

CLAIMS

What is claimed is:

1. A compound, 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH), that comprises one or more of the following:
 - (a) about $\leq 0.50\%$ to about $\geq 0.30\%$ or about $\leq 0.01\%$ of 8-(4-(2-ethoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-A);
 - (b) about $\leq 0.50\%$ to about $\geq 0.30\%$ or about $\leq 0.01\%$ of 1-isobutyl-8-(4-(2-propoxyethoxy)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-B);
 - (c) about $\leq 0.50\%$ to about $\geq 0.30\%$ of 4,4'-bis(2-butoxyethoxy)biphenyl (Compound VII); and
 - (d) about $\leq 0.50\%$ to about $\geq 0.30\%$ or about $\leq 0.01\%$ of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII); and optionally further comprises one or both of
 - about $\leq 0.50\%$ of 8-(4-butoxyphenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-C); and
 - about $\leq 0.50\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX).
2. The compound of claim 1, that comprises one or both of:
 - (a) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound II-OH-A; and
 - (b) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound II-OH-B; and optionally further comprises about $\leq 0.50\%$ of Compound II-OH-C.
3. The compound of claim 1, that comprises:
 - (a) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound II-OH-A;
 - (b) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound II-OH-B; and
 - (c) about $\leq 0.50\%$ of Compound II-OH-C.

4. The compound of claim 1, that comprises one or both of:
 - (a) about $\leq 0.01\%$ of Compound II-OH-A; and
 - (b) about $\leq 0.01\%$ of Compound II-OH-B; and optionally further comprises about $\leq 0.10\%$ of Compound II-OH-C.
5. The compound of claim 1, that comprises:
 - (a) about $\leq 0.01\%$ of Compound II-OH-A;
 - (b) about $\leq 0.01\%$ of Compound II-OH-B; and
 - (c) about $\leq 0.10\%$ of Compound II-OH-C.
6. The compound of claim 1, that comprises one or both of:
 - (a) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound VII; and
 - (b) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound VIII; and optionally further comprises about $\leq 0.50\%$ of Compound IX.
7. The compound of claim 1, that comprises:
 - (a) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound VII;
 - (b) about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound VIII; and
 - (c) about $\leq 0.50\%$ of Compound IX.
8. The compound of claim 1, that comprises about $\leq 0.01\%$ of Compound VIII, and optionally further comprises one or both of
about $\leq 0.05\%$ of Compound VII, and
about $\leq 0.15\%$ of Compound IX.
9. The compound of claim 1, that comprises:
 - (a) about $\leq 0.05\%$ of Compound VII;
 - (b) about $\leq 0.01\%$ of Compound VIII; and
 - (c) about $\leq 0.15\%$ of Compound IX.
10. The compound of claim 1, that comprises about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound II-OH-A.
11. The compound of claim 1, that comprises $\leq 0.01\%$ of Compound II-OH-A.

12. The compound of claim 1, that comprises about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound II-OH-B.
13. The compound of claim 1, that comprises $\leq 0.01\%$ of Compound II-OH-B.
14. The compound of claim 1, that comprises about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound VII.
15. The compound of claim 1, that comprises about $\leq 0.50\%$ to about $\geq 0.30\%$ of Compound VIII.
16. The compound of claim 1, that comprises $\leq 0.01\%$ of Compound VIII.
17. The compound of any one of claims 1-16, wherein the Compound II-OH has about $\geq 95.0\%$ to about $\leq 96.0\%$ purity.
18. The compound of any one of claims 1-16, wherein the Compound II-OH has about $>97.0\%$ purity.
19. A compound, 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH), with about $\geq 95.0\%$ to about $\leq 96.0\%$ purity.
20. The compound of claim 19, wherein 4,4'-bis(2-butoxyethoxy)biphenyl (Compound VII) is present in 0.20% or less.
21. The compound of claim 19 or 20, wherein 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII) is present in 0.50% or less.
22. The compound of any one of claims 19 to 21, wherein 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX) is present in 0.50% or less.

23. The compound of any one of claims 19 to 22, wherein 4,4'-bis(2-butoxyethoxy)biphenyl (Compound VII) is present in 0.10% or less; or 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII) is present in 0.10% or less; or 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX) is present in 0.15% or less.
24. The compound of any one of claims 19 to 23, wherein said compound comprises one or more of the following:
- (a) 0.50% or less of 8-(4-(2-ethoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-A);
 - (b) 0.50% or less of 1-isobutyl-8-(4-(2-propoxyethoxy)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-B);
 - (c) 0.50% or less of 8-(4-butoxyphenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-C);
 - (d) 0.50% or less of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII); and/or
 - (e) 0.50% or less of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX).
25. The compound of any one of claims 19 to 24, wherein 8-(4-(2-ethoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-A) is present in 0.10% or less.
26. The compound of any one of claims 19 to 25, wherein 1-isobutyl-8-(4-(2-propoxyethoxy)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-B) is present in 0.10% or less.
27. The compound of any one of claims 19 to 26, wherein 8-(4-butoxyphenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-C) is present in 0.10% or less.

28. The compound of any one of claims 19 to 27, wherein 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII) is present in 0.10% or less.

29. The compound of any one of claims 19 to 28, wherein 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX) is present in 0.20% or less.

30. The compound of any one of claims 19 to 29, wherein said compound comprises one or more of the following:

- (a) 0.05% or less of 8-(4-(2-ethoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-A);
- (b) 0.05% or less of 1-isobutyl-8-(4-(2-propoxyethoxy)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-B);
- (c) 0.05% or less of 8-(4-butoxyphenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-C);
- (d) 0.05% or less of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII); and/or
- (e) 0.15% or less of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX).

31. A compound, 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-N-(4-(2-(1-propyl-1H-imidazol-5-yl)acetyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH), or an enantiomer, a stereoisomer, or a combination thereof, with a purity of $\geq 96.0\%$ or $\geq 98.5\%$ or higher, wherein said compound comprises one or more of the following:

- (a) about $\leq 0.50\%$ to about $\geq 0.30\%$ of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII);
- (b) about $\leq 0.50\%$ to about $\geq 0.30\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX);
- (c) about $\leq 0.50\%$ to about $\geq 0.30\%$ of 8-(4-(2-ethoxyethoxy)phenyl)-1-isobutyl-N-(4-(((1-propyl-1H-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-A);

(d) about $\leq 0.50\%$ to about $\geq 0.30\%$ of 1-isobutyl-8-(4-(2-propoxyethoxy)phenyl)-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-B);

(e) about $\leq 0.50\%$ to about $\geq 0.45\%$ of 8-(4-butoxyphenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-C);

(f) about $\leq 0.50\%$ to about $\geq 0.45\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)thio)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-E);

(g) about $\leq 0.50\%$ to about $\geq 0.45\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-F); and

(h) about $\leq 0.50\%$ to about $\geq 0.45\%$ of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide) dimethanesulfonate (Compound I-MsOH-G).

32. The compound of claim 31, further comprising $\leq 1.0\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH).

33. The compound of claim 32, wherein $\leq 0.50\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH) is present.

34. The compound of claim 31, further comprising 2000 ppm or less of 4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)aniline (Compound III).

35. The compound of claim 34, wherein 4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)aniline (Compound III) is present in 1500 ppm or less.

36. The compound of claim 31, further comprising $\leq 2.0\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfonyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-D).

37. The compound of claim 36, wherein $\leq 1.0\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfonyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-D) is present.
38. The compound of claim 31, wherein $\leq 0.10\%$ of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII) is present, provided there is present one or more of compounds (b)-(h).
39. The compound of claim 31, wherein $\leq 0.10\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX) is present, provided there is present one or more of compounds (a) and (c)-(h).
40. The compound of claim 31, wherein $\leq 0.15\%$ of 8-(4-(2-ethoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-A) is present, provided there is present one or more of compounds (a)-(b) and (d)-(h).
41. The compound of claim 31, wherein $\leq 0.15\%$ of 1-isobutyl-8-(4-(2-propoxyethoxy)phenyl)-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-B) is present, provided there is present one or more of compounds (a)-(c) and (e)-(h).
42. The compound of claim 31, wherein $\leq 0.30\%$ of 8-(4-butoxyphenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-C) is present, provided there is present one or more of compounds (a)-(d) and (f)-(h).
43. The compound of claim 31, wherein $\leq 0.30\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)thio)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-E) is present, provided there is present one or more of compounds (a)-(e) and (g)-(h).

44. The compound of claim 31, wherein $\leq 0.20\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-F) is present, provided there is present one or more of compounds (a)-(f) and (h).
45. The compound of claim 31, wherein $\leq 0.15\%$ of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide) dimethanesulfonate (Compound I-MsOH-G) is present, provided there is present one or more of compounds (a)-(g).
46. The compound of claim 31, said compound comprises one or more of the following:
- (i) $\leq 0.30\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH);
 - (ii) $\leq 0.05\%$ of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid) (Compound VIII); and
 - (iii) $\leq 0.05\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX), provided there is present one or more of compounds (c)-(h)
47. The compound of claim 31, said compound comprises one or more of the following:
- (i) 1300 ppm or less wherein 4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)aniline (Compound III);
 - (ii) $\leq 0.10\%$ of 8-(4-(2-ethoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-A);
 - (iii) $\leq 0.10\%$ of 1-isobutyl-8-(4-(2-propoxyethoxy)phenyl)-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-B);
 - (iv) $\leq 0.20\%$ of 8-(4-butoxyphenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-C);
 - (v) $\leq 0.80\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfonyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-D);

(vi) $\leq 0.20\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)thio)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-E);

(vii) $\leq 0.15\%$ of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate (Compound I-MsOH-F); and

(viii) $\leq 0.10\%$ of 8,8'-(4-(2-butoxyethoxy)-1,3-phenylene)bis(1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide) dimethanesulfonate (Compound I-MsOH-G), provided there is present one or more of compounds (a)-(b).

48. The compound of any one of claims 31 to 47, wherein mesylate ester resulting from MsOH is present in 0.001% or less, or 10 ppm or less.

49. The compound of any one of claims 31 to 48, wherein said compound is (*S*)-8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate ((*S*)-Compound I-MsOH).

50. The compound of claim 49, wherein $\leq 0.5\%$ of (*R*)-8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate ((*R*)-Compound I-MsOH) is present.

51. The compound of any one of claim 50, wherein $\leq 0.2\%$ of (*R*)-8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-*N*-(4-(((1-propyl-1*H*-imidazol-5-yl)methyl)sulfinyl)phenyl)-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxamide methanesulfonate ((*R*)-Compound I-MsOH) is present.

52. The compound of claim 51, comprising 5.0% w/w or less or 2.0% w/w or less water content.

53. The compound of claim 1, wherein 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH) is prepared by reacting (4-

(2-butoxyethoxy)phenyl)boronic acid (Compound V-OH) with 8-bromo-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid.

54. The compound of claim 1, wherein 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH) is prepared by reacting 2,4,6-tris(4-(2-butoxyethoxy)phenyl)-1,3,5,2,4,6-trioxatriborinane (Compound V-3) with 8-bromo-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid.

55. The compound of claim 1, wherein 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH) is prepared by reacting a mixture of (4-(2-butoxyethoxy)phenyl)boronic acid (Compound V-OH) and 2,4,6-tris(4-(2-butoxyethoxy)phenyl)-1,3,5,2,4,6-trioxatriborinane (Compound V-3) with 8-bromo-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid.

56. The compound of claim 53 or 55, wherein (4-(2-butoxyethoxy)phenyl)boronic acid (Compound V-OH) is a crystalline form of Compound V-OH.

57. The compound of claim 54 or 55, wherein 2,4,6-tris(4-(2-butoxyethoxy)phenyl)-1,3,5,2,4,6-trioxatriborinane (Compound V-3) is a crystalline form of Compound V-3.

58. The compound of any one of claims 53 to 57, that comprises one or both of:

- (a) about $\leq 0.01\%$ of Compound II-OH-A; and
- (b) about $\leq 0.01\%$ of Compound II-OH-B; and optionally further comprises about $\leq 0.10\%$ of Compound II-OH-C.

59. The compound of any one of claims 53 to 57, that comprises:

- (a) about $\leq 0.01\%$ of Compound II-OH-A;
- (b) about $\leq 0.01\%$ of Compound II-OH-B; and
- (c) about $\leq 0.10\%$ of Compound II-OH-C.