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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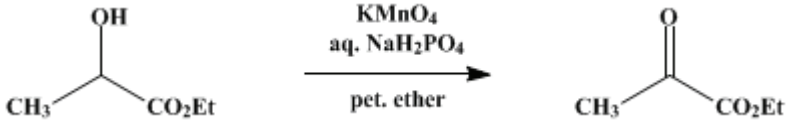
ETHYL PYRUVATE

[Pyruvic acid, ethyl ester]



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1. Procedure

In a 1-l. round-bottomed flask fitted with a thermometer and a mechanical stirrer are placed 130 ml. of saturated aqueous magnesium sulfate solution, 500 ml. of light petroleum ether (Note 1), 50 g. (0.42 mole) of ethyl lactate (Note 2), and 20 g. (0.13 mole) of sodium dihydrogen phosphate dihydrate. The stirrer is started (Note 3), the temperature is brought to 15° by means of an ice-water bath, and 55 g. (0.35 mole) of powdered potassium permanganate is added during 25–30 minutes. Stirring is continued until the oxidation is complete (Note 4), the temperature being kept near 15° throughout the process. The petroleum ether solution is decanted and the sludge stirred with three 50-ml. portions of light petroleum ether. The combined petroleum ether extracts are evaporated on a steam bath under a short fractionating column (Note 5). The residual oil is shaken thoroughly with two 10-ml. portions of a saturated aqueous calcium chloride solution (Note 6) and then distilled under reduced pressure. Almost the whole product boils at 56–57°/20 mm. The yield is 25–27 g. (51–54%) of nearly pure ethyl pyruvate, n_D^{20} 1.4053. This product compares favorably with material prepared by esterification of pyruvic acid (Note 7). Further purification may be effected through the sodium bisulfite compound (Note 8).

2. Notes

1. Petroleum ether, b.p. 40–60°, was washed with concentrated sulfuric acid before use. The checkers used the hexane fraction of petroleum.
2. The ethyl lactate should be of good quality, as its impurities tend to appear in the final product. The submitter used a good commercial grade supplied by British Industrial Solvents, Ltd. Its specification included an ester content of not less than 99% (calculated as ethyl lactate).
The commercial 99% ethyl lactate available to the checkers did not give satisfactory results. It was purified by distillation through a fractionating column 8 by ¾ in., packed with glass beads. The portion having the following properties was used: b.p. 154–155°, n_D^{20} 1.4125, d_4^{20} 1.0302.
3. The thick lower layer is stirred continuously and not too fast. Vigorous agitation of the upper layer is not advisable. A short Hershberg wire stirrer was used.
4. The oxidation requires about 2.5 hours. Unreduced permanganate is easily detected by spotting on filter paper. If a cake of manganese dioxide is formed beyond the compass of the stirrer, it should be pushed down. It is rarely necessary to do this more than once.
5. The distillate of petroleum ether, which contains ethanol and some ethyl pyruvate, can be recovered for another run by shaking with a little concentrated sulfuric acid.
6. This treatment removes unoxidized ethyl lactate. Each shaking should be continued for 5 minutes. It is convenient to separate the layers by centrifuging. Droplets of calcium chloride solution should not be present in the oil when it is to be distilled, or some polymerization will occur.
7. No satisfactory criterion of purity for ethyl pyruvate is available in the literature. The submitter used a method of assay which was devised[2] for the estimation of aldehydes. One hundred and sixteen milligrams of the ester is weighed in a 100-ml. conical flask, dissolved in 5 ml. of water, and treated with 0.3 ml. of saturated sodium bisulfite solution. After 1–2 minutes, a little starch solution is added, the mixture is chilled, and 0.1*N* iodine solution is run in as rapidly as possible until the blue color is stable for a few seconds (about 12 ml. is required). Six milliliters of saturated sodium bicarbonate

solution is added, and titration with iodine solution is carried out in the ordinary way. The end point is stable for 1 minute or more. The theoretical volume of 0.1*N* iodine required for pure ethyl pyruvate in the second stage is 20 ml. Thus if *n* ml. is required the estimated purity is 5*n*%. The results are perfectly consistent but may be slightly lower than the true values owing to dissociation of the bisulfite complex. The results from four different samples are as tabulated.

Method of Preparation	Estimated Ethyl Pyruvate Content, %
(1) Oxidation of ethyl lactate	95
(2) Esterification of once-distilled pyruvic acid	93–94
(3) Sample (2) twice redistilled; fraction b.p. 147–148° taken	96
(4) Sample (1) purified through bisulfite complex (Note 8)	98.5

8. The bisulfite compound is best made in small batches. The ester (2.2 ml.) in a large test tube is underlaid with 3.6 ml. of saturated sodium bisulfite solution. The tube is chilled in a freezing mixture, and the layers are shaken together. Crystallization occurs rapidly, especially if seed crystals are present. After 3 minutes, 10 ml. of ethanol is added and the crystalline product is washed on a filter with ethanol and ether. The yield is 3.0 g. Sixteen grams of the bisulfite complex is mixed with 32 ml. of saturated magnesium sulfate solution, and 5 ml. of 40% formaldehyde is added. After shaking, the oil is separated and the aqueous layer extracted with a little ether, which is added to the oil. After drying with magnesium sulfate the product is distilled at low pressure and affords 5.5 g. of ethyl pyruvate, b.p. 56°/20 mm. On redistillation, the purified ester boils at 147.5°/ 750 mm., n_D^{20} 1.4052, f.p. around −50°.

3. Discussion

Ethyl pyruvate can be prepared by esterification of pyruvic acid[3,4] or by catalytic oxidation of ethyl lactate with air or oxygen.[5,6] A process has been patented for the oxidation of ethyl lactate by acidified permanganate in dilute aqueous solution.[7] Ethyl pyruvate also has been obtained by the treatment of pyruvaldehyde diethyl acetal with N-bromosuccinimide,[8] by the reaction of pyruvyl chloride with ketene,[9] and by the reaction of pyruvic acid with diethyl pyrocarbonate.[10] Of minor interest are the preparations by pyrolysis of ethyl α-triphenylmethoxypropionate[11] and by the action of diethylamine on ethyl *meso*-α,α'-dibromoadipate.[12]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 610

References and Notes

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

petroleum ether

bisulfite complex

ethyl meso-α,α'-dibromoadipate

ethanol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

ether (60-29-7)

formaldehyde (50-00-0)

sodium bicarbonate (144-55-8)

potassium permanganate (7722-64-7)

oxygen (7782-44-7)

sodium bisulfite (7631-90-5)

iodine (7553-56-2)

manganese dioxide (1313-13-9)

diethylamine (109-89-7)

Ketene (463-51-4)

Pyruvic acid (127-17-3)

ethyl lactate (687-47-8)

pyruvyl chloride (78-95-5)

magnesium sulfate (7487-88-9)

N-bromosuccinimide (128-08-5)

hexane (110-54-3)

Ethyl pyruvate,

Pyruvic acid, ethyl ester (617-35-6)

sodium dihydrogen phosphate dihydrate (13472-35-0)

pyruvaldehyde diethyl acetal

diethyl pyrocarbonate (1609-47-8)

ethyl α-triphenylmethoxypropionate