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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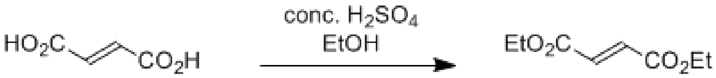
ETHYL FUMARATE



Submitted by B. B. Corson, Elizabeth Adams, and R. W. Scott.
Checked by Henry Gilman and J. B. Dickey.

1. Procedure

The apparatus is assembled as shown in Fig. 2. Alcohol vapor from vaporizer flask E is passed through the acid contained in esterification flask *J*. The ester which is formed remains in *J* whereas the excess alcohol and the water formed during esterification continuously distil through column *K* into condenser *L* (Note 1). Flask *E* is a 250-cc. Pyrex distilling flask equipped with an extra side-arm *D*. Alcohol is run from dropping funnel *F* into flask *E*, a sufficient head being maintained by the height of funnel *G*. Stopcock *G'* is kept open, the flow of alcohol being regulated by stopcock *F'*. Side-arm *H* may be wrapped with asbestos paper to lessen condensation.

Side-arm *D* connects with two mercury safety valves, *C and B*. Tube *C'* dips about 3 cm. under the surface of the mercury contained in test tube *C*. This valve guards against excess internal pressure sometimes caused by the plugging of delivery tube *I*. Loud bubbling in the mercury quickly results from any clogging (Note 2) in the apparatus. Glass tube *A* (preferably a large capillary) barely dips into the mercury which just seals the bend of U-tube *B*. This valve guards against any fall of pressure within the system (Note 3), which would result in the transfer of the contents of flask *J* into vaporizer *E*, were it not compensated by the inrush of air through *A*. Since there is some lag in this pressure compensation, the alcohol vapor delivery tube *I* should be about 30 cm. long; it should reach to within 2 or 3 cm. of the bottom of flask *J* and should extend about 10 cm. above the stopper of the flask. The delivery end may be drawn out to a coarse capillary (Note 4).

Esterification flask *J* is a 1-l. Pyrex round-bottom flask fitted with a 3-hole rubber stopper, carrying thermometer *T*, delivery tube *I* and column *K*. Thermometer *T* should reach to within a few centimeters of the bottom of the flask, so as to register the temperature of the liquid esterification mixture. Flask *J* is immersed in and heated by the oil contained in deep dish *O*. Thermometer *T'* dips into the oil bath. Fractionating column *K* (Note 5) leads the vapor mixture of alcohol and water into condenser *L*.

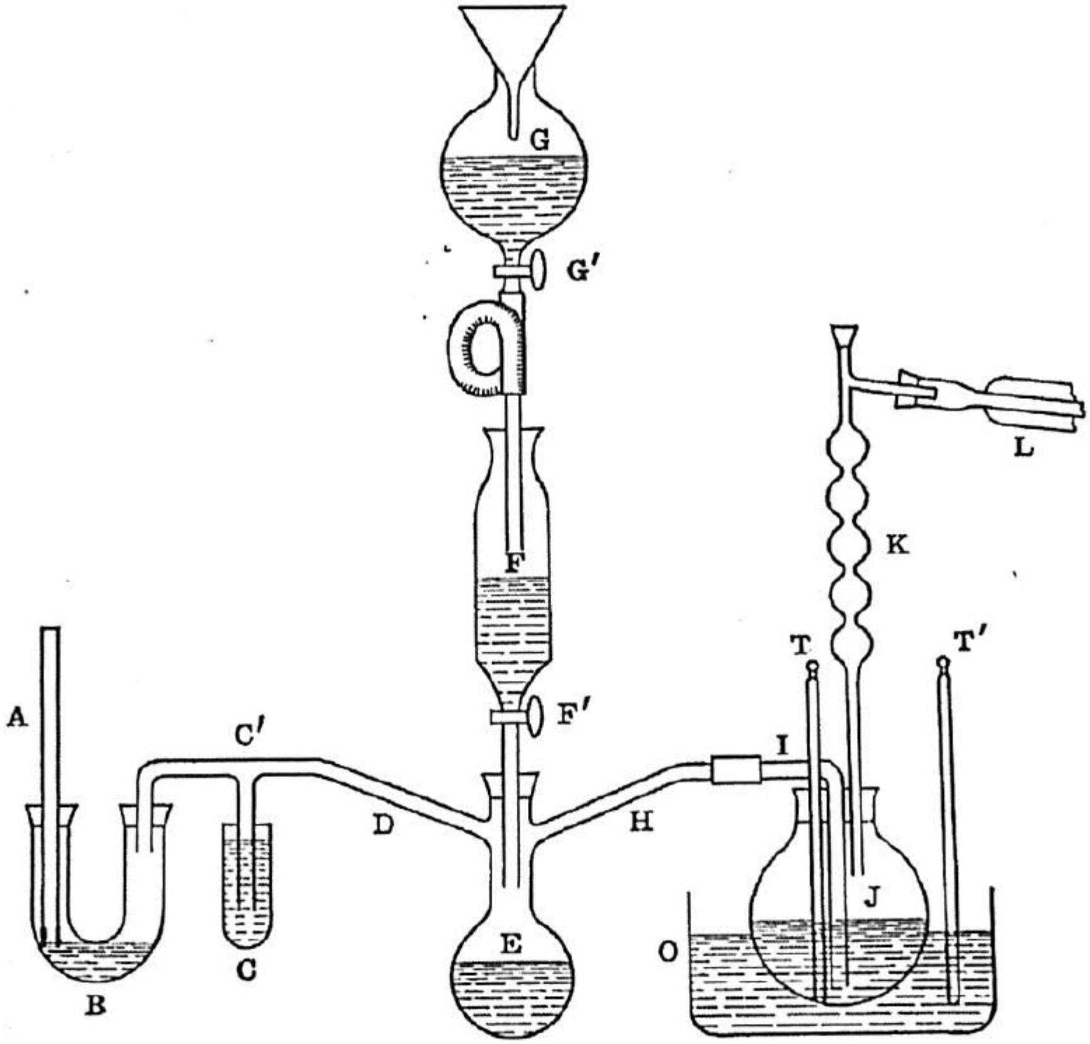


Fig. 2.

Esterification flask *J* is charged with 348 g. (3 moles) of fumaric acid and 350 cc. (Note 6) of 96 per cent ethyl alcohol containing 15 cc. of concentrated sulfuric acid. The oil bath is heated until the temperature of the reaction mixture in *J* is 110° (Note 7). During the preliminary heating about 200 cc. of alcohol distils from *J*. Then vaporizer *E* is heated over a gauze by a flame and the flow of 96 per cent (Note 8) alcohol (Note 9) from dropping tunnel *F* is so regulated that the temperature of the esterification mixture in *J* remains between 115° and 120°, the temperature of the oil bath being maintained at about 150°. The reaction is stopped when 910 cc. of distillate has been collected; this requires about two hours.

The reaction mixture is then cooled to room temperature and neutralized with sodium carbonate solution (Note 10). The ester is separated and the aqueous layer shaken with benzene (Note 11); the liquids are combined, the benzene is distilled through a fractionating column (Note 12), and the ester from a side-arm flask at ordinary pressure, and the portion boiling at 213–215° is collected. The yield is 410 g. (80 per cent of the theoretical amount) (Note 13).

2. Notes

1. This preparation avoids the two disadvantages of the ordinary method of esterification by removing the water from the esterification mixture and by raising the reaction temperature.
2. If tube *I* clogs, the solid can often be blown out by temporarily raising test tube *C*, thereby increasing the pressure within the system.
3. Too rapid an addition of alcohol to *E* might cause a sudden fall of pressure.
4. The capillary tube *I* which delivers into flask *J* should be coarse, so as not to clog. With salicylic acid, which is especially prone to plug the delivery tube, the capillary end is omitted.
5. If a simple bent tube is used instead of a column, as much as 10 per cent of the ester may be carried over with the alcohol-water vapor.
6. The amount of alcohol to be added depends upon the solubility of the acid in question. The esterification mixture when hot should be liquid enough to allow passage of the alcohol vapor. There should be no attempt to dissolve the acid completely. Complete solution occurs only after the esterification reaction has run for some time.
7. Should the acid tend to clog the delivery tube it is advisable to pass a slow stream of alcohol vapor through the esterification flask, in order to keep the tube open, even before the temperature of the esterification mixture has reached 110°.
8. If 99 per cent alcohol is used instead of 96 per cent, the yield of ethyl fumarate is 87 percent of the theoretical instead of 80 per cent. When large quantities of ester are being prepared it is easy to use dry alcohol, since the alcohol-water distillate can be dehydrated over quicklime and used again. The wet alcohol is conveniently dehydrated by refluxing six hours over quicklime in a 12-l. flask and then distilling.
9. Methyl esters are easily prepared by substituting methyl for ethyl alcohol.
10. Sometimes a white solid precipitates when sodium carbonate solution is shaken with the esterification mixture. This solid usually dissolves if some water is added.
11. If the benzene solution of ester is to stand several hours before distillation it should be dried with a small amount of anhydrous sodium carbonate.
12. If the benzene is distilled from an ordinary distilling flask or through a simple bent tube some of the ester passes over with the benzene. The ester-benzene should be heated until the temperature at the top of the column is 110°.
13. This apparatus can be used in the preparation of various high boiling esters. Its development was assisted by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

Following are the percentage yields obtained in the preparation of other esters; ethyl maleate, 73; ethyl salicylate, 70; ethyl oxalate, 80; ethyl benzoate, 92; methyl benzoate, 87. In the preparation of ethyl maleate troublesome emulsions were encountered in working up the product. Occasionally this happened with other esters. These emulsions can usually be broken by suction filtration. Salicylic acid esterifies more slowly than fumaric and requires a larger excess of alcohol.

3. Discussion

Various methods[1] of esterification, similar to the one described in the procedure, are to be found in the literature. In some methods[2] the process has been made continuous by passing the alcohol-water distillate through a dehydrator and then returning the vapor of the dried alcohol to the esterification mixture; in others,[3] a substance such as carbon tetrachloride, chloroform or benzene has been added, the water then being removed by means of a ternary mixture, for example, water-alcohol-benzene. When alcohol vapor is passed through the esterification mixture, as described above, the reaction temperature can be held as high as desired. The high temperature and the removal of water as fast as formed more than compensate for the absence of a large excess of alcohol.

Ethyl fumarate has been prepared from fumaric acid and ethyl alcohol, with or without sulfuric acid as catalyst,[4] from silver fumarate and ethyl iodide,[5] from silver maleate and ethyl iodide plus a trace of iodine,[6] from ethyl maleate by the action of iodine,[6] from ethyl maleate and phosphorous pentachloride,[7] and by passing hydrogen chloride into a boiling absolute alcohol solution of malic acid.[8]

4. References and Notes

1. Lea, Am. J. Sci. (2) **39**, 210 (1865); Frankland and Duppa, Phil. Trans. Roy. Soc. London **156**, 310 (1866); Phelps and Hubbard, Am. J. Sci. (4) **23**, 368 (1907); Phelps and Phelps, Am. J. Sci. (4) **24**, 194 (1907); Kohler and Allen, Org. Syn. **3**, 54 (1923).
2. Frankland and Aston, J. Chem. Soc. **79**, 517 (1901); Gibson, Proc. Roy. Soc. Edinburgh **28**, 703 (1908); Kenyon, Org. Syn. **5**, 59 (1925).
3. Taylor, Proc. Roy. Soc. Edinburgh **25**, 831 (1905); Clarke and Davis, Org. Syn. **2**, 23 (1922); Wahl, Bull. soc. chim. (4) **37**, 715 (1925).
4. Laubenheimer, Ann. **164**, 294 (1872); Purdie, J. Chem. Soc. **39**, 346 (1881); **47**, 856 (1885).
5. Anschütz, Ber. **11**, 1645 (1878); **12**, 2282 (1879); Purdie, J. Chem. Soc. **39**, 346 (1881).
6. Anschütz, Ber. **12**, 2282 (1879).
7. Henry, Ann. **156**, 177 (1870).
8. Laubenheimer, Ann**.** **164**, 295 (1872).

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

Fumaric acid: 2-Butenedioic acid, (2E)-; (110-17-8)

Diethyl fumarate: Diethyl (2E)-but-2-enedioate; (623-91-6)

Sulfuric acid; (7664-93-9)

Ethyl alcohol: Ethanol; (64-17-5)