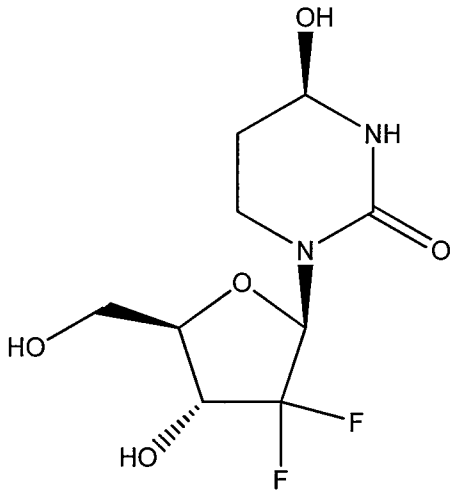
Claims

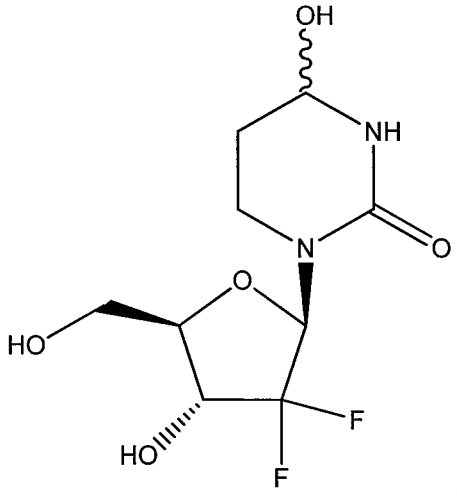
1. A method of producing compound 1:



1

or a salt thereof;

comprising precipitating or crystallizing compound 1 from a solution of compound 2:



2

in the presence of a catalyst,

wherein the solution comprises acetonitrile, acetone, tetrahydrofuran, dimethylsulfoxide (DMSO), or methanol, and

wherein the catalyst is 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU), acetic acid, trifluoroacetic acid, diisopropylethylamine, or ammonium hydroxide.

2. The method of claim 1, wherein the catalyst is a Bronsted-Lowry base.

3. The method of claim 1, wherein the catalyst is about 1 mol% to about 20 mol% DBU.

4. The method of claim 1, wherein the catalyst is about 5 mol% to about 10 mol% DBU.

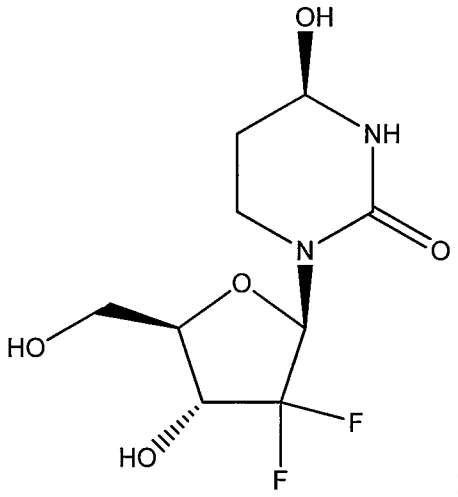
5. The method of claim 4, wherein the catalyst is about 5 mol% DBU.

6. The method of claim 1, wherein the catalyst is acetic acid, trifluoroacetic acid, diisopropylethylamine, or ammonium hydroxide.

7. The method of claim 1, wherein the solution comprises acetonitrile.

8. The method of claim 1, wherein the solution comprises acetone, tetrahydrofuran, DMSO, or methanol.

9. A method of producing compound 1:

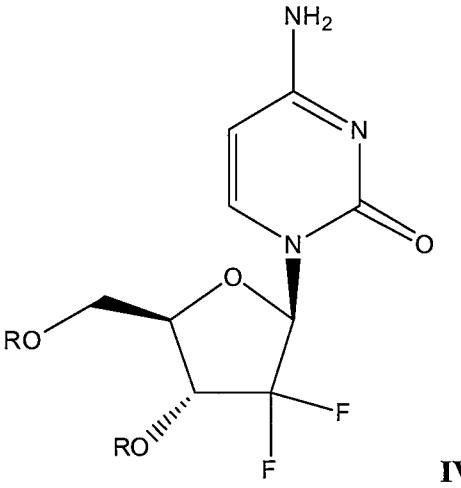


1

or a salt thereof;

comprising the steps of:

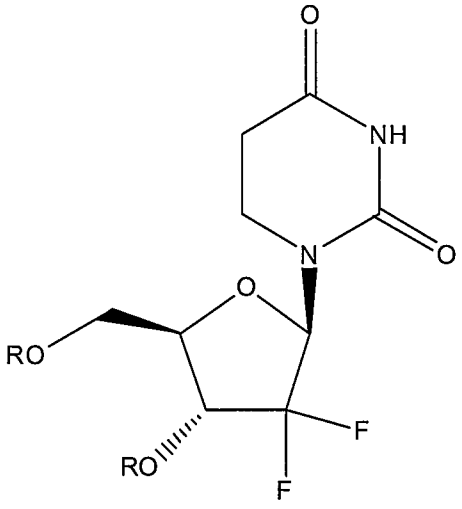
(a) hydrogenating a compound of Formula IV:



IV

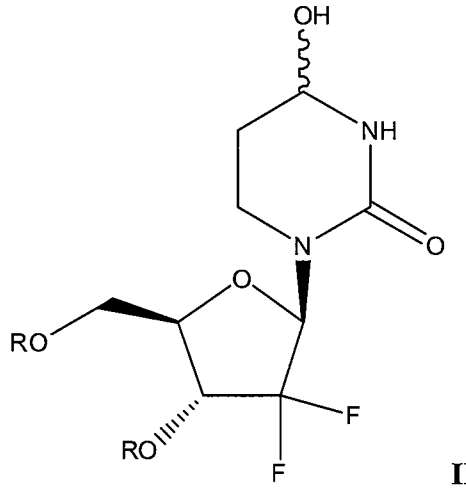
wherein R is a hydroxyl protecting group,

to produce a compound of Formula IIa:



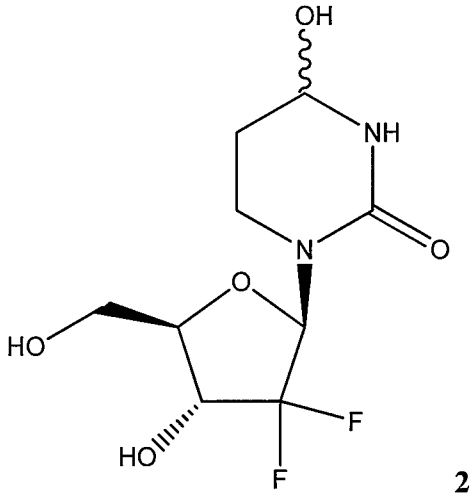
IIa;

(b) reducing the compound of Formula IIa to produce a compound of Formula IIIa:



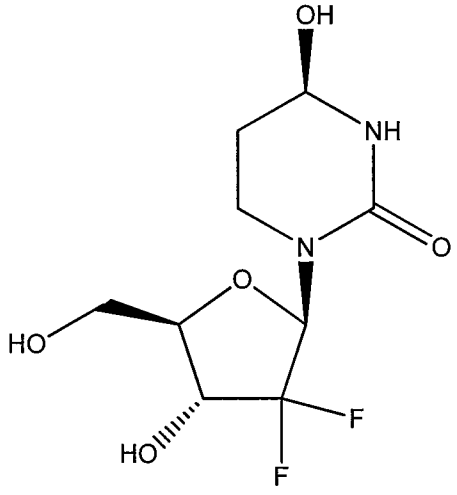
IIIa;

(c) deprotecting the compound of Formula IIIa to produce compound 2:



2; and

(d) precipitating or crystallizing compound 2 in the presence of a catalyst to produce compound 1:



1

or a salt thereof,

wherein the catalyst is DBU, acetic acid, trifluoroacetic acid, diisopropylethylamine, or ammonium hydroxide.

10. The method of claim 9, wherein the catalyst is about 1 mol% to about 20 mol% DBU

11. The method of claim 10, wherein the catalyst is about 5 mol% to about 10 mol% DBU.

12. The method of claim 11, wherein the catalyst is about 5 mol% DBU.

13. The method of claim 9, wherein the catalyst is acetic acid, trifluoroacetic acid, diisopropylethylamine, or ammonium hydroxide.

14. The method of claim 9, wherein the final product is recrystallized or slurrified.

15. The method of claim 9, wherein step (d) is carried out in the presence of a solution comprising acetonitrile.

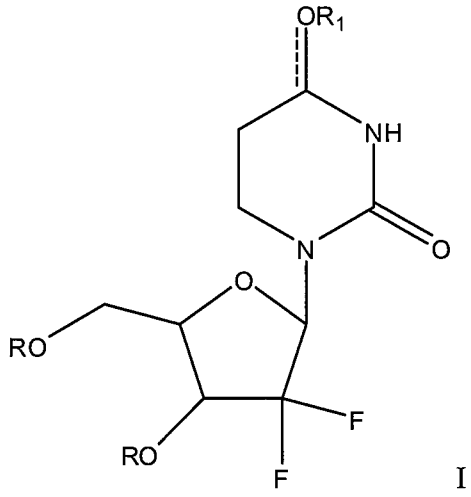
16. The method of claim 9, wherein step (d) is carried out in the presence of a solution comprising acetone or tetrahydrofuran.

17. The method of claim 9, wherein step (b) is carried out in the presence of $CeCl_3$.

18. The method of claim 9, further comprising a step of reducing the particle size of compound 1.

19. The method of claim 18, wherein the particle size is reduced to about 50 μm or less.

20. A compound of Formula I:



I

wherein R is a hydroxyl protecting group;

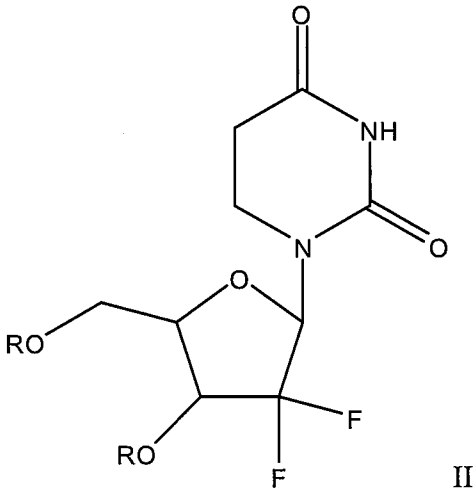
R_1 is H, a hydroxyl protecting group, or absent;

------ is a bond or absent; and

------ is absent when R_1 is H or a hydroxyl protecting group;

or a salt, or enantiomer, or diastereomer thereof.

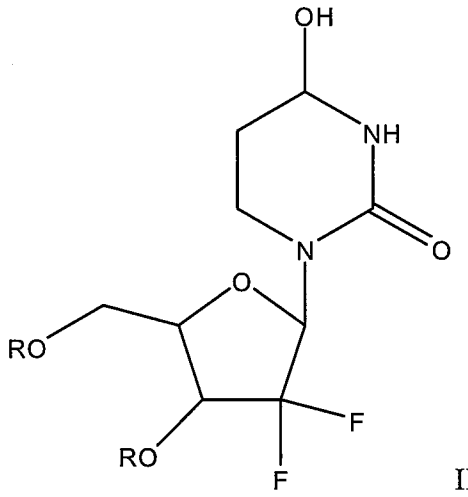
21. The compound of claim 20, having the structure of Formula II:



II

or a salt, or enantiomer, or diastereomer thereof.

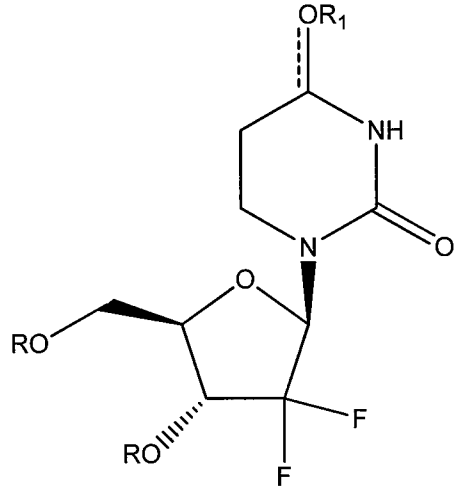
22. The compound of claim 20, having the structure of Formula III:



III

or a salt, or enantiomer, or diastereomer thereof.

23. The compound of claim 20, having the structure of Formula Ia:

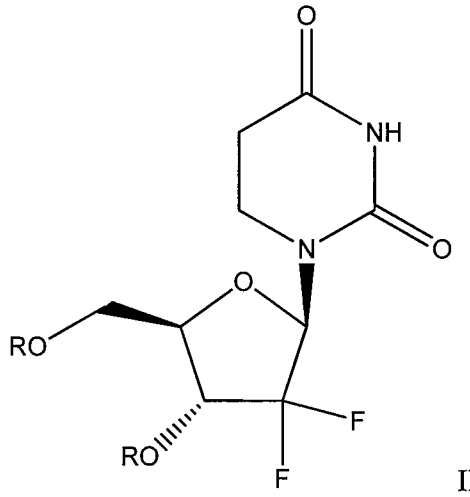


Ia

or a salt, or enantiomer, or diastereomer thereof.

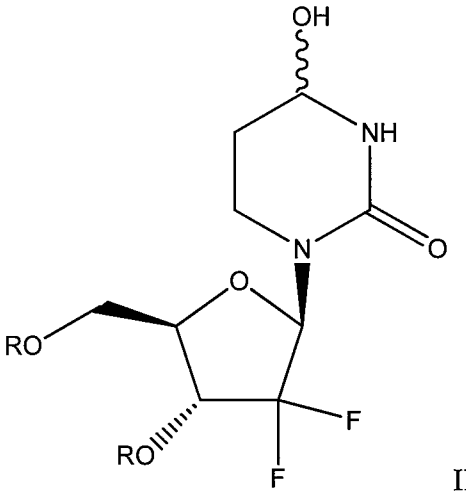
24. The compound of claim 20, wherein R_1 is H or absent.

25. The compound of claim 23, having the structure of Formula IIa:



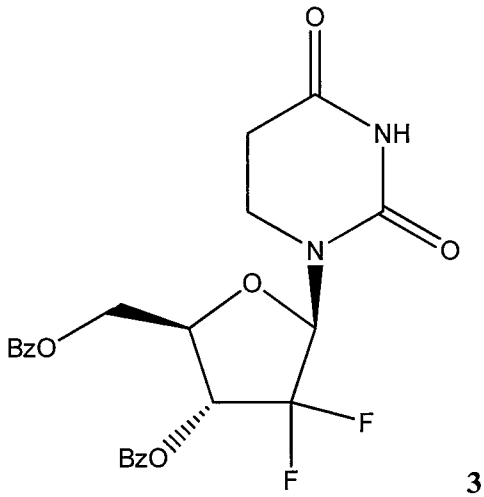
IIa.

26. The compound of claim 23, having the structure of Formula IIIa:



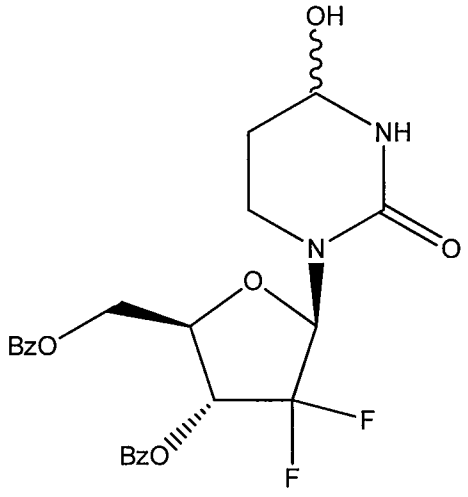
IIIa.

27. The compound of claim 25, wherein the compound is compound 3:



3.

28. The compound of claim 26, wherein the compound is compound 4:



4.