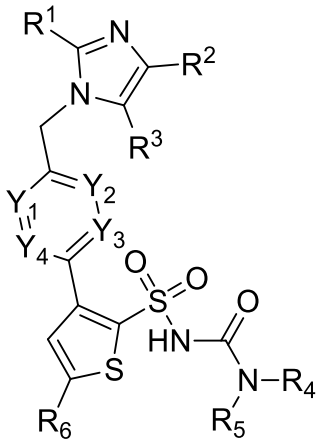
CLAIMS

1. A compound of formula I,



I

in which:

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

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

Y^1, Y^2, Y^3 and Y^4 independently represent -CH-, -CF- or -N-;

R^4 represents C_{1-7} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy-C_{1-6} alkyl, each of which are optionally substituted with one or more halogen atoms, 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 by one or more substituents selected from halogen, CF_3, CF_3O, C_{1-6} alkyl, and C_{1-6} alkoxy;

R^5 represents H or C_{1-6} alkyl, optionally substituted by one or more halogen atoms; and

R^6 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,

or a pharmaceutically-acceptable salt thereof.

2. A compound according to Claim 1, in which R^1 represents C_{1-3} alkyl group, optionally substituted by up to three fluorine atoms.

3. A compound according to Claim 1 or 2, in which R^2 and R^3 independently represent H, methyl or ethyl.

4. A compound according to Claim 1, 2 or 3, in which R^4 represents a C_{1-4} alkyl group, optionally substituted or terminated by up to three fluorine atoms; or a C_{1-2} alkoxy-C_{1-3} alkyl group, optionally substituted or terminated by up to three fluorine atoms; phenyl; C_{1-3} alkyl-aryl; or C_{1-3} alkylheteroaryl.

5. A compound according to any preceding claim, in which R^5 represents H or a C_{1-4} alkyl group.

6. A compound according to any preceding claim, in which R^6 represents a C_{1-4} alkyl group, optionally substituted or more preferably terminated by up to three fluorine atoms.

7. A compound according to any preceding claim, in which Y^1 represents -CH-, -CF- or -N-; Y^2 represents -CH- or -CF-; Y^3 represents -CH-; and/or Y^4 represents -CH- or -N-.

8. A compound according to Claim 7, in which Y^1 represents -CH- or -CF; and/or Y^2, Y^3 and Y^4 all represent -CH-.

9. A compound according to any preceding claim, which is:

1-benzyl-3-(5-isobutyl-3-{*p*-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-2 thienylsulfonyl)urea,

p-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-2-thienylsulfonyl)-1-[(2-pyridyl)methyl]urea,

p-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,

1-butyl-3-(5-isobutyl-3-{*p*-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-2-thienylsulfonyl)urea,

p-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-2-thienylsulfonyl)-1-(4,4,4-trifluorobutyl)urea,

1-benzyl-3-(3-{*p*-[(2-ethyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)urea,

p-[(2-ethyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(2-methoxyethyl)urea, or

p-[(2,4-dimethyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,

3-(3-{*p*-[(2-Ethyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-[(2-pyridyl)methyl]urea,

1-Benzyl-3-(3-{p-[(2,4-dimethyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)urea,

3-(3-{p-[(2,4-Dimethyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-[(2-pyridyl)methyl]urea,

1-benzyl-3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)urea,

3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-[(2-pyridyl)methyl]urea,

3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,

1-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-3-[(1-methyl-1H-imidazol-2-yl)methyl]urea,

1-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-3-[2-(1H-imidazol-4-yl)ethyl]urea,

3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-methyl-1-[(2-pyridyl)methyl]urea,

3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(4,4,4-trifluorobutyl)urea,

3-(5-isobutyl-3-{5-[(2-methyl-1H-imidazol-1-yl)methyl]-2-pyridyl}-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,

3-(5-isobutyl-3-{2-[(2-methyl-1H-imidazol-1-yl)methyl]-5-pyrimidinyl}-2-thienylsulfonyl)-1-(2-methoxyethyl)urea,

3-(5-isobutyl-3-{2-[(2-methyl-1H-imidazol-1-yl)methyl]-5-pyrimidinyl}-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,

3-(5-isobutyl-3-{2-[(2-methyl-1H-imidazol-1-yl)methyl]-5-pyrimidinyl}-2-thienylsulfonyl)-1-[(2-pyridyl)methyl]urea,

1-[(3,5-difluorophenyl)methyl]-3-(5-isobutyl-3-{5-[(2-methyl-1H-imidazol-1-yl)methyl]-2-pyridyl}-2-thienylsulfonyl)urea,

3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(2-methoxyethyl)urea,

3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-[1-(2-pyridyl)ethyl]urea,

3-(3-{2-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,

3-(3-{2-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(2,2,2-trifluoroethyl)urea,

1-(3-fluoropropyl)-3-(5-isobutyl-3-{p-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-2-thienylsulfonyl)urea,

1-(3,3-difluoropropyl)-3-(5-isobutyl-3-{p-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-2-thienylsulfonyl)urea,

1-[(3-{4-[(2-ethyl-1H-imidazol-1-yl)methyl]-3-fluorophenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-3-(3,3,3-trifluoropropyl)urea,

1-[(3-{4-[(2-ethyl-1H-imidazol-1-yl)methyl]-3-fluorophenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-3-(2-methoxyethyl)urea ,

3-[(3-{4-[(2-ethyl-1H-imidazol-1-yl)methyl]-3-fluorophenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-1-[(4-fluorophenyl)methyl]urea ,

1-[(3-{4-[(2-ethyl-1H-imidazol-1-yl)methyl]-3-fluorophenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-3-propylurea ,

1-[(3,4-difluorophenyl)methyl]-3-[(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]urea ,

1-[(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-3-[(thiophen-2-yl)methyl]urea ,

1-[(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-3-propylurea ,

1-[(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-3-(3,3,3-trifluoropropyl)urea ,

1-[(4-chloropyridin-2-yl)methyl]-3-[(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]urea ,

1-[(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]-3-(2-methylpropyl)urea ,

1-[(4,4-difluorocyclohexyl)methyl]-3-[(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-(2-methylpropyl)thiophen-2-yl)sulfonyl]urea ,

1-{[3-(3-fluoro-4-{[2-(propan-2-yl)-1H-imidazol-1-yl]methyl}phenyl)-5-(2-methylpropyl)thiophen-2-yl]sulfonyl}-3-(3,3,3-trifluoropropyl)urea ,

1-{[3-(3-fluoro-4-{[2-(propan-2-yl)-1H-imidazol-1-yl]methyl}phenyl)-5-(2-methylpropyl)thiophen-2-yl]sulfonyl}-3-(4,4,4-trifluorobutyl)urea ,

1-{[3-(3-fluoro-4-{[2-(propan-2-yl)-1H-imidazol-1-yl]methyl}phenyl)-5-(2-methylpropyl)thiophen-2-yl]sulfonyl}-3-propylurea,

1-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-3-propoxyurea,

3-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-(2,2,2-trifluoroethyl)-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea, and

3-(3-{3,5-difluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,

or a pharmaceutically-acceptable salt of any of the above compounds.

10. A compound according to Claim 9, which is 3-(3-{3-fluoro-4-[(2-methyl-1H-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-[(2-pyridyl)methyl]urea or a pharmaceutically acceptable salt thereof.

11. A compound according to Claim 9, which is *p*-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea or a pharmaceutically acceptable salt thereof.

12. A compound as defined in any preceding claim, for use as a pharmaceutical.

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

14. A compound as defined in any of Claims 1 to 11, for use in the treatment of an autoimmune disease, a fibrotic disease, a chronic kidney disease, pulmonary hypertension, heart failure and/or myocardial infarction.

15. Use of a compound as defined in any of Claims 1 to 11, for the manufacture of a medicament for the treatment of an autoimmune disease, a fibrotic disease, a chronic kidney disease, pulmonary hypertension, heart failure and/or myocardial infarction.

16. A compound for use according to Claim 14 or a use according to Claim 15, in which the disease is an interstitial lung disease.

17. A compound for use or a use according to Claim 16, in which the interstitial lung disease is idiopathic pulmonary fibrosis or sarcoidosis.

18. A compound for use according to Claim 14 or a use according to Claim 15, in which the autoimmune disease is rheumatoid arthritis or systemic sclerosis.

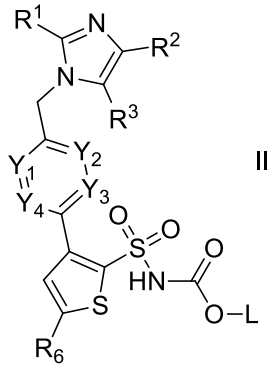
19. A compound for use according to Claim 14 or a use according to Claim 15, in which the chronic kidney disease is diabetic nephropathy.

20. A compound for use according to Claim 14 or a use according to Claim 15, in which the pulmonary hypertension is pulmonary arterial hypertension.

21. A compound for use according to Claim 14 or a use according to Claim 15, in which the heart failure is with preserved ejection fraction.

22. A process for the preparation of a compound of formula I as defined in any of Claims 1 to 11, which process comprises:

(i) reaction of a compound of formula II,



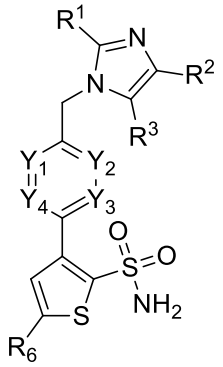
II

in which R^1, R^2, R^3, R^6, Y^1, Y^2, Y^3 and Y^4 are as defined in any one of Claims 1 to 9 as appropriate and L represents C_{1-6} alkyl with a compound of formula III,

NHR^4R^5 III

in which R^4 and R^5 are as defined in any one of Claims 1 to 11; or

(ii) for compounds of formula I in which R^5 represents H, reaction of a compound of formula IV,



IV

in which R^1, R^2, R^3, R^6, Y^1, Y^2, Y^3 and Y^4 are as defined in any one of Claims 1 to 11 as appropriate with a compound of formula V,

R^4-N=C=O V

in which R^4 is as defined in any one of Claims 1 to 11.