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.

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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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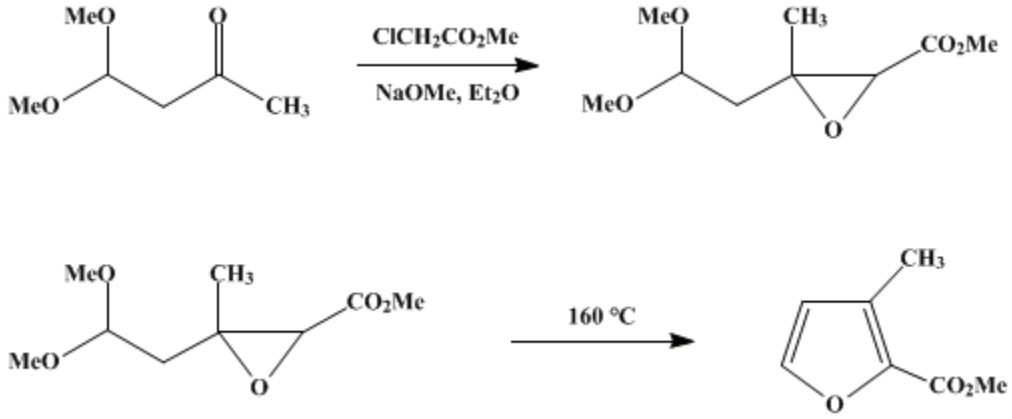
METHYL 3-METHYL-2-FUROATE

[2-Furoic acid, 3-methyl-, methyl ester]



Submitted by D. M. Burness[1]
Checked by James Cason and Robert B. Hutchison.

1. Procedure

A. *Methyl 5,5-dimethoxy-3-methyl-2,3-epoxypentanoate.* A 2-l. three-necked flask is equipped with a sealed centrifugal stirrer (Note 1), a thermometer inserted through an adapter with a side arm connected to a source of dry nitrogen, and a 250-ml. Erlenmeyer addition flask.[2] The apparatus is dried with a free flame in a slow stream of nitrogen; from this point the reaction is conducted in an atmosphere of nitrogen (Note 2).

A mixture of 132 g. (1.0 mole) of 4,4-dimethoxy-2-butanone (Note 3), 174 g. (1.6 moles) of methyl chloroacetate (Note 3), and 800 ml. of dry ether is placed in the reaction flask, then 86 g. (1.6 moles) of sodium methoxide (Note 4) is placed in the addition flask. The solution is cooled in an ice-salt bath to −10°, then the sodium methoxide is added gradually at a rate such that a temperature below −5° can be maintained (about 2 hours). The mixture is stirred for an additional 2 hours (Note 5) and then allowed to come to room temperature overnight. It is cooled again to 0° and made slightly acidic by the addition of a solution of 10 ml. of glacial acetic acid in 150 ml. of water. The ether is decanted, and the residual slurry is extracted with three 100-ml. portions of ether. The combined ether solutions are washed in a separatory funnel with 50 ml. of saturated sodium chloride solution to which is added 1-g. portions of sodium bicarbonate until the washings are no longer acidic. After each bicarbonate addition, the mixture is shaken for at least 1 minute before a test for acidity is made. Finally, the ether phase is washed with saturated sodium chloride solution, then dried over 20–25 g. of anhydrous magnesium sulfate. Distillation of the solvent leaves a nearly quantitative yield of crude glycidic ester (Note 6).

B. *Methyl 3-methyl-2-furoate.* The crude glycidic ester prepared as described above is placed in a 300-ml. flask which is attached to a 12-cm. column filled with 3/16-inch glass helices (or a 50-cm. simple Vigreux column) and heated in a liquid bath. When the pot temperature reaches about 160°, or before, methanol begins to distil. Heating is continued until the distillation of methanol essentially ceases and about the theoretical amount (64 g.) has been collected. After the heating bath has been allowed to cool, the product is distilled at reduced pressure; b.p. 72–78°/8 mm., yield 91–98 g. (65–70%) (Note 7). The ester solidifies in the receiver as an essentially pure compound, m.p. 34.5–36.5° (Note 8).

2. Notes

1. A stirring assembly which makes use of a lubricated ball-joint seal[3] is convenient. The checkers used

a Hershberg stirrer rather than a centrifugal stirrer.
2. Maintenance of a low positive pressure of nitrogen on the system is accomplished by insertion of a T-tube in the nitrogen line for attachment of a U-tube whose bend is just closed with mineral oil.
3. The 4,4-dimethoxy-2-butanone[4] may be obtained from Aldrich Chemical Co., Milwaukee, Wisconsin, under the name of 3-ketobutyraldehyde dimethyl acetal. This and the methyl chloroacetate are preferably dried over Drierite and distilled before use. The pure acetal has b.p. 55–56°/8 mm., n_D^{25} 1.4119. The presence of 4-methoxy-3-buten-2-one, which raises the index of refraction, can be tolerated as an impurity, for it leads to the same reaction product.[5] Commercial methyl chloroacetate usually contains considerable low-boiling material which is best separated by distillation through a 50-cm. simple Vigreux column. The chloroacetate is collected at 131–132°.
4. The submitter reports that the commercial 95% "Sodium Methylate" from Mathieson Chemical Corp. is satisfactory, provided that either fresh material or material which has been opened previously only under dry nitrogen is used. The checkers experienced such erratic results with commercial sodium methoxide (even previously unopened bottles) that freshly prepared material was used. For this purpose, 37 g. of clean sodium, cut in 1- to 3-g. pieces, was added portionwise to 800 ml. of stirred anhydrous methanol contained in a 2-l. three-necked flask equipped with a condenser. After the sodium had dissolved, the methanol was removed by distillation at reduced pressure, and the residual white sodium methoxide was dried by heating at 150° under aspirator vacuum.
5. The stream of nitrogen may be discontinued at this point if the outlet tube from the flask is closed with a Drierite tube.
6. The submitter reports that the residual glycidic ester was distilled through a 15-cm. Vigreux column to yield 185–195 g. of crude product, b.p. 113–122°/8 mm. Redistillation through a 25-cm. column packed with 3/16-inch glass helices was reported to give 157–164 g. (77–80%) of product; b.p. 93°/0.7 mm. to 89°/1 mm.; n_D^{25} 1.4405–1.4419. The drop in boiling point was attributed to decomposition during distillation to yield methanol and methyl 3-methyl-2-furoate. The checkers found that in most runs the product obtained from the first distillation consisted largely of the furoate.
The submitter has prepared methyl 5,5-dimethoxy-3-phenyl-2,3-epoxypentanoate by essentially the same procedure as here described.
7. In a run 15 times this size, a 71% yield was obtained by the submitter.
8. Recrystallization from ethanol raises the melting point to 36.5–37°.

3. Discussion

Methyl 5,5-dimethoxy-3-methyl-2,3-epoxypentanoate has been prepared only by the procedure described or in like manner from 4-methoxy-3-buten-2-one.[5]

Methyl 3-methyl-2-furoate has been prepared previously, presumably from the acid.[6]

References and Notes

1. Eastman Kodak Co., Rochester, New York.
2. *Org. Syntheses Coll. Vol.* **3**, 550 (1955).
3. *Organic Chemical Bulletin*, **24**, No. 3, Eastman Kodak Co., Rochester, New York, 1952.
4. Burness, U. S. pat. 2,760,985 [*C. A.*, **51**, 2854 (1957)].
5. Burness, *J. Org. Chem.*, **21**, 102 (1956); U. S. pat. 2,772,295 [*C. A.*, **51**, 7424 (1957)].
6. Asahina, *Acta phytochim. (Japan)*, **2**, 12 (1924) [*Chem. Zentr.*, **1924, II**, 1694].

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

Drierite

ethanol (64-17-5)

acetic acid (64-19-7)

methanol (67-56-1)

ether (60-29-7)

sodium bicarbonate (144-55-8)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

chloroacetate (79-11-8)

sodium methoxide,
sodium methylate (124-41-4)

sodium (13966-32-0)

methyl chloroacetate (96-34-4)

magnesium sulfate (7487-88-9)

bicarbonate (71-52-3)

Methyl 3-methyl-2-furoate,
2-Furoic acid, 3-methyl-, methyl ester (6141-57-7)

4,4-dimethoxy-2-butanone,
3-ketobutyraldehyde dimethyl acetal (5436-21-5)

4-methoxy-3-buten-2-one

furoate

methyl 5,5-dimethoxy-3-phenyl-2,3-epoxypentanoate

Methyl 5,5-dimethoxy-3-methyl-2,3-epoxypentanoate

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