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.

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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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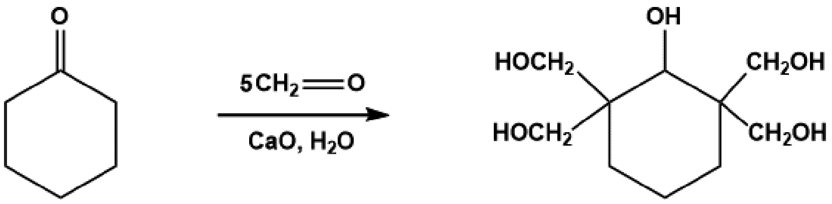
2,2,6,6-TETRAMETHYLOLCYCLOHEXANOL

[1,1,3,3-Cyclohexanetetramethanol, 2-hydroxy-]



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1. Procedure

[2]

A mixture of 196 g. (206 ml., 2 moles) of freshly distilled cyclohexanone, 332 g. (11 moles) of 99.5% paraformaldehyde (Note 1), and 1.8 l. of water is placed in a 5-l. flask equipped with a thermometer and an efficient stirrer. The mixture is cooled to 10–15° by an ice-water bath, and 70 g. (1.25 moles) of calcium oxide is added through a powder funnel over a period of 10–15 minutes. The temperature is allowed to rise slowly to 40° and is kept there by means of the cooling bath until the addition is complete. Stirring is maintained throughout. The reaction mixture is stirred for an additional 30 minutes. During this time the temperature usually falls to approximately 35°, and at this point the cooling bath is removed. The reaction mixture is then made slightly acid (pH 6–6.5) by the addition of 11–13 ml. of aqueous 87% formic acid. It is best to stir the reaction mixture for 30 minutes after neutralization in order to make sure that any suspended particles of lime are neutralized. If at the end of this time the solution is not acid, more formic acid should be added. The reaction mixture is then evaporated under reduced pressure to dryness (Note 2). The residue, which consists of a mixture of product and calcium formate, is mixed with 1 l. of absolute methanol. On warming, the organic material dissolves and the calcium formate settles to the bottom of the flask. A practically colorless solution of the product is obtained by filtration with suction (Note 3) through a heated funnel. The insoluble calcium formate is washed with about 50 ml. of methanol. Approximately one-half of the methanol is removed under reduced pressure, and the residual syrupy solution (Note 4) is allowed to crystallize in an ice chest for 24 hours. Thereafter the product is filtered and washed with 50 ml. of methanol. The mother liquor and washings are combined and set aside. With a mortar and pestle, the crystals are triturated successively with three 200–300-ml. portions of acetone, filtered, and air-dried. By continued evaporation of the mother liquor and washings, at least two successive crops of product are obtained, and these are processed as described above (Note 5). The total yield of product melting at 128–129° is 320–374 g. (73–85%). Recrystallization of 100 g. of material, m.p. 128–129°, from 175 ml. of absolute methanol yields 84 g. of pure product melting at 129–130°.

2. Notes

1. An equivalent quantity of aqueous formaldehyde free from methanol may be used.
2. The evaporation may be carried out in an ordinary distillation apparatus, but it is essential to stir the mixture to prevent bumping. It is advantageous from the point of view of speed and convenience to employ the method described below.

A 3-l. three-necked flask is fitted with an efficient rubber-sealed stirrer, an upright steam-heated condenser, the upper end of which is joined to a separatory funnel, and an outlet tube connected to a long water-cooled condenser placed for downward distillation. The end of this condenser is fitted to a 2-l. two-necked flask which is connected to a good water pump and immersed in an ice bath. The apparatus, with the exception of the separatory funnel, is placed under vacuum. The aqueous solution contained in a separatory funnel is slowly passed through the upright condenser into the three-necked flask heated on a steam bath. The syrupy residue collects in the flask, and the water vapor is removed through the condenser fitted for downward distillation. The residue is heated until no more water is removed. The total time required to strip off the water is 30 to 60 minutes.

3. The checkers found that suction filtration was very slow, owing to the very finely divided material that collected on the funnel. This was corrected by adding a filtering aid (Celite) to the crude mixture and filtering by suction, using an ordinary Büchner funnel (6-in. size). After removal of the solid by suction filtration, the methanol volume was reduced as indicated.

4. The submitter reported that it was preferable to carry out the crystallizations in metal beakers since the crystals were very hard to remove without breakage, but the checkers experienced no such difficulty. 5. Runs employing six times the quantities specified here have been carried out in 22-l. flasks with similar results.

3. Discussion

2,2,6,6-Tetramethylolcyclohexanol has been prepared by Mannich and Brose[3] by condensing cyclohexanone with formaldehyde in the presence of calcium oxide and precipitating the catalyst as calcium sulfate.

References and Notes

1. General Mills, Inc., Minneapolis, Minnesota.
2. This procedure forms a portion of the subject matter of U. S. pat. 2,462,031 [*C. A.*, **44**, 656 (1950)]; U. S. pat. 2,493,733 [*C. A.*, **44**, 3017 (1950)]; U. S. pat. 2,527,853 [*C. A.*, **45**, 2262 (1951)].
3. Mannich and Brose, *Ber.*, **56**, 833 (1923).

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

methanol (67-56-1)

formaldehyde (50-00-0)

Cyclohexanone (108-94-1)

formic acid (64-18-6)

calcium sulfate (7778-18-9)

acetone (67-64-1)

calcium oxide

calcium formate (544-17-2)

2,2,6,6-Tetramethylolcyclohexanol,
1,1,3,3-Cyclohexanetetramethanol, 2-hydroxy- (5416-55-7)

paraformaldehyde (30525-89-4)