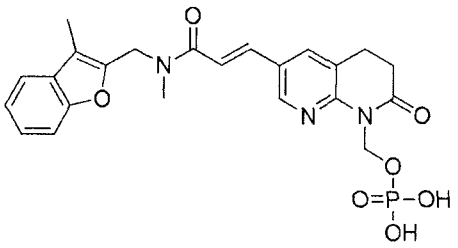
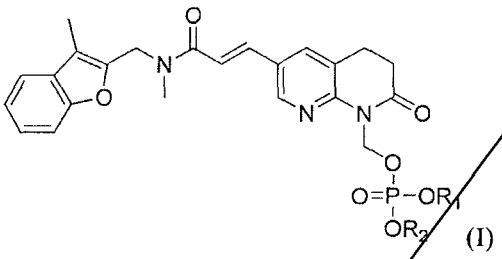
What is claimed is:

1. A compound represented by:



and pharmaceutically acceptable salts thereof

2. A compound represented by formula I:



(I)

wherein,

R_1 and R_2 are each independently selected from the group consisting of hydrogen, an alkali metal, NH_4^+, NH_3^+-(R_3), NH_2^+-(R_3)$_2$, and NH^+-(R_3)$_3$, or R_1 and R_2 taken together are an alkaline earth metal; and

R_3 is independently selected from the group consisting of C_{1-6}alkyl-, hydroxyC_{1-6}alkyl-, phenyl and benzyl.

3. The compound of claim 2, wherein R_1 and R_2 are each NH_3^+-(R_3).

4. The compound of claim 2, wherein one of R_1 and R_2 is H; and one of R_1 and R_2 is NH_4^+ or NH_3^+-(R_3).

5. The compound of any one of claims 2-4, wherein R_3 is $-CH_2CH_2OH$.

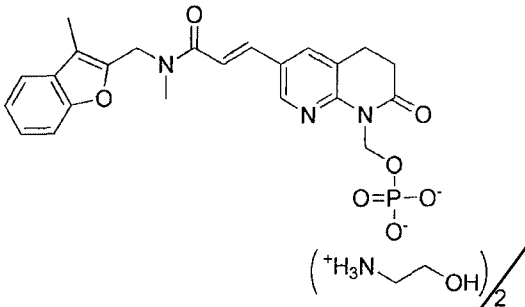
6. The compound of claim 2, wherein R_1 and R_2 are an alkali metal.

7. The compound of claim 6, wherein the alkali metal is selected from the group consisting of lithium, sodium and potassium.

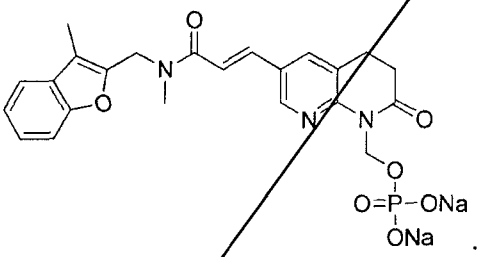
8. The compound of claim 2, wherein R_1 and R_2 taken together are an alkaline earth metal.

9. The compound of claim 8, wherein the alkaline earth metal is calcium or magnesium.

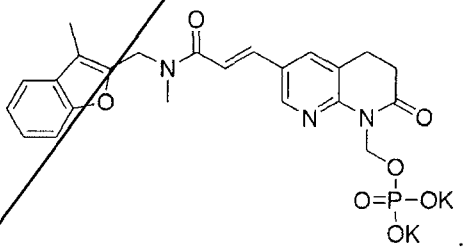
10. A compound represented by:



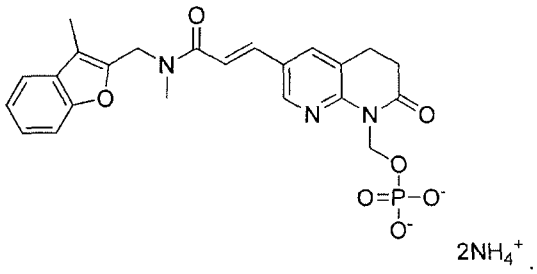
11. The compound of claim 2, wherein the compound is represented by:



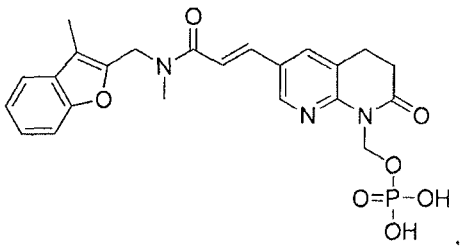
12. The compound of claim 2, wherein the compound is represented by:



13. The compound of claim 2, wherein the compound is represented by:



14. The compound of claim 2, wherein the compound is represented by:



15. The compound of any one of claims 1-14, wherein the compound has at least 2-fold greater oral bioavailability on a molar basis as compared to (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide or salts thereof.

16. The compound of any one of claims 1-14, wherein the compound has at least 2-fold greater bioavailability on a molar basis as compared to the p-toluenesulfonic salt of (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide.

17. A pharmaceutical composition comprising a compound of any one of claims 1-16 and a pharmaceutically acceptable excipient.

18. The pharmaceutical composition of claim 17, wherein the composition is formulated for one of: intravenous administration, injectable administration, topical administration, systemic administration, inhalation administration, or oral administration.

19. The pharmaceutically acceptable composition of claim 17 or 18, wherein the composition is a powder, tablet, pill, or capsule.

20. The pharmaceutically acceptable composition of claim 17 or 18, wherein the composition is a pharmaceutically-acceptable sterile isotonic aqueous or non-aqueous solution, dispersion, suspension or emulsion, or a sterile powder which may be reconstituted into sterile injectable solutions or dispersions.

21. Use of the pharmaceutical composition of claim 17 for treating a bacterial infection in a patient.

22. Use of the pharmaceutical composition of claim 17 for treating a bacterial infection in a patient, wherein the use provides a mean plasma level of the compound that is at least 2 times higher than that obtained by use of the same amount, on a molar basis, of (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide or salts thereof, at about 4 hours after the use.

23. Use of the pharmaceutical composition of claim 17 for treating a bacterial infection in a patient, wherein the use provides a mean plasma level of the compound that is at least 2 times higher than that obtained by use of the same amount, on a molar basis, of p-toluenesulfonic salt of (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide, at about 4 hours after the use.

24. Use of the pharmaceutical composition of claim 17 for treating or ameliorating cystic fibrosis in a patient.

25. The use of any one of claims 21-24, wherein the patient is a human.

26. The use of any one of claims 21-23, wherein the patient is a companion animal or food animal.

27. The use of any one of claims 21-26, wherein said use is by a route of administration selected from the group consisting of oral administration, intravenous administration, subcutaneous administration, topical administration, and inhalation.

28. The use of any one of claims 21-26, wherein said use is by oral administration.

29. The use of any one of claims 21-26, wherein said use is by injection.

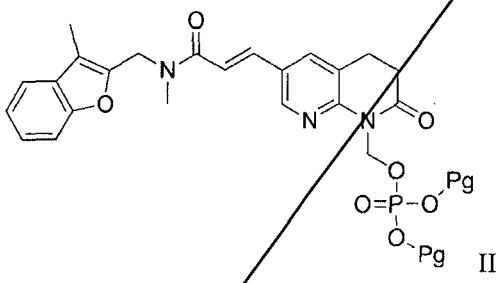
30. The use of any one of claims 21-29, further comprising use of a compound selected from the group consisting of an oxazolidinone, a lipoglycopeptide, vancomycin, teicoplanin, a glycopeptide, a penicillin, a cephalosporin, a puromutalin, a fusidane, a lincosamide, rifamycin and/or arbekacin.

31. The use of any one of claims 21-29, further comprising use of a compound selected from the group consisting of linezolid, daptomycin, teicoplanin, and telavancin.

32. The use of any one of claims 21-29, further comprising use of a compound selected from the group consisting of quinolones, fluoroquinolones, carbapenems, aminoglycosides, aminocyclitols, diaminopyrimidines, tetracyclines, glycyclines, streptogramins, macrolides, and /or sulfamides.

33. A kit comprising the pharmaceutical composition of any one of claims 17 to 20 and instructions for use thereof.

34. A method of preparing a compound represented by formula II:

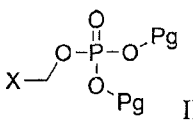


II

the method comprising:

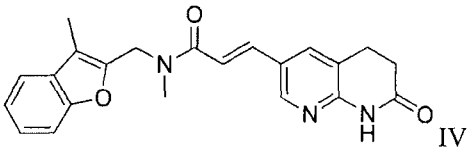
contacting a compound of formula III with a compound of formula IV or salt thereof; wherein:

formula III is represented by:



III;

formula IV is represented by:

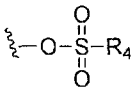
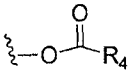


IV

wherein:

X represents a leaving group; and

Pg represents a protecting group.

35. The method of claim 34, wherein X is selected from the group consisting of: halogen,  , or  , wherein R_4 is $C_{1\text{-}6}$alkyl-, phenyl, benzyl, or halo$C_{1\text{-}6}$alkyl-.

36. The method of claim 34 or 35, wherein X is halogen.

37. The method of claim 36, wherein X is chloride.

38. The method of claim 34, wherein Pg is selected from the group consisting of -$C_{1\text{-}6}$alkyl-Si(R_5)$_3$ (wherein R_5 for each occurrence is $C_{1\text{-}6}$alkyl), $C_{1\text{-}6}$alkyl-, phenyl$C_{1\text{-}6}$alkyl-, $C_{1\text{-}6}$alkyloxycarbonyl-, and phenyl$C_{1\text{-}6}$alkyloxycarbonyl-.

39. The method of claim 38, wherein Pg is –$(CH_2)_2$-Si$(CH_3)_3$.

40. The method of claim 34, wherein Pg is –$(CH_2)_2$-Si$(CH_3)_3$.

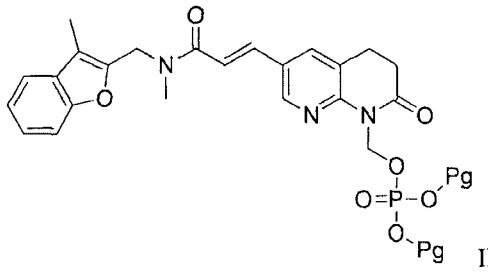
41. The method of claim 34, wherein Pg is selected from the group consisting of: t-butyl, benzyl, t-butyloxycarbonyl, and benzyloxycarbonyl

42. The method of any one of claims 34-41, wherein formula IV is the free base.

43. The method of any one of claims 34-42, wherein the method further comprises contacting formula IV with a base.

44. The method of claim 43, wherein contacting a compound of formula III with a compound of formula IV occurs in a solvent.

45. A compound represented by:



II

wherein:

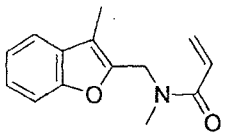
Pg is -$C_{1\text{-}6}$alkyl-$Si(R_5)_3$; and

R_5 for each occurrence is $C_{1\text{-}6}$alkyl.

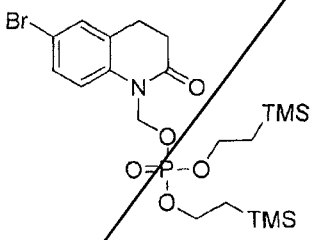
46. The compound of claim 45, wherein Pg is $-(CH_2)_2-Si(CH_3)_3$.

47. A method of preparing the compound represented by formula II of claim 45, comprising:

contacting a compound

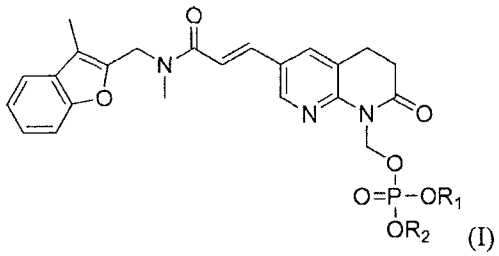


with a compound represented by:



under conditions suitable to prepare the compound of claim 45.

48. A method of preparing a compound represented by:



(I)

wherein,

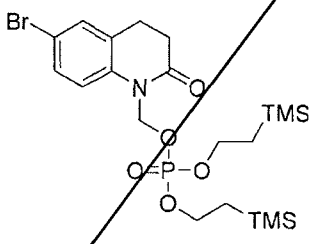
R_1 and R_2 are each independently selected from the group consisting of hydrogen, an alkali metal, NH_4^+, NH_3^+-(R_3), NH_2^+-(R_3)$_2$, and NH^+-(R_3)$_3$, or R_1 and R_2 taken together are an alkaline earth metal;

R_3 is independently selected for each occurence from the group consisting of C_{1-6}alkyl-, hydroxyC_{1-6}alkyl-, phenyl and benzyl;

comprising contacting a Brønsted acid and a compound of formula II prepared as in claim 34 or 47.

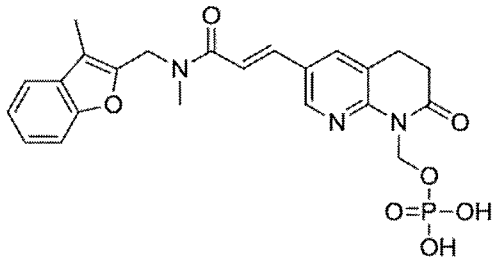
49. The method of claim 48, wherein the Brønsted acid is trifluoroacetic acid.

50. The compound represented by:



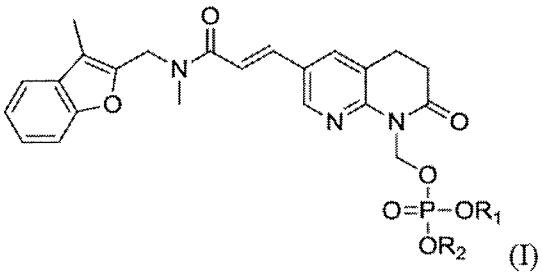
What is claimed is:

1. A compound represented by:



and pharmaceutically acceptable salts thereof.

2. A compound represented by formula I:



(I)

wherein,

R_1 and R_2 are each independently selected from the group consisting of hydrogen, an alkali metal, NH_4^+, NH_3^+-(R_3), NH_2^+-(R_3)$_2$, and NH^+-(R_3)$_3$, or R_1 and R_2 taken together are an alkaline earth metal; and

R_3 is independently selected from the group consisting of $C_{1\text{-}6}$alkyl-, hydroxy$C_{1\text{-}6}$alkyl-, phenyl and benzyl.

3. The compound of claim 2, wherein R_1 and R_2 are each NH_3^+-(R_3).

4. The compound of claim 2, wherein one of R_1 and R_2 is H; and one of R_1 and R_2 is NH_4^+ or NH_3^+-(R_3).

5. The compound of any one of claims 2-4, wherein R_3 is $-CH_2CH_2OH$.

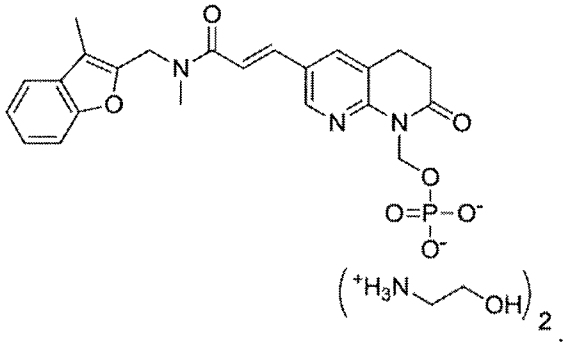
6. The compound of claim 2, wherein R_1 and R_2 are an alkali metal.

7. The compound of claim 6, wherein the alkali metal is selected from the group consisting of lithium, sodium and potassium.

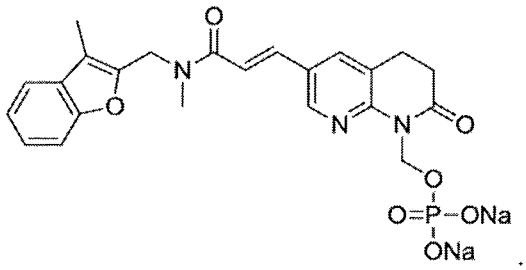
8. The compound of claim 2, wherein R_1 and R_2 taken together are an alkaline earth metal.

9. The compound of claim 8, wherein the alkaline earth metal is calcium or magnesium.

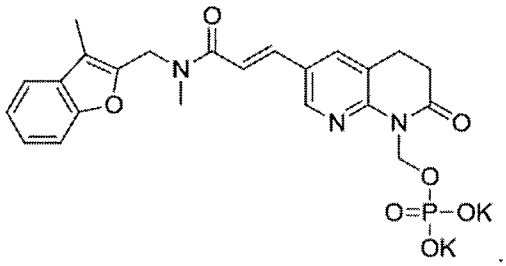
10. A compound represented by:



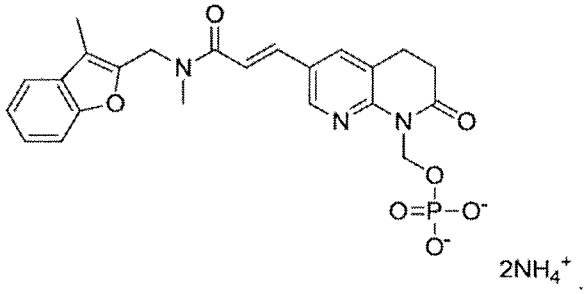
11. The compound of claim 2, wherein the compound is represented by:



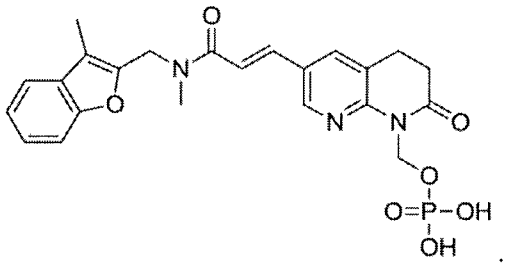
12. The compound of claim 2, wherein the compound is represented by:



13. The compound of claim 2, wherein the compound is represented by:



14. The compound of claim 2, wherein the compound is represented by:



15. The compound of any one of claims 1-14, wherein the compound has at least 2-fold greater oral bioavailability on a molar basis as compared to (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide or salts thereof.

16. The compound of any one of claims 1-14, wherein the compound has at least 2-fold greater bioavailability on a molar basis as compared to the p-toluenesulfonic salt of (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide.

17. A pharmaceutical composition comprising a compound of any one of claims 1-16 and a pharmaceutically acceptable excipient.

18. The pharmaceutical composition of claim 17, wherein the composition is formulated for one of: intravenous administration, injectable administration, topical administration, systemic administration, inhalation administration, or oral administration.

19. The pharmaceutically acceptable composition of claim 17 or 18, wherein the composition is a powder, tablet, pill, or capsule.

20. The pharmaceutically acceptable composition of claim 17 or 18, wherein the composition is a pharmaceutically-acceptable sterile isotonic aqueous or non-aqueous solution, dispersion, suspension or emulsion, or a sterile powder which may be reconstituted into sterile injectable solutions or dispersions.

21. Use of the compound or pharmaceutical composition of any one of claims 1 to 20 in the manufacture of a medicament for treating a bacterial infection in a patient.

22. Use of the compound or pharmaceutical composition of any one of claims 1 to 20 in the manufacture of a medicament for treating a bacterial infection in a patient, wherein the medicament provides a mean plasma level of the compound that is at least 2 times higher than that obtained by use of the same amount, on a molar basis, of (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide or salts thereof, at about 4 hours after the use.

23. Use of the compound or pharmaceutical composition of any one of claims 1 to 20 in the manufacture of a medicament for treating a bacterial infection in a patient, wherein the medicament provides a mean plasma level of the compound that is at least 2 times higher than that obtained by use of the same amount, on a molar basis, of p-toluenesulfonic salt of (E)-N-methyl-N-((3-methylbenzofuran-2-yl)methyl)-3-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)acrylamide, at about 4 hours after the use.

24. Use of the compound or pharmaceutical composition of any one of claims 1 to 20 in the manufacture of a medicament for treating or ameliorating cystic fibrosis in a patient.

25. The use of any one of claims 21-24, wherein the patient is a human.

26. The use of any one of claims 21-23, wherein the patient is a companion animal or food animal.

27. The use of any one of claims 21-26, wherein said medicament is formulated for a route of administration selected from the group consisting of oral administration, intravenous administration, subcutaneous administration, topical administration, and inhalation.

28. The use of any one of claims 21-26, wherein said medicament is formulated for oral administration.

29. The use of any one of claims 21-26, wherein said medicament is formulated for administration by injection.

30. The use of any one of claims 21-29, wherein the medicament further comprises or is formulated for use in combination with a compound selected from the group consisting of an

oxazolidinone, a lipoglycopeptide, vancomycin, teicoplanin, a glycopeptide, a penicillin, a cephalosporin, a pleuromutilin, a fusidane, a lincosamide, rifamycin and/or arbekacin.

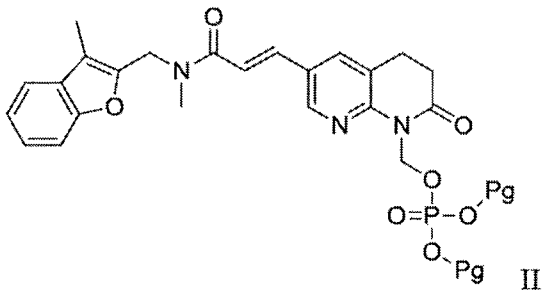
31. The use of any one of claims 21-29, wherein the medicament further comprises or is formulated for use in combination with a compound selected from the group consisting of linezolid, daptomycin, teicoplanin, and telavancin.

32. The use of any one of claims 21-29, wherein the medicament further comprises or is formulated for use in combination with a compound selected from the group consisting of quinolones, fluoroquinolones, carbapenems, aminoglycosides, aminocyclitols, diaminopyrimidines, tetracyclines, glycyclines, streptogramins, macrolides, and /or sulfamides.

33. The use of any one of claims 21-29, wherein the medicament comprises or is formulated for use in combination with a compound selected from the group consisting of sulfamethoxazole, gentamicin, ciprofloxin, levofloxin, aztreonam tobramycin, amoxicillin, nafcillin, rifabutin, rifampin and rifapentine.

34. A kit comprising the pharmaceutical composition of any one of claims 17 to 20 and instructions for use thereof.

35. A method of preparing a compound represented by formula II:



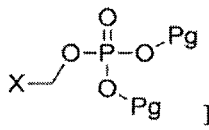
II

the method comprising:

contacting a compound of formula III with a compound of formula IV or salt thereof;

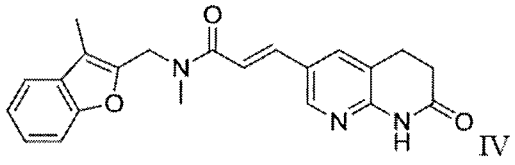
wherein:

formula III is represented by:



III;

formula IV is represented by:

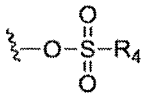
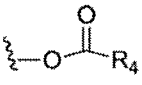


IV

wherein:

X represents a leaving group; and

Pg represents a protecting group.

36. The method of claim 35, wherein X is selected from the group consisting of: halogen, , or , wherein R_4 is $C_{1\text{-}6}$alkyl-, phenyl, benzyl, or halo$C_{1\text{-}6}$alkyl-.

37. The method of claim 35 or 36, wherein X is halogen.

38. The method of claim 37, wherein X is chloride.

39. The method of claim 35, wherein Pg is selected from the group consisting of -$C_{1\text{-}6}$alkyl-$Si(R_5)_3$ (wherein R_5 for each occurrence is $C_{1\text{-}6}$alkyl), $C_{1\text{-}6}$alkyl-, phenyl$C_{1\text{-}6}$alkyl-, $C_{1\text{-}6}$alkyloxycarbonyl-, and phenyl$C_{1\text{-}6}$alkyloxycarbonyl-.

40. The method of claim 39, wherein Pg is $-(CH_2)_2$-$Si(CH_3)_3$.

41. The method of claim 35, wherein Pg is $-(CH_2)_2$-$Si(CH_3)_3$.

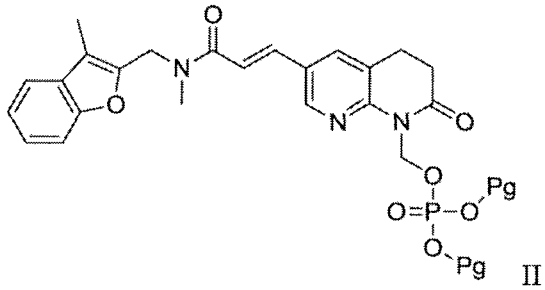
42. The method of claim 35, wherein Pg is selected from the group consisting of: t-butyl, benzyl, t-butyloxycarbonyl, and benzyloxycarbonyl.

43. The method of any one of claims 35-42, wherein formula IV is the free base.

44. The method of any one of claims 35-43, wherein the method further comprises contacting formula IV with a base.

45. The method of claim 44, wherein contacting a compound of formula III with a compound of formula IV occurs in a solvent.

46. A compound represented by:



II

wherein:

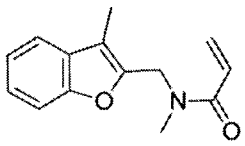
Pg is -$C_{1\text{-}6}$alkyl-$Si(R_5)_3$; and

R_5 for each occurrence is $C_{1\text{-}6}$alkyl.

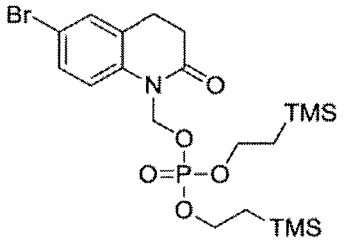
47. The compound of claim 46, wherein Pg is $-(CH_2)_2$-$Si(CH_3)_3$.

48. A method of preparing the compound represented by formula II of claim 46, comprising:

contacting a compound

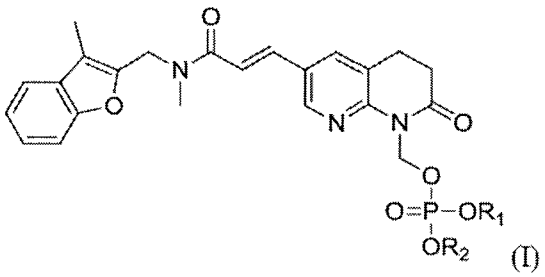


with a compound represented by:



under conditions suitable to prepare the compound of claim 46.

49. A method of preparing a compound represented by:



(I)

wherein,

R_1 and R_2 are each independently selected from the group consisting of hydrogen, an alkali metal, NH_4^+, NH_3^+-(R_3), NH_2^+-(R_3)$_2$, and NH^+-(R_3)$_3$, or R_1 and R_2 taken together are an alkaline earth metal;

R_3 is independently selected for each occurence from the group consisting of C_{1-6}alkyl-, hydroxyC_{1-6}alkyl-, phenyl and benzyl;

comprising contacting a Brønsted acid and a compound of formula II prepared as in claim 35 or 48.

50. The method of claim 49, wherein the Brønsted acid is trifluoroacetic acid.

51. The compound represented by:

