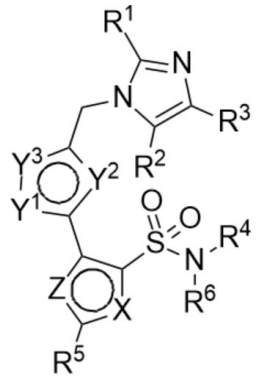
Claims

1. A compound of formula I,



I

wherein:

R^1 represents H, C_{1-6} alkyl, optionally substituted by one or more halogen atoms, CF_3 or OR^7;

R^2 and R^3 independently represent H or C_{1-6} alkyl, optionally substituted by one or more halogen atoms;

Y^1 is -CH-, -CF-, -N-, -NH-, O or S;
Y^2 is -CH-, -CF-, -CH=CH-, -CF=CH-, -CH=CF-, -CF=CF-, -N-, -NH-, O or S;
Y^3 is -CH- or -CF-,
provided that Y^1 and Y^2 are not the same;

R^4 represents C_{1-6} alkyl, C_{1-6} alkoxy or C_{1-6} alkoxy-C_{1-6} alkyl, the alkyl parts of each of which are optionally substituted and/or terminated by one or more halogen atoms or -OH groups, or
R^4 represents aryl, C_{1-6} alkylaryl, C_{1-3} alkenylaryl, heteroaryl, C_{1-6} alkylheteroaryl, or C_{1-3} alkenylheteroaryl, each of which are optionally substituted with one or more halogen, CF_3, CF_3O-, -CN, C_{1-6} alkyl and C_{1-6} alkoxy;

R^5 represents C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy-C_{1-6} alkyl, each of which are optionally substituted by one or more halogen atoms;

R^6 and R^7 independently represent H or C_{1-6} alkyl, optionally substituted by one or more halogen atoms;

X and Z independently represent CH=CH, CH, N, NH, O or S,
provided that:

(a) X and Z are not the same,

(b) when X represents CH=CH then Z may only represent CH, and

(c) when Z represents CH=CH then X may only represent CH,

or a pharmaceutically-acceptable salt thereof.

2. A compound as claimed in Claim 1, wherein R^1 represents tert-butyl or 2-hydroxypropan-2-yl.

3. A compound as claimed in any one of the preceding claims, wherein R^2 and R^3 both represent H.

4. A compound as claimed in any one of the preceding claims, wherein R^4 represents heteroaryl, optionally substituted by one or more halogen atoms, CF_3, -CN, Me or methoxy.

5. A compound as claimed in any one of the preceding claims, wherein R^5 represents isobutyl.

6. A compound as claimed in any one of the preceding claims, wherein R^6 represents H.

7. A compound as claimed in any one of the preceding claims, wherein Y^1 represents -CH-, Y^2 represents -CH=CH-, and/or Y^3 represents -CH- or -CF-.

8. A compound as claimed in any one of the preceding claims, which is:
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
3-(4-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)phenyl)-5-isobutyl-N-(pyrimidin-2-yl)thiophene-2-sulfonamide,
4'-((2-(2-hydroxypropan-2-yl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(5-chloropyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(5-fluoropyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,

4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(5-bromopyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(5-trifluoromethyl pyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(thiazol-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(5-cyanopyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-N-(thiazol-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-N-(5-fluoropyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-N-(5-chloropyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-N-(5-bromopyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-N-(5-cyanopyrimidin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(4,5-dimethyloxazol-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(6-methoxypyridazin-3-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(4-methoxypyrimidin-5-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(4,6-dimethoxypyrimidin-5-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(4,6-dimethoxy-1,3,5-triazin-2-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(5-methylpyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(5-methylisoxazol-3-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(4,5-dimethylisoxazol-3-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(3-methoxypyrazin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,

4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-5-isobutyl-N-(5-methoxypyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-N-(4-methoxypyrimidin-5-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(4,6-dimethoxypyrimidin-5-yl)-3'-fluoro-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-N-(4,5-dimethyloxazol-2-yl)-3'-fluoro-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-N-(6-methoxypyridazin-3-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-N-(5-(trifluoromethyl)pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-*N*-(5-methylpyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
3'-fluoro-5-isobutyl-4'-((2-isopropyl-1*H*-imidazol-1-yl)methyl)-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
3'-fluoro-5-isobutyl-4'-((2-methyl-1*H*-imidazol-1-yl)methyl)-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-ethyl-1*H*-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((1*H*-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-*N*-(5-methoxypyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-*N*-(isothiazol-3-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-5-isobutyl-*N*-(isothiazol-3-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-*N*-(2,6-dimethoxypyrimidin-4-yl)-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-*N*-(2,6-dimethoxypyrimidin-4-yl)-3'-fluoro-5-isobutyl-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-5-isobutyl-*N*-(5-methoxypyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
5-isobutyl-4'-((2-methyl-1*H*-imidazol-1-yl)methyl)-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((1*H*-imidazol-1-yl)methyl)-5-isobutyl-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,

5-isobutyl-4'-((2-isopropyl-1*H*-imidazol-1-yl)methyl)-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-ethyl-1*H*-imidazol-1-yl)methyl)-5-isobutyl-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-cyclopropyl-1*H*-imidazol-1-yl)methyl)-5-isobutyl-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
4'-((2-cyclopropyl-1*H*-imidazol-1-yl)methyl)-3'-fluoro-5-isobutyl-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
3-(4-((2-(tert-butyl)-1*H*-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
3-(3-fluoro-4-((2-methyl-1*H*-imidazol-1-yl)methyl)phenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
3-(4-((2-ethyl-1*H*-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
3-(3-fluoro-4-((2-isopropyl-1*H*-imidazol-1-yl)methyl)phenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
3-(4-((2-cyclopropyl-1*H*-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
3-(4-((1*H*-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
5-isobutyl-3-(4-((2-isopropyl-1*H*-imidazol-1-yl)methyl)phenyl)-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
5-isobutyl-3-(4-((2-methyl-1*H*-imidazol-1-yl)methyl)phenyl)-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
3-(4-((2-ethyl-1*H*-imidazol-1-yl)methyl)phenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide, or
3-(4-((2-cyclopropyl-1*H*-imidazol-1-yl)methyl)phenyl)-5-isobutyl-*N*-(pyrimidin-2-yl)thiophene-2-sulfonamide,
or a pharmaceutically-acceptable salt thereof.

9. A compound as claimed in Claim 8, which is:
3'-fluoro-5-isobutyl-4'-((2-isopropyl-1*H*-imidazol-1-yl)methyl)-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
3'-fluoro-5-isobutyl-4'-((2-methyl-1*H*-imidazol-1-yl)methyl)-*N*-(pyrimidin-2-yl)-[1,1'-biphenyl]-2-sulfonamide,
3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutyl-N-(pyrimidin-2-yl)thiophene-2-sulfonamide, or

3-(4-((2-ethyl-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutyl-N-(pyrimidin-2-yl)thiophene-2-sulfonamide,
or a pharmaceutically-acceptable salt thereof.

10. A compound as defined in any one of Claims 1 to 9, for use as a pharmaceutical.

11. A pharmaceutical formulation comprising a compound as defined in any one of Claims 1 to 9 in admixture with a pharmaceutically-acceptable, adjuvant, diluent or carrier.

12. The use of a compound as defined in any one of Claims 1 to 9, for the manufacture of a medicament for the treatment of an autoimmune disease, a viral respiratory tract infection and/or pneumonia as a consequence thereof, a fibrotic disease, a chronic kidney disease, pulmonary hypertension, heart failure and/or myocardial infarction.

13. A use as claimed in Claim 12, wherein the disease is an interstitial lung disease.

14. A use as claimed in Claim 13, wherein the interstitial lung disease is idiopathic pulmonary fibrosis or sarcoidosis.

15. A use as claimed in Claim 12, wherein the autoimmune disease is rheumatoid arthritis or systemic sclerosis.

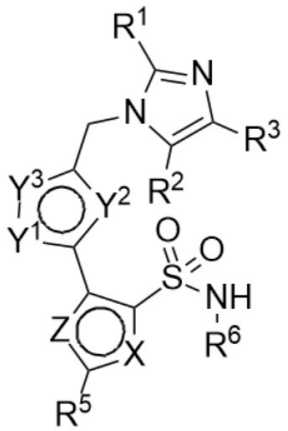
16. A use as claimed in Claim 12, wherein the chronic kidney disease is diabetic nephropathy.

17. A use as claimed in Claim 12, wherein the pulmonary hypertension is pulmonary arterial hypertension.

18. A use as claimed in Claim 12, wherein the heart failure is with preserved ejection fraction.

19. A use as claimed in Claim 12, wherein the viral respiratory tract infection results in virally-induced pneumonia.

20. A process for the preparation of a compound of formula I as defined in any one of the preceding claims, which process comprises reaction of a compound of formula II,



II

wherein R^1, R^2, R^3, R^5, R^6, X, Z, Y^1, Y^2 and Y^3 are as defined in any one of Claims 1 to 7 with a compound of formula III,

L^1R^4 III

wherein R^4 is as defined in any one of Claims 1, 4 or 7 and L^1 represents a suitable leaving group.