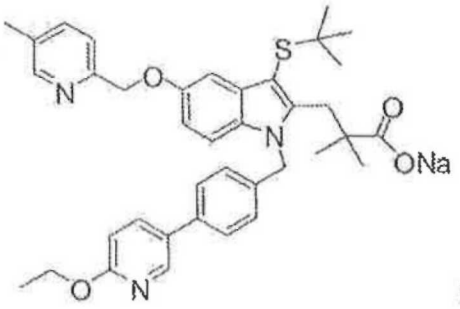
~~What is claimed is:~~

1. A pharmaceutically acceptable salt comprising 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionate as the anion and a cation selected from Na^+, K^+, Li^+, Ca^{2+}, NH_4^+, the protonated form of dicyclohexylamine, the protonated form of *N*-methyl-D-glucamine, the protonated form of tris(hydroxymethyl)methylamine, the protonated form of arginine, and the protonated form of lysine.

2. The pharmaceutically acceptable salt according to claim 1, which is sodium 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethylpropionate (Compound 2):



Compound 2.

3. The pharmaceutically acceptable salt according to claim 1 or claim 2 wherein the pharmaceutically acceptable salt is desolvated.

4. The pharmaceutically acceptable salt according to claim 1 or claim 2, wherein the pharmaceutically acceptable salt is solvated.

5. The pharmaceutically acceptable salt according to claim 4, wherein the pharmaceutically acceptable salt is solvated with a solvent selected from ethyl acetate, isopropyl acetate, methyl tert-butylether, heptane, isopropanol, and ethanol.

6. The pharmaceutically acceptable salt according to claim 5, wherein the pharmaceutically acceptable salt is solvated with methyl tert-butylether.

7. The pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein the pharmaceutically acceptable salt comprises a detectable amount of water.

8. The pharmaceutically acceptable salt according to any one of claims 1 to 7, wherein the pharmaceutically acceptable salt comprises a detectable amount of palladium that is less than 20ppm.

9. The pharmaceutically acceptable salt according to claim 8, wherein the pharmaceutically acceptable salt comprises a detectable amount of palladium that is less than 10ppm.

10. The pharmaceutically acceptable salt according to any one of claims 2 to 9, wherein Compound 2 has a solubility in water at about pH 10 and at about 25 °C that is greater than about 10 mg/mL.

11. The pharmaceutically acceptable salt according to any one of claims 2 to 10, wherein Compound 2 is in an amorphous phase, partially crystalline form, crystalline form, milled form, or nano-particulate form.

12. The pharmaceutically acceptable salt according to claim 11, wherein the pharmaceutically acceptable salt is crystalline.

13. The pharmaceutically acceptable salt according to claim 12, wherein Compound 2 is crystalline polymorph Form C.

14. The pharmaceutically acceptable salt according to claim 12 or claim 13, wherein Compound 2 is crystalline and was formed using methyl tert-butyl ether.

15. The pharmaceutically acceptable salt according to any one of claims 12 to 14 wherein Compound 2 has at least one of the following properties:

(1c) an X-ray powder diffraction (XRPD) pattern substantially similar to the one set forth in **Figure 1**;

(2c) an XRPD pattern with peaks at about 17.2°2-Theta, at about 18.4°2-Theta, at about 19.1° 2-Theta, at about 20.8°2-Theta, and at about 23.8°2-Theta;

(3c) a single melting point at about 290°C to about 295°C as measured by differential scanning calorimetry (DSC);

(4c) a DSC or a thermo-gravimetric analysis (TGA) substantially similar to the ones set forth in **Figure 15**;

(5c) physical and chemical stability (at 5°C, 25°C/60% relative humidity (RH), and/or 40°C/75% RH for at least one month in a humidity chamber);

(6c) non-hygroscopicity;

(7c) IR spectrum substantially similar to the one set forth in **Figure 19**; and/or

(8c) an X-ray powder diffraction (XRPD) pattern substantially similar to an XRPD pattern obtained for crystals of Compound 2 obtained from methyl tert-butyl ether (MTBE) or acetonitrile.

16. The pharmaceutically acceptable salt according to claim 12, wherein Compound 2 is crystalline polymorph Form B.

17. The pharmaceutically acceptable salt according to claim 16, wherein Compound 2 has at least one of the following properties:

(1b) an X-ray powder diffraction (XRPD) pattern substantially similar to the one set forth in **Figure 2**;

(2b) an XRPD pattern with peaks at about 6.6° 2-Theta, at about 8.1°2-Theta, at about 19.7°2-Theta, at about 21.0°2-Theta, at about 21.9°2-Theta, and at about 22.1°2-Theta.

18. The pharmaceutically acceptable salt according to claim 11, wherein the pharmaceutically acceptable salt is in an amorphous phase.

19. The pharmaceutically acceptable salt according to claim 18, wherein Compound 2 has at least one property selected from:

(1a) an XRPD pattern showing a lack of crystallinity;

(2a) at least one endotherm and at least one exotherm observed by differential scanning calorimetry (DSC);

(3a) a glass transition temperature of about 127°C;

(4a) a melting point at about 155°C followed by a re-crystallisation event at about 200°C followed by a second melting point at about 288°C to about 295 °C;

(5a) a phase change to a crystalline form when heated above about 200°C, wherein the crystalline form that is formed above about 200°C is characterized by an XRPD pattern substantially similar to any one of the XRPD patterns set forth in Figure 9;

(6a) a DSC or a TGA substantially similar to the ones set forth in **Figure 12**;

(7a) hygroscopicity; and/or

(8a) chemical stability.

20. The pharmaceutically acceptable salt according to any one of claims 1 to 19 for treating asthma, treating and/or preventing exercise-induced bronchoconstriction, treating and/or preventing allergic rhinitis, treating chronic obstructive pulmonary disease, treating cardiovascular disease, treating NSAID-indused gastric lesions, treating pain, treating ocular disease or treating skin disease in a human.

21. The pharmaceutically acceptable salt according to claim 20 for treating asthma, preventing exercise-induced bronchoconstriction, treating allergic rhinitis, treating chronic obstructive pulmonary disease, treating cardiovascular disease or treating NSAID-induced gastric lesions in a human.

22. The pharmaceutically acceptable salt according to any one of claims 1 to 19 for use in the treatment of asthma, prevention of exercise-induced bronchoconstriction,

treatment and/or prevention of allergic rhinitis, treatment of chronic obstructive pulmonary disease, treatment of cardiovascular disease, treatment of NSAID-induced gastric lesions, treatment of pain, treatment of ocular disease or treatment of skin disease in a human.

23. A pharmaceutical composition comprising:

a. a pharmaceutically acceptable salt according to any one of claims 1 to 22; and

b. at least one pharmaceutically acceptable inactive ingredient selected from among excipients, diluents, and carriers.

24. A pharmaceutical composition comprising:

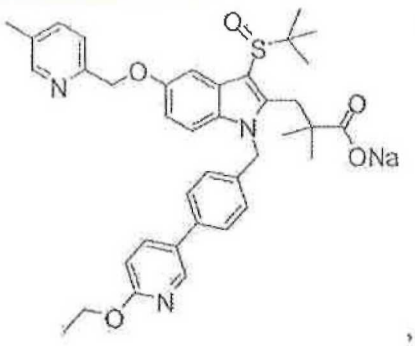
a. Compound 2 according to any one of claims 2 to 22; and

b. at least one pharmaceutically acceptable inactive ingredient selected from among excipients, diluents, and carriers.

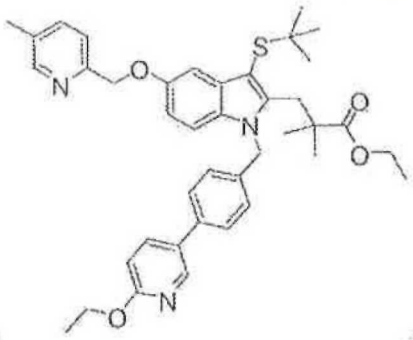
25. The pharmaceutical composition according to claim 23 or claim 24, wherein the composition comprises a detectable amount of solvent selected from 1,2-dimethoxyethane, ethyl acetate, methanol, ethanol, tetrahydrofuran, and methyl tert-butyl ether; wherein the solvents are detected at levels less than about 5000ppm.

26. The pharmaceutical composition according to claim 24 or claim 25, wherein Compound 2 underwent a crystal formation or was precipitated from methyl tert-butyl ether.

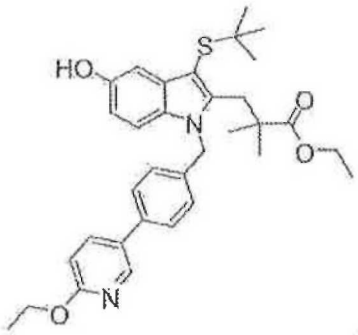
27. The pharmaceutical composition according to any one of claims 24 to 26, wherein the composition comprises a detectable amount of a compound selected from:



,



, and



.

28. The pharmaceutical composition according to any one of claims 24 to 27, wherein Compound 2 is greater than 97% pure.

29. The pharmaceutical composition according to claim 28, wherein Compound 2 is greater than 98% pure.

30. The pharmaceutical composition according to claim 29, wherein Compound 2 is greater than 99% pure.

31. The pharmaceutical composition according to any one of claims 23 to 30, wherein the pharmaceutical composition is in a form suitable for oral administration to a mammal.

32. The pharmaceutical composition according to claim 31, wherein the pharmaceutical composition is in the form of a pill, capsule, tablet, aqueous solution, or aqueous suspension.

33. An oral pharmaceutical composition comprising:

(a) a pharmaceutically acceptable salt according to any one of claims 1 to 22 wherein the cation is selected from Na^+, K^+, and Li^+;

(b) an aqueous buffer solution; and optionally

(c) ethanol or Poloxamer 124.

34. The oral pharmaceutical composition according to claim 33, wherein:

the cation is Na^+.

35. The oral pharmaceutical composition according to claim 33 or claim 34, wherein the aqueous buffer solution is an aqueous sodium carbonate buffer solution.

36. The oral pharmaceutical composition according to any one of claims 33 to 35, further comprising a pharmaceutically acceptable sweetener.

37. The oral pharmaceutical composition of claim 36, wherein the pharmaceutically acceptable sweetener is selected from sucrose, sorbitol, aspartame, sucralose, simple syrup, and syrpalta.

38. The oral pharmaceutical composition according to any one of claims 33 to 37, wherein the oral pharmaceutical composition has a concentration of up to about 60mg/mL of the sodium salt of 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid.

39. The oral pharmaceutical composition according to claim 38, wherein the oral pharmaceutical composition has a concentration of from about 10mg/mL to about 50mg/mL of the sodium salt of 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid.

40. The oral pharmaceutical composition according to claim 38, wherein the oral pharmaceutical composition has a concentration of from about 1mg/mL to about 20mg/mL of the sodium salt of 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid.

41. The oral pharmaceutical composition according to any on of claims 33 to 40, comprising:

a. about 1g of the sodium salt of 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid (Compound 2); and

b. about 100mL of a solution of 1% (w/w) Poloxamer 124 and 99% (w/w) aqueous sodium carbonate buffer (0.010M, pH9-10), sweetened with sucralose.

42. The oral pharmaceutical composition according to any one of claims 33 to 41, wherein a single dose of the pharmaceutical composition comprising from about 10mg to about 1000mg of the pharmaceutically acceptable salt of 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-

methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid when administered to healthy adult human subjects in the fasted state provides a C_{max} of about 0.2μM to about 30μM, a t_{max} of about 1 hour to about 4 hours, and an AUC_{0-24} of about 4 hr·μM to about 160 hr·μM.

43. The oral pharmaceutical composition according to any one of claims 33 to 41, wherein:
the single dose of the pharmaceutical composition when administered to healthy adult human subjects in the fasted state provides a C_{max} that is less than about 9μM.

44. The oral pharmaceutical composition according to claim 42, wherein the single dose of the oral pharmaceutical composition when administered to healthy adult human subjects in the fasted state provides after about 8 hours at least 70% reduction in blood ionophore-stimulated LTB_4 production and provides after about 24 hours at least 30% reduction in blood ionophore-stimulated LTB_4 production.

45. The oral pharmaceutical composition according to claim 42, wherein the single dose of the oral pharmaceutical composition when administered to healthy adult human subjects in the fasted state provides after about 24 hours at least 50% reduction in urinary LTE_4 levels.

46. The oral pharmaceutical composition according to any one of claims 42 to 45, wherein:
the single dose of the oral pharmaceutical composition comprises about 10mg, about 50mg, about 150mg, about 300mg, about 600mg, or about 1000mg of of the pharmaceutically acceptable salt of 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid.

47. An oral solid dosage form pharmaceutical composition comprising:
a) a pharmaceutically acceptable salt according to any one of claims 1 to 22; and
b) at least one inactive pharmaceutical ingredient.

48. An oral solid dosage form pharmaceutical composition according to claim 47 comprising:
a) from about 10mg to about 1000mg of the pharmaceutically acceptable salt; and
b) at least one inactive pharmaceutical ingredient.

49. The oral solid dosage form pharmaceutical composition according to claim 47 or claim 48, wherein the composition comprises about 10mg, about 50 mg, about 100mg, about 150mg, about 200mg, about 250mg, or about 300mg of Compound 2.

50. The oral solid dosage form pharmaceutical composition according to any one of claims 47 to 49, wherein the oral solid dosage form is in the form of a tablet.

51. The oral solid dosage form pharmaceutical composition according to claim 50, wherein:
the oral solid dosage form is in the form of an immediate release tablet.

52. The oral solid dosage form pharmaceutical composition according to claim 51, wherein:
the formulation exhibits an *in vitro* release of Compound 2 in about 1% sodium lauryl sulfate solution at pH of about 7 and about 37°C of more than about 90% after about 10 minutes.

53. The oral solid dosage form pharmaceutical composition according to claim 52, wherein:
the *in vitro* release is measured by a drug release test using the United States Pharmacopea (USP) Type 1, basket at about 100rpm with about 500mL of about 1% sodium lauryl sulfate solution at pH of about 7 and about 37°C.

54. The oral solid dosage form pharmaceutical composition according to any one of claim 47 to 51, wherein the oral solid dosage form when administered as a single dose to healthy adult human subjects in the fasted state provides a C_{max} less than about 5μM, and provides after about 8 hours at least 80% reduction in blood ionophore-stimulated LTB_4 production.

55. The oral solid dosage form pharmaceutical composition according to any one of claims 47 to 51, wherein the oral solid dosage form when administered as a single dose to healthy adult humans in the fasted state provides after about 24 hours at least 30% reduction in blood ionophore-stimulated LTB_4 production.

56. The oral solid dosage form pharmaceutical composition according to claim 54 or claim 55, wherein the oral solid dosage form when administered as a single dose to healthy adult human subjects in the fasted state provides after about 24 hours at least 80% reduction of urinary LTE_4 levels.

57. The oral solid dosage form pharmaceutical composition according to any one of claims 47 to 51, wherein the inactive pharmaceutical ingredients comprise a binding agent, a disintegrant, and a glidant.

58. The oral solid dosage form pharmaceutical composition according to claim 57, wherein the inactive pharmaceutical ingredients comprise silicified microcrystalline cellulose (SMCC), mannitol, crospovidone, and magnesium stearate.

59. The oral solid dosage form pharmaceutical composition according to any one of claims 47 to 51, wherein the oral solid dosage form pharmaceutical composition comprises from about 10% by weight to about 20% by weight of Compound 2.

60. The oral solid dosage form pharmaceutical composition according to any one of claims 47 to 49, wherein the oral solid dosage form pharmaceutical composition is in the form of a capsule.

61. The oral solid dosage form pharmaceutical composition according to claim 60, wherein the capsule is in the form of a hard gelatine capsule.

62. The oral solid dosage form pharmaceutical composition according to claim 61, wherein the capsule comprises at least one excipient in addition to the hard gelatine capsule.

63. A pharmaceutical composition that provides at least one metabolite of 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid after administration to a mammal.

64. The pharmaceutical composition according to claim 63, wherein the least one metabolite is selected from among:

a. 3-[3-*tert*-butylsulfinyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid;

b. 3-[3-*tert*-butylsulfanyl-1-[4-(6-hydroxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid;

c. 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-N-oxy-pyridin-2-ylmethoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid;

d. the acyl gluconuride of 3-[3-tert-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid; and

e. combinations thereof.

65. The pharmaceutical composition according to claim 63 or claim 64, wherein the least one metabolite is the acyl glucouuride of 3-[3-tert-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid.

66. A pharmaceutical composition comprising an active ingredient that inhibits 5-lipoxygenase-activating protein (FLAP) and does not substantially inhibit at least one Cytochrome P450 enzyme selected from CYP 3A4, CYP 1A2, CYP 2A6, CYP 2B6, CYP 2C8, CYP 2C9, CYP 2C19, CYP 2D6, and CYP 2E1 at doses up to 40μM.

67. The pharmaceutical composition according to claim 66, wherein:
the pharmaceutical composition does not substantially induce Cytochrome P450 CYP 3A4, CYP 2C9, CYP 1A2, CYP 2C19, or CYP 2D6 at doses up to 40μM.

68. The pharmaceutical composition according to claim 66 or claim 67, wherein the active ingredient is 3-[3-tert-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1H-indol-2-yl]-2,2-dimethyl-propionic acid, or a pharmaceutically acceptable salt thereof.

69. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of asthma in a human.

70. The pharmaceutical composition according to any one of claims 23 to 68 for use in the prevention of exercise-induced bronchoconstriction in a human.

71. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of allergic rhinitis in a human.

72. The pharmaceutical composition according to any one of claims 23 to 68 for use in the prevention of allergic rhinitis in a human.

73. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of chronic obstructive pulmonary disease in a human.

74. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of cardiovascular disease in a human.

75. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of NSAID-induced gastric lesions in a human.

76. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of ocular disease in a human.

77. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of pain in a human.

78. The pharmaceutical composition according to any one of claims 23 to 68 for use in the treatment of skin disease in a human.

79. The pharmaceutical composition according to of any one of claims 69 to 78, wherein the pharmaceutical composition further comprises at least one additional pharmaceutical agent selected from inhaled corticosteroids, short acting beta-agonists, long acting beta-agonists, and antihistamines.

80. An article of manufacture comprising multiple unit doses of the oral solid dosage form pharmaceutical composition according to any one of claims 23 to 79 in a high-density polyethylene (HDPE) bottle equipped with a high-density polyethylene (HDPE) cap.

81. The article of manufacture of claim 80, further comprising an aluminum foil induction seal and silica gel desiccant.

82. A method of treating asthma in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

83. A method of preventing exercise-induced bronchoconstriction in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

84. A method of treating allergic rhinitis in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

85. A method of preventing allergic rhinitis in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

86. A method of treating chronic obstructive pulmonary disease in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

87. A method of treating ocular disease in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

88. A method of treating skin disease in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

89. The method according to any one of claims 82 to 88, wherein the method further comprises administering at least one additional pharmaceutical agent selected from

inhaled corticosteroids, short acting beta-agonists, long acting beta-agonists, and antihistamines.

90. A method of treating chronic obstructive pulmonary disease in a human comprising administering to the human a pharmaceutical composition according to any one of claims 23 to 79.

91. A method of treating cardiovascular disease in a human comprising administering to the human a pharmaceutical composition according to any one of claims 23 to 79.

92. A method of treating NSAID-induced gastric lesions in a human comprising administering to the human a pharmaceutical composition according to any one of claims 23 to 79.

93. A method of treating pain in a human comprising administering to the human an oral pharmaceutical composition according to any one of claims 23 to 79.

94. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of asthma in a human.

95. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of allergic rhinitis in a human.

96. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the prevention of allergic rhinitis in a human.

97. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of chronic obstructive pulmonary disease in a human.

98. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of ocular disease in a human.

99. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of cardiovascular disease in a human.

100. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of skin disease in a human.

101. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of NSAID-induced gastric lesions in a human.

102. Use of a pharmaceutically acceptable salt according to any one of claims 1 to 22 for the manufacture of a medicament for the treatment of pain in a human.

103. A process for the preparation of a pharmaceutically acceptable salt according to any one of claims 12 to 17 comprising the steps of:

(1) adding Compound 2 to methyl tert-butylether to form a mixture;

(2) heating the mixture from step (1) and then cooling the solution; and

(3) isolating the solids that are formed from step (2) to provide a crystalline form of Compound 2.

104. A process for the preparation of a pharmaceutically acceptable salt according to any one of claims 2 to 22:

(a) reacting 4-methoxyphenylhydrazine hydrochloride with 4-bromobenzyl bromide in the presence of triethylamine and toluene to provide N-(4-bromo-benzyl)-N-(4-methoxy-phenyl)-hydrazine hydrochloride;

(b) treating the product of step (a) with HCl to provide N-(4-bromo-benzyl)-N-(4-methoxy-phenyl)-hydrazine hydrochloride;

(c) reacting N-(4-bromo-benzyl)-N-(4-methoxy-phenyl)-hydrazine hydrochloride with acetic acid, 5-*tert*-butylsulfanyl-2,2-dimethyl-4-oxo-pentanoic acid ethyl ester, and sodium acetate in toluene to provide 3-[1-(4-bromo-benzyl)-3-*tert*-butylsulfanyl-5-methoxy-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester;

(d) reacting 3-[1-(4-bromo-benzyl)-3-*tert*-butylsulfanyl-5-methoxy-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester with 2-methyl-2-propanethiol and aluminum chloride in dichloromethane to provide 3-[1-(4-bromo-benzyl)-3-*tert*-butylsulfanyl-5-hydroxy-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester;

(e) reacting 3-[1-(4-bromo-benzyl)-3-*tert*-butylsulfanyl-5-hydroxy-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester with bis(pinacolato)diboron using palladium mediated reaction conditions to provide 3-{3-*tert*-butylsulfanyl-5-hydroxy-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-1*H*-indol-2-yl}-2,2-dimethyl-propionic acid ethyl ester;

(f) reacting 3-{3-tert-butylsulfanyl-5-hydroxy-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-1H-indol-2-yl}-2,2-dimethyl-propionic acid ethyl ester with 5-bromo-2-ethoxypyridine using palladium mediated reaction conditions to provide 3-{3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-hydroxy-1*H*-indol-2-yl}-2,2-dimethyl-propionic acid ethyl ester;

(g) reacting 3-{3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-hydroxy-1*H*-indol-2-yl}-2,2-dimethyl-propionic acid ethyl ester with 2-chloro-5-

methylpyridine hydrochloride in the presence of a base and solvent to provide 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester;

(h) treating 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester with thiol derivatized silica gel; and

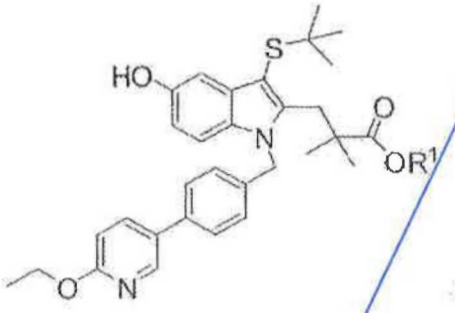
(i) forming Compound 2 from 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester.

105. The process of claim 104, wherein step (i) comprises reacting 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-ylmethoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionic acid ethyl ester with NaOH in a suitable solvent.

106. The process of claim104, wherein step (i) further comprises crystal formation of Compound 2 from methyl tert-butyl ether.

107. A process for the preparation of a pharmaceutically acceptable salt according to any one of claims 2 to 22 comprising the steps of:

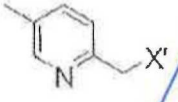
(A) reacting a compound of Formula (III)



Formula (III);

where R^1 is an alkyl;

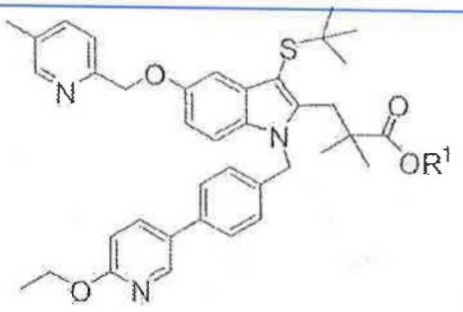
with a compound of Formula (II)



Formula (II);

wherein X' is a leaving group;

in the presence of a base and solvent to form a compound of Formula (I)



Formula (I);

and

(B) forming Compound 2 form the compound of Formula (I) of step (A).

108. The process according to claim 107, wherein step (A) further comprises isolating the compound of Formula (I) prior to step (B).

109. The process according to claim 107 or claim 108, wherein step (A) further comprises reducing the amount of palladium to less than about 20ppm.

110. The process according to claim 109, wherein reducing the amount of palladium comprises treatment of the compound of Formula (I) with thiol derivatized silica gel.

111. The process according to claim 107, wherein the reaction of step (A) is heated to a temperature of about 50°C to about 90°C.

112. The process according to claim 107, wherein step (B) comprises hydrolysis of the ester moiety of the product of step (A).

113. The process according to claim 112, wherein step (B) comprises treatment of the compound of Formula (I) from step (A) with:

a) LiOH, KOH, or $Ca(OH)_2$, followed by NaOH; or

b) NaOH.

114. The process according to claim 113, wherein step (B) comprises treatment of the compound of Formula (I) from step (i) with LiOH followed by NaOH.

115. The process according to claim 113, wherein step (B) comprises treatment of the compound of Formula (I) from step (i) with NaOH.

116. The process according to claim 115, whereinstep (B) is carried out in a solvent system comprising tetrahydrofuran, water and an alcohol selected from methanol and ethanol.

117. The process according to claim 116, wherein step (B) is carried out in a solvent system comprising tetrahydrofuran, water and ethanol.

118. The process according to claim 107, further comprising crystal formation of Compound 2 from methyl tert-butyl ether (MTBE).

119. The process according to claim 107, wherein R^1 is $-CH_3$ or $-CH_2CH_3$.

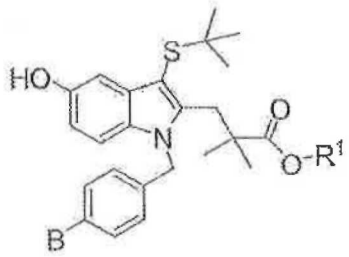
120. The process according to claim 107, wherein the base is a cesium base.

121. The process according to claim 107, wherein X' is selected from Cl, Br, I, $-OSO_2CF_3$, $-OSO_2$(4-methylphenyl), $-OSO_2$(phenyl) and $-OSO_2CH_3$.

122. The process according to claim 121, wherein X' is Cl.

123. The process according to claim 107, wherein the compound of Formula (III) is prepared by:

reacting a compound of formula (IV):

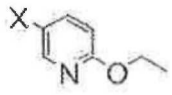


Formula (IV)

wherein R^1 is C_1-C_6 alkyl;

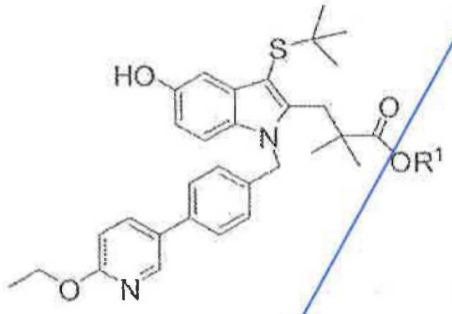
B is a boronic acid or boronate ester;

with a compound of Formula (IV) in the presence of a first coupling catalyst;



Formula (V)

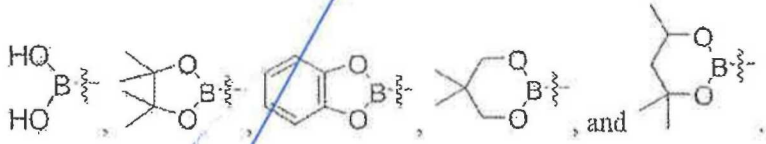
wherein X is a leaving group; to provide a compound of Formula (III)

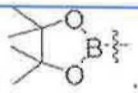


Formula (III).

124. The process according to claim 123, wherein X is selected from Cl, Br, I, or $-OSO_2CF_3$.

125. The process according to claim 123 or claim 124, wherein B is selected from



126. The process according to claim 125, wherein B is .

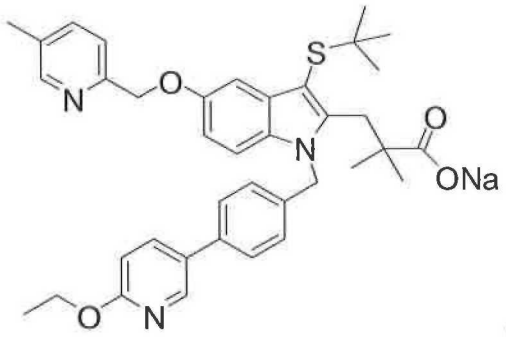
127. The process according to any one of claims 123 to 126, wherein the first coupling catalyst is a palladium catalyst.

128. The process of claim 127, wherein the palladium catalyst is tetrakis(triphenylphosphine)palladium.

129. The process according to any one of claims 123 to 128, wherein the reaction further comprises heating to a temperature of about 60°C to about 95°C.

Claims

1. A crystalline Form C of sodium 3-[3-(tert-butylsulfanyl)-1-[4-(6-ethoxy-pyridin-3-yl)benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1H-indol-2-yl]-2,2-dimethyl-propionate:



having an X-ray powder diffraction (XRPD) pattern with peaks at 17.2 °2-Theta, at 18.4 °2-Theta, at 19.1 °2-Theta, at 20.8 °2-Theta, and at 23.8 °2-Theta.

2. The crystalline Form C according to claim 1, having peaks comprising the 2-theta values listed below in the following Table, obtained with a diffractometer using copper Kα-radiation.

Angle 2-Theta °	Intensity %
15.6	42.7
16.6	43.3
17.2	69
17.8	42.6
18.4	49.2
19.1	100
19.8	40.5
20.8	91.6
23.1	47.8
23.8	59.2

3. The crystalline Form C of claim 1 or claim 2, exhibiting the following Infrared Vibrational (IR) Peaks: 2968 cm^{-1}, 2935 cm^{-1}, 2893 cm^{-1}, 2866 cm^{-1}, 1604 cm^{-1}, 1563 cm^{-1}, 1369 cm^{-1}, 1414 (1473) cm^{-1}, 1285 cm^{-1}, 815 cm^{-1}, and 796 cm^{-1}.

4. The crystalline Form C of any one of claims 1-3, wherein the crystalline Form C is desolvated.

5. The crystalline Form C of any of claims 1-4 for use in treating asthma, treating and/or preventing exercise-induced bronchoconstriction, treating and/or preventing rhinitis, treating chronic obstructive pulmonary disease, treating cardiovascular disease, treating non-steroidal anti-inflammatory drug (NSAID)-induced gastric lesions, treating pain, treating ocular disease or treating skin disease in a human.

6. The crystalline Form C of any one of claims 1-4 for use in treating asthma, preventing exercise-induced bronchoconstriction, treating allergic rhinitis, treating chronic obstructive pulmonary disease, treating cardiovascular disease or treating non-steroidal anti-inflammatory drug (NSAID)-induced gastric lesions in a human.

7. A pharmaceutical composition comprising:

   a. a crystalline Form C of any one of claims 1-4; and
   b. at least one pharmaceutically acceptable inactive ingredient selected from among excipients, diluents, and carriers.

8. A pharmaceutical combination comprising a crystalline Form C of any one of claims 1-4 and an additional pharmaceutical agent.

9. A process for the preparation of crystalline Form C of sodium 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionate comprising the steps of:

   (1) adding sodium 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionate to methyl tert-butylether to form a mixture;
   (2) heating the mixture from step (1) and then cooling the solution; and
   (3) isolating the solids that are formed from step (2) to provide crystalline Form C of sodium 3-[3-*tert*-butylsulfanyl-1-[4-(6-ethoxy-pyridin-3-yl)-benzyl]-5-(5-methyl-pyridin-2-yl-methoxy)-1*H*-indol-2-yl]-2,2-dimethyl-propionate.

10. A process, according to claim 9, in which crystalline Form C is obtained by ensuring removal of any protic co-solvents during the isolation from methyl tert-butylether.