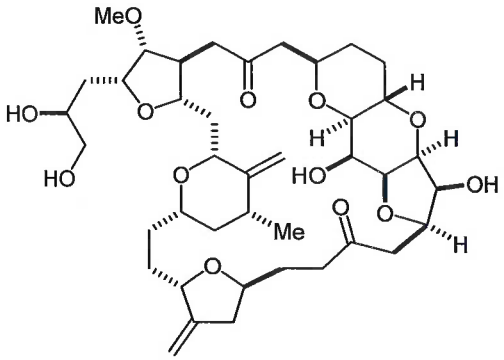
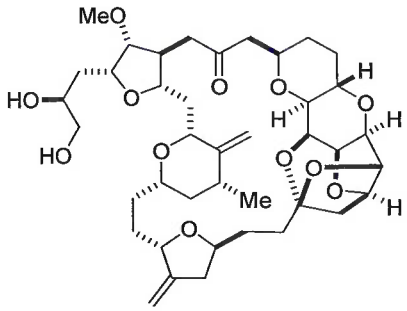
CLAIMS

1. A method of preparing an intermediate in the synthesis of eribulin, said method comprising reacting ER-811475:



ER-811475

with a conjugate acid of imidazole to produce the intermediate ER-076349:

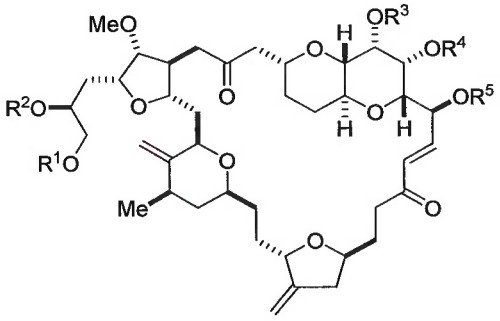


ER-076349.

2. The method of claim 1, wherein the reacting occurs in ethanol.

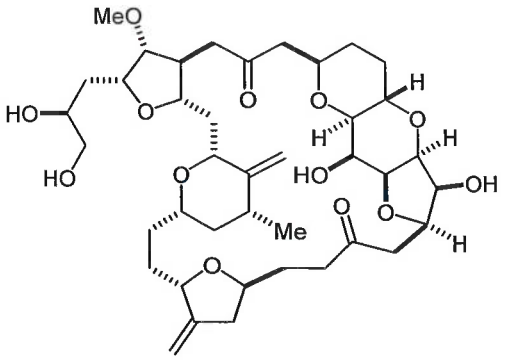
3. The method of claim 1, wherein the conjugate acid is imidazole hydrochloride.

4. The method of claim 1, wherein ER-811475 is produced by reacting a compound having formula (I):



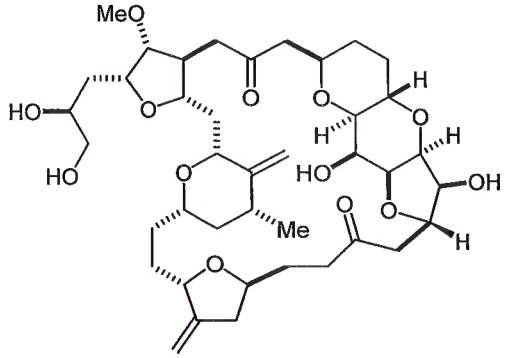
(I),

wherein each of R^1, R^2, R^3, R^4, and R^5 is independently a silyl group, with a fluoride source in a solvent comprising an amide to produce the intermediate ER-811475:



ER-811475.

5. The method of claim 4, wherein ER-811475 is produced in a mixture with an intermediate ER811474:



ER-811474.

6. The method of claim 5, further comprising adding a mixture of acetonitrile and water.

7. The method of claim 4, wherein each of R^1, R^2, R^3, R^4, and R^5 is t-butyldimethylsilyl.

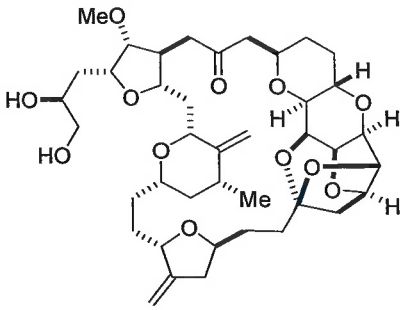
8. The method of claim 4, wherein the fluoride source is tetrabutylammonium fluoride.

9. The method of claim 4, wherein the solvent further comprises tetrahydrofuran.

10. The method of claim 4, wherein the amide is an N,N C1-C6 dialkyl C1-C6 alkyl amide or N C1-C6 alkyl C2-C6 lactam.

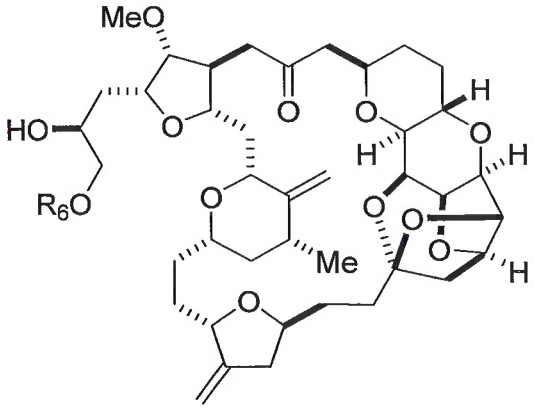
11. The method of claim 4, wherein the amide is N,N-dimethylacetamide, N,N-dimethylformamide, N-methyl-2-pyrrolidone, N, N-diethylacetamide, or N,N-dimethylpropionamide.

12. A method of preparing an intermediate in the synthesis of eribulin, said method comprising reacting ER-076349:



ER-076349

with a sulfonylating reagent in the presence of a metal catalyst to produce the intermediate:



,

wherein R_6 is sulfonyl, wherein sulfonyl is —$S(O)_2R$, wherein R is alkyl, alkenyl, aryl, arylalkyl, or silyl.

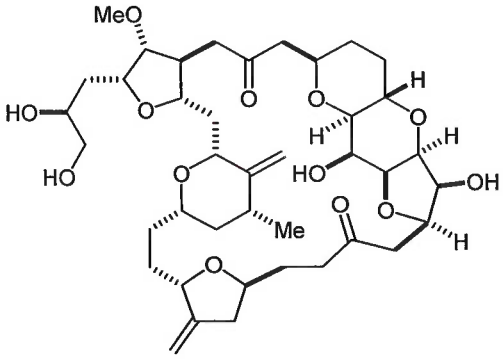
13. The method of claim 12, wherein the sulfonylating reagent is tosyl chloride.

14. The method of claim 12, wherein the reacting occurs in acetonitrile.

15. The method of claim 12, wherein said metal catalyst is dibutyltin oxide.

16. The method of claim 12, wherein the reacting occurs above 0 °C.

17. The method of claim 12, wherein ER-076349 is produced by reacting ER-811475:

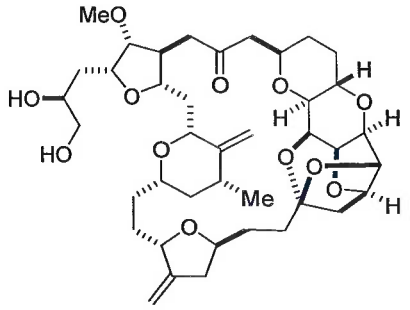


ER-811475

with a conjugate acid of imidazole.

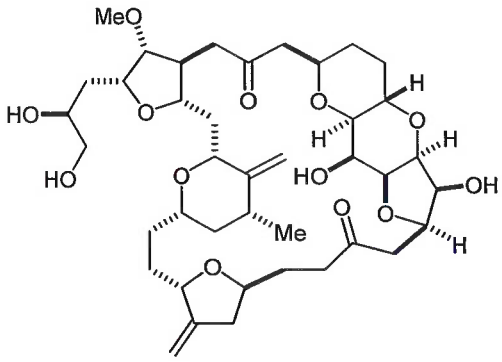
18. A method of producing eribulin, said method comprising the steps of:

a) producing the intermediate ER-076349:



ER-076349

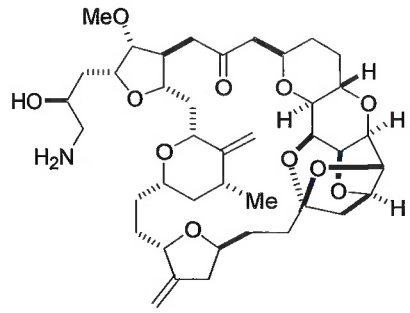
by reacting ER-811475



ER-811475

with a conjugate acid of imidazole to produce the intermediate ER-076349; and

b) aminating ER-076349 to produce eribulin:

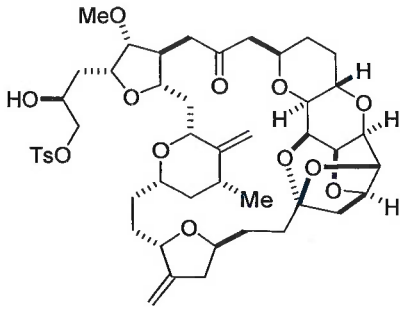


eribulin.

19. The method of claim 18, further comprising salifying eribulin to produce a pharmaceutically acceptable salt of eribulin.

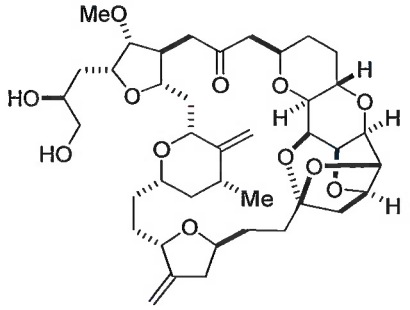
20. The method of claim 19, wherein said salt is the mesylate salt.

21. The method of claim 18, wherein step b) comprises converting ER-076349 to ER-082892:



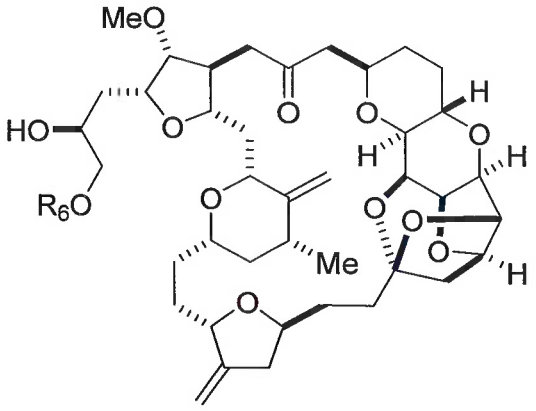
ER-082892

according to a method comprising reacting the intermediate ER-076349:



ER-076349

with a sulfonylating reagent in the presence of a metal catalyst to produce the intermediate:



wherein R_6 is sulfonyl, wherein sulfonyl is —$S(O)_2R$, wherein R is alkyl, alkenyl, aryl, arylalkyl, or silyl.

22. The method of claim 21, wherein the sulfonylating agent is tosyl chloride.

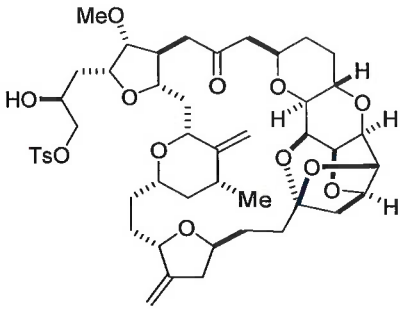
23. The method of claim 21, wherein the reacting occurs in acetonitrile.

24. The method of claim 21, wherein the metal catalyst is dibutyltin oxide.

25. The method of claim 21, wherein the reacting occurs above 0 °C.

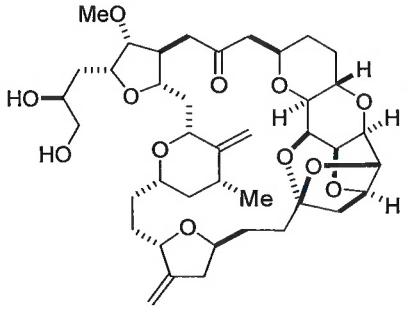
26. A method of producing eribulin, said method comprising the steps of:

a) producing the intermediate ER-082892:



ER-082892

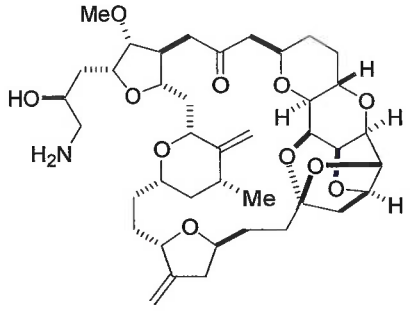
by reacting ER-076349



ER-076349

with a sulfonylating reagent in the presence of a metal catalyst; and

b) aminating ER-082892 to produce eribulin:



eribulin.

27. The method of claim 26, further comprising salifying eribulin to produce a pharmaceutically acceptable salt of eribulin.

28. The method of claim 27, wherein said salt is the mesylate salt.

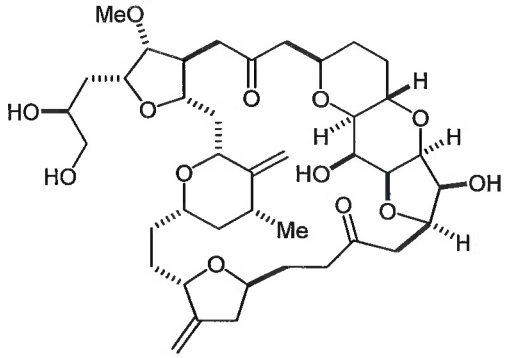
29. The method of claim 26, wherein the sulfonylating agent is tosyl chloride.

30. The method of claim 26, wherein the reacting occurs in acetonitrile.

31. The method of claim 26, wherein said metal catalyst is dibutyltin oxide.

32. The method of claim 26, wherein the reacting occurs above 0 °C.

33. The method of claim 26, wherein ER-076349 is produced by reacting ER-811475:



ER-811475

with a conjugate acid of imidazole.