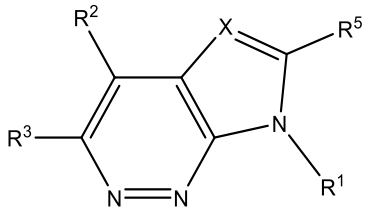
2019/034692, WO 2019/034690, WO 2019/034688, WO 2019/034686, WO 2019/008025, WO 2019/008029, WO 2019/023145, WO 2019/023147, WO 2019/025467, WO 2018/167468, WO 2018/015445, WO 2017/184746, WO 2017/184735, WO 2017/184623, WO 2017/184604, WO 2017/184624, WO 2017/140778, WO 2016/131098, US 11,319,319, US 2020/0361898, WO 2023/032987, WO 2023/032987, WO 2022/230912, WO 2023/275366, WO 2022/237781, WO 2022/036204, WO 2023/288039, WO 2022/204227, WO 2022/229315, WO 2022/184843, WO 2022/184842, WO 2022/063896, WO 2022/063876, WO 2021/219784, WO 2023/032987, WO 2022/166890, WO 2023/028534, WO 2023/028536, WO 2022/238347, WO 2022/253936, WO 2022/253326, WO 2022/135567, WO 2023/278438, and US 11,618,751.

SUMMARY

[0011] The present disclosure relates to novel compounds of structural formula I:



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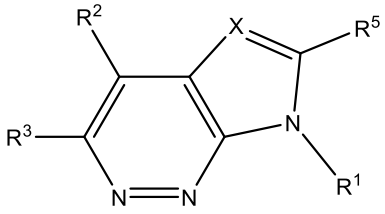
and pharmaceutically acceptable salts, hydrates and solvates thereof.

[0011a] In one aspect, there is provided a compound of structural formula I:



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or a pharmaceutically acceptable salt thereof, wherein

X is =N-;

R^1 is selected from the group:

(1) bicyclo[3.1.1]heptane,

(2) piperidine,

(3) 8-azabicyclo[3.2.1]octane, and

(4) octahydroindolizine,

wherein R^1 is unsubstituted or substituted with one to six substituents selected from R^a;

R^2 is $-CH_3$;

R^3 is phenyl, unsubstituted or substituted with one to five substituents selected from R^c;

R^5 is hydrogen or $-C_{1-6}$alkyl,

wherein each alkyl is unsubstituted or substituted with one to five substituents selected from R^e;

each R^a is independently selected from the group:

(1) CN,

(2) oxo,

(3) -OH,

(4) halogen,

(5) $-C_{1-6}$alkyl,

(6) $-C_{1-6}$alkyl-OH,

(7) $-O-C_{1-6}$alkyl,

(8) $-C_{3-6}$cycloalkyl,

(9) $–C_{1-6}$alkyl-C_{3-6}cycloalkyl,

(10) $–(CH_2)_p-S(O)_rR^f$, and

(11) $-N(R^g)_2$,

wherein each CH_2, alkyl, and cycloalkyl is independently unsubstituted or substituted with one to six substituents selected from halogen, CF_3, OH, C_{1-6}alkyl, and $-OC_{1-6}$alkyl;

each R^c is independently selected from the group:

(1) -OH,

(2) Cl,

(3) F,

(4) $-CH_3$,

(5) $-CF_3$,

(6) $-OCHF_2$,

(7) cyclopropyl, and

(8) NH_2;

each R^e is independently selected from the group:

(1) hydrogen,

(2) OH,

(3) halogen, and

(4) -C_{1-6}alkyl;

each R^f is independently selected from the group:

(1) hydrogen,

(2) -C_{1-6}alkyl,

(3) -C_{3-6}cycloalkyl, and

(4) -C_{2-6}cycloheteroalkyl;

each R^g is independently selected from the group:

(1) hydrogen,

(2) -C_{1-6}alkyl,

(3) -C_{3-6}cycloalkyl,

(4) -C_{2-6}cycloheteroalkyl,

(5) aryl,

(6) heteroaryl,

(7) -C(O)C_{1-6}alkyl, and

(8) -$S(O)_rR^f$,

wherein alkyl can be unsubstituted or substituted with one to three substituents selected from: CF_3, halogen, OH and -OC_{1-6}alkyl;

p is 0, 1, 2, 3, 4, 5 or 6; and

r is 1 or 2.

[0011b] In another aspect, there is provided a compound selected from:

(1) (*R*)-2-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

(2) (3*S*,4*R*)-3-(3-(2-hydroxy-4-(trifluoromethyl)phenyl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-7-yl)piperidin-4-ol;

(3) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

(4) (*R*)-3-(2-(difluoromethoxy)-4-(trifluoromethyl)phenyl)-7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazine;

(5) (3*S*,4*R*)-3-(3-(2-hydroxy-4-(trifluoro-methyl)phenyl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-7-yl)-1-methylpiperidin-4-ol; and

(6) (3*S*,4*R*)-1-ethyl-3-(3-(2-hydroxy-4-(trifluoro-methyl)phenyl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-7-yl)piperidin-4-ol;

(7) (*R*)-5-chloro-2-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)phenol;

(8) (*R*)-2-(4,6-dimethyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol; and

(9) (*R*)-5-chloro-2-(7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)phenol;

or a pharmaceutically acceptable salt thereof.

[0011c] In another aspect, there is provided a compound selected from:

1) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)-3-methyl-5-(trifluoromethyl)phenol;

2) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

3) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-3-methyl-5-(trifluoromethyl)phenol;

4) (*R*)-2-(7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

5) (*S*)-2-(7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

6) (*R*)-5-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)benzo[*b*]thiophen-4-ol;

7) (*R*)-5-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-2,3-dihydro-1*H*-inden-4-ol;

8) (*R*)-5-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-2,3-dihydro-1*H*-inden-4-ol; and

9) (*R*)-2,2-difluoro-5-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-2,3-dihydro-1*H*-inden-4-ol;

or a pharmaceutically acceptable salt thereof.

[0011d] In another aspect, there is provided a compound selected from:

1) (*R*)-2-fluoro-3-methyl-6-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)phenol;

2) (*R*)-2-(7-(1-isopropylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

3) (*R*)-2-(7-(1-cyclobutylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

4) 2-(7-((1*R*,2*R*,5*S*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

5) 2-(7-((1*S*,2*S*,5*R*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

6) (*R*)-3-cyclopropyl-2-fluoro-6-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)phenol;

7) 2-(4-methyl-7-((1*S*,2*S*,5*R*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

8) 2-(4-methyl-7-((1*R*,2*R*,5*S*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

9) 2-(7-((1*R*,2R,5*S*)-8-ethyl-8-aza-bicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoro-methyl)phenol;

10) 2-(7-((1*S*,2*S*,5*R*)-8-ethyl-8-aza-bicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoro-methyl)phenol;

11) 2-(7-(5-aminobicyclo[3.1.1]heptan-1-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

12) 2-(4-methyl-7-((8*S*,8a*R*)-octa-hydroindolizin-8-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoro-methyl)phenol; and

13) 2-(4-meth`yl-7-((8*R*,8a*S*)-octahydroindolizin-8-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

[0011e] In another aspect, there is provided a compound which is:
(*R*)-2-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol; or a pharmaceutically acceptable salt thereof.

[0011f] In another aspect, there is provided a compound which is:
2-(7-((1*R*,2*R*,5*S*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;
or a pharmaceutically acceptable salt thereof.
[0011g] In another aspect, there is provided a compound which is:
2-(7-((1*S*,2*S*,5*R*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;
or a pharmaceutically acceptable salt thereof.
[0011h] In another aspect, there is provided a compound which is:
2-(4-methyl-7-((1*S*,2*S*,5*R*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;
or a pharmaceutically acceptable salt thereof.
[0011i] In another aspect, there is provided a compound which is:
2-(4-methyl-7-((1*R*,2*R*,5*S*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;
or a pharmaceutically acceptable salt thereof.
[0011j] In another aspect, there is provided a compound which is:
2-(7-(5-aminobicyclo[3.1.1]heptan-1-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;
or a pharmaceutically acceptable salt thereof.
[0012] The compounds of structural formula I, and examples thereof, are inhibitors of NOD-like receptor protein 3 (NLRP3) and may be useful in the treatment and prevention of diseases, disorders and conditions mediated by NLRP3 such as, but not limited to, gout, pseudogout (chondrocalcinosis), cryopyrin-associated periodic syndromes (CAPS), NASH, fibrosis, heart failure, idiophathic pericarditis, atopic dermatitis, inflammatory bowel disease, Alzheimer's Disease, Parkinson's Disease and traumatic brain injury.
The present disclosure also relates to pharmaceutical compositions comprising the compounds of structural formula I, or a pharmaceutically acceptable salt, hydrate or solvate thereof, and a pharmaceutically acceptable carrier.
[0012a] In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

[0013] Also disclosed are methods for the treatment, management, prevention, alleviation, amelioration, suppression or control of disorders, diseases, and conditions that may be responsive to inhibition of the NLRP3 receptor in a subject in need thereof by administering the compounds and pharmaceutical compositions of the present disclosure.

[0014] The present disclosure also relates to the use of compounds of structural formula I for manufacture of a medicament useful in treating diseases, disorders and conditions that may be responsive to the inhibition of the NLRP3 receptor.

[0014a] In another aspect, there is provided the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament useful for the treatment of a disorder, condition, or disease that is responsive to the inhibition of NLRP3 in a mammal in need thereof.

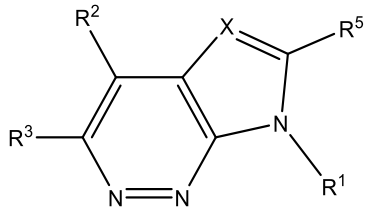
[0014b] In another aspect, there is provided the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment, prevention or control of an inflammatory disorder, a fibrotic disorder, a cardiovascular disorder, a metabolic disorder or a neurodegenerative disorder.

[0014c] In another aspect, there is provided a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in therapy.

[0015] The present disclosure is also concerned with treatment or prevention of these diseases, disorders and conditions by administering the compounds of structural formula I in combination with a therapeutically effective amount of another agent that may be useful to treat the disease, disorder and condition. The disclosure is further concerned with processes for preparing the compounds of structural formula I.

DETAILED DESCRIPTION

[0016] The present disclosure is concerned with novel compounds of structural Formula I:



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and pharmaceutically acceptable salts, hydrates and solvates thereof, wherein

X is independently selected from the group:

(1) =C(R^4)-, and

(2) =N-;

R^1 is selected from the group:

(1) -C_{3-12}cycloalkyl,

(2) -C_{3-12}cycloalkenyl,

(3) -C_{2-11}cycloheteroalkyl,

(4) -C_{2-11}cycloheteroalkenyl,

(5) aryl,

(6) heteroaryl,

(7) -C_{1-6}alkyl,

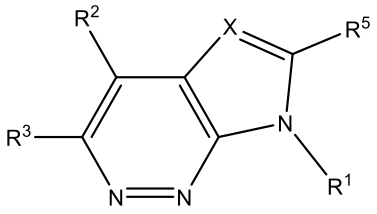
(8) -C_{1-6}alkyl-OH,

(9) -C_{1-6}alkyl-C_{3-12}cycloalkyl,

(10) -C_{1-6}alkyl-C_{3-12}cycloalkenyl,

WHAT IS CLAIMED IS:

1. A compound of structural formula I:



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or a pharmaceutically acceptable salt thereof, wherein

X is =N-;

R^1 is selected from the group:

(1) bicyclo[3.1.1]heptane,

(2) piperidine,

(3) 8-azabicyclo[3.2.1]octane, and

(4) octahydroindolizine,

wherein R^1 is unsubstituted or substituted with one to six substituents selected from R^a;

R^2 is -CH_3;

R^3 is phenyl, unsubstituted or substituted with one to five substituents selected from R^c;

R^5 is hydrogen or -C_{1-6}alkyl,

wherein each alkyl is unsubstituted or substituted with one to five substituents selected from R^e;

each R^a is independently selected from the group:

(1) CN,

(2) oxo,

(3) -OH,

(4) halogen,

(5) -C_{1-6}alkyl,

(6) -C_{1-6}alkyl-OH,

(7) -O-C_{1-6}alkyl,

(8) -C_{3-6}cycloalkyl,

(9) –C_{1-6}alkyl-C_{3-6}cycloalkyl,

(10) –$(CH_2)_p$-$S(O)_r$$R^f$, and

(11) -$N(R^g)_2$,

wherein each CH_2, alkyl, and cycloalkyl is independently unsubstituted or substituted with one to six substituents selected from halogen, CF_3, OH, C_{1-6}alkyl, and -OC_{1-6}alkyl;

each R^c is independently selected from the group:

(1) -OH,

(2) Cl,

(3) F,

(4) -CH_3,

(5) -CF_3,

(6) -$OCHF_2$,

(7) cyclopropyl, and

(8) NH_2;

each R^e is independently selected from the group:

(1) hydrogen,

(2) OH,

(3) halogen, and

(4) -C_{1-6}alkyl;

each R^f is independently selected from the group:

(1) hydrogen,

(2) -C_{1-6}alkyl,

(3) -C_{3-6}cycloalkyl, and

(4) -C_{2-6}cycloheteroalkyl;

each R^g is independently selected from the group:

(1) hydrogen,

(2) -C_{1-6}alkyl,

(3) -C_{3-6}cycloalkyl,

(4) -C_{2-6}cycloheteroalkyl,

(5) aryl,

(6) heteroaryl,

(7) -C(O)C_{1-6}alkyl, and

(8) -$S(O)_rR^f$,

wherein alkyl can be unsubstituted or substituted with one to three substituents selected from: CF_3, halogen, OH and -OC_{1-6}alkyl;

p is 0, 1, 2, 3, 4, 5 or 6; and

r is 1 or 2.

2. The compound according to Claim 1 wherein

R^5 is hydrogen;

or a pharmaceutically acceptable salt thereof.

3. The compound according to Claim 1 wherein

R^1 is bicyclo[3.1.1]heptane, wherein bicyclo[3.1.1]heptane is unsubstituted or substituted with one to six substituents selected from R^a;

or a pharmaceutically acceptable salt thereof.

4. The compound according to Claim 1 wherein

R^1 is 8-azabicyclo[3.2.1]octane, wherein R^1 is unsubstituted or substituted with one to six substituents selected from R^a;

or a pharmaceutically acceptable salt thereof.

5. A compound selected from:

(1) (*R*)-2-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

(2) (3*S*,4*R*)-3-(3-(2-hydroxy-4-(trifluoromethyl)phenyl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-7-yl)piperidin-4-ol;

(3) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

(4) (*R*)-3-(2-(difluoromethoxy)-4-(trifluoromethyl)phenyl)-7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazine;

(5) (3*S*,4*R*)-3-(3-(2-hydroxy-4-(trifluoro-methyl)phenyl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-7-yl)-1-methylpiperidin-4-ol; and

(6) (3*S*,4*R*)-1-ethyl-3-(3-(2-hydroxy-4-(trifluoro-methyl)phenyl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-7-yl)piperidin-4-ol;

(7) (*R*)-5-chloro-2-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)phenol;

(8) (*R*)-2-(4,6-dimethyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol; and

(9) (*R*)-5-chloro-2-(7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)phenol;

or a pharmaceutically acceptable salt thereof.

6. A compound selected from:

1) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)-3-methyl-5-(trifluoromethyl)phenol;

2) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-4-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

3) (*R*)-2-(7-(1-ethylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-3-methyl-5-(trifluoromethyl)phenol;

4) (*R*)-2-(7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

5) (*S*)-2-(7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

6) (*R*)-5-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)benzo[*b*]thiophen-4-ol;

7) (*R*)-5-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-2,3-dihydro-1*H*-inden-4-ol;

8) (*R*)-5-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-2,3-dihydro-1*H*-inden-4-ol; and

9) (*R*)-2,2-difluoro-5-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-2,3-dihydro-1*H*-inden-4-ol;

or a pharmaceutically acceptable salt thereof.

7. A compound selected from:

1) (*R*)-2-fluoro-3-methyl-6-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)phenol;

2) (*R*)-2-(7-(1-isopropylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

3) (*R*)-2-(7-(1-cyclobutylpiperidin-3-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

4) 2-(7-((1*R*,2*R*,5*S*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

5) 2-(7-((1*S*,2*S*,5*R*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

6) (*R*)-3-cyclopropyl-2-fluoro-6-(4-methyl-7-(1-methylpiperidin-3-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)phenol;

7) 2-(4-methyl-7-((1*S*,2*S*,5*R*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

8) 2-(4-methyl-7-((1*R*,2*R*,5*S*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

9) 2-(7-((1*R*,2R,5*S*)-8-ethyl-8-aza-bicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoro-methyl)phenol;

10) 2-(7-((1*S*,2*S*,5*R*)-8-ethyl-8-aza-bicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoro-methyl)phenol;

11) 2-(7-(5-aminobicyclo[3.1.1]heptan-1-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

12) 2-(4-methyl-7-((8*S*,8a*R*)-octa-hydroindolizin-8-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoro-methyl)phenol; and

13) 2-(4-meth`yl-7-((8*R*,8a*S*)-octahydroindolizin-8-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

8. A compound which is:

(*R*)-2-(4-methyl-7-(piperidin-3-yl)-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

9. A compound which is:

2-(7-((1*R*,2*R*,5*S*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

10. A compound which is:

2-(7-((1*S*,2*S*,5*R*)-8-azabicyclo[3.2.1]octan-2-yl)-4-methyl-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

11. A compound which is:

2-(4-methyl-7-((1*S*,2*S*,5*R*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

12. A compound which is:

2-(4-methyl-7-((1*R*,2*R*,5*S*)-8-methyl-8-azabicyclo[3.2.1]octan-2-yl)-7*H*-imidazo-[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

13. A compound which is:

2-(7-(5-aminobicyclo[3.1.1]heptan-1-yl)-4-methyl-7*H*-imidazo[4,5-*c*]pyridazin-3-yl)-5-(trifluoromethyl)phenol;

or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising a compound of any one of Claims 1 to 13, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

15. The use of a compound according to any one of Claims 1 to 13, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament useful for the treatment of a disorder, condition, or disease that is responsive to the inhibition of NLRP3 in a mammal in need thereof.

16. The use of a compound of any one of Claims 1 to 13, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment, prevention or control of an inflammatory disorder, a fibrotic disorder, a cardiovascular disorder, a metabolic disorder or a neurodegenerative disorder.

17. The use of Claim 16 wherein the disorder is an inflammatory disorder.

18. The use of Claim 17 wherein the inflammatory disorder is selected from: an auto-immune disorder, an auto-inflammatory disorder, an inflammatory joint disorder, an inflammatory skin disorder, and a neuroinflammatory disorder.

19. The use of Claim 15 wherein the disorder is selected from: atherosclerosis, non-alcoholic steatohepatitis, Alzheimer‘s disease and Parkinson’s disease.

20. A compound according to any one of Claims 1 to 13, or a pharmaceutically acceptable salt thereof, for use in therapy.