

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF WASHINGTON]

A STUDY OF THE CONDENSATION BETWEEN ALIPHATIC ESTERS AND KETONES<sup>1</sup>

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The condensation between ketones and esters has long served as a method for obtaining 1,3-diketones. In the case of unsymmetrical ketones the reaction can take place in either of two ways, and it has been found<sup>2</sup> that ketones of the type  $\text{CH}_3\text{COCH}_2\text{R}$  react through the methyl rather than the methylene group. This is not what might be expected from the fact that the reaction between 2-butanone and aldehydes<sup>3</sup> indicates the methylene as the more reactive group. That a methylene group is capable of reacting with esters was shown by Morgan, Drew and Porter,<sup>4</sup> who obtained diketones from 3-pentanone and from 4-heptanone. The same authors found that in the case of ethyl acetate and 3-pentanone the product was the expected 3-methyl-2,4-hexanedione when the reaction mixture was not heated, but was 2,4-hexanedione if the standard procedure was followed.

The 2,4-hexanedione apparently results from a reaction between the ethyl acetate and 2-butanone formed by alcoholysis of the 3-methyl-2,4-hexanedione.

In view of the above it seemed possible that under certain conditions ketones of the type  $\text{CH}_3\text{COCH}_2\text{R}$  might react through the methylene group and that, if alcoholysis could be prevented, the resulting diketones might be isolated. In none of the cases studied in this investigation was any evidence found that such a reaction occurred.

TABLE I  
EXPERIMENTAL RESULTS

No.	Ester	Ketone	Diketone	Yield, %
1	Ethyl acetate	2-Butanone	2,4-Hexanedione	11
2	Ethyl propionate	Acetone	2,4-Hexanedione	15
3	Ethyl propionate	2-Pentanone	3,5-Octanedione	9
4	Ethyl butyrate	2-Butanone	3,5-Octanedione	..
5	Ethyl acetate	3-Methyl-2-butanone	2-Methyl-3,5-hexanedione	14
6	Ethyl isobutyrate	Acetone	2-Methyl-3,5-hexanedione	6

<sup>1</sup> Presented at the Cincinnati Meeting of the American Chemical Society, September, 1930. This paper is taken from a thesis submitted by Keith M. Seymour in partial fulfillment of the requirements for the degree of Master of Science in the University of Washington.

<sup>2</sup> (a) Claisen and Ehrhardt, *Ber.*, **22**, 1009 (1889); (b) Morgan and Reeves, *J. Chem. Soc.*, **123**, 444 (1923); (c) Morgan and Drew, *ibid.*, **125**, 731 (1924); (d) Morgan and Holmes, *ibid.*, **127**, 2891 (1925).

<sup>3</sup> Zalkind, *J. Russ. Phys.-Chem. Soc.*, **37**, 484 (1905); *Chem. Zentr.*, **82**, II, 752 (1905); Merling and Kohler, U. S. Pat. 981,668, *Chem. Abstracts*, **5**, 1192 (1911); Powell, *THIS JOURNAL*, **46**, 2514 (1924).

<sup>4</sup> Morgan, Drew and Porter, *Ber.*, **53**, 338 (1925).

The course of the reaction when the standard procedure was followed was determined by preparing a diketone by two different ester-ketone combinations such that the identical product would be obtained if the reaction took place through the methyl group. The results are shown in Table I.

Of the three diketones obtained, 2,4-hexanedione and 3,5-octanedione have been previously prepared by reactions 1 and 4, respectively, whereas 2-methyl-3,5-hexanedione has not heretofore been prepared by the Claisen reaction, although obtained by other methods.<sup>5</sup>

The reaction was carried out as described by Claisen and Ehrhardt,<sup>6</sup> and by modifications of this method. Wherever the work was a repetition of that of others, our results were identical with theirs and are not described. According to the standard procedure as described by Claisen and Ehrhardt, the reaction mixture is allowed to stand for twelve hours and then refluxed for one hour. Since it has been shown that heating brings about alcoholysis in the case of the reaction between ethyl acetate and 3-pentanone, reactions 3, 4 and 5 (Table I) were repeated omitting the refluxing. In no case was there any evidence of the presence of any other diketone than the one resulting from the reaction between the ester and the methyl group of the ketone. Nor did omitting the refluxing in the reaction between ethyl acetate and 2-pentanone and between ethyl propionate and 2-butanone lead to any different results than those obtained by other investigators who used the standard procedure.

Reaction 1 (Table I) was repeated, changing the time of standing before refluxing from twelve hours to three hours in one case and to forty-eight hours in another. The sole effect seemed to be a diminution of the yield.

As reactions 2, 3, 5 and 6 have not been described heretofore, the results obtained in these cases are given. Unless otherwise stated all reactions were carried out using 0.5 atom of sodium, 0.5 mole of ketone and 1.0 mole of ester,<sup>7</sup> and following the standard procedure.

**Ethyl Propionate + Acetone.**—Diketone, b. p. 150–158°;  $n_D^{24}$  1.4505. Copper salt, m. p. 197°. 2,4-Hexanedione boils at 158° and its copper salt melts at 197–198°.<sup>8</sup> A second trial using 1 mole of acetone also gave 2,4-hexanedione in much smaller yield.

**Ethyl Propionate + 2-Pentanone.**—Refluxing omitted; diketone, b. p. 187–190°;  $n_D^{24}$  1.457. Copper salt, m. p. 157–158°. 3,5-Octanedione boils at 189–190° and its copper salt melts at 157°.<sup>9</sup>

**Ethyl Acetate + 3-Methyl-2-butanone.**—Twenty-five grams (0.3 mole) of the ketone, 7 g. (0.3 atom) of sodium and 26 g. (0.3 mole) of ester were used. No reaction

<sup>5</sup> (a) Conrad and Gast, *Ber.*, 31, 1339 (1898); (b) Bouveault, *Compt. rend.*, 131, 45 (1900).

<sup>6</sup> Claisen and Ehrhardt, *Ber.*, 22, 1009 (1889).

<sup>7</sup> Adkins, Kutz and Coffman, *THIS JOURNAL*, 52, 3218 (1930), have shown that the maximum yields are obtained by using sodium, ketone and ester in the molecular ratio 2 : 1 : 3.

<sup>8</sup> Morgan and Reeves, *J. Chem. Soc.*, 123, 444 (1923).

<sup>9</sup> Morgan and Drew, *ibid.*, 125, 731 (1924).

took place at 0° and it was slow at room temperature. Refluxing was omitted. Diketone, b. p. 164–166°; copper salt, m. p. 172°. 2-Methyl-3,5-hexanedione boils at 160–170° and its copper salt melts at 171°. <sup>10</sup>

**Ethyl Isobutyrate + Acetone.**—One-half mole of ester, ketone and sodium were used. The reaction was vigorous but only a small quantity of the copper salt melting at 171° was obtained. A mixture of this with that obtained in the preceding reaction also melted at 171°.

### Summary

1. The Claisen condensation between several esters and ketones has been studied and the diketones resulting have been identified.

2. Modifications of proportions and conditions did not change the course of the reaction in the cases studied.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE UNIVERSITY OF IOWA]

## BROMINE DERIVATIVES OF CERTAIN MIXED ETHERS AND SOME OF THEIR REACTIONS

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Previous work<sup>1</sup> in this Laboratory has shown that in the bromination of certain phenyl alkyl ethers the hydrogen bromide liberated may split them unless sodium acetate is present, and that the splitting is more pronounced when the alkyl radical is connected through a secondary or tertiary<sup>2</sup> carbon atom.

In cases where, as indicated below, the phenyl radical could not be further brominated under the conditions already described, and where, in consequence of this, no "nascent hydrogen bromide"<sup>3</sup> was produced during attempts at bromination, splitting of these ethers was not observed. Nevertheless, it was a matter of interest to test the behavior of such ethers toward hydrogen bromide under several conditions.

Graebe and Martz<sup>4</sup> found that heating trimethoxygallic acid with 48% hydrobromic acid in an open vessel surrounded by boiling water removed the methyl radical from position 4 to the extent of 90%. In the present work that method did not give satisfactory results. Refluxing 2,4,6-

<sup>10</sup> Conrad and Gast, *Ber.*, **31**, 1339 (1898).

<sup>1</sup> Raiford and Birosel, *THIS JOURNAL*, **51**, 1776 (1929).

<sup>2</sup> In the tertiary butyl derivative splitting occurred although sodium acetate was present. This may be due to a tendency of the ether to split off the unsaturated hydrocarbon isobutylene. Konowalow [*Z. physik. Chem.*, **1**, 67 (1887)] observed such a change in the study of tertiary amyl acetate.

<sup>3</sup> The small amount, if any, produced by the action of bromine on the alkyl radical of the ether was not detected and was disregarded.

<sup>4</sup> Graebe and Martz, *Ann.*, **340**, 220 (1905).