

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

## MODE OF FORMATION OF DISUBSTITUTED MALONIC ESTER DERIVATIVES<sup>1</sup>

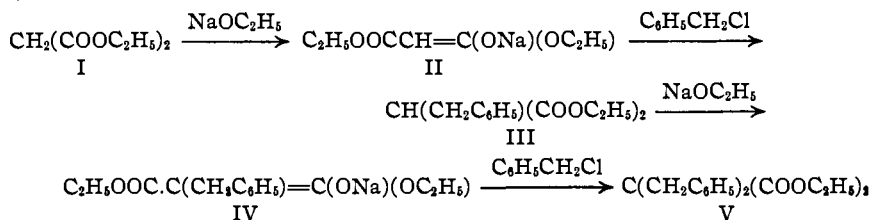
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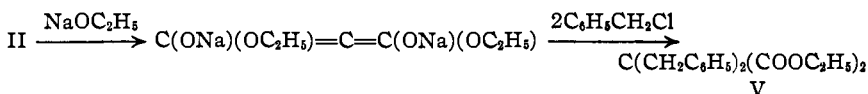
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Disubstituted malonic ester derivatives may be formed by three mechanisms according to the hypotheses which have been proposed. These reactions, using benzyl chloride as the halogen compound, are given in the accompanying chart.

### Consecutive Reaction Mechanism



### Disodium Malonic Ester Mechanism



### Leuchs Mechanism



The consecutive reaction mechanism is probably the principal one for sodium alcoholate solutions which favor the establishment of the necessary equilibria.<sup>2</sup> The hypothesis that disubstituted products may be formed through the agency of disodium malonic ester is still used by some authors despite the molecular weight experiments of Vorländer and von Schilling<sup>3</sup> and the spectroscopic investigations of Macbeth and Stewart,<sup>4</sup> which point to the non-existence of the disodium compound.

Support for the latter view and for the reactions postulated by Leuchs is obtained from the experiments reported in the present paper.

With equal molar proportion of reactants it is well known that the yield of disubstituted ester is much lower with aliphatic than with aromatic halides. In this connection Nef has stated that "the more negative the group introduced into the molecule the higher will be the proportion of the

<sup>1</sup> Presented at the Pasadena meeting of the American Association for the Advancement of Science, June, 1931. Financial assistance in this work has been received from the research funds of the University of California.

<sup>2</sup> Conrad and Guthzeit, *Ber.*, **15**, 2841 (1882); Nef, *Ann.*, **266**, 52 (1891).

<sup>3</sup> Vorländer and von Schilling, *Ber.*, **32**, 1876 (1899).

<sup>4</sup> Macbeth and Stewart, *J. Chem. Soc., Proc.*, **29**, 11 (1913).

disubstituted product." In our experiments with benzyl chloride, using methyl or ethyl alcohol as the solvent, mono- and dibenzylmalonic ester were formed in approximately a 2 to 1 molar ratio. With no solvent the ratio was increased. In this case the yield was lower than in the other experiments due to the formation of a crust of sodium malonic ester on the sodium<sup>5</sup> and to the condensation of two or three molecules of sodium malonic ester to give side reaction products.<sup>6</sup> The highest ratio (12.5 to 1) of mono and di-ester resulted when toluene was used as the liquid medium and the reaction mixture allowed to stand for forty-two days at room temperature.

By a quantitative study of the reaction between sodium and malonic ester in toluene evidence was obtained showing that an equal number of moles of sodium and malonic ester was used in bringing the reaction to completion and that only half the available sodium was utilized. Hence it may be concluded that no appreciable quantity of disodium malonic ester was formed under these conditions.

Clean, bright sodium was prepared by heating the commercial product in boiling toluene. Toluene was purified by refluxing it for three and a half hours with metallic sodium, after which it was fractionally distilled. This treatment was necessary to remove a reddish, gelatinous precipitate which formed when *c. p.* toluene was refluxed with sodium. Malonic ester, *b. p.* 103–104° (27 mm.) and *sp. gr.* 1.052, was used.

In each experiment 30 cc. of toluene, 2.00 cc. (0.013 mole) of malonic ester and about 0.7 g. (0.03 mole) of sodium, freshly purified and accurately weighed in toluene, were refluxed under anhydrous conditions in an oil-bath. The reaction mixture was chilled with ice, the liquid decanted and the residual sodium washed with three portions of toluene. The clean sodium was then dissolved in alcohol, diluted with water to a known volume and duplicate 25-cc. portions titrated with 0.1043 *N* sulfuric acid.

The results obtained from a series of such experiments are given in the table below. Since obvious quantitative difficulties are involved in handling metallic sodium, the final values are somewhat in excess of the theoretical.

Time of heating in minutes	Mole of sodium used	Molal ratio of sodium and malonic ester
5	0.00291	0.22
10	.00329	.26
20	.00468	.36
30	.00839	.64
50	.01137	.86
105	.01387	1.05
180	.01445	1.10

Further experiments, designed to test the postulates of Leuchs, were performed using toluene as the liquid medium in order that secondary reactions, initiated by sodium, might be avoided. Definite evidence was obtained for the formation of malonic ester from sodium malonic ester and benzylmalonic ester and of dibenzylmalonic ester from sodium benzyl-

<sup>5</sup> Conrad, *Ber.*, **12**, 749 (1879).

<sup>6</sup> Willstätter, *ibid.*, **32**, 1272 (1899); Baeyer, *ibid.*, **18**, 3454 (1885).

malonic ester and benzyl chloride. Hence it may be concluded that in toluene, and perhaps to some extent in alcoholic solutions, disubstituted derivatives of malonic ester are formed according to this hypothesis.

All substances used in these experiments were highly purified. Sodium malonic ester was prepared as a pale yellow powder by refluxing 23 g. of sodium and 160.5 g. of malonic ester in 1 liter of dry toluene until the sodium had disappeared. Then the toluene was removed by distillation and the residual material heated to 100° (11.5 mm.) for forty-five minutes to drive off the malonic ester. The residue of dry sodium malonic ester and 248.1 g. of added benzylmalonic ester were heated for three hours on a boiling water-bath and the resulting brown solution distilled *in vacuo*. The yield of product, b. p. 90–110° (33 mm.), was 81.5 g. After three additional fractionations at 98–100° (27 mm.), 37.4 g. of material, assumed to be pure malonic ester, was obtained. Equivalent weight values for this substance, found by saponification for thirty minutes with 1 *N* alcoholic potassium hydroxide, were 81.2, 81.5, 81.8 and 79.9 or an average value of 81.2 (calcd. 80.0).

The residual sodium benzylmalonic ester, from which the malonic ester had been completely removed, was refluxed for seven hours in an oil-bath with 126 g. of benzyl chloride and 500 cc. of toluene. The resulting mixture was filtered and the filtrate distilled *in vacuo*. The yield of product, b. p. 220–241° (27 mm.), was 99 g. Refractionation yielded 34 g. of viscous, golden oil, b. p. 233–243° (26 mm.). This product was assumed to be dibenzylmalonic ester since it was identical in appearance and boiling range with a highly purified, known sample of this ester. The unknown oil, saponified by heating it for two hours with 1 *N* alcoholic potassium hydroxide, gave on titration (with thymolphthalein) 178.8 and 170.3 (calcd. 170) as equivalent weight values. Difficulty was experienced in obtaining sharp end-points in titrating the solution due to its deep yellow color.

The assumption that benzylmalonic ester could be formed directly from malonic ester and benzyl chloride and that benzylmalonic ester and benzyl chloride react to give dibenzylmalonic ester is untenable as shown by the following experiments.

One mole each of purified benzyl chloride and malonic ester were refluxed with 235 cc. of anhydrous toluene for ten hours. During this time there was no visible sign of any reaction. Toluene, obtained as the first fraction in the vacuum distillation of the mixture, contained no detectable acid. The remaining liquid distilled completely below 200° (760 mm.). The boiling point of pure benzylmalonic ester is 297–300° (760 mm.).

One mole each of purified benzyl chloride and benzylmalonic ester were refluxed with 250 cc. of anhydrous toluene for ten hours. No evidence of a reaction was noted. On vacuum distillation the liquid distilled completely below 200° (25 mm.). The boiling point of pure dibenzylmalonic ester is 235–240° (28 mm.).

### Summary

1. The molal ratios of mono- and dibenzylmalonic ester, formed when equal molal quantities of sodium, malonic ester and benzyl chloride react, were found to be approximately 2 to 1 for methyl and ethyl alcohols, 1.2 to 1 with no solvent and ranging from 2.1 to 1 to 12.5 to 1 with toluene.
2. It was concluded from a quantitative study of the reaction between sodium and malonic ester in toluene that no appreciable quantity of disodium malonic ester was formed under the experimental conditions.
3. The view of Leuchs, that disubstituted derivatives of malonic ester may be formed directly from the reactants, is supported by our experiments.