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.

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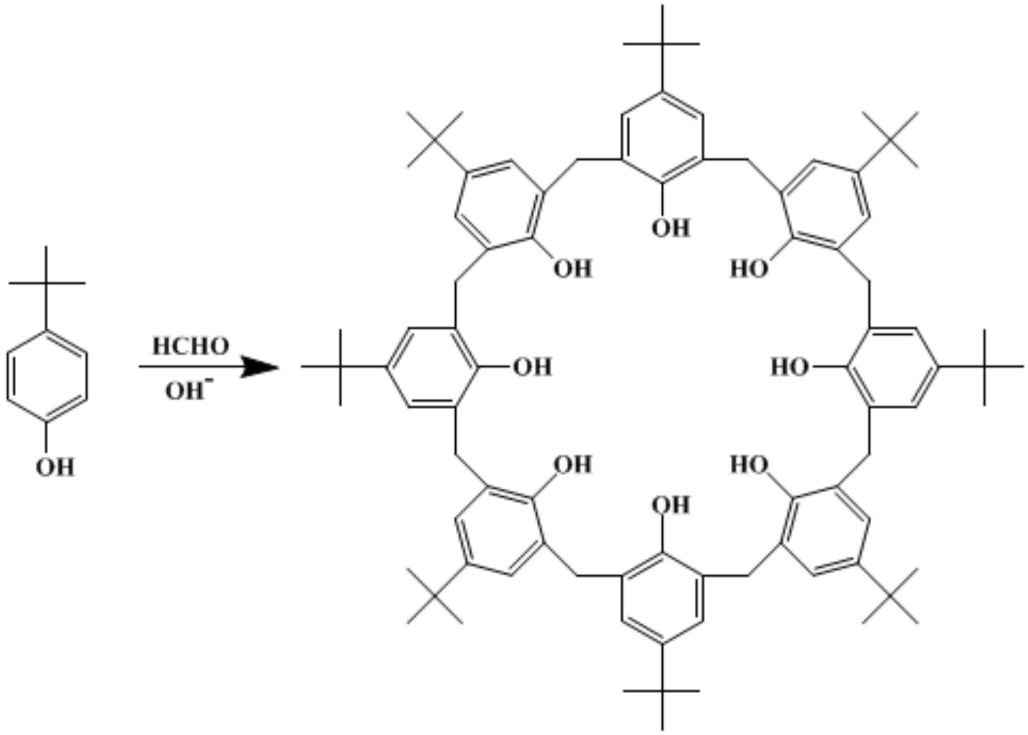
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.068.0243
Organic Syntheses, CV 8, 80

p-tert-BUTYLCALIX[8]ARENE



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Checked by Daniel T. Daly and James D. White.

1. Procedure

A slurry prepared from 100 g (0.67 mol) of *p-tert*-butylphenol, 35 g (ca. 1.1 mol) of paraformaldehyde (Note 1), and 2.0 mL (0.02 mol) of 10 *N* sodium hydroxide (Note 2) in 600 mL of xylene is placed in a 2-L, round-bottomed, three-necked flask fitted with a Dean–Stark water collector and a mechanical stirrer. The air in the flask is replaced with nitrogen, and the stirred contents of the flask are heated to reflux by means of a heating mantle. After 30 min a homogeneous solution is obtained, and after 1 hr a white precipitate begins to form. The reaction mixture is refluxed for 4 hr, the heating mantle is removed, the mixture is allowed to cool to room temperature, and the precipitate is removed by filtration. The crude product is washed, in succession, with 400-mL portions of toluene, ether, acetone, and water and is then dried under reduced pressure. It is dissolved in ca. 1600 mL of boiling chloroform. The chloroform is concentrated to ca. 1200 mL, the solution is cooled to room temperature, and the precipitate is collected by filtration to yield 67–70 g (62–65%) of a colorless powder, dec 418–420°C (Note 3) and (Note 4).

2. Notes

1. *p-tert*-Butylphenol from Aldrich Chemical Company, Inc., mp 98–101°C, and paraformaldehyde from Fisher Chemical Company, Certified ACS grade, were used.
2. Other bases, including KOH, RbOH, and CsOH, also work with approximately the same results, but LiOH is considerably inferior.
3. The (solvated) product can be obtained in crystalline form but, on standing in air for a few minutes, the colorless, glistening needles change to a white powder as the result of loss of solvent of crystallization. Considerable variation in the melting point of this material is noted. The product generally melts above 400°C, but sometimes the melting point falls to ca. 395°C or even lower. Undoubtedly, this is due to impurities such as metal ions and/or other cyclic oligomers that are

incompletely removed in the recrystallization (see (Note 4)).

4. Evaporation of the xylene filtrate and trituration of the residue with methylene chloride yields ca. 11 g of solid that consists mainly of cyclic hexamer and cyclic tetramer. The methylene chloride contains, inter alia, cyclic pentamer, cyclic heptamer, and bishomo compound, and these can be obtained as pure samples in low yield by fractional crystallization procedures. The composition of the reaction mixtures can be qualitatively established by TLC by means of the following R_f values in 9 : 1 petroleum ether/acetone and 1 : 1 petroleum ether/methylene chloride, respectively: (a) cyclic octamer—0.54, 0.85, (b) cyclic heptamer—0.40, 0.78, (c) cyclic hexamer—0.54, 0.76, (d) cyclic pentamer—0.74, 0.68, (e) cyclic tetramer—0.63, 0.66, and (f) bishomooxa compound—0.66, 0.56.

3. Discussion

This method for preparing *p*-*tert*-butylcalix[8]arene was first described in the patent literature[3] by chemists of the Petrolite Corporation, St. Louis, MO and, therefore, is often referred to as the "Petrolite procedure." It was introduced into journal literature by Gutsche et al.[4] Although the procedure is restricted to phenols substituted in the *p*-position with electronically neutral groups, it is more general in its application than the accompanying procedures for the calix[4]arenes and calix[6]arenes and has been used with *p*-isopropylphenol,[5] *p*-*tert*-pentylphenol,[5] *p*-(1,1,3,3-tetramethylbutyl)phenol,[6] and *p*-phenylphenol.[7]

References and Notes

1. Petrolite Corporation, St. Louis, MO 63119;
2. Department of Chemistry, Washington University, St. Louis, MO 63130.
3. Buriks, R. S.; Fauke, A. R.; Munch, J. H. U.S. Patent 4 259 464, 1981; *Chem. Abstr.* **1981**, *94*, P209, 722*x*.
4. Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782.
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6. Cornforth, J. W.; D'Arcy Hart, P.; Nicholls, G. A.; Rees, R. J. W.; Stock, J. A. *Br. J. Pharmacol.* **1955**, *10*, 73.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

petroleum ether

p-tert-Butylcalix[8]arene

ether (60-29-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

nitrogen (7727-37-9)

acetone (67-64-1)

toluene (108-88-3)

xylene (106-42-3)

methylene chloride (75-09-2)

p-phenylphenol (92-69-3)

p-tert-butylphenol (98-54-4)

p-isopropylphenol (99-89-8)

p-tert-pentylphenol (80-46-6)

p-(1,1,3,3-tetramethylbutyl)phenol (140-66-9)

paraformaldehyde (30525-89-4)