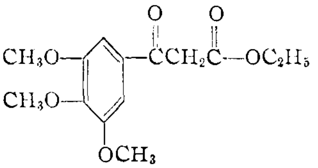
NOTES

Ethyl 3,4,5-Trimethoxybenzoylacetate

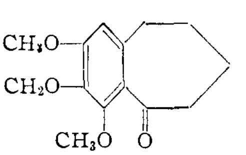
By A. G. Anderson, Jr., and Helen Frances Greef

Received January 7, 1952

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]

---

(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).

Department of Chemistry and Chemical Engineering
University of Washington
Seattle, Washington

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

By Paul Becher[4]

Received January 26, 1952

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-

---

(1) This work was supported by a Frederick Gardner Cottrell Grant of the Research Corporation.

(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).

hibited the reaction, but the essential nature of the reaction was not extensively studied. It was the purpose of this investigation to at least make a beginning in this direction.

Experimental

Reagents. Preparation of Trimethyl Phosphate.—This preparation is given in some detail since the general method for alkyl phosphates given in "Organic Syntheses"[7] is inapplicable because of the high solubility of trimethyl phosphate in water.

One pound (454 g., 8.4 moles) of sodium methylate[8] is suspended in 1200 ml., of dry C.P. benzene in a 3-neck, round-bottom, 5-liter flask, fitted with a reflux condenser, stirrer, and dropping funnel. To the flask is added in such a manner as to keep the temperature between 50 and 60°, 255 ml. (428 g., 2.8 moles) of phosphorus oxychloride, taking approximately four hours to complete the addition. The reaction is exothermic. The reaction mixture is allowed to stand overnight, and then most of the benzene layer is decanted off. The remaining sodium chloride is extracted with an additional 750 ml. of benzene in a Soxhlet extractor. The combined benzene solutions are concentrated under reduced pressure and the residue is distilled to yield 333.5 g. of trimethyl phosphate, b.p. 94° (22 mm.); $n^{25}\text{D}$ 1.3960; yield 85%.

The Reaction.—Metallic magnesium reacts with trimethyl phosphate, slowly at room temperature, vigorously at elevated temperatures. The reaction appears to be autocatalytic, and it is convenient to induce the room temperature reaction by initial heating for several minutes at temperatures just below boiling (*ca.* 160–170°). It may also be induced by the introduction of several crystals of iodine. Immediately vigorous reaction begins, the reaction vessel can be cooled down to room temperature, where it will continue at an appreciate rate. It is necessary, under these conditions, to cool the reaction vessel in a water-bath as the reaction is strongly exothermic.

Reaction is accompanied by the evolution of a gas which in a typical case contained 71.1% methane, 6.7% ethane, 13.8% acetylene, a trace of ethylene and no hydrogen, and the formation of a blackish-gray sludge. This sludge clings tenaciously to the magnesium particles and slows the reaction, and even may cause it to terminate before the magnesium is totally consumed.

The sludge may be separated from the supernatant liquid and, upon treatment with water, acetylene, identified by the formation of cuprous acetylide, is evolved, and white, gelatinous magnesium hydroxide is precipitated, indicating that one component of the sludge is probably magnesium carbide. Upon filtering off the magnesium hydroxide and evaporating the resulting solution to dryness, a glassy, difficultly crystallizable substance, soluble in water and methanol, is formed.

This solid residue upon solution in water, gave a qualitative test for magnesium, but none for phosphate. However, after heating with dilute hydrochloric acid, a positive test for phosphate ion was obtained, suggesting that the material was either magnesium monomethyl phosphate ($MgCH_3PO_4$) or magnesium dimethyl phosphate ($Mg[(CH_3)_2PO_4]_2$). The magnesium content of the product was determined by standard gravimetric procedures, with the following results: found 9.3%; calcd. for $MgCH_3PO_4$, 18.1%; calcd. for $Mg[(CH_3)_2PO_4]_2$, 8.9%. The agreement is not too good, but it is quite evident that the data favor the supposition that the material is magnesium dimethyl phosphate.

A possible mechanism for this reaction might be postulated as

$$(CH_3)_3PO_4 + Mg \longrightarrow PO(OCH_3)_2OMgCH_3 \quad (1)$$

$$PO(OCH_3)_2OMgCH_3 \xrightarrow{90\%} CH_3\cdot + Mg[(CH_3)_2PO_4]_2 \quad (2a)$$

$$PO(OCH_3)_2OMgCH_3 \xrightarrow{10\%} Mg(CH_3)_2 + Mg[(CH_3)_2PO_4]_2 \quad (2b)$$

$$CH_3\cdot \longrightarrow C_2H_2 + C_2H_6 + CH_4 \quad (3)$$

$$Mg(CH_3)_2 + C_2H_2 \text{ [from (3)]} \longrightarrow MgC_2 + CH_4 \quad (4)$$

The mode of formation of the MgC_2 is suggested by the analogous preparation of this compound from C_2H_5MgBr and C_2H_2 by Rueggeberg.[9] The hypothesized Grignard-like intermediate must, however, be extremely short-lived, since attempts to carry out Grignard methylations with aldehydes and ketones proved fruitless. Its existence is consistent, however, with the fact that small amounts of water inhibit this reaction.[6]

Acknowledgments.—The author wishes to acknowledge the continued advice and encouragement of Dr. Walter Schlesinger. Thanks are due to Dr. H. Adler of the Victor Chemical Company and Mr. William J. Bannister of the Commercial Solvents Corporation for advice on the synthesis of trimethyl phosphate.

---

[7] A. H. Blatt (Ed.), "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 109–111.

[8] Obtainable in one-pound containers of minimum 95% purity from the Mathieson Chemical Company, Niagara Falls, N. Y.

[9] W. H. C. Rueggeberg, THIS JOURNAL, **65**, 602 (1943).

DEPARTMENT OF CHEMISTRY
NORTH GEORGIA COLLEGE
DAHLONEGA, GA.

The Preparation of Suberone (Cycloheptanone)

BY F. F. BLICKE, NORMAN J. DOORENBOS AND R. H. COX

RECEIVED DECEMBER 11, 1951

The first step of a convenient procedure by means of which suberone can be obtained in comparatively large quantities consists in the condensation of cyclohexanone with nitromethane to form 1-(nitromethyl)-cyclohexanol. Upon electrolytic reduction of the latter substance, suspended in dilute sulfuric acid, a solution of 1-(aminomethyl)-cyclohexanol sulfate was obtained. Direct treatment of the solution with nitrous acid, without isolation of the sulfate, yielded suberone. The same route from cyclohexanone to suberone has been described by Dauben, *et al.*,[1] but these investigators employed catalytic reduction to convert 1-(nitromethyl)-cyclohexanol into the corresponding 1-(aminomethyl) derivative.

Recently, Wood and Cadorin[2] reported that interaction of cyclohexanone (2 moles) and nitromethane (1.5 moles) in methanol solution, in the presence of a very small amount (4 g.) of sodium hydroxide, yielded 1-(nitromethyl)-cyclohexanol in 51% yield.

Prior to their publication we had prepared large quantities of 1-(nitromethyl)-cyclohexanol by the use of sodium hydroxide as a condensation agent, and found that by reaction of cyclohexanone (1 mole), nitromethane (1 mole) and sodium hydroxide (1.25 moles) in methanol, and isolation of 1-(nitromethyl)-cyclohexanol in the form of its sodium derivative, the cyclohexanol can be isolated in 64–72% yields. The same yields were obtained by the use of fourfold quantities.

We have found that the cyclohexanol, suspended in dilute sulfuric acid, can be reduced electrolytically by the use of lead electrodes to 1-(amino-

---

[1] Hyp J. Dauben, Jr., H. J. Ringold, R. H. Wade and A. G. Anderson, Jr., THIS JOURNAL, **73**, 2359 (1951).

[2] T. F. Wood and R. J. Cadorin, *ibid.*, **73**, 5504 (1951).