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.

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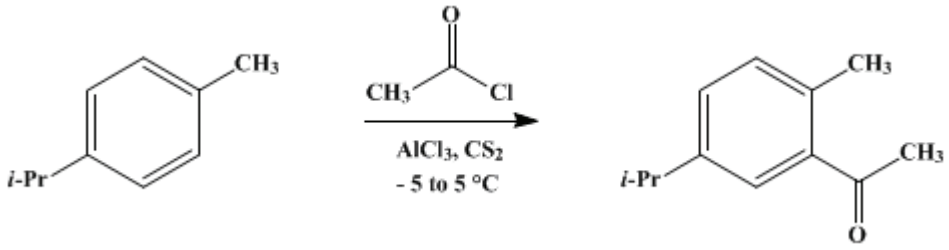
Organic Syntheses, Coll. Vol. 2, p.3 (1943); Vol. 14, p.1 (1934).

ACETO-*p*-CYMENE

[Acetophenone, 5-isopropyl-2-methyl-]



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Checked by Reynold C. Fuson and Charles F. Woodward.

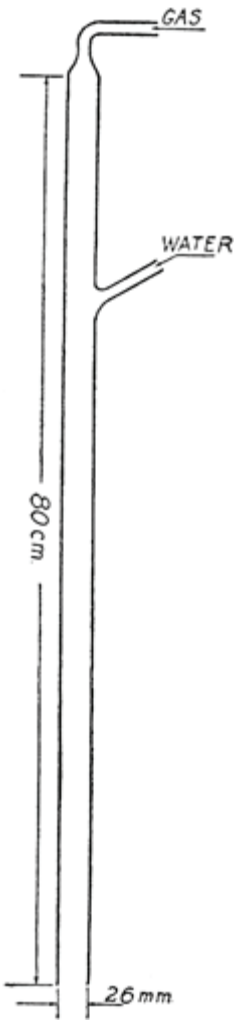
1. Procedure

A 1-l. three-necked flask is fitted with a dropping funnel, a stirrer, a thermometer for reading low temperatures (Note 1), and a condenser, to the upper end of which is attached a tube for disposing of the hydrogen chloride evolved (Note 2). A mixture of 200 cc. of carbon disulfide and 180 g. (1.35 moles) of anhydrous aluminum chloride is placed in the flask which is then immersed in an ice-salt freezing mixture and stirred very vigorously until the temperature of the mixture is −5° or below. A mixture of 175 g. (1.3 moles) of *p*-cymene and 110 g. (100 cc., 1.4 moles) of acetyl chloride is added from the dropping funnel at such a rate that the temperature never rises above 5°. This addition requires about three and one-third hours (Note 3). The mixture is allowed to stand overnight and is then poured upon 1 kg. of cracked ice to which 200 cc. of concentrated hydrochloric acid has been added. The mixture is extracted with three 700-cc. portions of ether; the ether solution is dried over anhydrous calcium chloride and distilled at ordinary pressure from a Claisen flask provided with an indented column, until the temperature reaches 190°. The material that remains in the flask is fractionally distilled twice under diminished pressure. The principal fraction is aceto-*p*-cymene, a pale yellow oil boiling at 124–125°/12 mm. (155–157°/30 mm.). It weighs 115–125 g. (50–55 per cent of the theoretical amount) (Note 4). About 50 g. of cymene is recovered (Note 5), and there is a small amount (10–12 g.) of residual oil left in the flask (Note 6).

2. Notes

1. Since it is impossible to read that part of the thermometer scale which extends into the reaction flask, a thermometer should be used which when in position has the zero point above the stopper of the flask. A thermometer reading from −50° to +50° is recommended.
2. A gas trap of the type shown in Fig. 1 is suitable for this purpose. Another gas trap is shown in Org. Syn. Coll. Vol. I, **1941**, 97.

Fig. 1



3. After about two-thirds of the mixture has been added the rate of addition may be increased somewhat. The time required for the addition depends on the efficiency of the cooling and stirring; the stirring must be vigorous. With one-half of these amounts in a 500-cc. flask, the time required is only about one and one-third hours since, under these conditions, it is easier to control the temperature.
4. From the first fractionation a fraction boiling over a 20° range is taken as crude ketone; e.g., at 28–30 mm. the fraction is taken which boils at 145–165°. Much trouble is caused by the tendency of the ketone to become superheated.
5. Acetyl chloride gives a better yield and less high-boiling residue than acetic anhydride.
6. This procedure has also been used successfully in the acetylation of cumene and *tert.*-butylbenzene. At the low temperatures employed there is very little decomposition, as is shown by the small amount of high-boiling residue.

3. Discussion

Aceto-*p*-cymene can be prepared by the action of acetyl chloride on *p*-cymene in the presence of anhydrous aluminum chloride[1] or ferric chloride.[2]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 24
- Org. Syn. Coll. Vol. 2, 543
- Org. Syn. Coll. Vol. 3, 23
- Org. Syn. Coll. Vol. 3, 446

- Org. Syn. Coll. Vol. 4, 42
- Org. Syn. Coll. Vol. 4, 62
- Org. Syn. Coll. Vol. 4, 157
- Org. Syn. Coll. Vol. 4, 162
- Org. Syn. Coll. Vol. 4, 364
- Org. Syn. Coll. Vol. 4, 387
- Org. Syn. Coll. Vol. 4, 404
- Org. Syn. Coll. Vol. 4, 554
- Org. Syn. Coll. Vol. 4, 590
- Org. Syn. Coll. Vol. 4, 715
- Org. Syn. Coll. Vol. 4, 746
- Org. Syn. Coll. Vol. 4, 755
- Org. Syn. Coll. Vol. 4, 804
- Org. Syn. Coll. Vol. 4, 807
- Org. Syn. Coll. Vol. 4, 844
- Org. Syn. Coll. Vol. 4, 960
- Org. Syn. Coll. Vol. 4, 984
- Org. Syn. Coll. Vol. 5, 196
- Org. Syn. Coll. Vol. 5, 572
- Org. Syn. Coll. Vol. 5, 580
- Org. Syn. Coll. Vol. 5, 1135

References and Notes

1. Lacourt, Bull. soc. chim. Belg. **38**, 17 (1929); Claus, Ber. **19**, 232 (1886); Klages and Lickroth, ibid. **32**, 1563 (1899); Verley, Bull. soc. chim. (3) **17**, 910 (1897).
2. Meissel, Ber. **32**, 2421 (1899).

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

Acetophenone, 5-isopropyl-2-methyl-

calcium chloride (10043-52-4)

hydrogen chloride,
hydrochloric acid (7647-01-0)

ether (60-29-7)

acetic anhydride (108-24-7)

acetyl chloride (75-36-5)

aluminum chloride (3495-54-3)

carbon disulfide (75-15-0)

ferric chloride (7705-08-0)

cymene,
p-cymene (99-87-6)

cumene (98-82-8)

Aceto-p-cymene

tert.-butylbenzene (98-06-6)