



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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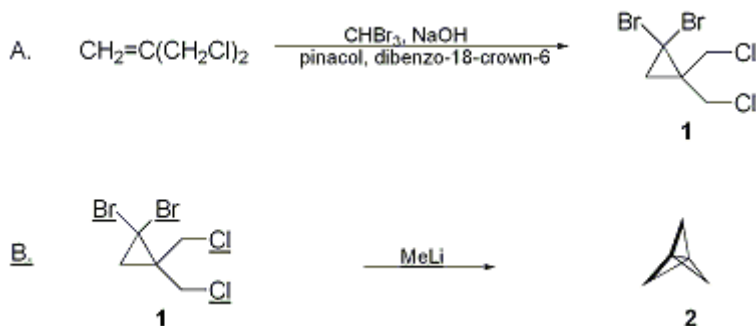
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 10, p.658 (2004); Vol. 75, p.98 (1998).

[1.1.1]PROPELLANE

[Tricyclo[1.1.1.0^{1,3}]pentane]



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Checked by Rajib Pal, Peter Belica, and Steven Wolff.

1. Procedure

A. *1,1-Dibromo-2,2-bis(chloromethyl)cyclopropane (1)*. Into a 1-L, three-necked, round-bottomed flask, equipped with an efficient mechanical stirrer, a thermometer, and a condenser equipped with a potassium hydroxide drying tube, are placed 54.1 g (0.403 mol) of *3-chloro-2-(chloromethyl)propene* (Note 1), 212 g (0.805 mol) of *bromoform* (Note 2), 1.70-2.00 g (14.4-16.9 mmol) of *pinacol* (Note 3), and 1.45 g (3.94 mmol) of *dibenzo-18-crown-6* (Note 4). With very vigorous stirring (Note 5), 312 g of an aqueous 50% *sodium hydroxide* solution that has been cooled to 15°C is added in one portion. The reaction mixture turns orange, then brown, then black within 5 min, and the temperature of the reaction mixture begins to rise. Within 20 min, the internal reaction temperature is 49-50°C at which point the reaction flask is cooled with a room-temperature water bath, and the reaction temperature decreases to ca. 20°C. After 1 hr, the bath is removed and the reaction mixture is heated to 40°C (internal temperature) with an oil bath. The vigorously stirred mixture is maintained at this temperature for 4 days (Note 6). The reaction mixture is cooled to room temperature, diluted with 500 mL of water, and filtered through a pad of Celite on a glass-fritted funnel (pore size C), using a water aspirator (Note 7). Up to an additional 1-L of water is used to rinse the thick black reaction mixture from the flask. The resulting golden-yellow filtrate is discarded (Note 8). The black, solid residue in the frit, and any material remaining in the reaction flask are transferred to a 1-L beaker with *pentane*, *acetone*, and a glass rod, and the solution is vigorously stirred with an additional 500 mL of a 1:1 (v/v) solution of *acetone* and *pentane* for 30 min. This mixture is filtered through a glass-fritted funnel using a minimal layer of Celite. The Celite pad is washed thoroughly with 1:1 *pentane/acetone* solution, and the resulting brown filtrate is dried over *magnesium sulfate*. Concentration using a rotary evaporator, followed by distillation under reduced pressure (bp 75-85°C/0.4 mm), and low temperature (ca. -20°C) recrystallization from *pentane* (ca. 1 mL/g of product), provide 70-95 g (60-80% yield) of the product as small, white crystals (mp 47.5-50°C) (Note 9) and (Note 10).

B. *[1.1.1]Propellane (2)*. A 500-mL, three-necked, round-bottomed flask that has been flame dried under reduced pressure and purged with *argon*, is equipped with a vacuum adapter equipped with an argon balloon, an efficient mechanical stirrer, and a pressure-equalizing, 150-mL addition funnel equipped with a rubber septum. The flask is charged with a 25-g (0.085 mol) portion of material obtained from part A, and 25 mL of *pentane* (Note 11). A *diethyl ether* solution of *methyllithium*, 132 mL of a 1.4 M (0.185 mol) solution (Note 12), is transferred to the addition funnel via cannula under a flow of *argon*. The reaction flask is cooled to -78°C and the *methyllithium* is added over 15 min with vigorous stirring. The reaction mixture is maintained at -78°C for 10 - 15 min; then the -78°C cooling bath is replaced with an ice-water bath (0°C), and the addition funnel is replaced with a rubber septum equipped with an *argon* balloon. Stirring is continued for an additional hour; then the volatile materials are transferred under reduced pressure to a flame-dried flask that is cooled to -196°C (Note 13). Based

on the recovery of the [thiophenol](#) adduct, the yield of [\[1.1.1\]propellane](#) is between 75 and 88%.

Determination of the yield of propellane. Wiberg and Waddell have shown that propellane reacts spontaneously in normal room light with [thiophenol](#) to yield [bicyclo\[1.1.1\]pentyl phenyl sulfide](#) in 98% yield.² A slight modification of their method provides a good estimate of the yield of propellane. Thus, a 3.0-mL portion of the propellane solution is transferred via a gas-tight syringe to a tared, flame-dried, argon-purged, 10-mL, round-bottomed flask equipped with a stirring bar and maintained under a static atmosphere of argon. [Thiophenol](#) is added in slight excess via syringe and the mixture is stirred under room light for 15 min. Concentration of the solution provides a mixture of [thiophenol](#) and [bicyclo\[1.1.1\]pentyl phenyl sulfide](#). The ratio of compounds may be determined by ¹H NMR or GLC, and the yield of propellane calculated ([Note 14](#)). Alternatively, the mixture may be diluted with [pentane](#), washed with 1 M [sodium hydroxide](#), dried with [magnesium sulfate](#), and concentrated to provide [bicyclo\[1.1.1\]pentyl phenyl sulfide](#) from which the yield of propellane is calculated. The reaction of [thiophenol](#) with propellane is assumed to be quantitative; thus yields for [bicyclo\[1.1.1\]pentyl sulfide](#) are 75 to 88% based on **1**.

Wiberg and Waddell also noted that propellane reacts with [iodine](#) in 88% yield.² Alber and Szeimies report a somewhat lower yield (61%) when an ethereal solution of propellane is treated with a solution of [iodine](#) in [ether/pentane](#) while being irradiated.³ Thus, titration of a portion of the resulting propellane solution with [iodine](#) provides an estimate of the minimum yield. A 3.0-mL portion of the propellane solution is transferred as noted above. Small pieces of [iodine](#) are added with stirring under room light over 10 min until just before the dark color persists. Concentration of the solution provides [1,3-diiodobicyclo\[1.1.1\]pentane](#) from which the minimal concentration of the propellane solution and minimal yield of propellane may be estimated if [iodine](#) is not added in excess. Alternatively, a solution of [iodine](#) in [diethyl ether/pentane](#) may be added instead of neat [iodine](#).

2. Notes

- [3-Chloro-2-\(chloromethyl\)propene](#) was prepared according to the method of Lynch and Dailey.⁴ Percent purity was determined by GLC, and 0.400 mol of starting material was calculated accordingly. A typical experiment used ca. 54 g of alkene that was 92-93% pure by GLC
- [Bromoform](#) (96%) stabilized with 1-3% [ethanol](#), was purchased from the Aldrich Chemical Company, Inc. , and used without further purification.
- [Pinacol](#) was purchased from the Aldrich Chemical Company, Inc. , and used without further purification.
- [Dibenzo-18-crown-6](#) (98%) was purchased from the Aldrich Chemical Company, Inc. , and used without further purification.
- A Glas Col GT-21 mechanical stirrer was used at maximum speed.
- In some runs, the internal temperature varied between 37-43°C over the 4-day period without a significant change in yield.
- Aspirator filtration through a pad of Celite was beneficial to prevent small particulate matter from clogging the fritted funnel. However, it was necessary to break up the pad of Celite to allow for effective filtration.
- [Pentane](#) extraction of the primarily aqueous filtrate provides only an additional 4 g (3%) of product.
- If solvents have not been evaporated completely, a forerun may be recovered with bp up to 50°C/0.5-1 mm. This should be trapped with a dry ice-acetone bath. If the sample is evaporated well prior to distillation, crystallization of the product will occur upon standing. Stirring a [pentane](#) solution of the crude product with decolorizing [carbon](#) , followed by filtration, and low temperature (ca. -20°C) recrystallization gives material that is suitable for many applications (mp 44-45°C); ¹H NMR (CDCl₃) δ: 1.80 (s, 2 H), 3.19 (s, 4 H) ; ¹³C NMR (CDCl₃) δ: 32.02 (s), 33.89 (t), 35.20 (s), 47.58 (t) .
- Reactions that were stirred for up to 5 or 6 days had slightly higher yields (up to 80%) and needed minimum purification. Reactions that were stirred for less than 3 days or more than 6 days had slightly lower yields (60% after recrystallization). The checkers found that distilled [1,1-dibromo-2,2-bis\(chloromethyl\)cyclopropane](#) was sufficiently pure (¹H NMR and mp) for the subsequent step and did not require recrystallization. The procedure has been carried out on a 1-mol scale with comparable results.
- High purity grade [pentane](#) was purchased from Fisher Scientific Company or Burdick and Jackson

Inc. and was used without further purification. Recently opened solvent was always used.

12. **Methylithium** (1.4 M, low halide) in **diethyl ether**, was purchased from the Aldrich Chemical Company, Inc. , and was used without further purification. Titration using the method of Watson and Eastham⁵ was used to determine the molarity. The best and most reproducible results (ca. 88% yield) were obtained when freshly opened **methylithium** was used. The yield was severely depressed when 0.86 M **methylithium** was used (< 33%). The checkers used a recently purchased, freshly opened bottle of **methylithium** and did not determine its molarity by titration.

13. The volatile materials are transferred under essentially static conditions. Bulb-to-bulb vacuum transfer may be accomplished with a standard 24/40 short path distillation apparatus. The reaction flask may be warmed slightly (40°C) with a water bath and the receiving flask is cooled in a liquid nitrogen bath. Vacuum is applied intermittently to allow for effective transfer of the volatile material. It is helpful to continue stirring the reaction flask during the transfer.

14. Integration and normalization of the ¹H NMR peaks for the acidic proton of **thiophenol** (d 3.4 ppm) and the **bicyclo[1.1.1]pentyl** group (d 1.96 ppm) were used to calculate the yield of propellane; ¹³C NMR (125 MHz, CDCl₃) δ: 1.0 and 74.2.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

This preparation of **1,1-dibromo-2,2-bis(chloromethyl)cyclopropane** is a modification of the method reported by Szeimies and co-workers,⁶ and represents a significant improvement in both the convenience of the workup and the yield of the reaction. In the present method, dilution and filtration of the reaction mixture leave behind a mostly solid residue from which the product is easily obtained. Most significantly, the problematic emulsion that forms in the Szeimies method is effectively eliminated.

The cocatalytic effects of **pinacol** in the phase transfer catalysis (PTC) of dihalocarbene additions to alkenes were noted by Dehmlow and co-workers who showed that **pinacol** accelerates the PTC deprotonation of substrates up to pKa 27.⁷ Dehmlow also studied the effects of various crown ethers as phase transfer catalysts in the addition of **dibromocarbene** to allylic bromides.⁸ In Dehmlow's study, elevated temperature (40°C) and **dibenzo-18-crown-6** did not give the highest ratio of addition/substitution to **allyl bromide**. However, the submitters' use of **pinacol**, **dibenzo-18-crown-6**, and heat in the addition of **dibromocarbene** to **3-chloro-2-(chloromethyl)propene** lead to good yields and a procedure with a significantly more facile work-up. In the course of the submitters' work in this area, Della and Taylor also reported an improvement in the synthesis of **1**;⁹ however, the submitters were unable to reproduce their results, even with several attempts.

The synthesis of **[1.1.1]propellane** from **1** is essentially as reported by Michl and co-workers,¹⁰ with only a slight modification in the process of transferring the crude propellane solution. As a result of the submitters' improvements in the preparation of **3-chloro-2-(chloromethyl)propene**⁴ and **1,1-dibromo-2,2-bis(chloromethyl)cyclopropane**, many of the difficulties in the Szeimies route to **[1.1.1]propellane** have been eliminated.

This preparation is referenced from:

- **Org. Syn. Coll. Vol. 10, 86**

References and Notes

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Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

[1.1.1]Propellane:

Tricyclo[1.1.1.0^{1,3}]pentane (9); (35634-10-7)

1,1-Dibromo-2,2-bis(chloromethyl)cyclopropane:

Cyclopropane, 1,1-dibromo-2,2-bis(chloromethyl)- (11); (98577-44-7)

3-Chloro-2-(chloromethyl)-1-propene:

1-Propene, 3-chloro-2-(chloromethyl)- (8,9); (1871-57-4)

Bromoform:

Methane, tribromo- (8,9); (75-25-2)

Pinacol:

2,3-Butanediol, 2,3-dimethyl- (8,9); (76-09-5)

Dibenzo-18-crown-6:

Dibenzo[b,k][1,4,7,10,13,16]hexaoxacyclooctadecin, 6,7,9,10,17,18,20,21- (8,9); (14187-32-7)

Methylolithium:

Lithium, methyl- (8,9); (917-54-4)

Bicyclo[1.1.1]pentyl phenyl sulfide:

Bicyclo[1.1.1]pentane, 1-(phenylthio)- (11); (98585-81-0)

Thiophenol:

Benzenethiol (8,9); (108-98-5)

Iodine (8,9); (7553-56-2)

1,3-Diiodobicyclo[1.1.1]pentane:

Bicyclo[1.1.1]pentane, 1,3-diiodo- (1); (105542-98-1)