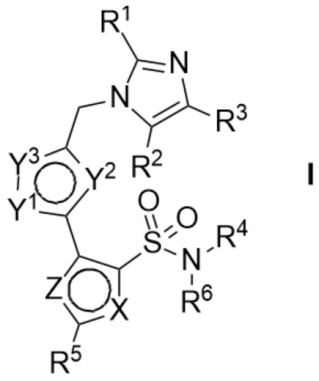
Claims

1. A pharmaceutical formulation comprising 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_{2-3} alkenylaryl, heteroaryl, C_{1-6} alkylheteroaryl, or C_{2-3} 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 in admixture with a pharmaceutically-acceptable, adjuvant, diluent or carrier.

2. The formulation as claimed in Claim 1 wherein R^1 represents methyl, ethyl, isopropyl, cyclopropyl or tert-butyl optionally substituted with CF_3 or OR^7.

3. The formulation as claimed in Claim 1 or Claim 2, wherein R^2 and R^3 both represent H.

4. The formulation 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, methyl or methoxy.

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

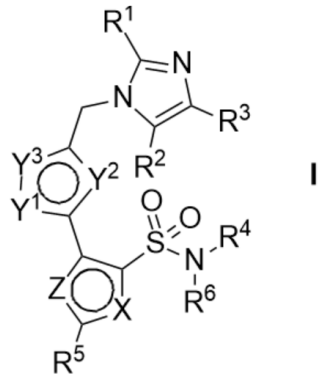
6. The formulation as claimed in any one of the preceding claims, wherein R^6 represents H.

7. The formulation as claimed in any one of the preceding claims, wherein R^7 represents H.

8. The formulation 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-.

9. The formulation as claimed in any one of the preceding claims, wherein X represents -CH=CH- or S.

10. 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 aryl, C_{1-6} alkylaryl, C_{2-3} alkenylaryl, heteroaryl, C_{1-6} alkylheteroaryl, or C_{2-3} 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.

11. The compound as claimed in Claim 10, 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.

12. The compound as claimed in Claim 11, 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.

13. A compound as defined in any one of Claims 1 to 12, for use as a medicament.

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

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

16. The use as claimed in Claim 14, wherein the autoimmune disease is rheumatoid arthritis or systemic sclerosis.

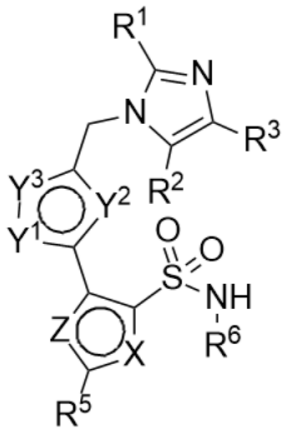
17. The use as claimed in Claim 14, wherein the chronic kidney disease is diabetic nephropathy.

18. The use as claimed in Claim 14, wherein the pulmonary hypertension is pulmonary arterial hypertension.

19. The use as claimed in Claim 14, wherein the heart failure is with preserved ejection fraction.

20. The use as claimed in Claim 14, wherein the viral respiratory tract infection results in virally-induced pneumonia.

21. A process for the preparation of a compound of formula I as claimed 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 claimed in any one of Claims 1 to 10 with a compound of formula III,

$$L^1R^4 \qquad \text{III}$$

wherein R^4 is as claimed in any one of Claims 1, 4 or 10 and L^1 represents a suitable leaving group.