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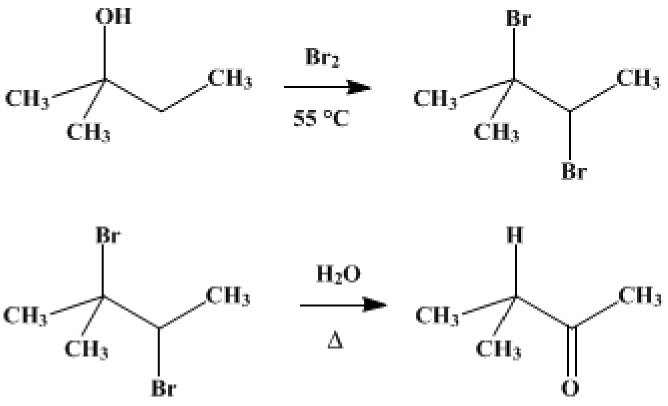
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.013.0068

Organic Syntheses, Coll. Vol. 2, p.408 (1943); Vol. 13, p.68 (1933).

METHYL ISOPROPYL KETONE

[2-Butanone, 3-methyl-]



Submitted by Frank C. Whitmore, W. L. Evers, and H. S. Rothrock.
Checked by W. W. Hartman and L. J. Roll.

1. Procedure

In a 1.5-l. round-bottomed Pyrex flask, fitted with a dropping funnel, an efficient mechanical stirrer, and a thermometer, is placed 176 g. (2 moles) of *tert.*-amyl alcohol (redistilled, b.p. range 0.5°). The flask is surrounded by a water bath, and the temperature of the alcohol is held at 50–60° while 320 g. (103 cc., 2 moles) of bromine is slowly added with stirring during about two hours (Note 1). The stirring is continued for a few minutes until the bromine color has disappeared (Note 2).

To the reaction flask containing the crude trimethylethylene dibromide is added 540 cc. of water, and the flask is fitted with a long reflux condenser and a mercury-sealed stirrer (Note 3). The mixture is refluxed with stirring for three to five hours until hydrolysis is practically complete (Note 4). The reflux condenser is then replaced by a condenser for distillation, and the crude methyl isopropyl ketone is removed from the reaction mixture by direct distillation, with stirring, until the temperature rises (Note 5) and the oil nearly stops coming over (about one and one-half hours), or until the oil coming over is heavier than water. The residue in the flask can be distilled to yield about 380 cc. of constant-boiling hydrobromic acid.

To the distillate, consisting of a yellow oil with a small lower water layer, powdered sodium carbonate (about 10 g.) is added, and the mixture is shaken until the water layer is alkaline and nearly saturated (Note 6). The layers are separated, and the oil is refluxed for about sixteen hours with 20 g. of powdered potassium carbonate and 5 cc. of water (Note 7). The oily layer is again separated and dried over about 6 g. of anhydrous calcium chloride or potassium carbonate (Note 8). It is then placed in a flask containing 2 g. of dry sodium carbonate and distilled through an efficient column. The yield of methyl isopropyl ketone boiling at 92–94° (Note 9) is about 102 g. (59 per cent of the theoretical amount). The product is slightly yellow.

2. Notes

1. The bromine is added at such a rate that only a small amount is present at any time, as shown by an orange-red color. The speed of the reaction depends on the temperature and efficiency of stirring. The temperature of the reaction mixture remains a few degrees above that of the water bath.
After about half the bromine has been added, the mixture becomes cloudy owing to the separation of water, and a somewhat lower temperature (40–45°) suffices to prevent the accumulation of unreacted bromine.
2. The crude trimethylethylene dibromide can be purified by washing with sodium carbonate solution

and water, drying, and distilling under reduced pressure; b.p. 49–51°/11 mm.; 60–70 per cent yield. Hydrolysis of the purified dibromide gives a 78 per cent yield of methyl isopropyl ketone. However, the losses in purifying the dibromide result in a slightly decreased over-all yield of ketone so that the purification of the dibromide is not recommended.

3. The quantity of water used is 50 per cent more than the theoretical amount for hydrolyzing the dibromide and converting all the bromine to constant-boiling (47.3 per cent) hydrobromic acid. Less water can be used, but more darkening of the reaction mixture occurs, and the yield of ketone is slightly decreased.

4. Efficient stirring lessens the time required for hydrolysis and avoids loss of material by intermittent sudden boiling. To be sure of complete hydrolysis, refluxing should be continued for at least an hour after the specific gravity of the oily layer becomes less than that of the water layer.

5. The distillate and residue contain a very powerful lachrymator and should be handled under a good hood.

6. The ketone is somewhat soluble in water, and the sodium carbonate serves to salt it out as well as to remove any hydrobromic acid.

7. The crude ketone contains small amounts of bromides, and it darkens even after repeated distillation unless first refluxed over potassium carbonate.

8. It is necessary to dry the ketone thoroughly since water distils with it at about 78°. This fraction can be dried again to recover the ketone.

9. A column 55 cm. high packed with glass tubes 6 mm. in length and diameter was employed with good results. A few grams of trimethylethylene, b.p. 34–36°/735 mm., is always obtained if adequate condensers have been used throughout the preparation. The presence of a little sodium carbonate during the final distillation hinders decomposition.

3. Discussion

Trimethylethylene dibromide has been obtained by the reaction between bromine and trimethylethylene[1] or tertiary amyl alcohol.[2]

Methyl isopropyl ketone has been obtained by the hydration of isopropylacetylene;[3] from isopropylmagnesium bromide and acetic anhydride;[4] from isopropylmagnesium chloride and ethyl acetate;[5] by the hydrolysis of ethyl dimethylacetoacetate;[6] by passing a mixture of the vapors of isobutyric and acetic acids over a thoria catalyst;[7] and from butane or isobutane, aluminum chloride, and carbon monoxide.[8] Methyl isopropyl ketone can also be obtained by rearrangement of methyl isopropenyl carbinol[9] or trimethylethylene oxide;[10] by heating trimethylethylene glycol with dilute hydrochloric acid;[11] by heating trimethylethylene chlorohydrin (2-methyl-2-hydroxy-3-chlorobutane) with water;[12] and by the hydrolysis of trimethylethylene dibromide.[13]

References and Notes

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

thoria

isobutyric and acetic acids

calcium chloride (10043-52-4)

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

ethyl acetate (141-78-6)

acetic anhydride (108-24-7)

carbon monoxide (630-08-0)

HYDROBROMIC ACID (10035-10-6)

sodium carbonate (497-19-8)

bromine (7726-95-6)

aluminum chloride (3495-54-3)

Methyl isopropyl ketone,
2-Butanone, 3-methyl- (563-80-4)

Trimethylethylene dibromide (594-51-4)

trimethylethylene (513-35-9)

tertiary amyl alcohol,
tert.-amyl alcohol (75-85-4)

isopropylacetylene (598-23-2)

isopropylmagnesium bromide (920-39-8)

isopropylmagnesium chloride (1068-55-9)

ethyl dimethylacetoacetate

butane (106-97-8)

methyl isopropenyl carbinol (10473-14-0)

trimethylethylene oxide

trimethylethylene glycol (7778-85-0)

trimethylethylene chlorohydrin

2-methyl-2-hydroxy-3-chlorobutane

isobutane (75-28-5)