



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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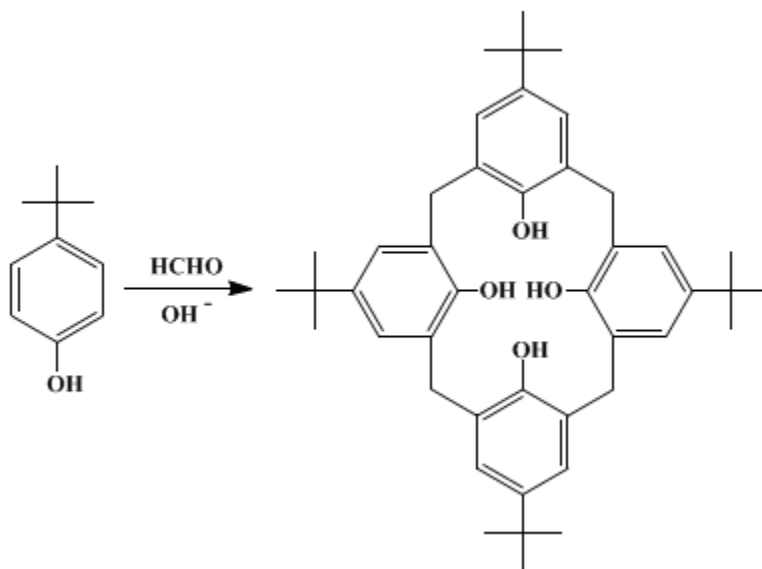
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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p-tert-BUTYLCALIX[4]ARENE



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1. Procedure

A. *Preparation of "precursor."* A mixture of 100 g (0.666 mol) of *p*-tert-butylphenol, 62 mL of 37% formaldehyde solution (0.83 mol of HCHO), and 1.2 g (0.03 mol) of sodium hydroxide (corresponding to 0.045 equiv with respect to phenol) (Note 1) in 3 mL of water is placed in a 3-L, three-necked, round-bottomed flask equipped with a mechanical stirrer. The contents of the open flask are allowed to stir for 15 min at room temperature, and then heated for 2 hr at 100–120°C by means of a heating mantle (Note 2). The reaction mixture, which is clear and colorless at the beginning, becomes light yellow after 30 min, a somewhat deeper yellow after 2 hr, and eventually changing to a thick slurry as the water evaporates and finally turning to a deep yellow or brown-yellow very viscous mass. During this period there is considerable frothing, and the reaction mixture fills most of the flask before shrinking back to the original volume. Stirring is discontinued, the reaction vessel is removed from the heating mantle, and the reaction mixture is allowed to cool to room temperature. To dissolve the residue 800–1000 mL of warm diphenyl ether (Note 3) is added to the flask and the contents are stirred, the process generally requiring at least 1 hr.

B. *Pyrolysis of the precursor.* The 3-L, three-necked flask is fitted with a nitrogen inlet. The contents of the flask are stirred and heated (110–120°C) with a heating mantle while a stream of nitrogen is blown rapidly over the reaction mixture to facilitate the removal of the water as it is evolved. During this period the color of the solution changes from yellow to a gray or a light brown. When the evolution of water subsides and a solid starts to form (prior to attaining the reflux temperature) (Note 4), the flask is fitted with a condenser, and the contents of the flask are stirred and heated to ca. 150–160°C (Note 5) for a few minutes and then at reflux for 3–4 hr under a gentle flow of nitrogen (Note 6). During this phase of the reaction the solid dissolves, and a clear dark-brown to grayish-black solution is formed. The reaction mixture is cooled to room temperature (some solid separates), and the product is precipitated by the addition of 1.5 L of ethyl acetate. The resulting mixture is stirred for 15–30 min and allowed to stand for at least 30 min (Note 7). Filtration yields material that is washed twice with 100-mL portions of ethyl acetate, once with 200 mL of acetic acid, twice with 100-mL portions of water, and twice with 50-mL portions of acetone to yield ca. 66 g (61%) of crude product (Note 8). The white-to-beige-colored crude product is dissolved in ca. 1600–1800 mL of boiling toluene that is concentrated to ca. 700–900 mL. On cooling, 61 g (49%) of product is obtained as glistening white rhombic crystals,

mp 342–344°C (Note 9) and (Note 10).

2. Notes

1. *p*-tert-Butylphenol from Aldrich Chemical Company, Inc., mp 98–101°C, and 37% formaldehyde solution from Fisher Chemical Company, Certified ACS grade, were used.
2. Care should be taken not to allow the heating mantle to get so hot as to char the solid material on the walls of the flask. Submitters have used an oil bath.
3. Diphenyl ether recovered from previous preparations of *p*-tert-butylcalix[4]arene can be used, resulting in some cases in slightly higher yields of product.
4. Stirring accelerates the rate of water removal, but is not necessary.
5. In some cases a solid does not form, and the solution remains clear throughout.
6. Cyclic octamer rather than cyclic tetramer has occasionally been reported as the major product, probably the result of insufficiently strenuous pyrolysis conditions (e.g., diphenyl ether not at reflux or too rapid a flow of nitrogen).
7. It may be convenient to transfer the contents of the three-necked flask to an Erlenmeyer flask prior to the addition of ethyl acetate.
8. The crude material is usually pure enough to be used in subsequent reactions without recrystallization.
9. The product of crystallization from toluene is a 1 : 1 complex of *p*-tert-butylcalix[4]arene and toluene, from which the toluene can be removed by drying under high vacuum (< 1 mm) and high temperature (> 140°C) for an extended period of time (48 hr).
10. The melting point is measured in an evacuated melting-point tube.

3. Discussion

A prototype of this procedure was first published in 1941 by Zinke and Ziegler,² although the unambiguous identity of the product was not established until some years later.³ A few other *p*-alkylcalix[4]arenes have been prepared by this procedure, but for practical purposes it appears to be restricted to *p*-alkylphenols in which the *p*-alkyl group is highly branched at the position adjacent to the phenyl ring. Thus, *p*-tert-pentylcalix[4]arene and *p*-(1,1,3,3-tetramethylbutyl)calix[4]arene⁴ are among the few other phenols that yield a tractable product in reasonable yield.

References and Notes

1. Department of Chemistry, Washington University, St. Louis, MO 63130.
2. Zinke, A.; Ziegler, E. *Ber.* **1941**, *74B*, 1729; Zinke, A.; Ziegler, E.; Martinowitz, E.; Pichelmayer, H.; Tomio, M.; Wittmann-Zinke, H.; Zwanziger, S. *Ber.* **1944**, *77B*, 264.
3. Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782.
4. Foia, D.; Pochini, A.; Ungaro, R. Andreotti, G. D. *Makromol. Chem., Rapid. Commun.* **1983**, *4*, 71.

Appendix

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

p-tert-Butylcalix[4]arene

HCHO

p-tert-pentylcalix[4]arene

p-(1,1,3,3-tetramethylbutyl)calix[4]arene

[acetic acid \(64-19-7\)](#)

[ethyl acetate \(141-78-6\)](#)

[sodium hydroxide \(1310-73-2\)](#)

[formaldehyde \(50-00-0\)](#)

[phenol \(108-95-2\)](#)

[nitrogen \(7727-37-9\)](#)

[acetone \(67-64-1\)](#)

[toluene \(108-88-3\)](#)

[diphenyl ether \(101-84-8\)](#)

[p-tert-butylphenol \(98-54-4\)](#)