NOTES

Ethyl 3,4,5-Trimethoxybenzoylacetate

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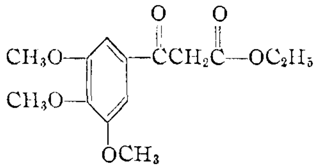
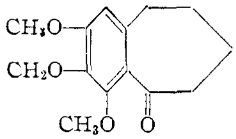
Ethyl 3,4,5-trimethoxybenzoylacetate (I) has been converted in good yield to 2′,3′,4′-trimethoxycyclohepten-2-one (II) by Haworth, *et al.*,[1] in their synthesis of purpurogallin. II is also of interest as an intermediate in the preparation of compounds related to colchicine.



I



II

The synthetic route to I employed by Haworth, *et al.*,[1] was that of Perkin and Weizmann[2] in which 3,4,5-trimethoxybenzoic acid was converted to the corresponding acid chloride, this product allowed to react with sodio ethyl acetoacetate, and the resulting ethyl trimethoxybenzoylacetoacetate cleaved with base. No yields were reported by either authors for any of the steps. In our hands the cleavage of the substituted acetoacetic ester with ammonia–ammonium chloride solution as described by Perkin[2] resulted in very low yields of I and the use of a stronger base (sodium methoxide or sodium hydroxide) resulted in acidic rather than ketonic cleavage.

We have found the following two step synthesis of I to be more satisfactory. Reaction of 3,4,5-trimethoxybenzoic acid with methyllithium yielded 3,4,5-trimethoxyacetophenone and condensation of this product with diethyl carbonate in the presence of sodium hydride gave I. The yield of the trimethoxyacetophenone was 38% although yields of 70–80% of acetophenone and 80–95% of *n*-valerophenone were obtained from the reaction of benzoic acid with the corresponding alkyl lithium under the same conditions. It was also observed that the concentration of the methyllithium solution could be varied from 0.5 to 2.0 molar without affecting the yield of ketone. Other workers[3] have specified the former concentration.

When the condensation of the trimethoxyacetophenone with diethyl carbonate was carried out in diethyl ether at reflux temperature, the yield of I was 54%. When di-*n*-butyl ether was used as the solvent and the reaction run at reflux temperature, the yield was raised to 84%.

Experimental

3,4,5-Trimethoxyacetophenone.—Methyllithium was prepared from 24 g. (3.4 gram atoms) of lithium wire and 200 g. (2.0 moles) of methyl bromide as described by Gilman, *et al.*[4] To a solution of the methyl lithium in one l. of sodium-dried ether was added dropwise at room temperature a suspension of 84 g. (0.4 mole) of 3,4,5-trimethoxybenzoic acid in 300 ml. of purified dioxane. The resulting mixture was refluxed for one to two hours and then poured onto 200–300 g. of ice. After separation of the layers, the aqueous phase was extracted several times with 100-ml. portions of ether. The combined ethereal solutions were washed with water (3–4 times) until neutral to litmus and dried over anhydrous sodium sulfate. After removal of the solvent, distillation *in vacuo* gave 32 g. (38%) of product (b.p. 132–134° at 1 mm.) which solidified in the receiver and melted at 73–74° (reported, 72°).[5]

Ethyl 3,4,5-Trimethoxybenzoylacetate (I).—A solution of 32 g. (0.15 mole) of 3,4,5-trimethoxyacetophenone in 500 ml. of sodium-dried di-*n*-butyl ether was added dropwise over a period of one to two hours to a gently refluxing mixture of 7.2 g. (0.3 mole) of sodium hydride in 100 ml. of dry di-*n*-butyl ether and 36 ml. (0.3 mole) of redistilled diethyl carbonate. The resultant mixture was refluxed for an additional six hours and then cooled to room temperature. The unreacted sodium hydride was destroyed by the addition of 30 ml. of ethanol and the mixture then neutralized with dilute hydrochloric acid. After separation of the layers and extraction of the aqueous phase several times with ether, the combined ethereal solutions were washed with 5% sodium bicarbonate, then with water, and dried over anhydrous sodium sulfate. Evaporation of the solvent left a yellow oil which slowly crystallized on standing. After one recrystallization from methanol, 35.6 g. (84%) of pale yellow crystals were obtained; m.p. 92–94° (reported 95°).[2]

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[1] R. D. Haworth, B. P. Moore and P. L. Pauson, *J. Chem. Soc.*, 1045 (1948); D. Caunt, W. D. Crow, R. D. Haworth and C. A. Vodoz, *ibid.*, 1631 (1950).

[2] W. H. Perkin, Jr., and C. Weizmann, *ibid.*, 1655 (1905).

[3] D. A. Van Doys and J. F. Arens, *Rec. trav. chim.*, **65**, 338 (1946); W. G. Dauben and E. Hoerger, This Journal, **73**, 1504 (1951).

[4] H. Gilman, J. A. Beel, C. G. Brannan, M. W. Bullock, G. E. Dunn and L. S. Miller, *ibid.*, **71**, 1499 (1949).

[5] F. Mauthner, *J. prakt. Chem.*, **190**, 275 (1910).

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The Reaction between Magnesium and Trimethyl Orthophosphate[1–3]

By Paul Becher[4]

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Although the trialkyl orthophosphate esters (including the trimethyl ester) have been known for more than half a century[5] and although many of these compounds have important applications as plasticizers, fire retardants, etc., the fact that trimethyl phosphate vigorously attacks metallic magnesium has apparently been overlooked. This reaction was first noted by W. Schlesinger and P. Becher[6] in connection with an investigation of the applicability of that compound as a base for non-inflammable aircraft hydraulic fluids and propeller de-icing fluids. It was found at that time that small amounts of water and of ketones in-

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[2] Presented, in part, in a paper delivered at the Southwide Chemical Conference, October 16–18, 1950, Atlanta, Georgia.

[3] Portions of the experimental work reported herein were performed by Messrs. Joseph L. Dobson, Thomas P. Garrett, Jr., John A. Simms and Robert B. Strickland.

[4] Colgate-Palmolive-Peet Company, Jersey City 2, New Jersey.

[5] G. N. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 211, *et seq.*

[6] W. Schlesinger and P. Becher, U. S. Patent 2,470,792 (1949).