CLAIMS:

1. A method for chlorinating a carbohydrate or a derivative thereof comprising reacting the carbohydrate or derivative thereof with a chlorinating agent and irreversibly removing hydrogen chloride produced during the chlorination of the carbohydrate or derivative thereof.

2. The method of claim 1, wherein the carbohydrate or derivative thereof is a sugar or derivative thereof.

3. The method of claim 2, wherein the sugar derivative is a sugar ester.

4. The method of claim 3, wherein the sugar ester is a sucrose-6-ester.

5. The method of claim 4, wherein the chlorinated product obtained is 4,1',6'-trichloro-4,1',6'-trideoxy-6-*O*-ester of galactosucrose (TGS-6E).

6. The method of any one of claims 1 to 5, wherein the chlorinating agent is an acid chloride.

7. The method of claim 6, wherein the acid chloride is selected from the group consisting of thionyl chloride, sulfuryl chloride, phosgene, phosphorus pentachloride, oxalyl chloride, methane sulfonyl chloride, and bis(trichloromethyl)carbonate.

8. The method of any one of claims 1 to 6, wherein the chlorinating agent is a Vilsmeier Reagent having the formula: $[XYC=N^{+}R_2]\ Cl^{-}$, wherein X is hydrogen, aryl, or alkyl, wherein the aryl or alkyl is optionally substituted with a halogen, alkoxy, thioalkoxy, amido, or cyano; Y is a leaving group; and R is hydrogen or alkyl which is optionally substituted with halogen, alkoxy, thioalkoxy, amido, or cyano.

9. The method of claim 8, wherein Y is halogen, heteroalkyl, or a group capable of being displaced by a heteroatomic nucleophile .

10. The method of claim 9, wherein the heteroatomic nucleophile is selected from the group consisting of tosylate, brosylate, besylate, nosylate, mesylate, alkylfluorosulfonates, triflates, nonaflates, and tresylates.

11. The method of claim 9, wherein Y is halogen.

12. The method of any one of claims 8, 9, and 11, wherein X is hydrogen, Y is chloro, and R is methyl.

13. The method of claim 12, wherein the Vilsmeier Reagent which is produced by the reaction of N,N-dimethylformamide with an acid chloride.

14. The method of claim 13, wherein the acid chloride is selected from the group consisting of thionyl chloride, sulfuryl chloride, phosgene, phosphorus pentachloride, oxalyl chloride, methane sulfonyl chloride, and bis(trichloromethyl)carbonate.

15. The method of any one of claims 1 to 14, wherein the chlorination reaction is carried out in a polar or non-polar solvent.

16. The method of claim 15, wherein the polar solvent is a polar aprotic solvent.

17. The method of claim 16, wherein the polar aprotic solvent is selected from the group consisting of N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl pyrrolidone, dimethylsulfoxide, sulfolane, glycol ethers, and the like.

18. The method of claim 17, wherein the polar aprotic solvent is N,N-dimethylformamide.

19. The method of any one of claims 1 to 18, wherein the chlorination is carried out at a temperature of 100 °C or below.

20. The method of claim 19, wherein the chlorination is carried out at a temperature of 85 °C or below.

21. The method of claim 20, wherein the reaction mixture is heated to a temperature not exceeding 85 °C after contacting the carbohydrate with the chlorinating agent.

22. The method of any one of claims 1 to 21, wherein hydrogen chloride is irreversibly removed from the reaction mixture by an irreversible physical process.

23. The method of claim 22, wherein the irreversible physical process comprises applying vacuum or sonic energy to, or inducing cavitation into, the reaction mixture, or distilling off solvent with HCl.

24. The method of claim 23, wherein the vacuum is applied when the reaction is mixture is being heated from a temperature of 50 °C or higher.

25. The method of claim 24, wherein the vacuum is applied until all or substantially all of the sucrose-6-ester is consumed.

26. The method of any one of claims 23 to 25, wherein the vacuum is applied for a period of about 5 minutes to about 12 hours.

27. The method of claim 26, wherein the vacuum is applied for a period of 30 minutes to about 2 hours.

28. The method of claim 23, wherein the distillation is carried out with or without vacuum.

29. The method of any one of claims 1 to 21, wherein hydrogen chloride is irreversibly removed from the reaction mixture by an irreversible chemical process.

30. The method of claim 29, wherein the irreversible chemical process comprises reacting hydrogen chloride with a material that forms a product that contains covalently bonded chlorine atom.

31. The method of claim 30, wherein the material is a cyclic ether or an olefin.

32. The method of claim 31, wherein the cyclic ether is propylene oxide.

33. The method of any one of claims 1 to 32, further comprising providing a moisture free gas atmosphere over the reaction mixture or sparging a moisture free gas through the reaction mixture.

34. The method of claim 33, wherein the moisture free gas is nitrogen, argon, helium, or air.

35. The method of any one of claims 1 to 34, further comprising contacting the reaction mixture with an adsorbent for hydrochloric acid.

36. The method of claim 35, wherein the adsorbent is placed in a scrubbing vessel located external to the chlorinating reactor.

37. The method of claim 36, wherein the adsorbent comprises an acid scavenger.

38. The method of claim 36 or 37, wherein the adsorbent or acid scavenger is selected from the group consisting of zeolites, activated carbon, organic amines, and polymeric resins.

39. A method for chlorinating a carbohydrate or a derivative thereof comprising:

(i) dissolving the carbohydrate or derivative thereof in a polar or non-polar aprotic solvent to obtain a solution of the carbohydrate or derivative thereof;

(ii) forming a chlorinating agent in and/or combining a pre-formed chlorinating agent in a solvent followed by dissolution of carbohydrate or derivative thereof to obtain a chlorination mixture;

(iii) irreversibly removing all or substantially all of the hydrogen chloride produced during reaction of the chlorinating agent with the hydroxy group or groups of the carbohydrate and/or during chlorination of the carbohydrate or derivative thereof;

(iv) optionally heating the reaction mixture from (iii) under an inert gas atmosphere to a temperature of 60 °C for a period of about 2 hours or more; and

(v) optionally heating the reaction mixture to a temperature not more than 85 °C, for a period of up to 16 hours, to obtain the chlorinated carbohydrate or derivative thereof.

40. The method of claim 39, wherein the irreversible removal of the hydrogen chloride produced during chlorination of the carbohydrate or derivative thereof is carried out by an irreversible physical process and/or an irreversible chemical process.

41. The method of claim 40, wherein the irreversible removal is carried out in an irreversible physical process.

42. The method of claim 41, wherein the irreversible physical process comprises applying vacuum or sonic energy or sparging a moisture free gas over the reaction mixture, inducing cavitation into the reaction mixture, or distilling off solvent with HCl.

43. The method of claim 40, wherein the irreversible removal is carried out in an irreversible chemical process or a physical process carried out external to the chlorinating reactor.

44. The method of claim 43, wherein the irreversible chemical process comprises reacting the hydrogen chloride with a material that forms an inert chlorinated product.

45. The method of claim 43, wherein the physical process comprises scrubbing hydrogen chloride on an adsorbent placed in a scrubbing vessel located external to the chlorinating reactor.

46. The method of any one of claims 39 to 45, wherein the chlorinated carbohydrate or derivative thereof is chlorinated sucrose-6-ester.

47. The method of claim 46, wherein the chlorinated sucrose-6-ester produced is free or substantially free of charred residues.

48. The method of claim 46 or 47, wherein the yield of sucralose-6-ester is at least 65%.

49. A method of preparing sucralose comprising de-esterifying the chlorinated sucrose 6-ester obtained according to any one of claims 1 to 48 to obtain the sucralose.

50. Sucralose prepared by the method of claim 49, which is free or substantially free of charred impurities.

51. Sucralose prepared by the method of claim 49, which is free or substantially free of overchlorinated impurities.

CLAIMS

1. A method for chlorinating a carbohydrate or an ester thereof comprising reacting the carbohydrate or ester thereof with a chlorinating agent and irreversibly removing during chlorination at least a portion of the hydrogen chloride produced by the reaction of the chlorinating agent with the carbohydrate or ester thereof, wherein the hydrogen chloride is removed by vacuum distillation.

2. The method of claim 1, wherein the carbohydrate or ester thereof is a sugar or ester thereof, preferably a sugar ester.

3. The method of claim 2, wherein the sugar ester is a sucrose-6-ester.

4. The method of claim 3, wherein the chlorinated product obtained is 4,1',6'-trichloro-4,1',6'-trideoxy-6-*O*-ester of galactosucrose (TGS-6E).

5. The method of any one of claims 1-4, wherein the chlorinating agent is an acid chloride.

6. The method of any one of claims 1-5, wherein the chlorinating agent is a Vilsmeier Reagent having the formula: $[XYC=N^{+}R_2]\ Cl^{-}$, wherein X is hydrogen, aryl, or alkyl, wherein the aryl or alkyl is optionally substituted with a halogen, alkoxy, thioalkoxy, amido, or cyano; Y is a leaving group; and R is hydrogen or alkyl which is optionally substituted with halogen, alkoxy, thioalkoxy, amido, or cyano,

preferably wherein, in the Vilsmeier Reagent, Y is halogen, heteroalkyl, or a group capable of being displaced by a heteroatomic nucleophile, wherein the heteroatomic nucleophile is preferably selected from tosylate, brosylate, besylate, nosylate, mesylate, alkylfluorosulfonate, triflate, nonaflate, and tresylate.

7. The method of claim 6, wherein Y is halogen.

8. The method of claim 6 or 7, wherein, in the Vilsmeier Reagent, X is hydrogen, Y is chloro, and R is methyl, and preferably wherein the Vilsmeier Reagent is produced by the

reaction of N,N-dimethylformamide with an acid chloride, preferably an acid chloride selected from thionyl chloride, sulfuryl chloride, phosgene, phosphorus pentachloride, oxalyl chloride, and methanesulfonyl chloride.

9. The method of any one of claims 1 to 8, wherein the chlorination reaction is carried out in a polar solvent, preferably a polar solvent selected from N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl pyrrolidone, dimethylsulfoxide, sulfolane, and glycol ethers, more preferably N,N-dimethylformamide.

10. The method of claim 1, wherein the chlorination is carried out at a temperature of 90 °C or below.

11. The method of claim 10, wherein the chlorination is carried out at a temperature of 50 °C to 90 °C.

12. The method of any one of claims 1-4, wherein the chlorinating agent is bis(trichloromethyl)carbonate.

13. A method for chlorinating a carbohydrate or an ester thereof, according to claim 1, comprising:

(i) dissolving the carbohydrate or ester thereof in a polar or non-polar aprotic solvent to obtain a solution of the carbohydrate or ester thereof;

(ii) forming a chlorinating agent in and/or combining a pre-formed chlorinating agent in a solvent followed by dissolution of carbohydrate or ester thereof to obtain a chlorination mixture;

(iii) irreversibly removing during chlorination at least a portion of the hydrogen chloride produced by the reaction of the chlorinating agent with the hydroxy group or groups of the carbohydrate and/or the carbohydrate or ester thereof, wherein the hydrogen chloride is irreversibly removed by vacuum distillation;

(iv) optionally heating the reaction mixture from (iii) under an inert gas atmosphere to a temperature of 60 °C for a period of 2 hours or more; and

(v) optionally heating the reaction mixture to a temperature not more than 90 °C, for a period of up to 16 hours, to obtain the chlorinated carbohydrate or ester thereof.

14. The method of claim 13, wherein the carbohydrate or ester thereof is a sugar or ester thereof, preferably a sugar ester, more preferably a sucrose-6-ester.

15. The method of claim 14, wherein the chlorinated product obtained is 4,1',6'-trichloro-4,1',6'-trideoxy-6-*O*-ester of galactosucrose (TGS-6E).

16. The method of claim 3, comprising reacting the sucrose-6-ester dissolved in an N,N-dialkylformamide or N,N-dialkylacetamide solvent with a chlorinating agent and irreversibly removing during chlorination at least a portion of the hydrogen chloride produced by the reaction of the chlorinating agent with the sucrose-6-ester, wherein the chlorination is conducted at a temperature of 50 °C to 90 °C, and the hydrogen chloride is irreversibly removed as a combination with the N,N-dialkylformamide or N,N-dialkylacetamide solvent by vacuum distillation.

17. The method of claim 14, comprising:

(i) dissolving the sucrose-6-ester in N,N-dimethylformamide to obtain a solution of the sucrose-6-ester;

(ii) forming a chlorinating agent in and/or combining a pre-formed chlorinating agent in N,N-dimethylformamide and combining the chlorinating agent or the pre-formed chlorinating agent with the solution of sucrose-6-ester obtained in (i) to obtain a chlorination mixture;

(iii) irreversibly removing during chlorination at least a portion of the hydrogen chloride produced by the reaction of the chlorinating agent with the hydroxy group or groups of the sucrose-6-ester, wherein the chlorination is conducted at a temperature of 50 °C to 90 °C, wherein the hydrogen chloride is irreversibly removed as a combination with N,N-dimethylformamide by vacuum distillation.