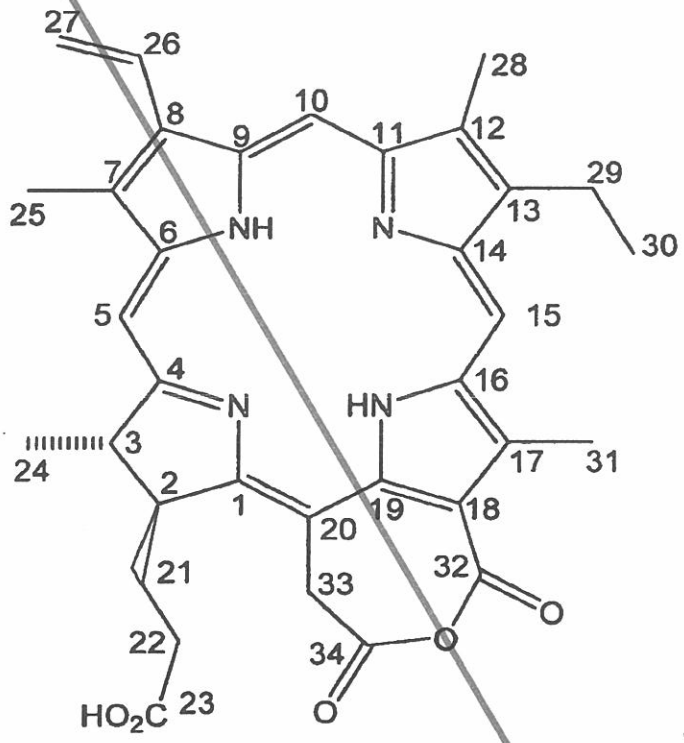
CLAIMS

What is claimed is:

1. A chemical reaction product of chlorin e_6 and a carbodiimide, the chemical reaction product comprising a chlorin e_6 anhydride of the form:



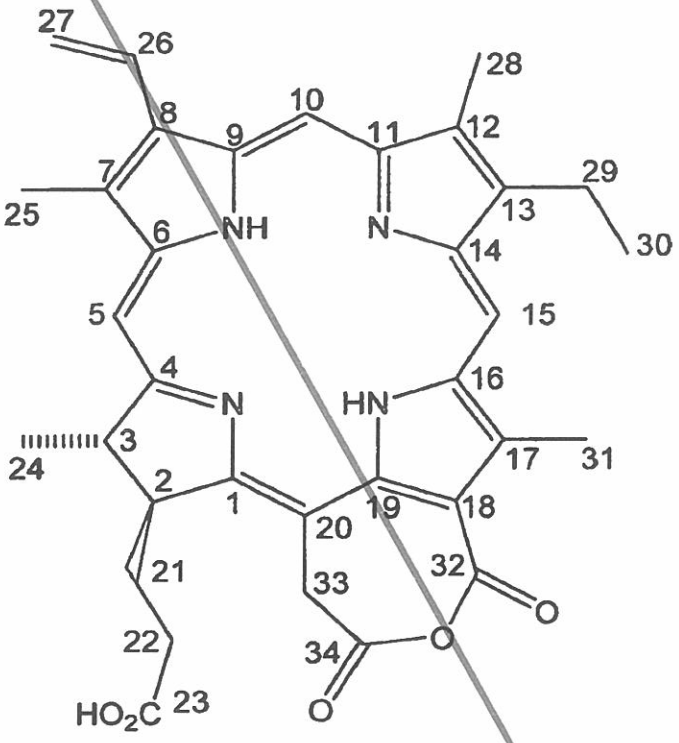
and precursors of diaspartyl chlorin e_6; wherein the precursors of diaspartyl chlorin e_6 comprise less than about 5 mol% based on the total amount of chlorin species present within the chemical reaction product.

2. The chemical reaction product of claim 1 wherein the precursors of diaspartyl chlorin e_6 comprise less than about 3 mol% based on the total amount of chlorin species present within the chemical reaction product.

3. The chemical reaction product of claim 1 wherein the chlorin e_6 anhydride comprises at least about 85 mol% of the chemical reaction product.

4. The chemical reaction product of claim 1 wherein the carbodiimide is N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride or N,N'-dicyclohexyl-carbodiimide.

5. A composition, comprising a compound of Formula I



Formula I,

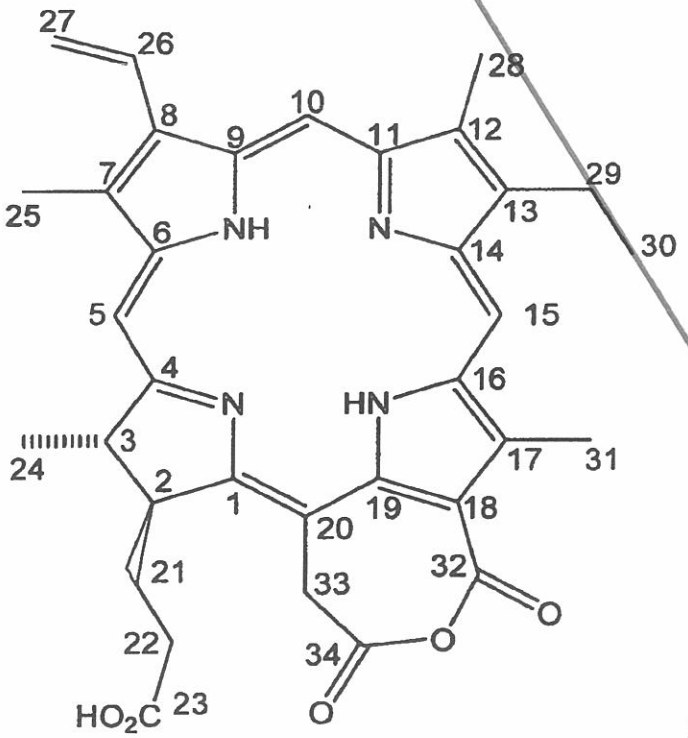
or a pharmaceutically acceptable salt thereof, in a substantially pure form.

6. The composition of claim 5 wherein a total content of the Formula I compound, or a pharmaceutically acceptable salt thereof, is greater than about 85 wt% of the composition.

7. The composition of claim 5 wherein a total content of the Formula I compound, or a pharmaceutically acceptable salt thereof, is greater than about 90 wt% of the composition.

8. The composition of claim 5 wherein a total content of the Formula I compound, or a pharmaceutically acceptable salt thereof, is greater than about 95 wt% of the composition.

9. A process for preparing a chlorin e_6 anhydride, or a pharmaceutically acceptable salt thereof, comprising combining chlorin e_6 with a carboxyl activating agent to obtain a mixture comprising a chlorin e_6 anhydride having the following formula



or pharmaceutically acceptable salt thereof; and purifying the chlorin e_6 anhydride or pharmaceutically acceptable salt thereof.

10. The process of claim 9 wherein the carboxyl activating agent is N,N'-dicyclohexyl-carbodiimide or N-ethyl-N'-(3 dimethylaminopropyl) carbodiimide hydrochloride.

11. The process of claim 9 wherein purifying the chlorin e_6 anhydride, or salt thereof, comprises isolating the chlorin e_6 anhydride, or salt thereof, from the mixture using one or more extraction, separation, chromatography, and/or purification techniques.

12. A method for preparing an intermediate, comprising activating chlorin e_6 with a carboxyl activating agent to obtain a mixture including an intermediate, the intermediate exhibiting a spectrum comprising chemical shifts in ppm at about 1.63 (t, 3H), 1.72/2.05 (m, 2H), 1.78 (d, 3H), 2.50/2.65 (m, 2H), 3.14 (s, 3H), 3.42 (s, 3H), 3.68 (br. q, 2H), 3.69 (s, 3H), 4.63 (br. q, 1H), 4.67 (br. d, 1H), 5.59/5.56 (d, 2H), 6.37/6.16 (d, 1H), 8.07 (dd, 1H), 8.86 (s, 1H), 9.35 (s, 1H), and 9.67 (s, 1H) when analyzed using proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy, at 500 MHz, using d_6-acetone/d_6-dimethyl sulfoxide as a solvent; and isolating the intermediate.

13. The method of claim 12 wherein isolating the intermediate comprises separating the intermediate from the mixture using one or more extraction, separation, chromatography, and/or purification techniques.

14. The method of claim 13 wherein the one or more extraction, separation, chromatography, and/or purification techniques includes contacting the mixture with activated silica.

15. The method of claim 12, further comprising drying the isolated intermediate in the presence of a vacuum.

16. A method for preparing Talaporfin, comprising combining an intermediate prepared according to claim 9 with an amine-containing reagent to form a mono amino acid chlorin e_6, or a pharmaceutically acceptable salt thereof.

17. The method of claim 16, wherein the amine-containing reagent is L-aspartic acid or an ester thereof.

18. A method for preparing Talaporfin, or a pharmaceutically acceptable salt thereof, comprising:

combining an aspartate salt composition having a pH ranging from about 10 to about 12 with a chemical reaction product according to claim 1 in the presence of an organic solvent to form a reaction mixture;

making the reaction mixture basic; and

precipitating the Talaporfin, or a pharmaceutically acceptable salt thereof, from the basic reaction mixture.

19. The method of claim 18, wherein the organic solvent is dimethyl formamide, dimethyl sulfoxide, tetrahydrofuran, ethyl acetate, methylene chloride, or mixtures thereof.

20. The method of claim 18, wherein making the reaction mixture basic comprises adding a hydroxide to maintain the pH of the reaction mixture within a range of about 8 to about 12.

21. The method of claim 18, wherein precipitating the Talaporfin, or a pharmaceutically acceptable salt thereof, comprises adding a suitable precipitation solvent to the basic reaction mixture.

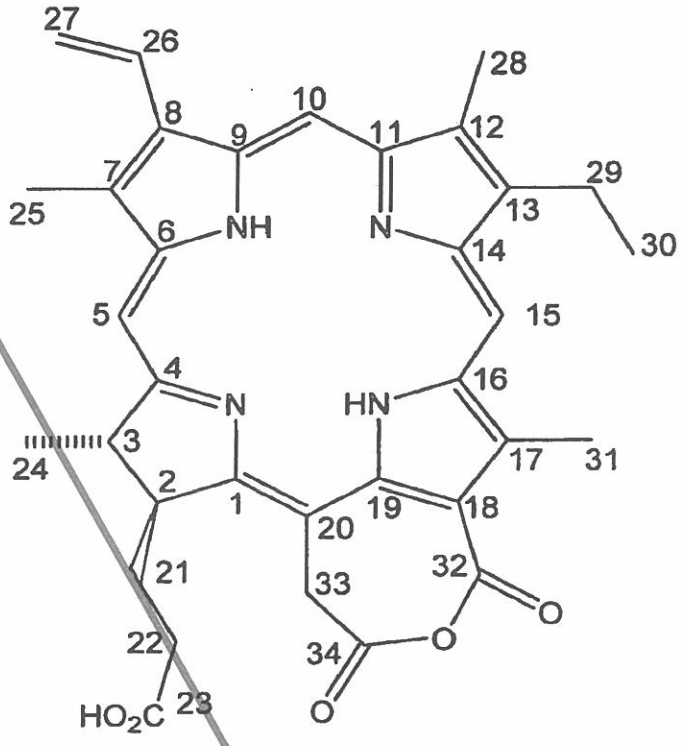
22. The method of claim 18, further comprising separating the Talaporfin, or a pharmaceutically acceptable salt thereof, precipitate from the basic reaction mixture by filtration and/or chromatography.

23. A method of preparing Talaporfin Sodium, comprising utilizing a purified intermediate reaction mixture in a reaction to prepare Talaporfin Sodium, the purified intermediate reaction mixture having been obtained from a crude reaction mixture comprising chlorin e_6, chlorin e_6 anhydride, and precursors of diaspartyl chlorin e_6 from which a significant proportion of the precursors of diaspartyl chlorin e_6 has been removed.

24. The method of claim 23 wherein the purified intermediate reaction mixture comprises less than about 5 mol% precursors of diaspartyl chlorin e_6 based on the total amount of chlorin species present within the purified intermediate reaction mixture.

25. The method of claim 23 wherein the purified intermediate reaction mixture comprises less than about 3 mol% precursors of diaspartyl chlorin e_6 based on the total chlorin species present within the purified intermediate reaction mixture.

26. The method of claim 23, wherein the chlorin e_6 cyclic anhydride is a Formula I chlorin e_6 cyclic anhydride



Formula I,

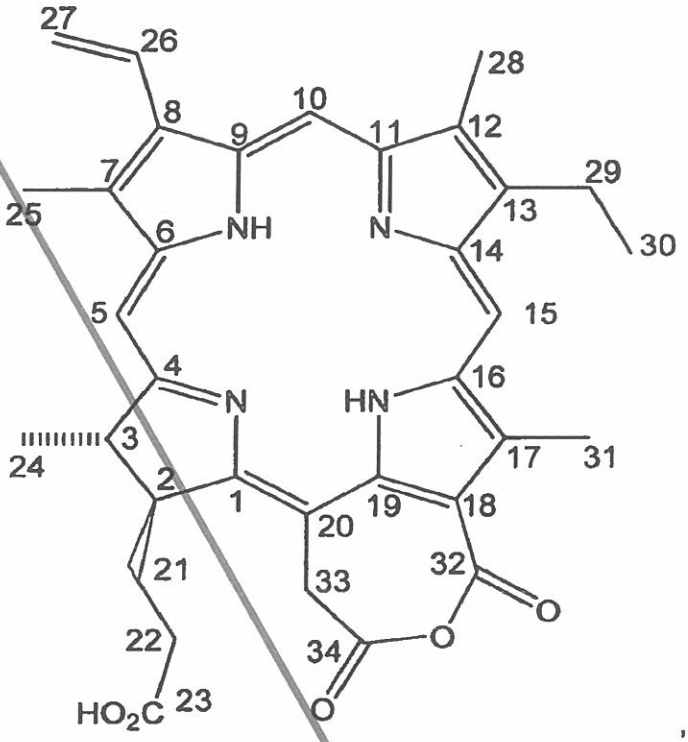
or salt thereof.

27. The method of claim 23, wherein the purified intermediate reaction mixture further comprises dimethyl sulfoxide.

28. The method of claim 23, wherein the purified intermediate reaction mixture further comprises N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride, N,N'-dicyclohexyl-carbodiimide, or dimethyl formamide, or combinations thereof.

29. The method of claim 23, wherein the significant proportion of the precursors of diaspartyl chlorin e_6 has been removed by using activated silica.

30. A reaction product, comprising: a product of a coupling reaction between a first reaction volume and a second reaction volume, the first reaction volume comprising a chlorin e_6 anhydride of the formula



and less than about 5 mol% precursors of diaspartyl chlorin e_6 based on total chlorin species present within the first reaction volume; and the second reaction volume comprising L-aspartic acid or ester thereof;

wherein the reaction product comprises mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, and diaspartyl chlorin e_6.

31. The reaction product of claim 30, wherein the reaction product comprises less than about 2 mol% diaspartyl chlorin e_6 based on total chlorin species present within the reaction product.

32. The reaction product of claim 30, wherein reaction product comprises less than about 1 mol% diaspartyl chlorin e_6 based on total chlorin species present within the reaction product.

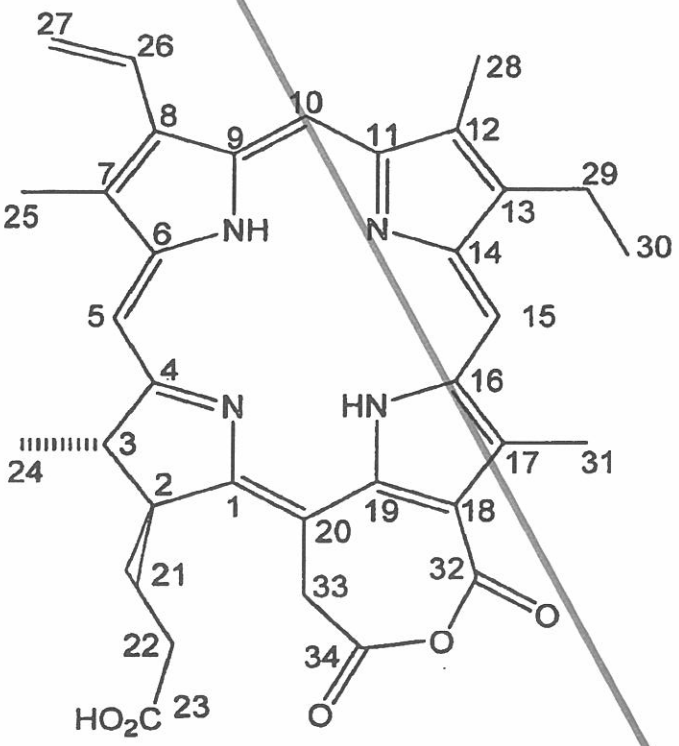
33. The reaction product of claim 30, wherein the first reaction volume further comprises dimethyl sulfoxide or dimethyl formamide.

34. The reaction product of claim 30, wherein the first reaction volume is purified to remove precursors of diaspartyl chlorin e_6 by a separation process.

35. The reaction product of claim 34, wherein the separation process is activated silica chromatography.

36. A process for preparing mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, comprising:

combining chlorin e_6 with a carboxyl activating agent to obtain a mixture comprising a Formula I intermediate



Formula I,

or a salt thereof;

isolating the Formula I intermediate, or salt thereof; and

combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent to form Talaporfin Sodium, or a pharmaceutically acceptable salt thereof.

37. The process of claim 36, wherein combining the chlorin e_6 with the carboxyl activating agent comprises reacting the chlorin e_6 with a carbodiimide.

38. The process of claim 37 wherein the carbodiimide is N,N'-dicyclohexyl-carbodiimide, N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide hydrochloride, N,N'-dicyclohexyl-carbodiimide, or mixtures thereof.

39. The process of claim 36, wherein combining the chlorin e_6 with the carboxyl activating agent comprises reacting the chlorin e_6 with a carbodiimide in the presence of dimethyl sulfoxide or dimethyl formamide.

40. The process of claim 36 wherein reacting the chlorin e_6 with the carboxyl activating agent comprises reacting the chlorin e_6 with N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide hydrochloride or N,N'-dicyclohexyl-carbodiimide.

41. The process of claim 36 wherein isolating the Formula I intermediate, or salt thereof, comprises separating the Formula I intermediate, or salt thereof, from the mixture by using activated silica to yield a substantially pure Formula I intermediate, or salt thereof.

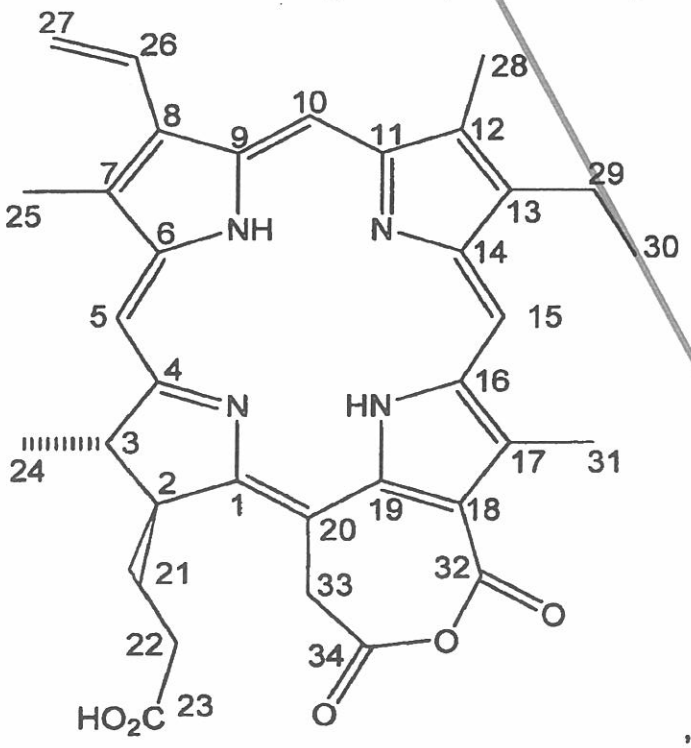
42. The process of claim 36 wherein combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent comprises reacting the isolated Formula I intermediate, or salt thereof, with sodium aspartate to form Talaporfin Sodium.

43. The process of claim 36 wherein combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent comprises combining the isolated Formula I intermediate, or salt thereof, in the presence of dimethyl sulfoxide, with L-aspartic acid or ester thereof to form Talaporfin Sodium.

44. The process of claim 36 wherein combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent comprises coupling the chlorin e_6 anhydride with L-aspartic acid or ester thereof in an aqueous alkaline solution to form a tetra-sodium salt of mono-L-aspartyl chlorin e_6.

45. A process for preparing a photoactive agent, or a pharmaceutically acceptable salt thereof, comprising:

combining a composition comprising a compound of the formula



, or a pharmaceutically acceptable salt thereof, an organic solvent, and one or more of diaspartyl chlorin e_6 precursors, with a basic aqueous sodium aspartate composition to form a crude mono-L-aspartyl chlorin e_6 reaction mixture, the crude reaction

mixture comprising less than about 2 mol% diaspartyl chlorin e_6 based on the total chlorin species within the composition.;

making the reaction mixture basic; and

precipitating a substantial amount of the mono-L-aspartyl chlorin e_6 from the reaction mixture.

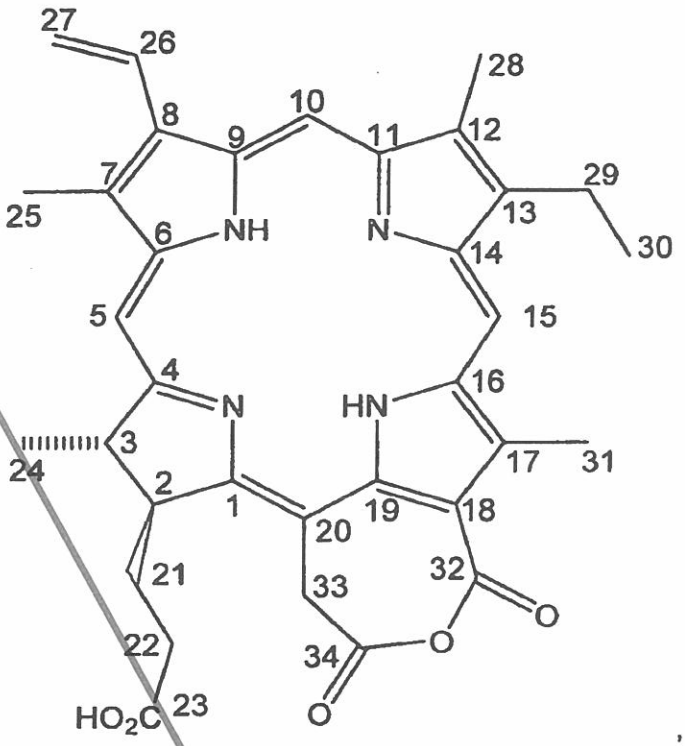
46. The process of claim 45 wherein the at least one diaspartyl chlorin e_6 precursor comprises less than about 5 mol% based on the total chlorin species within the composition.

47. The process of claim 45 wherein the at least one diaspartyl chlorin e_6 precursor comprises less than about 3 mol% based on the total chlorin species within the composition.

48. The process of claim 45 wherein making the reaction mixture basic comprises providing a sufficient amount of an alkaline agent to the reaction mixture to maintain a pH range from about 8 to about 12.

49. The process of claim 45 wherein precipitating a substantial amount of the mono-L-aspartyl chlorin e_6 from the reaction mixture comprises providing a sufficient amount of an organic solvent to cause the precipitation of more that 50 mol% of the mono-L-aspartyl chlorin e_6 present from the reaction mixture.

50. A chemical reaction product of chlorin e_6 and a dehydration agent, the chemical reaction product comprising a chlorin e_6 anhydride of the form:

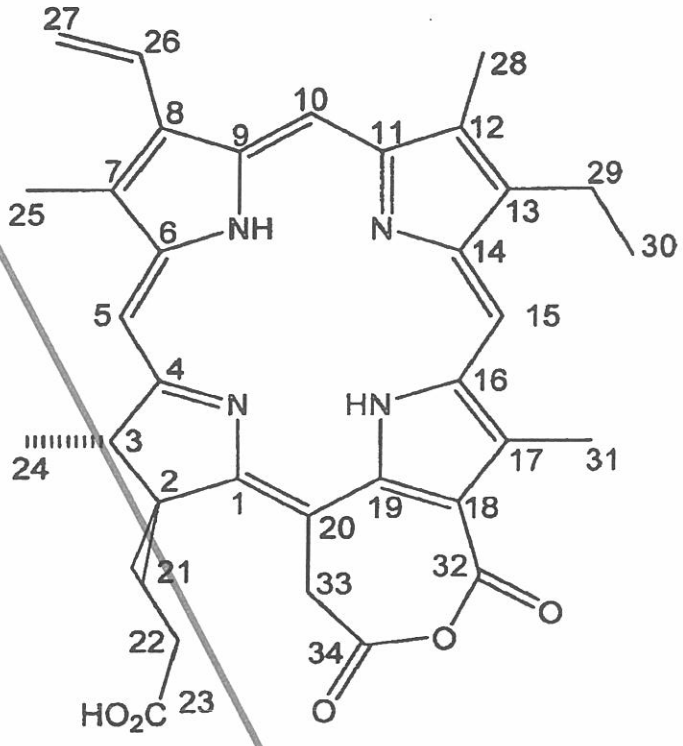


and precursors of diaspartyl chlorin e_6; wherein the precursors of diaspartyl chlorin e_6 comprise less than about 5 mol% based on the total amount of chlorin species present within the chemical reaction product.

51. The chemical reaction product of claim 50 wherein the dehydration agent is a carbodiimide.

52. The chemical reaction product of claim 51 wherein the carbodiimide is N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride or N,N'-dicyclohexyl-carbodiimide.

53. A composition, comprising a compound of Formula I



Formula I,

or a pharmaceutically acceptable salt thereof, in a substantially pure form.

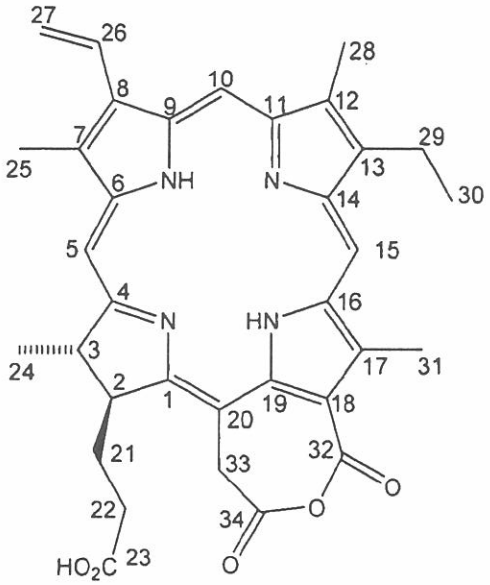
54, The composition of claim 53 wherein a total content of the Formula I compound is greater than about 85 mol% based on the total amount of chlorin species present within the composition.

55. The composition of claim 53 wherein a total content of the Formula I compound is greater than about 90 mol% based on the total amount of chlorin species present within the composition.

56. The composition of claim 53 wherein a total content of the Formula I compound is greater than about 95 mol% based on the total amount of chlorin species present within the composition.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A chemical reaction product of chlorin e_6 and a dehydration agent, the chemical reaction product comprising a chlorin e_6 anhydride of the form:



and precursors of diaspartyl chlorin e_6; wherein the precursors of diaspartyl chlorin e_6 comprise less than about 5 mol% based on the total amount of chlorin species present within the chemical reaction product.

2. The chemical reaction product of claim 1 wherein

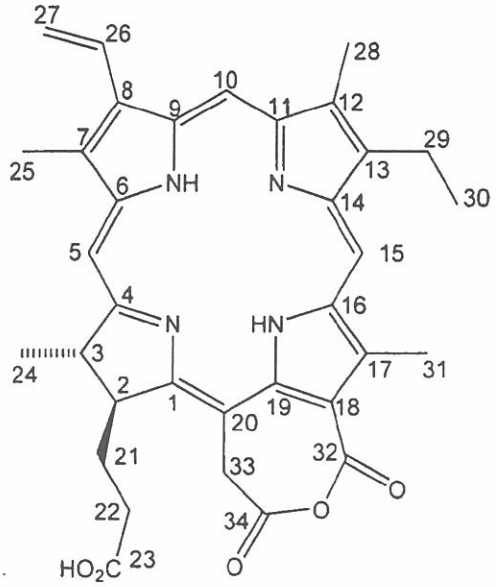
(1) the dehydration agent is a carbodiimide;

(2) the dehydration agent is a carbodiimide and the precursors of diaspartyl chlorin e_6 comprise less than about 3 mol% based on the total amount of chlorin species present within the chemical reaction product;

(3) the dehydration agent is a carbodiimide, and the chlorin e_6 anhydride comprises at least about 85 mol% of the chemical reaction product; or

(4) the dehydration agent is N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride or N,N'-dicyclohexyl-carbodiimide.

3. A composition, comprising a compound of Formula I



Formula I,

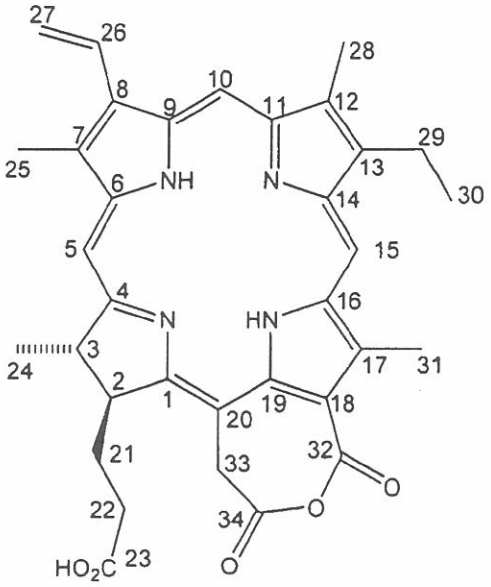
or a pharmaceutically acceptable salt thereof, in a substantially pure form.

4. The composition of claim 3 wherein

(1) a total content of the Formula I compound, or a pharmaceutically acceptable salt thereof, is greater than about 85 wt%, greater than about 90 wt%, or greater than about 95 wt% of the composition; or

(2) a total content of the Formula I compound is greater than about 85 mol%, greater than about 90 mol%, or greater than about 95 mole % based on the total amount of chlorin species present within the composition.

5. A process for preparing a chlorin e_6 anhydride, or a pharmaceutically acceptable salt thereof, comprising combining chlorin e_6 with a dehydration agent to obtain a mixture comprising a chlorin e_6 anhydride having the following formula (I)



(I)

or pharmaceutically acceptable salt thereof; and purifying the chlorin e_6 anhydride or pharmaceutically acceptable salt thereof.

6. The process of claim 5 wherein

(1) the dehydration agent is N,N'-dicyclohexyl-carbodiimide or N-ethyl-N'-(3 dimethylaminopropyl) carbodiimide hydrochloride; or

(2) purifying the chlorin e_6 anhydride, or salt thereof, comprises isolating the chlorin e_6 anhydride, or salt thereof, from the mixture using one or more extraction, separation, chromatography, and/or purification techniques.

7. A method for preparing an intermediate, comprising activating chlorin e_6 with a carboxyl activating agent to obtain a mixture including an intermediate, the intermediate exhibiting a spectrum comprising chemical shifts in ppm at about 1.63 (t, 3H), 1.72/2.05 (m, 2H), 1.78 (d, 3H), 2.50/2.65 (m, 2H), 3.14 (s, 3H), 3.42 (s, 3H), 3.68 (br. q, 2H), 3.69 (s, 3H), 4.63 (br. q, 1H), 4.67 (br. d, 1H), 5.59/5.56 (d, 2H), 6.37/6.16 (d, 1H), 8.07 (dd, 1H), 8.86 (s, 1H), 9.35 (s, 1H), and 9.67 (s, 1H) when analyzed using proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy, at 500 MHz, using d_6-acetone/d_6-dimethyl sulfoxide as a solvent; and isolating the intermediate.

8. The method of claim 7

(1) wherein isolating the intermediate comprises separating the intermediate from the mixture using one or more extraction, separation, chromatography, and/or purification techniques;

(2) wherein isolating the intermediate comprises separating the intermediate from the mixture using one or more extraction, separation, chromatography, and/or purification techniques, the one or more extraction, separation, chromatography, and/or purification techniques including contacting the mixture with activated silica; or

(3) further comprising drying the isolated intermediate in the presence of a vacuum.

9. A method for preparing mono-L-aspartyl chlorin e_6, the method comprising combining an intermediate prepared according to claim 7 with an amine-containing reagent, the amine-containing agent optionally being L-aspartic acid or an ester thereof, to form a mono amino acid chlorin e_6, or a pharmaceutically acceptable salt thereof.

10. A method for preparing mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, the method comprising:

combining an aspartate salt composition having a pH ranging from about 10 to about 12 with a chemical reaction product according to claim 1 in the presence of an organic solvent to form a reaction mixture;

making the reaction mixture basic; and

precipitating the mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, from the basic reaction mixture.

11. The method of claim 10,

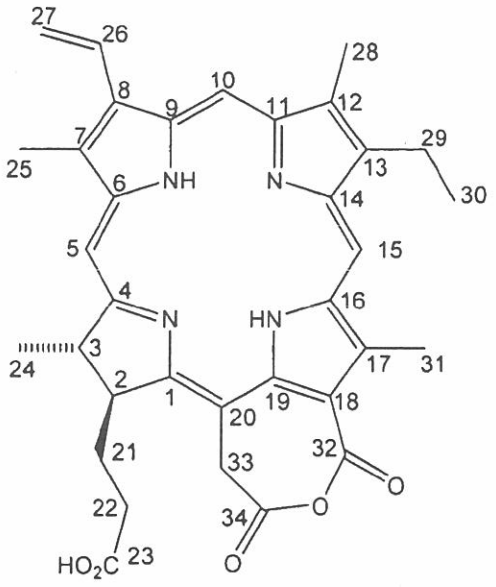
(1) wherein the organic solvent is dimethyl formamide, dimethyl sulfoxide, tetrahydrofuran, ethyl acetate, methylene chloride, or mixtures thereof;

(2) wherein making the reaction mixture basic comprises adding a hydroxide to maintain the pH of the reaction mixture within a range of about 8 to about 12;

(3) wherein precipitating the mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, comprises adding a suitable precipitation solvent to the basic reaction mixture; or

(4) further comprising separating the mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, precipitate from the basic reaction mixture by filtration and/or chromatography.

12. A method of preparing Talaporfin Sodium, comprising utilizing a purified intermediate reaction mixture in a reaction to prepare Talaporfin Sodium, the purified intermediate reaction mixture having been obtained from a crude reaction mixture comprising chlorin e_6, chlorin e_6 anhydride of Formula I:



(I)

or a salt thereof, and less than about 5 mol% precursors of diaspartyl chlorin e_6 based on the total amount of chlorin species present within the purified intermediate reaction mixture.

13. The method of claim 12 wherein

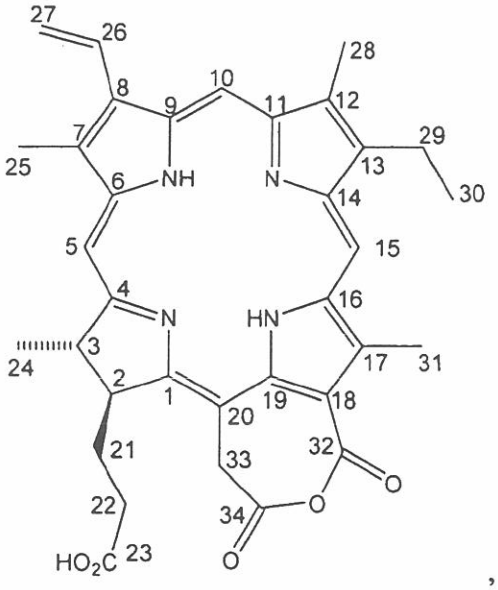
(1) the purified intermediate reaction mixture comprises less than about 3 mol% precursors of diaspartyl chlorin e_6 based on the total chlorin species present within the purified intermediate reaction mixture;

(2) the purified intermediate reaction mixture further comprises dimethyl sulfoxide;

(3) the purified intermediate reaction mixture further comprises N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride, N,N'-dicyclohexyl-carbodiimide, or dimethyl formamide, or combinations thereof; or

(4) the significant proportion of the precursors of diaspartyl chlorin e_6 has been removed by using activated silica.

14. A reaction product, comprising: a product of a coupling reaction between a first reaction volume and a second reaction volume, the first reaction volume comprising a chlorin e_6 anhydride of the formula



and less than about 5 mol% precursors of diaspartyl chlorin e_6 based on total chlorin species present within the first reaction volume; and the second reaction volume comprising L-aspartic acid or ester thereof;

wherein the reaction product comprises mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, and diaspartyl chlorin e_6.

15. The reaction product of claim 14, wherein

(1) the reaction product comprises less than about 2 mol% diaspartyl chlorin e_6 based on total chlorin species present within the reaction product;

(2) the reaction product comprises less than about 1 mol% diaspartyl chlorin e_6 based on total chlorin species present within the reaction product;

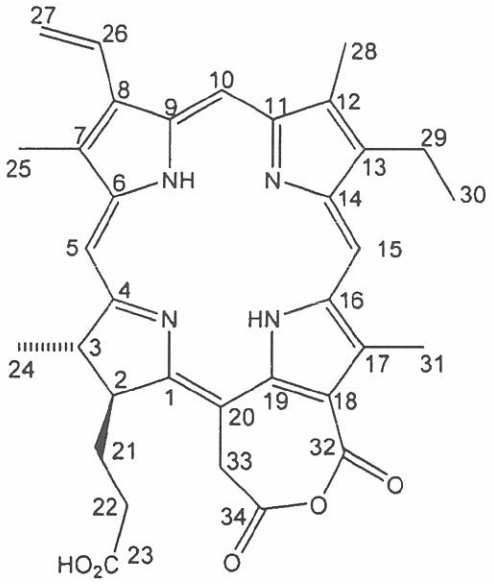
(3) the first reaction volume further comprises dimethyl sulfoxide or dimethyl formamide;

(4) the first reaction volume is purified to remove precursors of diaspartyl chlorin e_6 by a separation process; or

(5) the first reaction volume is purified to remove precursors of diaspartyl chlorin e_6 by activated silica chromatography.

16. A process for preparing mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, comprising:

combining chlorin e_6 with a dehydration agent to obtain a mixture comprising a Formula I intermediate



Formula I,

or a salt thereof;

isolating the Formula I intermediate, or salt thereof; and

combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent to form mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof.

17. The process of claim 16, wherein

(1) combining the chlorin e_6 with the dehydration agent comprises reacting the chlorin e_6 with a carbodiimide;

(2) combining the chlorin e_6 with the dehydration agent comprises reacting the chlorin e_6 with a carbodiimide, the carbodiimide being N,N'-dicyclohexyl-carbodiimide, N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide hydrochloride, or mixtures thereof;

(3) combining the chlorin e_6 with the dehydration agent comprises reacting the chlorin e_6 with a carbodiimide in the presence of dimethyl sulfoxide or dimethyl formamide;

(4) reacting the chlorin e_6 with the dehydration agent comprises reacting the chlorin e_6 with N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide hydrochloride or N,N'-dicyclohexyl-carbodiimide;

(5) isolating the Formula I intermediate, or salt thereof, comprises separating the Formula I intermediate, or salt thereof, from the mixture by using activated silica to yield a substantially pure Formula I intermediate, or salt thereof;

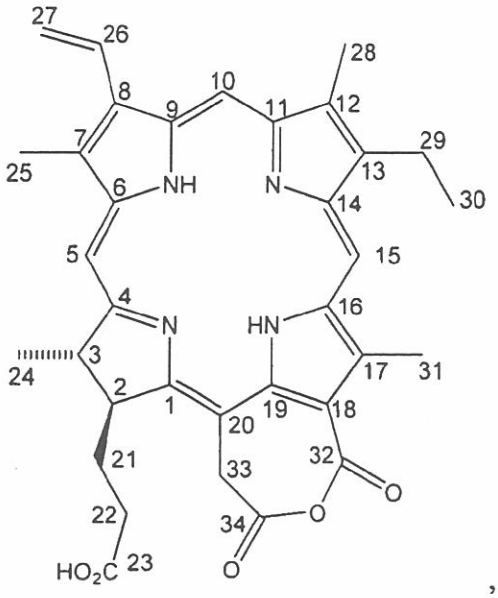
(6) combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent comprises reacting the isolated Formula I intermediate, or salt thereof, with sodium aspartate to form Talaporfin Sodium;

(7) combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent comprises combining the isolated Formula I intermediate, or salt thereof, in the presence of dimethyl sulfoxide, with L-aspartic acid or ester thereof to form mono-L-aspartyl chlorin e_6 or salt or ester thereof; or

(8) combining the isolated Formula I intermediate, or salt thereof, with an amine-containing reagent comprises coupling the chlorin e_6 anhydride with L-aspartic acid or ester thereof in an aqueous alkaline solution to form a tetra-sodium salt of mono-L-aspartyl chlorin e_6 or ester thereof.

18. A process for preparing mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, comprising:

combining a composition comprising a compound of the formula (I)



(I)

or a pharmaceutically acceptable salt thereof, an organic solvent, and one or more of diaspartyl chlorin e_6 precursors, with a basic aqueous sodium aspartate composition to form a crude mono-L-aspartyl chlorin e_6 reaction mixture, the crude reaction mixture comprising less than about 2 mol% diaspartyl chlorin e_6 based on the total chlorin species within the composition;

making the reaction mixture basic; and

precipitating a substantial amount of the mono-L-aspartyl chlorin e_6 or a pharmaceutically acceptable salt thereof, from the reaction mixture.

19. The process of claim 18 wherein

(1) the at least one diaspartyl chlorin e_6 precursor comprises less than about 5 mol% based on the total chlorin species within the composition;

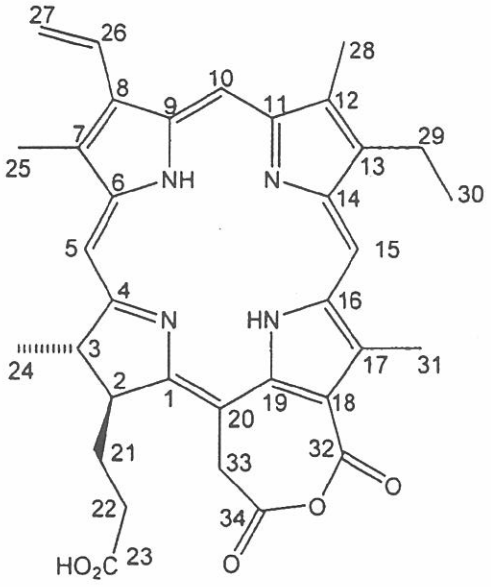
(2) the at least one diaspartyl chlorin e_6 precursor comprises less than about 3 mol% based on the total chlorin species within the composition;

(3) making the reaction mixture basic comprises providing a sufficient amount of an alkaline agent to the reaction mixture to maintain a pH range from about 8 to about 12; or

(4) precipitating a substantial amount of the mono-L-aspartyl chlorin e_6 or a pharmaceutically acceptable salt thereof, from the reaction mixture comprises providing a sufficient amount of an organic solvent to cause the precipitation of more than 50 mol% of

the mono-L-aspartyl chlorin e_6, or a pharmaceutically acceptable salt thereof, present from the reaction mixture.

20. An isolated compound having the following formula (I):



or a pharmaceutically acceptable salt thereof.

21. The compound of claim 20, wherein the compound has a purity of greater than 85 mol%, relative to total chlorin species, as determined by HPLC analysis.

22. The compound of claim 20, wherein the compound has a purity of greater than 90 mol%, relative to total chlorin species, as determined by HPLC analysis.

23. The compound of claim 20, wherein the compound has a purity of greater than 95 mol%, relative to total chlorin species, as determined by HPLC analysis.