WHAT IS CLAIMED IS:

1. A continuous flow process for making a bicyclic compound, comprising mixing 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane with an organometallic reagent in a continuous flow reactor under first reaction conditions selected to (a) react the 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane with the organometallic reagent to produce [1.1.1]propellane and a salt; and (b) minimize clogging of the continuous flow reactor by the salt, wherein additional mixing within the reactor minimizes clogging by the salt.

2. The process of Claim 1, wherein the organometallic reagent is selected from the group consisting of n-butyllithium, methyllithium, methyllithium lithium bromide complex, and phenyllithium.

3. The process of Claim 1 or 2, wherein the salt comprises LiCl, LiBr, or both.

4. The process of any one of Claims 1 to 3, wherein the first reaction conditions comprise mixing a solvent with the 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane and the organometallic reagent in the continuous flow reactor, wherein the solvent is selected from the group consisting of diethylether, diethoxymethane, dibutylether, methyl tert-butyl ether tetrahydrofuran, 2-methyltetrahydrofuran and mixtures thereof.

5. The process of any one of Claims 1 to 4, wherein the continuous flow reactor comprises a static mixer and wherein the mixing of the 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane with an organometallic reagent is conducted with the static mixer at a mixing rate that is effective to minimize clogging of the continuous flow reactor by the salt.

6. The process of any one of Claims 1 to 5, wherein the continuous flow reactor comprises a first stage and a second stage.

7. The process of Claim 6, wherein the reaction conditions further comprise a first reaction temperature in the range of about -50º C to about 0º C during the first stage.

8. The process of Claim 7, wherein the reaction conditions further comprise a second reaction temperature in the range of about -10º C to about 25º C during the second stage.

9. The process of any one of Claims 6 to 8, wherein the continuous flow reactor further comprises a third stage.

10. The process of Claim 9, wherein the third stage comprises mixing an aqueous composition with the produced [1.1.1]propellane and the salt in the continuous flow reactor to form a salt-containing aqueous phase.

11. The process of Claim 10, wherein the aqueous composition comprises a buffer.

12. The process of Claim 10 or 11, further comprising separating the salt-containing aqueous phase from the produced [1.1.1]propellane to thereby produce a substantially salt-free [1.1.1]propellane composition.

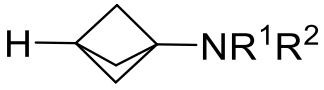
13. The process of Claim 9, wherein the third stage comprises distilling the produced [1.1.1]propellane to thereby produce a substantially salt-free [1.1.1]propellane composition.

14. The process of Claim 12 or 13, further comprising mixing the substantially salt-free [1.1.1]propellane composition with 2,3-butanedione in the continuous flow reactor under second reaction conditions selected to react the produced [1.1.1]propellane with the 2,3-butanedione to produce 1,3-diacetylbicyclo[1.1.1]pentane, wherein the second reaction conditions comprise exposing the produced [1.1.1]propellane and the 2,3-butanedione to a light source.

15. The process of Claim 14, wherein the light source is a source of radiation in the range of about 350 nm to about 380 nm.

16. The process of Claim 14, wherein the light source comprises a light emitting diode.

17. The process of any one of Claims 1 to 13, further comprising mixing the produced [1.1.1]propellane or the substantially salt-free [1.1.1]propellane composition with a magnesium amide reagent in the continuous flow reactor under second reaction conditions selected to react the produced [1.1.1]propellane with the magnesium amide reagent to produce a compound of Formula (I):



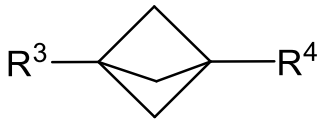

(I)

wherein $R^1$ and $R^2$ are each individually selected from the group consisting of hydrogen, an optionally substituted $C_{1-10}$ alkyl, an optionally substituted $C_{3-10}$ monocyclic cycloalkyl, an optionally substituted $C_{6-10}$ aryl, an optionally substituted ($C_{6-10}$ aryl)alkyl, an

optionally substituted $C_{5-10}$ heteroaryl, an optionally substituted ($C_{5-10}$ heteroaryl)alkyl, phenyl and benzyl; or $R^1$, $R^2$ and the nitrogen to which they are attached together form an optionally substituted heterocyclyl.

18. The process of Claim 17, wherein the magnesium amide reagent comprises at least one selected from $R^1R^2NMgCl$, $R^1R^2NMgBr$, $R^1R^2NMgCl\bullet LiCl$ and $R^1R^2NMgBr\bullet LiBr$.

19. The process of any one of Claims 1 to 13, further comprising mixing the produced [1.1.1]propellane with a reagent of the formula $R^3$-$MX^1$ and a compound of the formula $R^4$-$X^2$ in the continuous flow reactor under second reaction conditions selected to react the produced [1.1.1]propellane with the reagent of the formula $R^3$-$MX^1$ and the compound of the formula $R^4$-$X^2$ to produce a compound of Formula (II):




(II)

wherein $R^3$ is selected from the group consisting of an optionally substituted $C_{1-10}$ alkyl, an optionally substituted $C_{2-10}$ alkenyl, an optionally substituted $C_{3-10}$ cycloalkyl, an optionally substituted $C_{5-10}$ cycloalkenyl, an optionally substituted $C_{6-10}$ aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl;

wherein $R^4$ is selected from the group consisting of an optionally substituted $C_{1-10}$ alkyl, an optionally substituted $C_{2-10}$ alkenyl, an optionally substituted $C_{3-10}$ cycloalkyl, an optionally substituted $C_{5-10}$ cycloalkenyl, an optionally substituted $C_{6-10}$ aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl

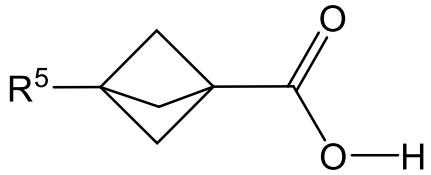
wherein $X^1$ and $X^2$ are each independently selected from the group consisting of a halide and a pseudohalide;

wherein M is magnesium or lithium; and

wherein the second reaction conditions comprise the presence of a transition metal catalyst that is selected from the group consisting of a Pd catalyst and a Ni catalyst.

20. The process of Claim 19, wherein the second reaction conditions comprise mixing a zinc salt with the produced [1.1.1]propellane, the reagent of the formula $R^3$-$MX^1$ and the compound of the formula $R^4$-$X^2$ in the continuous flow reactor prior to mixing with the transition metal catalyst.

21. The process of any one of Claims 1 to 13, further comprising mixing the produced [1.1.1]propellane with a compound of the formula $R^5$-$X^3$ and carbon dioxide in the continuous flow reactor under second reaction conditions selected to react the produced [1.1.1]propellane with the compound of the formula $R^5X^3$ and the carbon dioxide to produce a compound of Formula (III):

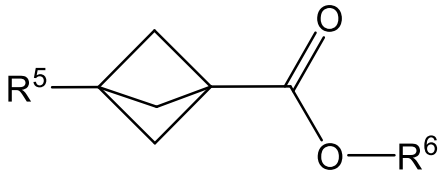


(III)

wherein $R^5$ is selected from the group consisting of an optionally substituted $C_{1-10}$ alkyl, an optionally substituted $C_{2-10}$ alkenyl, an optionally substituted $C_{3-10}$ cycloalkyl, an optionally substituted $C_{5-10}$ cycloalkenyl, an optionally substituted $C_{6-10}$ aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl; and

wherein $X^3$ is selected from the group consisting of a lithium halide, a lithium pseudohalide, a zinc halide, a zinc pseudohalide, a magnesium halide, and a magnesium pseudohalide.

22. The process of any one of Claims 1 to 13, further comprising mixing the produced [1.1.1]propellane with a compound of the formula $R^5$-$X^3$ and a compound of the formula $X^4$-$CO_2R^6$ in the continuous flow reactor under second reaction conditions selected to react the produced [1.1.1]propellane with the compound of the formula $R^5X^3$ and the compound of the formula $X^4$-$CO_2R^6$ to produce a compound of Formula (IV):



(IV)

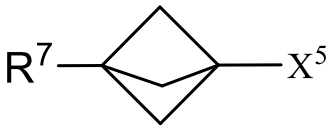
wherein $R^5$ is selected from the group consisting of an optionally substituted $C_{1-10}$ alkyl, an optionally substituted $C_{2-10}$ alkenyl, an optionally substituted $C_{3-10}$ cycloalkyl, an optionally substituted $C_{5-10}$ cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl;

wherein $R^6$ is an optionally substituted $C_{1-10}$ alkyl or an optionally substituted $C_{6-10}$ aryl;

wherein $X^3$ is selected from the group consisting of a lithium halide, a lithium pseudohalide, a magnesium halide, and a magnesium pseudohalide; and

wherein $X^4$ is a halide or a pseudohalide.

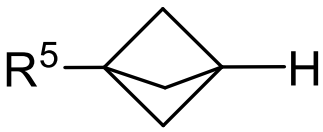
23. The process of any one of Claims 1 to 13, further comprising mixing the produced [1.1.1]propellane with a compound of the formula $R^7$-$X^5$ in the continuous flow reactor under second reaction conditions selected to react the produced [1.1.1]propellane with the compound of the formula $R^7$-$X^5$ to produce a compound of Formula (V):



(V)

wherein $X^5$ is iodide (I) or bromide (Br) and $R^7$ is selected from the group consisting of an optionally substituted $C_{1-10}$ alkyl, an optionally substituted $C_{2-10}$ alkenyl, an optionally substituted $C_{3-10}$ cycloalkyl, an optionally substituted $C_{5-10}$ cycloalkenyl, an optionally substituted $C_{6-10}$ aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl.

24. The process of any one of Claims 1 to 13, further comprising mixing the produced [1.1.1]propellane with a compound of the formula $R^5X^3$ and water in the continuous flow reactor under second reaction conditions selected to react the produced [1.1.1]propellane with the compound of the formula $R^5X^3$ and the water to produce a compound of Formula (VI):



(VI)

wherein $R^5$ is selected from the group consisting of an optionally substituted $C_{1-10}$ alkyl, an optionally substituted $C_{2-10}$ alkenyl, an optionally substituted $C_{3-10}$ cycloalkyl, an optionally substituted $C_{5-10}$ cycloalkenyl, an optionally substituted $C_{6-10}$ aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl; and

wherein $X^3$ is selected from the group consisting of a lithium halide, a lithium pseudohalide, a zinc halide, a zinc pseudohalide, a magnesium halide, and a magnesium pseudohalide.

25. A continuous flow process for making 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane, comprising mixing 3-chloro-2-(chloromethyl)prop-1-ene with $CHBr_3$ in a continuous flow reactor under reaction conditions selected to produce the 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane.

26. The process of Claim 25, wherein the reaction conditions comprise mixing an aqueous base with the 3-chloro-2-(chloromethyl)prop-1-ene and the $CHBr_3$ in the continuous flow reactor.

27. The process of Claim 26, wherein the aqueous base is aqueous NaOH, aqueous KOH or a mixture thereof.

28. The process of any one of Claims 25-27, wherein the reaction conditions comprise phase transfer conditions.

29. The process of Claim 28, wherein the phase transfer conditions comprise a catalytically effective amount of a phase transfer catalyst selected from pinacol, a crown ether or a mixture thereof.

30. The process of Claim 29, wherein the crown ether is 18-crown-6.

31. The process of Claim 25, wherein the reaction conditions comprise mixing an organic solvent, an aqueous base, and a phase transfer catalyst with the 3-chloro-2-(chloromethyl)prop-1-ene and the $CHBr_3$ in the continuous flow reactor under phase transfer reaction conditions.