



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.

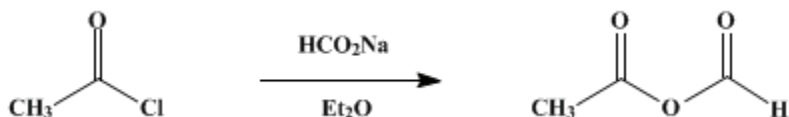
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ACETIC FORMIC ANHYDRIDE

[Acetic acid, anhydride with formic acid]



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Checked by James Savage and Peter Yates.

1. Procedure

A dry, 2-l., three-necked, round-bottomed flask equipped with a stirrer, a thermometer, a reflux condenser fitted with a calcium chloride tube, and a dropping funnel is charged with 300 g. (4.41 moles) of sodium formate (Note 1) and 250 ml. of anhydrous diethyl ether (Note 2). To this stirred mixture is added 294 g. (266 ml., 3.75 moles) of acetyl chloride (Note 3) as rapidly as possible, while the temperature is maintained at 23–27° (Note 4). After the addition is complete, the mixture is stirred for 5.5 hours at 23–27° to ensure complete reaction. The mixture is then filtered with suction, the solid residue is rinsed with 100 ml. of ether, and the washings are added to the original filtrate (Note 5). The ether is removed by distillation at reduced pressure, and the residue is distilled, yielding 212 g. (64%) of colorless acetic formic anhydride, b.p. 27–28° (10 mm.), 38–38.5° (39 mm.); n_D^{20} 1.388 (Note 6).

2. Notes

1. Reagent grade sodium formate from J. T. Baker Chemical Co. was used; it was finely ground to ensure better contact. It is imperative that extreme care be taken to ensure anhydrous conditions throughout the procedure, since hydrolysis produces formic and acetic acids, which are very difficult to remove from the product. A slight excess of sodium formate ensures a product free of acetyl chloride.
2. Mallinckrodt AR grade ether was used without further drying by the submitter. The checkers, working at half scale, found it essential to dry the ether over sodium.
3. Acetyl chloride from Matheson, Coleman and Bell was used without further purification.
4. The addition of acetyl chloride is mildly exothermic; the exotherm can be controlled by slower addition or by the use of a cooling bath (20–24°). The addition is completed in *ca.* 5 minutes.
5. The filtration and subsequent ether rinse should be carried out quickly in order to keep the filtrate dry.
6. The acetic formic anhydride may be stored at 4° in a standard-taper, round-bottomed flask fitted with a polyethylene stopper. Moisture catalyzes the decomposition of the product to acetic acid, with the evolution of carbon monoxide. *The material must not be stored in sealed containers!*
7. The IR spectrum of neat acetic formic anhydride shows two bands in the carbonyl region at 1765 and 1791 cm^{-1} and carbon-oxygen-carbon stretching absorption at 1050 cm^{-1} (a band at 1180 cm^{-1} could also be due to C-O-C). The ¹H NMR spectrum (neat) shows a singlet at δ 2.25 (acetyl protons) and a singlet at δ 9.05 (formyl proton). If the product is not pure, the following peaks may also be observed: δ 2.05 ($\text{CH}_3\text{CO}_2\text{H}$), 2.20 [$(\text{CH}_3\text{CO})_2\text{O}$], 2.68 (CH_3COCl), 8.05 (HCOOH), 8.85 [$(\text{HCO})_2\text{O}$]. The spectrum of the product obtained by the checkers showed slight contamination with acetic anhydride and formic anhydride.

3. Discussion

Acetic formic anhydride has been prepared by the reaction of formic acid with acetic anhydride^{2,3} and ketene,^{4,5} and of acetyl chloride with sodium formate.⁶ The present procedure is essentially that of Muramatsu.⁶ It is simpler than others previously described, gives better yields, and is easily adapted to the preparation of large quantities, usually with an increase in yield. Acetic formic anhydride is a useful intermediate for the formylation of amines,^{3,7} amino acids,^{8,9} and alcohols,^{2,10} for the synthesis of aldehydes from Grignard reagents,¹¹ and for the preparation of formyl fluoride.¹²

References and Notes

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

Acetic formic anhydride

Acetic acid, anhydride with formic acid

acetic acid (64-19-7)

ether,
diethyl ether (60-29-7)

acetic anhydride (108-24-7)

carbon monoxide (630-08-0)

acetyl chloride (75-36-5)

formic acid (64-18-6)

sodium (13966-32-0)

sodium formate

formyl fluoride (1493-02-3)

FORMIC ANHYDRIDE

carbon-oxygen-carbon