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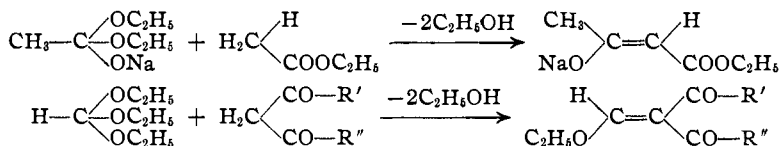
CONDENSATION OF ORTHO ESTERS WITH ACETOACETIC ESTER AND MALONIC ESTER¹

BY PETER P. T. SAH

RECEIVED DECEMBER 19, 1930

PUBLISHED MAY 6, 1931

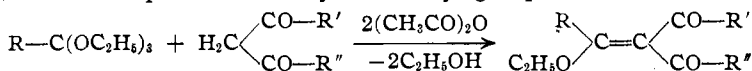
The condensation of ortho-formic ester with compounds containing a reactive methylene group between two carbonyl groups, such as acetoacetic ester, malonic ester, acetylacetone, etc., was a classical piece of work of Claisen,² who compared the analogy of this type of condensation to the formation of acetoacetic ester



where R' and R'' are alkyl, aryl or alkoxy groups.

The condensation products, esters of hydroxymethylene acids, formed very stable inorganic salts. The unstable acids were also isolated by Claisen and found to be exceedingly strong acids. They may be considered as derivatives of formic acid in which the carbonyl oxygen is replaced by a carbon atom attached to two negative groups.

By using triethyl ortho-acetate³ and triethyl orthobenzoate⁴ in place of triethyl ortho-formate in the above condensation, we have been able to isolate the methyl and the phenyl derivatives of ethoxymethylene esters and identify them through their copper salts. The condensation is, therefore, a general reaction for the class of ortho esters. The mechanism of the reaction may be expressed according to the following general equation, where R represents an alkyl or an aryl group



Experimental

General Procedure for the Condensation.⁵—All the reagents used were freshly distilled and the apparatus kept absolutely anhydrous. One

¹ This paper was constructed from a part of a thesis, presented by Peter P. T. Sah to the Faculty of the Graduate School of the University of Wisconsin in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June 21, 1926. The investigation was carried out under the direction of Professor Richard Fischer.

² Claisen, *Ber.*, **26**, 2731 (1893); *Ann.*, **295**, 311 (1897); *ibid.*, **297**, 1-98 (1897).

³ Geuther, *Z. Chemie*, 128 (1871); Reitter and Hess, *Ber.*, **40**, 3020 (1907); Sah, *THIS JOURNAL*, **50**, 516 (1928).

⁴ Limpricht, *Ann.*, **135**, 87 (1865); Tschitschibabin, *Ber.*, **38**, 563 (1905).

⁵ Wheeler and Johns, *Am. Chem. J.*, **40**, 237-238 (1908).

mole of ortho ester, one mole of acetoacetic ester or malonic ester and two moles of acetic anhydride (freshly distilled over sodium, b. p. 137°) were mixed and refluxed vigorously for four hours on an oil-bath with or without the addition of fused zinc chloride to catalyze the condensation. The resulting ethyl acetate and acetic acid were removed by distillation at atmospheric pressure till the thermometer, which was immersed in the solution, registered 120°. The mixture was then again refluxed for an hour and some more ethyl acetate was distilled out.⁶ The residue was then fractionated under a reduced pressure of 3 mm. produced by an oil pump. A small amount of acetic acid and acetic anhydride distilled over first, then the unreacted esters and finally the condensation product. The yield of the ethoxymethylene esters thus obtained varied exceedingly, depending upon the following factors: (1) purity of the reagents used, (2) time of reaction, (3) stability of the ortho ester used, (4) stability of the condensation product and (5) the presence of catalysts. With this procedure, Claisen's experiments could be easily repeated with a yield of 50–60% under the best condition.

Description of the Condensation Products

Ethyl methyl-ethoxymethylene-acetoacetate, from triethyl ortho-acetate (b. p. 144–146°) and ethyl acetoacetate, was a yellowish-white glycol-thick liquid, boiling unsteadily between 108 to 123° at 3 mm. The low yield of the product, the color, and the unsteadiness of its boiling point were undoubtedly due to partial decomposition during distillation. On standing, the compound deepened in color; yield, about 8 g. from 162 g. of triethyl ortho-acetate used. The addition of fused zinc chloride during the condensation produced no favorable effect upon the yield.

Diethyl methyl-ethoxymethylene-malonate, from triethyl ortho-acetate and diethyl malonate, was a glycol-thick liquid distilling unsteadily from 123 to 128° at 3 mm. The reddish-brown color due to partial decomposition could not be removed by redistillation; yield, about 5 g. from 162 g. of triethyl ortho-acetate used. The greater part of the ortho ester was decomposed by acetic anhydride to 3 moles of ethyl acetate.⁶ Addition of fused zinc chloride produced no favorable effect upon the yield.

Ethyl phenyl-ethoxymethylene-acetoacetate, from triethyl ortho-benzoate⁷ and ethyl acetoacetate, was a glycol-thick liquid, boiling very steadily at 185–186° at 3 mm. without any decomposition; d_4^{25} 1.0949; n_D^{25} 1.5512. Freshly distilled, the liquid was practically colorless. It may be kept in a well-stoppered bottle for months without any noticeable change; yield, over 40 g. from 124 g. of triethyl orthobenzoate used. Addition of fused zinc chloride increased the yield slightly.

Diethyl phenyl-ethoxymethylene-malonate, from triethyl ortho-benzoate and diethyl malonate, was a stable, colorless, glycol-thick liquid, boiling very constantly at 188–190° at 3 mm. without any decomposition; d_4^{25} 1.0738; n_D^{25} 1.4928; yield, over

⁶ The enormous amount of ethyl acetate formed during the condensation was undoubtedly due to the side reaction between acetic anhydride and ortho ester as mentioned by Sawitsch, *Jahrsb. über die Fortschritte der Chemie*, 391 (1860).

⁷ This was prepared by adding an alcoholic solution of sodium ethoxide to benzo-trichloride: b. p. 240° at atm. pressure; 128–130° at 3 mm.; n_D^{25} 1.4938; d_4^{25} 1.0325. Compare with Röse, *Ann.*, 205, 250 (1880).

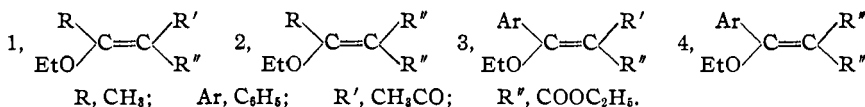
25 g. from 75 g. of triethyl ortho-benzoate used. Addition of fused zinc chloride increased the yield considerably.

All these condensation products were insoluble in water, but very soluble in ether, ethyl alcohol, ethyl acetate, glacial acetic acid, acetone, benzene, chloroform and carbon tetrachloride. Warm water decomposed them to their corresponding constituents, the double bond being very sensitive to hydrolysis.²

TABLE I
ANALYSES OF THE CONDENSATION PRODUCTS

No.	Formula	Calcd.	Carbon, %		Calcd.	Hydrogen, %			
			Found	Found		Calcd.	Found	Found	
1	C ₁₀ H ₁₆ O ₄	59.96	58.79	59.01	59.22	8.06	7.59	7.49	7.51
2	C ₁₁ H ₁₈ O ₆	57.36	56.48	56.64	56.50	7.88	7.10	7.08	7.09
3	C ₁₆ H ₁₈ O ₄	68.66	69.02	68.51	68.39	6.92	6.96	7.01	6.90
4	C ₁₆ H ₂₀ O ₅	65.72	65.85	65.78	65.87	6.90	6.92	6.87	6.95

Structures:

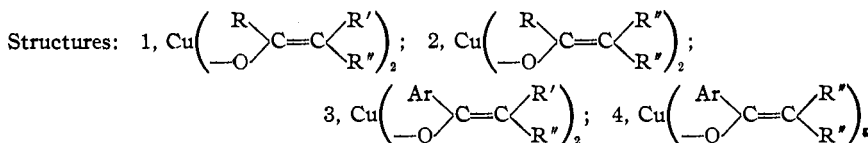


Copper Salts of the Condensation Products.—These were easily obtained by shaking the ester with a cold saturated solution of copper acetate. They were quite stable and served to characterize these new condensation products. The copper salts of the methyl homologs had the same solubility as those of the hydroxymethylene acids described by Claisen.² They were insoluble in cold concentrated copper acetate solution, soluble in ethyl alcohol, isoamyl alcohol, acetone and hot benzene, from which they reprecipitated on cooling. With pyridine they formed a beautiful violet solution, which distinguished them from copper acetoacetate and copper malonate. Warm water hydrolyzed them to copper oxide. Both are greenish-blue in color.

The copper salts of the phenyl analogs, light blue in color, were very insoluble in the ordinary solvents. Warm water hydrolyzed them to copper oxide and their corresponding constituents, the odor of which, especially ethyl benzoate, could be easily identified. They gave no violet color with pyridine.

TABLE II
ANALYSES OF THE COPPER SALTS^a

No.	Formula	Subs., mg.	Na ₂ S ₂ O ₃ , N/100, cc.		Calcd.	Copper, %		
			Calcd.	Found		Calcd.	Found	
1	C ₁₆ H ₂₈ O ₈ Cu	20.62	22.71	5.10	5.65	15.67	15.72	15.82
2	C ₁₈ H ₂₈ O ₁₀ Cu	25.03	20.02	5.35	4.35	13.65	13.59	13.81
3	C ₂₀ H ₂₈ O ₈ Cu	31.50	33.86	5.86	6.38	12.00	11.83	11.98
4	C ₂₈ H ₃₀ O ₁₀ Cu	33.33	30.06	5.73	5.15	10.78	10.93	10.89



^a Abderhalden and Schnitzler, *Z. physiol. Chem.*, **163**, 95 (1926).

Summary

1. Triethyl ortho-acetate condensed only with difficulty with either ethyl acetoacetate or diethyl malonate in the presence of acetic anhydride, forming the methyl homologs of ethoxymethylene esters. They were unstable liquids, decomposing partially on distillation. They formed, however, characteristic copper salts which could be purified and identified.

2. Triethyl ortho-benzoate condensed easily with either ethyl acetoacetate or diethyl malonate, forming very stable phenyl analogs of ethoxymethylene esters with definite physical properties. Their copper salts were also made and analyzed.

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MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

STUDIES IN THE 3-NITROPHTHALIC ACID SERIES

BY H. W. UNDERWOOD, JR., AND R. L. WAKEMAN¹

RECEIVED DECEMBER 29, 1930

PUBLISHED MAY 6, 1931

I. Phenol-3-nitrophthalein and Resorcinol-3-nitrophthalein.—This paper gives an account of the preparation of phenol-3-nitrophthalein and resorcinol-3-nitrophthalein and a comparison of the properties of these compounds with those of phenolphthalein and fluorescein. In previous contributions² dealing with derivatives of phthalic and diphenic acids, it was pointed out that the groups in diphenic anhydride give the sodium salt of phenoldiphenic acid a light yellow instead of a red color and that an alkaline solution of resorcinoldiphenic acid does not show fluorescence.

Discussion of Experiments

All of the temperatures given are uncorrected.

Phenol-3-nitrophthalein.—Fifteen grams of 3-nitrophthalic anhydride, 16.1 g. of phenol (calcd. amt. $\times 1.1$) and 3 g. of concd. sulfuric acid (d 1.84) were placed in a loosely stoppered Erlenmeyer flask and heated in an oil-bath which was rapidly raised to 170°, maintained at this temperature for about two and one-half hours and then at 215–220° for three hours longer. After the reaction product had cooled, it was powdered and added to about 600 cc. of water in a beaker. The mixture was boiled for four hours to remove the excess of phenol; the water lost by evaporation was replaced from time to time. The insoluble solid was collected on a filter, transferred to a beaker and stirred with three 60-cc. portions of 3.5% sodium hydroxide solution. Acidification of the combined, filtered alkaline liquids yielded a dark colored precipitate. This material was collected on a filter, dried for forty-eight hours at room temperature and then ground with six 100-cc. portions of ether in a mortar. The ether

¹ Some of the experimental results described in this paper are taken from a thesis submitted to the Faculty of the Massachusetts Institute of Technology by R. L. Wakeman in partial fulfillment of the requirements for the degree of Bachelor of Science.

² Underwood and Kochmann, *THIS JOURNAL*, **45**, 3071 (1923); **46**, 2069 (1924).