

CLAIMS

What is claimed is:

1. A method of preparing a salt of urolithin A, comprising: combining in an alkaline aqueous solution a copper-containing catalyst, 2-bromo-5-hydroxybenzoic acid, and resorcinol, thereby forming the salt of urolithin A.
2. The method of claim 1, wherein the copper-containing catalyst is selected from the group consisting of copper powder, copper-bronze couple, CuSO₄ pentahydrate, CuSO₄ hydrate, anhydrous CuSO₄, Cu(acac)₂, CuCl, CuCl₂, CuBr, CuBr₂, CuI, Cu₂O, CuO, CuOTf, CuCN, and mixtures thereof.
3. The method of claim 2, wherein the copper-containing catalyst is CuSO₄ pentahydrate.
4. The method of claim 1, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃.
5. The method of claim 4, wherein the alkaline aqueous solution comprises NaOH.
6. The method of claim 1, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃, and the copper-containing catalyst is CuSO₄ pentahydrate.
7. The method of claim 1, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, or CsOH, and the copper-containing catalyst is CuSO₄ pentahydrate.
8. The method of claim 1, wherein the alkaline aqueous solution comprises NaOH or KOH, and the copper-containing catalyst is CuSO₄ pentahydrate.
9. The method of claim 1, wherein the alkaline aqueous solution comprises KOH, and the copper-containing catalyst is CuSO₄ pentahydrate.
10. The method of claim 1, wherein the alkaline aqueous solution comprises NaOH, and the copper-containing catalyst is CuSO₄ pentahydrate.
11. The method of any one of claims 1-10, wherein the amount of the copper-containing catalyst is at least a trace amount but no more than 0.01 molar equivalents relative to the amount of 2-bromo-5-hydroxybenzoic acid.

12. The method of any one of claims 1-11, wherein the molar ratio of resorcinol to 2-bromo-5-hydroxybenzoic acid is about 3.5:1 to about 5:1.

13. The method of any one claims 1-11, wherein the molar ratio of resorcinol to 2-bromo-5-hydroxybenzoic acid is about 3.5:1 to about 4.5:1.

14. The method of any one claims 1-11, wherein the molar ratio of resorcinol to 2-bromo-5-hydroxybenzoic acid is about 3.8:1 to about 4.2:1.

15. The method of any one claims 1-11, wherein the molar ratio of resorcinol to 2-bromo-5-hydroxybenzoic acid is about 4.0:1.

16. The method of any one of claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃; and the molar ratio of LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃ to 2-bromo-5-hydroxybenzoic acid is about 2.8:1 to about 5:1.

17. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃; and the molar ratio of LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃ to 2-bromo-5-hydroxybenzoic acid is about 3.0:1 to about 4.8:1.

18. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃; and the molar ratio of LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃ to 2-bromo-5-hydroxybenzoic acid is about 3.2:1 to about 4.6:1.

19. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃; and the molar ratio of LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃ to 2-bromo-5-hydroxybenzoic acid is about 4.2:1 to about 4.6:1.

20. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃; and the molar ratio of LiOH, NaOH, KOH, CsOH, Na₂CO₃, CaCO₃, or Cs₂CO₃ to 2-bromo-5-hydroxybenzoic acid is about 4.4:1.

21. The method of any one of claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, or CsOH; and the molar ratio of LiOH, NaOH, KOH, or CsOH to 2-bromo-5-hydroxybenzoic acid is about 2.8:1 to about 5:1.

22. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, or CsOH; and the molar ratio of LiOH, NaOH, KOH, or CsOH to 2-bromo-5-hydroxybenzoic acid is about 3.0:1 to about 4.8:1.

23. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, or CsOH; and the molar ratio of LiOH, NaOH, KOH, or CsOH to 2-bromo-5-hydroxybenzoic acid is about 3.2:1 to about 4.6:1.

24. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, or CsOH; and the molar ratio of LiOH, NaOH, KOH, or CsOH to 2-bromo-5-hydroxybenzoic acid is about 4.2:1 to about 4.6:1.

25. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises LiOH, NaOH, KOH, or CsOH; and the molar ratio of LiOH, NaOH, KOH, or CsOH to 2-bromo-5-hydroxybenzoic acid is about 4.4:1.

26. The method of any one of claims 1-15, wherein the alkaline aqueous solution comprises NaOH or KOH; and the molar ratio of NaOH or KOH to 2-bromo-5-hydroxybenzoic acid is about 2.8:1 to about 5:1.

27. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH or KOH; and the molar ratio of NaOH or KOH to 2-bromo-5-hydroxybenzoic acid is about 3.0:1 to about 4.8:1.

28. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH or KOH; and the molar ratio of NaOH or KOH to 2-bromo-5-hydroxybenzoic acid is about 3.2:1 to about 4.6:1.

29. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH or KOH; and the molar ratio of NaOH or KOH to 2-bromo-5-hydroxybenzoic acid is about 4.2:1 to about 4.6:1.

30. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH or KOH; and the molar ratio of NaOH or KOH to 2-bromo-5-hydroxybenzoic acid is about 4.4:1.

31. The method of any one of claims 1-15, wherein the alkaline aqueous solution comprises KOH; and the molar ratio of KOH to 2-bromo-5-hydroxybenzoic acid is about 2.8:1 to about 5:1.

32. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises KOH; and the molar ratio of KOH to 2-bromo-5-hydroxybenzoic acid is about 3.0:1 to about 4.8:1.

33. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises KOH; and the molar ratio of KOH to 2-bromo-5-hydroxybenzoic acid is about 3.2:1 to about 4.6:1.

34. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises KOH; and the molar ratio of KOH to 2-bromo-5-hydroxybenzoic acid is about 4.2:1 to about 4.6:1.

35. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises KOH; and the molar ratio of KOH to 2-bromo-5-hydroxybenzoic acid is about 4.4:1.

36. The method of any one of claims 1-15, wherein the alkaline aqueous solution comprises NaOH; and the molar ratio of NaOH to 2-bromo-5-hydroxybenzoic acid is about 2.8:1 to about 5:1.

37. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH; and the molar ratio of NaOH to 2-bromo-5-hydroxybenzoic acid is about 3.0:1 to about 4.8:1.

38. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH; and the molar ratio of NaOH to 2-bromo-5-hydroxybenzoic acid is about 3.2:1 to about 4.6:1.

39. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH; and the molar ratio of NaOH to 2-bromo-5-hydroxybenzoic acid is about 4.2:1 to about 4.6:1.

40. The method of any one claims 1-15, wherein the alkaline aqueous solution comprises NaOH; and the molar ratio of NaOH to 2-bromo-5-hydroxybenzoic acid is about 4.4:1.

41. The method of any one of claims 1-40, wherein the molar yield of the salt of urolithin A is at least about 40% relative to the amount of 2-bromo-5-hydroxybenzoic acid.

42. The method of any one of claims 1-41, wherein the salt of urolithin A is

urolithin A monosodium salt.

43. The method of any one of claims 1-41, wherein the salt of urolithin A is urolithin A disodium salt.

44. The method of any one of claims 1-43, wherein the alkaline aqueous solution is heated at a temperature in the range of about 60 °C to about 90 °C.

45. The method of claim 44, wherein the alkaline aqueous solution is heated at a temperature in the range of about 70 °C to about 80 °C.

46. The method of claim 45, wherein the alkaline aqueous solution is heated at a temperature of about 75 °C.

47. The method of any one of claims 1-46, further comprising isolating the salt of urolithin A, to give an isolated salt of urolithin A.

48. The method of claim 47, wherein the isolated salt of urolithin A is isolated by filtration.

49. The method of claim 47 or 48, wherein the isolated salt of urolithin A contains less than about 1 ppm copper.

50. The method of any one of claims 47-49, further comprising combining a Bronsted acid and the isolated salt of urolithin A, to give a slurry.

51. The method of claim 50, wherein the Bronsted acid is a carboxylic acid.

52. The method of claim 51, wherein the carboxylic acid is acetic acid.

53. The method of claim 51, wherein the carboxylic acid is glacial acetic acid.

54. The method of any one of claims 47-53, wherein the isolated salt of urolithin A is urolithin A monosodium salt.

55. The method of any one of claims 47-53, wherein the isolated salt of urolithin A is urolithin A disodium salt.

56. The method of any one of claims 47-55, wherein the isolated salt of urolithin is at least 95% pure.

57. The method of claim 56, wherein the isolated salt of urolithin is at least 97% pure.

58. The method of claim 57, wherein the isolated salt of urolithin is at least 98% pure.
59. The method of claim 58, wherein the isolated salt of urolithin is at least 99% pure.
60. The method of claim 59, wherein the isolated salt of urolithin is at least 99.5% pure.
61. The method of any one of claims 50-60, wherein the slurry is heated at a temperature in the range of about 100 °C to about 130 °C.
62. The method of claim 61, wherein the slurry is heated at a temperature in the range of about 110 °C to about 120 °C.
63. The method of claim 62, wherein the slurry is heated at a temperature of about 115 C.
64. The method of any one of claims 50-60, wherein the slurry is maintained at a temperature in the range of about 10 °C to about 30 °C.
65. The method of claim 64, wherein the slurry is maintained at a temperature in the range of about 15 °C to about 25 °C.
66. The method of claim 65, wherein the slurry is maintained at a temperature of about 20 °C.
67. The method of any one of claims 50-66, further comprising isolating urolithin A from the slurry.
68. The method of claim 67, wherein the urolithin A is isolated by filtration.
69. The method of claim 67 or 68, wherein the isolated urolithin A is at least 99% pure.
70. The method of claim 69, wherein the isolated urolithin A is at least 99.5% pure.
71. The method of claim 70, wherein the isolated urolithin A is at least 99.8% pure.
72. The method of claim 71, wherein the isolated urolithin A is at least 99.9% pure.