That which is claimed is:

1. A process for making a compound of **Formula I,**

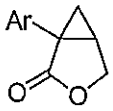


I

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl,

comprising the steps of :

i) providing a composition comprising a compound of **Formula II**:



II

wherein Ar is as given above, and an organic solvent, wherein said composition is at a temperature of from -30 to 40 °C; and

ii) adding to said composition a hydride reducing agent, wherein said agent reduces said compound of **Formula II** into said compound of **Formula I,**

to thereby make said compound of **Formula I.**

2. The process of claim 1, wherein Ar is unsubstituted or substituted 1 – 3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

3. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -30 to 30 °C.

4. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -30 to 10 °C.

5. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -10 to 0 °C.

6. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -10 to -5 °C.

7. The process of any of claims 1-6, wherein the organic solvent is an aromatic hydrocarbon solvent, an aliphatic hydrocarbon solvent, a halogenated hydrocarbon solvent or an ether solvent.

8. The process of any of claims 1-6, wherein the organic solvent is tetrahydrofuran or toluene.

9. The process of any of claims 1-6, wherein the organic solvent is a mixture of tetrahydrofuran and 2-methyltetrahydrofuran.

10. The process of any of claims 1-9, wherein the hydride reducing agent is selected from the group consisting of: sodium borohydride, lithium borohydride, lithium aluminum hydride, lithium tributoxy aluminum hydride, diisobutylaluminum hydride, zinc borohydride, and lithium triethyl borohydride.

11. The process of any of claims 1-9, wherein the hydride reducing agent is lithium borohydride or lithium triethyl borohydride.

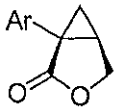
12. The process of any of claims 1-11, further comprising the step of mixing the composition after said adding step for a time of 12 to 24 hours.

13. The process of claim 11, further comprising the step of quenching the reduction by adding to said composition a mild aqueous acid.

14. The process of claim 13, wherein said mild aqueous acid is citric acid, EDTA or tartaric acid.

15. The process of claim 13, wherein said mild aqueous acid is citric acid.

16. The process of any of claims 1-15, wherein the compound of **Formula II** has the absolute stereochemistry of **Formula IIa**:



IIa

17. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 80%.

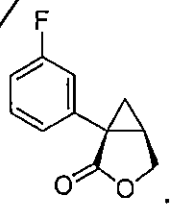
18. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 85%.

19. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 90%.

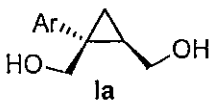
20. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 95%.

21. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 98%.

22. The process of any of claims 1-16, wherein the compound of **Formula II** is the compound:



23. The process of any of claims 1-22, wherein the compound of **Formula I** has the absolute stereochemistry of **Formula Ia**:



Ia

24. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 80%.

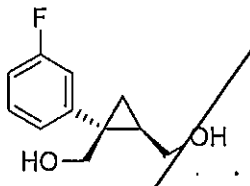
25. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 85%.

26. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 90%.

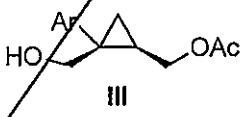
27. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 95%.

28. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 98%.

29. The process of any of claims 1-28, wherein the compound of **Formula I** is:



30. A compound of **Formula III**:

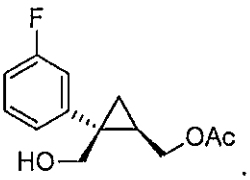


III

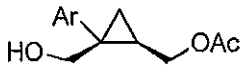
wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently chosen from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl.

31. The compound of claim 30, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

32. The compound of claim 30, wherein said compound is:



33. A process for making a compound of **Formula III**:



III

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl,

comprising reacting a mixture of:

i) a compound of **Formula Ia:**



Ia

wherein Ar is as given above,

ii) vinyl acetate,

iii) a lipase, and

iv) an organic solvent

for a time of from 5 to 36 hours,

to thereby make the compound of **Formula III.**

34. The process of claim 33, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

35. The process of claim 33 or claim 34, wherein the organic solvent is tetrahydrofuran, 2-methyltetrahydrofuran, an ether solvent, acetone, or acetonitrile.

36. The process of any of claims 33-35, wherein the reacting step is carried out for a time of from 7 to 18 hours.

37. The process of any of claims 33-36, wherein said lipase is a *Candida Antarctica* lipase.

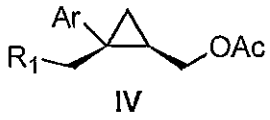
38. The process of any of claims 33-36, wherein said lipase is a *Candida Antarctica* B lipase coupled to an acrylic resin.

39. The process of any of claims 33-38, further comprising the step of filtering the mixture after said reacting to produce a filtrate, and concentrating the filtrate to produce a concentrated filtrate.

40. The process of claim 39, further comprising the step of washing the concentrated filtrate with water or water comprising a salt.

41. The process of claim 39, further comprising the step of washing the concentrated filtrate with a solution of 15-20% NaCl in water.

42. A compound of **Formula IV**:



IV

wherein:

Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_1 is a leaving group.

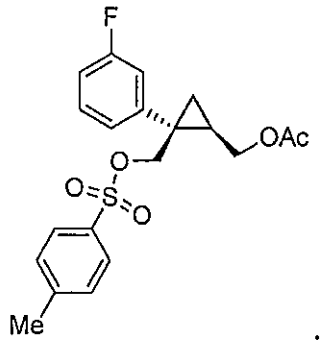
43. The compound of claim 42, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

44. The compound of claim 42 or claim 43, wherein the leaving group is a sulfonate ester leaving group selected from the group consisting of: mesylate, tosylate, nosylate, benzene sulfonate, and brosylate.

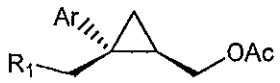
45. The compound of claim 42 or claim 43, wherein the leaving group is mesylate.

46. The compound of claim 42 or claim 43, wherein the leaving group is tosylate.

47. The compound of claim 42, wherein said compound is:



48. The compound of any of claims 42-47, wherein the compound of **Formula IV** has the absolute stereochemistry of **Formula IVa:**



IVa

49. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 80%.

50. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 85%.

51. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 90%.

52. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 95%.

53. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 98%.

54. A process for making a compound of **Formula IV**:

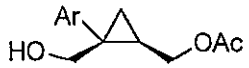


IV

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_1 is a sulfonate ester leaving group,

said process comprising reacting a compound of **Formula III**:



III

wherein Ar is as given above,

with a compound selected from the group consisting of: tosyl chloride, mesyl chloride, nosyl chloride, toluenesulfonyl chloride, toluenesulfonic anhydride and methanesulfonic anhydride, wherein said reacting is carried out in an organic solvent in the presence of a base,

to thereby make said compound of **Formula IV**.

55. The process of claim 54, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

56. The process of claim 54 or claim 55, where said reacting is carried out for a time of from 10 minutes to 2 hours.

57. The process of any of claims 54-56 wherein the base is an organic amine or potassium carbonate.

58. The process of any of claims 54-56, wherein the base is an organic amine selected from the group consisting of: triethylamine, diisopropylethylamine, and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).

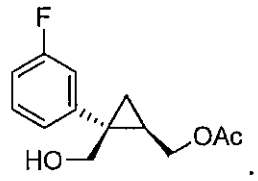
59. The process of any of claims 54-56, wherein the base is pyridine.

60. The process of any of claims 54-59, wherein the organic solvent is selected from the group consisting of: dichloromethane, tetrahydrofuran, 2-methyltetrahydrofuran, toluene, acetonitrile, and ethyl acetate.

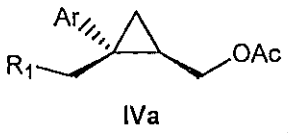
61. The process of any of claims 54-59, wherein the organic solvent is dichloromethane.

62. The process of any of claims 54-59, wherein the organic solvent is 2-methyltetrahydrofuran.

63. The process of any of claims 54-62, wherein said compound of **Formula III** is:



64. The process of any of claims 54-63, wherein the compound of **Formula IV** has the absolute stereochemistry of **Formula IVa**:



IVa

65. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 80%.

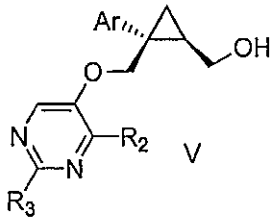
66. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 85%.

67. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 90%.

68. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 95%.

69. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 98%.

70. A process for making a compound of **Formula V**,



V

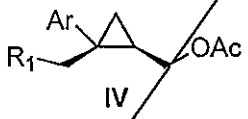
wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl,

comprising the steps of:

a) stirring a mixture of:

i) a compound of **Formula IV**:

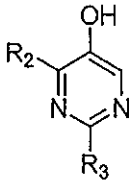


IV

wherein Ar is as given above; and

R_1 is a leaving group,

ii) a substituted pyrimidine of **Formula VI**:



VI ,

wherein R_2 and R_3 are as given above;

iii) a base; and

iv) an organic solvent,

at a temperature of from 65-70 °C, for 1 to 12 hours; and then

b) reacting the mixture with an aqueous base for a time of from 2 to 20 hours,

to thereby make said compound of **Formula V**.

71. The process of claim 70, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

72. The process of claim 70 or claim 71, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

73. The process of any of claims 70-72, wherein the base of step a) is cesium carbonate or DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).

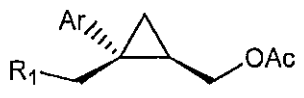
74. The process of any of claims 70-73, wherein the aqueous base of step b) is an aqueous hydroxide or carbonate.

75. The process of any of claims 70-73, wherein the aqueous base of step b) is aqueous sodium hydroxide.

76. The process of any of claims 70-73, wherein the aqueous base of step b) is aqueous potassium hydroxide.

77. The process of any of claims 70-76, wherein the organic solvent is selected from the group consisting of: acetonitrile, acetone, ethyl acetate and tetrahydrofuran.

78. The process of any of claims 70-77, wherein the compound of **Formula IV** has the absolute stereochemistry of **Formula IVa**:



IVa

79. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 80%.

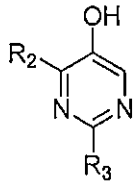
80. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 85%.

81. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 90%.

82. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 95%.

83. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 98%.

84. A process for making a compound of **Formula VI**:

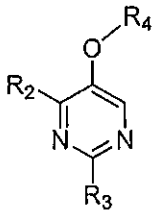


VI

wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6} alkyl,

comprising the step of heating a mixture of:

i) a compound of **Formula B**:



B

wherein:

R_2 and R_3 are as given above; and

R_4 is C_{1-6} alkyl,

ii) an alkoxide or hydroxide salt,

iii) a thiol, and

iv) an organic solvent,

to thereby make said compound of **Formula VI**.

85. The process of claim 84, wherein said heating is to a temperature of from 50 to 140 °C.

86. The process of claim 84, wherein said heating comprises boiling said mixture.

87. The process of claim 84, wherein said heating comprises refluxing said mixture.

88. The process of any of claims 84-87, wherein said heating is carried out in a time of from 5 to 50 hours.

89. The process of any of claims 84-88, wherein said alkoxide salt is an ethoxide, *t*-butoxide, 3-methyl-3-pentoxide, or 7-amyloxide salt.

90. The process of any of claims 84-88, wherein said alkoxide salt is a *t*-butoxide salt.

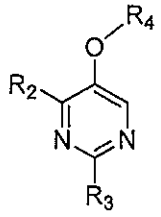
91. The process of any of claims 84-88, wherein said alkoxide is potassium *t*-butoxide.

92. The process of any of claims 84-91, wherein said thiol is 1-decanethiol or 1-dodecanethiol.

93. The process of any of claims 84-92, wherein said organic solvent is, *N,N*-Dimethylformamide, *N,N*-Dimethylacetamide, *N*-Methylpyrrolidone, 1-butanol, 2-butanol, *tert*-butanol, *iso*-butanol.

94. The process of any of claims 84-92, wherein said organic solvent is 1-butanol.

95. A process for making a compound of **Formula B:**



B

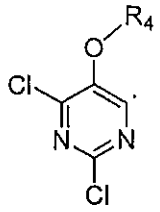
wherein:

R_2 and R_3 are each independently selected from the group consisting of hydrogen and C_{1-6} alkyl; and

R_4 is C_{1-6} alkyl,

comprising mixing:

i) a compound of **Formula A**:



A

wherein R_4 is as given above,

ii) trimethylaluminum,

iii) a palladium catalyst, and

iv) an organic solvent,

to thereby make said compound of **Formula B**.

96. The process of claim 95, wherein said palladium catalyst is tetrakis-(triphenylphosphine)palladium(0).

97. The process of claim 95 or claim 96, wherein said organic solvent is tetrahydrofuran or 2-methyltetrahydrofuran.

98. The process of any of claims 95-97, wherein said mixing step is carried out for a time of from 12 to 48 hours.

99. The process of any of claims 95-98, wherein said mixing step is carried out at a temperature of from 20 to 110 °C.

100. The process of any of claims 95-99, further comprising the step of quenching the reaction with water comprising a base.

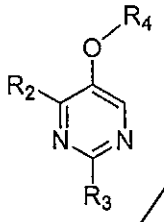
101. The process of claim 100, wherein said base is sodium hydroxide.

102. The process of any of claims 95-101, further comprising the step of treating said compound of **Formula B** with a solution comprising hydrogen chloride and an alcohol to obtain said compound of **Formula B** as a hydrochloride salt.

103. The process of claim 102, wherein said alcohol is selected from the group consisting of methanol, ethanol, n-propanol, isopropyl alcohol, n-butanol, amyl alcohol, ethylene glycol, propylene glycol, butyl carbitol acetate, glycerin and a combination thereof.

104. The process of claim 102, wherein said alcohol is isopropyl alcohol.

105. A process for making a compound of **Formula B**:



B

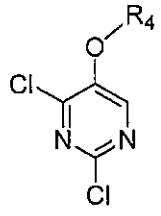
wherein:

R_2 and R_3 are each independently selected from the group consisting of hydrogen and C_{1-6} alkyl; and

R_4 is C_{1-6} alkyl;

comprising mixing:

i) a compound of **Formula A**:



A

wherein R_4 is as given above,

ii) a nickel catalyst,

iii) an alkylmagnesium halide, and

iv) an organic solvent,

to thereby make said compound of **Formula B**.

106. The process of claim 105, wherein said nickel catalyst is selected from the group consisting of: $Ni(acac)_2$, $Ni(PPh_3)_2Cl_2$, or $Ni(dppp)Cl_2$.

107. The process of claim 105, wherein said nickel catalyst is $Ni(dppp)Cl_2$.

108. The process of any of claims 105-107, wherein said alkylmagnesium halide is methyl magnesium chloride.

109. The process of any of claims 105-108, wherein said organic solvent is tetrahydrofuran or 2-methyltetrahydrofuran.

110. The process of any of claims 105-109, wherein said mixing is carried out for a time of from 6 to 36 hours.

111. The process of any of claims 105-110, wherein said mixing is carried out at a temperature of from 10 to 30 °C.

112. The process of any of claims 105-111, further comprising the step of quenching the reaction with water comprising an acid.

113. The process of claim 112, wherein said acid is citric acid.

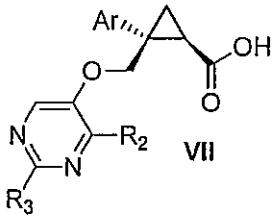
114. The process of claim 112 or claim 113, further comprising the step of adding ammonium hydroxide after said quenching step.

115. The process of any of claims 105-114, wherein said process further comprises reacting the compound of **Formula B** with a solution comprising hydrogen chloride and an alcohol to obtain said compound of **Formula B** as a hydrochloride salt.

116. The process of claim 115, wherein said alcohol is selected from the group consisting of methanol, ethanol, n-propanol, isopropyl alcohol, n-butanol, amyl alcohol, ethylene glycol, propylene glycol, butyl carbitol acetate, glycerin and a combination thereof.

117. The process of claim 115, wherein said alcohol is isopropyl alcohol.

118. A process for making a compound of **Formula VII**:



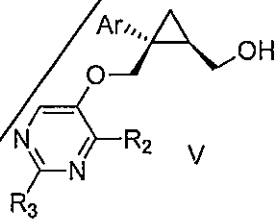
VII

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl,

comprising the steps of :

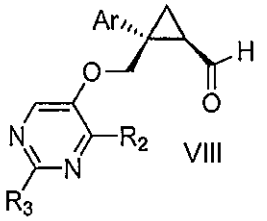
a) oxidizing a compound of **Formula V**:



V

wherein Ar, R_2 and R_3 are as given above,

with a first oxidizing agent, to form an aldehyde of Formula **VIII**:



VIII

wherein Ar, R_2 and R_3 are as given above; and then

b) oxidizing the aldehyde of **Formula VIII** with a second oxidizing agent, to thereby make said compound of **Formula VII**.

119. The process of claim 118, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

120. The process of claim 118 or claim 119, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

121. The process of any of claims 118-120, wherein the first oxidizing agent is sodium hypochlorite.

122. The process of claim 121, wherein said oxidizing of step a) is catalyzed with an effective amount of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO).

123. The process of any of claims 118-122, wherein the second oxidizing agent is sodium chlorite.

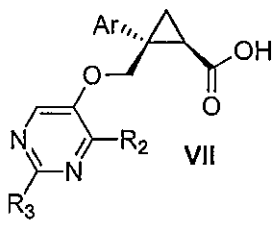
124. The process of any of claims 118-122, wherein the first oxidizing agent and the second oxidizing agent are the same.

125. The process of any of claims 118-122, wherein the first oxidizing agent and the second oxidizing agent are different.

126. The process of any of claims 118-125, wherein said oxidizing of step a) and/or step b) is carried out in an organic solvent selected from the group consisting of dichloromethane, tetrahydrofuran, 2-methyltetrahydrofuran, toluene, acetonitrile, and ethyl acetate.

127. The process of claim 126, wherein said organic solvent is toluene.

128. A process for preparing a compound of **Formula VII**,

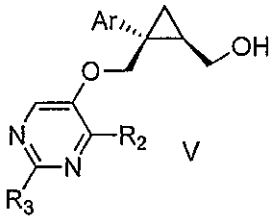


VII

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl,

comprising: oxidizing a compound of **Formula V**:



V

wherein Ar, R_2 and R_3 are as given above,

with sodium hypochlorite and sodium chlorite,

to thereby make said compound of **Formula VII**.

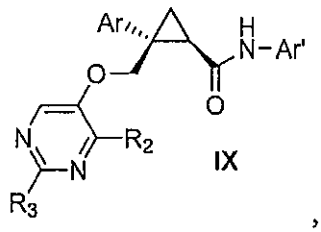
129. The process of claim 128, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

130. The process of claim 128 or claim 129, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

131. The process of any of claims 128-130, wherein said oxidizing with sodium hypochlorite and sodium chlorite is carried out simultaneously.

132. The process of any of claims 128-131, wherein said oxidizing is catalyzed with an effective amount of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO).

133. A process for making a compound of **Formula IX**:



IX

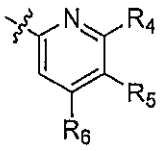
,

wherein:

Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl;

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl; and

Ar' is a pyridine group:



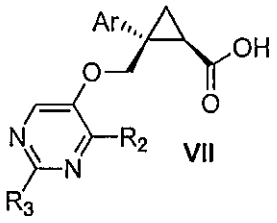
wherein:

R_4 is selected from the group consisting of: hydrogen, halo, C_{1-6}alkyl, C_{1-6}alkoxy, and (C_{1-6}alkoxy)C_{1-6}alkyl;

R_5 is selected from the group consisting of: hydrogen, halo, C_{1-6}alkyl, and haloC_{1-6}alkyl; and

R_6 is selected from the group consisting of: hydrogen, halo, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, (C_{1-6}alkoxy)C_{1-6}alkyl, and cyano;

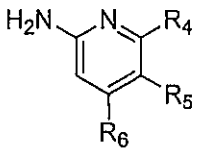
comprising the step of reacting a compound of **Formula VII**:



VII

wherein Ar, R_2 and R_3 are as given above,

with a compound of **Formula X**:



X ;

wherein R_4, R_5, and R_6 are as given above,

said reacting carried out in an organic solvent in the presence of an organic amine and an amide coupling agent,
to prepare said compound of **Formula IX**.

134. The process of claim 133, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

135. The process of claim 133 or claim 134, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

136. The process of any of claims 133-135, wherein said organic solvent is selected from the group consisting of: *N,N*-dimethylformamide (DMF), *N,N*-dimethylacetamide (DMA), *N*-methyl-2-pyrrolidone (NMP), acetone, toluene, acetonitrile, and dichloromethane.

137. The process of any of claims 133-136, wherein said amide coupling agent is an alkyl phosphonic anhydride.

138. The process of any of claims 133-136, wherein said amide coupling agent is a propyl phosphonic anhydride.

139. The process of any of claims 133-136, wherein said amide coupling agent is tri-n-propyl phosphonic anhydride.

Claims

1. A process for making a compound of **Formula I**,

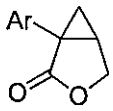


I

wherein Ar is phenyl, which phenyl is substituted 1-3 times with halo, or haloC_{1-6}alkyl,

comprising the steps of :

i) providing a composition comprising a compound of **Formula II**:



II

wherein Ar is as given above, and an organic solvent, wherein said composition is at a temperature of from -30 to 40 °C; and

ii) adding to said composition a hydride reducing agent, wherein said agent reduces said compound of **Formula II** into said compound of **Formula I**,

to thereby make said compound of **Formula I**.

2. The process of claim 1, wherein Ar is substituted 1 time with a halo selected from the group consisting of: chloro, fluoro, bromo, and iodo.

3. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -30 to 30 °C.

4. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -30 to 10 °C.

5. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -10 to 0 °C.

6. The process of claim 1 or claim 2, wherein said composition is provided at a temperature of from -10 to -5 °C.

7. The process of any of claims 1-6, wherein the organic solvent is an aromatic hydrocarbon solvent, an aliphatic hydrocarbon solvent, a halogenated hydrocarbon solvent or an ether solvent.

8. The process of any of claims 1-6, wherein the organic solvent is tetrahydrofuran or toluene.

9. The process of any of claims 1-6, wherein the organic solvent is a mixture of tetrahydrofuran and 2-methyltetrahydrofuran.

10. The process of any of claims 1-9, wherein the hydride reducing agent is selected from the group consisting of: sodium borohydride, lithium borohydride, lithium aluminum hydride, lithium tributoxy aluminum hydride, diisobutylaluminum hydride, zinc borohydride, and lithium triethyl borohydride.

11. The process of any of claims 1-9, wherein the hydride reducing agent is lithium borohydride or lithium triethyl borohydride.

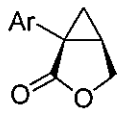
12. The process of any of claims 1-11, further comprising the step of mixing the composition after said adding step for a time of 12 to 24 hours.

13. The process of claim 11, further comprising the step of quenching the reduction by adding to said composition a mild aqueous acid.

14. The process of claim 13, wherein said mild aqueous acid is citric acid, EDTA or tartaric acid.

15. The process of claim 13, wherein said mild aqueous acid is citric acid.

16. The process of any of claims 1-15, wherein the compound of **Formula II** has the absolute stereochemistry of **Formula IIa**:



IIa .

17. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 80%.

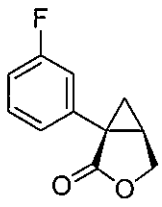
18. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 85%.

19. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 90%.

20. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 95%.

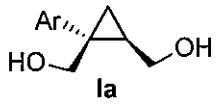
21. The process of claim 16, wherein the compound has an enantiomeric excess (ee) of the **Formula IIa** stereoisomer of at least 98%.

22. The process of any of claims 1-16, wherein the compound of **Formula II** is the compound:



.

23. The process of any of claims 1-22, wherein the compound of **Formula I** has the absolute stereochemistry of **Formula Ia**:



Ia

24. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 80%.

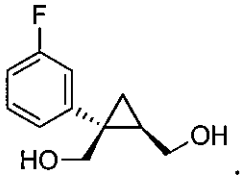
25. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 85%.

26. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 90%.

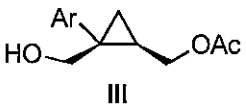
27. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 95%.

28. The process of claim 23, wherein the compound has an enantiomeric excess (ee) of the **Formula Ia** stereoisomer of at least 98%.

29. The process of any of claims 1-28, wherein the compound of **Formula I** is:



30. A compound of **Formula III**:

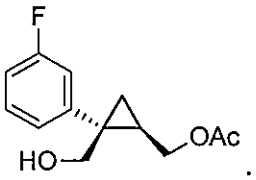


III

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently chosen from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl.

31. The compound of claim 30, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

32. The compound of claim 30, wherein said compound is:



33. A process for making a compound of **Formula III**:



III

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl,

comprising reacting a mixture of:

i) a compound of **Formula Ia:**



Ia

wherein Ar is as given above,

ii) vinyl acetate,

iii) a lipase, and

iv) an organic solvent

for a time of from 5 to 36 hours,

to thereby make the compound of **Formula III**.

34. The process of claim 33, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

35. The process of claim 33 or claim 34, wherein the organic solvent is tetrahydrofuran, 2-methyltetrahydrofuran, an ether solvent, acetone, or acetonitrile.

36. The process of any of claims 33-35, wherein the reacting step is carried out for a time of from 7 to 18 hours.

37. The process of any of claims 33-36, wherein said lipase is a *Candida Antarctica* lipase.

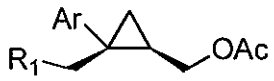
38. The process of any of claims 33-36, wherein said lipase is a *Candida Antarctica* B lipase coupled to an acrylic resin.

39. The process of any of claims 33-38, further comprising the step of filtering the mixture after said reacting to produce a filtrate, and concentrating the filtrate to produce a concentrated filtrate.

40. The process of claim 39, further comprising the step of washing the concentrated filtrate with water or water comprising a salt.

41. The process of claim 39, further comprising the step of washing the concentrated filtrate with a solution of 15-20% NaCl in water.

42. A compound of **Formula IV**:



IV

wherein:

Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_1 is a leaving group.

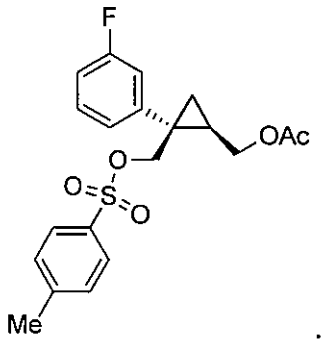
43. The compound of claim 42, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

44. The compound of claim 42 or claim 43, wherein the leaving group is a sulfonate ester leaving group selected from the group consisting of: mesylate, tosylate, nosylate, benzene sulfonate, and brosylate.

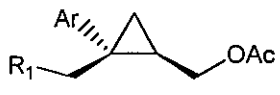
45. The compound of claim 42 or claim 43, wherein the leaving group is mesylate.

46. The compound of claim 42 or claim 43, wherein the leaving group is tosylate.

47. The compound of claim 42, wherein said compound is:



48. The compound of any of claims 42-47, wherein the compound of **Formula IV** has the absolute stereochemistry of **Formula IVa**:



IVa

49. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 80%.

50. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 85%.

51. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 90%.

52. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 95%.

53. The compound of claim 48, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 98%.

54. A process for making a compound of **Formula IV**:



IV

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_1 is a sulfonate ester leaving group,

said process comprising reacting a compound of **Formula III**:



III

wherein Ar is as given above,

with a compound selected from the group consisting of: tosyl chloride, mesyl chloride, nosyl chloride, toluenesulfonyl chloride, toluenesulfonic anhydride and methanesulfonic anhydride, wherein said reacting is carried out in an organic solvent in the presence of a base,

to thereby make said compound of **Formula IV**.

55. The process of claim 54, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

56. The process of claim 54 or claim 55, where said reacting is carried out for a time of from 10 minutes to 2 hours.

57. The process of any of claims 54-56 wherein the base is an organic amine or potassium carbonate.

58. The process of any of claims 54-56, wherein the base is an organic amine selected from the group consisting of: triethylamine, diisopropylethylamine, and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).

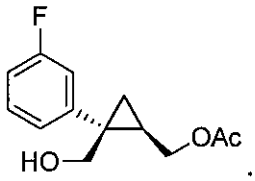
59. The process of any of claims 54-56, wherein the base is pyridine.

60. The process of any of claims 54-59, wherein the organic solvent is selected from the group consisting of: dichloromethane, tetrahydrofuran, 2-methyltetrahydrofuran, toluene, acetonitrile, and ethyl acetate.

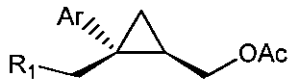
61. The process of any of claims 54-59, wherein the organic solvent is dichloromethane.

62. The process of any of claims 54-59, wherein the organic solvent is 2-methyltetrahydrofuran.

63. The process of any of claims 54-62, wherein said compound of **Formula III** is:



64. The process of any of claims 54-63, wherein the compound of **Formula IV** has the absolute stereochemistry of **Formula IVa**:



IVa

65. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 80%.

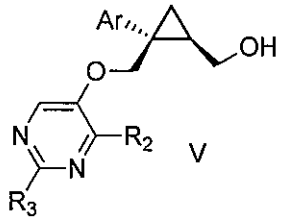
66. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 85%.

67. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 90%.

68. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 95%.

69. The process of claim 64, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 98%.

70. A process for making a compound of **Formula V**,



V

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl,

comprising the steps of:

a) stirring a mixture of:

i) a compound of **Formula IV**:

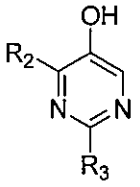


IV

wherein Ar is as given above; and

R_1 is a leaving group,

ii) a substituted pyrimidine of **Formula VI**:



VI ,

wherein R_2 and R_3 are as given above;

iii) a base; and

iv) an organic solvent,

at a temperature of from 65-70 °C, for 1 to 12 hours; and then

b) reacting the mixture with an aqueous base for a time of from 2 to 20 hours,

to thereby make said compound of **Formula V**.

71. The process of claim 70, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

72. The process of claim 70 or claim 71, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

73. The process of any of claims 70-72, wherein the base of step a) is cesium carbonate or DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).

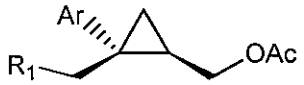
74. The process of any of claims 70-73, wherein the aqueous base of step b) is an aqueous hydroxide or carbonate.

75. The process of any of claims 70-73, wherein the aqueous base of step b) is aqueous sodium hydroxide.

76. The process of any of claims 70-73, wherein the aqueous base of step b) is aqueous potassium hydroxide.

77. The process of any of claims 70-76, wherein the organic solvent is selected from the group consisting of: acetonitrile, acetone, ethyl acetate and tetrahydrofuran.

78. The process of any of claims 70-77, wherein the compound of **Formula IV** has the absolute stereochemistry of **Formula IVa**:



IVa

79. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 80%.

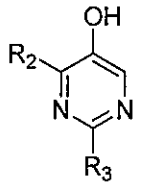
80. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 85%.

81. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 90%.

82. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 95%.

83. The process of claim 78, wherein the compound has an enantiomeric excess (ee) of the **Formula IVa** stereoisomer of at least 98%.

84. A process for making a compound of **Formula VI**:

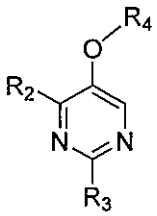


VI

wherein R_2 and R_3 are each independently C_{1-6} alkyl,

comprising the step of heating a mixture of:

i) a compound of **Formula B**:



B

wherein:

R_2 and R_3 are as given above; and

R_4 is C_{1-6} alkyl,

ii) an alkoxide or hydroxide salt,

iii) a thiol, and

iv) an organic solvent,

to thereby make said compound of **Formula VI**.

85. The process of claim 84, wherein said heating is to a temperature of from 50 to 140 °C.

86. The process of claim 84, wherein said heating comprises boiling said mixture.

87. The process of claim 84, wherein said heating comprises refluxing said mixture.

88. The process of any of claims 84-87, wherein said heating is carried out in a time of from 5 to 50 hours.

89. The process of any of claims 84-88, wherein said alkoxide salt is an ethoxide, *t*-butoxide, 3-methyl-3-pentoxide, or 7-amyloxide salt.

90. The process of any of claims 84-88, wherein said alkoxide salt is a *t*-butoxide salt.

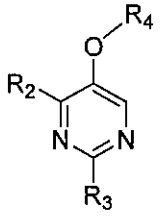
91. The process of any of claims 84-88, wherein said alkoxide is potassium *t*-butoxide.

92. The process of any of claims 84-91, wherein said thiol is 1-decanethiol or 1-dodecanethiol.

93. The process of any of claims 84-92, wherein said organic solvent is, *N,N*-Dimethylformamide, *N,N*-Dimethylacetamide, *N*-Methylpyrrolidone, 1-butanol, 2-butanol, *tert*-butanol, *iso*-butanol.

94. The process of any of claims 84-92, wherein said organic solvent is 1-butanol.

95. A process for making a compound of **Formula B**:



B

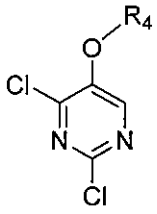
wherein:

R_2 and R_3 are each methyl; and

R_4 is C_{1-6} alkyl,

comprising mixing:

i) a compound of **Formula A**:



A

wherein R_4 is as given above,

ii) trimethylaluminum,

iii) a palladium catalyst, and

iv) an organic solvent,

to thereby make said compound of **Formula B**.

96. The process of claim 95, wherein said palladium catalyst is tetrakis-(triphenylphosphine)palladium(0).

97. The process of claim 95 or claim 96, wherein said organic solvent is tetrahydrofuran or 2-methyltetrahydrofuran.

98. The process of any of claims 95-97, wherein said mixing step is carried out for a time of from 12 to 48 hours.

99. The process of any of claims 95-98, wherein said mixing step is carried out at a temperature of from 20 to 110 °C.

100. The process of any of claims 95-99, further comprising the step of quenching the reaction with water comprising a base.

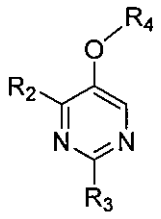
101. The process of claim 100, wherein said base is sodium hydroxide.

102. The process of any of claims 95-101, further comprising the step of treating said compound of **Formula B** with a solution comprising hydrogen chloride and an alcohol to obtain said compound of **Formula B** as a hydrochloride salt.

103. The process of claim 102, wherein said alcohol is selected from the group consisting of methanol, ethanol, n-propanol, isopropyl alcohol, n-butanol, amyl alcohol, ethylene glycol, propylene glycol, butyl carbitol acetate, glycerin and a combination thereof.

104. The process of claim 102, wherein said alcohol is isopropyl alcohol.

105. A process for making a compound of **Formula B**:



B

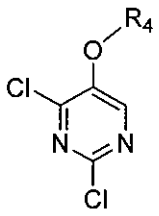
wherein:

R_2 and R_3 are each independently selected from the group consisting of hydrogen and C_{1-6} alkyl; and

R_4 is C_{1-6} alkyl;

comprising mixing:

i) a compound of **Formula A**:



A

wherein R_4 is as given above,

ii) a nickel catalyst,

iii) an alkylmagnesium halide, and

iv) an organic solvent,

to thereby make said compound of **Formula B**.

106. The process of claim 105, wherein said nickel catalyst is selected from the group consisting of: $Ni(acac)_2$, $Ni(PPh_3)_2Cl_2$, or $Ni(dppp)Cl_2$.

107. The process of claim 105, wherein said nickel catalyst is $Ni(dppp)Cl_2$.

108. The process of any of claims 105-107, wherein said alkylmagnesium halide is methyl magnesium chloride.

109. The process of any of claims 105-108, wherein said organic solvent is tetrahydrofuran or 2-methyltetrahydrofuran.

110. The process of any of claims 105-109, wherein said mixing is carried out for a time of from 6 to 36 hours.

111. The process of any of claims 105-110, wherein said mixing is carried out at a temperature of from 10 to 30 °C.

112. The process of any of claims 105-111, further comprising the step of quenching the reaction with water comprising an acid.

113. The process of claim 112, wherein said acid is citric acid.

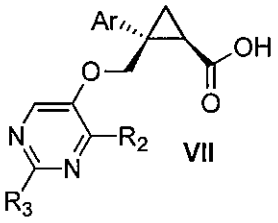
114. The process of claim 112 or claim 113, further comprising the step of adding ammonium hydroxide after said quenching step.

115. The process of any of claims 105-114, wherein said process further comprises reacting the compound of **Formula B** with a solution comprising hydrogen chloride and an alcohol to obtain said compound of **Formula B** as a hydrochloride salt.

116. The process of claim 115, wherein said alcohol is selected from the group consisting of methanol, ethanol, n-propanol, isopropyl alcohol, n-butanol, amyl alcohol, ethylene glycol, propylene glycol, butyl carbitol acetate, glycerin and a combination thereof.

117. The process of claim 115, wherein said alcohol is isopropyl alcohol.

118. A process for making a compound of **Formula VII**:



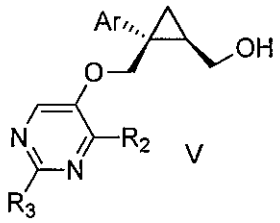
VII

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl,

comprising the steps of :

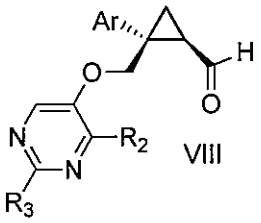
a) oxidizing a compound of **Formula V**:



V

wherein Ar, R_2 and R_3 are as given above,

with a first oxidizing agent, to form an aldehyde of Formula **VIII**:



VIII

wherein Ar, R_2 and R_3 are as given above; and then

b) oxidizing the aldehyde of **Formula VIII** with a second oxidizing agent, to thereby make said compound of **Formula VII**.

119. The process of claim 118, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

120. The process of claim 118 or claim 119, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

121. The process of any of claims 118-120, wherein the first oxidizing agent is sodium hypochlorite.

122. The process of claim 121, wherein said oxidizing of step a) is catalyzed with an effective amount of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO).

123. The process of any of claims 118-122, wherein the second oxidizing agent is sodium chlorite.

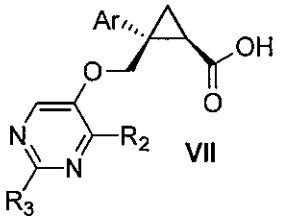
124. The process of any of claims 118-122, wherein the first oxidizing agent and the second oxidizing agent are the same.

125. The process of any of claims 118-122, wherein the first oxidizing agent and the second oxidizing agent are different.

126. The process of any of claims 118-125, wherein said oxidizing of step a) and/or step b) is carried out in an organic solvent selected from the group consisting of dichloromethane, tetrahydrofuran, 2-methyltetrahydrofuran, toluene, acetonitrile, and ethyl acetate.

127. The process of claim 126, wherein said organic solvent is toluene.

128. A process for preparing a compound of **Formula VII**,

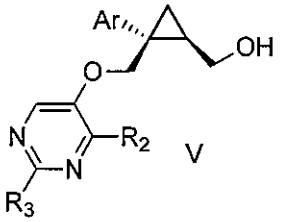


VII

wherein Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl; and

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl,

comprising: oxidizing a compound of **Formula V**:



V

wherein Ar, R_2 and R_3 are as given above,

with sodium hypochlorite and sodium chlorite,

to thereby make said compound of **Formula VII.**

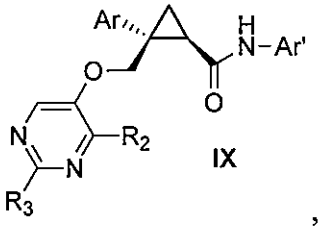
129. The process of claim 128, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

130. The process of claim 128 or claim 129, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

131. The process of any of claims 128-130, wherein said oxidizing with sodium hypochlorite and sodium chlorite is carried out simultaneously.

132. The process of any of claims 128-131, wherein said oxidizing is catalyzed with an effective amount of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO).

133. A process for making a compound of **Formula IX**:



IX

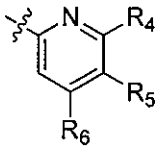
,

wherein:

Ar is phenyl, which phenyl may be unsubstituted, or substituted 1-3 times with substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, and haloC_{1-6}alkyl;

R_2 and R_3 are each independently selected from the group consisting of: hydrogen, C_{1-6}alkyl, haloC_{1-6} alkyl, C_{1-6}alkoxy, and hydroxyC_{1-6}alkyl; and

Ar' is a pyridine group:



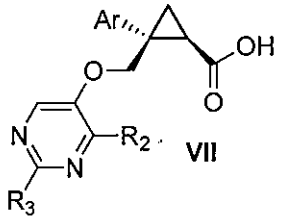
wherein:

R_4 is selected from the group consisting of: hydrogen, halo, C_{1-6}alkyl, C_{1-6}alkoxy, and (C_{1-6}alkoxy)C_{1-6}alkyl;

R_5 is selected from the group consisting of: hydrogen, halo, C_{1-6}alkyl, and haloC_{1-6}alkyl; and

R_6 is selected from the group consisting of: hydrogen, halo, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, (C_{1-6}alkoxy)C_{1-6}alkyl, and cyano;

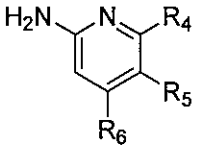
comprising the step of reacting a compound of **Formula VII**:



VII

wherein Ar, R_2 and R_3 are as given above,

with a compound of **Formula X**:



X ;

wherein R_4, R_5, and R_6 are as given above,

said reacting carried out in an organic solvent in the presence of an organic amine and an amide coupling agent,

to prepare said compound of **Formula IX**.

134. The process of claim 133, wherein Ar is unsubstituted or substituted 1-3 times with a halo independently selected from the group consisting of: chloro, fluoro, bromo, and iodo.

135. The process of claim 133 or claim 134, wherein R_2 and R_3 are each independently selected from the group consisting of: hydrogen and C_{1-6}alkyl.

136. The process of any of claims 133-135, wherein said organic solvent is selected from the group consisting of: *N,N*-dimethylformamide (DMF), *N,N*-dimethylacetamide (DMA), *N*-methyl-2-pyrrolidone (NMP), acetone, toluene, acetonitrile, and dichloromethane.

137. The process of any of claims 133-136, wherein said amide coupling agent is an alkyl phosphonic anhydride.

138. The process of any of claims 133-136, wherein said amide coupling agent is a propyl phosphonic anhydride.

139. The process of any of claims 133-136, wherein said amide coupling agent is tri-n-propyl phosphonic anhydride.