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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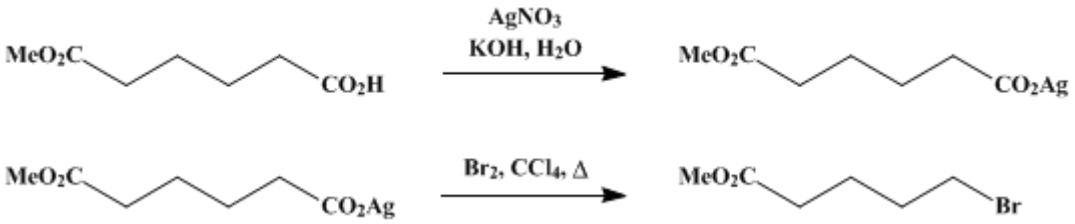
METHYL 5-BROMOVALERATE

[Valeric acid, δ-bromo-, methyl ester]



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1. Procedure

To a solution of 33 g. (0.5 mole) of potassium hydroxide (Note 1) in 1.5 l. of distilled water in a 5-l. flask or other appropriate container fitted with a mechanical stirrer is added 80 g. (0.5 mole) of methyl hydrogen adipate (Note 2). With continuous stirring a solution of 85 g. (0.5 mole) of silver nitrate in 1 l. of distilled water is added rapidly (about 15 minutes). The precipitated methyl silver adipate is collected on a Büchner funnel, washed with methanol, and dried in an oven at 50–60°. For the next step the dried silver salt is finely powdered and sieved through a 40-mesh screen. The combined yield from two such runs is 213 g. (80%).

The 213 g. (0.8 mole) of finely powdered silver salt is placed in a 1-l. three-necked flask (Note 3); two necks of the flask are stoppered, and the third is connected to a water pump through a U-tube or flask containing Drierite. The flask is then placed in an oil bath and evacuated to a pressure of about 15 mm. The temperature of the oil bath is maintained at 100–110° for 36 hours (Note 4) and (Note 5).

The pressure in the flask is restored to that of the atmosphere. The flask is removed from the oil bath and equipped with a dropping funnel, condenser, and mechanical stirrer (Note 6). To the salt is added 350 ml. of dry carbon tetrachloride (Note 7); the stirrer is started, and 117 g. (40 ml., 0.73 mole) of dry bromine (p. 790, Note 2) is added through the dropping funnel over a 30- to 40-minute period. Occasional cooling may be necessary as the reaction is quite vigorous at first. When all the bromine has been added, the mixture is heated for 1 hour on a steam bath. It is then filtered and the silver bromide washed thoroughly on the filter with 100 ml. of warm carbon tetrachloride. The filtrate is washed once with 100 ml. of 10% sodium carbonate solution and dried over 30–40 g. of Drierite. The solvent is removed and the residue distilled under reduced pressure. The yield of product boiling at 75–80°/4 mm. is 101–106 g. The yield is 65–68% based on the weight of the methyl silver adipate before drying under reduced pressure, or 52–54% based upon methyl hydrogen adipate.

2. Notes

1. Reagent grade potassium hydroxide containing 85% potassium hydroxide is used.
2. The methyl hydrogen adipate was Eastman Kodak grade.
3. Drying is carried out in the flask in which the final reaction is to be run in order to avoid a transfer. The success of this preparation depends upon the exclusion of moisture. The silver salt retains traces of water tenaciously.
4. If the indicated pressure is maintained the water pump may be disconnected, but owing to leaks it will usually be found necessary to re-evacuate several times over the 36-hour period.
5. A good vacuum oven would serve for drying just as well, but the temperature of the salt should not exceed 110°.
6. For best results all equipment should be thoroughly dried.
7. The carbon tetrachloride is dried over phosphorus pentoxide or some other drying agent.

3. Discussion

This method with some slight modifications is applied in the synthesis of ω-bromo esters from C_5 to C_{17}.[1] Methyl 5-bromovalerate has been prepared by treating the silver salt of methyl hydrogen adipate with bromine.[1] The ethyl ester has been prepared from the acid by esterification[2,3] or through the acid chloride.[3]

References and Notes

1. Hunsdiecker and Hunsdiecker, *Ber.*, **75**, 296 (1942).
2. Cloves, *Ann.*, **319**, 367 (1901).
3. Merchant, Wickert, and Marvel, *J. Am. Chem. Soc.*, **49**, 1829 (1927).

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

Drierite

silver salt of methyl hydrogen adipate

methanol (67-56-1)

silver nitrate (7761-88-8)

sodium carbonate (497-19-8)

bromine (7726-95-6)

carbon tetrachloride (56-23-5)

potassium hydroxide (1310-58-3)

Methyl 5-bromovalerate,
Valeric acid, δ-bromo-, methyl ester (5454-83-1)

methyl hydrogen adipate (627-91-8)

methyl silver adipate

silver bromide (7785-23-1)

phosphorus pentoxide (1314-56-3)