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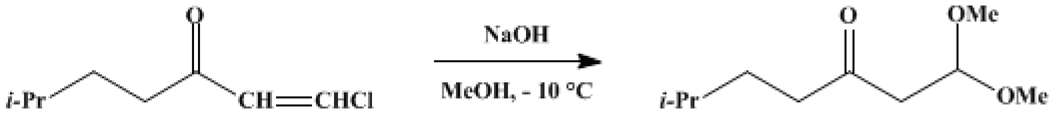
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.032.0079

Organic Syntheses, Coll. Vol. 4, p.558 (1963); Vol. 32, p.79 (1952).

β-KETOISOÖCTALDEHYDE DIMETHYL ACETAL

[Heptanal, 6-methyl-3-oxo-, 1-dimethyl acetal]



Submitted by Charles C. Price and Joseph A. Pappalardo[1].
Checked by R. S. Schreiber, Wm. Bradley Reid, Jr., and R. W. Jackson.

1. Procedure

A dry 1-l. three-necked flask fitted with a mercury-sealed stirrer, a calcium chloride drying tube, and a 500-ml. dropping funnel, protected by a calcium chloride drying tube, is surrounded by an ice-salt mixture at −11°. Anhydrous methanol (130 ml.) (Note 1) and (Note 2) and 161 g. (1 mole) of β-chlorovinyl isoamyl ketone (p. 186) are poured into the flask (Note 3). A solution of 43 g. (1.04 moles) of sodium hydroxide (97%) and 350 ml. of absolute methanol (Note 4) is added dropwise with stirring over a period of 2 hours, during which time the bath temperature is kept between −11° and −8°.

The reaction mixture is poured, with stirring, into 1 kg. of a saturated sodium chloride solution (Note 5). The mixture is extracted with four 100-ml. portions of low-boiling petroleum ether. The extracts are combined and dried over anhydrous potassium carbonate. The liquid is decanted, the potassium carbonate is washed with 25 ml. of low-boiling petroleum ether, and the solution is added to the main fraction. A pinch of anhydrous potassium carbonate is added to the petroleum ether solution, and the solution is then distilled from a Claisen flask to give a colorless liquid; yield 151–169 g. (80–90%); b.p. 122–125°/25 mm.; n_D^{25} 1.4260; d_4^{25} 0.932 (Note 6).

2. Notes

1. Absolute methanol (C.P. grade) was used.
2. The checkers ran this preparation at one-third the scale described here and obtained equivalent results.
3. When this procedure is used to make the dimethyl acetal of β-ketobutyraldehyde, the methanol and β-chlorovinyl methyl ketone must be mixed quickly and cooled well. If these two liquids are placed in the same flask without immediate cooling and mixing, the ketone may decompose rapidly with the evolution of heat and large amounts of hydrogen chloride.
4. It takes about 1 hour of shaking to dissolve the sodium hydroxide pellets.
5. If this reaction is used to prepare the water-soluble dimethyl acetal of β-ketobutyraldehyde, the product of the reaction is not poured into the saturated sodium chloride solution. Instead, the methanol solution is filtered from the sodium chloride and distilled.
6. The product darkens a little on standing but undergoes no change in refractive index.

3. Discussion

The preparation described[2] has been used by Nelles[3] to make a variety of β-ketoacetals.

References and Notes

1. University of Notre Dame, Notre Dame, Indiana.
2. Price and Pappalardo, *J. Am. Chem. Soc.*, **72**, 2613 (1950).
3. Nelles, U. S. pat. 2,091,373 [*C. A.*, **31**, 7444 (1937)]; Brit. pat. 466,890 [*C. A.*, **31**, 7886 (1937)].

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

petroleum ether

dimethyl acetal

potassium carbonate (584-08-7)

hydrogen chloride (7647-01-0)

methanol (67-56-1)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

β-ketobutyraldehyde

β-Chlorovinyl isoamyl ketone (18378-90-0)

β-chlorovinyl methyl ketone

Heptanal, 6-methyl-3-oxo-, 1-dimethyl acetal

β-Ketoisooctaldehyde dimethyl acetal (53684-58-5)