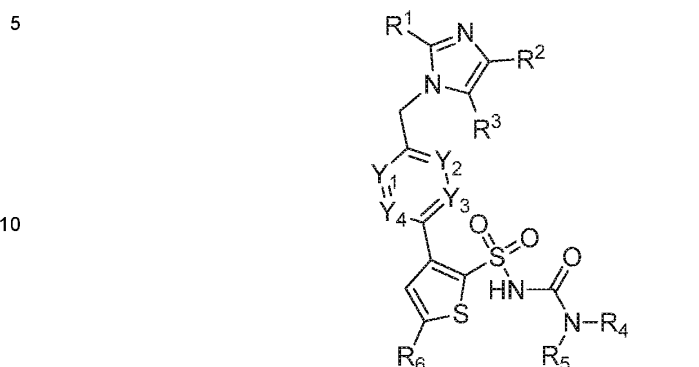


Claims

1. A compound of formula I,



15 wherein:

R¹ represents C₁₋₆ alkyl, optionally substituted by one or more halogen atoms;

20 R² and R³ independently represent H or C₁₋₆ alkyl, optionally substituted by one or more halogen atoms;

Y¹, Y², Y³ and Y⁴ independently represent -CH-, -CF- or -N-;

25 R⁴ represents C₁₋₇ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy-C₁₋₆ alkyl, each of which are optionally substituted with one or more halogen atoms, or

R⁴ represents aryl, C₁₋₆ alkylaryl, C₁₋₃ alkenylaryl, heteroaryl, C₁₋₆ alkylheteroaryl or C₁₋₃ alkenylheteroaryl, each of which are optionally substituted by one or more substituents selected from halogen, CF₃, CF₃O, C₁₋₆ alkyl, and C₁₋₆ alkoxy;

30 R⁵ represents H or C₁₋₆ alkyl, optionally substituted by one or more halogen atoms; and

R⁶ represents C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy-C₁₋₆ alkyl, each of which are optionally substituted by one or more halogen atoms,

35 or a pharmaceutically-acceptable salt thereof.

2. A compound as claimed in Claim 1, wherein R¹ represents C₁₋₃ alkyl group, optionally substituted by up to three fluorine atoms.

3. A compound as claimed in Claim 1 or Claim 2, wherein R² and R³ independently represent H, methyl or ethyl.
- 5 4. A compound as claimed in any one of the preceding claims, wherein R⁴ represents a C₁₋₄ alkyl group, optionally substituted or terminated by up to three fluorine atoms; or a C₁₋₂ alkoxy-C₁₋₃ alkyl group, optionally substituted or terminated by up to three fluorine atoms; phenyl; C₁₋₃ alkylaryl; or C₁₋₃ alkylheteroaryl.
- 10 5. A compound as claimed in any one of the preceding claims, wherein R⁵ represents H or a C₁₋₄ alkyl group.
6. A compound as claimed in any one of the preceding claims, wherein R⁶ represents a C₁₋₄ alkyl group, optionally substituted or more preferably terminated by up to three fluorine atoms.
- 15 7. A compound as claimed in any one of the preceding claims, wherein Y¹ represents -CH-, -CF- or -N-; Y² represents -CH- or -CF-; Y³ represents -CH-; and/or Y⁴ represents
- 20 -CH- or -N-.
8. A compound as claimed in Claim 7, wherein Y¹ represents -CH- or -CF; and/or Y², Y³ and Y⁴ all represent -CH-.
- 25 9. A compound as claimed in any one of the preceding claims, 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,
30 *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,
35 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,
- 5 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-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)urea,
- 3-(3-{*p*-[(2,4-Dimethyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-
- 10 thienylsulfonyl)-1-[(2-pyridyl)methyl]urea,
- 1-benzyl-3-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)urea,
- 3-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-[(2-pyridyl)methyl]urea,
- 15 3-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,
- 1-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-3-[(1-methyl-1*H*-imidazol-2-yl)methyl]urea,
- 1-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-
- 20 thienylsulfonyl)-3-[2-(1*H*-imidazol-4-yl)ethyl]urea,
- 3-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-methyl-1-[(2-pyridyl)methyl]urea,
- 3-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(4,4,4-trifluorobutyl)urea,
- 25 3-(5-isobutyl-3-{5-[(2-methyl-1*H*-imidazol-1-yl)methyl]-2-pyridyl}-2-thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,
- 3-(5-isobutyl-3-{2-[(2-methyl-1*H*-imidazol-1-yl)methyl]-5-pyrimidinyl}-2-thienylsulfonyl)-1-(2-methoxyethyl)urea,
- 3-(5-isobutyl-3-{2-[(2-methyl-1*H*-imidazol-1-yl)methyl]-5-pyrimidinyl}-2-
- 30 thienylsulfonyl)-1-(3,3,3-trifluoropropyl)urea,
- 3-(5-isobutyl-3-{2-[(2-methyl-1*H*-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-1*H*-imidazol-1-yl)methyl]-2-pyridyl}-2-thienylsulfonyl)urea,
- 35 3-(3-{3-fluoro-4-[(2-methyl-1*H*-imidazol-1-yl)methyl]phenyl}-5-isobutyl-2-thienylsulfonyl)-1-(2-methoxyethyl)urea,
- 3-(3-{3-fluoro-4-[(2-methyl-1*H*-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,
- 5 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,
- 10 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 ,
- 15 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 ,
- 20 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 ,
- 25 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 ,
- 30 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 ,
- 35 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-1H-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,
5 or a pharmaceutically-acceptable salt of any of the above compounds.
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
10 Claims 1 to 9 in admixture with a pharmaceutically- or cosmetically-acceptable, adjuvant, diluent or carrier.
12. A compound as defined in any one of Claims 1 to 9, for use in the treatment of
an autoimmune disease, a fibrotic disease, a chronic kidney disease, pulmonary
15 hypertension, heart failure and/or myocardial infarction.
13. 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 fibrotic
disease, a chronic kidney disease, pulmonary hypertension, heart failure and/or
20 myocardial infarction.
14. A method of treatment of an autoimmune disease, a fibrotic disease, a chronic
kidney disease, pulmonary hypertension, heart failure and/or myocardial infarction,
which comprises administering a compound as defined in any one of Claims 1 to 9 to
25 a patient in need of such treatment.
15. A compound for use as claimed in Claim 12, a use as claimed in Claim 13, or a
method of treatment as claimed in Claim 14, wherein the disease is an interstitial lung
disease.
30
16. A compound for use, a use, or a method of treatment as claimed in Claim 15,
wherein the interstitial lung disease is idiopathic pulmonary fibrosis or sarcoidosis.
17. A compound for use as claimed in Claim 12, a use as claimed in Claim 13, or a
35 method of treatment as claimed in Claim 14, wherein the autoimmune disease is
rheumatoid arthritis or systemic sclerosis.

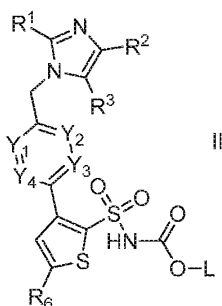
18. A compound for use as claimed in Claim 12, a use as claimed in Claim 13, or a method of treatment as claimed in Claim 14, wherein the chronic kidney disease is diabetic nephropathy.

19. A compound for use as claimed in Claim 12, a use as claimed in Claim 13, or a method of treatment as claimed in Claim 14, wherein the pulmonary hypertension is pulmonary arterial hypertension.

20. A compound for use as claimed in Claim 12, a use as claimed in Claim 13, or a method of treatment as claimed in Claim 14, wherein the heart failure is with preserved ejection fraction.

21. A process for the preparation of a compound of formula I as defined in any one of Claims 1 to 9, which process comprises:

(i) reaction of a compound of formula II,

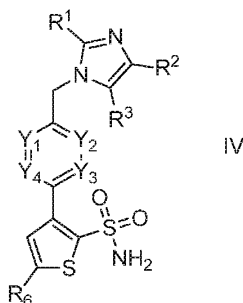


wherein R^1 , R^2 , R^3 , R^6 , Y^1 , Y^2 , Y^3 and Y^4 are as defined in any one of Claims 1 to 9 as appropriate and L represents C_{1-6} alkyl with a compound of formula III,



wherein R^4 and R^5 are as defined in any one of Claims 1 to 9; or

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



wherein 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 with a compound of formula V,



wherein R^4 is as defined in any one of Claims 1 to 9.