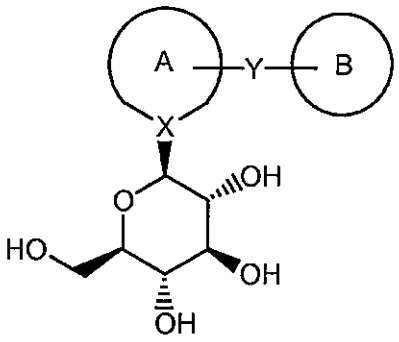
We Claim

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



(I)

wherein Ring A and Ring B are one of the following:

(1) Ring A is an optionally substituted unsaturated monocyclic heterocyclic ring, and Ring B is an optionally substituted unsaturated monocyclic heterocyclic ring, an optionally substituted unsaturated fused heterobicyclic ring, or an optionally substituted benzene ring; or

(2) Ring A is an optionally substituted benzene ring, and Ring B is an optionally substituted unsaturated monocyclic heterocyclic ring, or an optionally substituted unsaturated fused heterobicyclic ring wherein Y is linked to the heterocyclic ring of the fused heterobicyclic ring; or

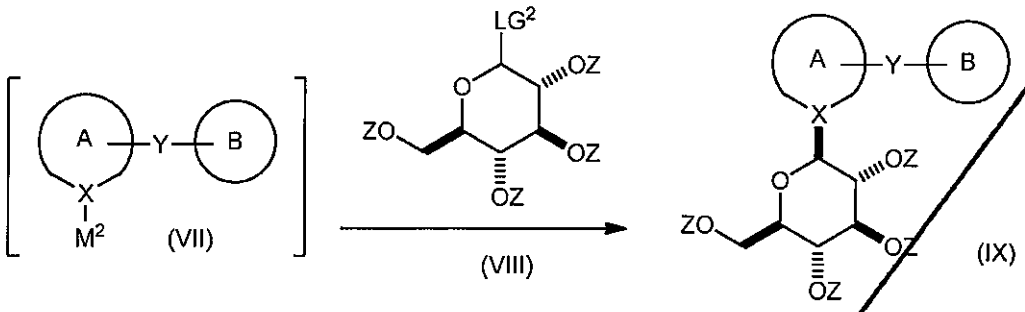
(3) Ring A is an optionally substituted unsaturated fused heterobicyclic ring, wherein the sugar moiety X-(sugar) and the moiety –Y-(Ring B) are both on the same heterocyclic ring of the fused heterobicyclic ring, and Ring B is an optionally substituted unsaturated monocyclic heterocyclic ring, an optionally substituted unsaturated fused heterobicyclic ring, or an optionally substituted benzene ring;

X is a carbon atom;

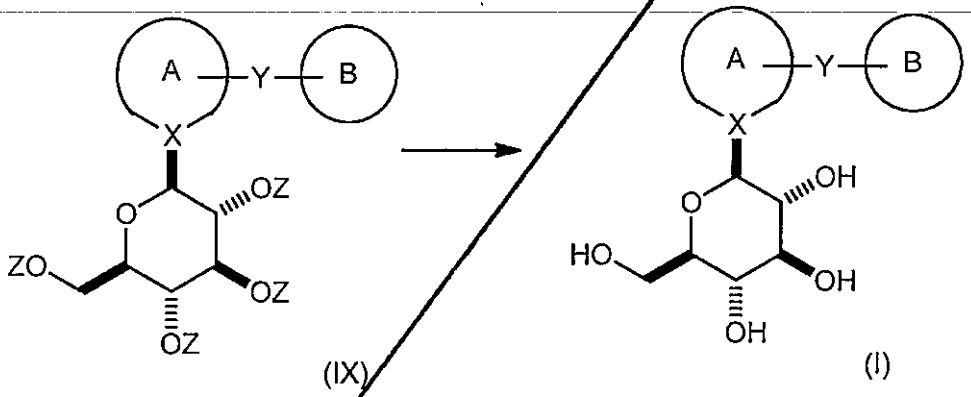
Y is $-(CH_2)_n-$; wherein n is 1 or 2;

provided that in Ring A, X is part of an unsaturated bond;

or a pharmaceutically acceptable salt or solvate thereof; comprising

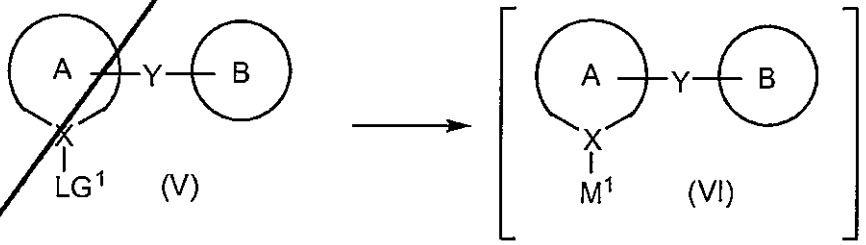


reacting a compound of formula (VII), wherein M^2 is a zinc species, with a compound of formula (VIII), wherein each Z is an independently selected oxygen protecting group and wherein LG^2 is a leaving group, in a mixture of an ether solvent and a hydrocarbon solvent; to yield the corresponding compound of formula (IX);



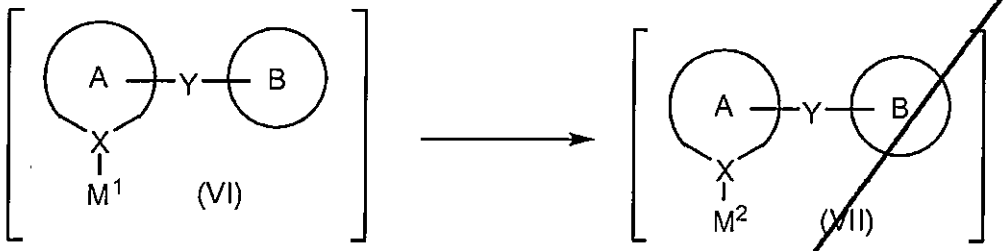
de-protecting the compound of formula (IX); to yield the corresponding compound of formula (I).

2. A process as in Claim 1, further comprising



reacting a compound of formula (V), wherein LG^1 is a leaving group, with an organo-lithium reagent; in a mixture of an ether solvent and a hydrocarbon

solvent; to yield the corresponding compound of formula (VI), wherein M^1 is lithium;



reacting the compound of formula (VI) with a zinc salt or an amine complex of zinc halide; in a mixture of an ether solvent and a hydrocarbon solvent; to yield the corresponding compound of formula (VII).

3. A process as in Claim 1, wherein M^2 is ZnBr, Z is pivaloyl and LG^2 is bromo.

4. A process as in Claim 1, wherein the compound of formula (VIII) is present in an amount in the range of from about 1.0 to about 1.1 molar equivalents.

5. A process as in Claim 1, wherein the ether solvent is di-n-butyl ether or cyclopentyl methyl ether and wherein the hydrocarbon solvent is toluene.

6. A process as in Claim 2, wherein the organo-lithium reagent is n-hexyl lithium; and wherein the n-hexyl lithium is present in an amount in the range of from about 1.0 to about 1.2 molar equivalents.

7. A process as in Claim 2, wherein the ether solvent is di-n-butyl ether or cyclopentyl methyl ether and wherein the hydrocarbon solvent is toluene.

8. A process as in Claim 2, wherein the zinc salt is selected from the group consisting of zinc dibromide ($ZnBr_2$), zinc diiodide (ZnI_2) and zinc ditriflate; and wherein the amine complex of zinc halide is selected from the group consisting

of pyridine zinc bromide complex and N-methylmorpholine zinc bromide complex.

9. A process as in Claim 2, wherein the compound of formula (VI) is reacted with a zinc salt; wherein the zinc salt is zinc dibromide and wherein the zinc dibromide is present in an amount in the range of from about 0.33 to about 1.0 molar equivalents.

10. A process as in Claim 1, wherein

X is a carbon atom;

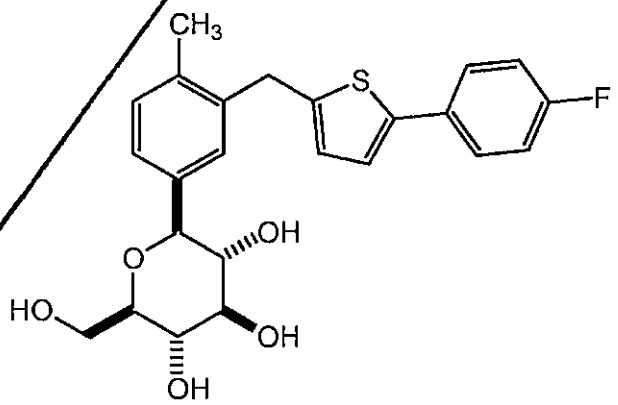
Ring A is selected from the group consisting of 4-methylphenyl and 4-chlorophenyl;

Y is $-CH_2-$ and is bound at the 3-position of Ring A; and

Ring B is selected from the group consisting of 2-(5-(4-fluorophenyl)-thienyl) and 2-(5-(6-fluoro-pyrid-3-yl)-thienyl).

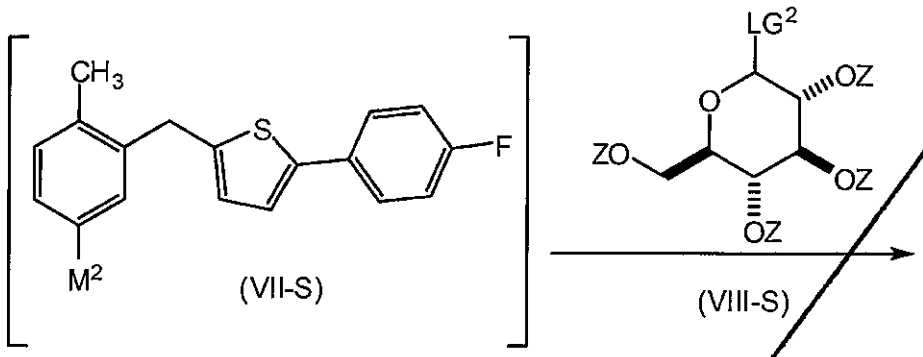
11. A process as in Claim 1, wherein X is a carbon atom; Ring A is 4-methyl-phenyl; Y is $-CH_2-$ and is bound at the 3-position of Ring A; and Ring B is 5-(4-fluorophenyl)-thien-5-yl.

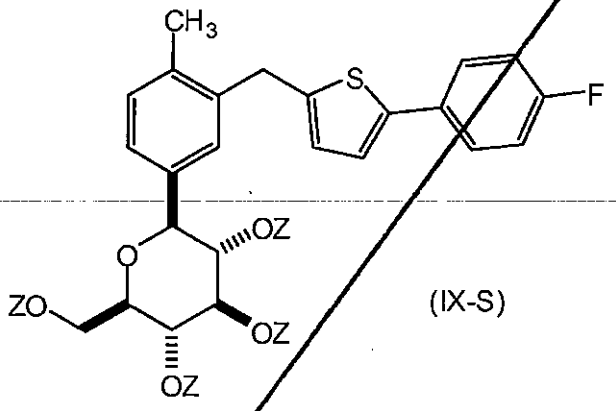
12. A process for the preparation of a compound of formula (I-S)



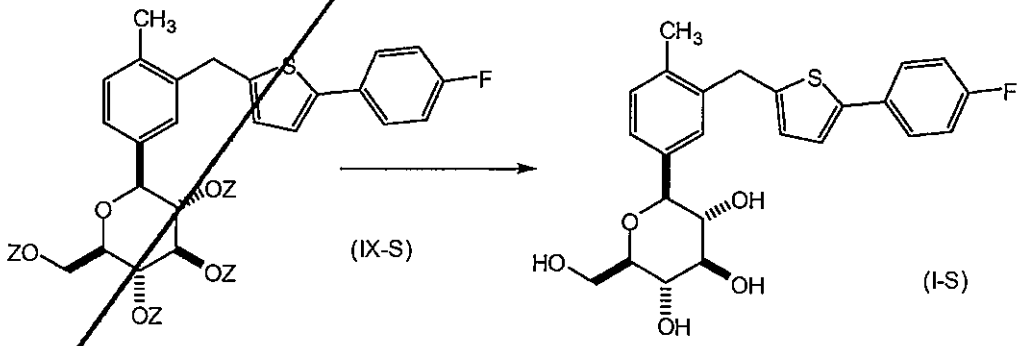
(I-S)

or solvate thereof; comprising





reacting a compound of formula (VII-S), wherein M^2 is a zinc species, with a compound of formula (VIII-S), wherein each Z is an independently selected oxygen protecting group and wherein LG^2 is a leaving group; in a mixture of an ether solvent and a hydrocarbon solvent; to yield the corresponding compound of formula (IX-S);



de-protecting the compound of formula (IX-S); to yield the corresponding compound of formula (I-S).

13. A process as in Claim 12, wherein M^2 is ZnBr.

14. A process as in Claim 12, wherein each Z is pivaloyl and wherein LG^2 is bromo.

15. A process as in Claim 12, wherein the compound of formula (VIII-S) is present in an amount in the range of from about 0.8 to about 1.25 molar equivalents.

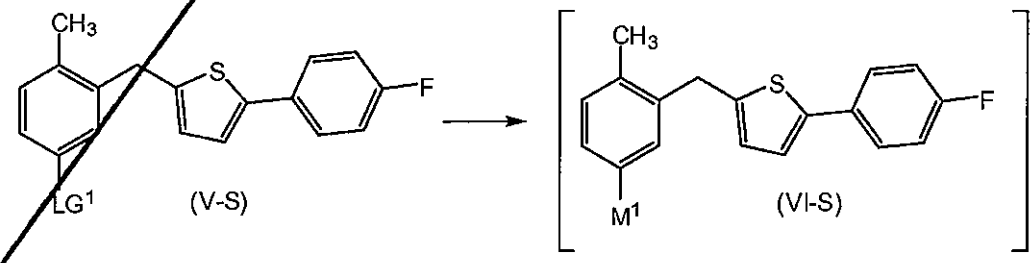
16. A process as in Claim 15, wherein the compound of formula (VIII-S) is present in an amount in the range of from about 1.0 to about 1.1 molar equivalents.

17. A process as in Claim 12, wherein the ether solvent is di-n-butyl ether or cyclopentyl methyl ether and wherein the hydrocarbon solvent is toluene.

18. A process as in Claim 12, wherein the compound of formula (VIII-S) in a solution of the hydrocarbon solvent is added to the compound of formula (VII-S) in a solution of the ether solvent.

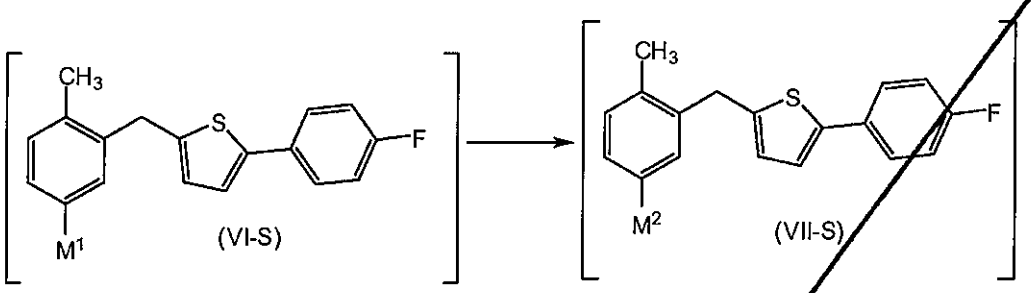
19. A process as in Claim 12, wherein the compound of formula (VII-S) is reacted with the compound of formula (VIII-S) at a temperature in the range of from about 60°C to about 95°C.

20. A process as in Claim 12, further comprising



reacting a compound of formula (V-S), wherein LG^1 is a leaving group; with an organo-lithium reagent; in a mixture of an ether solvent and a

hydrocarbon solvent; to yield the corresponding compound of formula (VI-S), wherein M^1 is lithium;



reacting the compound of formula (VI-S) with a zinc salt or an amine complex of zinc halide; in a mixture of an ether solvent and a hydrocarbon solvent; to yield the corresponding compound of formula (VII-S).

21. A process as in Claim 20, wherein the organo-lithium reagent is n-hexyl lithium.

22. A process as in Claim 20, wherein the organo-lithium reagent is present in an amount in the range of from about 0.5 to about 2.0 molar equivalents.

23. A process as in Claim 22, wherein the organo-lithium reagent is present in an amount in the range of from about 1.0 to about 1.2 molar equivalents.

24. A process as in Claim 20, wherein the ether solvent is di-n-butyl ether or cyclopentyl methyl ether and wherein the hydrocarbon solvent is toluene.

25. A process as in Claim 20, wherein the compound of formula (V-S) is reacted with the organo-lithium reagent at a temperature in the range of from about -78°C to about room temperature.

26. A process as in Claim 20, wherein the zinc salt is selected from the group consisting of zinc dibromide ($ZnBr_2$), zinc diiodide (ZnI_2) and zinc ditriflate; and wherein the amine complex of zinc halide is selected from the

group consisting of pyridine zinc bromide complex and N-methylmorpholine zinc bromide complex.

27. A process as in Claim 20, wherein the compound of formula (VI-S) is reacted with a zinc salt; and wherein the zinc salt is zinc dibromide.

28. A process as in Claim 27, wherein the zinc dibromide is present in an amount in the range of from about 0.33 to about 1.0 molar equivalents.

29. A process as in Claim 28, wherein the zinc dibromide is present in an amount of about 0.5 molar equivalents.

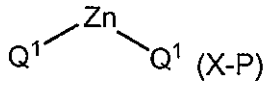
30. A process as in Claim 20, wherein the compound of formula (VI-S) is reacted with a zinc salt in the presence of an amine or lithium salt.

31. A process as in Claim 30, wherein the amine or lithium salt is selected from the group consisting of lithium bromide, lithium iodide, pyridine, N-methyl morpholine, 2,6-lutidine and TMEDA; and wherein the amine or lithium salt is preferably present in an amount in the range of from about 1.0 to about 2.0 molar equivalent.

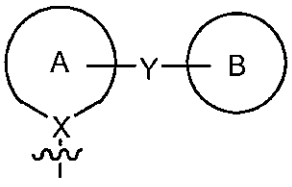
32. A compound prepared according to a process as in Claim 1.

33. A compound prepared according to a process as in Claim 12.

34. A process for the preparation of a compound of formula (X-P)



(X-P)

wherein both Q^1 groups are the same and are 

;

and wherein Ring A and Ring B are one of the following:

(1) Ring A is an optionally substituted unsaturated monocyclic heterocyclic ring, and Ring B is an optionally substituted unsaturated monocyclic heterocyclic ring, an optionally substituted unsaturated fused heterobicyclic ring, or an optionally substituted benzene ring; or

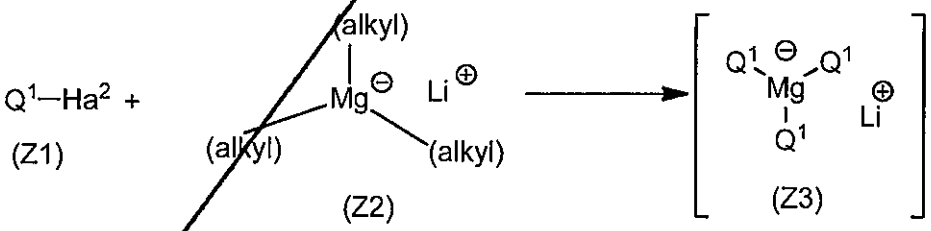
(2) Ring A is an optionally substituted benzene ring, and Ring B is an optionally substituted unsaturated monocyclic heterocyclic ring, or an optionally substituted unsaturated fused heterobicyclic ring wherein Y is linked to the heterocyclic ring of the fused heterobicyclic ring; or

(3) Ring A is an optionally substituted unsaturated fused heterobicyclic ring, wherein the sugar moiety X-(sugar) and the moiety –Y-(Ring B) are both on the same heterocyclic ring of the fused heterobicyclic ring, and Ring B is an optionally substituted unsaturated monocyclic heterocyclic ring, an optionally substituted unsaturated fused heterobicyclic ring, or an optionally substituted benzene ring;

X is a carbon atom;

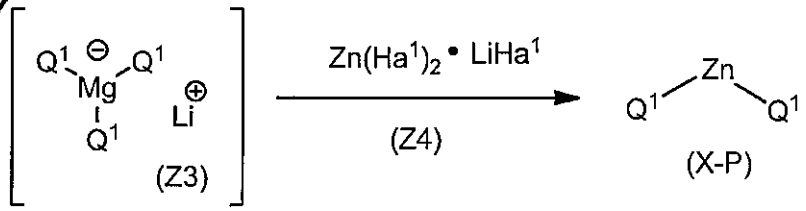
Y is $-(CH_2)_n-$; wherein n is 1 or 2;

provided that in Ring A, X is part of an unsaturated



bond;

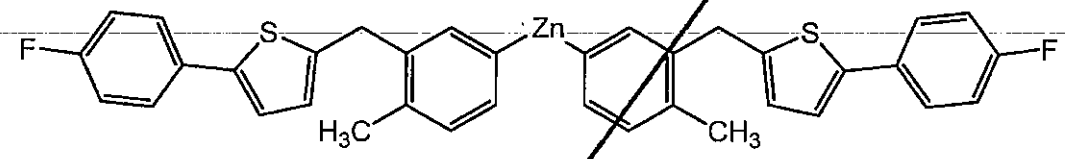
reacting a compound of the formula (Z1), wherein Ha^2 is a halogen, with a lithium trialkyl magnesate, a compound of formula (Z2); in a suitably selected anhydrous organic solvent or mixture or anhydrous organic solvents; to yield the corresponding compound of formula (Z3);



reacting the compound of formula (Z3) with a zinc halide•lithium halide complex, a compound of formula (Z4), wherein Ha^1 is a halogen; in a suitably selected anhydrous organic solvent or mixture or anhydrous organic solvents; to yield the corresponding compound of formula (X-P).

35. A process as in Claim 34, wherein the compound of formula (Z2) is lihtiun dibutyl hexylmagnesate; and wherein the compound of formula (Z4) is zinc bromide•lithium bromide complex.

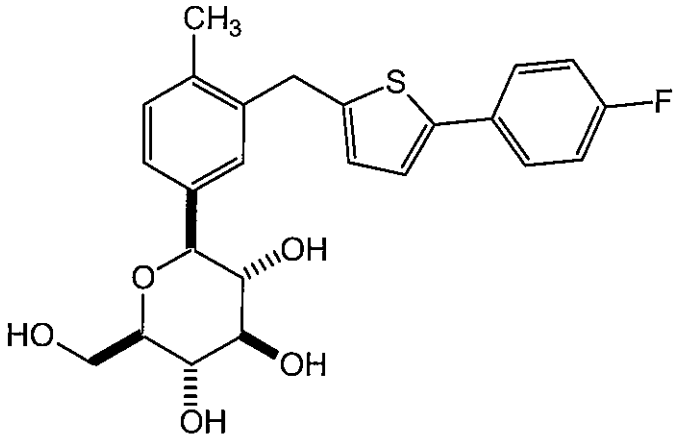
36. A process as in Claim 34, wherein the compound of formula (X-P) is a compound of formula (X-S)



(X-S).

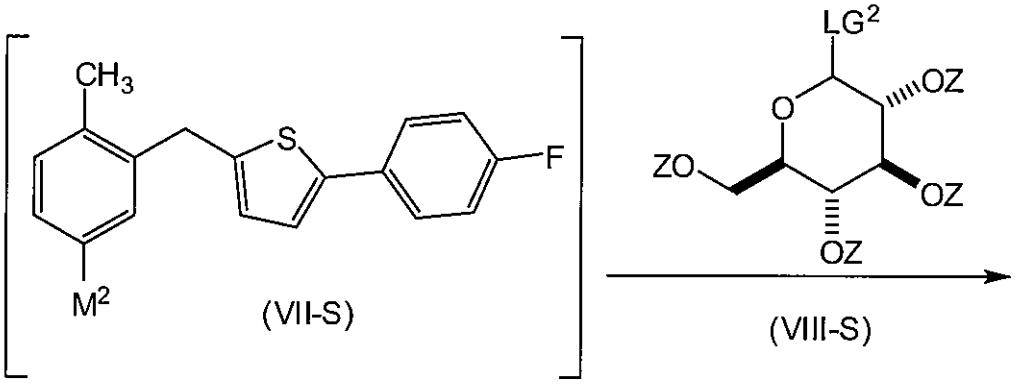
Claims

1. A compound prepared according to a process for the preparation of a compound of formula (I-S)



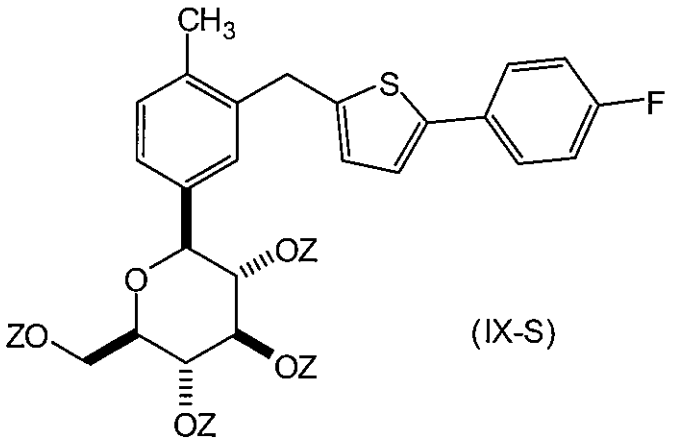
(I-S)

or solvate thereof; comprising



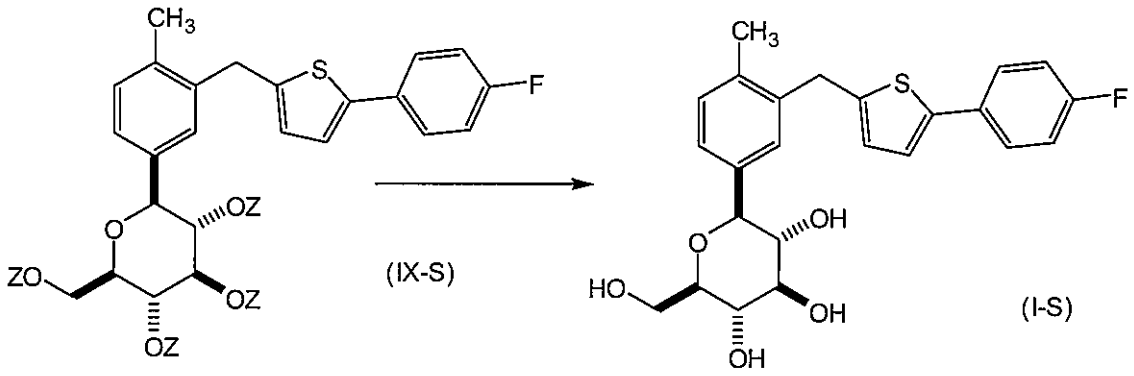
(VII-S)

(VIII-S)



(IX-S)

reacting a compound of formula (VII-S), wherein M^2 is a zinc species, with a compound of formula (VIII-S), wherein each Z is an independently selected oxygen protecting group and wherein LG^2 is a leaving group; in a mixture of an ether solvent and a hydrocarbon solvent; to yield the corresponding compound of formula (IX-S);



de-protecting the compound of formula (IX-S); to yield the corresponding compound of formula (I-S).