

of nitric nitrogen found had no apparent relationship to the amount of nitric nitrogen actually present. It may thus be seen that the chloroform in the presence of calcium hydroxide very materially interferes with the accurate determination of the nitric nitrogen.

The discussion so far has had to do only with the determination of the nitrates in solution. The soil factor must be considered. Accordingly, it was decided to determine the nitric nitrogen content in two soils, one a very rich, hothouse soil, the other a field soil, poor in nitric nitrogen. The nitric nitrogen was determined by the lime method both with and without chloroform. The results obtained are recorded in Table IV.

TABLE IV.—COMPARATIVE DETERMINATION OF NITRIC NITROGEN IN A SOIL.

Sample No.		Soil rich in nitrates.	Soil poor in nitrates.
	Without chloroform.		
1	Lime 1 gram per 50 grams of soil.....	27.0	0.36
	Lime 1 gram per 50 grams of soil.....	27.5	0.36
	With chloroform.		
7	Lime and chloroform.....	22.5	0.22
8	Lime and chloroform.....	22.0	0.14

Again the marked influence of chlorine is demonstrated. In the rich soil where chloroform and lime are used, there is a loss of 5 mg. of nitric nitrogen, while in the soil poor in nitric nitrogen there is a loss of over 50% of the nitrates, and furthermore, the results obtained are not concordant.

It is seen, therefore, that the lime method is highly desirable for use in soils rich in nitrates and organic matter, since a clear solution is thus obtained and there is no interference in the determination of the nitrates, provided chloroform is not also used.

Ionic chlorine has a marked influence on the determination of the nitrates in the solution whether the ionic chlorine is derived from the chlorides of the soil or by decomposition of the added chloroform. The result obtained also indicated clearly that chloroform should not be added to the soil extract obtained by the lime method.

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[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

THE FORMATION OF β -KETONE ESTERS BY THE APPLICATION OF REFORMATSKY'S REACTION.

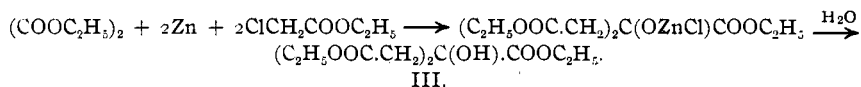
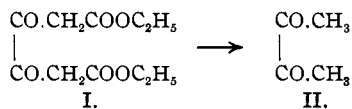
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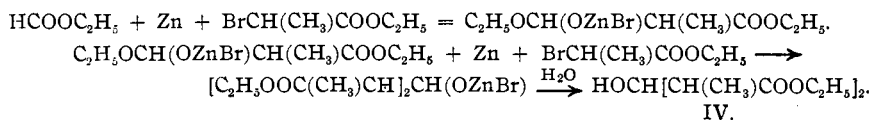
In 1887, Fittig and Daimler¹ investigated the action of ethyl chloroacetate on diethyl oxalate in the presence of amalgamated zinc. They observed that this halide reacted with the oxalate, in an unique manner,

¹ *Ber.*, 20, 202; *Ann.*, 249, 182.

forming diethyl ketipate I, while triethyl citrate III, would have been the normal product of the reaction if this halide had reacted with a carbethoxy group of the oxalate in a manner analogous to that of alkylhalides (Frankland's reaction). The constitution of their condensation-product I, was established by the fact that it underwent a ketone hydrolysis normally giving an orthodiketone, which was identical with Pechmann's¹ diacetyl II.



No further attention was paid, apparently to the behavior of esters of halogen-substituted fatty acids on esters, in the presence of zinc, until eight years later, in 1895, when Reformatsky² developed his important synthesis of hydroxydibasic acids. He found, for example, that ethyl α -bromopropionate reacted with ethyl formate, giving an excellent yield of diethyl α,α -dimethyl- β -hydroxyglutarate IV. He obtained no evidence, apparently, of the formation of ethyl formylpropionate $\text{HCO.CH}(\text{CH}_3)\text{COOC}_2\text{H}_5$ corresponding to Fittig and Daimler's diethyl ketipate I. In other words, this halide functionated, in this case, as a true alkyl halide, and the transformation may be expressed by the following equations:



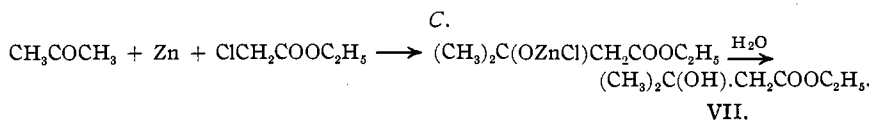
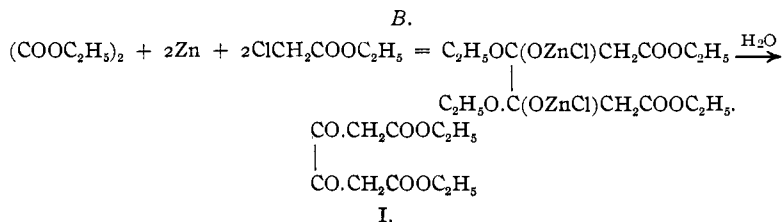
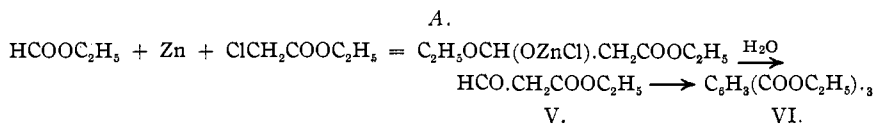
While this reaction of Reformatsky's has received wide application, nevertheless, it is interesting to note that an attempt, by this investigator, to prepare diethyl β -hydroxyglutarate $\text{HOCH}(\text{CH}_2\text{COOC}_2\text{H}_5)_2$ from ethyl formate and ethyl chloroacetate was unsuccessful.³ He made the interesting observation that this halide reacted abnormally, and he obtained as the chief product of his reaction ethyl trimesinate VI. This ester was the product of the second phase of his reaction, and was formed by a trimolecular-condensation of ethyl formylacetate V. The reactions involved in the formation of this ester (ethylformylacetate), and that of diethyl ketipate I from diethyl oxalate and ethyl chloroacetate are, therefore, perfectly analogous and represent the first phase only of Reformatsky's synthesis. In fact, the various

¹ *Ber.*, 20, 3164.

² *Ber.*, 28, 3262; *Jahresbr.*, 1097 (1898). Michailenko, *Ibid.*, 1098 (1898).

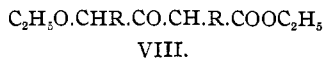
³ *Chem. Centr.*, 2, 472 (1898).

changes involved here are perfectly analogous to those involved in the formation of esters of β -hydroxy acids VII, from ketones and aldehydes.¹ The relationship between these reactions is apparent by inspection of the following equations.



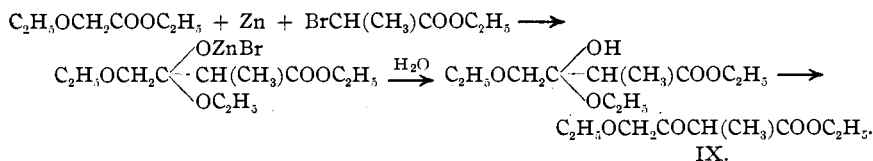
These results obtained by Fittig and Reformatsky suggested to the writer that other esters besides ethyl formate and diethyl oxalate would be found to undergo analogous condensations with halogen esters, in the presence of amalgamated-zinc, giving β -ketone esters. The data which I now introduce in this preliminary paper, and unpublished observations, confirm such an assumption. In fact, it appears very probable now from the evidence available, that the first phase of Reformatsky's synthesis may be the most important of the two in many cases where this reaction has been applied with only partial success.

I now find that Fittig's and Daimler's reaction can be applied successfully with esters of α -ethoxyacids and have succeeded in preparing by this method several β -ketone esters corresponding to the general formula



VIII. In fact every ester of this type, which I have so far examined, has reacted in this manner. For example: during the progress of synthetical work on pyrimidine-nucleosides it was necessary to obtain ethyl α -methyl- γ -ethoxyacetoacetate IX. We succeeded in preparing it without difficulty by condensation of ethyl ethoxyacetate with ethyl α -bromopropionate in the presence of amalgamated-zinc and the reaction may be expressed by the following equations:

¹ Reformatsky, *Ber.*, 20, 1210; 28, 2463.



We have used so far in our work ethyl ethoxyacetate, ethyl α -ethoxypropionate, ethyl bromoacetate and ethyl α -bromopropionate and have synthesized all four of the theoretically possible β -ketone esters by application of this reaction. The boiling points of these new ketone esters are recorded below. The description of their syntheses and chemical behavior will be discussed in future papers.

Ethyl γ -Ethoxyacetoacetate, $\text{C}_2\text{H}_5\text{OCH}_2\text{COCH}_2\text{COOC}_2\text{H}_5$.—Boiling points: 120–125° at 30 mm.; 130–136° at 45 mm.; 116–120° at 26–27 mm.; 110° at 20–21 mm.; 132° at 52 mm.; 135° at 55 mm.

Ethyl α -Methyl- γ -ethoxyacetoacetate, $\text{C}_2\text{H}_5\text{OCH}_2\text{COCH}(\text{CH}_3)\text{COOC}_2\text{H}_5$.—Boiling points: 116° at 24 mm.; 113–116° at 18–20 mm.

Ethyl γ -Methyl- γ -ethoxyacetoacetate, $\text{C}_2\text{H}_5\text{OCH}(\text{CH}_3)\text{COCH}_2\text{COOC}_2\text{H}_5$.—Boiling points: 110–115° at 19 mm.

Ethyl α -Methyl- γ -methyl- γ -ethoxyacetoacetate, $\text{C}_2\text{H}_5\text{OCH}(\text{CH}_3)\text{COCH}(\text{CH}_3)\text{COOC}_2\text{H}_5$.—Boiling points: 108–115° at 16 mm.

The synthesis of ethyl γ -ethoxyacetoacetate is incorporated in the following paper by L. H. Chernoff and the writer.

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[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON PYRIMIDINES. LXII. THE SYNTHESIS OF PYRIMIDINES RELATED STRUCTURALLY TO PYRIMIDINE-NUCLEOSIDES.

BY TREAT B. JOHNSON AND LEWIS H. CHERNOFF.

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Through the investigations of Levene and his co-workers¹ it seems to have been definitely established that the highly complex nucleic acids are composed of characteristic complexes designated by the term *nucleotides*. The latter are compounds consisting of phosphoric acid conjugated with a complex composed of a carbohydrate and a purine or pyrimidine. In other words, substances like yeast and thymus nucleic acids may be viewed as *polynucleotides*, corresponding to the polysaccharides in the sugar series, and consist of combinations of the molecules of *mononucleotides*, with loss of the elements of water. The latter correspond to the monosaccharides of the sugar series, and are represented in nature by the

¹ *Ber.*, 41, 1905; 42, 2703, 2744; 43, 3150, 3164; 44, 1027; 45, 608. THIS JOURNAL, 12, 411, 421; 11, 85.