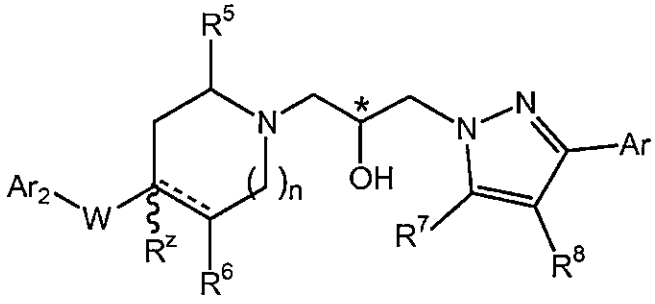
We claim:

1. A process for the preparation of a compound of formula (I)



(I)

wherein

Ar_2 is a monocyclic or bicyclic ring system, unsaturated, saturated or aromatic, optionally fused, optionally including between 1 and 5 heteroatom ring moieties independently selected from the group consisting of O, S, N, SO_2 and C=O; wherein said Ar_2 ring system is optionally substituted with between 1 and 4 substituents;

W represents O, S, NR^{27}, C=O, (C=O)NH, NH(C=O),CHR^{28}, or a covalent bond;

R^{27} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, naphthyl, benzyl, phenethyl, C_{1-5}heterocyclyl, C_{2-8}acyl, aroyl, $R^{29}OC=O$, $R^{30}R^{31}NC=O$, $R^{29}SO$, $R^{29}S$, $R^{29}SO_2$ or $R^{30}R^{31}NSO_2$; or alternatively, R^{27} and part of Ar_2 can be taken together to form an optionally substituted 5- to 6-membered heterocyclic ring with optionally 1 to 3 additional heteroatom moieties in the ring selected from O, NR^9, NR^{10}, N, SO_2, C=O and S; which ring may be saturated, unsaturated or aromatic; wherein R^9 and R^{10} are independently selected from the group consisting of H, C_{1-3}alkyl, and $–CH_2CO_2(C_{1-4}alkyl)$;

R^{28} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, hydroxy, phenyl, benzyl, C_{1-5}heterocyclyl, $R^{29}O$, $R^{30}R^{31}NC=O$, $R^{29}S$, $R^{29}SO$, $R^{29}SO_2$ or $R^{30}R^{31}NSO_2$;

R^{29} is C_{1-5}alkyl, C_{3-5}akenyl, phenyl, benzyl or C_{1-5}heterocyclyl;

R^{30} and R^{31} are each independently selected from the group consisting of hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl, phenethyl, naphthyl, and C_{1-5}heteroaryl; alternatively R^{30} and R^{31} can be taken together to form an optionally substituted 4- to 7-membered ring carbocyclic or heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

R^z is H or OH and the dashed line is absent; or R^z is absent where the dashed line is an sp^2 bond;

R^5 and R^6 are each independently selected from the group consisting of hydrogen and C_{1-5}alkyl;

n is an integer selected from 0, 1 or 2;

R^7 and R^8 are each independently hydrogen, C_{1-5}alkyl, C_{2-5}alkenyl, C_{1-5}alkoxy, C_{1-5}alkylthio, halogen, or a 4-7 membered carbocyclyl or heterocyclyl;

alternatively, R^7 and R^8 can be taken together to form an optionally substituted 5- to 7-membered carbocyclyc or heterocyclic ring, which ring may be unsaturated or aromatic, and may be optionally substituted with between one and three substituents independently selected from the group consisting of halo, cyano, amino, hydroxy, nitro, R^4, R^4O-, R^4S-, $R^4O(C_{1-5}alkylene)$-, $R^4O(C=O)$-, $R^4(C=O)$-, $R^4(C=S)$-, $R^4(C=O)O$-, $R^4O(C=O)(C=O)$-, R^4SO_2, $NHR^{44}(C=NH)$-, $NHR^{44}SO_2$-, an $NHR^{44}(C=O)$-;

R^4 is H, C_{1-5}alkyl, C_{2-5}alkenyl, C_{1-5}heterocyclyl, (C_{1-5}heterocyclyl)C_{1-6}alkylene, phenyl, benzyl, phenethyl, NH_2, mono- or di(C_{1-6}alkyl)N-, (C_{1-6}alkoxy)carbonyl- or $R^{42}OR^{43}$-; wherein R^{42} is H, C_{1-5}alkyl, C_{2-5}alkenyl, phenyl, benzyl, phenethyl, C_{1-5}heterocyclyl, or (C_{1-5}heterocyclyl)C_{1-6}alkylene- and R^{43} is C_{1-5}alkylene, phenylene, or divalent C_{1-5}heterocyclyl;

R^{44} is H, C_{1-5}alkyl, C_{2-5}alkenyl, C_{1-5}heterocyclyl, (C_{1-5}heterocyclyl)C_{1-6}alkylene, phenyl, benzyl, phenethyl, NH_2, mono- or di(C_{1-6}alkyl)N-, (C_{1-6}alkoxy)carbonyl- or $R^{42}OR^{43}$-; wherein R^{42} is H, C_{1-5}alkyl, C_{2-5}alkenyl, phenyl, benzyl, phenethyl, C_{1-5}heterocyclyl, or (C_{1-5}heterocyclyl)C_{1-6}alkylene- and R^{43} is C_{1-5}alkylene, phenylene, or divalent C_{1-5}heterocyclyl;

Ar represents a monocyclic or bicyclic aryl or heteroaryl ring, optionally substituted with between 1 and 3 substituents independently selected from the group consisting of halogen, C_{1-5}alkoxy, C_{1-5}alkyl, C_{2-5}alkenyl, cyano, azido, nitro, $R^{22}R^{23}N$, $R^{24}SO_2$, $R^{24}SO$, $R^{24}OC=O$, $R^{22}R^{23}NC=O$, C_{1-5}haloalkyl, C_{1-5}haloalkoxy, C_{1-5}haloalkylthio and C_{1-5}alkylthio;

R^{22} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, phenethyl, benzyl, C_{1-5}heterocyclyl, C_{2-8}acyl, aroyl, $R^{38}OC=O$, $R^{25}R^{26}NC=O$, $R^{38}SO$, $R^{38}SO2$, $R^{38}S$, or $R^{25}R^{26}NSO_2$;

R^{23} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl or C1-5heterocyclyl; alternatively, R^{22} and R^{23} can be taken together to form an optionally substituted 4- to 7-membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

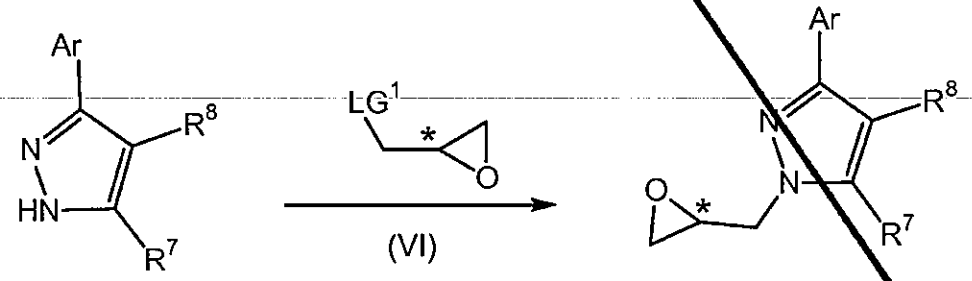
R^{24} is C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl, or C_{1-5}heterocyclyl;

R^{25} and R^{26} independently are hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl or C_{1-5}heterocyclyl; or alternatively, R^{25} and R^{26} can be taken together to form an optionally substituted 4- to 7-membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

R^{38} is H, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl, phenethyl or C_{1-5}heterocyclyl;

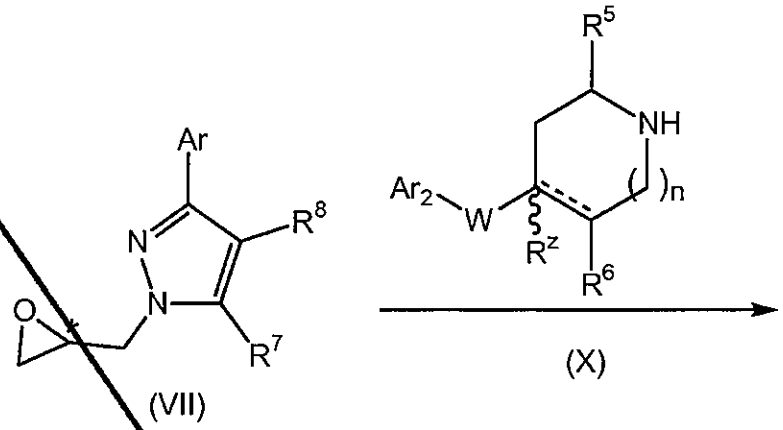
wherein each of the above hydrocarbyl or heterocarbyl groups, unless otherwise indicated, and in addition to any specified substituents, is optionally and independently substituted with between 1 and 3 substituents selected from the group consisting of methyl, halomethyl, hydroxymethyl, halo, hydroxy, amino, nitro, cyano, C_{1-5}alkyl, C_{1-5}alkoxy, -COOH, C_{2-6}acyl, [di(C_{1-4}alkyl)amino]C_{2-5}alkylene, [di(C_{1-4}alkyl)amino]C_{2-5}alkyl-NH-CO-, and C_{1-5}haloalkoxy;

or a pharmaceutically acceptable salt, amide or ester thereof; or a stereoisomeric form thereof; comprising

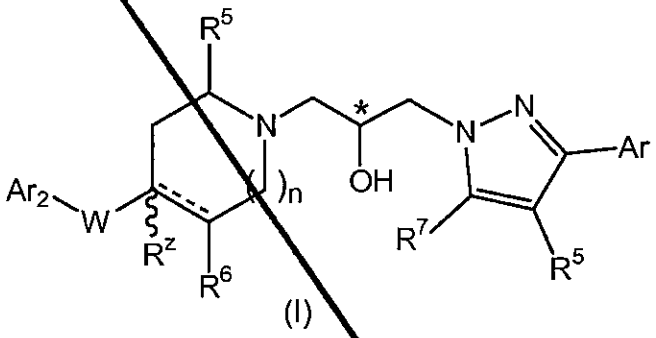


(V) (VII)

reacting a compound of formula (V) with a compound of formula (VI), wherein LG^1 is a leaving group; in the presence of an organic or inorganic base; to yield the corresponding compound of formula (VII);



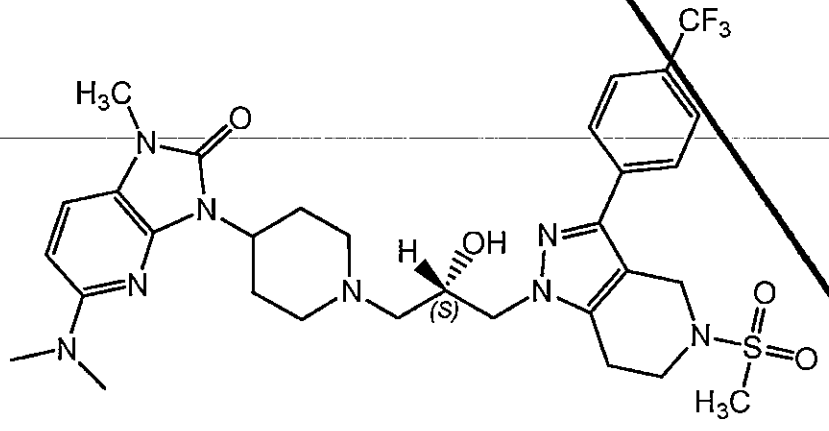
(VII) (X)



(I)

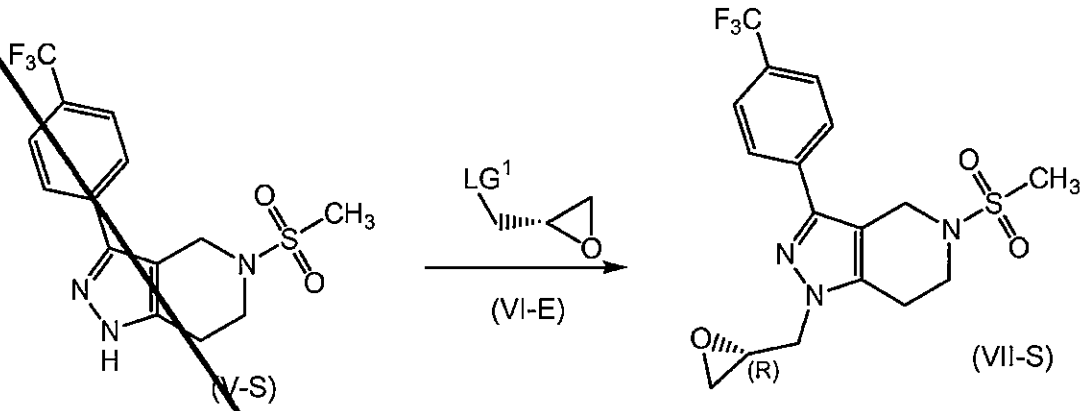
reacting the compound of formula (VII) with a compound of formula (X); in an organic solvent; to yield the corresponding compound of formula (I).

2. A process for the preparation of a compound of formula (I-S)



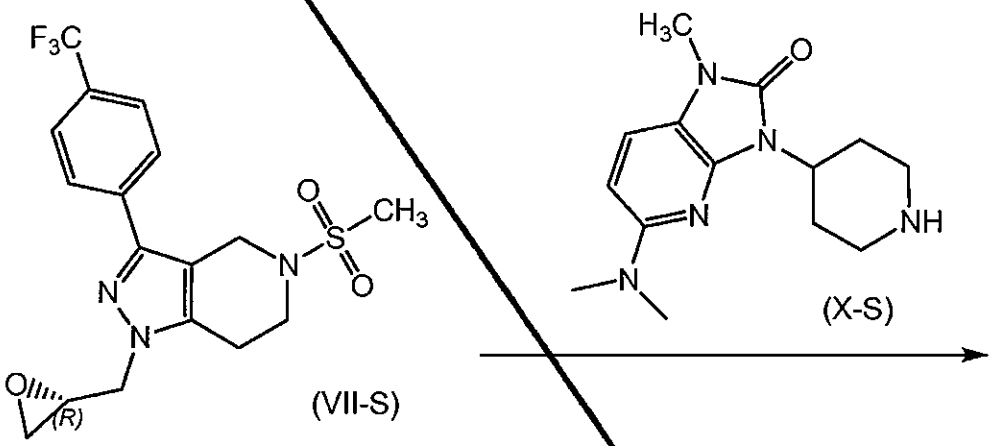
(I-S)

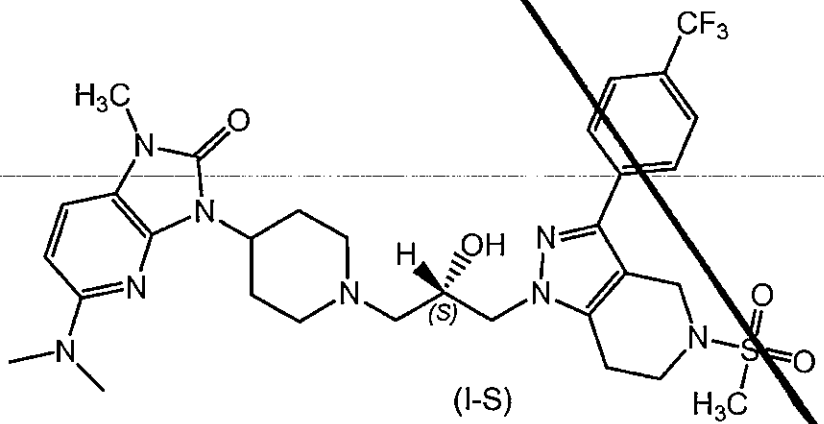
or a pharmaceutically acceptable salt, amide or ester thereof; or a stereoisomeric form thereof; comprising



(V-S) (VII-S)

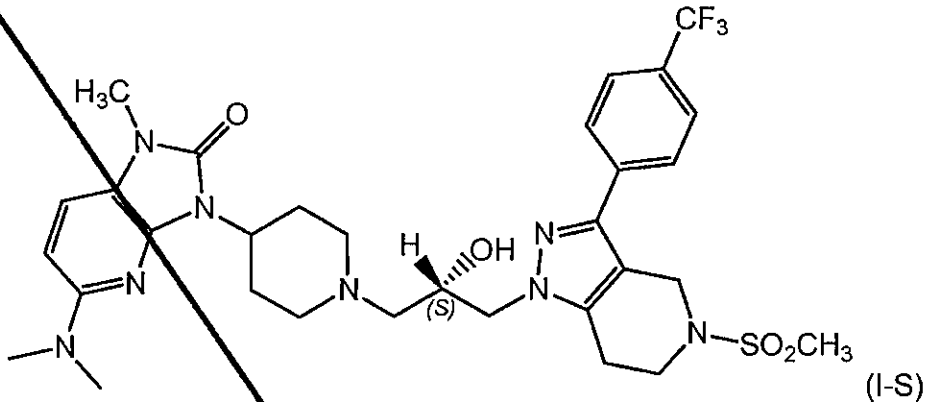
reacting a compound of formula (V-S) with a compound of formula (VI-E), wherein LG^1 is a leaving group; in the presence of an organic or inorganic base; to yield the corresponding compound of formula (VII-S);





reacting the compound of formula (VII-S) with a compound of formula (X-S); in an organic solvent; to yield the corresponding compound of formula (I-S).

3. A crystalline, hexahydrate mono-HCl salt of a compound of formula (I-S)



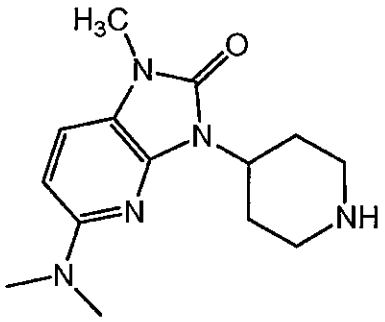
(I-S)

comprising the following X-ray diffraction peaks:

Angle (°2θ)	d-spacing (Å)
4.33	20.42
7.58	11.67
8.39	10.54
8.80	10.04
9.16	9.66
12.71	6.96
13.30	6.66
13.69	6.47
14.69	6.03
15.55	5.70
15.96	5.55
18.44	4.81
18.69	4.75
19.07	4.65

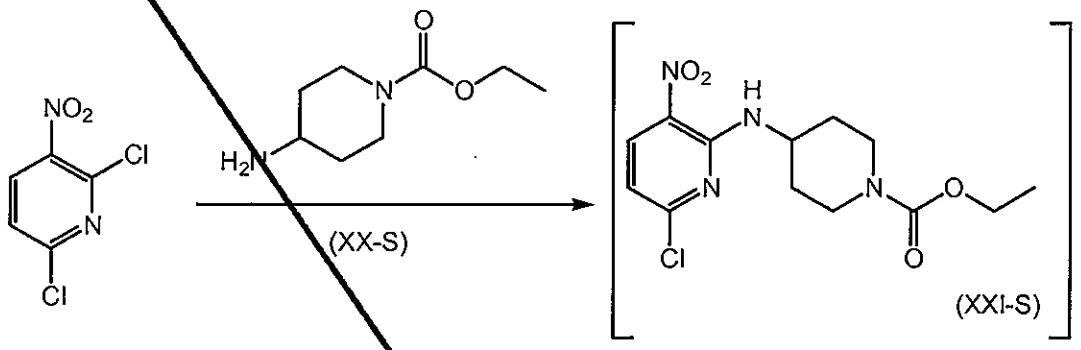
.

4. A process for the preparation of a compound of formula (X-S)

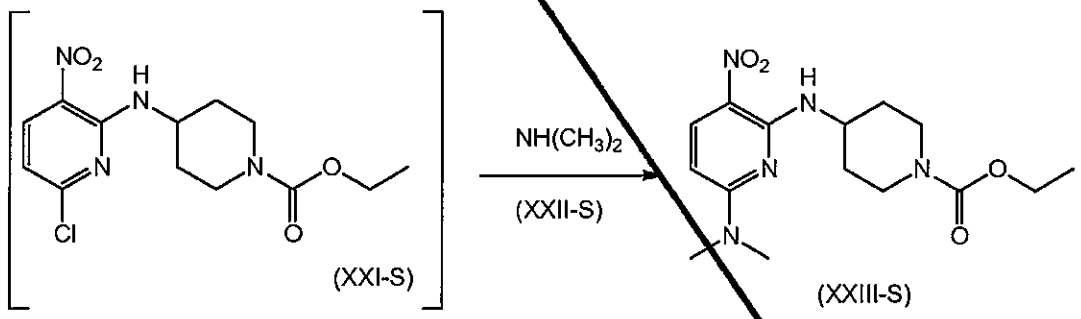


(X-S)

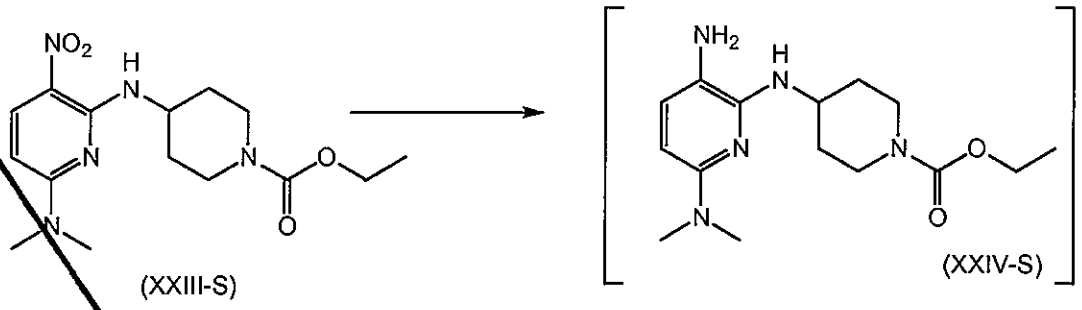
comprising



reacting 2,6-dichloro-3-nitro-pyridine with a compound of formula (XX-S), wherein PG^5 is a nitrogen protecting group; in the presence of an organic or inorganic base; in an organic solvent; to yield the corresponding compound of formula (XXI-S);

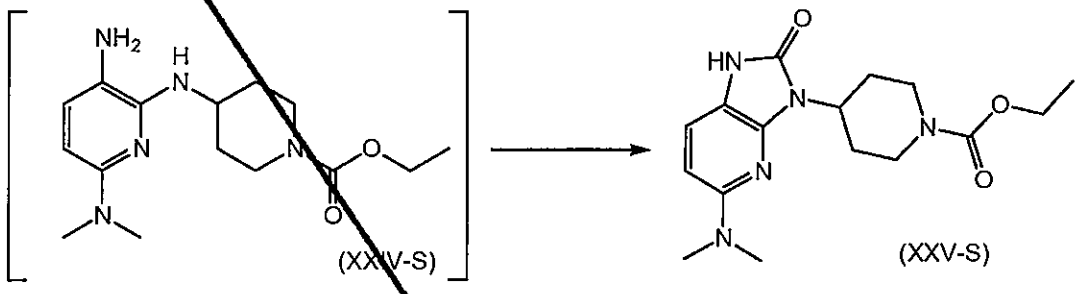


reacting the compound of formula (XXI-S) with a compound of formula (XXII-S); in an organic solvent; to yield the corresponding compound of formula (XXIII-S);



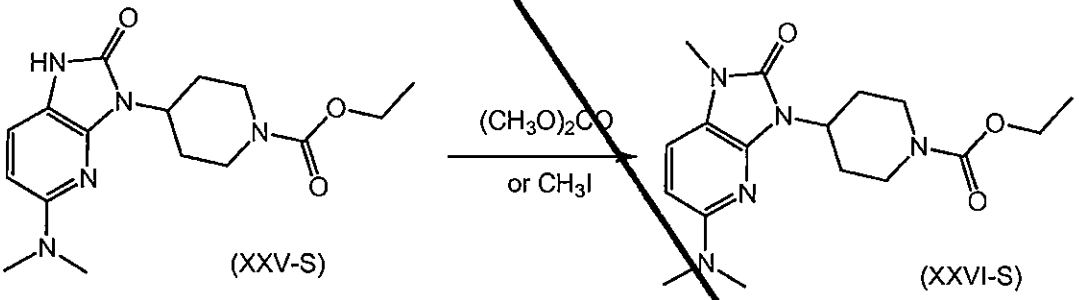
(XXIII-S) (XXIV-S)

reacting the compound of formula (XXIII-S) with a reducing agent; in the presence of a catalyst; in an organic solvent; to yield the corresponding compound of formula (XXIV-S);



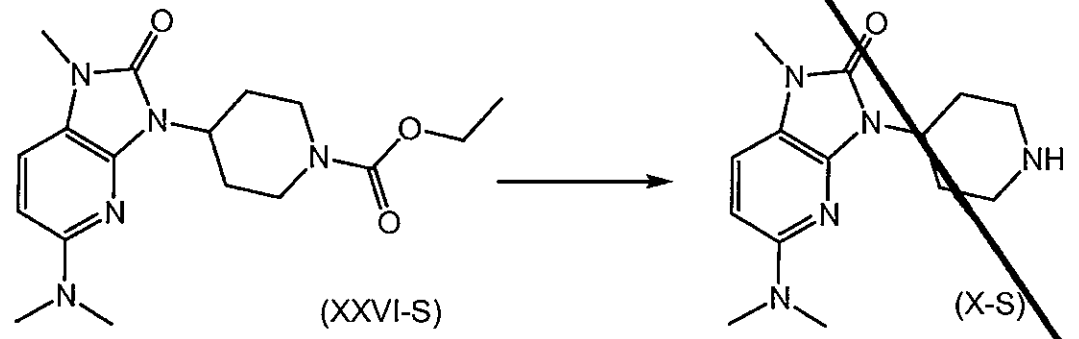
(XXIV-S) (XXV-S)

reacting the compound of formula (XXIV-S) with a reagent selected from the group consisting of CDI, N-methylcarbodiimide, phosgene and triphosgene; in an organic solvent; to yield the corresponding compound of formula (XXV-S);



(XXV-S) (XXVI-S)

reacting the compound of formula (XXV-S) with carbonic acid dimethyl ester or CH_3I; in the presence of an inorganic base; in an organic solvent; to yield the corresponding compound of formula (XXVI-S);

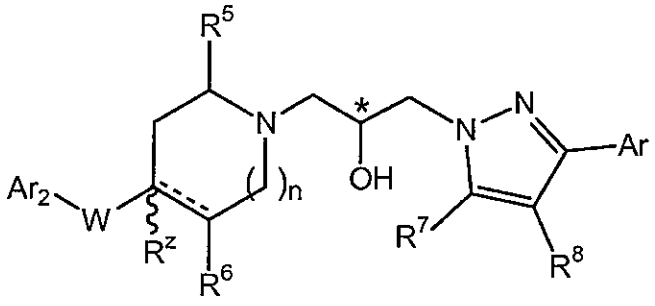


(XXVI-S) (X-S)

de-protecting the compound of formula (XXVI-S); to yield the corresponding compound of formula (X-S).

Claims:

1. A process for the preparation of a compound of formula (I)



(I)

wherein

Ar_2 is a monocyclic or bicyclic ring system, unsaturated, saturated or aromatic, optionally fused, optionally including between 1 and 5 heteroatom ring moieties independently selected from the group consisting of O, S, N, SO_2 and C=O; wherein said Ar_2 ring system is optionally substituted with between 1 and 4 substituents;

W represents O, S, NR^{27}, C=O, (C=O)NH, NH(C=O),CHR^{28}, or a covalent bond;

R^{27} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, naphthyl, benzyl, phenethyl, C_{1-5}heterocyclyl, C_{2-8}acyl, aroyl, $R^{29}OC=O$, $R^{30}R^{31}NC=O$, $R^{29}SO$, $R^{29}S$, $R^{29}SO_2$ or $R^{30}R^{31}NSO_2$; or alternatively, R^{27} and part of Ar_2 can be taken together to form an optionally substituted 5- to 6-membered heterocyclic ring with optionally 1 to 3 additional heteroatom moieties in the ring selected from O, NR^9, NR^{10}, N, SO_2, C=O and S; which ring may be saturated, unsaturated or aromatic; wherein R^9 and R^{10} are independently selected from the group consisting of H, C_{1-3}alkyl, and $-CH_2CO_2(C_{1-4}$alkyl);

R^{28} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, hydroxy, phenyl, benzyl, C_{1-5}heterocyclyl, $R^{29}O$, $R^{30}R^{31}NC=O$, $R^{29}S$, $R^{29}SO$, $R^{29}SO_2$ or $R^{30}R^{31}NSO_2$;

R^{29} is C_{1-5}alkyl, C_{3-5}akenyl, phenyl, benzyl or C_{1-5}heterocyclyl;

R^{30} and R^{31} are each independently selected from the group consisting of hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl, phenethyl, naphthyl, and C_{1-5}heteroaryl; alternatively R^{30} and R^{31} can be taken together to form an optionally substituted 4- to 7-membered ring carbocyclic or heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

R^z is H or OH and the dashed line is absent; or R^z is absent where the dashed line is an sp^2 bond;

R^5 and R^6 are each independently selected from the group consisting of hydrogen and C_{1-5}alkyl;

n is an integer selected from 0, 1 or 2;

R^7 and R^8 are each independently hydrogen, C_{1-5}alkyl, C_{2-5}alkenyl, C_{1-5}alkoxy, C_{1-5}alkylthio, halogen, or a 4-7 membered carbocyclyl or heterocyclyl;

alternatively, R^7 and R^8 can be taken together to form an optionally substituted 5- to 7-membered carbocyclyc or heterocyclic ring, which ring may be unsaturated or aromatic, and may be optionally substituted with between one and three substituents independently selected from the group consisting of halo, cyano, amino, hydroxy, nitro, R^4, R^4O-, R^4S-, $R^4O(C_{1-5}alkylene)$-, $R^4O(C=O)$-, $R^4(C=O)$-, $R^4(C=S)$-, $R^4(C=O)O$-, $R^4O(C=O)(C=O)$-, R^4SO_2, $NHR^{44}(C=NH)$-, $NHR^{44}SO_2$-, an $NHR^{44}(C=O)$-;

R^4 is H, C_{1-5}alkyl, C_{2-5}alkenyl, C_{1-5}heterocyclyl, (C_{1-5}heterocyclyl)C_{1-6}alkylene, phenyl, benzyl, phenethyl, NH_2, mono- or di(C_{1-6}alkyl)N-, (C_{1-6}alkoxy)carbonyl- or $R^{42}OR^{43}$-; wherein R^{42} is H, C_{1-5}alkyl, C_{2-5}alkenyl, phenyl, benzyl, phenethyl, C_{1-5}heterocyclyl, or (C_{1-5}heterocyclyl)C_{1-6}alkylene- and R^{43} is C_{1-5}alkylene, phenylene, or divalent C_{1-5}heterocyclyl;

R^{44} is H, C_{1-5}alkyl, C_{2-5}alkenyl, C_{1-5}heterocyclyl, (C_{1-5}heterocyclyl)C_{1-6}alkylene, phenyl, benzyl, phenethyl, NH_2, mono- or di(C_{1-6}alkyl)N-, (C_{1-6}alkoxy)carbonyl- or $R^{42}OR^{43}$-; wherein R^{42} is H, C_{1-5}alkyl, C_{2-5}alkenyl, phenyl, benzyl, phenethyl, C_{1-5}heterocyclyl, or (C_{1-5}heterocyclyl)C_{1-6}alkylene- and R^{43} is C_{1-5}alkylene, phenylene, or divalent C_{1-5}heterocyclyl;

Ar represents a monocyclic or bicyclic aryl or heteroaryl ring, optionally substituted with between 1 and 3 substituents independently selected from the group consisting of halogen, C_{1-5}alkoxy, C_{1-5}alkyl, C_{2-5}alkenyl, cyano, azido, nitro, $R^{22}R^{23}N$, $R^{24}SO_2$, $R^{24}SO$, $R^{24}OC=O$, $R^{22}R^{23}NC=O$, C_{1-5}haloalkyl, C_{1-5}haloalkoxy, C_{1-5}haloalkylthio and C_{1-5}alkylthio;

R^{22} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, phenethyl, benzyl, C_{1-5}heterocyclyl, C_{2-8}acyl, aroyl, $R^{38}OC=O$, $R^{25}R^{26}NC=O$, $R^{38}SO$, $R^{38}SO2$, $R^{38}S$, or $R^{25}R^{26}NSO_2$;

R^{23} is hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl or C1-5heterocyclyl; alternatively, R^{22} and R^{23} can be taken together to form an optionally substituted 4- to 7-membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

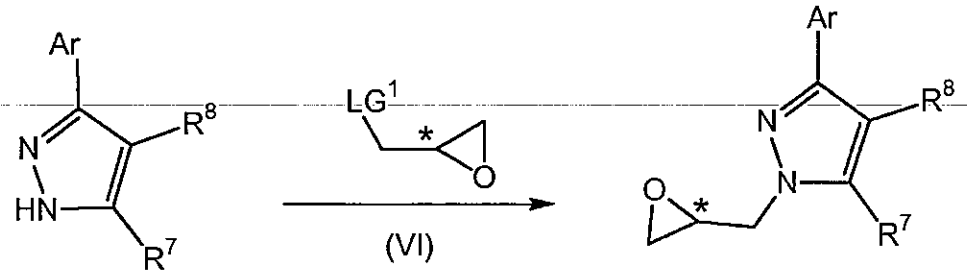
R^{24} is C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl, or C_{1-5}heterocyclyl;

R^{25} and R^{26} independently are hydrogen, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl or C_{1-5}heterocyclyl; or alternatively, R^{25} and R^{26} can be taken together to form an optionally substituted 4- to 7-membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

R^{38} is H, C_{1-5}alkyl, C_{3-5}alkenyl, phenyl, benzyl, phenethyl or C_{1-5}heterocyclyl;

wherein each of the above hydrocarbyl or heterocarbyl groups, unless otherwise indicated, and in addition to any specified substituents, is optionally and independently substituted with between 1 and 3 substituents selected from the group consisting of methyl, halomethyl, hydroxymethyl, halo, hydroxy, amino, nitro, cyano, C_{1-5}alkyl, C_{1-5}alkoxy, -COOH, C_{2-6}acyl, [di(C_{1-4}alkyl)amino]C_{2-5}alkylene, [di(C_{1-4}alkyl)amino]C_{2-5}alkyl-NH-CO-, and C_{1-5}haloalkoxy;

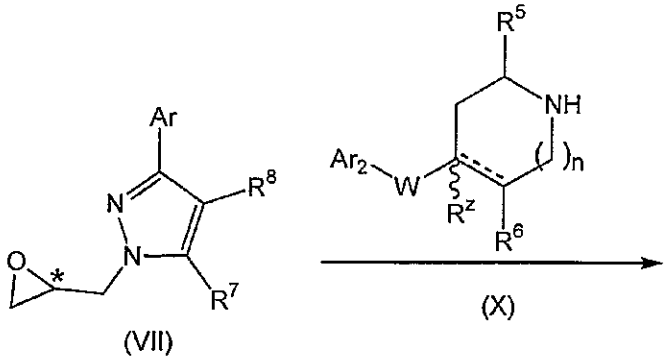
or a pharmaceutically acceptable salt, amide or ester thereof; or a stereoisomeric form thereof; comprising



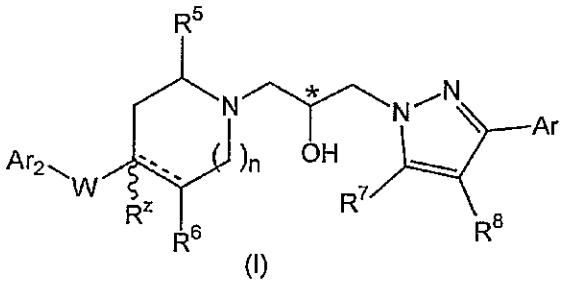
(V) (VII)

reacting a compound of formula (V) with a compound of formula (VI), wherein LG^1 is a leaving group selected from 4-nitrophenyl-sulfonyl, 3-

nitrophenyl-sulfonyl, mesyl, tosyl, trifluoromethane sulfonyl, 3-fluoro-benzensulfonyl, 3-(trifluoromethyl)-benzene sulfonyl, 4-chloro-benzenesulfonyl and 3-chloro-benzenesulfonyl; in the presence of an organic or inorganic base; to yield the corresponding compound of formula (VII);



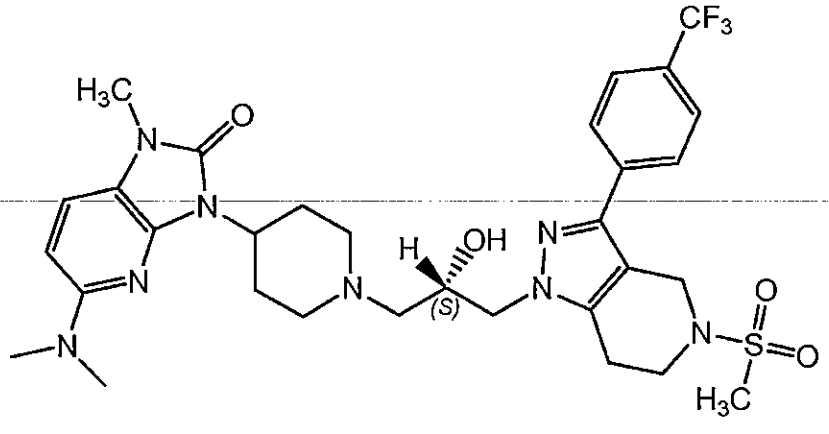
(VII) (X)



(I)

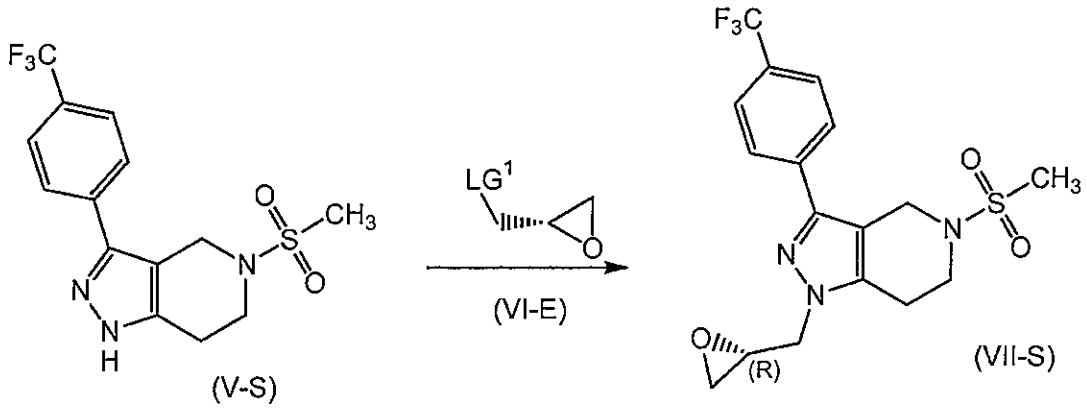
reacting the compound of formula (VII) with a compound of formula (X); in an organic solvent; to yield the corresponding compound of formula (I).

2. A process for the preparation of a compound of formula (I-S)

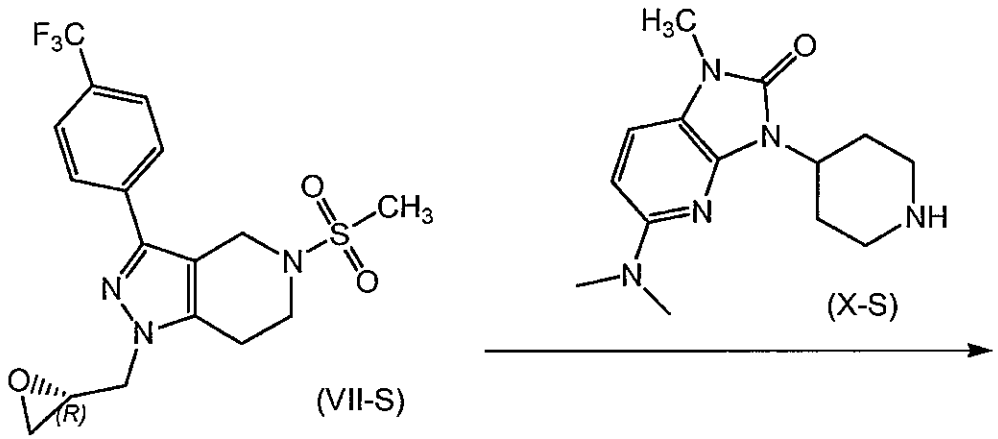


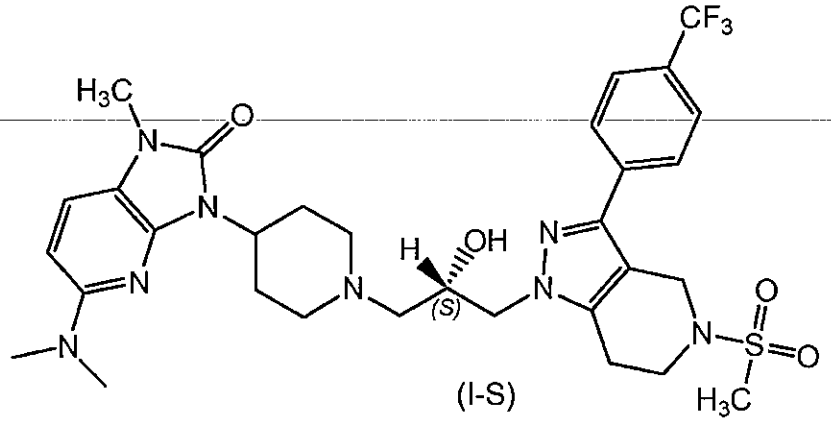
(I-S)

or a pharmaceutically acceptable salt, amide or ester thereof; or a stereoisomeric form thereof; comprising



reacting a compound of formula (V-S) with a compound of formula (VI-E), wherein LG^1 is a leaving group selected from 4-nitrophenyl-sulfonyl, 3-nitrophenyl-sulfonyl, mesyl, tosyl, trifluoromethane sulfonyl, 3-fluoro-benzensulfonyl, 3-(trifluoromethyl)-benzene sulfonyl, 4-chloro-benzenesulfonyl and 3-chloro-benzenesulfonyl; in the presence of an organic or inorganic base; to yield the corresponding compound of formula (VII-S);





reacting the compound of formula (VII-S) with a compound of formula (X-S); in an organic solvent; to yield the corresponding compound of formula (I-S).

3. The process according to claim 2, wherein LG^1 is 3-nitrophenyl-sulfonyl.

4. The process according to claim 2, wherein the compound of formula (VI-E) is present in an amount in the range of from about 0.5 to about 3.0 molar equivalents, or wherein the compound of formula (VI-E) is present in about 1.0 to about 1.5 molar equivalents.

5. The process according to claim 2, wherein the organic or inorganic base is selected from the group consisting of TEA, DIPEA, pyridine, NaH, KOt-Bu, NaOt-Bu, Cs_2CO_3, K_2CO_3, Na_2CO_3 and CsF, or wherein the organic or inorganic base is Cs_2CO_3.

6. The process according to claim 2, wherein when the compound of formula (V-S) is reacted with the compound of formula (VI-E) in an organic solvent, the organic solvent is DMF.

7. The process according to claim 2, wherein the compound of formula (V-S) is reacted with the compound of formula (VI-E) at a temperature in the range of from about 0°C to about 5°C, followed by heating to a temperature in the range of from about room temperature to about 60°C.

8. The process according to claim 2, wherein the compound of formula (X-S) is present in an amount in the range of from about 0.5 to about 3.0 molar equivalents, or wherein the compound of formula (X-S) is present in an amount of about 1.1 molar equivalents.

9. The process according to claim 2, wherein when the compound of formula (VII-S) is reacted with the compound of formula (X-S) in an organic

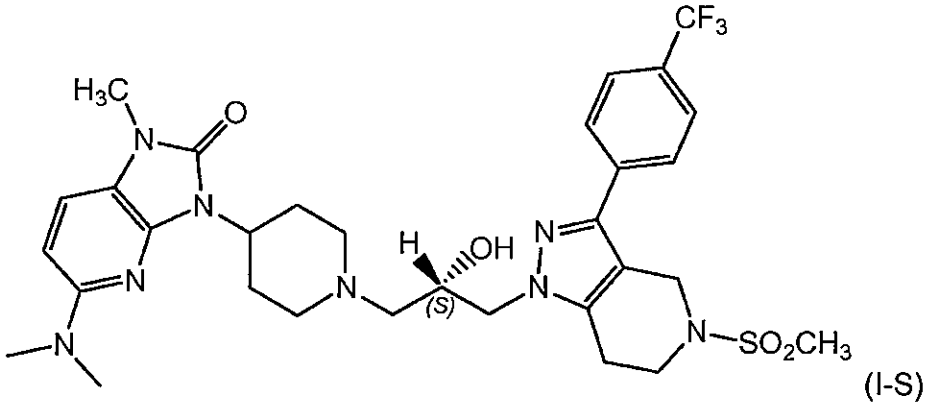
solvent, the organic solvent is selected from the group consisting of DCE, ethanol, isopropyl alcohol and DMF, or wherein the organic solvent is ethanol.

10. The process according to claim 2, wherein the compound of formula (VII-S) is reacted with the compound of formula (X-S) at about solvent reflux temperature,

11. The process according to claim 2, wherein the compound of formula (VII-S) is reacted with the compound of formula (X-S) in the presence of a Lewis acid selected from the group consisting of titanium propoxide, $Yb(OTf)_3$ and $Al(OTf)_3$.

12. The process according to claim 11, wherein the Lewis acid is present in a catalytic amount.

13. A crystalline, hexahydrate mono-HCl salt of a compound of formula (I-S)



(I-S)

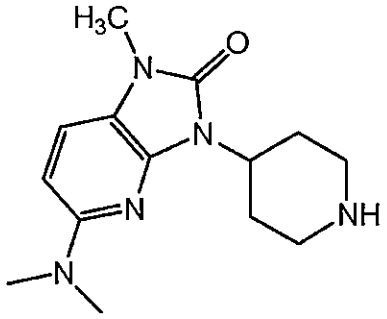
comprising the following X-ray diffraction peaks:

Angle (°2θ)	d-spacing (Å)
4.33	20.42
7.58	11.67
8.39	10.54
8.80	10.04
9.16	9.66
12.71	6.96
13.30	6.66
13.69	6.47
14.69	6.03
15.55	5.70

15.96	5.55
18.44	4.81
18.69	4.75
19.07	4.65

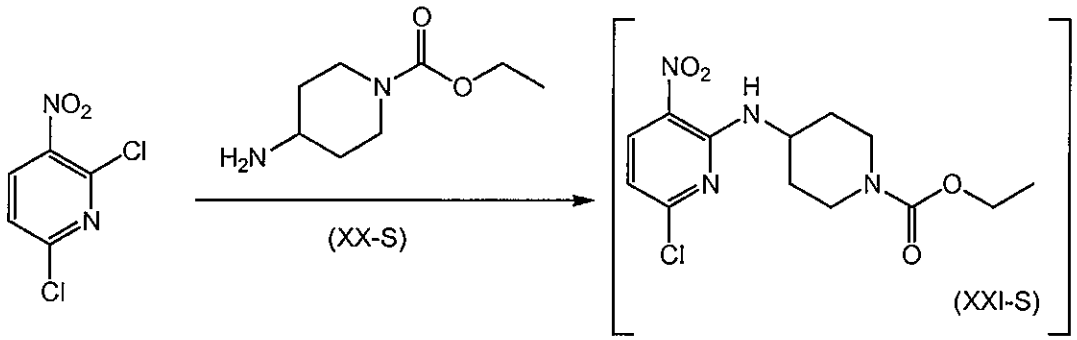
14. A process for the preparation of a crystalline, mono-HCl, hexahydrate salt of claim 13 comprising reacting a compound of formula (I-S) with HCl acid in water.

15. A process for the preparation of a compound of formula (X-S)



(X-S)

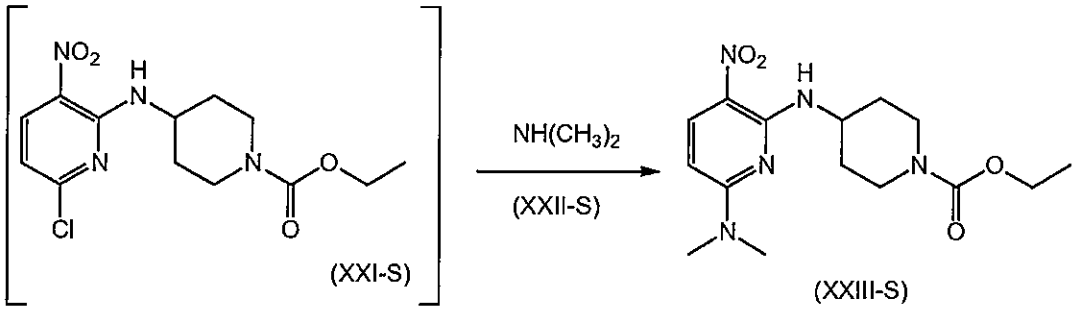
comprising



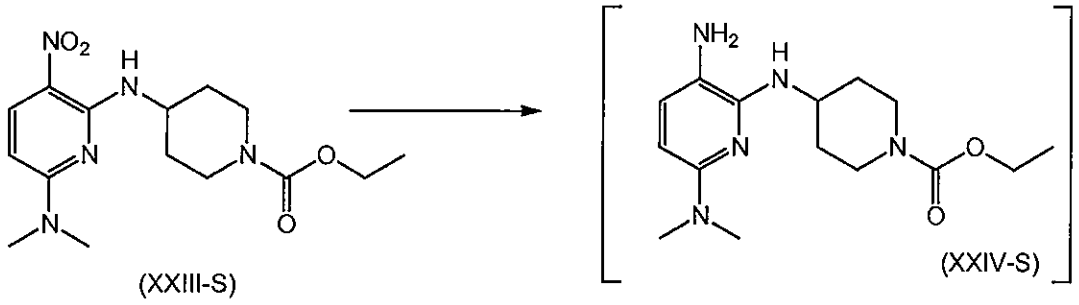
(XX-S)

(XXI-S)

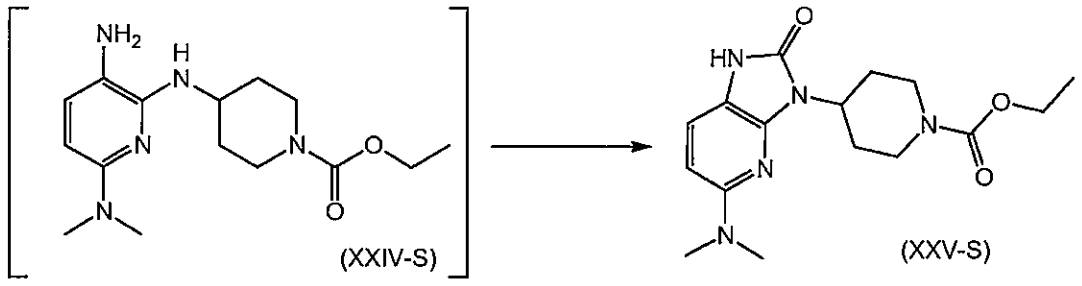
reacting 2,6-dichloro-3-nitro-pyridine with a compound of formula (XX-S), wherein PG^5 is a nitrogen protecting group; in the presence of an organic or inorganic base; in an organic solvent; to yield the corresponding compound of formula (XXI-S);



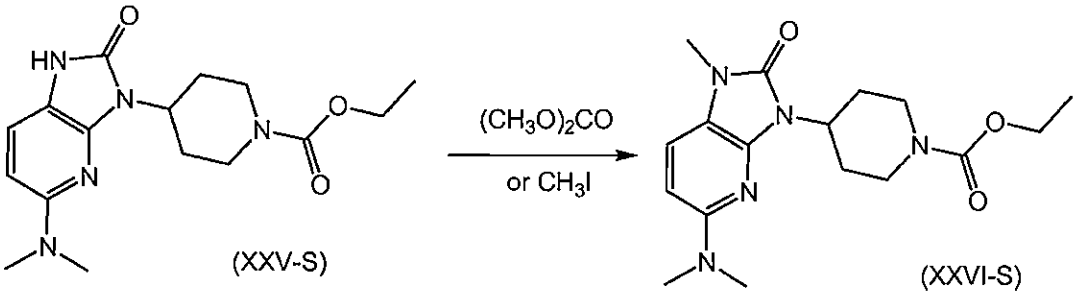
reacting the compound of formula (XXI-S) with a compound of formula (XXII-S); in an organic solvent; to yield the corresponding compound of formula (XXIII-S);



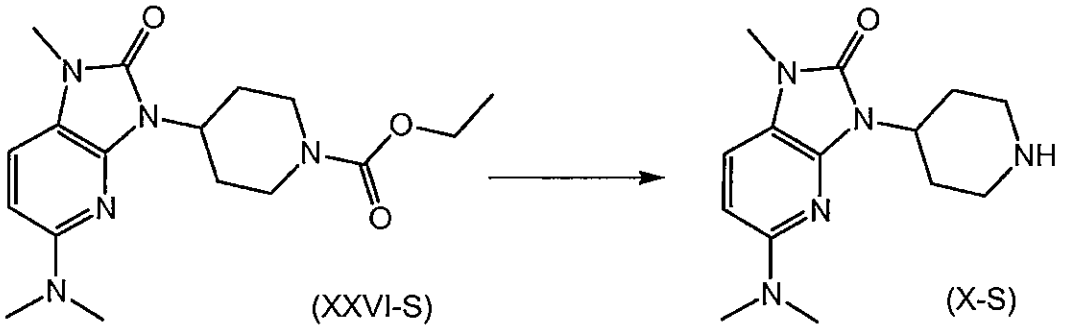
reacting the compound of formula (XXIII-S) with a reducing agent; in the presence of a catalyst; in an organic solvent; to yield the corresponding compound of formula (XXIV-S);



reacting the compound of formula (XXIV-S) with a reagent selected from the group consisting of CDI, N-methylcarbodiimide, phosgene and triphosgene; in an organic solvent; to yield the corresponding compound of formula (XXV-S);



reacting the compound of formula (XXV-S) with carbonic acid dimethyl ester or CH_3I; in the presence of an inorganic base; in an organic solvent; to yield the corresponding compound of formula (XXVI-S);



(XXVI-S) (X-S)

de-protecting the compound of formula (XXVI-S); to yield the corresponding compound of formula (X-S).