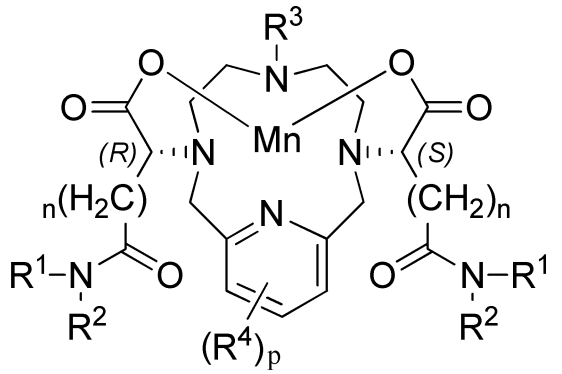


(IA)

or a salt or solvate thereof, and a pharmaceutically acceptable excipient, wherein:

each R^1 is independently selected from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl, or $C_{3–6}$ aryl optionally-substituted with one or more substituents selected from halo and -C(=O)-NH-$C_{1–6}$ hydroxyalkyl;

each R^2 is independently selected from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl or hydrogen;

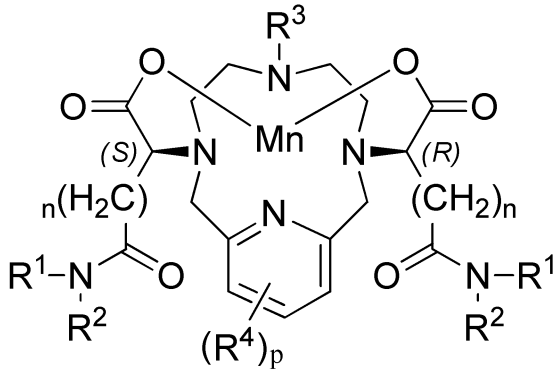
R^3 is selected from C_{1-3} alkyl or -$(CH_2)_m$-C(=0)- NR^5R^6, wherein m is an integer from 2–5, wherein R^5 and R^6 are independently selected from hydrogen, from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl, or $C_{3–6}$ aryl optionally-substituted with one or more substituents selected from halo and -C(=O)-NH-$C_{1–6}$ hydroxyalkyl;

R^4 is selected from hydroxy, $C_{1–6}$ alkyl and C_{1-6} hydroxyalkyl;

p is 0-3; and,

each n is an integer from 0–4,

wherein the composition lack detectable amounts of the compound of Formula (IB):



(IB)

or a salt or solvate thereof.

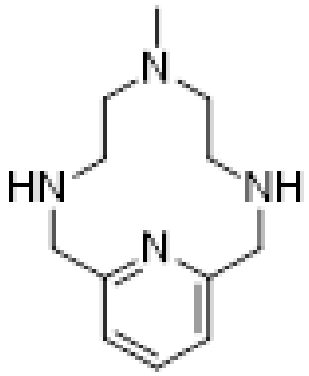
[0026] In one example, the disclosure involves a method of imaging a patient comprising administering the contrast agent, or contrast agent composition, followed by acquiring an MRI image of the patient.

[0026a] In another aspect, there is provided a method of imaging a patient comprising administering the compound as defined above to a patient in need thereof, followed by acquiring an MRI image of the patient.

[0027] In one example, the disclosure involves a method of making the imaging agent as described above. The method may involve enantioselective synthesis, or isomerization from compounds of Formula (1A) to compounds of Formula (1B).

[0027a] In another aspect, there is provided a method of enantioselective synthesis of the compound of Formula (1A) as defined above comprising:

(a) monoalkylation using a first enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate of a compound of formula (III)



(III);

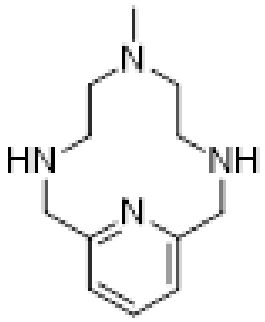
(b) followed by alkylation of the compound from step (a) with a second enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate, the second enantiomer being opposite the first enantiomer;

(c) reacting the product of step (b) with Mn; and

(d) reacting the product of step (c) with an aminoalcohol.

[0027b] In another aspect, there is provided a method of enantioselective synthesis of a composition comprising Formula (1A) as defined above comprising:

(a) monoalkylation using a first enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate of a compound of formula (III)



(III);

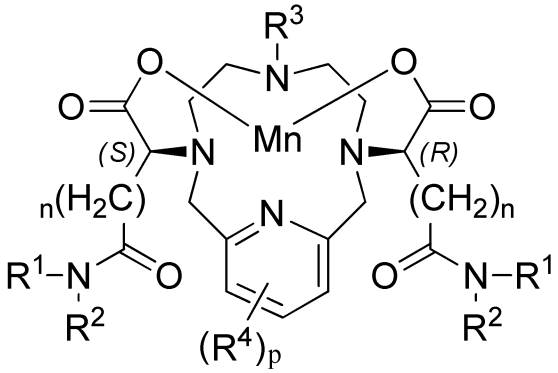
(b) followed by alkylation of the compound from step (a) with a second enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate, the second enantiomer being opposite the first enantiomer;

(c) reacting the product of step (b) with Mn; and

(d) reacting the product of step (c) with an aminoalcohol.

[0027c] In another aspect, there is provided a method of making the composition as defined above, wherein the method comprises:

heating a composition comprising the compound of Formula (1B):



(IB)

or a salt or solvate thereof;

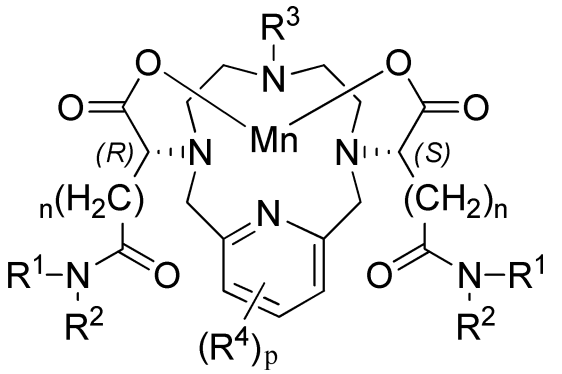
wherein the heating is for a sufficient time and temperature to convert substantially all of the compound of Formula (1B) into the compound of Formula (1A).

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] Fig. 1 shows the predicted stereoisomers of Mn Chelate-5.

WHAT IS CLAIMED IS:

1. A compound of formula IA:



,

(IA)

or a salt or solvate thereof, wherein:

each R^1 is independently selected from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl or $C_{3–6}$ aryl optionally-substituted with one or more substituents selected from halo and -C(=O)-NH-$C_{1–6}$ hydroxyalkyl;

each R^2 is independently selected from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl or hydrogen;

R^3 is selected from C_{1-3} alkyl or -$(CH_2)_m$-C(=0)- NR^5R^6, wherein m is an integer from 2–5, wherein R^5 and R^6 are independently selected from hydrogen, from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl, or $C_{3–6}$ aryl optionally-substituted with one or more substituents selected from halo and -C(=O)-NH-$C_{1–6}$ hydroxyalkyl;

R^4 is selected from hydroxy, $C_{1–6}$ alkyl and C_{1-6} hydroxyalkyl;

p is 0-3; and,

each n is an integer from 0–4.

2. The compound of claim 1, where the compound comprises at least two hydroxy groups.

3. The compound of claim 1, wherein the compound is of Formula IA.

4. The compound of claim 1, wherein the compound is of Formula IA,

each R^1 is $C_{1–20}$ hydroxyalkyl;

R3 is methyl;

R^2 is hydrogen;

p is 0; and

n is 2.

5. The compound of claim 1, wherein each R^1 is $C_{1–20}$ hydroxyalkyl.

6. The compound of claim 1, wherein R^3 is methyl.

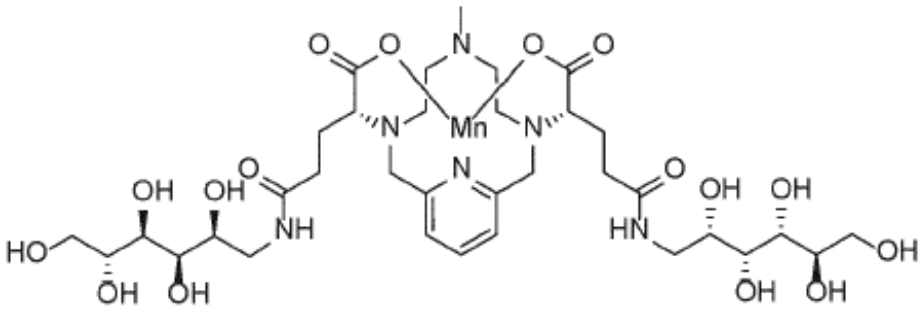
7. The compound of claim 1, wherein R^2 is hydrogen; and p is 0.

8. The compound of claim 1, wherein n is 2.

9. The compound of claim 1, wherein each R^1 is independently $C_{3–9}$ hydroxyalkyl.

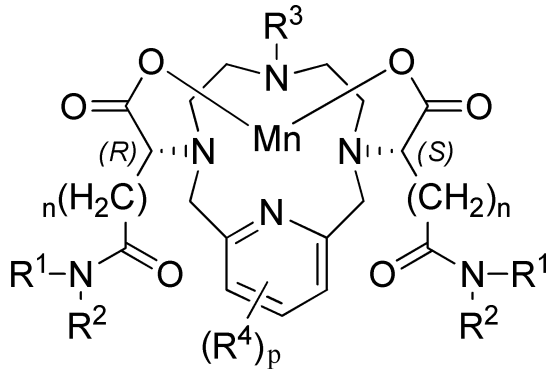
10. The compound of claim 1, wherein each R^1 is independently $C_{3–6}$ hydroxyalkyl.

11. A compound having the structure;



.

12. A composition comprising a compound of formula IA:



(IA)

or a salt or solvate thereof, and a pharmaceutically acceptable excipient, wherein:

each R^1 is independently selected from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl, or $C_{3–6}$ aryl optionally-substituted with one or more substituents selected from halo and -C(=O)-NH-$C_{1–6}$ hydroxyalkyl;

each R^2 is independently selected from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl or hydrogen;

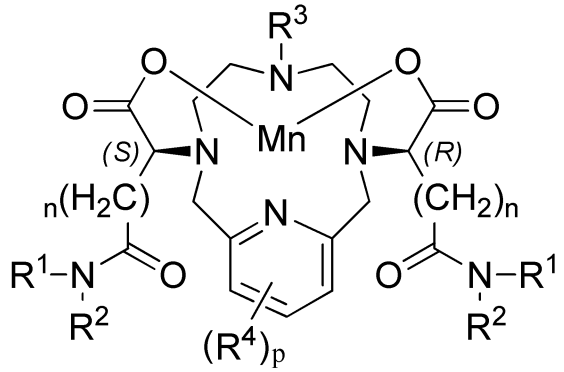
R^3 is selected from C_{1-3} alkyl or -$(CH_2)_m$-C(=0)- NR^5R^6, wherein m is an integer from 2–5, wherein R^5 and R^6 are independently selected from hydrogen, from $C_{1–20}$ hydroxyalkyl, C_{1-6} alkyl, or $C_{3–6}$ aryl optionally-substituted with one or more substituents selected from halo and -C(=O)-NH-$C_{1–6}$ hydroxyalkyl;

R^4 is selected from hydroxy, $C_{1–6}$ alkyl and C_{1-6} hydroxyalkyl;

p is 0-3; and,

each n is an integer from 0–4,

wherein the composition lacks detectable amounts of the compound of Formula (IB):

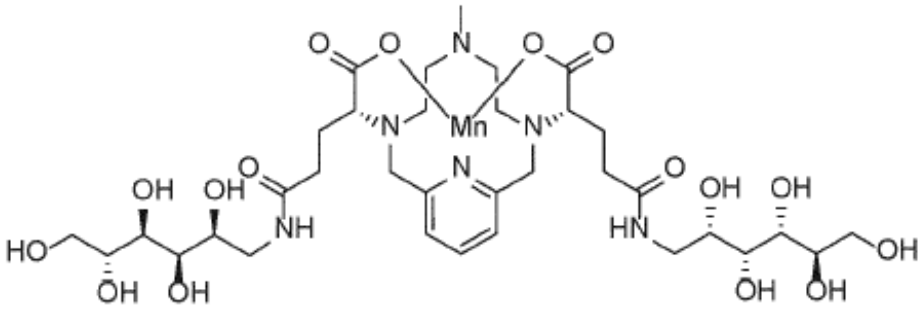


(IB)

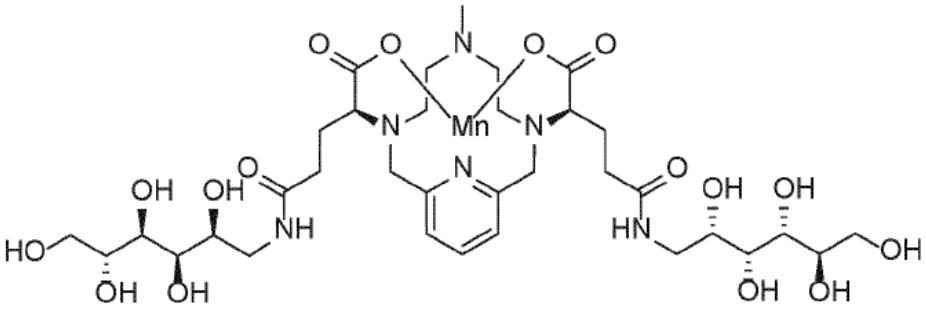
or a salt or solvate thereof.

13. The composition of claim 12, where the compound of Formula IA comprises at least two hydroxy groups.

14. The composition of claim 12, wherein the compound of Formula IA has the structure:



15. The composition of claim 12, wherein the compound of Formula (IB) has the structure:



16. The composition of claim 12, wherein the composition further comprises Mn Chelates having (*R,R*) and/or (*S,S*) stereochemistry.

17. The composition of claim 12, wherein each R^1 is $C_{1–20}$ hydroxyalkyl.

18. The composition of claim 12, wherein R^3 is methyl.

19. The composition of claim 12, wherein R^2 is hydrogen; and p is 0.

20. The composition of claim 12, wherein n is 2.

21. The composition of claim 12, wherein each R^1 is independently $C_{3–9}$ hydroxyalkyl.

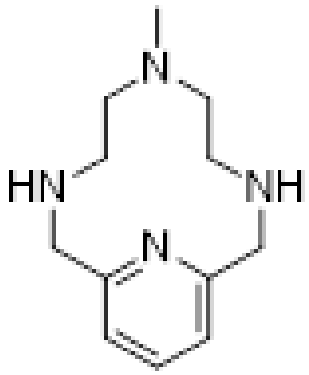
22. The composition of claim 12, wherein each R^1 is independently $C_{3–6}$ hydroxyalkyl.

23. A method of imaging a patient comprising administering the compound of claim 1 or claim 11 to a patient in need thereof, followed by acquiring an MRI image of the patient.

24. A method of imaging a patient comprising administering the composition of claim 12 or claim 14 to a patient in need thereof, followed by acquiring an MRI image of the patient.

25. A method of enantioselective synthesis of the compound of Formula (1A) of claim 1 comprising:

(a) monoalkylation using a first enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate of a compound of formula (III)



(III);

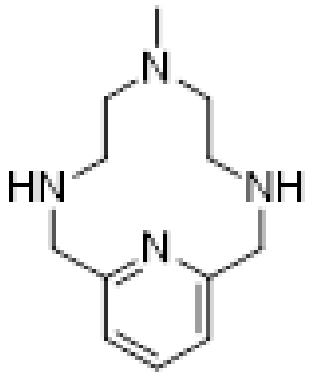
(b) followed by alkylation of the compound from step (a) with a second enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate, the second enantiomer being opposite the first enantiomer;

(c) reacting the product of step (b) with Mn; and

(d) reacting the product of step (c) with an aminoalcohol.

26. A method of enantioselective synthesis of a composition comprising Formula (1A) of claim 12 comprising:

(a) monoalkylation using a first enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate of a compound of formula (III)



(III);

(b) followed by alkylation of the compound from step (a) with a second enantiomer of 5-benzyl 1-*tert*-butyl 2-(methylsulfonyloxy) pentanedioate, the second enantiomer being opposite the first enantiomer;

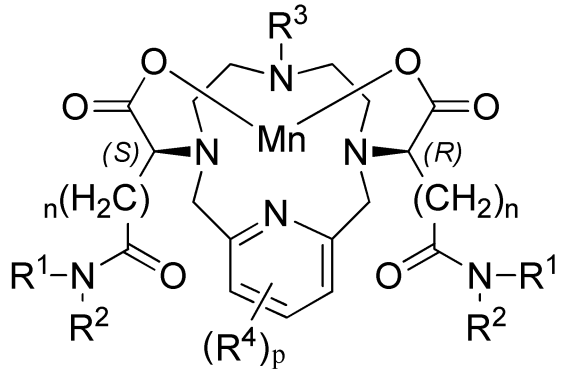
(c) reacting the product of step (b) with Mn; and

(d) reacting the product of step (c) with an aminoalcohol.

27. The method of claim 26, wherein the method results in a composition comprising Formula (IA).

28. A method of making the composition of claim 12, wherein the method comprises:

heating a composition comprising the compound of Formula (1B):



(IB)

or a salt or solvate thereof;

wherein the heating is for a sufficient time and temperature to convert substantially all of the compound of Formula (1B) into the compound of Formula (1A).