Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

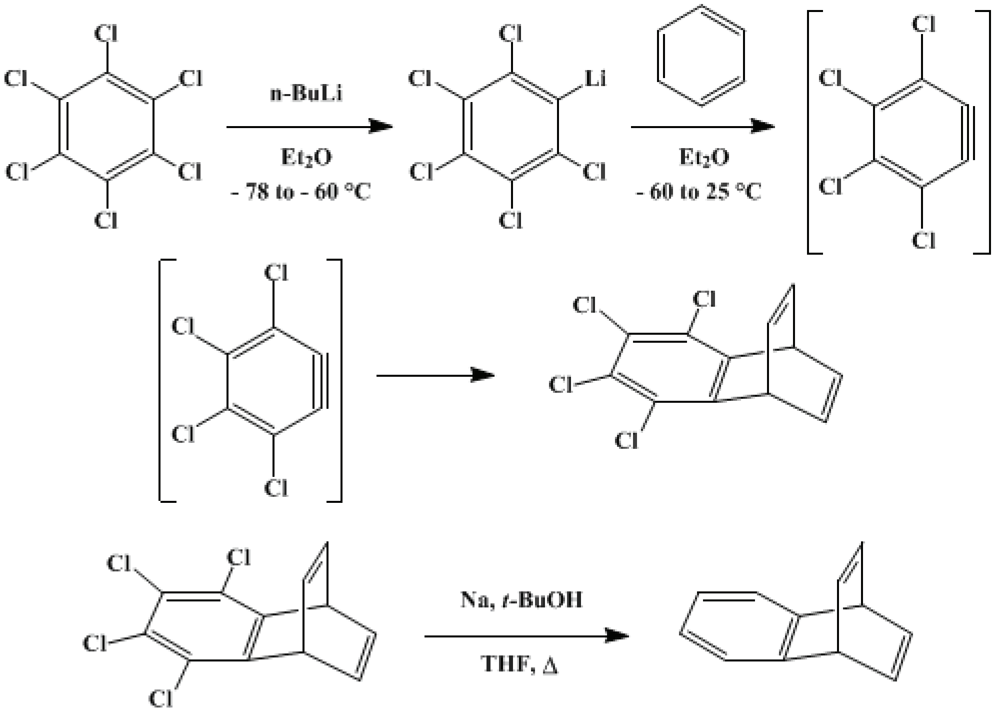
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.059.0071

Organic Syntheses, Coll. Vol. 6, p.82 (1988); Vol. 59, p.71 (1979).

DIELS-ALDER ADDITION OF PERCHLOROBENZYNE: BENZOBARRELENE

[1,4-Ethenonaphthalene, 1,4-dihydro]



Submitted by Neil J. Hales, Harry Heaney[1], John H. Hollinshead, and Pritpal Singh.
Checked by G. Crass, M. Pohmakotr, and D. Seebach.

1. Procedure

Caution! Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A. *Tetrachlorobenzobarrelene*. A carefully dried, 5-l., three-necked, round-bottomed flask equipped with a large magnetic stirring bar, a low-temperature thermometer, a 500-ml., pressure-equalizing dropping funnel bearing a gas-inlet tube, and a Nujol bubbler (Note 1) is charged with 28.5 g. (0.100 mole) of hexachlorobenzene (Note 2). The apparatus is flushed with argon or nitrogen (Note 3) before 600 ml. of dry diethyl ether (Note 4) is added. The resulting suspension is stirred and cooled to −72° to −78° in a 4-l. acetone–dry ice bath. A solution of *n*-butyllithium (0.110 mole) in hexane (Note 5) is added over a 30-minute period such that the temperature does not exceed −70° (Note 6). The mixture is then allowed to warm to −60° over an additional 1.5 hours. Four liters of dry, thiophene-free benzene (Note 4) is added to the pentachlorophenyllithium solution (Note 7) over a 1-hour interval, during which the temperature rises to *ca.* + 10° (Note 8). The mixture is allowed to warm slowly to room temperature over a period of at least 14 hours and then is heated at +30° for another 2 hours to ensure complete reaction (Note 9). A 10-g. portion of solid ammonium chloride is added, and 15 minutes later the contents of the flask are filtered through 20 g. of Celite. The volume of the filtrate is reduced to 75 ml. with a rotary evaporator, and 100 g. of alumina (Note 10) is added to the concentrate in a 250-ml. flask. The rotary evaporation is continued until the weight remains constant and a free-flowing consistency is attained. The material is placed on a column packed with 800 g. of alumina and eluted with low-boiling petroleum ether (Note 11). Fractions of *ca.* 200 ml. are collected and analyzed by GC or TLC ((Note 6)), with the appropriate fractions combined and evaporated, providing 16.9–17.5 g. (58–60%, (Note 12)) of essentially pure tetrachlorobenzobarrelene, m.p. 127–129° (Note 13).

B. *Benzobarrelene*. A dry, 1-l., three-necked, round-bottomed flask equipped with a magnetic stirring bar, a combined gas-inlet tube and rubber septum, a 500-ml., pressure-equalizing dropping funnel, and a reflux condenser connected to a Nujol bubbler is charged with 500 ml. of dry tetrahydrofuran (Note 14) and 17 g. (0.74 mole) of sodium wire having a diameter of *ca.* 0.5 mm. The mixture is stirred and heated at reflux under an atmosphere of argon or nitrogen while 50 ml. of freshly distilled *tert*-butyl alcohol is added. Immediately afterward a solution of 15 g. (0.051 mole) of tetrachlorobenzobarrelene in 200 ml. of tetrahydrofuran is added over a 15-minute period. After 4 hours under reflux (Note 15) the contents of the flask are cooled to room temperature and filtered through a plug of glass wool (Note 16) into a 2-l. beaker containing 50 ml. of methanol. After any remaining pieces of sodium have reacted with the methanol, 400 ml. of water is added, and the mixture is extracted with six 150-ml. portions of ether. The combined ether layers are washed with two 200-ml. portions of aqueous saturated sodium chloride, dried over magnesium sulfate, and evaporated with a rotary evaporator operated at water aspirator pressure and room temperature. The semicrystalline residue (7.3–8.1 g.) is mixed with 40 g. of alumina (Note 10) and swirled at room temperature under reduced pressure until it attains a free-flowing consistency. The material is then placed on a column packed with 600 g. of alumina and eluted with low-boiling petroleum ether (Note 11). Fractions of *ca.* 200 ml. are collected, evaporated, and assayed by GC (Note 15) and (Note 17). Combination of the appropriate fractions yields 5.9–6.8 g. (75–86%) of benzobarrelene, m.p. 62–64.5° (Note 18).

2. Notes

1. The dropping funnel must be arranged so that the drops fall directly into the solution and not onto the side of the flask. The checkers used a 4-l., four-necked flask equipped with a mechanical stirrer and a ground-glass stirring assembly, and carried out the reaction on four-fifths scale.
2. Technical-grade hexachlorobenzene was purchased by the submitters from BDH Chemicals, Ltd., and recrystallized twice from benzene: m.p. 227°. The submitters found that if the technical-grade material is used without purification, some insoluble material remains after the reaction with *n*-butyllithium, though the yield of tetrachlorobenzobarrelene is only slightly reduced. The checkers used 22.8 g. (0.0800 mole) of hexachlorobenzene of 98% purity, purchased as a fine powder from EGA-Chemie K. G., an affiliate of Aldrich Chemical Company, Inc., without further purification.
3. The flushing operation was accomplished by replacing the bubbler with a stop-cock and alternately evacuating and filling the apparatus with inert gas three times. A slight outflow of inert gas should be maintained during all subsequent operations. When the flask is being cooled, it is necessary to increase the gas flow.
4. Dry ether and dry, thiophene-free benzene were prepared by the submitters according to procedures presented in reference [2].
5. *n*-Butyllithium as 1.5–3.0 *M* solutions in hexane is available from the following firms: Pfizer, Ltd., Sandwich, England; Metallgesellschaft, Frankfurt, Germany; Alfa Division, Ventron Corporation. The appropriate volume of the solution is transferred with a 50-ml. syringe to the dropping funnel with care being taken to exclude air. An excess of *n*-butyllithium above the 10% recommended here may lead to the formation of dilithiotetrachlorobenzene.
6. The reaction of *n*-butyllithium and hexachlorobenzene and, later, the formation of tetrachlorobenzobarrelene may be monitored by GC or TLC. Samples withdrawn from the reaction mixture with a syringe are injected into a small amount of water, and the organic layer is analyzed. GC was carried out by the submitters with flame ionization detection and 1.5 m. × 4 mm. (inside diameter) glass column packed with 3% silicone rubber (SE-30) supported on 80–100 mesh Gaschrom Q. With a column temperature of 150° and a nitrogen carrier gas flow rate of 45 ml. per minute, the retention times of pentachlorobenzene, hexachlorobenzene, and tetrachlorobenzobarrelene are *ca.* 2, 4, and 18 minutes, respectively. Normally trace amounts of hexachlorobenzene are still detectable at the end of the reaction with *n*-butyllithium. TLC was performed on silica gel with 5% ether in pentane as developing solvent. The R_f value of tetrachlorobenzobarrelene is less than that of chlorobenzenes.
7. A clear yellow solution is usually obtained at this stage; however, some suspended material may be present, particularly when technical grade hexachlorobenzene is used.

8. For proper temperature control the cooling bath should be free from excess amounts of dry ice. The benzene should be added in the following manner (volume of benzene added, period of addition, final temperature reached): 0.5 l., 15 minutes, *ca.* −20°; 0.5 l., 15 minutes, *ca.* −10°; 3.0 l., 30 minutes, *ca.* +10°.

9. The reaction is relatively slow at a laboratory temperature of 18–20° and may require as much as 40 hours to reach completion.

10. The submitters used Activity I (Brockmann) Camag alumina, which was purchased from Hopkins and Williams. The checkers used comparable material obtained from E. Merck, Darmstadt, Germany.

11. Low-boiling petroleum ether (b.p. 30–50° or 40–60°) was distilled from calcium chloride prior to use.

12. The submitters usually combined fractions 5–14 and obtained 18–19.5 g. (62–67%) of tetrachlorobenzobarrelene, m.p. 127–131°. The checkers, using a 3.5 cm. × 1 m. column for the chromatography, isolated 13.5–14 g. (58–60%) of product from fractions 10–25.

13. ^{1}H NMR ($CDCl_3$): δ (multiplicity, number of protons, assignment): 5.45 (m, 2H, bridgehead *H*), 6.95 (m, 4H, vinyl *H*). A melting point of 125° is reported in the literature.[3]

14. The tetrahydrofuran was freshly distilled from lithium aluminum hydride. For a warning regarding this method of purifying tetrahydrofuran, see *Org. Synth.*, **Coll. Vol. 5**, 976 (1973).

15. An aliquot may be removed at this stage and analyzed by either GC or TLC to ensure that the reaction is complete. Benzobarrelene has a retention time of *ca.* 5 minutes under the conditions stated in (Note 6), but with a column temperature of 104°. The completion of the reaction is also indicated by a purple coloration of the precipitated sodium chloride.

16. The glass wool removes the larger pieces of unreacted sodium and much of the purple sodium chloride.

17. The dimensions of the column used by the checkers were the same as those specified in (Note 12), and the product was obtained from fractions 10–20. The submitters evaporated the fractions with a rotary evaporator operated at water aspirator pressure and room temperature (*ca.* 20°); however, the checkers caution that the product sublimes very readily.

18. IR cm.$^{-1}$, strong peaks: 1460, 1325, 790, 750, 690, 660; ^{1}H NMR ($CDCl_3$): δ (multiplicity, number of protons, assignment): 4.9 (m, 2H, bridgehead *H*), 6.8–7.3 (m, 8H, aryl and vinyl *H*). The reported melting point is 65.5–66°.[4] From 20 g. of tetrachlorobenzobarrelene the submitters obtained 8.3–8.8 g. (79–83%) of benzobarrelene, m.p. 64–65°.

3. Discussion

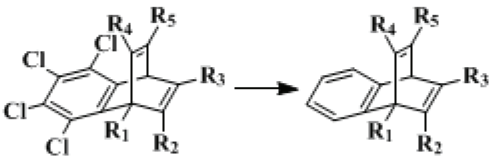
Although benzobarrelene has been used in a number of recent studies, the best available published synthesis[4] starts with the Diels-Alder reaction of β-naphthol and maleic anhydride, affording benzobarrelene in *ca.* 1% yield after five additional steps. Minor improvements allow small quantities of benzobarrelene to be prepared in an overall yield of *ca.* 10%.[5] The reaction of benzyne with benzene is relatively inefficient, giving benzobarrelene in *ca.* 2% yield.[6] When benzyne is generated by decomposition of benzenediazonium-2-carboxylate at high dilution in benzene, the yield of benzobarrelene is raised to 14%.[7] The reactions of benzyne with other aromatic substrates are equally inefficient.

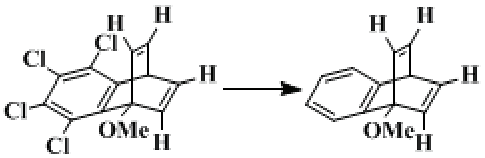
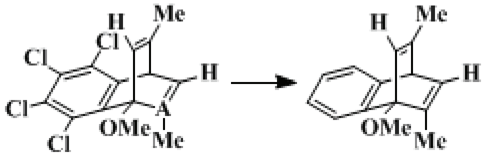
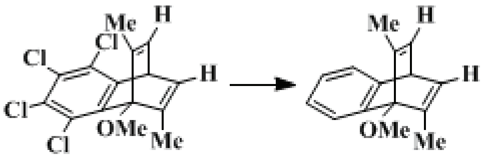
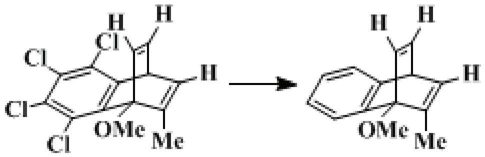
Tetrahalobenzynes, however, react with a variety of aromatic compounds to afford tetrahalobenzobarrelene derivatives in good yields, frequently in the range of 55 to 75%.[8] The dehalogenation of a variety of alkenyl chlorides with alkali metals in tetrahydrofuran containing *tert*-butyl alcohol[9] suggested this approach to the dechlorination of tetrachlorobenzobarrelenes.

The generation of pentachlorophenyllithium by the reaction of *n*-butyllithium with hexachlorobenzene has been reported previously by Rausch, Tibbetts, and Gordon.[10] The present procedure for the preparation of benzobarrelene is based on the submitters' previously published note.[11] By this method 10-g. quantities of benzobarrelene may be obtained in *ca.* 3 working days without the use of large-scale apparatus. The generality of the procedure is shown by the examples given in Table I.

TABLE I

PREPARATION OF SUBSTITUTED BENZOBARRELENES



Tetrachlorobenzobarrelenes	Yield of Benzobarrelenes (%)
R^1 = OMe; R^2 = R^3 = R^4 = R^5 = H 	100
R^1 = OMe; R^2 = R^5 = Me; R^3 = R^4 = H 	90
R^1 = OMe; R^2 = R^4 = Me; R^3 = R^5 = H 	95
R^1 = OMe; R^2 = Me; R^3 = R^4 = R^5 = H 	95

References and Notes

1. Department of Chemistry, The University of Technology, Loughborough, Leicestershire, England, LE11 3 TU.
2. J. A. Riddick and E. Toops, Jr., "Organic Solvents," Vol. VII of "Technique of Organic Chemistry," A. Weissburger, Ed., Interscience, New York, 1955; A. I. Vogel, "A Text-Book of Practical Organic Chemistry," 3rd ed., Longmans, Green, London, 1956, pp. 163–165, 172–173.
3. H. Heaney and J. M. Jablonski, *J. Chem. Soc. C*, 1895 (1968).
4. H. E. Zimmerman, R. S. Givens, and R. M. Pagni, *J. Am. Chem. Soc.*, **90**, 6096 (1968).
5. H. Hart and G. M. Love, personal communication; L. A. Paquette, personal communication.
6. R. G. Miller and M. Stiles, *J. Am. Chem. Soc.*, **85**, 1798 (1963); L. Friedman, *J. Am. Chem. Soc.*, **89**, 3071 (1967).
7. H. E. Zimmerman, R. J. Boettcher, N. E. Buehler, G. E. Keck, and M. G. Steinmetz, *J. Am. Chem. Soc.*, **98**, 7680 (1976).
8. H. Heaney, *Fortschr. Chem. Forsch.*, **16**, 35 (1970).
9. P. Bruck, D. Thompson, and S. Winstein, *Chem. Ind. (London)*, 405 (1960); P. G. Gassman and P. G. Pape, *J. Org. Chem.*, **29**, 160 (1964); G. W. Griffin and A. K. Price, *J. Org. Chem.*, **29**, 3192 (1964); P. G. Gassman and J. L. Marshall, *Org. Synth.*, **Coll. Vol. 5**, 424 (1973).

10. M. D. Rausch, F. E. Tibbetts, and H. B. Gordon, *J. Organomet. Chem.*, **5**, 493 (1966).
11. N. J. Hales, H. Heaney, and J. H. Hollinshead, *Synthesis*, 707 (1975).

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

alumina

petroleum ether

Tetrachlorobenzobarrelene

Benzobarrelene

Dry ether

calcium chloride (10043-52-4)

Benzene,
benzyne (71-43-2)

methanol (67-56-1)

ether,
diethyl ether (60-29-7)

ammonium chloride (12125-02-9)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

β-naphthol (135-19-3)

sodium (13966-32-0)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

n-butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

maleic anhydride (108-31-6)

lithium aluminum hydride (16853-85-3)

hexane (110-54-3)

argon (7440-37-1)

tert-butyl alcohol (75-65-0)

Benzenediazonium-2-carboxylate (1608-42-0)

hexachlorobenzene (118-74-1)

PERCHLOROBENZYNE (634-66-2)

1,4-Ethenonaphthalene, 1,4-dihydro (7322-47-6)

pentachlorophenyllithium

dilithiotetrachlorobenzene

pentachlorobenzene (608-93-5)