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.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 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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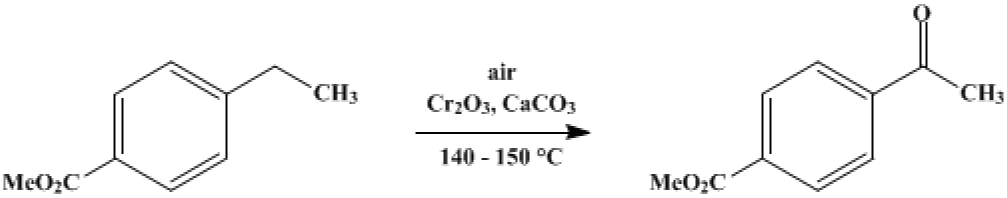
METHYL *p*-ACETYLBENZOATE

[Benzoic acid, *p*-acetyl-, methyl ester]



Submitted by William S. Emerson and George F. Deebel[1].
Checked by Arthur C. Cope and Warren N. Baxter.

1. Procedure

A 200-ml. three-necked flask is equipped with a thermometer, a mechanical stirrer, a gas inlet tube extending as far into the flask as the stirrer permits, and a trap (designed to return the heavier layer of the condensate) (Note 1) which is attached to a bulb and a coil-type reflux condenser connected in series. Methyl *p*-ethylbenzoate (98 g., 0.6 mole) (Note 2) and a mixture of 1 g. of chromium oxide and 4 g. of calcium carbonate, prepared by grinding the solids together in a mortar, are added. An air line with a bleed control valve (Note 3) is connected from the top of the condenser to a water aspirator. The flask is heated with a hemispherical electric mantle (Note 4).

The mixture is stirred vigorously at a temperature of 140–150°, and air is drawn through it (Note 5). for 24 hours while the water formed is collected in the trap (Note 6). At the end of this period, the mixture is cooled, diluted with 100 ml. of benzene (Note 7), and filtered with suction to remove the catalyst (Note 8). The catalyst is washed with 10 ml. of benzene on the funnel, and the washings are combined with the filtrate. The benzene is distilled from the clear, yellow solution (conveniently at a pressure of 100 mm. or lower to avoid superheating and partial decomposition of the product) through a fractionating column (Note 9). After removal of the benzene, the pressure is reduced and the residue is fractionally distilled. There is obtained 29–32 g. of unreacted methyl *p*-ethylbenzoate (b.p. 118–121°/16 mm.), and 43–45 g. (40–42% conversion and 60% yield) of methyl *p*-acetylbenzoate; b.p. 149–150°/7 mm. (Note 10) and (Note 11). The high-boiling residue weighs 13–18 g. The crude methyl *p*-acetylbenzoate can be purified by crystallization from the minimum amount of 1:1 benzene-commercial hexane required for solution with a recovery of 82–85%, collected in two crops; m.p. 92–95°.

2. Notes

1. A Dean and Stark trap[2] modified to provide for continuous return of the heavier organic layer is most convenient. Such a trap can be constructed like a small Wehrli extractor.[3]
2. Methyl *p*-ethylbenzoate was prepared from ethylbenzene (1 kg.), which was converted to *p*-ethylacetophenone by adding aluminum chloride (792 g.), followed by acetyl chloride (462 g.), which was added with stirring at 0–5° over a period of 3 hours. The mixture was stirred for 1 hour longer, allowed to stand overnight, and washed with iced dilute hydrochloric acid. The ethylbenzene was removed by distillation, and the crude product was oxidized to *p*-ethylbenzoic acid with alkaline hypochlorite.[4] Recrystallization of the crude acid from 95% ethanol yielded 350 g. (41%) of the pure acid; m.p. 110–112°. Esterification with methanol in the presence of hydrogen chloride[4] yielded methyl *p*-ethylbenzoate (77–79%).
3. A T-tube in the connection between the top of the condenser and the water aspirator is attached to a Bunsen burner. The needle valve of the burner serves as a bleed control valve, regulating the amount of air drawn through the reaction mixture.
4. An oil bath can be used.
5. The air stream should be introduced as rapidly as possible, preferably at a rate which will just permit return of the liquid from the coil condenser. It is equally satisfactory to force air through the mixture

from a cylinder or compressed-air line if the air is clean and free from oil. Use of a rapid stream of air and vigorous stirring prevents the catalyst from settling.

6. Removal of the water should be as complete as possible, in order to prevent coagulation of the catalyst, which retards the oxidation.

7. The benzene serves to keep the methyl *p*-acetylbenzoate in solution. If crystallization occurs, the mixture should be warmed to dissolve the ester before filtration.

8. The catalyst should be removed completely, because distillation of the product in the presence of small amounts of the catalyst results in some decomposition with a corresponding lowering of the yield. Use of a filter aid such as Super-Cel aids in separating the catalyst.

9. The submitters used a 120-cm. Vigreux column in distilling the benzene and a 60-cm. Vigreux column in fractionating the product. The checkers used a Widmer column with a 17-cm. spiral for the entire distillation.

10. Cooling water should not be circulated through the condenser during distillation of the product, because the methyl *p*-acetylbenzoate tends to crystallize in the condenser.

11. The submitters have obtained similar yields (40–54% conversion and 60–66% yield) in oxidations on 10 times this scale.

3. Discussion

Methyl *p*-acetylbenzoate has been prepared by the esterification of *p*-acetylbenzoic acid with methanol in the presence of hydrogen chloride,[5] by the hydrogenation of methyl *p*-trichloroacetylbenzoate in the presence of a palladium on calcium carbonate catalyst,[6] and by the air oxidation of methyl *p*-ethylbenzoate.[4]

References and Notes

1. Monsanto Chemical Company, Dayton, Ohio.
2. Dean and Stark, *Ind. Eng. Chem.*, **12**, 486 (1920).
3. Wehrli, *Helv. Chim. Acta*, **20**, 927 (1937).
4. Emerson, Heyd, Lucas, Chapin, Owens, and Shortridge, *J. Am. Chem. Soc.*, **68**, 674 (1946); Monsanto Chemical Co., Brit. pat. 636,196 [*C. A.*, **44**, 8951 (1950)].
5. Meyer, *Ann.*, **219**, 234 (1883); Bergmann and Blum, *J. Org. Chem.*, **24**, 549 (1959); Sergeev and Sladkov., *Zhur. Obshchei Khim.*, **27**, 817 (1957) [*C. A.*, **51**, 16348 (1957)].
6. Feist, *Ber.*, **67**, 938 (1934).

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

benzene-commercial hexane

ethanol (64-17-5)

hydrogen chloride,
hydrochloric acid (7647-01-0)

Benzene (71-43-2)

methanol (67-56-1)

acetyl chloride (75-36-5)

calcium carbonate (471-34-1)

aluminum chloride (3495-54-3)

palladium (7440-05-3)

ethylbenzene (100-41-4)

chromium oxide (1308-38-9)

Methyl p-acetylbenzoate,
Benzoic acid, p-acetyl-, methyl ester (3609-53-8)

Methyl p-ethylbenzoate (7364-20-7)

p-ethylacetophenone (937-30-4)

p-ethylbenzoic acid (619-64-7)

p-acetylbenzoic acid (586-89-0)

methyl p-trichloroacetylbenzoate