



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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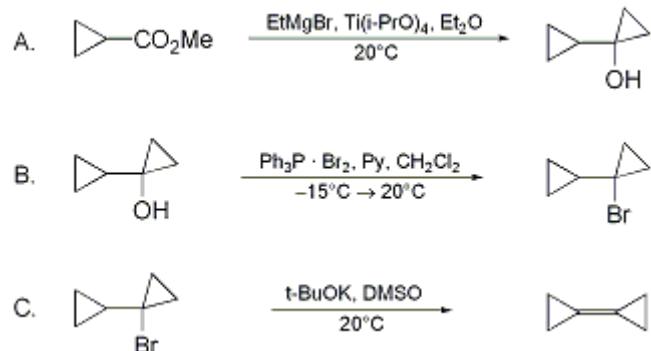
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions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

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BICYCLOPROPYLIDENE

[Cyclopropane, cyclopropylidene]



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1. Procedure

A. *1-Cyclopropylcyclopropanol*. A 4-L, four-necked, round-bottomed flask equipped with a mechanical stirrer, thermometer and reflux condenser is charged under **nitrogen** with 120.2 g (122 mL, 1.2 mol) of **methyl cyclopropanecarboxylate** (Note 1), 85.3 g (89.3 mL; 0.30 mol) of **titanium tetrakisopropoxide**, and 1.45 L of anhydrous ether (Note 2). To the well-stirred solution, 840 mL (2.52 mol) of **ethylmagnesium bromide** as a 3 M solution in ether is added over a period of 4 hr (Notes 3, 4). The temperature is maintained between 20°C and 25°C with a water bath. After the addition is complete the black or dark-brown mixture is stirred for an additional 0.5 hr at the same temperature, then cooled to -5°C, and the reaction is quenched by careful addition of 1.56 L of ice-cold aqueous 10% **sulfuric acid** while the temperature is maintained between -5°C and 0°C with an acetone-dry ice bath. The mixture is stirred at 0°C for an additional 1 hr, in which time the precipitate should have completely dissolved (Note 5), and then is transferred to a 4-L separatory funnel. The inorganic phase is extracted with 360 mL of ether (Note 6). The combined ethereal phases are washed with two 600-mL portions of saturated **sodium hydrogen carbonate** solution, 600 mL of saturated brine, dried over anhydrous **magnesium sulfate**, and filtered. The solvent is removed from the filtrate under water-aspirator vacuum at 20°C (Note 7) to give 116 g (99%) of **1-cyclopropylcyclopropanol** that is used without further purification (Note 8).

B. *1-Bromo-1-cyclopropylcyclopropane*. In a well-ventilated hood, a 2-L, three-necked, round-bottomed flask, equipped with a magnetic stirrer, thermometer, dropping funnel, and a reflux condenser, is charged under **nitrogen** with 327 g (1.24 mol) of **triphenylphosphine**, and 1.24 L of anhydrous **dichloromethane**. The solution is vigorously stirred under acetone-dry ice cooling, as 199 g (64.1 mL, 1.25 mol) of **bromine** (Note 9) is added over a period of 0.5 hr at -30°C to -15°C under **nitrogen** (Note 10). After an additional 15 min of stirring, a mixture of 116 g (1.18 mol) of **1-cyclopropylcyclopropanol** and 93.5 g (95.6 mL, 1.18 mol) of anhydrous **pyridine** is added dropwise at -15°C over a period of 2 hr. The mixture is stirred at 20°C for an additional 24 hr under **nitrogen**. The reflux condenser and the dropping funnel are removed. The flask is immersed in an oil bath and connected to a 2-L, two-necked, round-bottomed flask via a 90° angle glass tube (Note 11). The second flask is cooled with acetone-dry ice. All the volatile material is bulb-to-bulb distilled, at first under water-aspirator vacuum and 30°C oil bath temperature, and then under further reduced pressure (0.1 mm) with a 100°C oil bath. The distillation is continued until the temperature in the first flask reaches 80°C (Note 12). The receiver flask is allowed to warm to 20°C, and the solvent is removed by distillation at atmospheric pressure using a 30-cm Vigreux column. The residue is distilled under reduced pressure to give 117.1 g (62%) of **1-bromo-1-cyclopropylcyclopropane** (Note 13).

C. Bicyclopolydene. A 2-L, three-necked, round-bottomed flask equipped with a magnetic stirrer, thermometer, dropping funnel, and a reflux condenser is charged under **nitrogen** with 109 g (0.971 mol) of **potassium tert-butoxide** (Note 14), and 1 L of **dimethyl sulfoxide** (Note 15). The solution is vigorously stirred as 105 g (0.65 mol) of neat **1-bromo-1-cyclopropylcyclopropane** is added over a period of 2 hr under **nitrogen**. The temperature is maintained between 20°C and 25°C with a water bath. The mixture is stirred under a blanket of **nitrogen** (Note 16) at 20°C for an additional 24 hr. The reflux condenser and the dropping funnel are removed. The flask is immersed in a water bath and connected via a 90° angle glass tube to a 200-mL trap cooled with acetone-dry ice. All the volatile material is bulb-to-bulb distilled into the cold trap under reduced pressure (0.1 mm) at a maximum temperature of 35°C to 40°C inside the flask (Note 17). The contents of the cold trap are allowed to warm to 20°C, transferred into a 150-mL separatory funnel, washed with four 50-mL portions of ice-cold water, and then transferred into a preweighed bottle containing 2-3 g of 4 Å molecular sieves. The yield is: 44 g (84%) of **bicyclopolydene** (Note 18).

2. Notes

1. **Methyl cyclopropanecarboxylate** is obtained from Aldrich Chemical Company, Inc. The corresponding ethyl ester can also be used, but esters of higher alcohols are undesirable because the isolation of **1-cyclopropylcyclopropanol** becomes difficult.
2. Ether is obtained from E. Merck or Aldrich Chemical Company, Inc., and dried using a common procedure. **titanium tetraisopropoxide** is obtained from ABCR or Aldrich Chemical Company, Inc. (97% purity).
3. **Ethylmagnesium bromide** (EtMgBr) in ether (3 M) was purchased from Aldrich Chemical Company, Inc. The submitters also prepared it from **bromoethane** and **magnesium**. The concentration of EtMgBr was determined as follows: 1 mL of the Grignard solution was poured into 30 mL of ice-cold water; 4.00 mL of 1 N HCl solution was added, and the mixture was stirred until a clear solution was formed. Excess HCl was measured by titration with 0.1 N NaOH solution.
4. In the course of addition, the extensive evolution of **ethane** is observed, and therefore it is not necessary to maintain a stream of **nitrogen**.
5. While the precipitate is dissolving, an ice bath should be used to keep the mixture cool. The dissolution proceeds more rapidly when the precipitate is scraped off the walls of the flask from time to time with a spatula (the stirrer should be stopped for this operation).
6. Only one extraction with ether is necessary.
7. It is desirable to monitor this evaporation by ¹H NMR spectroscopy to remove as much **2-propanol** (originating from **titanium tetraisopropoxide**) as possible.
8. **1-Cyclopropylcyclopropanol** is a rather unstable compound that rapidly rearranges into **cyclopropyl ethyl ketone** (IR 1707 cm⁻¹) in the presence of acids and bases or upon heating. Therefore, it should be used immediately. The checkers stored the sample overnight at -78°C. If necessary, it should be stored no longer than 2-3 days at -78°C. Quantities of 20-30 g can be distilled, bp 65-68°C (32 mm); distillation of larger quantities is accompanied by the formation of a significant amount of **cyclopropyl ethyl ketone**. The physical properties are as follows: IR (film) cm⁻¹: 3332, 3084, 3007, 1217, 1009 and 935; ¹H NMR (250 MHz, CDCl₃) δ: 0-0.9 (m, 2 H), 0.21 (dd, 2 H, J = 6.5, 5.1), 0.25-0.33 (m, 2 H), 0.50 (dd, 2 H, J = 6.5, 5.1), 1.1-1.2 (m, 1 H), 3.83 (s, 1 H), [impurities at 0.6-0.9 (m), 1.1 (d, J = 6.2), 3.83 (m)]; ¹³C NMR (62.5 MHz, CDCl₃) δ: 2.51, 11.20, 16.20, 56.37, [impurities at 8.07, 21.59, 24.89, 63.84]; MS (ES⁺) m/z (rel intensity) 121 [100, (M + Na)⁺]. Anal. Calcd for C₆H₁₀O: C, 73.4; H, 10.3. Found: C, 71.7; H, 10.4.
9. Technical grade **triphenylphosphine** as obtained from BASF or Aldrich Chemical Company, Inc., is satisfactory. **Dichloromethane** is obtained from E. Merck or Fluka Chemical Corp. and dried according to commonly used procedures. **Pyridine** is obtained from Aldrich Chemical Company, Inc., or J. T. Baker ("Baker" grade) and dried by distillation over calcium hydride. **Bromine** was obtained from Aldrich Chemical Company, Inc., and used as supplied. **CAUTION: Bromine is a severe irritant, causes burns, and is very poisonous.**
10. The checkers added pellets of dry ice continuously to the acetone, cooling the bath to maintain the required temperature.
11. The checkers bent Pyrex glass tubing (o.d. 2 cm) to a 90° angle. The arm lengths were 17 and 16 cm and terminated in a male 24/29 ground glass joint. The longer arm was inserted in the distillation flask to accommodate bumping during the distillation.

12. The conditions of this bulb-to-bulb distillation are of prime importance: the oil bath must not be overheated, and the distillation performed with strict temperature control inside the first flask, otherwise lower yields are obtained. This operation takes 2-3 hr.

13. The submitters obtained 99.4-120.9 g (66-79%) from 1 mol of [cyclopropylecyclopropanol](#); they found it essential to carry out the last 5 min of the bulb-to-bulb distillation under full pumping power with the valve between the pump and the receiving flask completely open; bp 69-73°C (88 mm). The physical properties are as follows: IR (film) cm^{-1} : 3084, 3039, 1724, 1446, 1415, 1381, 1188, 1112, 1099, 1020 and 955 ; ^1H NMR (250 MHz, CDCl_3) δ : 0.25-0.30 (m, 2 H), 0.56-0.60 (m, 2 H), 0.70 (dd, 2 H, J = 6.5, 6.5), 1.03 (dd, 2 H, J = 6.5, 6.5), 1.51-1.66 (m, 1 H) ; ^{13}C NMR (62.5 MHz, CDCl_3) δ : 6.07, 14.24, 20.58, 36.80 . High resolution mass spectrum is as follows: (EI) m/z 160.9965 [(M+H) $^+$; calcd for C_6H_{10} ^{79}Br : 160.9966]. Anal. Calcd for $\text{C}_6\text{H}_9\text{Br}$: C, 44.75 ; H, 5.6. Found: C, 45.3, H, 5.7. The mixture has a tendency to foam upon distillation; if desired, a vacuum distillation capillary can be used to facilitate the distillation.

14. [Potassium tert-butoxide](#) is obtained from ABCR GmbH & Co., Karlsruhe, Germany or Aldrich Chemical Company, Inc. (95% purity).

15. The checkers purchased dimethyl sulfoxide from Aldrich Chemical Company, Inc. , and dried it by distillation (water aspirator) from calcium hydride. The submitters obtained [dimethyl sulfoxide](#) from J. T. Baker ("Baker" grade) and used it without purification.

16. During this stirring, the nitrogen inlet and outlet are at the top of the reflux condenser to avoid losses of the volatile product by evaporation. The [nitrogen](#) flow rate was kept to a minimum.

17. In several cases, the bulb-to-bulb distillation of bicyclopypylidene from the reaction mixture was incomplete when the system was evacuated only once. Therefore, it is recommended that distillation be interrupted as soon as no more condensation of product in the receiving flask is observed, that the apparatus be flushed with nitrogen, and then evacuation of the apparatus be repeated to continue bulb-to-bulb distillation. This procedure may have to be repeated one or two more times. Because the melting point of bicyclopypylidene is only -10°C, care must be taken to prevent the connecting tube from clogging with solid bicyclopypylidene. The checkers used a cold trap similar in design to the Aldrich cold trap, catalog No Z10, 310-1.

18. The submitters obtained a yield of 39.1-42.2 g (75-81%) from 1 mol of [1-bromo-1-cyclopropylcyclopropane](#) . [Bicyclopypylidene](#) can be distilled (bp 100-102°C); however, polymerization may occur in the distillation flask reducing the yield. The physical properties are as follows: IR (film) cm^{-1} : 3051, 2983, 1410, 1247, 1071 1046, 1016 and 994 ; ^1H NMR (250 MHz, CDCl_3) δ : 1.17 (s, 8 H); ^{13}C NMR (62.5 MHz, CDCl_3) δ : 2.8, 110.2 . The ^1H and ^{13}C NMR spectra indicated a sample purity = 95% (the submitters reported 95-97%). Anal. Calcd for C_6H_8 : C, 89.94 ; H, 10.06. Found: C, 89.03, H, 10.04. The sample was analyzed by gas chromatography (retention time 2.8 min) on an SGE capillary column BP5 (5% [methylphenylsiloxane](#)), internal diameter 0.32 mm, film thickness 0.25 μm , length 25 m, flow velocity 30 cm/s, injection temp 150°C, flame ionization detector 300°C. The column temperature was raised from 50°C at 10°C/min to 250°C. The checkers found that within a retention time of 3 min the sample purity ranged from 91-97%, but over 25 min the purity ranged from 88-91%. The checkers were unable to record a mass spectrum.

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 procedure is also applicable to the production of a number of spirocyclopropanated bicyclopypylidenes² in good yields. Bicyclopypylidene with its high-lying HOMO³ was demonstrated to possess unique reactivity toward a wide range of electrophiles and cyclophiles including nucleophilic carbenes to give complex skeletons and heterocycles in high yields.⁴ Functional derivatives can also be prepared directly from bicyclopypylidene.⁵ Transition metal-catalyzed reactions of bicyclopypylidene⁶ including Heck coupling⁷ allow the preparation of carbocycles, polyenes and heterocyclic compounds⁸ that are not readily available by other synthetic methods. [Bicyclopypylidene](#) has also been prepared by Simmons-Smith monocyclopropanation of the terminal double bond in [ethenylidenecyclopropane](#)(15% yield),⁹ dimerization of [1-lithiocyclopropene](#) in the presence of [lithium amide](#) in liquid ammonia over a

period of 1 month (30% yield),¹⁰ and several multistep syntheses starting from acetyl cyclopropane (15-30% overall yields).^{11 12 13 14}

References and Notes

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

Bicyclopropylidene (8);
Cyclopropane, cyclopropylidene- (9); (27567-82-4)

1-Cyclopropylcyclopropanol:
[1,1'-Bicyclopropyl]-1-ol (9); (54251-80-8)

Methyl cyclopropanecarboxylate:
Cyclopropanecarboxylic acid, methyl ester (8,9); (2868-37-3)

Titanium tetraisopropoxide:
Isopropyl alcohol, titanium(4+) salt (8);
2-Propanol, titanium(4+) salt (9); (546-68-9)

Ethylmagnesium bromide:
Magnesium, bromoethyl- (9); (925-90-6)

1-Bromo-1-cyclopropylcyclopropane:
1,1'-Bicyclopentyl, 1-bromo- (9); (60629-95-0)

Triphenylphosphine:
Phosphine, triphenyl- (8,9); (603-35-0)

Bromine (8,9); (7726-95-6)

Pyridine (8,9); (110-86-1)

Potassium tert-butoxide:
tert-Butyl alcohol, potassium salt (8);
2-Propanol, 2-methyl-, potassium salt (9); (865-47-4)

Dimethyl sulfoxide:
Methyl sulfoxide (8):
Methane, sulfinyl bis- (9); (67-68-5)

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