Organic Syntheses

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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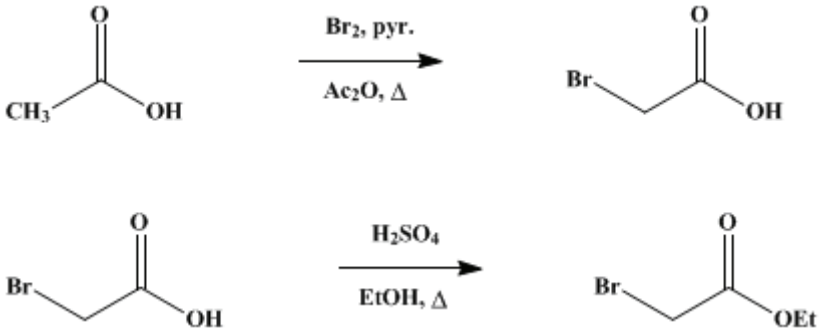
ETHYL BROMOACETATE

[Acetic acid, bromo-, ethyl ester]



Submitted by Samuel Natelson and Sidney Gottfried.
Checked by Nathan L. Drake and Stuart Haywood..

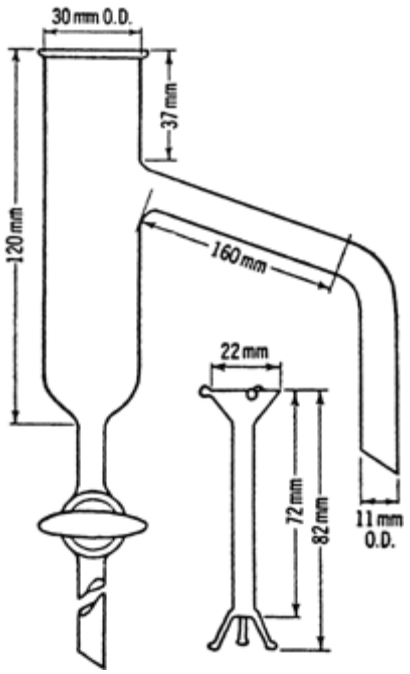
1. Procedure

A. *Bromoacetic acid.* (Note 1). A mixture of 1 l. (17.5 moles, excess) of glacial acetic acid, 200ml. of acetic anhydride, and 1 ml. of pyridine is placed in a 3-l. flask fitted with a dropping funnel and a reflux condenser, the end of which is protected with a drying tube (Note 2); the tip of the dropping funnel should reach below the level of the liquid. Some glass beads are added, and the mixture is heated to boiling. The flame is then removed, approximately 1 ml. of bromine is added, and the reaction is allowed to proceed until the liquid becomes colorless (Note 3). Then the remainder of 1124 g. (360 ml., 7.03 moles) of bromine (Note 4) is added as rapidly as it will *react* (Note 5); during this period (about 2.5 hours), the acid is kept boiling *gently* by means of a flame. After about half the bromine has been added, the liquid assumes a cherry color which is retained throughout the remainder of the bromination. After all the bromine has been added, the mixture is heated until it becomes colorless.

The mixture is allowed to cool, and 75 ml. of water is added slowly to destroy the acetic anhydride. Excess acetic acid and water are now removed on a boiling water bath under a pressure of approximately 35 mm. When the evaporation is complete, the residue will crystallize on cooling; this residue, which is almost pure bromoacetic acid, weighs 845–895 g. (Note 6).

B. *Ethyl bromoacetate.* For the esterification, an apparatus similar to that used in the preparation of anhydrous oxalic acid [*Org. Syntheses*, Coll. Vol. 1, 422 (1941)] may be used, but with the outlets from the trap reversed so that the lighter liquid returns to the mixture and the heavier liquid (water) is drawn off at the bottom. A somewhat simpler apparatus may be built using the water trap shown in Fig. 12 (Note 7). The crude bromoacetic acid is placed in a 3-l. flask, together with 610 ml. of ethanol (9.9 moles, excess) and 950 ml. of benzene. About 1.5 ml. of concentrated sulfuric acid is added to hasten the reaction (Note 8), and the mixture is refluxed on a boiling water bath while the water is separated and measured. Approximately 296 ml. of liquid (whose composition is approximately 50% ethanol and water) separates from the benzene; this includes all the water formed in the reaction, together with the excess ethanol. When no more water separates from the benzene, 75 ml. of ethanol is added to the reaction mixture and heating is continued for 30 minutes. If the reaction has been completed, there will not be a second phase in the distillate. The end of the reaction is also indicated when the benzene flowing through the side tube becomes clear and the rate of refluxing decreases considerably. At this point, 150 ml. of benzene is condensed and removed through the trap.

Fig. 12.



The mixture is transferred to a separatory funnel and washed once with 1.5 l. of water, once with 1.5 l. of 1% sodium bicarbonate solution, and finally with 1.5 l. of water. It is then dried over anhydrous sodium sulfate and fractionated at atmospheric pressure from an oil bath using a Vigreux column 1 ft. in length (Note 9). The fraction boiling at 154–155°/759 mm. is collected (Note 10). The yield is approximately 818 g. (65–70%).

2. Notes

1. The vapors of ethyl bromoacetate are extremely irritating to the eyes. Care should be taken to keep the material in closed containers and to manipulate it in open vessels only in a good hood.
2. An all-glass apparatus is advisable. If it is not available, one-holed asbestos stoppers may be made by soaking strips of asbestos in water, wrapping them around pieces of glass tubing of suitable size until the desired diameter has been reached, and then allowing them to dry at 110°.
3. At the beginning there is a lag of about 10 minutes before the reaction starts and the color of the bromine disappears.
4. If C.P. bromine is available it may be used directly. Technical bromine should be dried with concentrated sulfuric acid.
5. The bromine should not be added so rapidly that loss occurs through the condenser.
6. Pure bromoacetic acid may be obtained by distillation of this crude product from a Claisen flask immersed in an oil bath and fitted with an 8-in. insulated Vigreux column. The fraction boiling at 108–110°/30 mm. is collected. The yield is 775–825 g. (80–85%).
7. The trap shown in Fig. 12 is a modification of the moisture trap designed by Dean and Stark.[1] The dimensions may be varied to suit individual purposes, for the size is largely a matter of convenience. The trap may be used without the inner funnel, but with this funnel (C. F. Koelsch, private communication) the condensate separates into two layers rapidly and completely, and the liquid falling from the condenser does not agitate the two phases in the trap. The funnel tube must be of such a length that the top of the funnel is above the side arm of the trap. The tube of the trap may be graduated, but this is not necessary.
8. In the absence of a catalyst the reaction proceeds more slowly and smaller yields are obtained. Phosphoric acid may be substituted for sulfuric acid, but the use of sulfuric acid results in the best yield in the shortest time.
9. If a fractionating column is not used, as much as 15–20% of the product may be lost in the fore-run.
10. The fraction boiling over a 1-degree range is collected. The boiling point has been observed to range from 154–155° to 158–159° on different days.

3. Discussion

Bromoacetic acid has been prepared by direct bromination of acetic acid at elevated temperatures and pressures,[2,3,4] or with dry hydrogen chloride as a catalyst;[5] and with red phosphorus as a catalyst with the formation of bromoacetyl bromide.[6,7,8,9,10] Bromoacetic acid has also been prepared from chloroacetic acid and hydrogen bromide at elevated temperatures;[6] by oxidation of ethylene bromide with fuming nitric acid;[7] by oxidation of an ethanolic solution of bromoacetylene by air;[8] and from ethyl α,β-dibromovinyl ether by hydrolysis.[9] Acetic acid has been converted into bromoacetyl bromide by action of bromine in the presence of red phosphorus, and ethyl bromoacetate has been obtained by action of ethanol upon the acid bromide.[10,11,12,13,14] Ethyl bromoacetate has also been prepared by direct bromination of ethyl acetate at elevated temperatures;[15,16] by action of ethanol upon bromoacetic anhydride;[17] by action of phosphorus tribromide upon ethyl glycollate;[18] and by action of hydrogen bromide upon ethyl diazoacetate.[19] The method described above is based upon the procedure of Natelson and Gottfried.[20]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 408
- Org. Syn. Coll. Vol. 4, 573
- Org. Syn. Coll. Vol. 4, 605
- Org. Syn. Coll. Vol. 5, 277
- Org. Syn. Coll. Vol. 5, 303
- Org. Syn. Coll. Vol. 5, 762
- Org. Syn. Coll. Vol. 5, 808
- Org. Syn. Coll. Vol. 5, 883
- Org. Syn. Coll. Vol. 5, 1060
- Org. Syn. Coll. Vol. 6, 520
- Org. Syn. Coll. Vol. 7, 135

References and Notes

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

red phosphorus

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrogen chloride (7647-01-0)

acetic acid (64-19-7)

Benzene (71-43-2)

ethyl acetate (141-78-6)

acetic anhydride (108-24-7)

sodium bicarbonate (144-55-8)

nitric acid (7697-37-2)

hydrogen bromide (10035-10-6)

bromine (7726-95-6)

sodium sulfate (7757-82-6)

phosphorus tribromide (7789-60-8)

Oxalic acid (144-62-7)

chloroacetic acid (79-11-8)

pyridine (110-86-1)

phosphoric acid (7664-38-2)

ethylene bromide (106-93-4)

bromoacetyl bromide (598-21-0)

Bromoacetic acid (79-08-3)

ethyl diazoacetate (623-73-4)

Ethyl bromoacetate,
Acetic acid, bromo-, ethyl ester (105-36-2)

bromoacetylene (593-61-3)

ethyl α,β-dibromovinyl ether

bromoacetic anhydride (13094-51-4)

ethyl glycollate (623-50-7)