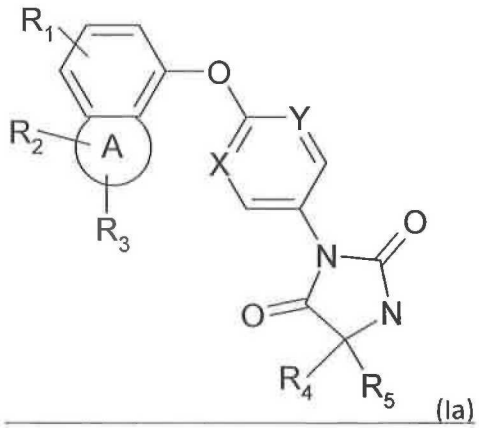
modulators of Kv3 channels in auditory brainstem nuclei could have a benefit in the treatment of disorders of hearing, including tinnitus and auditory hyper-acuity associated with Fragile X syndrome and autism.

Summary ~~of the invention~~

According to one aspect, there is provided a compound of formula (Ia):



(Ia)

wherein

R_1 is H, or C_{1-4}alkyl, halo, haloC_{1-4}alkyl, CN, C_{1-4}alkoxy, haloC_{1-4}alkoxy;

R_2 is H, C_{1-4}alkyl, C_{3-4} spiro carbocycly, haloC_{1-4}alkyl or halo;

R_3 is H, C_{1-4}alkyl, haloC_{1-4}alkyl, halo;

A is a 5 or 6 membered saturated or unsaturated heterocycle, with at least one O atom; which heterocycle is optionally fused with a cyclopropyl group to form a tricycle when considered together with the phenyl;

X is C or N;

Y is C or N;

R_4 is C_{1-4} alkyl;

R_5 is H, Deuterium, C_{1-4} alkyl;

or R_4 and R_5 can be fused to form C_{3-4} spiro carbocycly;

wherein R_2 and R_3 may be attached to the same or a different ring atom;

and wherein R_2 may be attached to a fused ring atom;

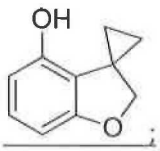
or a pharmaceutically acceptable salt thereof.

According to another aspect, there is provided a use of a compound as disclosed in the preceding aspect in the manufacture of a medicament for the prophylaxis or treatment of hearing disorders, schizophrenia, bipolar disorder or sleep disorders.

According to another aspect, there is provided a pharmaceutical composition comprising a compound as disclosed in the preceding aspect and a pharmaceutically acceptable carrier or excipient.

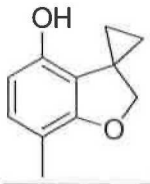
According to another aspect, there is provided a compound selected from:

spiro[1-benzofuran-3,1'-cyclopropan]-4-ol



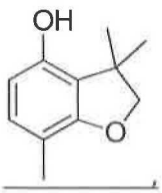
;

7-methylspiro[2H-benzofuran-3,1'-cyclopropane]-4-ol



; and

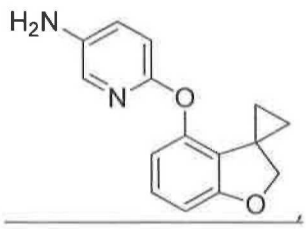
3,3,7-trimethyl-2,3-dihydro-1-benzofuran-4-ol



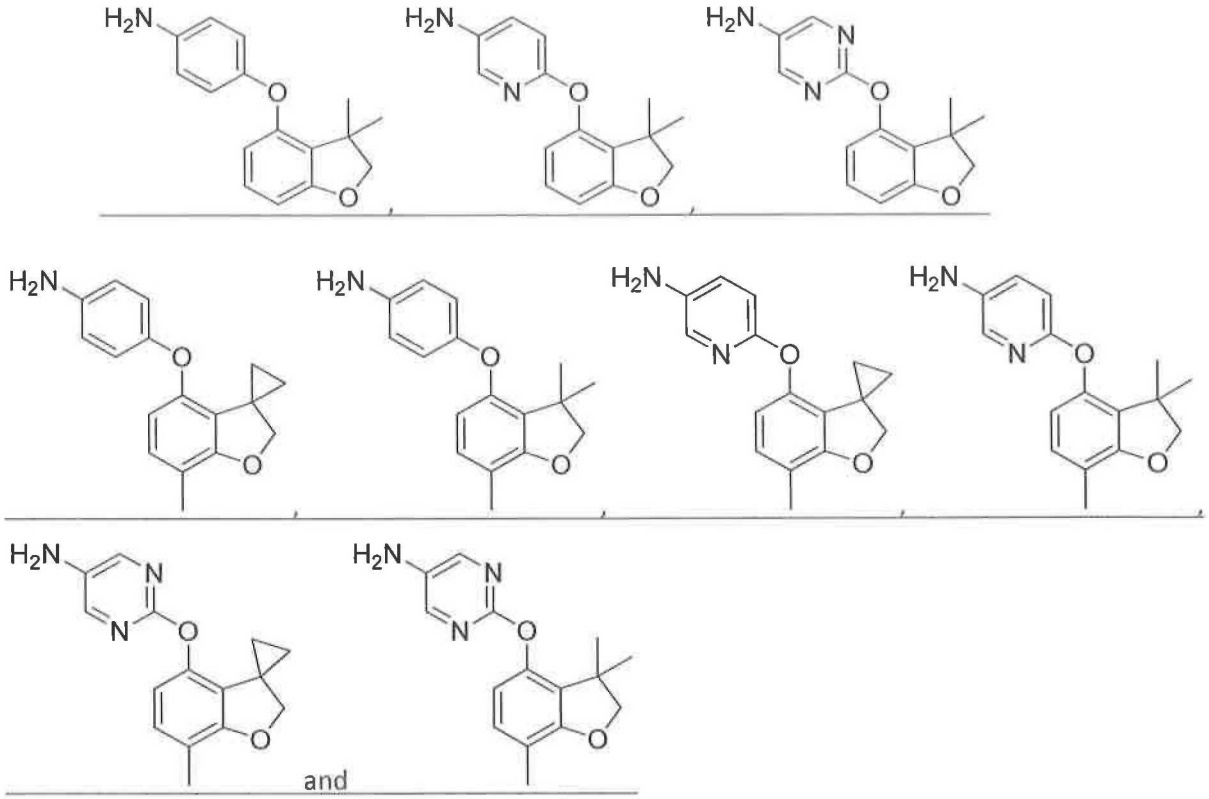
,

or a salt thereof.

According to another aspect, there is provided a compound which is selected from the group consisting of:



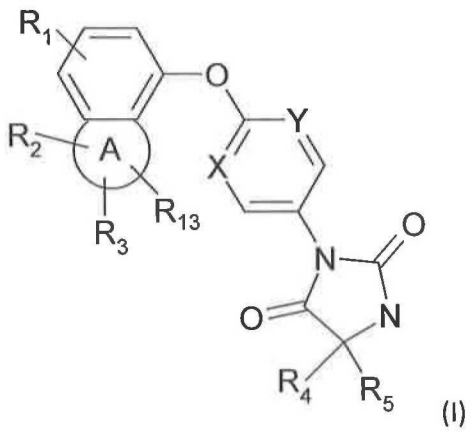
,



and

or a salt thereof.

The present ~~invention~~ disclosure provides compounds of formula (I):



(I)

wherein:

R_1 is is H, or C_{1-4}alkyl, halo, haloC_{1-4}alkyl, CN, C_{1-4}alkoxy, haloC_{1-4}alkoxy;

R_2 is H, C_{1-4}alkyl, C_{3-4} spiro carbocycly, haloC_{1-4}alkyl or halo;

R_3 is H, C_{1-4}alkyl, haloC_{1-4}alkyl, halo; or R_3 is absent;

R_{13} is H, C_{1-4}alkyl, haloC_{1-4}alkyl, halo; or R_{13} is absent;

A is a 5 or 6 membered saturated or unsaturated heterocycle, with at least one O atom; which heterocycle is optionally fused with a cyclopropyl group to form a tricycle when considered together with the phenyl;

X is C or N;

Y is C or N;

R_4 is C_{1-4} alkyl;

R_5 is H, Deuterium, C_{1-4} alkyl;

or R_4 and R_5 can be fused to form C_{3-4} spiro carbocycly;

wherein R_2 and R_3 may be attached to the same or a different ring atom; and wherein R_2 may be attached to a fused ring atom.

Compounds of formula (I) may be provided in the form of a pharmaceutically acceptable salt and/or solvate. In one embodiment of the ~~invention~~ disclosure a compound of formula (I) is provided in the form of a pharmaceutically acceptable salt.

The compounds of formula (I) may be used as medicaments, in particular for the prophylaxis or treatment of hearing disorders, including hearing loss and tinnitus, as well as schizophrenia, bipolar disorder, epilepsy and sleep disorders.

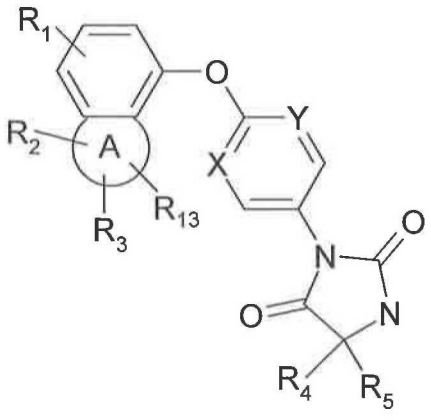
Further, there is provided a method for the prophylaxis or treatment of hearing disorders, including hearing loss and tinnitus, as well as schizophrenia, bipolar disorder, epilepsy and sleep disorders by administering to a subject a compound of formula (I).

Compounds of formula (I) may be used in the manufacture of a medicament for the prophylaxis or treatment of hearing disorders, including hearing loss and tinnitus, as well as schizophrenia, bipolar disorder, epilepsy and sleep disorders.

Also provided are pharamaceuticual compositions containg a compound of formula (I) and a pharmaceutically acceptable carrier or excipient.

Detailed description of the invention

The present invention provides compounds of formula (I):

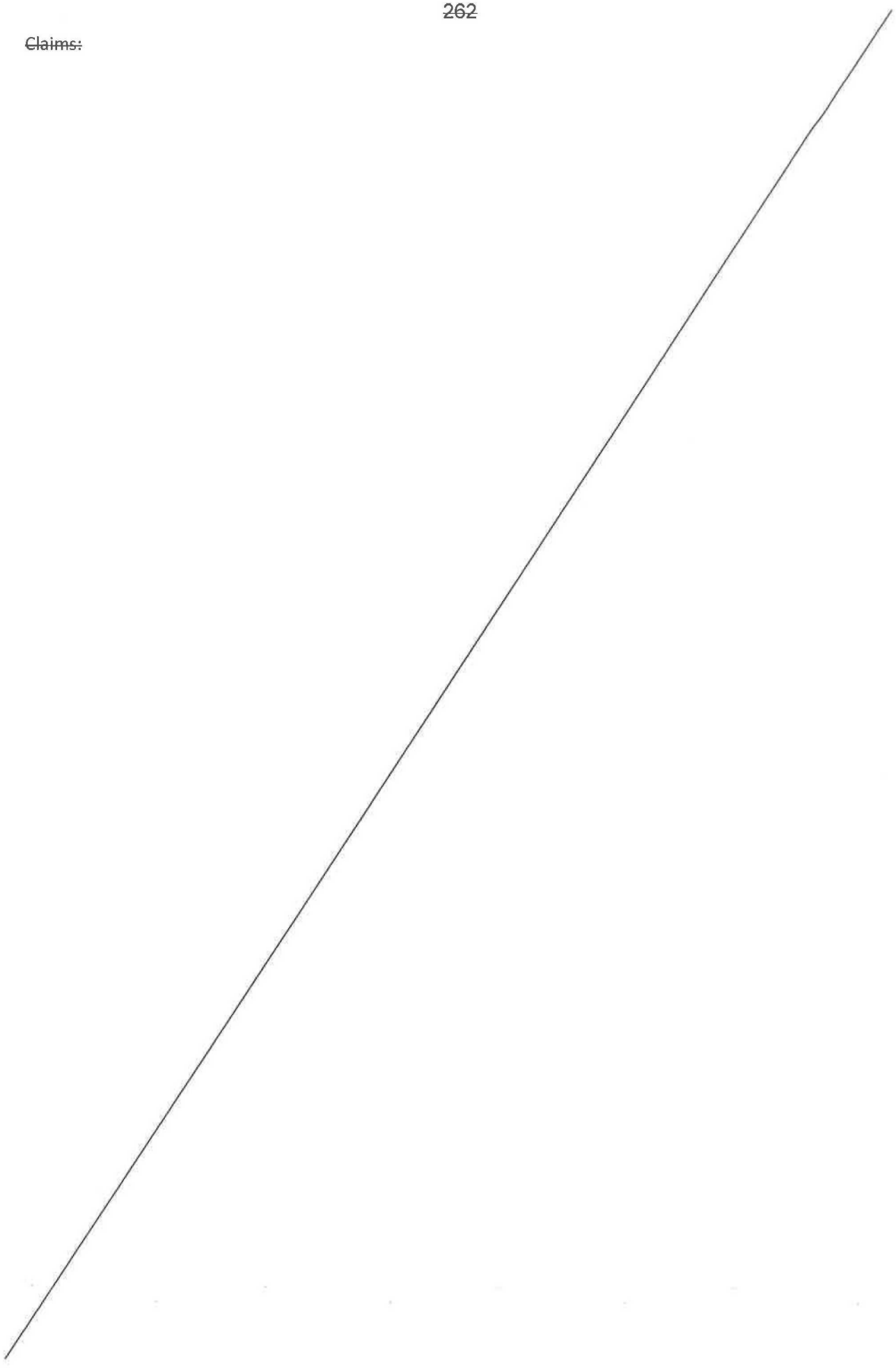


(I)

wherein:

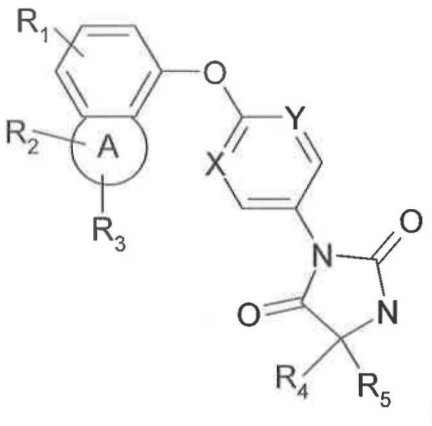
R_1 is is H, or $C_{1\text{-}4}$alkyl, halo, halo$C_{1\text{-}4}$alkyl, CN, $C_{1\text{-}4}$alkoxy, halo$C_{1\text{-}4}$alkoxy;

~~Claims:~~



Claims:

1. A compound of formula (Ia):



(Ia)

wherein

R_1 is H, or C_{1-4}alkyl, halo, haloC_{1-4}alkyl, CN, C_{1-4}alkoxy, haloC_{1-4}alkoxy;

R_2 is H, C_{1-4}alkyl, C_{3-4} spiro carbocycly, haloC_{1-4}alkyl or halo;

R_3 is H, C_{1-4}alkyl, haloC_{1-4}alkyl, halo;

A is a 5 or 6 membered saturated or unsaturated heterocycle, with at least one O atom; which heterocycle is optionally fused with a cyclopropyl group to form a tricycle when considered together with the phenyl;

X is C or N;

Y is C or N;

R_4 is C_{1-4} alkyl;

R_5 is H, Deuterium, C_{1-4} alkyl;

or R_4 and R_5 can be fused to form C_{3-4} spiro carbocycly;

wherein R_2 and R_3 may be attached to the same or a different ring atom;

and wherein R_2 may be attached to a fused ring atom;

or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein R_1 is H or methyl.

3. The compound according to claim 1 or claim 2, wherein R_2 is H, methyl or a C_3 spiro group.

4. The compound according to any one of claims 1 to 3, wherein R_3 is H or methyl.

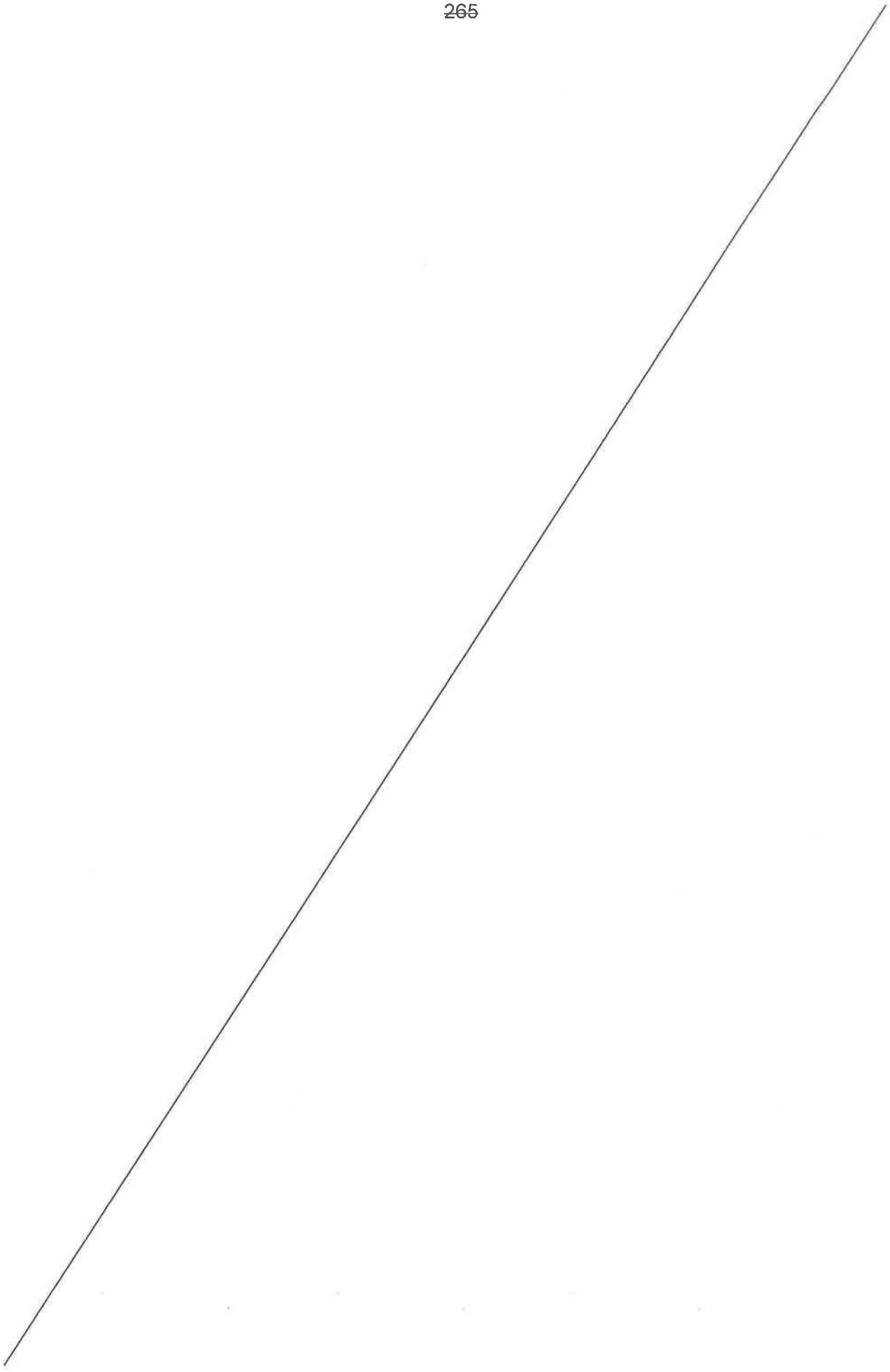
5. The compound according to any one of claims 1 to 4, wherein X is C and Y is C.

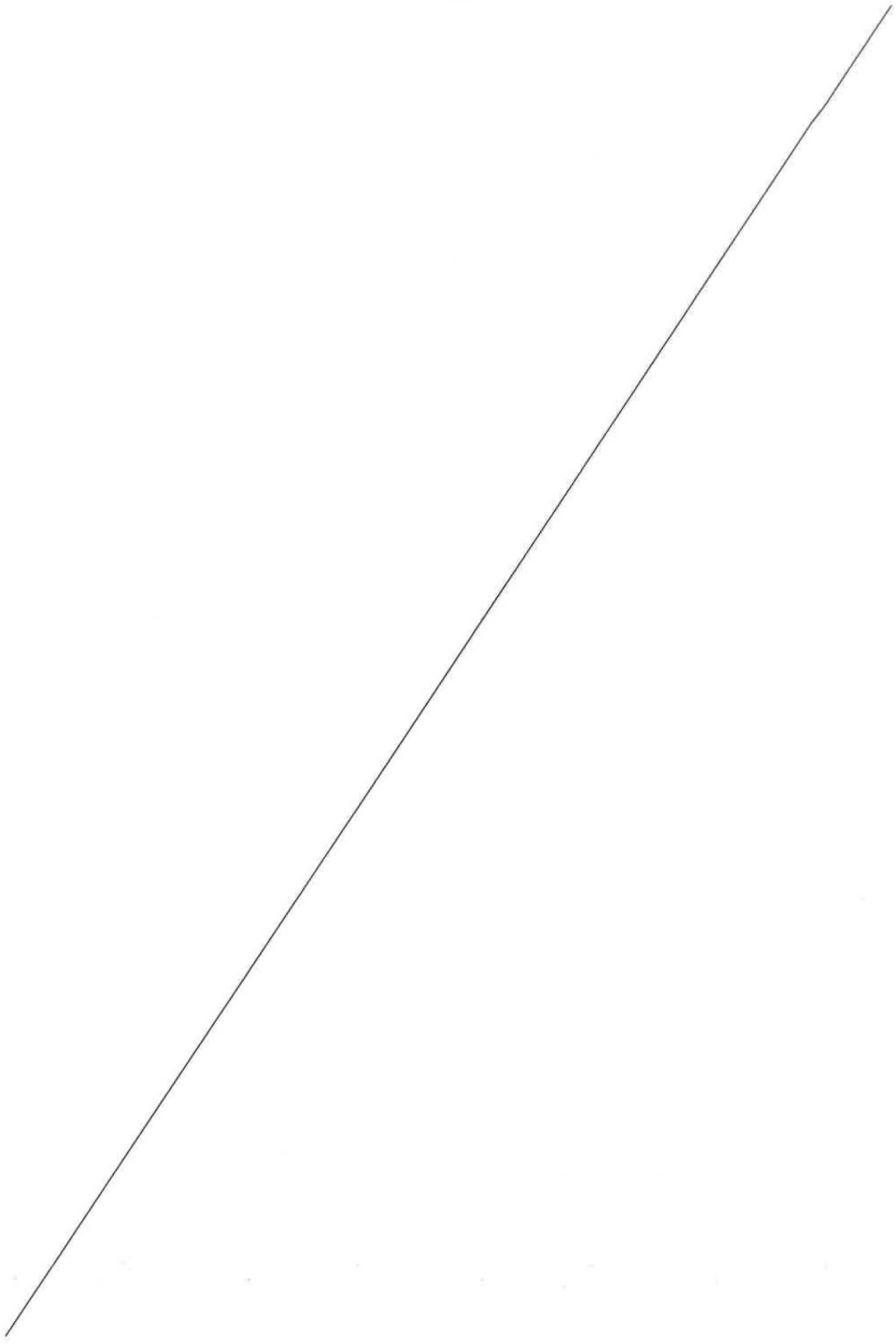
6. The compound according to any one of claims 1 to 4, wherein X is C and Y is N.

7. The compound according to any one of claims 1 to 4, wherein X is N and Y is N.

8. The compound according to any one of claims 1 to 7, wherein R_4 is methyl or ethyl.

9. The compound according to any one of claims 1 to 8, wherein R_5 is H or methyl.





10. The compound according to claim 1, selected from the group consisting of:

(5R)-3-[4-(1,3-dihydro-2-benzofuran-4-yloxy)phenyl]-5-methyl-2,4-imidazolidinedione;

(5R)-5-methyl-3-{4-[(3-methyl-1,2-benzisoxazol-4-yl)oxy]phenyl}-2,4-imidazolidinedione;

(5R)-3-{4-[(3,6-dimethyl-1,2-benzisoxazol-4-yl)oxy]phenyl}-5-methyl-2,4-imidazolidinedione;

5,5-dimethyl-3-{4-[(3-methyl-1,2-benzisoxazol-4-yl)oxy]phenyl}-2,4-imidazolidinedione;

(5R)-5-ethyl-3-{6-[(3-ethyl-1,2-benzisoxazol-4-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione;

(5R)-5-ethyl-3-(6-{[3-(1-methylethyl)-1,2-benzisoxazol-4-yl]oxy}-3-pyridinyl)-2,4-imidazolidinedione;

(5R)-3-{4-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]phenyl}-5-methyl-2,4-imidazolidinedione;

(5R)-3-{6-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-3-pyridinyl}-5-methyl-2,4-imidazolidinedione;

(5R)-3-{6-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-3-pyridinyl}-5-ethyl-2,4-imidazolidinedione;

(5R)-3-{2-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-5-pyrimidinyl}-5-ethyl-2,4-imidazolidinedione;

7-{6-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-3-pyridinyl}-5,7-diazaspiro[3.4]octane-6,8-dione;

6-{6-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-3-pyridinyl}-4,6-diazaspiro[2.4]heptane-5,7-dione;

3-{6-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-3-pyridinyl}-5,5-dimethyl-2,4-imidazolidinedione;

(5R)-3-{2-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-5-pyrimidinyl}-5-(1,1-dimethylethyl)-2,4-imidazolidinedione;

(5R)-5-ethyl-3-[6-(spiro[1-benzofuran-3,1'-cyclopropan]-4-yloxy)-3-pyridinyl]-2,4-imidazolidinedione;

5,5-dimethyl-3-[6-(spiro[1-benzofuran-3,1'-cyclopropan]-4-yloxy)-3-pyridinyl]-2,4-imidazolidinedione;

(5R)-5-ethyl-5-methyl-3-[6-(spiro[1-benzofuran-3,1'-cyclopropan]-4-yloxy)-3-pyridinyl]-2,4-imidazolidinedione;

(5R)-5-ethyl-3-(6-{[(3S/R)-3-methyl-1,3-dihydro-2-benzofuran-4-yl]oxy}-3-pyridinyl)-2,4-imidazolidinedione (diastereoisomeric mixture);

(5R)-5-ethyl-3-{6-[(3-methyl-1,3-dihydro-2-benzofuran-4-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (diastereoisomers 1 and 2);

(5R)-5-ethyl-3-{6-[(3-ethyl-1,3-dihydro-2-benzofuran-4-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (distereoisomeric mixture);

(5R)-5-ethyl-3-{6-[(3-ethyl-1,3-dihydro-2-benzofuran-4-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (diastereoisomers 1 and 2);

5,5-dimethyl-3-{6-[(3-methyl-3,4-dihydro-2H-chromen-5-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (racemic mixture);

5,5-dimethyl-3-{6-[(3-methyl-3,4-dihydro-2H-chromen-5-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (enantiomers 1 and enantiomer 2);

5,5-dimethyl-3-{6-[(1a-methyl-1,1a,2,7b-tetrahydrocyclopropa[c]chromen-7-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (racemic mixture);

5,5-dimethyl-3-{6-[(1a-methyl-1,1a,2,7b-tetrahydrocyclopropa[c]chromen-7-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (enantiomer 1 and enantiomer 2);

(5R)-5-ethyl-5-methyl-3-[6-(1H-spiro[2-benzopyran-4,1'-cyclopropan]-5-yloxy)-3-pyridinyl]-2,4-imidazolidinedione;

3-{2-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-5-pyrimidinyl}-5,5-dimethyl-2,4-imidazolidinedione;

(5R)-3-{2-[(3,3-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-5-pyrimidinyl}-5-(1-methylethyl)-2,4-imidazolidinedione;

(5R)-3-{6-[(2,2-dimethyl-2,3-dihydro-1-benzofuran-4-yl)oxy]-3-pyridinyl}-5-ethyl-2,4-imidazolidinedione;

5,5-dimethyl-3-[6-(1H-spiro[2-benzopyran-4,1'-cyclopropan]-5-yloxy)-3-pyridinyl]-2,4-imidazolidinedione;

(5R)-3-[2-(2,3-dihydrospiro[chromene-4,1'-cyclopropan]-5-yloxy)-5-pyrimidinyl]-5-ethyl-5-methyl-2,4-imidazolidinedione;

5,5-dimethyl-3-{6-[(4-methyl-3,4-dihydro-2H-chromen-5-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (racemate mixture, enantiomer 1, enantiomer 2);

(5R)-5-ethyl-5-methyl-3-{6-[(3-methyl-3,4-dihydro-2H-chromen-5-yl)oxy]-3-pyridinyl}-2,4-imidazolidinedione (diastereoisomeric mixture, diastereoisomer 1, diastereoisomer 2);

(5R)-5-ethyl-5-methyl-3-[6-(1,1a,2,7b-tetrahydrocyclopropa[c]chromen-7-yloxy)-3-pyridinyl]-2,4-imidazolidinedione (diastereoisomeric mixture, diastereoisomer 1, diastereoisomer 2); and

3-{6-[(3-ethyl-1,3-dihydro-2-benzofuran-4-yl)oxy]-3-pyridinyl}-5,5-dimethyl-2,4-imidazolidinedione (racemate mixture, enantiomer 1, enantiomer 2).

11. Use of a compound according to any one of claims 1 to 10 in the manufacture of a medicament for the prophylaxis or treatment of hearing disorders, schizophrenia, bipolar disorder or sleep disorders.

12. The use according to claim 11 in manufacture of a medicament for the the prophylaxis or treatment of hearing disorders.

13. The use according to claim 11 or claim 12, wherein the hearing disorder is selected from the group consisting of auditory neuropathy, auditory processing disorder, hearing loss, which includes sudden hearing loss, noise induced hearing loss, substance-induced hearing loss, hearing loss in adults over 60 (presbycusis), and tinnitus.

14. The use according to claim 11 or claim 12, wherein the hearing disorder is hearing loss.

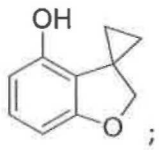
15. The use according to claim 11 or claim 12, wherein the hearing disorder is tinnitus.

16. The use according to claim 11, in the manufacture of a medicament for the prophylaxis or treatment of schizophrenia.

17. A pharmaceutical composition comprising a compound according to any one of claims 1 to 10 and a pharmaceutically acceptable carrier or excipient.

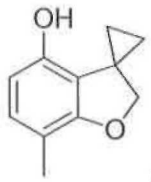
18. A compound selected from:

spiro[1-benzofuran-3,1'-cyclopropan]-4-ol



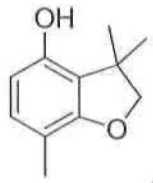
;

7-methylspiro[2H-benzofuran-3,1'-cyclopropane]-4-ol



; and

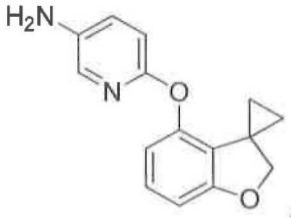
3,3,7-trimethyl-2,3-dihydro-1-benzofuran-4-ol

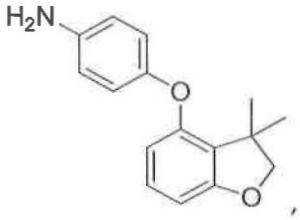


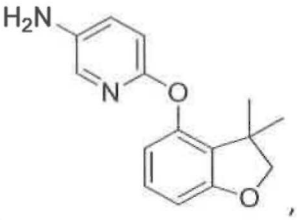
,

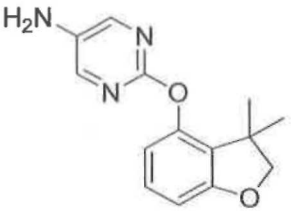
or a salt thereof.

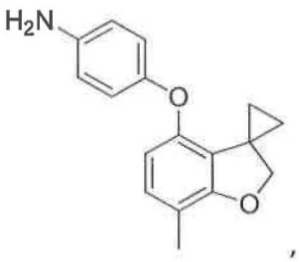
19. A compound which is selected from the group consisting of:

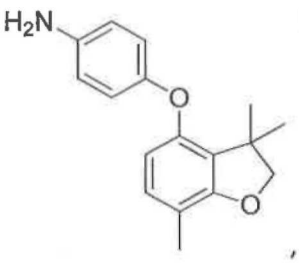


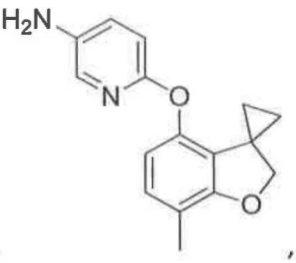


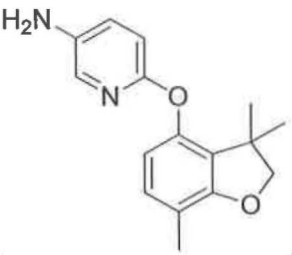


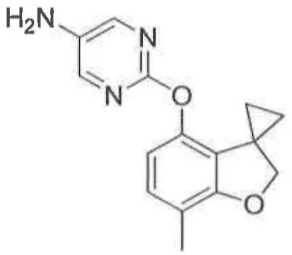




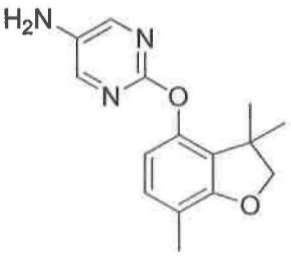








and



or a salt thereof.