

## The Reaction between Acetylacetone and Citraconic Anhydride\*

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As previously described by the author<sup>1</sup> acetylacetone and maleic anhydride formed an adduct when heated together or when the mixture was left for a long time at room temperature. The original object of the investigation was to find out if a dienol of acetylacetone existed containing conjugated carbon-to-carbon double bonds. The reaction which took place did not, however, proceed as expected according to a simple Diels-Alder scheme, but it was found that the adduct was built up of one molecule of acetylacetone and two molecules of maleic anhydride. The explanation of the course of the reaction arrived at was that in a first step two molecules of maleic anhydride by way of a substitution addition formed a double-molecule which, due to an enolization, acted as a dien and to which the mono-enol of acetylacetone was added in a second step.

It has now been found that acetylacetone forms an adduct also with citraconic anhydride. In this case, however, each molecule of the diketone reacts with one molecule only of the acid anhydride. The fact that the new adduct is a monocarboxylic acid indicates that neither in this case has a simple Diels-Alder reaction taken place. Evidently one of the carbonyl groups of the citraconic anhydride or the anhydride bond itself must be involved in the formation of the adduct. Before discussing the structural formula of the adduct and the mode of its formation it will be necessary to describe briefly the reactions of the adduct.

The excellently crystallizing adduct was only slightly soluble in cold water but dissolved readily on boiling. It did not reduce silver nitrate in the presence of ammonia. The iodoform reaction was positive, and the adduct gave with bromine-water a monobromo derivative. With dinitrophenylhydrazine and semicarbazid it gave crystalline monoderivatives. An aqueous solution of the

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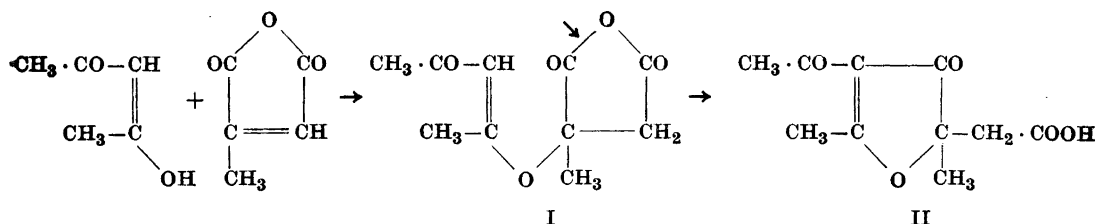
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adduct did not give any colour with ferric chloride but under certain conditions the adduct showed a pronounced tendency of enolizing which will be evident from the following. On dissolving the adduct in an excess of sodium carbonate the solution remained colourless and after it had been acidified no colour appeared after the addition of ferric chloride. If, however, the adduct was dissolved in more than one equivalent of alkali hydroxide the solution became strongly yellow. When this solution was acidified the yellow colour disappeared and the solution now gave a deep red-violet colour with ferric chloride. Leaving the acidified solution at room temperature the strength of the colour reaction decreased and disappeared nearly completely in the course of a few days. At the same time most of the unchanged adduct crystallized from the solution. It is quite remarkable that although a keto-form evidently was the stable form in acid medium the conversion of the enol-form into the ketoform proceeded so slowly. On dissolving the adduct in more than two equivalents of alkali a spontaneous degradation took place which will be discussed below.

Another example of the enolizing tendency of the adduct was found in the case of the ester. By means of diazomethane a methyl ester with one methoxyl group was obtained as a colourless crystalline substance. A solution of the ester in ethanol turned yellow on the addition of sodium ethoxide but the colour disappeared again on acidifying. On the other hand a solution of the methyl ester in ether containing a little methanol turned permanent yellow when treated with an excess of diazomethane. From this solution an orange-yellow syrup was obtained which did not crystallize and which obviously contained the methyl ether of the enol-form of the ester. The same enol-ether was formed to a certain degree also in an acid medium, viz. when hydrogen chloride was added to a solution of the methyl ester or of the adduct itself in methanol. Such a solution rapidly took on a yellow, later an orange, colour, and after removing the hydrogen chloride and the methanol an orange syrup was obtained, being a mixture of ordinary colourless ester and the coloured methyl ether of the enol-form from which a part of the former separated as crystals on standing.

The adduct was exceedingly stable in acid medium. It could be boiled with dilute sulphuric acid for half an hour without giving any degradation products. It could even be recovered unchanged after having been dissolved in concentrated sulphuric acid.

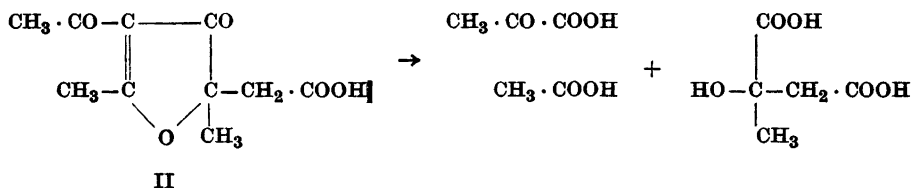
By the oxidation of the adduct with potassium permanganate acetic acid, pyruvic acid, and citramalic acid ( $\alpha$ -hydroxy- $\alpha$ -methylsuccinic acid) were isolated. Considering this result and the facts given above the following scheme is suggested for the formation of the adduct:



In a first step a substitution addition takes place, the acetylacetone reacting in its mono-enol-form. In the intermediate product (I) which has not as yet been isolated the second mobile hydrogen atom then attacks the anhydride bond as indicated by the arrow. This leads to the adduct (II) which can accordingly be designated as 4-acetyl-2,5-dimethyl-3-keto-2,3-dihydrofuryl-2-acetic acid.

It should be remarked that the sequence of the two steps of the reaction may be the reverse of that given in the scheme, but this will make no difference in the formula for the adduct. At the present time it has not been possible to make a decision between the two alternatives.

The result of the oxidation mentioned above is in full agreement with formula II:



The degradation of the adduct by means of alkali could be carried out either at room temperature or by heating on the steam-bath. At room temperature the degradation was followed by titration showing that the requirement of alkali per mole adduct increased to nearly three equivalents. The two main products of degradation were acetic acid and  $\beta$ -hydroxy- $\beta$ -methyl- $\gamma$ -ketovaleric acid, and the result of the titration was therefore in agreement with the following scheme according to which each mole of the adduct gave two mole of acetic acid and one mole of the keto-acid.

As acetone was found to be a minor product of degradation it is reasonable to suggest that the intermediate product III is degraded partly as indicated by the dotted arrow. It has, however, not been possible to isolate citramalic acid from its mixture with the keto-acid which is an oil. The keto-acid gave a



another month gave 95 g more of the adduct. The overall yield was therefore 47.5 % of theory. The crude adduct was washed with cold ethyl acetate and then recrystallized twice from ethyl acetate when it was obtained quite colourless and had m.p. 130°. The same m.p. was found after recrystallization from water.

	0.2229 g required 10.51 ml N/10 NaOH		
$C_{10}H_{12}O_5$	Calc.	C 56.60	H 5.70
	Found	» 56.73, 56.77	» 5.49, 5.58
			M 212.2
			» 212.1

*Dinitrophenylhydrazone*: Adding to the aqueous solution of the adduct a solution of 2,4-dinitrophenylhydrazine in 2N hydrochloric acid the hydrazone at first separated amorphous but rapidly turned into red crystals. Recrystallized from ethanol, m.p. 203°.

$C_{16}H_{16}O_8N_4$ (392.3)	Calc.	C 48.98	H 4.11	N 14.28
	Found	» 49.29, 48.98	» 4.18, 4.08	» 14.27, 14.13

*Semicarbazone* prepared in the usual way and recrystallized from water had m.p. 194°.

$C_{11}H_{15}O_5N_3$ (269.3)	Calc.	C 49.06	H 5.62	N 15.61
	Found	» 49.06	» 5.56	» 15.16

*Reaction with bromine*: To a little of the adduct dissolved in water bromine-water was added. The colour of the bromine disappeared instantaneously and an oil separated which crystallized in a few minutes. M.p. 95°.

$C_{10}H_{11}O_5Br$	Calc.	Br 27.45	Found	27.65
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*The adduct in acid medium*: A little of the adduct was dissolved in conc. sulphuric acid giving a yellow solution. After 15 minutes a part of the solution was poured on ice when the adduct separated as crystals with m.p. 130°. The rest of the solution was left for two days and also then the adduct was recovered unchanged. In another experiment the adduct (2 g) was boiled for half an hour with 2N sulphuric acid (25 ml) and a few ml distilled off. The distillate contained no acid and gave no reaction on acetone with o-nitrobenzaldehyde. From the rest of the solution which gave no colour with ferric chloride 1.75 g of the adduct crystallized on cooling, m.p. 128°.

#### Methyl ester of adduct

The pulverized adduct dissolved easily in an ethereal solution of diazomethane. On distilling off the ether a colourless liquid remained which crystallized in the course of a couple of months. After recrystallization from petroleum ether the ester had m.p. 55°.

$C_{11}H_{14}O_5$ (226.2)	Calc.	C 58.40	H 6.24	$CH_3O$ 13.70
	Found	» 58.58, 58.69	» 6.14, 6.24	» 15.04

0.2085 g in 17.42 g benzene,  $\Delta$  0.267° M 224

As already stated above the ester with an excess of diazomethane gave the methyl ether of an enol-form. The high content found for methoxyl may therefore be due to a contamination of the ester by a little of the ether.

In an attempt to prepare the ester in the usual way the following observations were made. In a solution of 1.3 g adduct in 15 ml methanol a current of dry hydrogen chloride was led until the weight had increased with 4 g. Shortly after starting the current the solution turned yellow and soon became orange (the same colours appeared when starting with a methanolic solution of the ester prepared by means of diazomethane). Next day the solution was placed in a vacuum desiccator above calcium chloride and potassium hydroxide when a dark orange syrup was obtained. In a couple of weeks a little crystalline material had been formed in the syrup. It was pressed on a porous plate and then recrystallized from petroleum ether. M.p. 55°.

## Oxidation of the adduct

A solution of the adduct (10 g) in a little more than one equivalent of sodium carbonate and diluted to 300 ml was vigorously stirred and a 5 per cent solution of potassium permanganate (350 ml) added in the course of two and a half hour, keeping the temperature at about 0°. After coagulating the manganese dioxide by heating gently and shaking the filtered colourless solution was concentrated on the steam-bath to 100 ml. Sulphuric acid (40 ml 5 N) was added and nearly two third of the solution distilled off. The distillate needed for its neutralization 41.4 ml N NaOH, corresponding to 2.48 g acetic acid (one mole per mole adduct would correspond to 2.83 g acetic acid). The neutralized distillate evaporated to dryness gave 3.6 g salt in which acetic acid was identified by well-known methods. The rest of the solution from the distillation (55 ml) was extracted thoroughly with ether giving 3.95 g of a syrup which partly crystallized. The crystalline substance (1.6 g) separated from the syrup on a porous plate was recrystallized twice from ethyl acetate. M.p. 118–120°, alone and after mixing with an authentic sample of citramalic acid.

$C_5H_8O_5$ (148.1)	Calc.	C 40.54	H 5.44
	Found	» 40.23, 40.18	» 5.59, 5.45

The presence of pyruvic acid amongst the oxidation products was proved in another experiment. Having oxidized 4.24 g adduct as above and acidified with sulphuric acid a solution of 2,4-dinitrophenylhydrazine in 2 N hydrochloric acid was added at about 50°. The orange-yellow precipitate (1.5 g) was recrystallized from ethanol when it had the m.p. 220°, alone or mixed with the hydrazone of pyruvic acid.

$C_9H_8O_6N_4$ (268.2)	Calc.	C 40.31	H 3.01	N 20.89
	Found	» 40.54, 40.37	» 2.92, 3.07	» 21.09, 21.15

## Degradation of adduct with alkali

The adduct (4.24 g) was dissolved in 5 equivalents sodium hydroxide diluted to 40 ml and excess of alkali determined by titrating samples of 2 ml of the solution from day to day. The yellow colour of the fresh solution became very faint in the course of one day. The consumption of alkali which just after dissolving the adduct was 1.026 equiv. per mole increased in 1, 2, 3, and 4 days to 2.396, 2.716, 2.782 and 2.816 equiv. respectively. To the rest of the solution (30 ml) 5 N sulphuric acid (15 ml) was added and the solution extracted two times with ether, each time with 450 ml. From the dried ethereal solution a yellow syrup was obtained which had a strong smell of acetic acid. It was placed in a vacuum desiccator above potassium hydroxide until the weight remained constant (1.9 g). The syrup would not crystallize. It was readily soluble in water and gave a crystalline orange-coloured dinitrophenylhydrazone which after recrystallization from ethanol had m.p. 175°.

$C_{12}H_{14}O_7N_4$ (326.3)	Calc.	C 44.17	H 4.32	N 17.17
	Found	» 44.18, 44.16	» 4.50, 4.56	» 17.51, 17.45

This correspond to the formula  $C_6H_{10}O_4$  for the syrupy degradation product. That the product was a monobasic acid was verified by esterifying a sample with diazomethane and preparing the dinitrophenylhydrazone of the ester. Recrystallized from ethanol, m.p. 132°.

$C_{13}H_{16}O_7N_4$ (340.3)	Calc.	C 45.88	H 4.74	N 16.47
	Found	» 45.95, 45.94	» 4.73, 4.85	» 16.44, 16.51

The composition of the semicarbazone corresponded to the same formula of the degradation product. The semicarbazone showed dimorphism. On crystallization from water a labile modification consisting of thin needles appeared first followed by dense prisms which were stable and into which the needles were transformed on standing. The stable modification had m.p. 204°.

$C_7H_{13}O_4N_3$ (203.2)	Calc. C 41.38	H 6.45	N 20.68
	Found » 41.32, 41.40	» 6.30, 6.33	» 20.69, 20.64

The presence of acetone amongst the degradation products was proved in a separate experiment. After the alkaline degradation had taken place the acidified solution was distilled. A part of the distillate on addition of *o*-nitrobenzaldehyde and alkali gave indigo. Another part on addition of dinitrophenylhydrazine in hydrochloric acid gave a crystalline hydrazone which after recrystallization from ethanol had m.p. 127°, alone and mixed with the hydrazone of acetone.

$C_9H_{10}O_4N_4$ (238.2)	Calc. C 45.38	H 4.23	N 23.52
	Found » 45.63	» 4.18	» 23.09

#### Investigation of $C_6H_{10}O_4$

(With stud. real. Svein Ramstad)

Greater quantities of the degradation product  $C_6H_{10}O_4$  were prepared in the following way. Batches of 10 g adduct were heated with 125 ml 2 *N* sodium hydroxide for two hours on the steam-bath. After adding 30 ml 5 *N* sulphuric acid and concentrating to two third of the volume a solution containing hydrochloride of semicarbazide (5 g) and potassium acetate (5 g) was added. Each batch gave from 7.9 to 8.2 g semicarbazone.

The semicarbazone was decomposed by heating 34 g with 50 ml water and 100 ml 5 *N* sulphuric acid on the steam-bath till it had dissolved completely. The solution on shaking six times with ether, each time with 600 ml, gave 19.9 g of the degradation product as a nearly colourless syrup.

*Reduction:* To a solution of the syrup (3.5 g) in ether (400 ml) amalgamated aluminium turnings (30 g) and from time to time small quantities of water were added. The reaction which thus proceeded smoothly was continued for 20 hours. After evaporating the ether sulphuric acid was added and the solution distilled with steam. From the distillate an oil (1.5 g) was obtained which had a pronounced smell of fatty acid and boiled at about 190°. By treatment with phosphorus trichloride it was transformed into an acid chloride which on pouring into conc. ammonia gave a crystalline amide. After recrystallization from ethyl acetate the amide had m.p. 125°, alone and mixed with an authentic sample of the amide of  $\beta$ -methylvaleric acid.

$C_6H_{13}ON$	Calc. N 12.16;	Found 11.90, 12.03
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*Oxidation with hypobromite:* To a solution of sodium hydroxide (3.3 g = 8 ¼/100 mole) in water (15 ml) bromine (4.8 g = 3/100 mole) was added while the solution was cooled with ice and shaken vigorously. Under continued cooling and shaking a solution of  $C_6H_{10}O_4$  (1.46 g = 1/100 mole) was added. The reaction proceeded rapidly and in a short time the solution became colourless. After adding 10 ml 5 *N* sulphuric acid bromoform was separated in a funnel and the aqueous solution concentrated on the steam-bath. On extracting two times with ether, each time with 500 ml, a viscous syrup (1.2 g) was obtained which crystallized immediately after inoculating with citramalic acid. After recrystallization from ethyl acetate, m.p. 119–120°, alone and mixed with pure citramalic acid.

## Adduct from propionylacetone

Propionylacetone (20 ml) and citraconic anhydride (16 ml) were mixed and left for seven weeks at 80°. The brown reaction product was dissolved in sodium carbonate and excess of propionylacetone extracted with ether. The aqueous solution was acidified and extracted with ether when a dark yellow syrup (10 g) was obtained which could not be brought to crystallize. On treating 1 g of the syrup with dinitrophenylhydrazine 1 g of a red crystalline hydrazone separated. Recrystallized from dilute ethanol, m.p. 194°.

$C_{17}H_{18}O_8N_4$ (396.3)	Calc.	C 50.25	H 4.46	N 13.79
	Found	» 50.14	» 4.55	» 14.13

## SUMMARY

A crystalline adduct is formed from one molecule of acetylacetone and one molecule of citraconic anhydride. The adduct which is a monocarboxylic acid was found to be a derivative of dihydrofuran. It is suggested that the reaction takes place in two steps but it has as yet not been possible to decide about the sequence of the steps. The adduct is enolized either by the action of alkali or excess of diazomethane or by treatment with methanolic hydrogen chloride. The adduct is remarkably stable against acids but is rapidly degraded in alkaline medium.

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