



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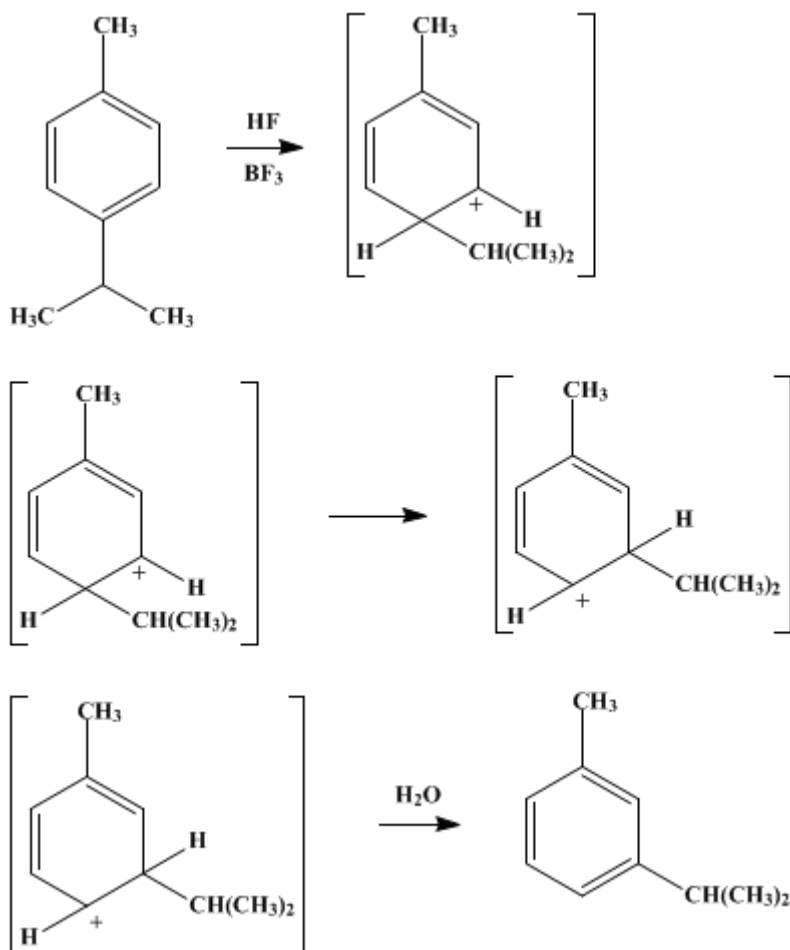
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.332 (1973); Vol. 47, p.40 (1967).

m-CYMENE

[*m*-Isopropyltoluene]



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1. Procedure

Caution! It is necessary to carry out the entire operation including the workup in a well-ventilated hood. Rubber gloves and safety glasses should be worn (Note 1).

Anhydrous hydrogen fluoride (135 ml., approx. 7 moles) is liquefied by passing the gas through an 8-ft. spiral of ¼-in. I.D. copper tubing surrounded by an isopropyl alcohol-dry ice bath (Note 2). The liquid is delivered to a 500-ml. polyethylene squeeze bottle (Note 3) containing a magnetic stirring bar via a polyethylene tube inserted through the screw cap of the bottle. The squeeze bottle is contained in a 2-l. beaker and is surrounded by powdered dry ice (Note 4). After the hydrogen fluoride is collected, the cap and delivery tube are removed, and *p*-cymene (terpene-free, 67 g., 0.5 mole), precooled to -50° to -60°, just above the slush point, is added to the hydrogen fluoride. The cap and polyethylene tube assembly is now attached to deliver boron trifluoride. The delivery tube in this case dips below the surface of the hydrogen fluoride, the bottom layer. Boron trifluoride is bubbled through while the mixture is efficiently stirred with a magnetic stirrer (Note 5). A light orange color develops immediately, and the two layers become one in about 30 minutes (Note 6). Additional powdered dry ice

must be added to the beaker during the boron trifluoride addition. The volume of the complex increases about 25%. After homogeneity is effected (in 30 minutes), a somewhat slower stream of boron trifluoride is added for an additional 30 minutes (Note 7). The delivery tube is replaced by a cap on the polyethylene bottle, the drying tube is removed, and the original side-arm tube is lowered to the bottom of the container. The cold reaction mixture is squirted, by squeezing the bottle, in a continuous small stream into a 4-l. beaker half-filled with cracked ice, vigorously hand-stirred. The bottle is rinsed, and the contents of the beaker are placed in a large separatory funnel. The upper colorless layer is separated, and the aqueous phase is extracted 3 times with 50-ml. portions of hexane. The combined organic layers are washed with three 50-ml. portions of water and dried overnight with anhydrous sodium sulfate under refrigeration (Note 8). The hexane solution at this point contains *m*-cymene with about 8% disproportionation impurities including toluene. The solution is fractionated through a 1-ft. helices-packed column, with the *m*-cymene at boiling point 173–176°, 50–54 g. (75–80%) being collected (Note 9).

2. Notes

1. In the event of accidental contact of hydrogen fluoride with the skin, the affected area must be washed immediately and thoroughly with cold water. Additional treatment has been described.²
2. If one half the given quantity of hydrogen fluoride is used, all other factors being kept the same, the *m*-cymene formed contains as much as 5% of *p*-cymene.
3. A Nalgene "15–500" polyethylene bottle (Nalge Co., Rochester, New York) was used. The side arm coming off the shoulder of the bottle is kept well above the liquid level, the constricted tip removed, and the end of the tube connected to a drying tube containing clay plate chips impregnated with concentrated sulfuric acid.
A squeeze bottle can be simply made from a 500-ml. narrow-mouthed polyethylene bottle and polyethylene tubing. Holes in the bottle cap and shoulder are made with a sharp cork borer of the appropriate size to ensure a tight fit with the inserted tubing.
4. A polyethylene or copper foil loop 1 in. wide is placed between the squeeze bottle and the side of the beaker in such a position as to exclude the dry ice from the space and to provide a window to permit one to see that the liquid hydrogen fluoride fills the bottle to a premarked level. The frost on the beaker must be scraped off to allow inspection through the window.
5. The stirring motor is housed in a polyethylene bag to protect it from acid fumes.
6. Larger quantities of boron trifluoride are evolved from the drying tube at this point. During the first 30 minutes, boron trifluoride is added at a rate which gives a slow emanation of fuming vapor from the drying tube. The checkers found that the product was contaminated by *p*-cymene when inefficient stirring and slow boron trifluoride addition rates were employed (Note 7).
7. The checkers used a flowmeter to monitor boron trifluoride addition and found that an indicated addition rate of 1800 ml./min. (calibrated with air) for the first 5 minutes followed by an average rate of 600 ml./min. gave homogeneity in the prescribed time. A rate of 150 ml./min. was used for the second 30 minutes.
8. All glassware is rinsed with water immediately after use to prevent etching.
9. The product is analyzed by vapor phase chromatography using a 6-ft., 1/4-in. O.D. copper tube, packed with 5% Bentone-34 (Wilkins Instrument Co.) and 0.5% XF-1150 (General Electric Silicone Products) on Diatoport-S (80–100 mesh) (F and M Co.); flow rate of helium 60 ml./min., oven temperature 85°. This column separates *m*-cymene (retention time 12 minutes) from *p*-cymene (retention time 10 minutes) but does not resolve the *ortho* isomer. The purity of the distilled *m*-cymene is above 98%.

3. Discussion

m-Cymene has been prepared from the Grignard reagent of *m*-bromotoluene and acetone followed by conversion of the carbinol to the chloride and reduction with sodium in liquid ammonia.³ It also has been prepared from *m*-toluoyl chloride and excess methylmagnesium bromide followed by catalytic reduction of the olefin formed.⁴ The best set of physical properties for the isomeric cymenes appears to be that of Birch and co-workers.⁴ Many examples of Friedel-Crafts alkylation of toluene with propylene are described; apparently the best of them gives a 90% yield of cymenes containing 65–70% *m*-cymene.⁵

The method of preparation in this procedure is adapted from that of McCauley and Lien by which they obtained *m*-cymene in unstated yields.⁶ The procedure has been altered to operate at -78° rather than -20° .

4. Merits of the Preparation

Aromatic hydrocarbons substituted by alkyl groups other than methyl are notorious for their tendency to disproportionate in Friedel-Crafts reactions. This tendency has previously limited the application of the isomerization of *para*-(or *ortho*-)dialkylbenzenes to the corresponding *meta* compounds. At the lower temperature of the present modification, disproportionation can be minimized.

References and Notes

1. Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37203.
2. G. A. Olah and S. J. Kuhn, *this volume*, p. 66.
3. P. E. Verkade, K. S. deVries, and B. M. Wepster, *Rec. Trav. Chim.*, **82**, 637 (1963).
4. S. F. Birch, R. A. Dean, F. A. Fidler, and R. A. Lowry, *J. Am. Chem. Soc.*, **71**, 1362 (1949).
5. B. L. Kozik, I. S. Vol'fson, M. B. Vol'f, and L. I. Germash, *Khim. i Tekhnol. Topliva i Masel*, **6**, (10) 9 (1961); G. A. Olah, "Friedel-Crafts and Related Reactions," Vol. II, Part I, Interscience Publishers, New York, 1964, p. 149 (summary of the alkylation of toluene by propylene).
6. D. A. McCauley and A. P. Lien, U.S. Patent 2,741,647 [*C.A.*, **50**, 11658 (1956)].

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

sulfuric acid (7664-93-9)

ammonia (7664-41-7)

propylene (115-07-1)

sodium sulfate (7757-82-6)

hydrogen fluoride (7664-39-3)

acetone (67-64-1)

toluene (108-88-3)

sodium (13966-32-0)

methyl (2229-07-4)

p-cymene (99-87-6)

boron trifluoride (7637-07-2)

methylmagnesium bromide (75-16-1)

hexane (110-54-3)

helium (7440-59-7)

m-Bromotoluene (591-17-3)

m-toluoyl chloride (1711-06-4)

m-Cymene,
m-Isopropyltoluene (535-77-3)