A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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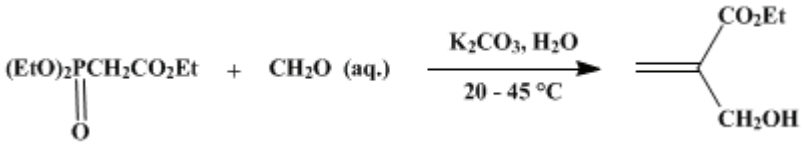
ETHYL α-(HYDROXYMETHYL)ACRYLATE

[2-Propenoic acid, 2-(hydroxymethyl)-, ethyl ester]



Submitted by J. Villieras and M Rambaud[1].
Checked by Christina M. J. Fox and James D. White.

1. Procedure

A. *Ethyl α-(hydroxymethyl)acrylate*. (See (Note 1)). A 1000-mL, four-necked, round-bottomed flask is fitted with mechanical stirrer, 250-mL equalizing funnel, condenser, and thermometer. Paraformaldehyde (48 g, 1.6 mol), 1 *N* phosphoric acid (4 mL), and water (110 mL) are heated at 90°C for 1.5 hr to form a clear aqueous formaldehyde solution. This solution is cooled to room temperature. Triethyl phosphonoacetate (89.6 g, 0.4 mol) is added to the flask and the solution is stirred at room temperature at 1000 rpm. A solution of potassium carbonate (60.7 g, 0.44 mol) in water (60 mL) is added at room temperature (first slowly: 10 mL in 10 min) and then more rapidly (40 min). The temperature reaches 35–40°C and must be maintained at this level (with a water bath if necessary). Stirring is continued for 5 min at 40°C after the end of the addition; then the mixture (liquid–liquid heterogenous mixture) must be cooled rapidly to room temperature using an ice bath (Note 2) while diethyl ether (200 mL) and brine (150 mL) are added. After decantation, the mixture is extracted with ether (three 100-mL portions). The combined organic layers are washed with brine (two 100-mL portions) (Note 3) and dried over magnesium sulfate; the solvents are evaporated under reduced pressure and the remaining oil is distilled to give a fraction at 65–70°C (1 mm) that weighs 38.5–41.6 g (74–80%), n_D^{20} 1.4494. The hydroxy ester is of high purity as shown by GLC analysis (25-m silica capillary OV-1 column) and spectral data (Note 4) and (Note 5).

2. Notes

1. All manipulations should be carried out in a well-ventilated hood. The preparation requires the use of formaldehyde solution and gives rise to ethyl acrylate as a secondary product, the amount of which increases if the addition of the carbonate solution, is too rapid and the temperature rises to 45°C. A freshly opened supply of paraformaldehyde purchased from Aldrich Chemical Company, Inc. was used by the checkers. The use of commercial formaldehyde solutions that now contain up to 15% methanol leads to the formation of several by-products that cannot be separated by distillation from the α-(hydroxymethyl)acrylate.
2. This experimental procedure must be followed carefully to avoid partial decomposition of ethyl α-(hydroxymethyl) acrylate. The reaction is stopped rapidly after the addition of the carbonate solution (5 min) to prevent formation of high molecular weight by-products which result from transesterification and Michael addition, both of which occur in the basic medium. However, about 25% of the product is lost. Addition of diethyl ether during cooling minimizes side reactions.
3. Treatment with brine allows total elimination of base in the organic layer and prevents any side reaction during the distillation.
4. The spectral properties of ethyl α-(hydroxymethyl) acrylate are as follows: ^{1}H NMR (CCl_4) δ: 4.20 (2 H, CH_2-OH), 5.80 and 6.15 (2 H, CH_2=); ^{13}C NMR ($CDCl_3$) δ: 60.9 (CH_2OH), 124.8 (CH_2=C), 140.2 (CH_2=C), 166.5 (COOEt).
5. α-(Bromomethyl)-, α-(chloromethyl)-, α-(iodomethyl)-, and α-(fluoromethyl)acrylates are easily obtained from the α-(hydroxymethyl)acrylate[2] as illustrated in the following procedure.
A 500-mL, four-necked, round-bottomed flask is fitted with a mechanical stirrer, a 100-mL pressure-equalizing addition funnel, a reflux condenser capped with a drying tube (silica gel), and a thermometer

(range −90° to +60°C). The flask is charged with a stirred solution of ethyl α-(hydroxymethyl)acrylate (33.84 g, 0.26 mol) in dry ether (250 mL) at −10°C. Phosphorus tribromide (34 g, 11.5 mL, 0.12 mol) is added slowly (15 min). The temperature is allowed to rise to 20°C and stirring is continued for 3 hr. Water (150 mL) is added at −10°C and the mixture is extracted with technical-grade hexane (three 50-mL portions). The organic phase is washed twice with a saturated sodium chloride solution (50 mL) and dried over magnesium sulfate. The solvents are removed with a rotary evaporator under reduced pressure, and the remaining oil is distilled to give ethyl α-(bromomethyl)acrylate, bp 85–87°C (20 mm), which weighs 43.8 g (87%), n_D^{20} 1.4502. The ester is of high purity as shown by GLC analysis on a capillary OV-1 column, and spectral data.

The spectral properties of ethyl α-(bromomethyl)acrylate are as follows: ^{1}H NMR (CCl_4) δ: 4.15 (2 H, CH_2Br), 5.90 and 6.22 (2 H, H_2C=); ^{13}C NMR ($CDCl_3$) δ: 29.2 (CH_2Br), 126.5 (CH_2=C), 137.8 (CH_2=C), 164.5 (COOEt).

3. Discussion

Ethyl α-(hydroxymethyl)acrylate can be used for the synthesis of chloro and bromomethyl acrylates. The fluoro and iodo compounds have been prepared easily by halogen exchange from ethyl α-(bromomethyl)acrylate.[2]

The same procedure can be applied to the synthesis of diethyl α-(bromomethyl)vinylphosphonate.[3,4] The keto analogs can be obtained in the same way.[5]

The procedure described here is relatively new and gives improved overall yields of 60–67% for the preparation of ethyl α-(bromomethyl)acrylate in two stages from commercially available starting materials. Other more complex and less productive procedures have been described.[6]

Ethyl α-(bromomethyl)acrylate has been used extensively for the synthesis of α-methylene lactones from ketones and aldehydes,[7] and α-methylene lactams, which are known for their cytotoxic activity,[7,8,9] from imines.[8]

References and Notes

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

brine

potassium carbonate (584-08-7)

methanol (67-56-1)

ether,
diethyl ether (60-29-7)

formaldehyde (50-00-0)

sodium chloride (7647-14-5)

phosphorus tribromide (7789-60-8)

phosphoric acid (7664-38-2)

magnesium sulfate (7487-88-9)

keto

hexane (110-54-3)

triethyl phosphonoacetate (867-13-0)

Ethyl α-(bromomethyl)acrylate (17435-72-2)

Ethyl α-(hydroxymethyl)acrylate,
2-Propenoic acid, 2-(hydroxymethyl)-, ethyl ester,
ethyl α-(hydroxymethyl) acrylate (10029-04-6)

diethyl α-(bromomethyl)vinylphosphonate

paraformaldehyde (30525-89-4)