 3-chloropyrid-2-yl.

30 Table 44

Table 44 consists of 26 compounds of the general formula (4), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28, R^7 is methyl and R^{20} is 4-substituted 2,6-difluorophenyl.

Table 45

Table 45 consists of 26 compounds of the general formula (4), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28, R^7 is methyl and R^{20} is 4-substituted 2-chloro-6-fluorophenyl.

5

Table 46

Table 46 consists of 26 compounds of the general formula (4), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28, R^7 is methyl and R^{20} is 4-substituted 2-chlorophenyl.

10

Table 47

Table 47 consists of 26 compounds of the general formula (4), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28, R^7 is methyl and R^{20} is 5-substituted 3-fluoropyrid-2-yl.

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Table 48

Table 48 consists of 26 compounds of the general formula (4), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28, R^7 is methyl and R^{20} is 5-substituted 3-chloropyrid-2-yl.

20

Table 49

Table 49 consists of 26 compounds of the general formula (4), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28, R^7 is ethyl and R^{20} is 4-substituted 2,6-difluorophenyl.

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Table 50

Table 50 consists of 26 compounds of the general formula (4), where R^1 is R^{20} , W, X, Y, Z and B have the values given in Table 28, R^7 is ethyl and R^{20} is 4-substituted 2-chloro-6-fluorophenyl.

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Table 51

Table 51 consists of 26 compounds of the general formula (4), where R¹ is R²⁰, W, X, Y, Z and B have the values given in Table 28, R⁷ is ethyl and R²⁰ is 4-substituted 2-chlorophenyl.

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Table 52

Table 52 consists of 26 compounds of the general formula (4), where R¹ is R²⁰, W, X, Y, Z and B have the values given in Table 28, R⁷ is ethyl and R²⁰ is 5-substituted 3-fluoropyrid-2-yl.

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Table 53

Table 53 consists of 26 compounds of the general formula (4), where R¹ is R²⁰, W, X, Y, Z and B have the values given in Table 28, R⁷ is ethyl and R²⁰ is 5-substituted 3-chloropyrid-2-yl.

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The compounds of formula (1) are active fungicides and may be used to control one or more of the following pathogens: *Pyricularia oryzae* (*Magnaporthe grisea*) on rice and wheat and other *Pyricularia* spp. on other hosts; *Puccinia triticina* (or *recondita*), *Puccinia striiformis* and other rusts on wheat, *Puccinia hordei*, *Puccinia striiformis* and other rusts on barley, and rusts on other hosts (for example turf, rye, coffee, pears, apples, peanuts, sugar beet, vegetables and ornamental plants); *Erysiphe cichoracearum* on cucurbits (for example melon); *Blumeria* (or *Erysiphe*) *graminis* (powdery mildew) on barley, wheat, rye and turf and other powdery mildews on various hosts, such as *Sphaerotheca macularis* on hops, *Sphaerotheca fusca* (*Sphaerotheca fuliginea*) on cucurbits (for example cucumber), *Leveillula taurica* on tomatoes, aubergine and green pepper, *Podosphaera leucotricha* on apples and *Uncinula necator* on vines; *Cochliobolus* spp., *Helminthosporium* spp., *Drechslera* spp. (*Pyrenophora* spp.), *Rhynchosporium* spp., *Mycosphaerella graminicola* (*Septoria tritici*) and *Phaeosphaeria nodorum* (*Stagonospora nodorum* or *Septoria nodorum*), *Pseudocercospora herpotrichoides* and *Gaeumannomyces graminis* on cereals (for example wheat, barley, rye), turf and other hosts; *Cercospora arachidicola* and *Cercosporidium personatum* on peanuts and other *Cercospora* spp. on other hosts, for example sugar beet, bananas, soya beans and rice; *Botrytis cinerea* (grey mould) on tomatoes, strawberries, vegetables, vines and other hosts and other *Botrytis* spp. on other

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hosts; *Alternaria* spp. on vegetables (for example carrots), oil-seed rape, apples, tomatoes, potatoes, cereals (for example wheat) and other hosts; *Venturia* spp. (including *Venturia inaequalis* (scab)) on apples, pears, stone fruit, tree nuts and other hosts; *Cladosporium* spp. on a range of hosts including cereals (for example wheat) and tomatoes; *Monilinia* spp. on

5 stone fruit, tree nuts and other hosts; *Didymella* spp. on tomatoes, turf, wheat, cucurbits and other hosts; *Phoma* spp. on oil-seed rape, turf, rice, potatoes, wheat and other hosts; *Aspergillus* spp. and *Aureobasidium* spp. on wheat, lumber and other hosts; *Ascochyta* spp. on peas, wheat, barley and other hosts; *Stemphylium* spp. (*Pleospora* spp.) on apples, pears, onions and other hosts; summer diseases (for example bitter rot (*Glomerella cingulata*), black

10 rot or frog-eye leaf spot (*Botryosphaeria obtusa*), Brooks fruit spot (*Mycosphaerella pomi*), Cedar apple rust (*Gymnosporangium juniperi-virginianae*), sooty blotch (*Gloeodes pomigena*), flyspeck (*Schizothyrium pomi*) and white rot (*Botryosphaeria dothidea*)) on apples and pears; *Plasmopara viticola* on vines; other downy mildews, such as *Bremia lactucae* on lettuce, *Peronospora* spp. on soybeans, tobacco, onions and other hosts,

15 *Pseudoperonospora humuli* on hops and *Pseudoperonospora cubensis* on cucurbits; *Pythium* spp. (including *Pythium ultimum*) on turf and other hosts; *Phytophthora infestans* on potatoes and tomatoes and other *Phytophthora* spp. on vegetables, strawberries, avocado, pepper, ornamentals, tobacco, cocoa and other hosts; *Thanatephorus cucumeris* on rice and turf and other *Rhizoctonia* spp. on various hosts such as wheat and barley, peanuts, vegetables, cotton

20 and turf; *Sclerotinia* spp. on turf, peanuts, potatoes, oil-seed rape and other hosts; *Sclerotium* spp. on turf, peanuts and other hosts; *Gibberella fujikuroi* on rice; *Colletotrichum* spp. on a range of hosts including turf, coffee and vegetables; *Laetisaria fuciformis* on turf; *Mycosphaerella* spp. on bananas, peanuts, citrus, pecans, papaya and other hosts; *Diaporthe* spp. on citrus, soybean, melon, pears, lupin and other hosts; *Elsinoe* spp. on citrus, vines,

25 olives, pecans, roses and other hosts; *Verticillium* spp. on a range of hosts including hops, potatoes and tomatoes; *Pyrenopeziza* spp. on oil-seed rape and other hosts; *Oncobasidium theobromae* on cocoa causing vascular streak dieback; *Fusarium* spp., *Typhula* spp., *Microdochium nivale*, *Ustilago* spp., *Urocystis* spp., *Tilletia* spp. and *Claviceps purpurea* on a variety of hosts but particularly wheat, barley, turf and maize; *Ramularia* spp. on sugar

30 beet, barley and other hosts; post-harvest diseases particularly of fruit (for example *Penicillium digitatum*, *Penicillium italicum* and *Trichoderma viride* on oranges, *Colletotrichum musae* and *Gloeosporium musarum* on bananas and *Botrytis cinerea* on grapes); other pathogens on vines, notably *Eutypa lata*, *Guignardia bidwellii*, *Phellinus*

igniarius, *Phomopsis viticola*, *Pseudopeziza tracheiphila* and *Stereum hirsutum*; other pathogens on trees (for example *Lophodermium seeditiosum*) or lumber, notably *Cephaloascus fragrans*, *Ceratocystis* spp., *Ophiostoma piceae*, *Penicillium* spp., *Trichoderma pseudokoningii*, *Trichoderma viride*, *Trichoderma harzianum*, *Aspergillus niger*, *Leptographium lindbergi* and *Aureobasidium pullulans*; and fungal vectors of viral diseases (for example *Polymyxa graminis* on cereals as the vector of barley yellow mosaic virus (BYMV) and *Polymyxa betae* on sugar beet as the vector of rhizomania).

A compound of formula (1) may move acropetally, basipetally or locally in plant tissue to be active against one or more fungi. Moreover, a compound of formula (1) may be volatile enough to be active in the vapour phase against one or more fungi on the plant.

The invention therefore provides a method of combating or controlling phytopathogenic fungi which comprises applying a fungicidally effective amount of a compound of formula (1), or a composition containing a compound of formula (1), to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other plant growth medium, e.g. nutrient solution.

The term "plant" as used herein includes seedlings, bushes and trees. Furthermore, the fungicidal method of the invention includes protectant, curative, systemic, eradicator and antisporeulant treatments.

The compounds of formula (1) are preferably used for agricultural, horticultural and turfgrass purposes in the form of a composition.

In order to apply a compound of formula (1) to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other growth medium, a compound of formula (1) is usually formulated into a composition which includes, in addition to the compound of formula (1), a suitable inert diluent or carrier and, optionally, a surface active agent (SFA). SFAs are chemicals that are able to modify the properties of an interface (for example, liquid/solid, liquid/air or liquid/liquid interfaces) by lowering the interfacial tension and thereby leading to changes in other properties (for example dispersion, emulsification and wetting). It is preferred that all compositions (both solid and liquid formulations) comprise, by weight, 0.0001 to 95%, more preferably 1 to 85%, for example 5 to 60%, of a compound of formula (1). The composition is generally used for the control of fungi such that a compound of formula (1) is applied at a rate of from 0.1g to 10kg per hectare, preferably from 1g to 6kg per hectare, more preferably from 1g to 1kg per hectare.

When used in a seed dressing, a compound of formula (1) is used at a rate of 0.0001g to 10g (for example 0.001g or 0.05g), preferably 0.005g to 10g, more preferably 0.005g to 4g, per kilogram of seed.

In another aspect the present invention provides a fungicidal composition comprising
5 a fungicidally effective amount of a compound of formula (1) and a suitable carrier or diluent therefor.

In a still further aspect the invention provides a method of combating and controlling fungi at a locus, which comprises treating the fungi, or the locus of the fungi with a fungicidally effective amount of a composition comprising a compound of formula (1).

10 The compositions can be chosen from a number of formulation types, including dustable powders (DP), soluble powders (SP), water soluble granules (SG), water dispersible granules (WG), wettable powders (WP), granules (GR) (slow or fast release), soluble concentrates (SL), oil miscible liquids (OL), ultra low volume liquids (UL), emulsifiable concentrates (EC), dispersible concentrates (DC), emulsions (both oil in water (EW) and
15 water in oil (EO)), micro-emulsions (ME), suspension concentrates (SC), aerosols, fogging/smoke formulations, capsule suspensions (CS) and seed treatment formulations. The formulation type chosen in any instance will depend upon the particular purpose envisaged and the physical, chemical and biological properties of the compound of formula (1).

Dustable powders (DP) may be prepared by mixing a compound of formula (1) with
20 one or more solid diluents (for example natural clays, kaolin, pyrophyllite, bentonite, alumina, montmorillonite, kieselguhr, chalk, diatomaceous earths, calcium phosphates, calcium and magnesium carbonates, sulphur, lime, flours, talc and other organic and inorganic solid carriers) and mechanically grinding the mixture to a fine powder.

Soluble powders (SP) may be prepared by mixing a compound of formula (1) with
25 one or more water-soluble inorganic salts (such as sodium bicarbonate, sodium carbonate or magnesium sulphate) or one or more water-soluble organic solids (such as a polysaccharide) and, optionally, one or more wetting agents, one or more dispersing agents or a mixture of said agents to improve water dispersibility/solubility. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water soluble granules (SG).

30 Wettable powders (WP) may be prepared by mixing a compound of formula (1) with one or more solid diluents or carriers, one or more wetting agents and, preferably, one or more dispersing agents and, optionally, one or more suspending agents to facilitate the

dispersion in liquids. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water dispersible granules (WG).

Granules (GR) may be formed either by granulating a mixture of a compound of formula (1) and one or more powdered solid diluents or carriers, or from pre-formed blank granules by absorbing a compound of formula (1) (or a solution thereof, in a suitable agent) in a porous granular material (such as pumice, attapulgate clays, fuller's earth, kieselguhr, diatomaceous earths or ground corn cobs) or by adsorbing a compound of formula (1) (or a solution thereof, in a suitable agent) on to a hard core material (such as sands, silicates, mineral carbonates, sulphates or phosphates) and drying if necessary. Agents which are commonly used to aid absorption or adsorption include solvents (such as aliphatic and aromatic petroleum solvents, alcohols, ethers, ketones and esters) and sticking agents (such as polyvinyl acetates, polyvinyl alcohols, dextrans, sugars and vegetable oils). One or more other additives may also be included in granules (for example an emulsifying agent, wetting agent or dispersing agent).

Dispersible Concentrates (DC) may be prepared by dissolving a compound of formula (1) in water or an organic solvent, such as a ketone, alcohol or glycol ether. These solutions may contain a surface active agent (for example to improve water dilution or prevent crystallisation in a spray tank).

Emulsifiable concentrates (EC) or oil-in-water emulsions (EW) may be prepared by dissolving a compound of formula (1) in an organic solvent (optionally containing one or more wetting agents, one or more emulsifying agents or a mixture of said agents). Suitable organic solvents for use in ECs include aromatic hydrocarbons (such as alkylbenzenes or alkylnaphthalenes, exemplified by SOLVESSO 100, SOLVESSO 150 and SOLVESSO 200; SOLVESSO is a Registered Trade Mark), ketones (such as cyclohexanone or methylcyclohexanone), alcohols (such as benzyl alcohol, furfuryl alcohol or butanol), *N*-alkylpyrrolidones (such as *N*-methylpyrrolidone or *N*-octylpyrrolidone), dimethyl amides of fatty acids (such as C₈-C₁₀ fatty acid dimethylamide) and chlorinated hydrocarbons. An EC product may spontaneously emulsify on addition to water, to produce an emulsion with sufficient stability to allow spray application through appropriate equipment. Preparation of an EW involves obtaining a compound of formula (1) either as a liquid (if it is not a liquid at room temperature, it may be melted at a reasonable temperature, typically below 70°C) or in solution (by dissolving it in an appropriate solvent) and then emulsifying the resultant liquid or solution into water containing one or more SFAs, under high shear, to produce an

emulsion. Suitable solvents for use in EWs include vegetable oils, chlorinated hydrocarbons (such as chlorobenzenes), aromatic solvents (such as alkylbenzenes or alkyl naphthalenes) and other appropriate organic solvents that have a low solubility in water.

Microemulsions (ME) may be prepared by mixing water with a blend of one or more solvents with one or more SFAs, to produce spontaneously a thermodynamically stable isotropic liquid formulation. A compound of formula (1) is present initially in either the water or the solvent/SFA blend. Suitable solvents for use in MEs include those hereinbefore described for use in ECs or in EWs. An ME may be either an oil-in-water or a water-in-oil system (which system is present may be determined by conductivity measurements) and may be suitable for mixing water-soluble and oil-soluble pesticides in the same formulation. An ME is suitable for dilution into water, either remaining as a microemulsion or forming a conventional oil-in-water emulsion.

Suspension concentrates (SC) may comprise aqueous or non-aqueous suspensions of finely divided insoluble solid particles of a compound of formula (1). SCs may be prepared by ball or bead milling the solid compound of formula (1) in a suitable medium, optionally with one or more dispersing agents, to produce a fine particle suspension of the compound. One or more wetting agents may be included in the composition and a suspending agent may be included to reduce the rate at which the particles settle. Alternatively, a compound of formula (1) may be dry milled and added to water, containing agents hereinbefore described, to produce the desired end product.

Aerosol formulations comprise a compound of formula (1) and a suitable propellant (for example *n*-butane). A compound of formula (1) may also be dissolved or dispersed in a suitable medium (for example water or a water miscible liquid, such as *n*-propanol) to provide compositions for use in non-pressurised, hand-actuated spray pumps.

A compound of formula (1) may be mixed in the dry state with a pyrotechnic mixture to form a composition suitable for generating, in an enclosed space, a smoke containing the compound.

Capsule suspensions (CS) may be prepared in a manner similar to the preparation of EW formulations but with an additional polymerisation stage such that an aqueous dispersion of oil droplets is obtained, in which each oil droplet is encapsulated by a polymeric shell and contains a compound of formula (1) and, optionally, a carrier or diluent therefor. The polymeric shell may be produced by either an interfacial polycondensation reaction or by a coacervation procedure. The compositions may provide for controlled release of the

compound of formula (1) and they may be used for seed treatment. A compound of formula (1) may also be formulated in a biodegradable polymeric matrix to provide a slow, controlled release of the compound.

5 A composition may include one or more additives to improve the biological performance of the composition (for example by improving wetting, retention or distribution on surfaces; resistance to rain on treated surfaces; or uptake or mobility of a compound of formula (1)). Such additives include surface active agents, spray additives based on oils, for example certain mineral oils or natural plant oils (such as soy bean and rape seed oil), and blends of these with other bio-enhancing adjuvants (ingredients which may aid or modify the
10 action of a compound of formula (1)).

A compound of formula (1) may also be formulated for use as a seed treatment, for example as a powder composition, including a powder for dry seed treatment (DS), a water soluble powder (SS) or a water dispersible powder for slurry treatment (WS), or as a liquid composition, including a flowable concentrate (FS), a solution (LS) or a capsule suspension
15 (CS). The preparations of DS, SS, WS, FS and LS compositions are very similar to those of, respectively, DP, SP, WP, SC and DC compositions described above. Compositions for treating seed may include an agent for assisting the adhesion of the composition to the seed (for example a mineral oil or a film-forming barrier).

Wetting agents, dispersing agents and emulsifying agents may be SFAs of the
20 cationic, anionic, amphoteric or non-ionic type.

Suitable SFAs of the cationic type include quaternary ammonium compounds (for example cetyltrimethyl ammonium bromide), imidazolines and amine salts.

Suitable anionic SFAs include alkali metals salts of fatty acids, salts of aliphatic monoesters of sulphuric acid (for example sodium lauryl sulphate), salts of sulphonated
25 aromatic compounds (for example sodium dodecylbenzenesulphonate, calcium dodecylbenzenesulphonate, butylnaphthalene sulphonate and mixtures of sodium di-*isopropyl*- and tri-*isopropyl*-naphthalene sulphonates), ether sulphates, alcohol ether sulphates (for example sodium laureth-3-sulphate), ether carboxylates (for example sodium laureth-3-carboxylate), phosphate esters (products from the reaction between one or more fatty alcohols and phosphoric acid (predominately mono-esters) or phosphorus pentoxide (predominately di-esters),
30 for example the reaction between lauryl alcohol and tetraphosphoric acid; additionally these products may be ethoxylated), sulphosuccinamates, paraffin or olefine sulphonates, taurates and lignosulphonates.

Suitable SFAs of the amphoteric type include betaines, propionates and glycines.

Suitable SFAs of the non-ionic type include condensation products of alkylene oxides, such as ethylene oxide, propylene oxide, butylene oxide or mixtures thereof, with fatty alcohols (such as oleyl alcohol or cetyl alcohol) or with alkylphenols (such as octylphenol, nonylphenol or octylcresol); partial esters derived from long chain fatty acids or hexitol anhydrides; condensation products of said partial esters with ethylene oxide; block polymers (comprising ethylene oxide and propylene oxide); alkanolamides; simple esters (for example fatty acid polyethylene glycol esters); amine oxides (for example lauryl dimethyl amine oxide); and lecithins.

10 Suitable suspending agents include hydrophilic colloids (such as polysaccharides, polyvinylpyrrolidone or sodium carboxymethylcellulose) and swelling clays (such as bentonite or attapulgite).

15 A compound of formula (1) may be applied by any of the known means of applying fungicidal compounds. For example, it may be applied, formulated or unformulated, to any part of the plant, including the foliage, stems, branches or roots, to the seed before it is planted or to other media in which plants are growing or are to be planted (such as soil surrounding the roots, the soil generally, paddy water or hydroponic culture systems), directly or it may be sprayed on, dusted on, applied by dipping, applied as a cream or paste formulation, applied as a vapour or applied through distribution or incorporation of a composition (such as a granular composition or a composition packed in a water-soluble bag) in soil or an aqueous environment.

20 A compound of formula (1) may also be injected into plants or sprayed onto vegetation using electrodynamic spraying techniques or other low volume methods, or applied by land or aerial irrigation systems.

25 Compositions for use as aqueous preparations (aqueous solutions or dispersions) are generally supplied in the form of a concentrate containing a high proportion of the active ingredient, the concentrate being added to water before use. These concentrates, which may include DCs, SCs, ECs, EWs, MEs SGs, SPs, WPs, WGs and CSs, are often required to withstand storage for prolonged periods and, after such storage, to be capable of addition to water to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. Such aqueous preparations may contain varying amounts of a compound of formula (1) (for example 0.0001 to 10%, by weight) depending upon the purpose for which they are to be used.

30

A compound of formula (1) may be used in mixtures with fertilisers (for example nitrogen-, potassium- or phosphorus-containing fertilisers). Suitable formulation types include granules of fertiliser. The mixtures suitably contain up to 25% by weight of the compound of formula (1).

5 The invention therefore also provides a fertiliser composition comprising a fertiliser and a compound of formula (1).

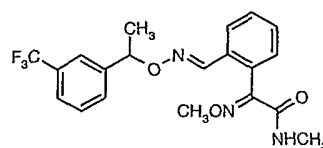
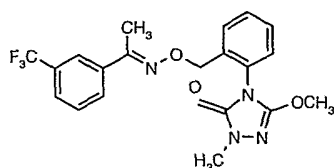
 The compositions of this invention may contain other compounds having biological activity, for example micronutrients or compounds having similar or complementary fungicidal activity or which possess plant growth regulating, herbicidal, insecticidal,
10 nematicidal or acaricidal activity.

 By including another fungicide, the resulting composition may have a broader spectrum of activity or a greater level of intrinsic activity than the compound of formula (1) alone. Further the other fungicide may have a synergistic effect on the fungicidal activity of the compound of formula (1).

15 The compound of formula (1) may be the sole active ingredient of the composition or it may be admixed with one or more additional active ingredients such as a pesticide, fungicide, synergist, herbicide or plant growth regulator where appropriate. An additional active ingredient may: provide a composition having a broader spectrum of activity or increased persistence at a locus; synergise the activity or complement the activity (for
20 example by increasing the speed of effect or overcoming repellency) of the compound of formula (1); or help to overcome or prevent the development of resistance to individual components. The particular additional active ingredient will depend upon the intended utility of the composition.

 Examples of fungicidal compounds which may be included in the composition of the
25 invention are AC 382042 (*N*-(1-cyano-1,2-dimethylpropyl)-2-(2,4-dichlorophenoxy) propionamide), acibenzolar-*S*-methyl, alanycarb, aldimorph, anilazine, azaconazole, azafenidin, azoxystrobin, benalaxyl, benomyl, benthiavalicarb, biloxazol, bitertanol, blasticidin *S*, boscalid (new name for nicobifen), bromuconazole, bupirimate, captafol, captan, carbendazim, carbendazim chlorhydrate, carboxin, carpropamid, carvone, CGA 41396, CGA
30 41397, chinomethionate, chlorbenzthiazole, chlorothalonil, chlorozolate, clozylacon, copper containing compounds such as copper oxychloride, copper oxyquinolate, copper sulphate, copper tallate, and Bordeaux mixture, cyamidazosulfamid, cyazofamid (IKF-916), cyflufenamid, cymoxanil, cyproconazole, cyprodinil, debacarb, di-2-pyridyl disulphide

- 1,1'-dioxide, dichlofluanid, diclocymet, diclomezine, dicloran, diethofencarb, difenoconazole, difenzoquat, diflumetorim, *O,O*-di-*iso*-propyl-*S*-benzyl thiophosphate, dimefluazole, dimetconazole, dimethirimol, dimethomorph, dimoxystrobin, diniconazole, dinocap, dithianon, dodecyl dimethyl ammonium chloride, dodemorph, dodine, doguadine, edifenphos, epoxiconazole, ethaboxam, ethirimol, ethyl (*Z*)-*N*-benzyl-*N*[(methyl(methyl-thioethylideneaminooxycarbonyl)amino]thio)- β -alaninate, etridiazole, famoxadone, fenamidone, fenarimol, fenbuconazole, fenfuram, fenhexamid, fenoxanil (AC 382042), fempiclonil, fenpropidin, fenpropimorph, fentin acetate, fentin hydroxide, ferbam, ferimzone, fluazinam, fludioxonil, flumetover, flumorph, fluoroimide, fluoxastrobin, fluquinconazole, flusilazole, flusulfamide, flutolanil, flutriafol, folpet, fosetyl-aluminium, fuberidazole, furalaxyl, furametpyr, guazatine, hexaconazole, hydroxyisoxazole, hymexazole, imazalil, imibenconazole, iminoctadine, iminoctadine triacetate, ipconazole, iprobenfos, iprodione, iprovalicarb, isopropanyl butyl carbamate, isoprothiolane, kasugamycin, kresoxim-methyl, LY186054, LY211795, LY 248908, mancozeb, maneb, mefenoxam, mepanipyrim, mepronil, metalaxyl, metalaxyl M, metconazole, metiram, metiram-zinc, metominostrobin, metra-fenone, MON65500 (*N*-allyl-4,5-dimethyl-2-trimethylsilylthiophene-3-carboxamide), myclobutanil, NTN0301, neoasozin, nickel dimethyldithiocarbamate, nitrothale-isopropyl, nuarimol, ofurace, organomercury compounds, orysastrobin, oxadixyl, oxasulfuron, oxolinic acid, oxpoconazole, oxycarboxin, pefurazoate, penconazole, pencycuron, phenazin oxide, phosphorus acids, phthalide, picoxystrobin, polyoxin D, polyram, probenazole, prochloraz, procymidone, propamocarb, propamocarb hydrochloride, propiconazole, propineb, propionic acid, proquinazid, prothioconazole, pyraclostrobin, pyrazophos, pyrifenox, pyrimethanil, pyroquilon, pyroxyfur, pyrrolnitrin, quaternary ammonium compounds, quinomethionate, quinoxifen, quintozone, silthiofam (MON 65500), *S*-imazalil, simeconazole, sipconazole, sodium pentachlorophenate, spiroxamine, streptomycin, sulphur, tebuconazole, tecloftalam, tecnazene, tetraconazole, thiabendazole, thifluzamide, 2-(thiocyanomethylthio)-benzothiazole, thiophanate-methyl, thiram, tiadinil, timibenconazole, tolclofos-methyl, tolylfluanid, triadimefon, triadimenol, triazbutil, triazoxide, tricyclazole, tridemorph, trifloxystrobin, triflumizole, triforine, triticonazole, validamycin A, vapam, vinclozolin, XRD-563, zineb, ziram, zoxamide and compounds of the formulae:



The compounds of formula (1) may be mixed with soil, peat or other rooting media for the protection of plants against seed-borne, soil-borne or foliar fungal diseases.

Some mixtures may comprise active ingredients, which have significantly different physical, chemical or biological properties such that they do not easily lend themselves to the same conventional formulation type. In these circumstances other formulation types may be prepared. For example, where one active ingredient is a water insoluble solid and the other a water insoluble liquid, it may nevertheless be possible to disperse each active ingredient in the same continuous aqueous phase by dispersing the solid active ingredient as a suspension (using a preparation analogous to that of an SC) but dispersing the liquid active ingredient as an emulsion (using a preparation analogous to that of an EW). The resultant composition is a suspoemulsion (SE) formulation.

The invention is illustrated by the following Examples in which the following abbreviations are used:

ml = millilitres

g = grammes

ppm = parts per million

s = singlet

d = doublet

t = triplet

q = quartet

m = multiplet

b = broad

f = fine

THF = tetrahydrofuran

DCM = dichloromethane

DMF = *N,N*-dimethylformamide

DMSO = dimethylsulphoxide

DMAP = 4-dimethylaminopyridine

NMR = nuclear magnetic resonance

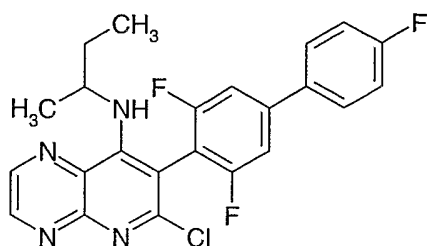
HPLC = high performance liquid

chromatography

EXAMPLES

EXAMPLE 1

This example illustrates the preparation of sec-butyl-[6-chloro-7-[(4-fluorophenyl)-2,6-difluorophenyl]-pyrido[2,3-b]pyrazin-8-yl]-amine of the formula below, Compound 3.002.



3.002

Step 1: The preparation of 2,6-difluoro-4-bromobenzyl methanesulphonate

2,6-difluoro-4-bromobenzyl alcohol (9.50 g) and triethylamine (5.0 g) were dissolved in THF cooled to 10°C with stirring. Methanesulphonyl chloride (4.8 g) was added in a solution of THF (10ml) over 10 minutes, and a white solid precipitated from the solution. The reaction was then warmed to room temperature for one hour and then the solid was collected and washed with diethyl ether. The filtrate was evaporated to give 2,6-difluoro-4-bromobenzyl methanesulphonate (13.0 g) as a golden oil which slowly crystallised.

¹H NMR (CDCl₃) δ ppm: 3.05 (s,3H), 5.3 (s,2H), 7.15 (t,2H).

10

Step 2: The preparation of 2,4-difluoro-4-bromobenzyl cyanide

Potassium cyanide (2.8 g) was dissolved in water and was added to a stirred solution of the product of Step 1 (13.0 g) in ethanol (100 ml). The reaction was refluxed for 2 hours, and was then cooled and the solvent evaporated to give a sludge. Water was added and the mixture was extracted with DCM and dried over magnesium sulphate. The solution was evaporated and to give a sludge which was triturated with a small amount of diethyl ether to give 2,4-difluoro-4-bromobenzyl cyanide as a light brown solid (5.2 g).

¹H NMR (CDCl₃) δ ppm: 3.7 (s,2H), 7.18 (t,2H).

Step 3: The preparation of 2,6-difluoro-4-bromophenyl acetic acid

The product from Step 2 (4.2 g) was dissolved in a mixture of water (25 ml) and concentrated sulphuric acid (25 ml), and the reaction was refluxed for 3 hours. The reaction was then cooled and the solid collected was washed with water and dried to give 2,6-difluoro-4-bromophenyl acetic acid as a light brown crystalline solid (3.8 g).

¹H NMR (CDCl₃) δ ppm: 3.75 (s,2H), 7.1 (t,2H).

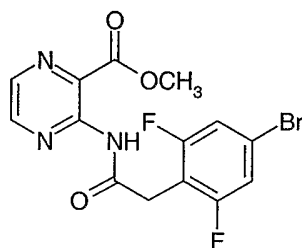
25

Step 4: The preparation of 2,6-difluoro-4-bromophenyl acetyl chloride

The product from Step 3 (3.6 g) was added portionwise to thionyl chloride (10 ml), pre-heated to 60°C, with two drops of DMF. Reaction was immediate and after the addition the reaction was refluxed for a further 1 hour, and was then cooled and evaporated to give the acid chloride as a brown liquid (3.6 g), which was used in the next reaction without further purification.

Step 5: The preparation of methyl 3-[2-(4-bromo-2,6-difluoro-phenyl)-acetyl-amino]-pyrazine-2-carboxylate:

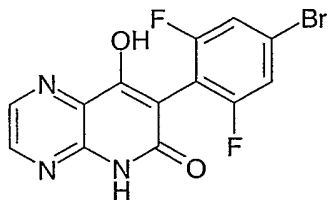
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A solution of the crude acid chloride from Step 4 (3.6 g) in DCM (10ml) was added dropwise to a stirred solution of methyl 2-aminopyrazine carboxylate (2.2 g) and pyridine (5 ml) stirred at 10°C in DCM. The reaction was stirred for 15 hours at room temperature, and the solvent was evaporated and water was added, followed by extraction with ethyl acetate. The organic fraction was washed with water and aqueous sodium carbonate, followed by dilute hydrochloric acid. The ethyl acetate was dried over magnesium sulphate and evaporated to give a dark sludge, which was triturated with diethyl ether, and methyl 3-[2-(4-bromo-2,6-difluoro-phenyl)-acetyl-amino]-pyrazine-2-carboxylate was isolated as a buff solid (2.9 g).

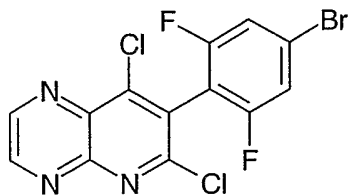
¹H NMR (CDCl₃) δ ppm: 4.0 (s,2H), 4.05 (s,3H), 7.15 (dd,2H), 8.4 (d,1H), 8.6 (d, 1H).

Step 6: The preparation of 7-(4-bromo-2,6-difluoro-phenyl)-8-hydroxy-5H-pyrido[2,3-]pyrazin-6-one:



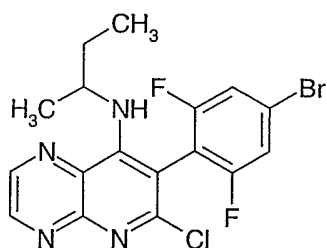
- The product from Step 5 (2.9 g) and potassium carbonate (2.1 g) in dry DMF (20 ml) were heated to 100°C (oil bath) for 4 hours, giving a yellow suspension. The solvent was evaporated to dryness and the dark sludge was triturated with diethyl ether, and the pale green solid collected. This solid was dissolved in water and acidified with 4M hydrochloric acid, and the precipitated solid was collected and dried to give 7-(4-bromo-2,6-difluoro-phenyl)-8-hydroxy-5H-pyrido[2,3-]pyrazin-6-one as a buff solid (1.6 g).
- ¹H NMR (CDCl₃) δ ppm: 7.3 (d,2H), 8.55 (d,1H), 8.65 (d,1H).

Step 7: The preparation of 7-(4-bromo-2,6-difluoro-phenyl)-6,8-dichloro-pyrido[2,3-b]pyrazine



- The product from Step 6 (0.353 g) and phosphorus oxychloride (3 ml) were mixed together at room temperature and then refluxed with stirring for 6 hours. The reaction was cooled and evaporated to dryness and water and DCM were added.
- The DCM extract was washed with aqueous sodium carbonate, dried with magnesium sulphate, and evaporated to give an oil which was purified by flash column chromatography on silica gel eluting with diethyl ether to give 7-(4-bromo-2,6-difluoro-phenyl)-6,8-dichloro-pyrido[2,3-b]pyrazine as a reddish solid (0.205 g), which was used without further purification.

Step 8: The preparation of [7-(4-Bromo-2,6-difluoro-phenyl)-6-chloro-pyrido[2,3-b]pyrazin-8-yl]-sec-butyl-amine



- 5 The product from Step 7 (0.205 g) and s-butylamine (1.0 ml) were mixed together in a sealed tube and were stirred at room temperature for 4 days. The reaction mixture was evaporated to give a sludge, which was then purified by flash column chromatography on silica gel eluting with diethyl ether:hexane 1:2, and then diethyl ether:hexane 4:1, to give [7-(4-Bromo-2,6-difluoro-phenyl)-6-chloro-pyrido[2,3-b]pyrazin-8-yl]-sec-butyl-amine as a yellow solid
- 10 (0.095 g).
- ¹H NMR (CDCl₃) δ ppm: 0.8 (t,3H), 1.1 (d,3H), 1.45 (m,2H), 3.15 (m,2H), 6.95 (bd,1H), 7.3 (d,2H), 8.7 (d,1H), 9.0 (d,1H).

- Step 9: The preparation of sec-butyl-[6-chloro-7-[(4-fluorophenyl)-2,6-difluorophenyl]-pyrido[2,3-b]pyrazin-8-yl]-amine, Compound 3.002
- 15

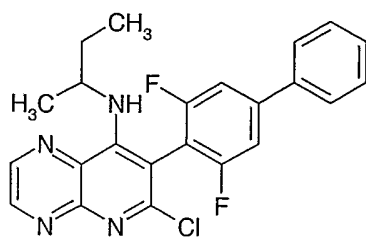
The product from Step 8 (0.027 g), 4-fluorophenyl boronic acid (0.012 g), potassium carbonate (0.020 g) and tetrakis(triphenylphosphine)palladium (0.001 g) were mixed and brought to reflux for 6 hours in toluene (2.0 ml). The reaction was cooled and evaporated and the crude product was dissolved in diethyl ether and then purified by flash column

20 chromatography on silica gel eluting with diethyl ether, to give the title product as a white gum (0.010 g).

¹H NMR (CDCl₃) δ ppm: 0.7 (t,3H), 1.1 (d,3H), 1.45 (m,2H), 3.2 (m,1H), 6.95 (bd,1H), 7.15 (d,2H), 7.2 (d,2H), 7.65 (m,2H), 8.7 (d,1H), 9.0 (d,1H).

25 EXAMPLE 2

This example illustrates the preparation of sec-butyl-[6-chloro-7-[phenyl-2,6-difluorophenyl]-pyrido[2,3-b]pyrazin-8-yl]-amine, Compound 2.002



2.002

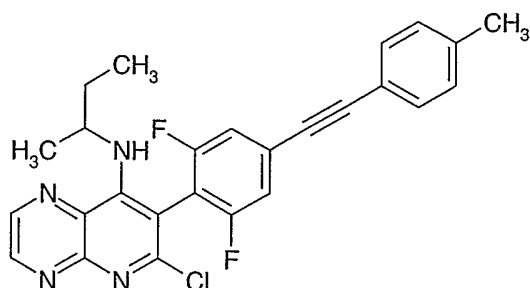
The compound was prepared analogous to Step 9 from Example 1 from the product of Step 8 of Example 1, but the coupling reaction was carried out with phenyl boronic acid instead of 4-fluorophenyl boronic acid.

^1H NMR (CDCl_3) δ ppm: 0.75 (t,3H), 1.1 (d,3H), 1.45 (m,2H), 3.2 (m,1H), 6.95 (bd,1H), 7.3 (d,2H), 7.45-7.5 (m,3H), 7.65 (d,2H), 8.65 (fd,1H), 9.0 (fd,1H).

EXAMPLE 3

10

This example illustrates the preparation of sec-butyl-[6-chloro-7-(2,6-difluoro-(4-methylphenylethynyl)-phenyl)-pyrido[2,3-b]pyrazin-8-yl]-amine of the formula below, Compound 9.002.



9.002

15

[7-(4-Bromo-2,6-difluoro-phenyl)-6-chloro-pyrido[2,3-b]pyrazin-8-yl]-sec-butyl-amine (0.030 g), 4-methylphenyl acetylene (0.016 g), cuprous iodide (0.001 g), dichlorobis (triphenylphosphine)palladium (0.003 g) and triethylamine (5 ml) were refluxed for 7 hours. The reaction was cooled and evaporated to give a sludge, which was taken up in diethyl ether and purified by flash column chromatography on silica gel eluting with diethyl ether, to give the title compound as a gum (0.008 g).

^1H NMR (CDCl_3) δ ppm: 0.75 (t,3H), 1.05 (d,3H), 1.45 (m,1H), 2.4 (s,3H), 3.15 (m,1H), 6.95 (bd,1H), 7.2 (d,4H), 7.45 (d,2H), 8.15 (bs,1H), 9.0 (bs,1H).

EXAMPLE 4

This Example illustrates the fungicidal properties of the compounds of the general formula (1).

5 *Septoria tritici* (leaf blotch): Conidia of the fungus from cryogenic storage were directly mixed into nutrient broth (PDB potato dextrose broth). After placing a (DMSO) solution of the test compounds into a microtiter plate (96-well format) the nutrient broth containing the fungal spores was added. The test plates were incubated at 24 C and the inhibition of growth was determined photometrically after 72 hours.

10 *Pyricularia oryzae* (rice blast): Conidia of the fungus from cryogenic storage were directly mixed into nutrient broth (PDB potato dextrose broth). After placing a (DMSO) solution of the test compounds into a microtiter plate (96-well format) the nutrient broth containing the fungal spores was added. The test plates were incubated at 24° C and the inhibition of growth was determined photometrically after 72 hours.

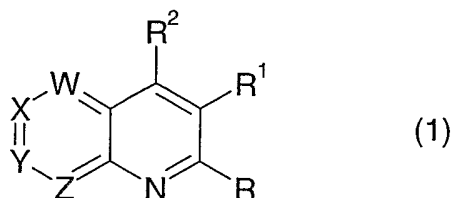
15 The following compounds gave greater than 60% control of disease:

Septoria tritici: 2.002

Pyricularia oryzae: 2.002

CLAIMS

1. The compound of the general formula (1):



- 5 wherein

W, X, Y and Z can be N or CR⁸, with at least one and no more than three of W, X, Y and Z being N, but excluding compounds where W, X, Y = N and Z = CR⁸, and X, Y, Z = N and Z = CR⁸;

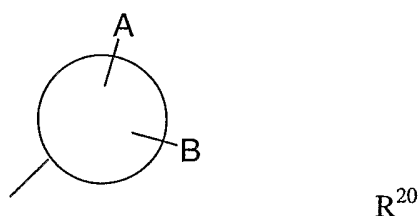
- R⁸ is H, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy or halo(C₁₋₄)alkyl, CN, C₁₋₄alkylthio, C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, aryl, heteroaryl, halo(C₁₋₆)alkoxy, halo(C₁₋₄)alkylthio, C₂₋₄alkenyl, C₂₋₄alkynyl, C₂₋₆cycloalkyl, or NR³R⁴;

R is H, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, cyano, halogen or NR³R⁴;

R² is halo or NR³R⁴;

R¹ is an aryl or heteroaryl ring R²⁰, of the general formula

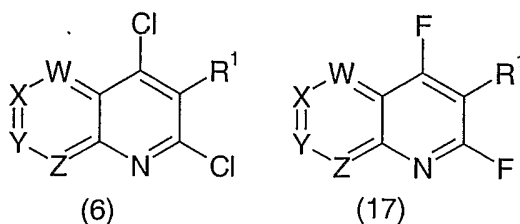
15



- where A can be one to four optional substituents independently selected from halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl,
- and B is at least one or more substituents independently selected from aryl, heteroaryl, aryloxy (except that phenoxy must be substituted), heteroaryloxy, aryl(C₁₋₄)alkoxy (except that benzyloxy must be substituted), heteroaryl(C₁₋₄)alkoxy, arylthio, arylsulphinyl, arylsulphonyl, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, aryl(C₂₋₄)alkenyl, aryl(C₂₋₄)alkynyl, heteroaryl(C₂₋₄)alkenyl, heteroaryl(C₂₋₄)alkynyl, aryl(C₁₋₄)alkyl,

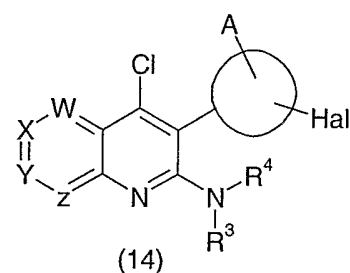
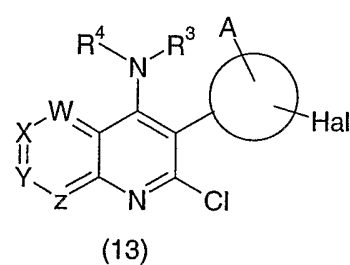
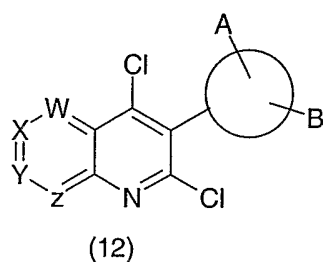
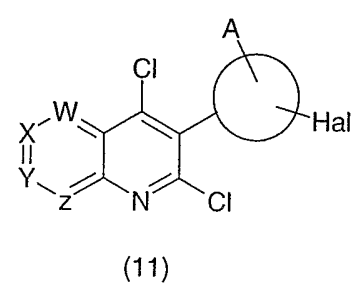
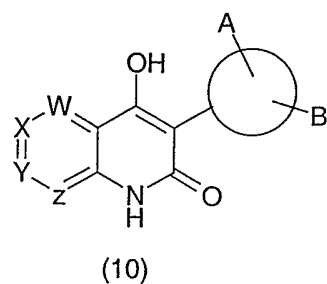
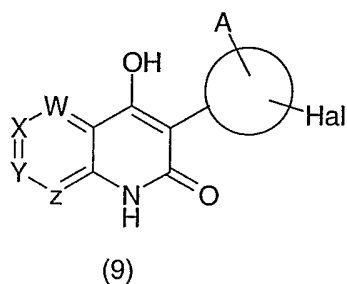
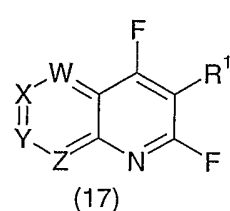
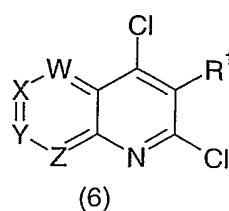
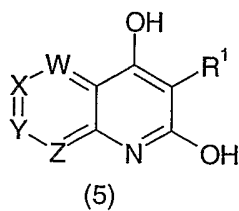
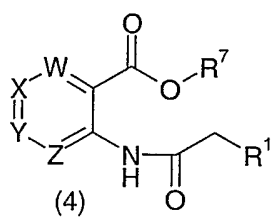
- heteroaryl(C₁₋₄)alkyl, with any of the forgoing aryl or heteroaryl substituents being optionally substituted with halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)-alkylthio, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, cyano or nitro;
- 5 R³ and R⁴ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₈)alkyl, NR⁵R⁶ or R³ and R⁴ together form a C₃₋₇ alkylene or C₃₋₇ alkenylene chain optionally substituted with one or more C₁₋₄ alkyl or C₁₋₄ alkoxy groups, or,
- 10 together with the nitrogen atom to which they are attached, R³ and R⁴ form a morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide ring or a piperazine or piperazine *N*-(C₁₋₄)alkyl ring, and R⁵ and R⁶ are independently H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, aryl, aryl(C₁₋₈)alkyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₆)alkyl, heteroaryl or heteroaryl(C₁₋₈)alkyl; any of the foregoing alkyl, alkenyl, alkynyl or cycloalkyl groups or moieties (other than for R⁸) being optionally substituted with halogen, cyano, C₁₋₆ alkoxy,
- 15 C₁₋₆ alkylcarbonyl, C₁₋₆ alkoxycarbonyl, C₁₋₆ haloalkoxy, C₁₋₆ alkylthio, tri(C₁₋₄)alkylsilyl, C₁₋₆ alkylamino or C₁₋₆ dialkylamino, any of the foregoing morpholine, thiomorpholine, piperidine, piperazine and pyrrolidine rings being optionally substituted with C₁₋₄ alkyl (especially methyl), and any of the foregoing aryl or heteroaryl groups or moieties in R³, R⁴, R⁵, R⁶ or R⁸ being optionally substituted with one or more substituents selected from halo,
- 20 hydroxy, mercapto, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆ alkylthio, halo(C₁₋₆)alkylthio, hydroxy(C₁₋₆)alkyl, C₁₋₄ alkoxy(C₁₋₆)alkyl, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR¹³R¹⁴, -NHCOR¹³, -NHCONR¹³R¹⁴, -CONR¹³R¹⁴, -SO₂R¹³, -OSO₂R¹³, -COR¹³, -CR¹³=NR¹⁴ or
- 25 -N=CR¹³R¹⁴, in which R¹³ and R¹⁴ are independently hydrogen, C₁₋₄ alkyl, halo(C₁₋₄)alkyl, C₁₋₄ alkoxy, halo(C₁₋₄)alkoxy, C₁₋₄ alkylthio, C₃₋₆ cycloalkyl, C₃₋₆ cycloalkyl(C₁₋₄)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C₁₋₄ alkyl or C₁₋₄ alkoxy.
- 30 2. A compound according to claim 1 wherein W and Z are N and X and Y are CH.
3. A compound according to claim 1 or 2 wherein R² is NR³R⁴.

4. A compound according to claim 3 wherein R is halo.
5. A compound according to any one of the preceding claims wherein
 R^3 is C_{1-8} alkyl, halo(C_{1-8})alkyl, halo C_{1-4} alkoxy(C_{1-8})alkyl, C_{1-4} alkoxyhalo(C_{1-8})alkyl
 5 C_{1-4} alkoxy carbonyl(C_{1-8})alkyl, C_{1-4} alkoxy carbonylhalo(C_{1-8})alkyl, phenyl($_{1-4}$)alkyl,
 C_{2-8} alkenyl, halo(C_{2-8})alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl optionally substituted
 with chloro, fluoro or methyl, C_{3-8} cycloalkyl(C_{1-4})alkyl, phenylamino, piperidino or
 morpholino, the phenyl ring of phenylalkyl or phenylamino being optionally
 substituted with one, two or three substituents selected from halo, C_{1-4} alkyl, halo(C_{1-}
 10 $_4$)alkyl, C_{1-4} alkoxy and halo(C_{1-4})alkoxy; and
 R^4 is H, C_{1-4} alkyl, halo(C_{1-4})alkyl or amino, or
 R^3 and R^4 together form a C_{3-7} alkylene or alkenylene chain optionally substituted
 with methyl, or,
 together with the nitrogen atom to which they are attached, R^3 and R^4 form a
 15 morpholine, thiomorpholine, thiomorpholine S-oxide or thiomorpholine S-dioxide
 ring or a piperazine or piperazine N -(C_{1-4})alkyl (especially N -methyl) ring, in which
 the morpholine or piperazine rings are optionally substituted with methyl.
6. A process for preparing a compound of the general formula (1) according to claim 1
 20 wherein one of R and R^2 is chloro or fluoro and the other is NR^3R^4 and W, X, Y, Z,
 R^1 , R^3 and R^4 are as defined in claim 1, which comprises reacting an amine of the
 general formula NR^3R^4 with a compound of the general formula (6) or (17):



25

7. The intermediate chemicals having the general formulae (4), (5), (6), (9), (10), (11),
 (12), (13) (14) and (17):



wherein W, X, Y, Z, R¹, R³, R⁴, Hal, A and B are as defined in claim 1 and R⁷, is C₁₋₄ alkyl.

- 5 8. A plant fungicidal composition comprising a fungicidally effective amount of a compound as defined in claim 1 and a suitable carrier or diluent therefor.
9. A method of combating or controlling phytopathogenic fungi which comprises applying to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or to any other plant growth medium, a fungicidally effective amount of a compound according to claim 1 or a composition according to claim 15.
- 10

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2005/006687

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D241/36 A01N43/60

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A01N

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 801 592 A (GRAF ET AL) 31 January 1989 (1989-01-31) the whole document	1-9
P, X	WO 2004/056824 A (SYNGENTA LIMITED; SYNGENTA PARTICIPATIONS AG; CROWLEY, PATRICK, JELF;) 8 July 2004 (2004-07-08) the whole document	1-9
P, X	WO 2004/056825 A (SYNGENTA LIMITED; SYNGENTA PARTICIPATIONS AG; CROWLEY, PATRICK, JELF;) 8 July 2004 (2004-07-08) the whole document	1-9
P, X	WO 2004/056826 A (SYNGENTA LIMITED; SYNGENTA PARTICIPATIONS AG; CROWLEY, PATRICK, JELF;) 8 July 2004 (2004-07-08) the whole document	1-9



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

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

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

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

Z document member of the same patent family

Date of the actual completion of the international search

22 September 2005

Date of mailing of the international search report

05/10/2005

Name and mailing address of the ISA

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Timmermans, M

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/006687

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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