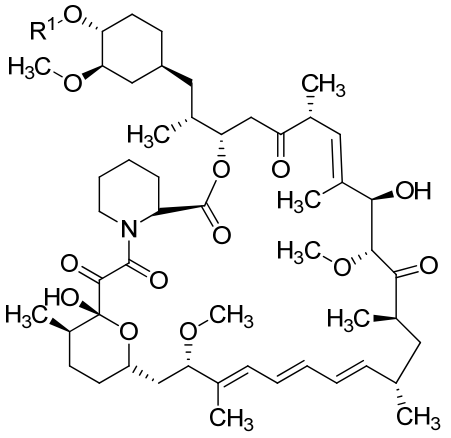
[0004] The chemical structure of BA9 compared to sirolimus and other sirolimus derivatives is provided in Figure 1. BA9 is structurally related to rapamycin (also known as sirolimus). The structure consists of the rapamycin 31-membered macrolide triene lactone ring with ethoxyethylation at position 40.

[0005] BA9, like sirolimus, binds to the intracellular immunophilin protein FKBP12. It is believed that the resulting macrolide/FKBP12 complex then binds, in a manner similar to sirolimus, to mTOR, a protein critical for cell cycle progression. Inactivation of mTOR results in suppression of several specific signal transduction pathways and arrest of the cell cycle at the G1 to S phase.

[0006] Given the therapeutic value of BA9 and other rapamycin derivatives, improved processes for preparation of this family of active agents is desired. The present invention addresses this and other needs.

BRIEF SUMMARY

[0006a] In one aspect of the present disclosure, there is provided a method for obtaining a purified, solid compound having a structure according to Formula I:



Formula I

,

wherein R^1 is CH_2-CH_2-O-CH_2-CH_3;

the method comprising:

a) forming a mixture consisting essentially of a crude compound having a structure according to Formula I and a non-polar organic solvent under conditions sufficient to dissolve the compound, wherein the dielectric constant of the non-polar organic solvent is less than 5, and wherein forming the mixture comprises heating the mixture;

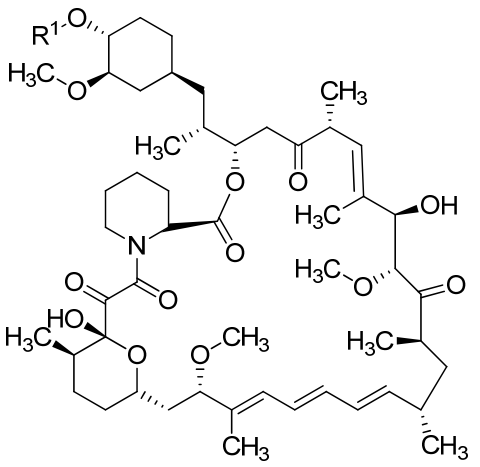
b) solidifying at least a portion of the compound having the structure according to Formula I, wherein the solidifying comprises cooling the mixture; and

c) separating at least a portion of the solidified compound from the solvent in the mixture;

thereby obtaining the purified, solid compound.

WHAT IS CLAIMED IS:

1. A method for obtaining a purified, solid compound having a structure according to Formula I:



Formula I

,

wherein R^1 is CH_2-CH_2-O-CH_2-CH_3;

the method comprising:

a) forming a mixture consisting essentially of a crude compound having a structure according to Formula I and a non-polar organic solvent under conditions sufficient to dissolve the compound, wherein the dielectric constant of the non-polar organic solvent is less than 5, and wherein forming the mixture comprises heating the mixture;

b) solidifying at least a portion of the compound having the structure according to Formula I, wherein the solidifying comprises cooling the mixture; and

c) separating at least a portion of the solidified compound from the solvent in the mixture;

thereby obtaining the purified, solid compound.

2. The method of claim 1, wherein the non-polar organic solvent is selected from the group consisting of hexane, heptane, methyl *t*-butyl ether, ligroin, octane, cyclohexane, and mixtures thereof.

3. The method of claim 2, wherein the non-polar organic solvent is hexane.

4. The method of claim 2, wherein the non-polar organic solvent is heptane.

5. The method of claim 1, wherein forming the mixture in step a) comprises heating the mixture to a temperature of from 35 °C to 100 °C.

6. The method of claim 1, wherein forming the mixture in step a) comprises heating the mixture to reflux.

7. The method of claim 1, wherein cooling the mixture in step b) comprises cooling the mixture to a temperature of from -78 °C to 25 °C.

8. The method of claim 7, wherein cooling the mixture in step b) comprises cooling the mixture to a temperature of 15 °C.

9. The method of claim 1, wherein the purified, solid compound is obtained in a crystalline form.

10. The method of claim 1, further comprising:

d) solubilizing the solidified compound in a polar organic solvent to form a solution;

e) contacting the solution with water to precipitate at least a portion of the compound; and

f) drying the precipitated compound.

11. The method of claim 10, wherein the polar organic solvent is selected from the group consisting of methanol, ethanol, isopropanol, *t*-butanol, tetrahydrofuran, and acetone.

12. The method of claim 11, wherein the polar organic solvent is methanol.

13. The method of claim 10, wherein the drying is conducted under reduced pressure.

14. The method of claim 1, wherein the purity of the purified, solid compound is increased by from 1% to 20% with respect to the crude compound.

15. The method of claim 1, wherein the purity of the purified, solid compound is increased by from 1% to 10% with respect to the crude compound.

16. The method of claim 1, wherein the purity of the purified, solid compound is increased by 3% with respect to the crude compound.