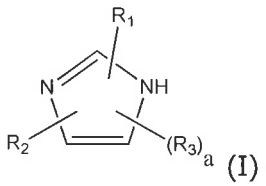
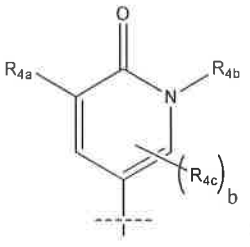
CLAIMS

1. A compound of formula (I), or a salt thereof:



(I)

wherein



R_1 represents ;

R_2 is hydrogen, C_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl, heterocycloalkyl or $-CHR_5(CH_2)_cR_6$;

each R_3 is independently selected from the group consisting of halogen, -CN, C_{1-3}alkyl, C_{1-3}alkoxy, $-NO_2$, $-CONR_7R_8$, $-NR_7COR_8$, $-OCOR_8$, $-CO_2R_8$, $-SO_2NR_7R_8$, $-NR_7SO_2R_8$, $-SO_2R_8$, $-R_8$, $-NR_7R_8$, and $-OR_8$, with the proviso that when a is 2, one R_3 is selected from the group consisting of halogen, -CN, C_{1-3}alkyl and C_{1-3}alkoxy;

R_{4a} is hydrogen, C_{1-3}alkyl, C_{1-3}alkoxy, halogen, -CN, -OH, $-NR_9R_{10}$;

R_{4b} is hydrogen or C_{1-3}alkyl;

each R_{4c} is independently selected from the group consisting of C_{1-3}alkyl, C_{1-3}alkoxy, halogen, -CN, -OH, and $-NR_9R_{10}$;

R_5 is hydrogen, C_{1-3}alkyl, or $-(CH_2)_dOR_{11}$;

R_6 is hydrogen, C_{1-3}alkyl, $-(CH_2)_dOR_{11}$, C_{3-7}cycloalkyl, or heterocycloalkyl, wherein the C_{1-3}alkyl, $-(CH_2)_dOR_{11}$, C_{3-7}cycloalkyl, heterocycloalkyl groups can be optionally substituted with one or two substituents independently selected from the group consisting of C_{1-3}alkyl, C_{1-3}alkoxy, halogen, $-CH_2OH$, -COOH, and $-COCH_3$;

R_7 is hydrogen or C_{1-3}alkyl and R_8 is –Y-Z, or when R_3 is $-CONR_7R_8$, R_7 and R_8 together with the nitrogen to which they are attached may form a heterocycloalkyl, wherein the heterocycloalkyl group can be optionally substituted with one or two groups independently selected from C_{1-3}alkyl, halogen, $-NH_2$, $-CH_2NH_2$, $-CO_2H$, -OH, -CN, and $-CH_2OH$;

Y is a bond or C_{1-3}alkylene, wherein the C_{1-3}alkylene group can be optionally substituted with one or two groups independently selected from C_{1-3}alkyl;

Z is hydrogen, C_{1-3}alkyl, C_{3-7}cycloalkyl, heterocycloalkyl, aryl, heteroaryl, $-SO_2NR_{12}R_{13}$, $-NR_{12}SO_2R_{13}$, $-SO_2R_{12}$, or $-NR_{12}R_{13}$, wherein C_{1-3}alkyl, C_{3-7}cycloalkyl, heterocycloalkyl, aryl or heteroaryl can be optionally substituted with one or two groups independently selected from C_{1-3}alkyl, C_{1-3}alkoxy, halogen, $-NH_2$, $-CH_2NH_2$, $-CO_2H$, -OH, -CN, and $-CH_2OH$;

R_9 is hydrogen or CH_3;

R_{10} is hydrogen or C_{1-3}alkyl;

R_{11} is hydrogen or C_{1-3}alkyl;

R_{12} is hydrogen or C_{1-3}alkyl;

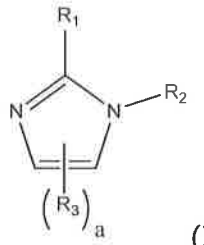
R_{13} is hydrogen or C_{1-3}alkyl;

a represents 0, 1 or 2;

b represents 0, 1 or 2;

each c and d independently represent 0 or 1.

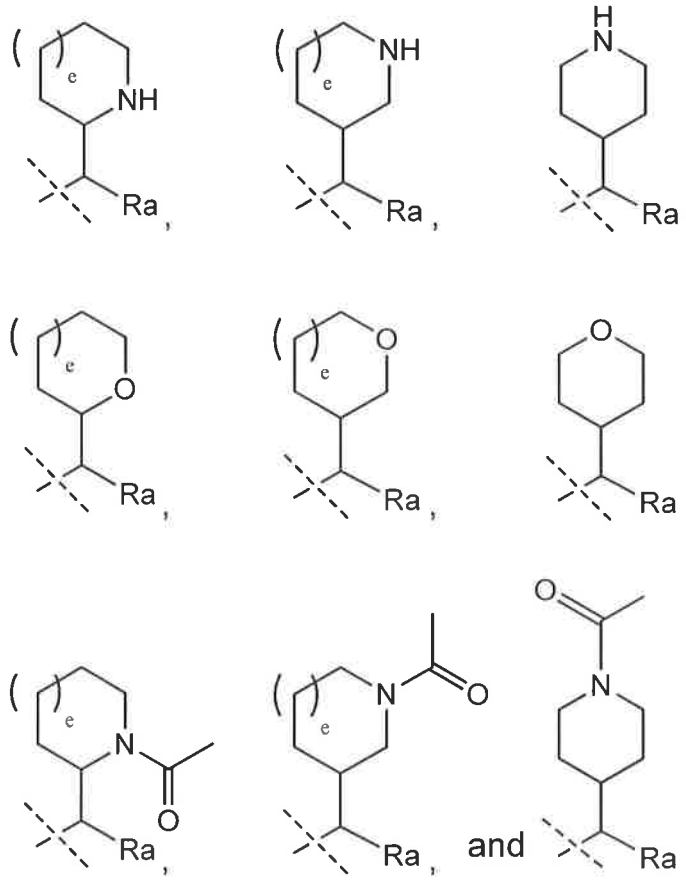
2. A compound according to claim 1, comprising a compound of formula (Ia), or a salt thereof:



(Ia)

wherein R_1, R_2, R_3 and a are as defined in claim 1.

3. A compound or salt according to claim 1 or 2, wherein R_2 is selected from the group consisting of:



wherein Ra is hydrogen or C_{1-3} alkyl; and e is 0 or 1.

4. A compound or salt according to any of claims 1 to 3, wherein R_{4a} is CH_3.

5. A compound or salt according to any one of claims 1 to 4, wherein R_{4b} is CH_3.

6. A compound or salt according to any one of claims 1 to 5, wherein b is 0.

7. A compound or salt according to any one of claims 1 to 6, wherein a is 1 or 2 and each R_3 is selected from the group consisting of halogen, -CN, C_{1-3}alkyl, and C_{1-3}alkoxy.

8. A compound or salt according to claim 7, wherein R_3 is at the 4-position on the imidazole ring.

9. A compound according to claim 1, which is selected from the group consisting of

5-(1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(4-bromo-1-ethyl-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(1-(cyclopropylmethyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(4-bromo-1-(cyclopropylmethyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1H)-one;

5-(1-isobutyl-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

1,3-dimethyl-5-(1-((tetrahydro-2*H*-pyran-4-yl)methyl)-1*H*-imidazol-2-yl)pyridin-2(1*H*)-one;

1,3-dimethyl-5-(1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)pyridin-2(1*H*)-one;

(*R*)-1,3-dimethyl-5-(1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)pyridin-2(1*H*)-one;

(*S*)-1,3-dimethyl-5-(1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)pyridin-2(1*H*)-one;

1,3-dimethyl-5-(1-(piperidin-4-ylmethyl)-1*H*-imidazol-2-yl)pyridin-2(1*H*)-one;

1,3-dimethyl-5-(1-((tetrahydrofuran-2-yl)methyl)-1*H*-imidazol-2-yl)pyridin-2(1*H*)-one;

5-(1-(2-methoxyethyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(1-(1,3-dimethoxypropan-2-yl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

Methyl 2-(1,5-dimethyl-6-oxo-1,6-dihydropyridin-3-yl)-1H-imidazole-5-carboxylate;

5-(5-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

2-(1,5-dimethyl-6-oxo-1,6-dihydropyridin-3-yl)-1*H*-imidazole-5-carboxamide;

2-(1,5-dimethyl-6-oxo-1,6-dihydropyridin-3-yl)-1*H*-imidazole-4,5-dicarbonitrile;

5-(1-(1,3-dimethoxypropan-2-yl)-4,5-dimethyl-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(4-(4-bromophenyl)-1-(1,3-dimethoxypropan-2-yl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(4-chloro-1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*R*)-5-(4-chloro-1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*S*)-5-(4-chloro-1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(5-chloro-1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*R*)-5-(5-chloro-1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*S*)-5-(5-chloro-1-((tetrahydro-2*H*-pyran-2-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(5-chloro-1-((tetrahydro-2*H*-pyran-4-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(5-chloro-1-((tetrahydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*R*)-5-(5-chloro-1-((tetrahydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*S*)-5-(5-chloro-1-((tetrahydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(4-chloro-1-(1,3-dimethoxypropan-2-yl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(1-((1-acetylpiperidin-3-yl)methyl)-5-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*R*)-5-(1-((1-acetylpiperidin-3-yl)methyl)-5-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*S*)-5-(1-((1-acetylpiperidin-3-yl)methyl)-5-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(1-((1-acetylpiperidin-3-yl)methyl)-4-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*R*)-5-(1-((1-acetylpiperidin-3-yl)methyl)-4-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*S*)-5-(1-((1-acetylpiperidin-3-yl)methyl)-4-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(1-((1-acetylpiperidin-3-yl)methyl)-4-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*R*)-5-(1-((1-acetylpiperidin-3-yl)methyl)-4-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one

(*S*)-5-(1-((1-acetylpiperidin-3-yl)methyl)-4-chloro-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one

5-(4-chloro-1-((tetrahydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*R*)-5-(4-chloro-1-((tetrahydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

(*S*)-5-(4-chloro-1-((tetrahydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(4-chloro-1-((tetrahydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazol-2-yl)-1,3-dimethylpyridin-2(1*H*)-one;

5-(4-chloro-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazol-2-yl)-1,3-dimethylpyridin-2(1H)-one;

5-(1-ethyl-1H-imidazol-5-yl)-1,3-dimethylpyridin-2(1H)-one;

rac-1-(4-chloro-1-((tetrahydro-2H-pyran-3-yl)methyl)-1H-imidazol-2-yl)-3,5-dimethylpyridin-4(1H)-one;

methyl 2-(1,5-dimethyl-6-oxo-1,6-dihydropyridin-3-yl)-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazole-4-carboxylate;

methyl 2-(1,5-dimethyl-6-oxo-1,6-dihydropyridin-3-yl)-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazole-5-carboxylate;

2-(1,5-dimethyl-6-oxo-1,6-dihydropyridin-3-yl)-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazole-4-carboxylic acid;

rac-5-(4-bromo-1-((tetrahydro-2H-pyran-3-yl)methyl)-1H-imidazol-2-yl)-1,3-dimethylpyridin-2(1H)-one;

rac-1-(4-bromo-1-((tetrahydro-2H-pyran-3-yl)methyl)-1H-imidazol-2-yl)-3,5-dimethylpyridin-4(1H)-one;

1-(4-bromo-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazol-2-yl)-3,5-dimethylpyridin-4(1H)-one;

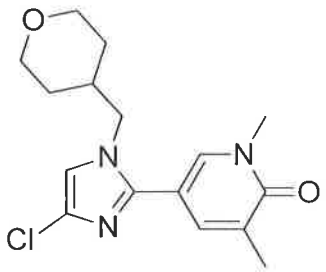
5-(4-bromo-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazol-2-yl)-1,3-dimethylpyridin-2(1H)-one;

rac-5-(1-((1-acetylpiperidin-3-yl)methyl)-4-bromo-1H-imidazol-2-yl)-1,3-dimethylpyridin-2(1H)-one;

1-(4-chloro-1-(1,3-dimethoxypropan-2-yl)-1H-imidazol-2-yl)-3,5-dimethylpyridin-4(1H)-one; and

1-(4-chloro-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazol-2-yl)-3,5-dimethylpyridin-4(1H)-one, or a salt thereof.

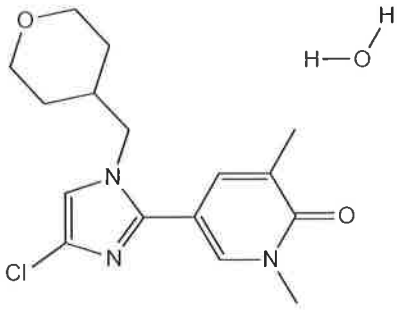
10. A compound according to claim 1, which is 5-(4-chloro-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazol-2-yl)-1,3-dimethylpyridin-2(1H)-one, of formula:



or a salt thereof.

11. A compound or salt according to any of claims 1 to 10, which is in the form of a pharmaceutically acceptable salt.

12. A compound according to claim 1, which is 5-(4-chloro-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-imidazol-2-yl)-1,3-dimethylpyridin-2(1H)-one monohydrate, of formula:



13. A compound according to claim 12, which is in crystalline form having:

a) an X-ray powder diffraction pattern (XRPD) substantially as shown in Fig. 1; and/or

b) an X-ray powder diffraction pattern (XRPD) with specific peaks at 2θ values, ± 0.1° 2θ experimental error, of 10.0, 12.4, 13.1, 14.8, 15.8, 17.9, 19.6, 20.2, 21.2, 23.3, and 24.4 degrees; and/or

c) a FT Raman spectrum substantially as shown in Fig. 2.

14. A pharmaceutical composition comprising a compound or salt as defined in any of claims 1 to 13, and one or more pharmaceutically acceptable excipients.

15. A compound or salt as defined in any of claims 1 to 13 for use in therapy.

16. A compound or salt as defined in any of claims 1 to 13 for use in the treatment of rheumatoid arthritis.

17. Use of a compound or salt as defined in any of claims 1 to 13 in the manufacture of a medicament for the treatment of rheumatoid arthritis.