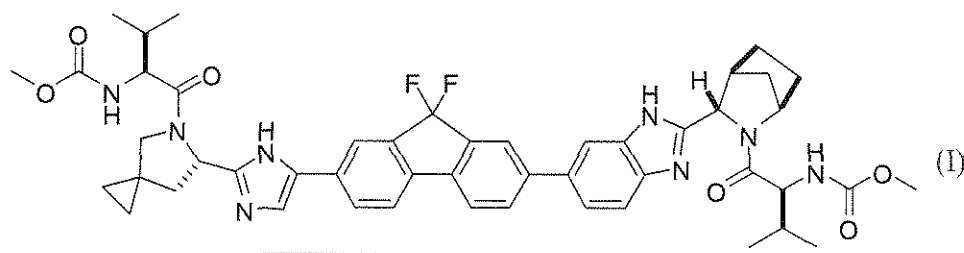


[0007] The substituents R and R' are independently selected from the group consisting of hydrogen and straight or branched C₁₋₈-alkyl, or R and R' together represent a straight or branched C₁₋₈-alkylene, C₃₋₈-cycloalkylene, or C₆₋₁₂-arylene.

[0008] Any alkyl, alkylene, cycloalkylene, or arylene as defined herein is optionally substituted with one or more substituents selected from the group consisting of C₁₋₆-alkyl, -C(O)N(C₁₋₆-alkyl)₂, and -C(O)O(C₁₋₆-alkyl).

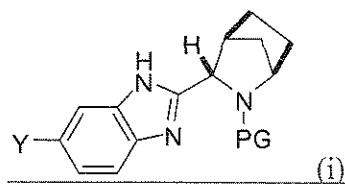
[0009] More specific embodiments are described below.

[0009a] In one aspect, there is provided a process for making a compound of formula I:

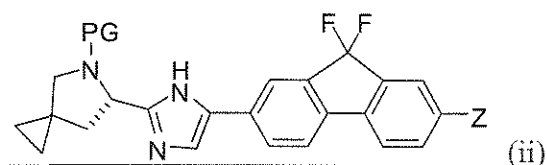


or a pharmaceutically acceptable salt thereof, comprising

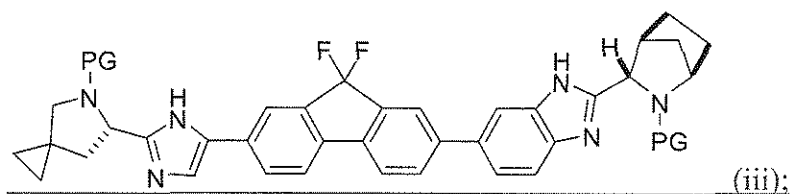
(A) coupling a compound of formula (i)



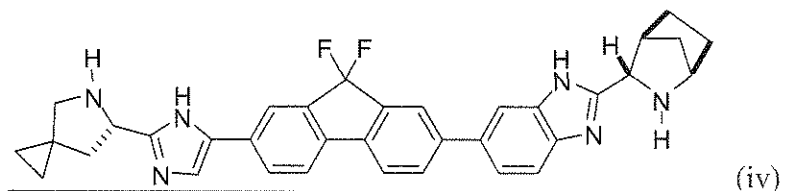
with a compound of formula (ii)



in the presence of a metal catalyst and base to yield a compound of formula (iii) or a salt thereof:

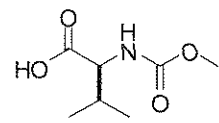


(B) deprotecting a compound of formula (iii) to yield a compound of formula (iv):



or a salt thereof;

(C) contacting the compound of formula (iv) with (S)-2-(methoxycarbonylamino)-3-methylbutanoic acid:



to yield a compound of formula I; wherein

each PG independently is an amine protecting group;

Y and Z are independently selected from Br and -B(OR)(OR') wherein when

Y is -B(OR)(OR'), then Z is Br and

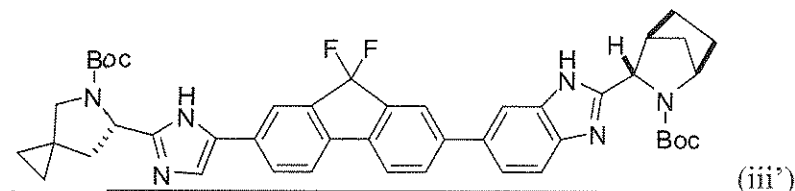
Y is Br, then Z is -B(OR)(OR'); and

R and R' are independently selected from the group consisting of hydrogen and straight or branched C₁₋₈-alkyl,

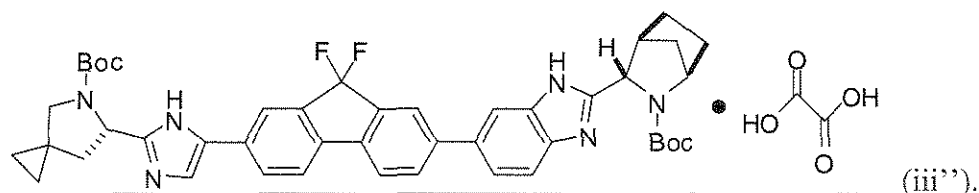
or R and R' together represent a straight or branched C₁₋₈-alkylene, C₃₋₈-cycloalkylene, or C₆₋₁₂-arylene,

wherein any alkyl, alkylene, cycloalkylene, or arylene is optionally substituted with one or more substituents selected from the group consisting of C₁₋₆-alkyl, -C(O)N(C₁₋₆-alkyl)₂, and -C(O)O(C₁₋₆-alkyl).

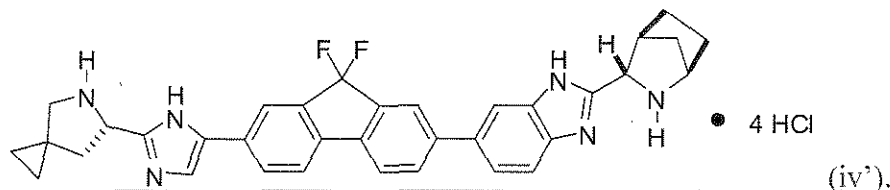
[0009b] In one aspect, there is provided a compound of formula (iii'):



or an oxalate thereof according to formula (iii''):



[0009c] In one aspect, there is provided a compound of formula (iv'):



[0009d] In one aspect, there is provided a crystalline compound of formula iv' (Form I) as described herein characterized by an X-ray powder diffractogram comprising the following peaks: 7.1, 8.2, 10.8 $2\theta \pm 0.2^\circ 2\theta$, as determined on a diffractometer using Cu-K α radiation at a wavelength of 1.54060 Å.

[0009e] In one aspect, there is provided a crystalline compound of formula iv' (Form II) as described herein characterized by an X-ray powder diffractogram comprising the following peaks: 7.4, 9.4, and 11.6 $2\theta \pm 0.2^\circ 2\theta$ as determined on a diffractometer at 25 °C using Cu-K α radiation at 1.54060 Å.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIGURE 1 is an X-ray powder diffractogram of Form I, a crystalline polymorph of compound 30 as described hereinbelow.

[0011] FIGURE 2 is an X-ray powder diffractogram of Form II, a crystalline polymorph of compound 30 as described hereinbelow.

DETAILED DESCRIPTION

[0012] Definitions

[0013] As used in the present specification, the following words and phrases are generally intended to have the meanings as set forth below, except to the extent that the context in which they are used indicates otherwise.

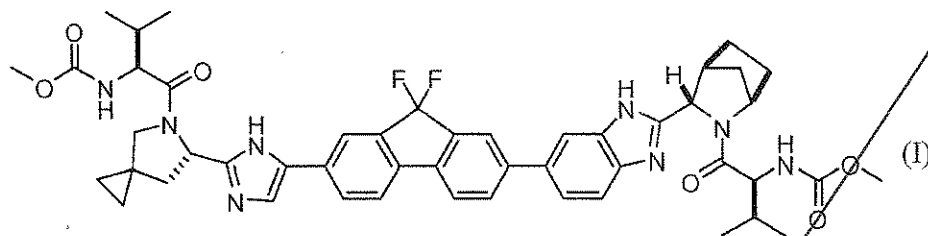
[0014] The term “alkyl” as used herein refers to a straight or branched chain, saturated hydrocarbon having the indicated number of carbon atoms. For example, (C₁-C₈)alkyl is meant to include, but is not limited to methyl, ethyl, propyl, isopropyl, butyl, *sec*-butyl, *tert*-butyl, pentyl, isopentyl, neopentyl, hexyl, isohexyl, and neohehexyl. An alkyl group can be unsubstituted or optionally substituted with one or more substituents as described herein throughout.

[0015] The term “substituted alkyl” refers to:

1) an alkyl group as defined above, having 1, 2, 3, 4 or 5 substituents, (in some embodiments, 1, 2 or 3 substituents) selected from the group consisting of alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, cycloalkoxy, cycloalkenyloxy, acyl, acylamino, acyloxy, amino, substituted amino, aminocarbonyl, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, keto, thiocarbonyl, carboxy, carboxyalkyl, arylthio, heteroarylthio, heterocyclylthio,

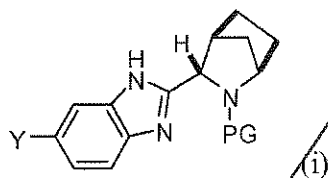
WE CLAIM:

1. A process for making a compound of formula I:

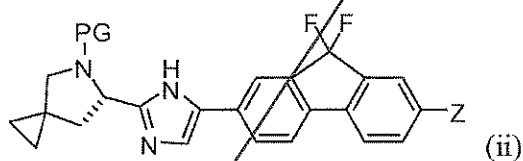


or a pharmaceutically acceptable salt thereof, comprising

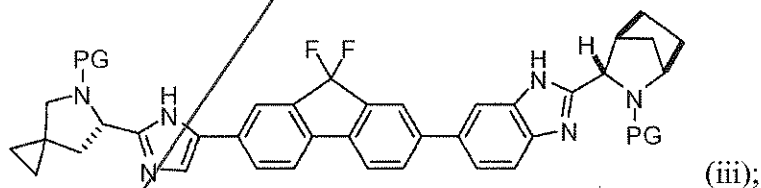
- (A) coupling a compound of formula (i)



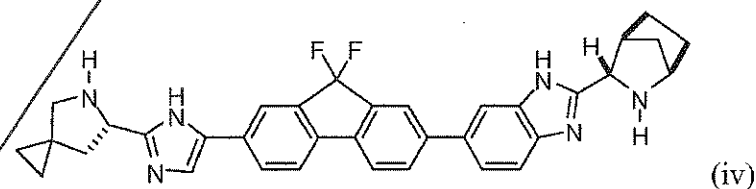
with a compound of formula (ii)



in the presence of a metal catalyst and base to yield a compound of formula (iii) or a salt thereof:

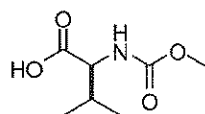


- (B) deprotecting a compound of formula (iii) to yield a compound of formula (iv):



or a salt thereof;

- (C) contacting the compound of formula (iv) with (*S*)-2-(methoxycarbonylamino)-3-methylbutanoic acid:



to yield a compound of formula I; wherein

each PG independently is an amine protecting group;

Y and Z are independently selected from Br and $-B(OR)(OR')$ wherein when

Y is $-B(OR)(OR')$, then Z is Br and

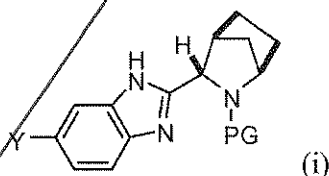
Y is Br, then Z is $-B(OR)(OR')$; and

R and R' are independently selected from the group consisting of hydrogen and straight or branched C_{1-8} -alkyl,

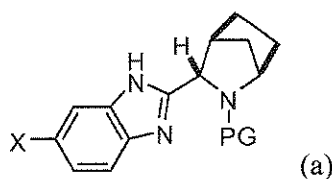
or R and R' together represent a straight or branched C_{1-8} -alkylene, C_{3-8} -cycloalkylene, or C_{6-12} -arylene,

wherein any alkyl, alkylene, cycloalkylene, or arylene is optionally substituted with one or more substituents selected from the group consisting of C_{1-6} -alkyl, $-C(O)N(C_{1-6}\text{-alkyl})_2$, and $-C(O)O(C_{1-6}\text{-alkyl})$.

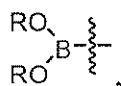
2. The process according to claim 1, wherein Y is $-B(OR)(OR')$ and Z is Br.
3. The process according to claim 2, further comprising the step of *in situ* generation of the compound of formula (i),



comprising sequentially contacting a compound of formula (a)

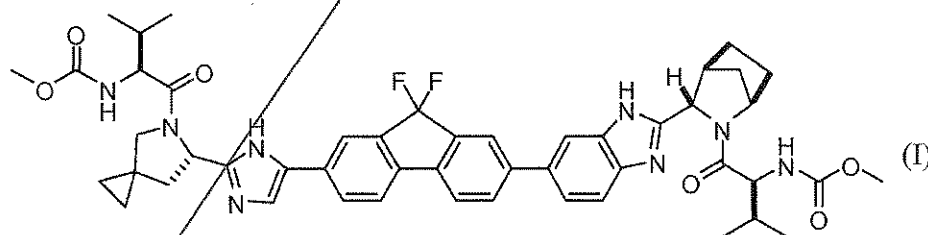


with a source of palladium and then a borylation agent comprising the moiety



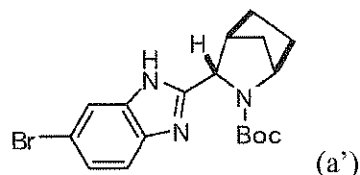
in the presence of a second base, whereby the compound of formula (i) is formed *in situ*, and X is a halide selected from Cl, Br, and I.

4. The process according to claim 3, wherein the step of *in situ* generation of the compound of formula (i) and step (A) are carried out sequentially in one pot.
5. The process according to claim 3, where the borylation agent is selected from bis(pinacolato)diboron and bis(neopentylglycolato)diboron.
6. The process according to claim 5, where the borylation agent is bis(pinacolato)diboron.
7. The process according to claim 5, where the borylation agent is bis(neopentylglycolato)diboron.
8. The process according to claim 4, wherein X is Br and PG is *tert*-butoxycarbonyl.
9. The process according to claim 2, wherein the metal catalyst is a Pd(0) or Pd(II) compound.
10. The process according to claim 9, wherein the metal catalyst is PdCl₂[P(*t*-Bu)₂Ph]₂.
11. The process according to claim 9, wherein the metal catalyst is Pd(OAc)₂-dicyclohexylphosphino-2'-methylbiphenyl.
12. The process according to claim 9, wherein the metal catalyst is dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloromethane adduct.
13. The process according to claim 3, wherein the second base is a propionate salt.
14. The process according to claim 13, wherein the propionate salt is potassium propionate.
15. A process for making a compound of formula I:

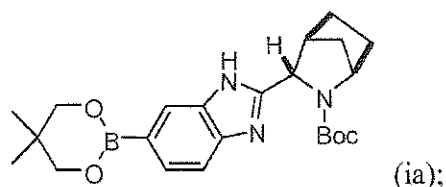


or a pharmaceutically acceptable salt thereof, comprising

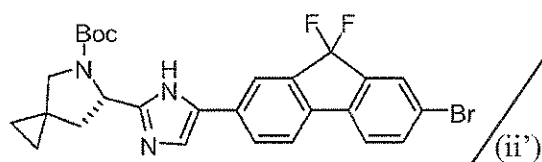
- (1) sequentially contacting a compound of formula (a')



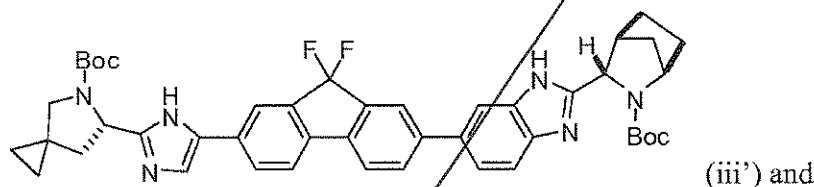
with a catalytically effective amount of $\text{PdCl}_2[\text{P}(t\text{-Bu})_2\text{Ph}]_2$ and bis(neopentylglycolato)diboron in the presence of potassium propionate to yield a reaction mixture comprising a compound of formula (ia):



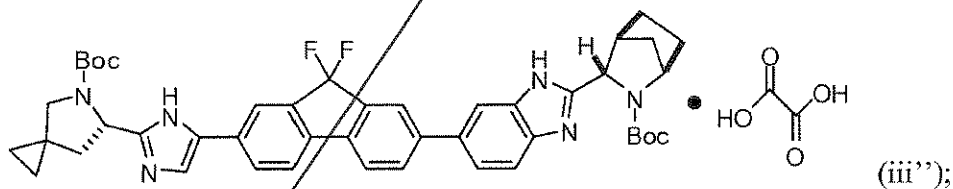
(2) contacting the reaction mixture from step (1) with a compound of formula (ii'):



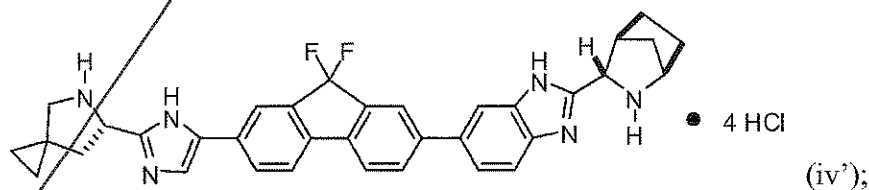
and potassium phosphate to yield a compound of formula (iii'):



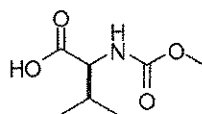
optionally contacting the compound of formula (iii') with oxalic acid to yield an oxalate salt of formula (iii''):



(3) contacting the compound of formula (iii') or formula (iii'') with HCl to yield a compound of formula (iv').



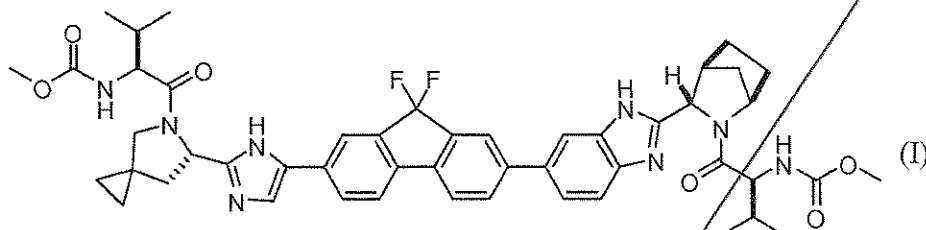
(4) contacting the compound of formula (iv') with (S)-2-(methoxycarbonylamino)-3-methylbutanoic acid:



to yield a compound of formula I;

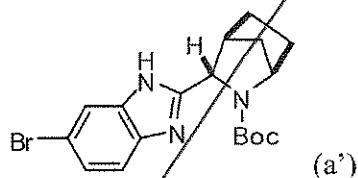
wherein Boc in each instance represents *tert*-butoxycarbonyl.

16. A process for making a compound of formula I:



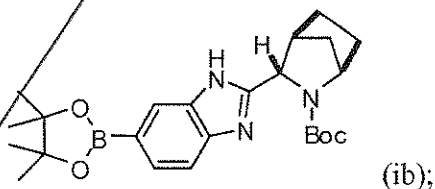
or a pharmaceutically acceptable salt or solvate thereof, comprising

(1) sequentially contacting a compound of formula (a')

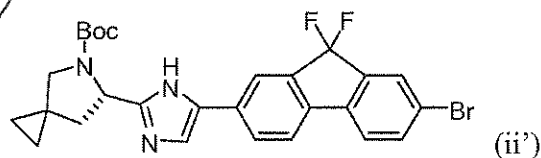


with a catalytically effective amount of $\text{PdCl}_2[\text{P}(t\text{-Bu})_2\text{Ph}]_2$ and

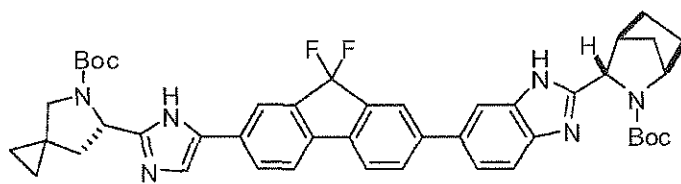
bis(pinacolato)diboron in the presence of potassium propionate to yield a reaction mixture comprising a compound of formula (ib):



(2) contacting the reaction mixture from step (1) with a compound of formula (ii'):

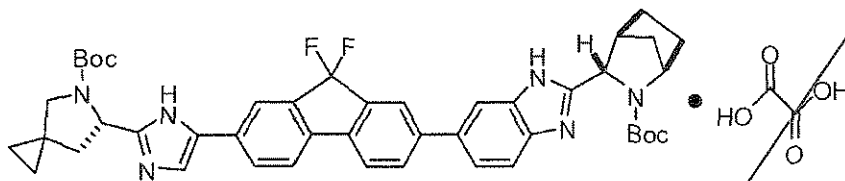


and potassium phosphate to yield a compound of formula (iii'):



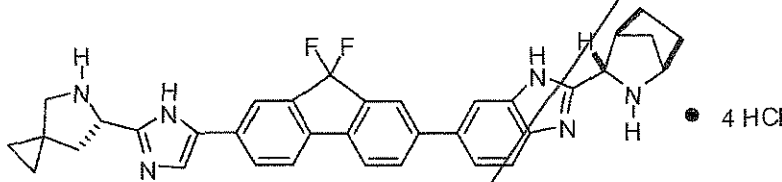
(iii')

optionally contacting the compound of formula (iii') with oxalic acid to yield an oxalate salt of formula (iii''):



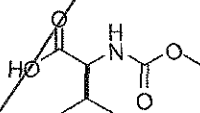
(iii'')

(3) contacting the compound of formula (iii') or formula (iii'') with HCl to yield a compound of formula (iv'):



(iv')

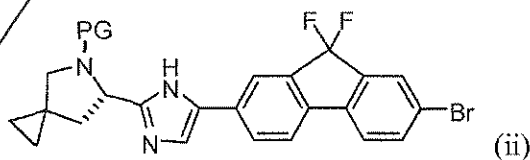
(4) contacting the compound of formula (iv') with (*S*)-2-(methoxycarbonylamino)-3-methylbutanoic acid:



to yield a compound of formula I;

wherein Boc in each instance represents *tert*-butoxycarbonyl.

17. A compound of formula (ii):

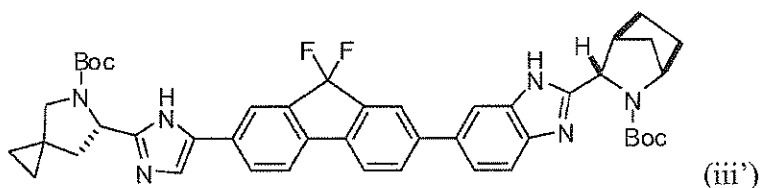


(ii)

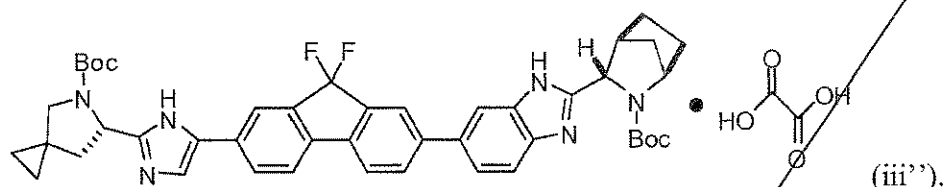
wherein PG is an amine protecting group.

18. The compound according to claim 17, wherein PG is *tert*-butoxycarbonyl.

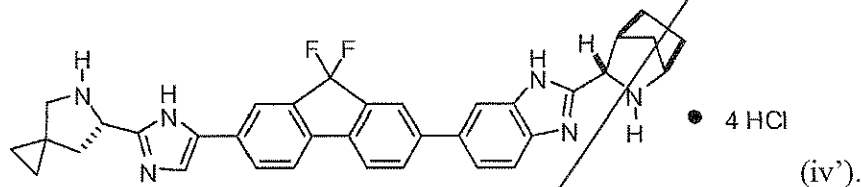
19. A compound of formula (iii'):



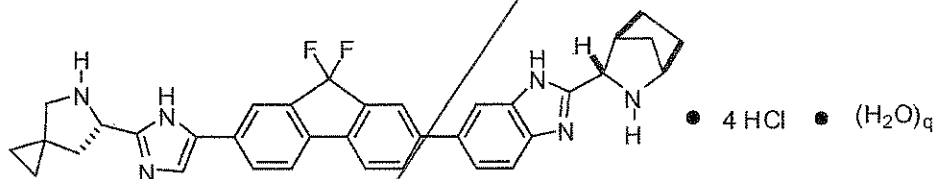
or an oxalate thereof according to formula (iii''):



20. A compound of formula (iv'):



21. The compound according to claim 20, wherein the compound of formula (iv') is a hydrate according to the formula:



wherein q is a number, fractional or otherwise, between 0 and 7.

22. The compound according to claim 21, wherein q is a number between 0 and 6 inclusive.

23. Crystalline compound of formula iv' (Form I) according to claim 20 characterized by an X-ray powder diffractogram comprising the following peaks: 7.1, 8.2, 10.8 $^{\circ}2\theta \pm 0.2^{\circ}2\theta$, as determined on a diffractometer using Cu-K $_{\alpha}$ radiation at a wavelength of 1.54060 Å.

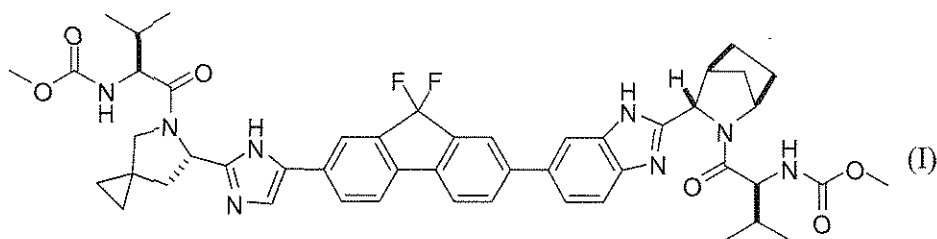
24. Crystalline Form I according to claim 23, wherein the diffractogram further comprises peaks at 11.1, 12.8, 14.1, 14.8, 16.1, 18.9, 24.5, 24.9, and 25.9 $^{\circ}2\theta \pm 0.2^{\circ}2\theta$.

25. Crystalline Form I according to claim 23, wherein the diffractogram is substantially as shown in Figure 1.

26. Crystalline compound of formula iv' (Form II) according to claim 20 characterized by an X-ray powder diffractogram comprising the following peaks: 7.4, 9.4, and 11.6 $2\theta \pm 0.2^\circ 2\theta$ as determined on a diffractometer at 25 °C using Cu-K $_{\alpha}$ radiation at 1.54060 Å.
27. Crystalline Form II according to claim 26, wherein the diffractogram further comprises peaks at 7.5, 14.9, 15.2, 22.5, 23.2, and 26.3 $2\theta \pm 0.2^\circ 2\theta$.
28. Crystalline Form II according to claim 26, wherein the diffractogram is substantially as shown in Figure 2.

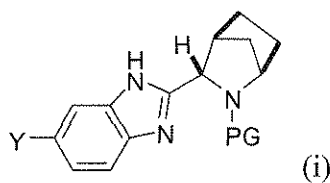
WE CLAIM:

1. A process for making a compound of formula I:

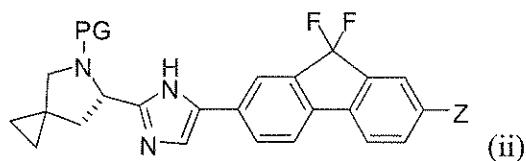


or a pharmaceutically acceptable salt thereof, comprising

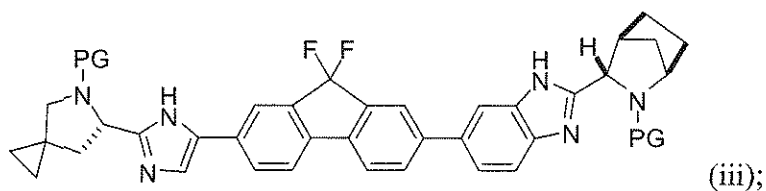
- (A) coupling a compound of formula (i)



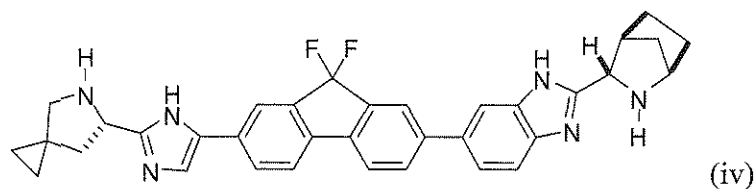
with a compound of formula (ii)



in the presence of a metal catalyst and base to yield a compound of formula (iii) or a salt thereof:

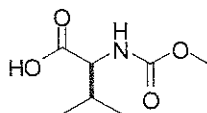


- (B) deprotecting a compound of formula (iii) to yield a compound of formula (iv):



or a salt thereof;

- (C) contacting the compound of formula (iv) with (*S*)-2-(methoxycarbonylamino)-3-methylbutanoic acid:



to yield a compound of formula I; wherein

each PG independently is an amine protecting group;

Y and Z are independently selected from Br and $-B(OR)(OR')$ wherein when

Y is $-B(OR)(OR')$, then Z is Br and

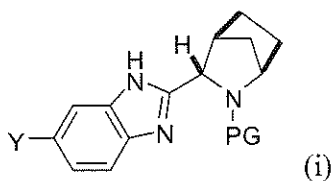
Y is Br, then Z is $-B(OR)(OR')$; and

R and R' are independently selected from the group consisting of hydrogen and straight or branched C_{1-8} -alkyl,

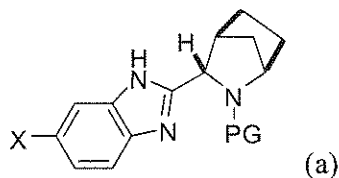
or R and R' together represent a straight or branched C_{1-8} -alkylene, C_{3-8} -cycloalkylene, or C_{6-12} -arylene,

wherein any alkyl, alkylene, cycloalkylene, or arylene is optionally substituted with one or more substituents selected from the group consisting of C_{1-6} -alkyl, $-C(O)N(C_{1-6}\text{-alkyl})_2$, and $-C(O)O(C_{1-6}\text{-alkyl})$.

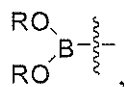
- The process according to claim 1, wherein Y is $-B(OR)(OR')$ and Z is Br.
- The process according to claim 2, further comprising the step of *in situ* generation of the compound of formula (i),



comprising sequentially contacting a compound of formula (a)

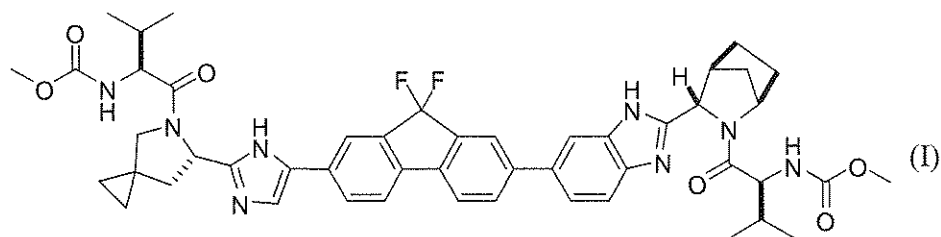


with a source of palladium and then a borylation agent comprising the moiety



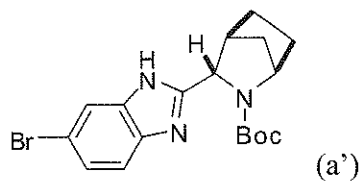
in the presence of a second base, whereby the compound of formula (i) is formed *in situ*, and X is a halide selected from Cl, Br, and I.

4. The process according to claim 3, wherein the step of *in situ* generation of the compound of formula (i) and step (A) are carried out sequentially in one pot.
5. The process according to claim 3, where the borylation agent is selected from bis(pinacolato)diboron and bis(neopentylglycolato)diboron.
6. The process according to claim 5, where the borylation agent is bis(pinacolato)diboron.
7. The process according to claim 5, where the borylation agent is bis(neopentylglycolato)diboron.
8. The process according to claim 4, wherein X is Br and PG is *tert*-butoxycarbonyl.
9. The process according to claim 2, wherein the metal catalyst is a Pd(0) or Pd(II) compound.
10. The process according to claim 9, wherein the metal catalyst is $\text{PdCl}_2[\text{P}(t\text{-Bu})_2\text{Ph}]_2$.
11. The process according to claim 9, wherein the metal catalyst is $\text{Pd}(\text{OAc})_2/2$ -dicyclohexylphosphino-2'-methylbiphenyl.
12. The process according to claim 9, wherein the metal catalyst is dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloromethane adduct.
13. The process according to claim 3, wherein the second base is a propionate salt.
14. The process according to claim 13, wherein the propionate salt is potassium propionate.
15. The process according to claim 1 for making a compound of formula I:

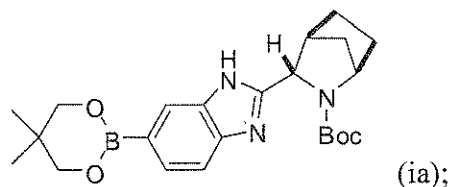


or a pharmaceutically acceptable salt thereof, comprising

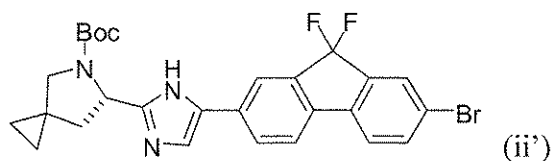
- (1) sequentially contacting a compound of formula (a')



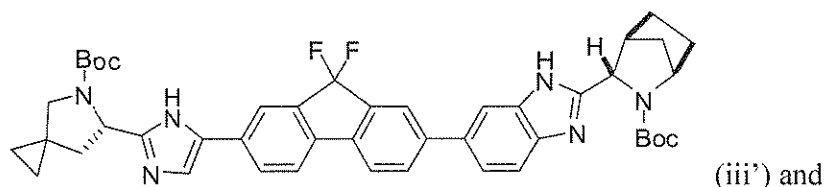
with a catalytically effective amount of $\text{PdCl}_2[\text{P}(t\text{-Bu})_2\text{Ph}]_2$ and bis(neopentylglycolato)diboron in the presence of potassium propionate to yield a reaction mixture comprising a compound of formula (ia):



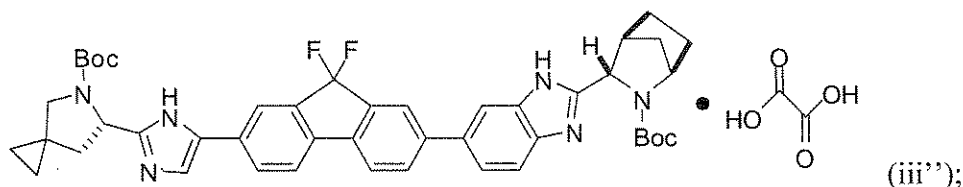
(2) contacting the reaction mixture from step (1) with a compound of formula (ii'):



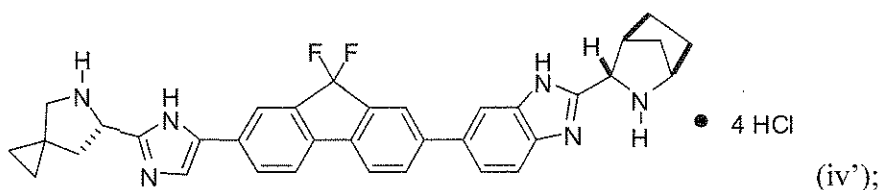
and potassium phosphate to yield a compound of formula (iii'):



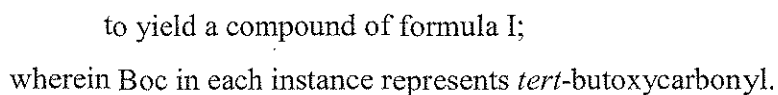
optionally contacting the compound of formula (iii') with oxalic acid to yield an oxalate salt of formula (iii''):



(3) contacting the compound of formula (iii') or formula (iii'') with HCl to yield a compound of formula (iv'):



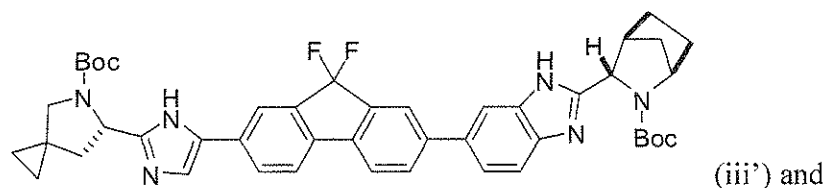
(4) contacting the compound of formula (iv') with (*S*)-2-(methoxycarbonylamino)-3-methylbutanoic acid:

CCOC(=O)NC(C)C(=O)N1C[C@H](C2CC2)C[C@H]1C3=NC=CC=C3C4=CC=C5C(=C4)C(F)(F)C6=CC=C(C=C5)C7=CC=C8C(=C7)N=C(N8)C9C10C11C20C11C9C(=O)NC(C)C(=O)OC (I)O=C1C(=Nc2cc(Br)ccc2N1)C3C4C(C3)C5C4C(C5)N(C6C7C(C6)C8C7C(C8)C(C9C10C(C8)C(C9)C(C10)C(C11C12C(C9)C(C11)C(C12)C(C13C14C(C11)C(C13)C(C14)C(C15C16C(C13)C(C15)C(C16)C(C17C18C(C15)C(C17)C(C18)C(C19C20C(C17)C(C19)C(C20)C(C21C22C(C19)C(C21)C(C22)C(C23C24C(C21)C(C23)C(C24)C(C25C26C(C23)C(C25)C(C26)C(C27C28C(C25)C(C27)C(C28)C(C29C30C(C27)C(C29)C(C30)C(C31C32C(C29)C(C31)C(C32)C(C33C34C(C31)C(C33)C(C34)C(C35C36C(C33)C(C35)C(C36)C(C37C38C(C35)C(C37)C(C38)C(C39C40C(C37)C(C39)C(C40)C(C41C42C(C39)C(C41)C(C42)C(C43C44C(C41)C(C43)C(C44)C(C45C46C(C43)C(C45)C(C46)C(C47C48C(C45)C(C47)C(C48)C(C49C50C(C47)C(C49)C(C50)C(C51C52C(C49)C(C51)C(C52)C(C53C54C(C51)C(C53)C(C54)C(C55C56C(C53)C(C55)C(C56)C(C57C58C(C55)C(C57)C(C58)C(C59C60C(C57)C(C59)C(C60)C(C61C62C(C59)C(C61)C(C62)C(C63C64C(C61)C(C63)C(C64)C(C65C66C(C63)C(C65)C(C66)C(C67C68C(C65)C(C67)C(C68)C(C69C70C(C67)C(C69)C(C70)C(C71C72C(C69)C(C71)C(C72)C(C73C74C(C71)C(C73)C(C74)C(C75C76C(C73)C(C75)C(C76)C(C77C78C(C75)C(C77)C(C78)C(C79C80C(C77)C(C79)C(C80)C(C81C82C(C79)C(C81)C(C82)C(C83C84C(C81)C(C83)C(C84)C(C85C86C(C83)C(C85)C(C86)C(C87C88C(C85)C(C87)C(C88)C(C89C90C(C87)C(C89)C(C90)C(C91C92C(C89)C(C91)C(C92)C(C93C94C(C91)C(C93)C(C94)C(C95C96C(C93)C(C95)C(C96)C(C97C98C(C95)C(C97)C(C98)C(C99C100C(C97)C(C99)C(C100)C(C101C102C(C99)C(C101)C(C102)C(C103C104C(C101)C(C103)C(C104)C(C105C106C(C103)C(C105)C(C106)C(C107C108C(C105)C(C107)C(C108)C(C109C110C(C107)C(C109)C(C110)C(C111C112C(C109)C(C111)C(C112)C(C113C114C(C111)C(C113)C(C114)C(C115C116C(C113)C(C115)C(C116)C(C117C118C(C115)C(C117)C(C118)C(C119C120C(C117)C(C119)C(C120)C(C121C122C(C119)C(C121)C(C122)C(C123C124C(C121)C(C123)C(C124)C(C125C126C(C123)C(C125)C(C126)C(C127C128C(C125)C(C127)C(C128)C(C129C130C(C127)C(C129)C(C130)C(C131C132C(C129)C(C131)C(C132)C(C133C134C(C131)C(C133)C(C134)C(C135C136C(C133)C(C135)C(C136)C(C137C138C(C135)C(C137)C(C138)C(C139C140C(C137)C(C139)C(C140)C(C141C142C(C139)C(C141)C(C142)C(C143C144C(C141)C(C143)C(C144)C(C145C146C(C143)C(C145)C(C146)C(C147C148C(C145)C(C147)C(C148)C(C149C150C(C147)C(C149)C(C150)C(C151C152C(C149)C(C151)C(C152)C(C153C154C(C151)C(C153)C(C154)C(C155C156C(C153)C(C155)C(C156)C(C157C158C(C155)C(C157)C(C158)C(C159C160C(C157)C(C159)C(C160)C(C161C162C(C159)C(C161)C(C162)C(C163C164C(C161)C(C163)C(C164)C(C165C166C(C163)C(C165)C(C166)C(C167C168C(C165)C(C167)C(C168)C(C169C170C(C167)C(C169)C(C170)C(C171C172C(C169)C(C171)C(C172)C(C173C174C(C171)C(C173)C(C174)C(C175C176C(C173)C(C175)C(C176)C(C177C178C(C175)C(C177)C(C178)C(C179C180C(C177)C(C179)C(C180)C(C181C182C(C179)C(C181)C(C182)C(C183C184C(C181)C(C183)C(C184)C(C185C186C(C183)C(C185)C(C186)C(C187C188C(C185)C(C187)C(C188)C(C189C190C(C187)C(C189)C(C190)C(C191C192C(C189)C(C191)C(C192)C(C193C194C(C191)C(C193)C(C194)C(C195C196C(C193)C(C195)C(C196)C(C197C198C(C195)C(C197)C(C198)C(C199C200C(C197)C(C199)C(C200)C(C201C202C(C199)C(C201)C(C202)C(C203C204C(C201)C(C203)C(C204)C(C205C206C(C203)C(C205)C(C206)C(C207C208C(C205)C(C207)C(C208)C(C209C210C(C207)C(C209)C(C210)C(C211C212C(C209)C(C211)C(C212)C(C213C214C(C211)C(C213)C(C214)C(C215C216C(C213)C(C215)C(C216)C(C217C218C(C215)C(C217)C(C218)C(C219C220C(C217)C(C219)C(C220)C(C221C222C(C219)C(C221)C(C222)C(C223C224C(C221)C(C223)C(C224)C(C225C226C(C223)C(C225)C(C226)C(C227C228C(C225)C(C227)C(C228)C(C229C230C(C227)C(C229)C(C230)C(C231C232C(C229)C(C231)C(C232)C(C233C234C(C231)C(C233)C(C234)C(C235C236C(C233)C(C235)C(C236)C(C237C238C(C235)C(C237)C(C238)C(C239C240C(C237)C(C239)C(C240)C(C241C242C(C239)C(C241)C(C242)C(C243C244C(C241)C(C243)C(C244)C(C245C246C(C243)C(C245)C(C246)C(C247C248C(C245)C(C247)C(C248)C(C249C250C(C247)C(C249)C(C250)C(C251C252C(C249)C(C251)C(C252)C(C253C254C(C251)C(C253)C(C254)C(C255C256C(C253)C(C255)C(C256)C(C257C258C(C255)C(C257)C(C258)C(C259C260C(C257)C(C259)C(C260)C(C261C262C(C259)C(C261)C(C262)C(C263C264C(C261)C(C263)C(C264)C(C265C266C(C263)C(C265)C(C266)C(C267C268C(C265)C(C267)C(C268)C(C269C270C(C267)C(C269)C(C270)C(C271C272C(C269)C(C271)C(C272)C(C273C274C(C271)C(C273)C(C274)C(C275C276C(C273)C(C275)C(C276)C(C277C278C(C275)C(C277)C(C278)C(C279C280C(C277)C(C279)C(C280)C(C281C282C(C279)C(C281)C(C282)C(C283C284C(C281)C(C283)C(C284)C(C285C286C(C283)C(C285)C(C286)C(C287C288C(C285)C(C287)C(C288)C(C289C290C(C287)C(C289)C(C290)C(C291C292C(C289)C(C291)C(C292)C(C293C294C(C291)C(C293)C(C294)C(C295C296C(C293)C(C295)C(C296)C(C297C298C(C295)C(C297)C(C298)C(C299C300C(C297)C(C299)C(C300)C(C301C302C(C299)C(C301)C(C302)C(C303C304C(C301)C(C303)C(C304)C(C305C306C(C303)C(C305)C(C306)C(C307C308C(C305)C(C307)C(C308)C(C309C310C(C307)C(C309)C(C310)C(C311C312C(C309)C(C311)C(C312)C(C313C314C(C311)C(C313)C(C314)C(C315C316C(C313)C(C315)C(C316)C(C317C318C(C315)C(C317)C(C318)C(C319C320C(C317)C(C319)C(C320)C(C321C322C(C319)C(C321)C(C322)C(C323C324C(C321)C(C323)C(C324)C(C325C326C

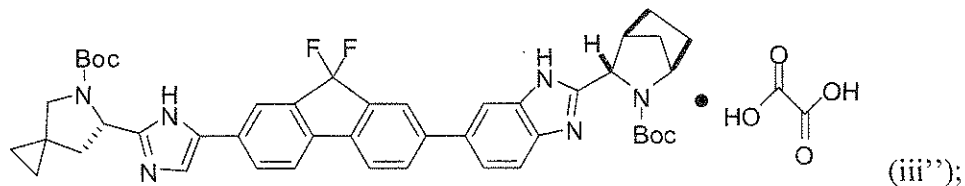
(ib);

C1CC2(C1)CCN(C2)C[C@H]3C=NC=C(C3)c4ccc5c(c4)c6cc(Br)ccc6C(F)(F)c5 (ii')

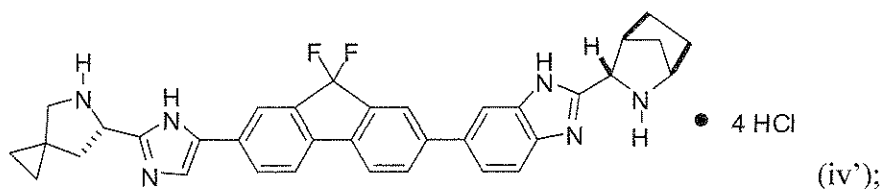
62



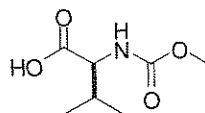
optionally contacting the compound of formula (iii') with oxalic acid to yield an oxalate salt of formula (iii'');



(3) contacting the compound of formula (iii') or formula (iii'') with HCl to yield a compound of formula (iv'):



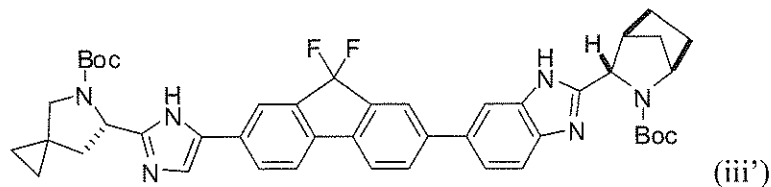
(4) contacting the compound of formula (iv') with (*S*)-2-(methoxycarbonylamino)-3-methylbutanoic acid:



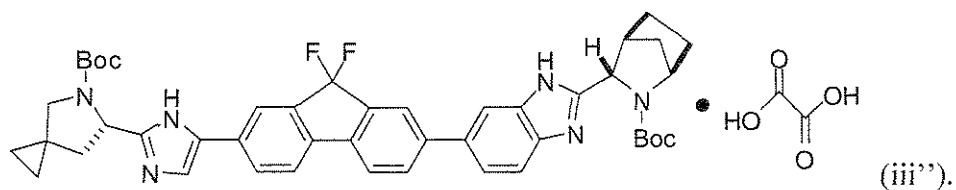
to yield a compound of formula I;

wherein Boc in each instance represents *tert*-butoxycarbonyl.

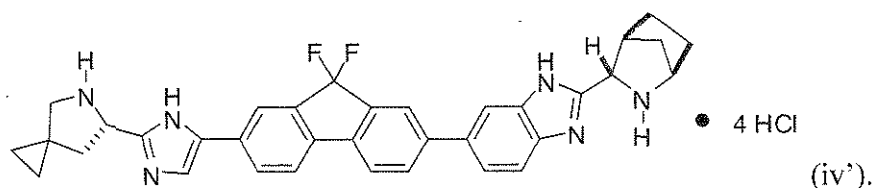
17. A compound of formula (iii'):



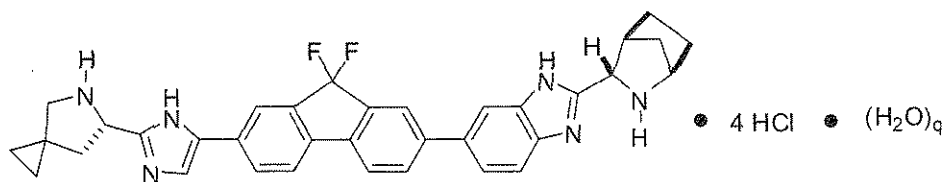
or an oxalate thereof according to formula (iii'');



18. A compound of formula (iv'):



19. The compound according to claim 18, wherein the compound of formula (iv') is a hydrate according to the formula:



wherein q is a number, fractional or otherwise, between 0 and 7.

20. The compound according to claim 19, wherein q is a number between 0 and 6 inclusive.

21. Crystalline compound of formula iv' (Form I) according to claim 18 characterized by an X-ray powder diffractogram comprising the following peaks: 7.1, 8.2, 10.8 $^{\circ}2\theta \pm 0.2^{\circ}2\theta$, as determined on a diffractometer using Cu-K $_{\alpha}$ radiation at a wavelength of 1.54060 Å.

22. Crystalline Form I according to claim 21, wherein the diffractogram further comprises peaks at 11.1, 12.8, 14.1, 14.8, 16.1, 18.9, 24.5, 24.9, and 25.9 $^{\circ}2\theta \pm 0.2^{\circ}2\theta$.

23. Crystalline Form I according to claim 21, wherein the diffractogram is substantially as shown in Figure 1.

24. Crystalline compound of formula iv' (Form II) according to claim 18 characterized by an X-ray powder diffractogram comprising the following peaks: 7.4, 9.4, and 11.6 $2\theta \pm 0.2^{\circ}2\theta$ as determined on a diffractometer at 25 °C using Cu-K $_{\alpha}$ radiation at 1.54060 Å.

25. Crystalline Form II according to claim 24, wherein the diffractogram further comprises peaks at 7.5, 14.9, 15.2, 22.5, 23.2, and 26.3 $^{\circ}2\theta \pm 0.2^{\circ}2\theta$.

26. Crystalline Form II according to claim 24, wherein the diffractogram is substantially as shown in Figure 2.