CLAIMS

What is claimed is:

1. A composition of 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 ≤0.50% to about ≥0.30% or about ≤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 ≤0.50% to about ≥0.30% or about ≤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 ≤0.50% to about ≥0.30% of 4,4'-bis(2-butoxyethoxy)biphenyl (Compound VII); and

(d) about ≤0.50% to about ≥0.30% or about ≤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 ≤0.50% of 8-(4-butoxyphenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH-C); and

about ≤0.50% of 8-(4-(2-butoxyethoxy)phenyl)-1-butyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound IX).

2. The composition of claim 1, that comprises one or both of:

(a) about ≤0.50% to about ≥0.30% of Compound II-OH-A; and

(b) about ≤0.50% to about ≥0.30% of Compound II-OH-B; and optionally further comprises about ≤0.50% of Compound II-OH-C.

3. The composition of claim 1, that comprises one or both of:

(a) about ≤0.01% of Compound II-OH-A; and

(b) about ≤0.01% of Compound II-OH-B; and optionally further comprises about ≤0.10% of Compound II-OH-C.

4. The composition of claim 1, that comprises one or both of:

(a) about ≤0.50% to about ≥0.30% of Compound VII; and

(b) about ≤0.50% to about ≥0.30% of Compound VIII; and optionally further comprises about ≤0.50% of Compound IX.

5. The composition of claim 1, that comprises about ≤0.01% of Compound VIII, and optionally further comprises one or both of

about ≤0.05% of Compound VII, and

about ≤0.15% of Compound IX.

6. The composition of claim 1, wherein the Compound II-OH has about >97.0% purity.

7. A composition comprising 8-(4-(2-butoxyethoxy)phenyl)-1-isobutyl-1,2,3,4-tetrahydrobenzo[b]azocine-5-carboxylic acid (Compound II-OH), with ≥95.0% to ≤96.0% purity.

8. The composition of claim 7, wherein 4,4'-bis(2-butoxyethoxy)biphenyl (Compound VII) is present in 0.20% or less.

9. The composition of claim 7, 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.

10. The composition of claim 7, wherein said composition 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).

11. The composition of claim 7, wherein said composition 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).

12. The composition 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;

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; or

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.

13. The composition of claim 12, wherein (4-(2-butoxyethoxy)phenyl)boronic acid (Compound V-OH) is a crystalline form of Compound V-OH.

14. The composition of claim 12, 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.

15. The composition of claim 12, that comprises one or both of:

(a) about ≤0.01% of Compound II-OH-A; and

(b) about ≤0.01% of Compound II-OH-B; and optionally further comprises about ≤0.10% of Compound II-OH-C.

16. The composition of claim 12, that comprises:

(a) about ≤0.01% of Compound II-OH-A;

(b) about ≤0.01% of Compound II-OH-B; and

(c) about ≤0.10% of Compound II-OH-C.