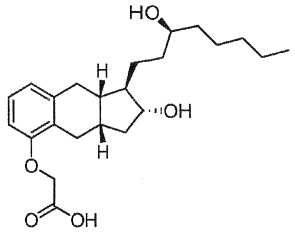
~~What is claimed is:~~

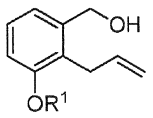
1. A method of generating a compound of Formula **I**



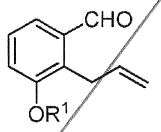
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent in the presence of an organic solvent to generate a compound of Formula **10**



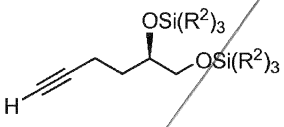
9



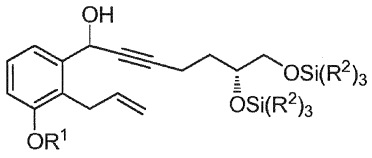
10

wherein R^1 is C_{1-6} alkyl and the oxidizing agent comprises MnO_2 or Dess-Martin periodinane;

ii) reacting the compound of Formula **10** with a compound of Formula **5** in the presence of a base and an organic solvent to generate a compound of Formula **11**, wherein each R^2 is independently selected from C_{1-6} alkyl or phenyl; and



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iii) converting the compound of Formula **11** to the compound of Formula **I**.

2. The method of claim 1, wherein the organic solvent of step **i)** comprises a halogenated organic solvent.

3. The method of claim 2, wherein the halogenated organic solvent comprises dichloromethane, chloroform, or any combination thereof.

4. The method of claim 1, wherein the base of step **ii)** comprises an alkyllithium reagent.

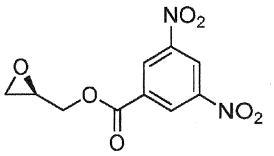
~~5. The method of claim 4, wherein the alkyllithium reagent is *sec*-butyllithium.~~

6. ~~The method of claim 1, wherein the organic solvent of step **ii)** comprises pentane, hexane,~~ cyclohexane, heptane, tetrahydrofuran, 1,4-dioxane, diethyl ether, petro ether, methyl-*tert*-butylether, or any combination thereof.

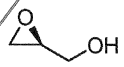
7. The method of claim 6, wherein the organic solvent of step **ii)** comprises methyl-*tert*-butylether.

8. The method of claim 1, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

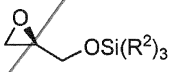


1a



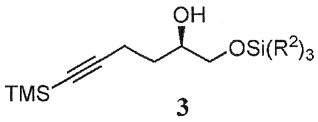
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v) reacting the compound of Formula **1** with $SiCl(R^2)_3$ under basic conditions to generate the compound of Formula **2**;



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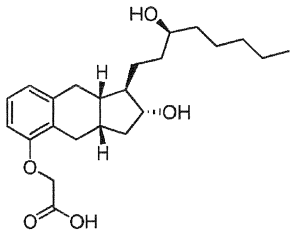
vi) reacting the compound of Formula **2** with 1-TMS-1-propyne to generate the compound of Formula **3**; and



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vii) converting the compound of Formula **3** to the compound of Formula **5**.

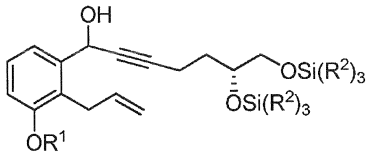
9. A method of generating a compound of Formula **I**



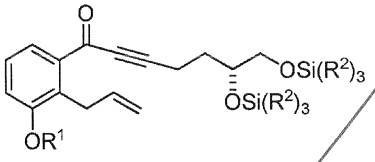
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~~or a pharmaceutically acceptable salt thereof, comprising the steps of:~~

viii) reacting a compound of Formula **11** with an oxidizing agent in the presence of an organic solvent to generate a compound of Formula **12**



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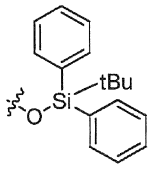


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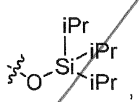
wherein R^1 is C_{1-6} alkyl, each R^2 is independently selected from C_{1-6} alkyl or phenyl, and the oxidizing agent comprises MnO_2; and

ix) converting the compound of Formula **12** to the compound of Formula **I**.

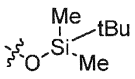
10. The method of claim 9, wherein each of the $-OSi(R^2)_3$ groups in the compounds of Formulae **11** and **12** is independently selected from



,



, or



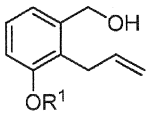
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11. The method of claim 9, wherein the organic solvent of step **viii)** comprises a halogenated organic solvent.

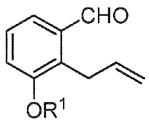
12. The method of claim 11, wherein the halogenated organic solvent comprises dichloromethane, chloroform, or any combination thereof.

13. The method of claim 9, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent in the presence of an organic solvent to generate a compound of Formula **10**



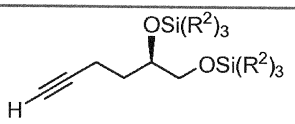
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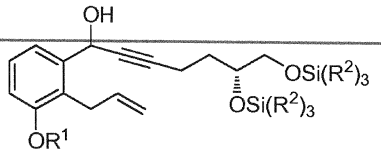
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wherein R^1 is C_{1-6} alkyl and the oxidizing agent comprises MnO_2 or Dess-Martin periodinane; and

ii) ~~reacting the compound of Formula **10** with a compound of Formula **5**~~



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in the presence of a base and an organic solvent to generate a compound of Formula **11**.

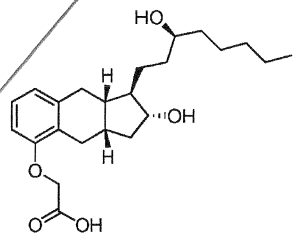
14. The method of claim 13, wherein the base of step **ii)** comprises an alkyllithium reagent.

15. The method of claim 14, wherein the alkyllithium reagent is *sec*-butyllithium.

16. The method of claim 13, wherein the organic solvent of step **ii)** comprises pentane, hexane, cyclohexane, heptane, tetrahydrofuran, 1,4-dioxane, diethyl ether, petro ether, methyl-*tert*-butylether, or any combination thereof.

17. The method of claim 16, wherein the organic solvent of step **ii)** comprises methyl-*tert*-butylether.

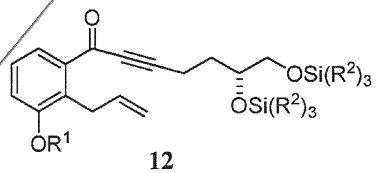
18. A method of generating a compound of Formula **I**



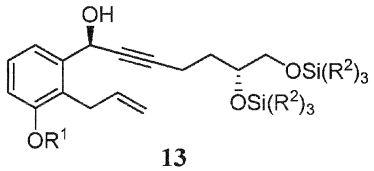
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or a pharmaceutically acceptable salt thereof, comprising the steps of:

x) reacting a compound of Formula **12** with a reducing agent in the presence of an organic solvent to generate a compound of Formula **13**



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wherein the organic solvent comprises THF, R^1 is $C_{1\text{-}6}$ alkyl, and each R^2 is independently selected from $C_{1\text{-}6}$ alkyl or phenyl; and

xi) converting the compound of Formula **13** to the compound of Formula **I**.

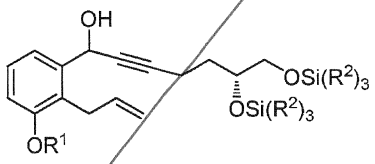
19. The method of claim 18, wherein the reducing agent of step **x)** comprises a chiral borane compound.

20. The method of claim 19, wherein the chiral borane compound is selected from (R)-1-methyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-1-butyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-tetrahydro-1,3,3-triphenyl-1H,3H-pyrrolo[1,2-c][1,3,2]oxaborole, (4S)- 2-methyl-4,5,5-triphenyl-1,3,2-oxazaborolidine, or any combination thereof.

21. The method of claim 18, wherein the organic solvent of step **x)** further comprises toluene.

22. The method of claim 18, further comprising the step of:

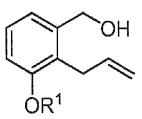
viii) reacting a compound of Formula **11** with an oxidizing agent to generate the compound of Formula **12**, wherein the oxidizing agent comprises MnO_2



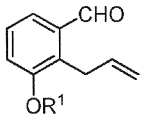
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23. The method of claim 22, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent to generate a compound of Formula **10**; and

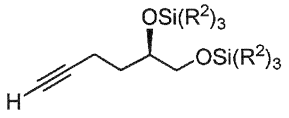


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ii) reacting the compound of Formula **10** with a compound of Formula **5** in the presence of a base and an organic solvent to generate a compound of Formula **11**



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~~24. The method of claim 23, wherein the oxidizing agent comprises MnO_2 or Dess-Martin~~ periodinane.

25. The method of claim 23, wherein the base of step **ii)** comprises an alkyllithium reagent.

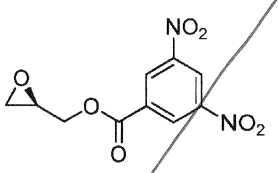
26. The method of claim 25, wherein the alkyllithium reagent is *sec*-butyllithium.

27. The method of claim 23, wherein the organic solvent of step **ii)** comprises pentane, hexane, cyclohexane, heptane, tetrahydrofuran, 1,4-dioxane, diethyl ether, petro ether, methyl-*tert*-butylether, or any combination thereof.

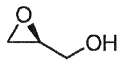
28. The method of claim 27, wherein the organic solvent of step **ii)** comprises methyl-*tert*-butylether.

29. The method of claim 23, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

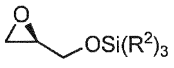


1a



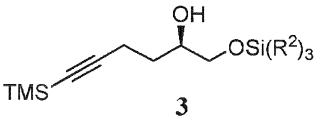
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v) reacting the compound of Formula **1** with $SiCl(R^2)_3$ under basic conditions to generate the compound of Formula **2**;



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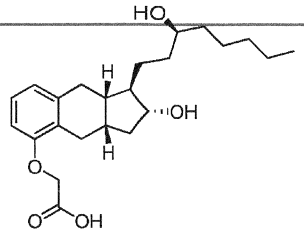
vi) reacting the compound of Formula **2** with 1-TMS-1-propyne to generate the compound of Formula **3**; and



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vii) converting the compound of Formula **3** to the compound of Formula **5**.

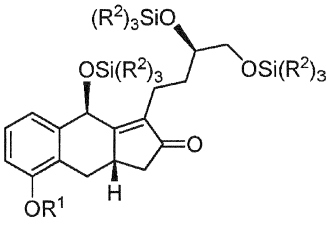
~~30. A method of generating a compound of Formula **I**~~



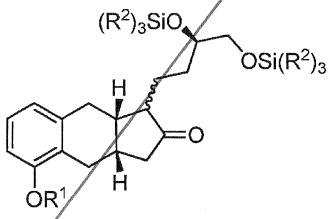
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

xii) hydrogenating a compound of Formula **15** in the presence of an alcohol (e.g., methanol or ethanol), optionally substituted THF (e.g., THF or 2-Me-THF), or any combination thereof to generate the compound of Formula **16**



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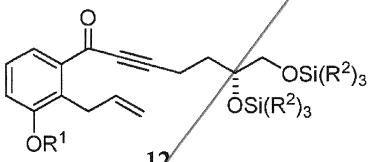
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wherein R^1 is C_{1-6} alkyl, and each R^2 is independently selected from C_{1-6} alkyl or phenyl; and

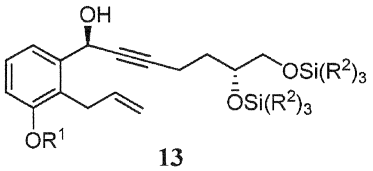
xiii) converting the compound of Formula **16** to the compound of Formula **I**.

31. The method of claim 30, further comprising the steps of:

x) reacting a compound of Formula **12** with a reducing agent in the presence of an organic solvent to generate a compound of Formula **13**



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wherein the organic solvent comprises THF; and

xiv) converting the compound of Formula **13** to the compound of Formula **15**.

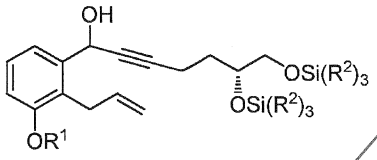
32. The method of claim 31, wherein the reducing agent of step **x)** comprises a chiral borane compound.

33. The method of claim 32, wherein the chiral borane compound is selected from ~~(R)-1-methyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole,~~

~~(R)-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-1-butyl-3,3-~~ diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-tetrahydro-1,3,3-triphenyl-1H,3H-pyrrolo[1,2-c][1,3,2]oxaborole, (4S)- 2-methyl-4,5,5-triphenyl-1,3,2-oxazaborolidine, or any combination thereof.

34. The method of claim 31, further comprising the steps of:

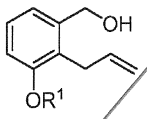
viii) reacting a compound of Formula **11** with an oxidizing agent to generate the compound of Formula **12**, wherein the oxidizing agent comprises MnO_2



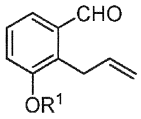
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35. The method of claim 34, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent to generate a compound of Formula **10**; and

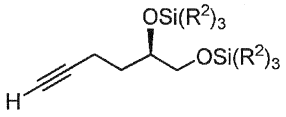


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ii) reacting the compound of Formula **10** with a compound of Formula **5** in the presence of a base and an organic solvent to generate a compound of Formula **11**



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36. The method of claim 35, wherein the oxidizing agent of step **i)** comprises MnO_2 or Dess-Martin periodinane.

37. The method of claim 35, wherein the base of step **ii)** comprises an alkyllithium reagent.

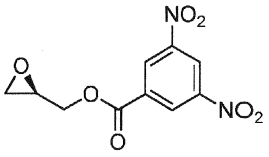
~~38. The method of claim 37, wherein the alkyllithium reagent is *sec*-butyllithium.~~

39. The method of claim 35, wherein the organic solvent of step **ii)** comprises pentane, hexane, cyclohexane, heptane, tetrahydrofuran, 1,4-dioxane, diethyl ether, petro ether, methyl-*tert*-butylether, or any combination thereof.

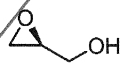
40. The method of claim 39, wherein the organic solvent of step **ii)** comprises methyl-*tert*-butylether.

41. The method of claim 35, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

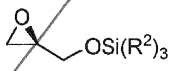


1a



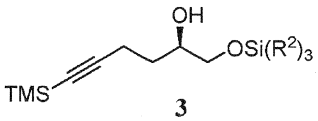
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v) reacting the compound of Formula **1** with $SiCl(R^2)_3$ under basic conditions to generate the compound of Formula **2**;



2

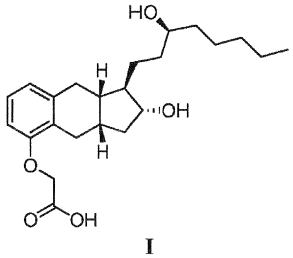
vi) reacting the compound of Formula **2** with 1-TMS-1-propyne to generate the compound of Formula **3**; and



3

vii) converting the compound of Formula **3** to the compound of Formula **5**.

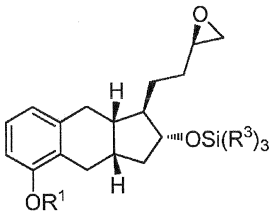
42. A method of generating a compound of Formula **I**



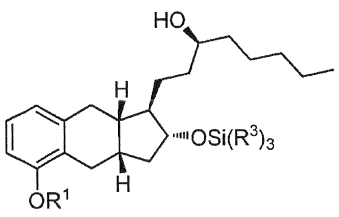
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

xv) reacting a compound of Formula **21** with n-butyllithium in the presence of an organic solvent and a transition metal catalyst to generate a compound of Formula **22**



21



22

wherein R^3 is $C_{1\text{-}6}$ alkyl or phenyl; and

xvi) converting the compound of Formula **22** to the compound of Formula **I**.

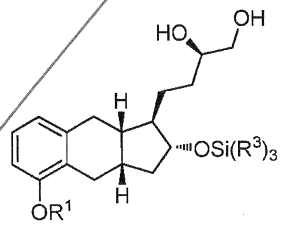
43. The method of claim 42, wherein the transition metal catalyst of step **xv)** comprises a compound or complex either of which comprises Cu having a +1 oxidation state.

44. The method of claim 43, wherein the transition metal catalyst of step **xv)** comprises CuX, wherein X is selected from halogen, acetate, benzoate, cyanide, hydroxide, nitrate, or any combination thereof.

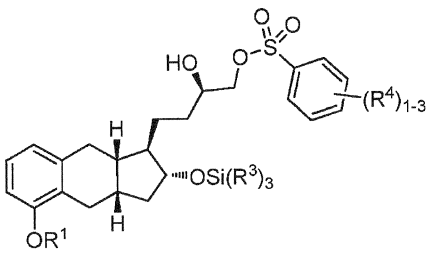
45. The method of claim 44, wherein the transition metal catalyst of step **xv)** comprises CuI.

46. The method of claim 42, further comprising the steps of:

xvii) reacting a compound of Formula **19** with R^4-substituted benzenesulfonyl chloride under basic conditions to generate a compound of Formula **20**, wherein each R^4 is independently selected from –H or $C_{1\text{-}3}$ alkyl; and



19

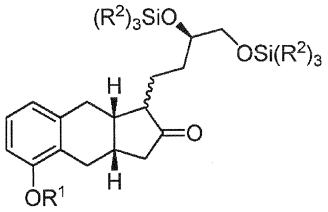


20

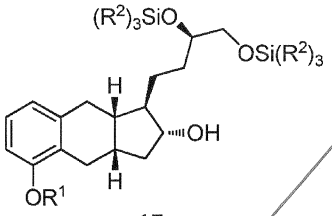
xviii) reacting the compound of Formula **20** with methanol under basic conditions to generate the compound of Formula **21**.

47. The method of claim 46, further comprising the steps of

xix) reacting a compound of Formula **16** with a reducing agent to generate a compound of Formula **17**;

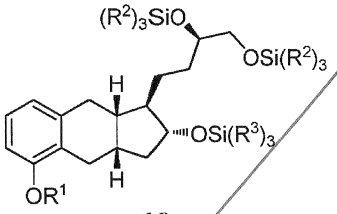


16



17

xx) reacting the compound of claim **17** with $Si(R^3)_3Cl$ under basic conditions to generate a compound of Formula **18**; and

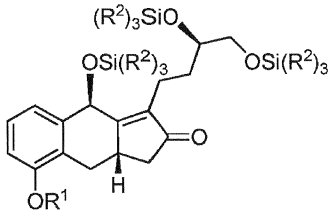


18

xxi) selectively deprotecting the compound of Formula **18** to generate the compound of Formula **19**.

48. The method of claim 47, further comprising the steps of:

xii) hydrogenating a compound of Formula **15**

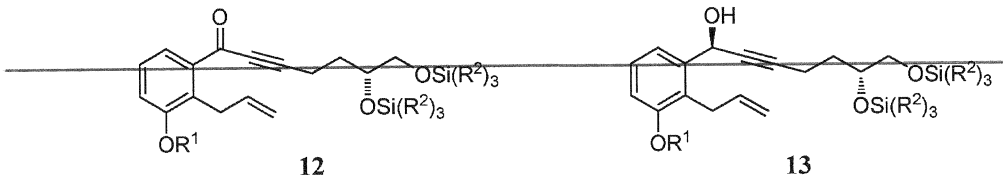


15

in the presence of an alcohol or optionally substituted THF to generate the compound of Formula **16**.

49. The method of claim 48, further comprising the steps of:

x) reacting a compound of Formula **12** with a reducing agent to generate a compound of Formula **13**; and



12 **13**

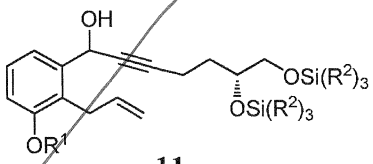
xiv) converting the compound of Formula **13** to the compound of Formula **15**.

50. The method of claim 49, wherein the reducing agent of step **x)** comprises a chiral borane compound.

51. The method of claim 50, wherein the chiral borane compound is selected from (R)-1-methyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-1-butyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-tetrahydro-1,3,3-triphenyl-1H,3H-pyrrolo[1,2-c][1,3,2]oxaborole, (4S)- 2-methyl-4,5,5-triphenyl-1,3,2-oxazaborolidine, or any combination thereof.

52. The method of claim 49, further comprising the step of:

viii) reacting a compound of Formula **11**



11

with an oxidizing agent to generate the compound of Formula **12**, wherein the oxidizing agent comprises MnO_2.

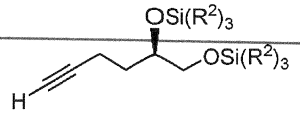
53. The method of claim 52, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent to generate a compound of Formula **10**; and



9 **10**

ii) reacting the compound of Formula **10** with a compound of Formula **5** in the presence of a base and an organic solvent to generate a compound of Formula **11**



5

54. The method of claim 53, wherein the oxidizing agent of step **i)** comprises MnO_2 or Dess-Martin periodinane.

55. The method of claim 53, wherein the base of step **ii)** comprises an alkyllithium reagent.

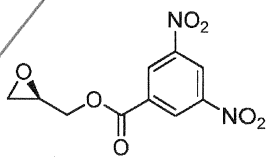
56. The method of claim 55, wherein the alkyllithium reagent is *sec*-butyllithium.

57. The method of claim 53, wherein the organic solvent of step **ii)** comprises pentane, hexane, cyclohexane, heptane, tetrahydrofuran, 1,4-dioxane, diethyl ether, petro ether, methyl-*tert*-butylether, or any combination thereof.

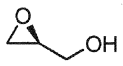
58. The method of claim 57, wherein the organic solvent of step **ii)** comprises methyl-*tert*-butylether.

59. The method of claim 53, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having greater than about 99% e.e.;

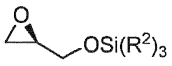


1a



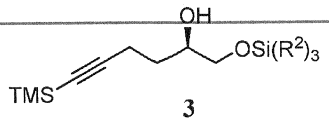
1

v) reacting the compound of Formula **1** with $SiCl(R^2)_3$ under basic conditions to generate the compound of Formula **2**;



2

vi) reacting the compound of Formula **2** with 1-TMS-1-propyne to generate the compound of Formula **3**; and

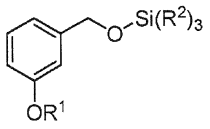


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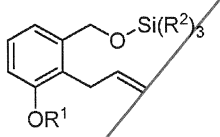
vii) converting the compound of Formula **3** to the compound of Formula **5**.

60. The method of claim 59, further comprising the steps of:

xxii) reacting a compound of Formula **7** with a 3-haloprop-1-ene in the presence of a base and an organic solvent to generate a compound of Formula **8**; and



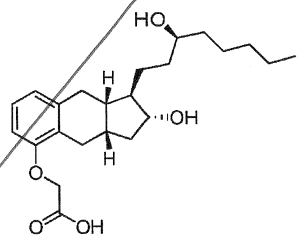
7



8

xxiii) deprotecting the compound of Formula **8** to generate the compound of Formula **9**.

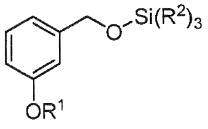
61. A method of generating a compound of Formula **I**



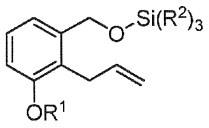
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

xxii) reacting a compound of Formula **7**, wherein R^1 is C_{1-6} alkyl and each R^2 is independently selected from C_{1-6} alkyl or phenyl, with a 3-haloprop-1-ene in the presence of a base and an organic solvent to generate a compound of Formula **8**;

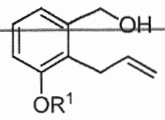


7



8

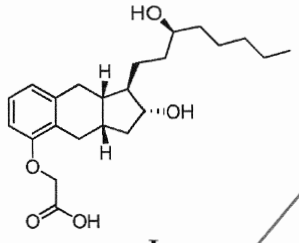
xxiii) deprotecting the compound of Formula **8** to generate the compound of Formula **9**, and



9

xxiv) converting the compound of Formula **9** to the compound of Formula **I,** wherein the base of step **xxii)** comprises sec-butyl lithium.

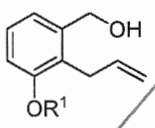
62. A method of generating a compound of Formula **I**



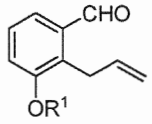
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent in the presence of an organic solvent to generate a compound of Formula **10**



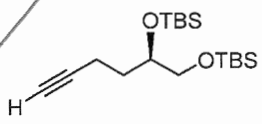
9



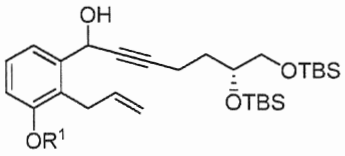
10

wherein R^1 is C_{1-6} alkyl and the oxidizing agent comprises MnO_2 or Dess-Martin periodinane;

ii) reacting the compound of Formula **10** with a compound of Formula **5a** in the presence of a base and an organic solvent to generate a compound of Formula **11a**; and



5a



11a

iii) converting the compound of Formula **11a** to the compound of Formula **I.**

63. The method of claim 62, wherein the organic solvent of step **i)** comprises a halogenated organic solvent.

64. The method of claim 63, wherein the halogenated organic solvent comprises dichloromethane, chloroform, or any combination thereof.

65. The method of claim 62, wherein the base of step **ii)** comprises an alkyllithium reagent.

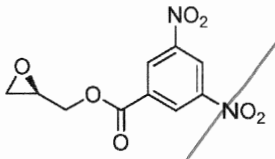
66. The method of claim 65, wherein the alkyllithium reagent is *sec*-butyllithium.

67. The method of claim 62, wherein the organic solvent of step **ii)** comprises pentane, hexane, cyclohexane, heptane, tetrahydrofuran, 1,4-dioxane, diethyl ether, petro ether, methyl-*tert*-butylether, or any combination thereof.

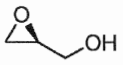
68. The method of claim 67, wherein the organic solvent of step **ii)** comprises methyl-*tert*-butylether.

69. The method of claim 62, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

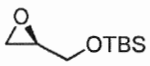


1a



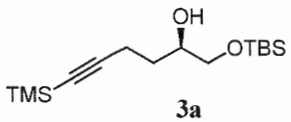
1

v) reacting the compound of Formula **1** with TBSCl under basic conditions to generate the compound of Formula **2a**;



2a

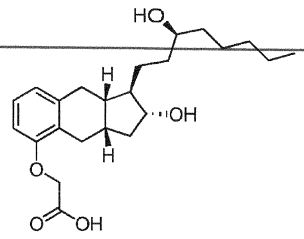
vi) reacting the compound of Formula **2a** with 1-TMS-1-propyne to generate the compound of Formula **3a**; and



3a

vii) converting the compound of Formula **3a** to the compound of Formula **5a**.

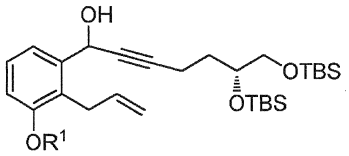
70. A method of generating a compound of Formula **I**



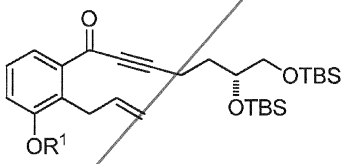
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

viii) reacting a compound of Formula **11a** with an oxidizing agent in the presence of an organic solvent to generate a compound of Formula **12a**



11a



12a

wherein R^1 is $C_{1\text{-}6}$ alkyl and the oxidizing agent comprises MnO_2; and

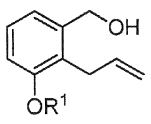
ix) converting the compound of Formula **12a** to the compound of Formula **I**.

71. The method of claim 70, wherein the organic solvent of step **viii)** comprises a halogenated organic solvent.

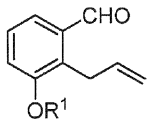
72. The method of claim 71, wherein the halogenated organic solvent comprises dichloromethane, chloroform, or any combination thereof.

73. The method of claim 70, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent in the presence of an organic solvent to generate a compound of Formula **10**



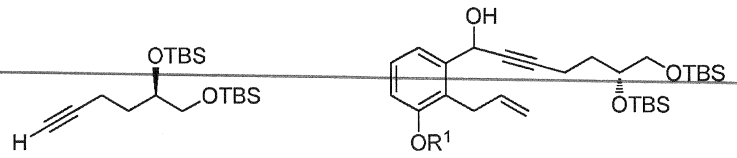
9



10

wherein the oxidizing agent comprises MnO_2 or Dess-Martin periodinane; and

~~**ii)** reacting the compound of Formula **10** with a compound of Formula **5a**~~



5a **11a**

in the presence of a base and an organic solvent to generate a compound of Formula **11a**.

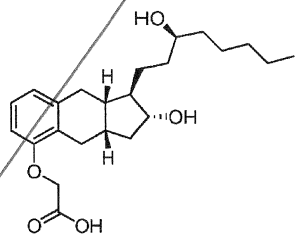
74. The method of claim 73, wherein the base of step **ii)** comprises an alkyllithium reagent.

75. The method of claim 74, wherein the alkyllithium reagent is *sec*-butyllithium.

76. The method of claim 73, wherein the organic solvent of step **ii)** comprises pentane, hexane, cyclohexane, heptane, tetrahydrofuran, 1,4-dioxane, diethyl ether, petro ether, methyl-*tert*-butylether, or any combination thereof.

77. The method of claim 76, wherein the organic solvent of step **ii)** comprises methyl-*tert*-butylether.

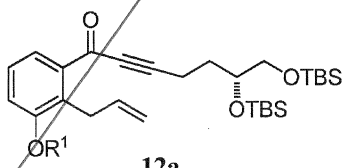
78. A method of generating a compound of Formula **I**



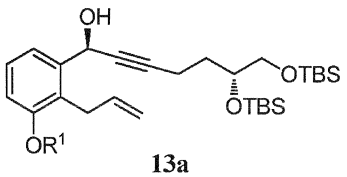
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

x) reacting a compound of Formula **12a** with a reducing agent in the presence of an organic solvent to generate a compound of Formula **13a**



12a



13a

wherein the organic solvent comprises THF, R^1 is $C_{1\text{-}6}$ alkyl, and each R^2 is independently ~~selected from $C_{1\text{-}6}$ alkyl or phenyl; and~~

~~xi) converting the compound of Formula 13 to the compound of Formula I.~~

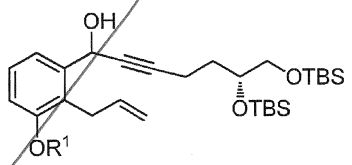
79. The method of claim 78, wherein the reducing agent of step **x)** comprises a chiral borane compound.

80. The method of claim 79, wherein the chiral borane compound is selected from (R)-1-methyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-1-butyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole, (R)-tetrahydro-1,3,3-triphenyl-1H,3H-pyrrolo[1,2-c][1,3,2]oxaborole, (4S)- 2-methyl-4,5,5-triphenyl-1,3,2-oxazaborolidine, or any combination thereof.

81. The method of claim 80, wherein the organic solvent of step **x)** further comprises toluene.

82. The method of claim 78, further comprising the step of:

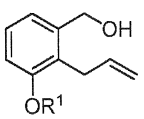
viii) reacting a compound of Formula **11a** with an oxidizing agent to generate the compound of Formula **12a**, wherein the oxidizing agent comprises MnO_2



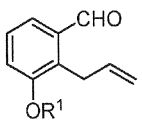
11a

83. The method of claim 81, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent to generate a compound of Formula **10**; and

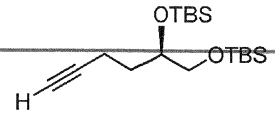


9



10

ii) reacting the compound of Formula **10** with a compound of Formula **5a** in the ~~presence of a base and an organic solvent to generate a compound of Formula 11a~~

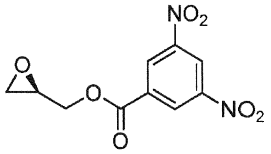


5a

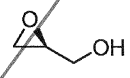
84. The method of claim 83, wherein the oxidizing agent comprises MnO_2 or Dess-Martin periodinane.

85. The method of claim 83, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

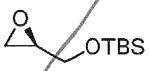


1a



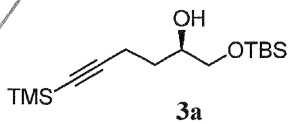
1

v) reacting the compound of Formula **1** with TBSCl under basic conditions to generate the compound of Formula **2a**;



2a

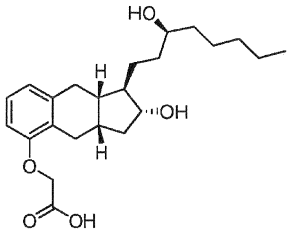
vi) reacting the compound of Formula **2a** with 1-TMS-1-propyne to generate the compound of Formula **3a**; and



3a

vii) converting the compound of Formula **3a** to the compound of Formula **5a**.

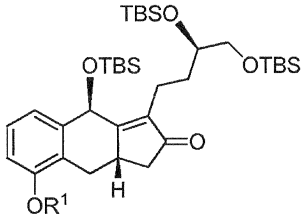
86. A method of generating a compound of Formula **I**



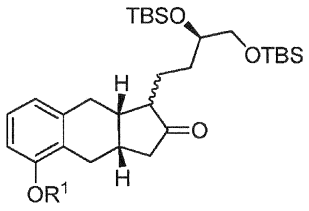
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

xii) hydrogenating a compound of Formula **15a** in the presence of methanol, ethanol, THF, 2-methyl-THF, or any combination thereof to generate the compound of Formula **16a**



15a



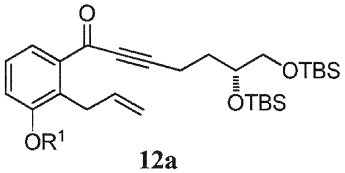
16a

wherein R^1 is $C_{1\text{-}6}$ alkyl; and

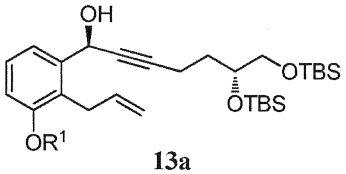
xiii) converting the compound of Formula **16a** to the compound of Formula **I**.

87. The method of claim 86, further comprising the steps of:

x) reacting a compound of Formula **12a** with a reducing agent in the presence of an organic solvent to generate a compound of Formula **13a**



12a



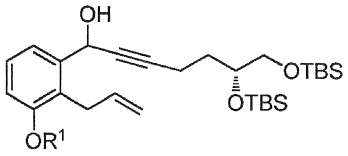
13a

wherein the organic solvent comprises THF; and

xiv) converting the compound of Formula **13a** to the compound of Formula **15a**.

88. The method of claim 87, further comprising the steps of:

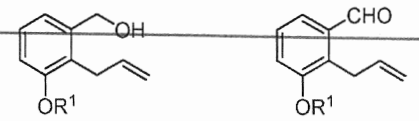
viii) reacting a compound of Formula **11a** with an oxidizing agent to generate the compound of Formula **12a**, wherein the oxidizing agent comprises MnO_2



11a

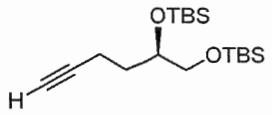
89. The method of claim 87, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent to generate a compound of Formula **10**; and



9 **10**

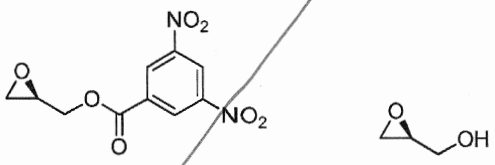
ii) reacting the compound of Formula **10** with a compound of Formula **5a** in the presence of a base and an organic solvent to generate a compound of Formula **11a**



5a

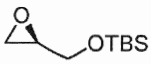
90. The method of claim 89, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;



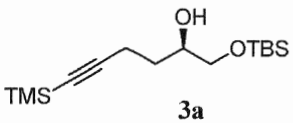
1a **1**

v) reacting the compound of Formula **1** with TBSCl under basic conditions to generate the compound of Formula **2a**;



2a

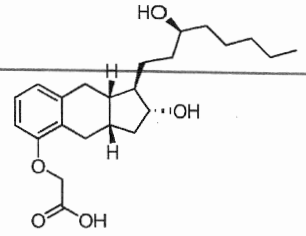
vi) reacting the compound of Formula **2a** with 1-TMS-1-propyne to generate the compound of Formula **3a**; and



3a

vii) converting the compound of Formula **3a** to the compound of Formula **5a**.

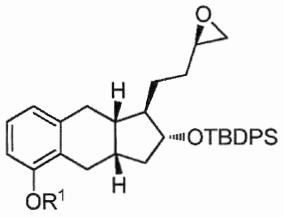
~~91. A method of generating a compound of Formula I~~



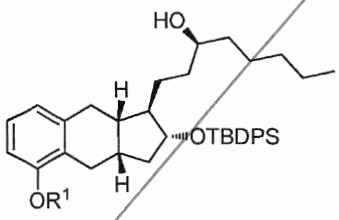
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

xv) reacting a compound of Formula **21a** with n-butyllithium in the presence of an organic solvent and a transition metal catalyst to generate a compound of Formula **22a**



21a



22a

wherein R^1 is C_{1-6} alkyl; and

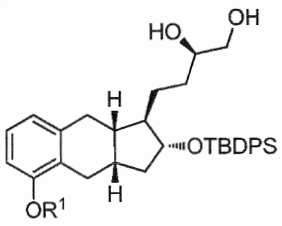
xvi) converting the compound of Formula **22a** to the compound of Formula **I**.

92. The method of claim 91, wherein the transition metal catalyst comprises a compound or complex either of which comprises copper having a +1 oxidation state.

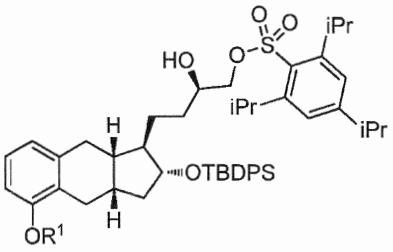
93. The method of claim 92, wherein the transition metal catalyst comprises CuI.

94. The method of claim 91, further comprising the steps of:

xvii) reacting a compound of Formula **19a** with triisopropylbenzenesulfonyl chloride under basic conditions to generate a compound of Formula **20a**; and



19a

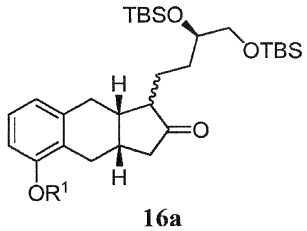


20a

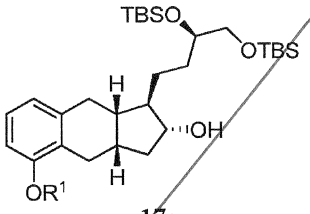
~~xviii) reacting the compound of Formula **20a** with methanol under basic conditions to~~ generate the compound of Formula **21a**.

95. The method of claim 94, further comprising the steps of

xix) reacting a compound of Formula **16a** with a reducing agent to generate a compound of Formula **17a**;

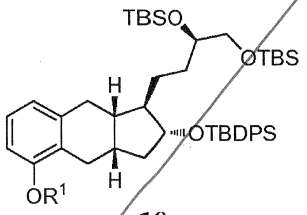


16a



17a

xx) reacting the compound of Formula **17a** with TBDPSCl under basic conditions to generate a compound of Formula **18a**; and

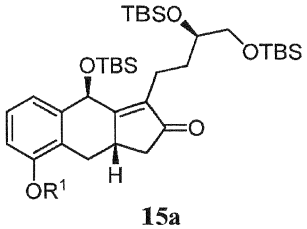


18a

xxi) selectively deprotecting the compound of Formula **18a** to generate the compound of Formula **19a**.

96. The method of claim 95, further comprising the steps of:

xii) hydrogenating a compound of Formula **15a**

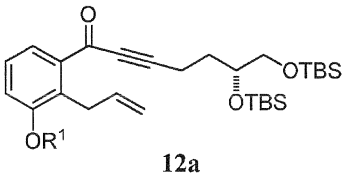


15a

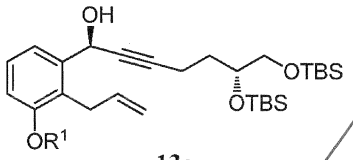
in the presence of an alcohol, optionally substituted THF, or any combination thereof to generate the compound of Formula **16a**.

~~97. The method of claim 96, further comprising the steps of:~~

x) reacting a compound of Formula **12a** with a reducing agent to generate a compound of Formula **13a**; and



12a

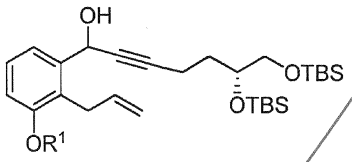


13a

xiv) converting the compound of Formula **13a** to the compound of Formula **15a**.

98. The method of claim 97, further comprising the step of:

viii) reacting a compound of Formula **11a**

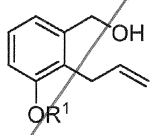


11a

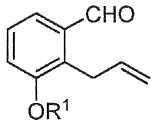
with an oxidizing agent to generate the compound of Formula **12a**, wherein the oxidizing agent comprises MnO_2.

99. The method of claim 97, further comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent to generate a compound of Formula **10**; and

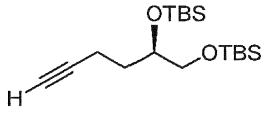


9



10

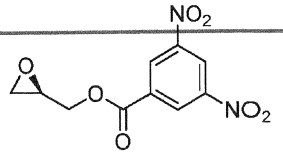
ii) reacting the compound of Formula **10** with a compound of Formula **5a** in the presence of a base and an organic solvent to generate a compound of Formula **11a**



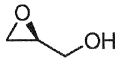
5a

100. The method of claim 99, further comprising the steps of:

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

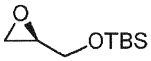


1a



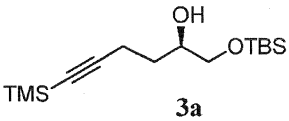
1

v) reacting the compound of Formula **1** with TBSCl under basic conditions to generate the compound of Formula **2a**;



2a

vi) reacting the compound of Formula **2a** with 1-TMS-1-propyne to generate the compound of Formula **3a**; and

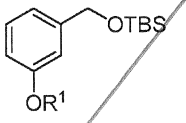


3a

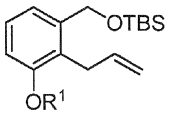
vii) converting the compound of Formula **3a** to the compound of Formula **5a**.

101. The method of claim 100, further comprising the steps of:

xxii) reacting a compound of Formula **7a** with a 3-haloprop-1-ene in the presence of a base and an organic solvent to generate a compound of Formula **8a**; and



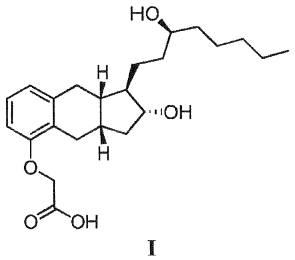
7a



8a

xxiii) deprotecting the compound of Formula **8a** to generate the compound of Formula **9**.

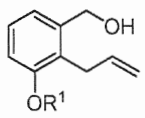
102. A method of generating a compound of Formula **I**



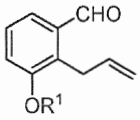
I

or a pharmaceutically acceptable salt thereof, comprising the steps of:

i) reacting a compound of Formula **9** with an oxidizing agent to generate a compound of Formula **10**;

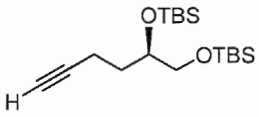


9

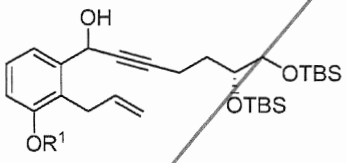


10

ii) reacting the compound of Formula **10** with a compound of Formula **5a** in the presence of a base and an organic solvent to generate a compound of Formula **11a**;

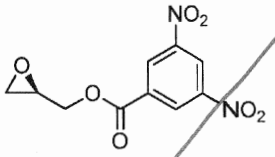


5a

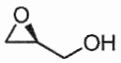


11a

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

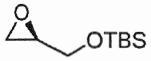


1a



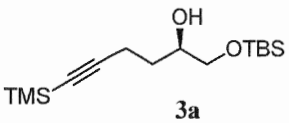
1

v) reacting the compound of Formula **1** with TBSCl under basic conditions to generate the compound of Formula **2a**;



2a

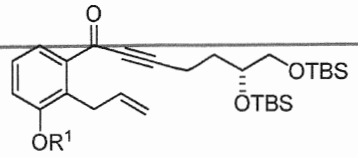
vi) reacting the compound of Formula **2a** with 1-TMS-1-propyne to generate the compound of Formula **3a**;



3a

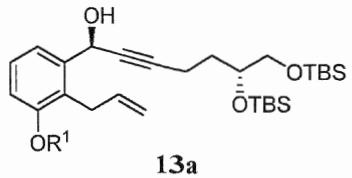
vii) converting the compound of Formula **3a** to the compound of Formula **5a;**

viii) reacting a compound of Formula **11a** with an oxidizing agent to generate the compound of Formula **12a**, wherein the oxidizing agent comprises MnO_2;



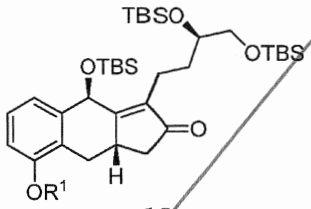
12a

x) reacting a compound of Formula **12a** with a reducing agent to generate a compound of Formula **13a**;



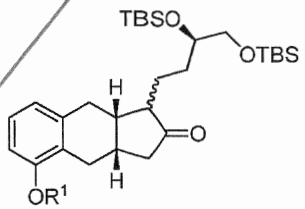
13a

xiv) converting the compound of Formula **13a** to the compound of Formula **15a**;



15a

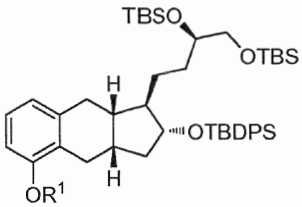
xii) hydrogenating a compound of Formula **15a** in the presence of methanol, ethanol, THF, 2-methyl-THF, or any combination thereof to generate the compound of Formula **16a**;



16a

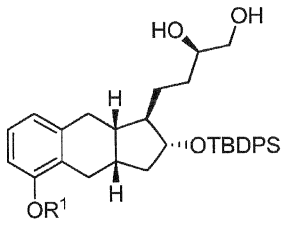
xix) reacting a compound of Formula **16a** with a reducing agent to generate a compound of Formula **17a**;

xx) reacting the compound of Formula **17a** with TDPSCl under basic conditions to generate a compound of Formula **18a**;



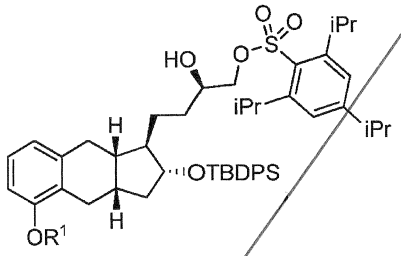
18a

~~xxi) selectively deprotecting the compound of Formula **18a** to generate the compound~~ of Formula **19a**;



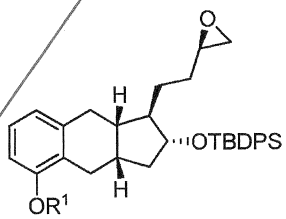
19a

xvii) reacting a compound of Formula **19a** with triisopropylbenzenesulfonyl chloride under basic conditions to generate a compound of Formula **20a**;



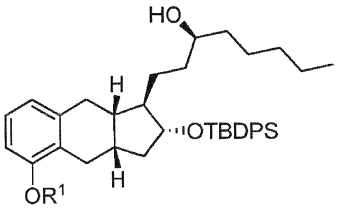
20a

xviii) reacting the compound of Formula **20a** with methanol under basic conditions to generate the compound of Formula **21a**;



21a

xv) reacting a compound of Formula **21a** with n-butyllithium in the presence of an organic solvent and a transition metal catalyst to generate a compound of Formula **22a**; and



22a

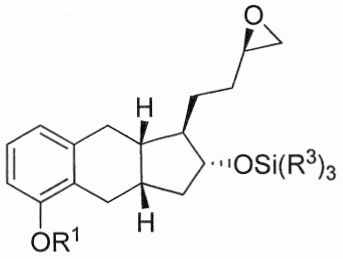
~~**xvi)** converting the compound of Formula **22a** to the compound of Formula **I.**~~

~~103. The method of claim 102, further comprising the step of:~~

~~**xxiv)** reacting the compound of Formula **I** with diethanolamine in the presence of an organic solvent to generate the diethanolamine salt of the compound of Formula **I**.~~

CLAIMS

~~104~~1. A compound of Formula **21**

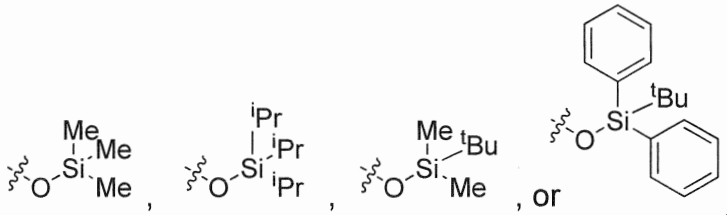


21

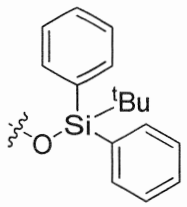
wherein R^1 is C_{1-6} alkyl and each R^3 is independently C_{1-6} alkyl or phenyl.

~~105~~2. The compound of claim ~~104~~1, wherein R^1 is methyl, ethyl, propyl, *iso*-propyl, butyl, *sec*-butyl, or *tert*-butyl.

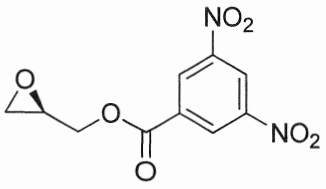
~~106~~3. The compound of claim ~~104~~1, wherein the $-OSi(R^3)_3$ group is selected from



~~107~~4. The compound of claim ~~104~~1, wherein R^1 is methyl and the $-OSi(R^3)_3$ group is

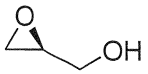


~~108~~5. A compound of Formula **1a**



1a

~~1096~~. A method of purifying a compound of Formula **1** comprising:



1

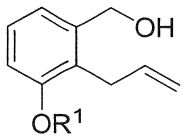
xxx) reacting a compound of Formula **1** with a derivatizing reagent to generate a precipitate that is substantially insoluble in dichloromethane or mixtures thereof;

xxxi) collecting the precipitate and refluxing the precipitate in a solvent comprising an alcohol to generate the compound of Formula **1** having a chemical purity of about 98% or greater and an e.e. of about 98% or greater;

wherein the method excludes the use of any column chromatography.

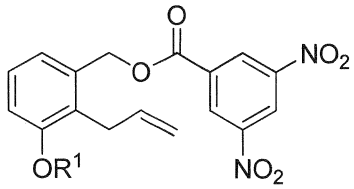
~~1107~~. The method of claim ~~1096~~, wherein the derivitizing reagent comprises 3,5-dinitrobenzoyl chloride and the alcohol comprises methanol.

~~1118~~. A method of purifying a compound of Formula **9** comprising:



9

xl) reacting a compound of Formula **9**, wherein R^1 is C_{1-6} alkyl, with 3,5-dinitrobenzoyl chloride to generate a precipitate comprising a compound of Formula **9A**; and



9A

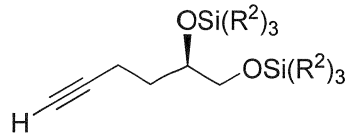
xli) collecting the precipitate and treating the precipitate with a base in the presence of an alcohol to generate the compound of Formula **9** having a chemical purity of about 95% or greater;

wherein the method excludes the use of any column chromatography.

~~1129~~. The method of claim ~~1118~~, further comprising the step:

xlii) recrystallizing the precipitate of step **xli)**.

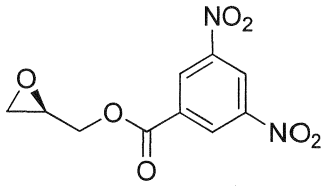
~~113~~10. A method of generating a compound of Formula **5**



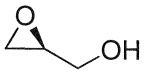
5

wherein each R^2 is independently selected from a C_{1-6} alkyl or phenyl, comprising

iv) refluxing the compound of Formula **1a** in the presence of methanol to generate a compound of Formula **1** having an e.e. of greater than about 98%;

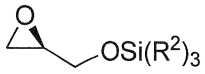


1a



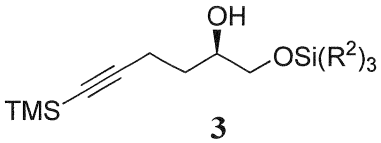
1

v) reacting the compound of Formula **1** with $SiCl(R^2)_3$, wherein each R^2 is independently selected from C_{1-6} alkyl or phenyl, under basic conditions to generate the compound of Formula **2**;



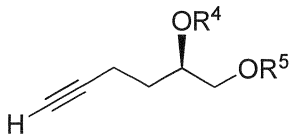
2

vi) reacting the compound of Formula **2** with 1-TMS-1-propyne to generate the compound of Formula **3**;



3

l) deprotecting the compound Formula **3** under basic condition to generate a compound of Formula **4**, wherein each of R^4 and R^5 are H or $-OSi(R^2)_3$; and

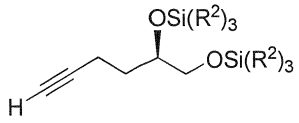


4

li) reacting the compound of Formula **4** with $SiCl(R^2)_3$ under basic conditions to generate the compound of Formula **5**,

wherein the compound of Formula **5** has a chemical purity of about 98% or greater and an e.e. of about 98% or greater.

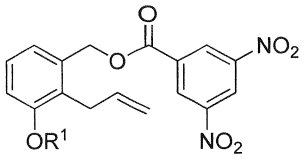
~~114~~11. A compound of Formula **5**



5

wherein each of R^2 is independently selected from a $C_{1\text{-}6}$ alkyl or phenyl.

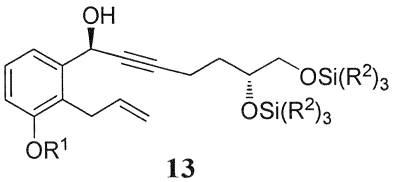
~~115~~12. A compound of Formula **9a**



9A

wherein R^1 is $C_{1\text{-}6}$ alkyl.

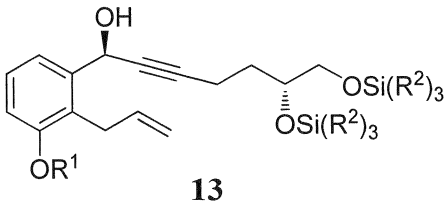
~~116~~13. A compound of Formula **13**



13

wherein R^1 is $C_{1\text{-}6}$ alkyl and each R^2 is independently selected from $C_{1\text{-}6}$ alkyl or phenyl.

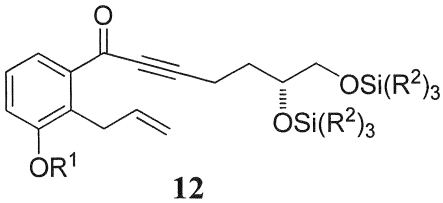
~~117~~14. A method of generating a compound of Formula **13**



13

wherein R^1 is $C_{1\text{-}6}$ alkyl and each R^2 is independently selected from $C_{1\text{-}6}$ alkyl or phenyl, comprising

x) reacting a compound of Formula **12** with (R)-1-methyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2]oxazaborole in the presence of an organic solvent comprising THF and toluene to generate a compound of Formula **13**



12

wherein the compound of Formula **13** has a chemical purity of about 97% or greater and a d.e. of about 97% or greater.