LXXXIX.—*Contributions to the Knowledge of the β -Ketonic acids. Part II.*

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IN a paper recently published by one of us and E. A. Tyler (Trans., 1896, **69**, 530), it was shown that the sodium derivative of ethylic acetoacetate readily reacts with ethylic chlorofumarate with the formation of a compound for which the formula

was brought forward. This constitution was derived from the chemical and physical properties of the substance, and also from the fact that the same compound is produced by using ethylic chloromaleate. It is, moreover, supported by the following considerations.

If the interaction of ethylic sodioacetoacetate and ethylic chlorofumarate were to take place as indicated by the equation

it might be expected that at the same time alcohol would be eliminated with the formation of the ethereal salt of a dicarboxylic acid, namely, ethylic methylcoumalindicarboxylate. This conclusion would follow from the synthesis of the ethereal salt of isodehydracetic acid, which is brought about by the action of ethylic sodioacetoacetate on ethylic β -chlorisocrotonate (Anschütz, Bendix, and Kerp, *Annalen*, **259**, 179), as indicated by the following symbols

The result of the action of the sodium derivative of ethylic acetate and ethylic chlorofumarate is, however, the ethereal salt of a tricarboxylic acid. The view of the constitution of this ethereal salt as expressed by the name ethylic methyldihydrofurfurantricarboxylate, is also supported by the experiments recorded in this communication.

Action of Ethylic Chlorofumarate on Ethylic Benzoylacetate.

Forty grams of ethylic benzoylacetate are added to the solution of 4.8 grams of sodium in 100 grams of absolute alcohol, and 43 grams of ethylic chlorofumarate are then gradually introduced. A reaction sets in immediately, and is complete after an hour's heating on the water bath. On removing the alcohol by distillation, and adding water, an oil separates, which is taken up with ether. The ethereal extract is dried with calcium chloride, the ether evaporated, and the oily residue distilled in a vacuum. Almost the total quantity comes over at $242\text{--}245^\circ$, under a pressure of 20 mm., as a yellow oil with a green fluorescence. The compound is very viscous, and does not solidify in a freezing mixture of ice and salt. It is insoluble in dilute potash, and does not react with phenylhydrazine.

On analysis, it gave numbers corresponding with the formula $\text{C}_{19}\text{H}_{22}\text{O}_7$.

0.2252 gave 0.5206 CO_2 and 0.1128 H_2O . $\text{C} = 63.04$; $\text{H} = 6.06$.

$\text{C}_{19}\text{H}_{22}\text{O}_7$, requires $\text{C} = 62.98$; $\text{H} = 6.07$ per cent.

The compound resembles in its chemical behaviour the product of the interaction of ethylic sodioacetoacetate on the ethereal salts of chlorofumaric and chloromaleic acids, and it may be regarded as ethylic phenyldihydrofurfurantricarboxylate,

Action of Potash.—Like the corresponding methyl compound, this ethereal salt is readily hydrolysed. By boiling the solution of the furfuran compound in alcoholic potash in a flask with a reflux condenser on the water bath, a red oil collects at the bottom of the

vessel, which is undoubtedly the potassium salt of the acid. After four hours' heating, the alcohol is distilled off, and the residue treated with an excess of hydrochloric acid, when carbon dioxide is evolved, and a crystalline precipitate separates, which increases on standing over night. The solid is collected on a filter, and the mother liquor, which still contains a small quantity of the substance, is extracted with ether. This compound readily dissolves in boiling water, and the solution, after being decolorised by animal charcoal, deposits, on cooling, bunches of colourless needles, which melt with slight decomposition at 172° , having begun to soften a few degrees lower.

On analysis, the following numbers were obtained, corresponding with the formula $C_{12}H_{12}O_6$.

0.2068 gave 0.4342 CO_2 and 0.0920 H_2O . C = 56.98; H = 4.91.

$C_{12}H_{12}O_6$ requires C = 57.14; H = 4.76 per cent.

The hydrolysis of the furfuran compound leads also in this case to the formation of an acid, namely, acetophenylmalic acid, the constitution of which is to be expressed by the formula

The *silver salt* of this acid is obtained on the addition of silver nitrate to the solution of the acid neutralised by ammonia. For analysis it was dried first in a vacuum over sulphuric acid, and then at 100° .

0.2542 left on ignition 0.1176 Ag. Ag = 46.26.

$C_{12}H_{10}Ag_2O_6$ requires 46.35 per cent.

The aqueous solution of the acid gives a white precipitate with lead acetate, which dissolves in water with great difficulty. Copper sulphate, when added to the solution of the acid neutralised with ammonia, throws down a bluish-green salt.

Action of Ammonia on Ethylic Phenyldihydrofurfurantricarboxylate.

Ammonia reacts with this ethereal salt as it does with ethylic methyldihydrofurfurantricarboxylate. On allowing the ethereal salt to remain in contact with strong aqueous ammonia for three days, the contents of the vessel are transformed into a semi-solid mass of crystals, which readily dissolves in hot water, and, on cooling, comes down in long, thin needles, softening at 180° and melting at $185-186^{\circ}$.

A nitrogen determination leads to the formula $C_{15}H_{16}N_2O_6$.

0.2194 gave 17.5 c.c. moist nitrogen at 16° and 759 mm. N = 9.28.

$C_{15}H_{16}N_2O_6$ requires N = 9.21.

The constitution of this compound is no doubt similar to that of the substance produced from ethylic methylhydrofurfurantricarboxylate, and is probably expressed by one of the following formulæ:

Action of the Sodium Derivative of Ethylic Methylacetoacetate on Ethylic Chlorofumarate.

The interaction of ethylic chlorofumarate and the sodium derivatives of ethylic acetoacetate and ethylic benzoylacetate was explained by the assumption that the hydrogen atom of the α -hydrocarbon group, contained in the ethereal salts of these β -ketonic acids, shifts and brings about the closing of the ring in the following manner

If this explanation be correct, it may be expected that by using the sodium derivative of ethylic acetomethylacetate instead of ethylic sodioacetoacetate, either the ethereal salt of a tricarboxylic acid of the formula

would be produced, or that the interaction of these substances would be accompanied by the splitting off of ethylic acetate with the formation of the compound

which is to be regarded as ethylic methylfurfurandicarboxylate. That the reaction takes place in the latter manner is proved by experiment, and this fact affords a further support to the constitution given above for the compounds formed by the interaction of ethylic chlorofumarate and the sodium derivatives of ethylic acetoacetate and ethylic benzoylacetate. The reaction is carried out in the following way.

Thirty grams of ethylic acetomethylacetate are mixed with a cold solution of 4.8 grams of sodium in 100 grams of absolute alcohol, and 43 grams of ethylic chlorofumarate gradually added, when the

mixture turns deep red. On allowing it to stand over night, the cake of ethylic sodioacetomethylacetate disappears with precipitation of sodium chloride. The reaction is complete after about an hour's heating at 100° , the contents of the flask having a strong odour of ethylic acetate. On distilling on the water bath, the ethylic acetate passes over together with the alcohol; water is added to the residue, which throws down an oil; this is taken up with ether, the solvent evaporated, and the remaining oil allowed to stand in a vacuum over sulphuric acid, when, after several hours, crystals separate and gradually increase in quantity.

A certain amount of the same compound is still contained in the red aqueous solution, and may be obtained by adding an excess of hydrochloric acid and extracting with ether. The oil which is left, partially solidifies on standing in a vacuum.

The substance obtained from the product of the reaction, before and after acidification, is collected on a filter, washed with benzene to remove adhering oil, and dissolved in hot, dilute spirit, from which, on cooling, it separates in colourless plates, melting at 132° .

The thick, yellow oil formed along with this substance does not deposit any crystals; on distillation in a vacuum, it suffers decomposition, leaving a black mass in the distilling flask. It is a mixture of the furfuran derivative of ethylic acetomethylacetate, ethylic chlorofumarate, and other compounds.

Analysis of the compound melting at 132° gave the following numbers, which correspond with the formula for ethylic methylfurfurandicarboxylate

0.2196 gave 0.4692 CO_2 and 0.1180 H_2O . C = 58.27; H = 5.97.

0.2136 „ 0.4584 „ „ 0.1194 „ C = 58.51; H = 6.21.

$\text{C}_{11}\text{H}_{14}\text{O}_5$ requires C = 58.40; H = 6.19 per cent.

The ethereal salt readily dissolves in alcohol and glacial acetic acid, but with difficulty in benzene. The alcoholic solution of the compound is coloured red-violet on the addition of ferric chloride. The substance is soluble in ammonia and in dilute alkalis, and is reprecipitated unchanged from the yellow solution on the addition of hydrochloric acid. This behaviour explains why a certain amount of the furfuran derivative is contained as a sodium compound in the aqueous solution of the product of the interaction of ethylic chlorofumarate and ethylic acetomethylacetate. The solubility of ethylic methylfurfurandicarboxylate may be attributed either to a splitting of the furfuran ring or to the negative characters of the $-\text{CH}$ group.

1388 RUHEMANN AND WOLF: THE β -KETONIC ACIDS.

The remarkable properties of the product formed from the ethereal salt on hydrolysis rendered it desirable to fix its formula by the determination of the molecular weight.

(1.) 0.3468 gram dissolved in 23.309 grams of glacial acetic acid produced a depression of 0.25° .

(2.) 0.3884 gram dissolved in 24.671 grams of glacial acetic acid produced a depression of 0.26° .

(3.) 0.7616 gram dissolved in 32.022 grams of absolute alcohol, distilled from sodium, increased the boiling point by 0.12° .

(4.) 1.2256 grams dissolved in 33.6680 grams of absolute alcohol increased the boiling point by 0.18° .

	Calculated for $C_{11}H_{14}O_6$.	Found.			
		I.	II.	III.	IV.
M	226	232	236	228	232

Hydrolysis of Ethylic Methylfurfurandicarboxylate.

The compound formed from the ethereal salt on hydrolysis is, on account of its remarkable properties, of considerable interest. Its study, which has occupied us for some time, led to the following result.

The hydrolysis of ethylic methylfurfurandicarboxylate is accompanied by elimination of carbon dioxide, and yields a compound which, when dried at 100° , has the composition $C_6H_6O_3$, and this formula agrees also with the determination of its molecular weight. The synthesis of this substance from the furfuran derivative would lead to the view that it is to be regarded as methylfurfuranmonocarboxylic acid,

Its behaviour, however, as described below, points to the conclusion that it is to be looked upon as methylhydroxycoumalin, and that by the action of the hydrolysing agent on the ethereal salt at the same time, a destruction of the furfuran ring takes place as indicated by the following symbols

This anhydride exists only when the compound is dried at 100° , or in solution in solvents free from water, such as acetone or absolute alcohol. In the presence of water, however, it is partially trans-

formed into the dihydroxy-acid,
$$\begin{array}{c} \text{CH}_3 \cdot \text{C} = \text{CH} \\ | \quad | \\ \text{OH} \quad \text{CH} \\ | \quad | \\ \text{C} \cdot \text{OH} \\ | \\ \text{COOH} \end{array}$$
 the aqueous solu-

tion of which decomposes barium carbonate with evolution of carbon dioxide.

The analytical results lead to the view that in aqueous solution an equilibrium is established between the acid and its internal anhydride which is reached when the system has the composition

and which is also maintained in the air-dried substance.

The hydrolysis of ethylic methylfurfurandicarboxylate may be effected by boiling the solution of the ethereal salt with a concentrated aqueous solution of potash, or by heating it with hydrochloric acid. In the former case, the reaction is complete after three hours; on addition of hydrochloric acid, carbon dioxide is evolved, and a crystalline precipitate is thrown down, which increases on standing; the mother liquor contains a quantity of the substance, which may be extracted by frequently shaking with ether. It is, however, more convenient to bring about the hydrolysis of the ethereal salt by boiling it with concentrated hydrochloric acid in a flask provided with a reflux condenser. The salt melts and gradually disappears; after two hours' heating, a dark coloured solution is obtained which, on evaporation on the water bath, leaves a dark residue. This is dissolved in water, and the solution, after being decolorised by animal charcoal, deposits, on cooling, colourless prisms, which melt at 244° to a brown liquid.

On drying the compound at 100° , the crystals become opaque, and have then the composition $\text{C}_6\text{H}_6\text{O}_3$, as indicated by the results of the following analyses, of which the first was made with a specimen obtained by hydrolysis with potash; the second by hydrolysis with hydrochloric acid.

0.2252 gave 0.4727 CO_2 and 0.0966 H_2O . C = 57.2; H = 4.76.

0.2102 „ 0.4384 „ „ 0.0950 „ C = 56.88; H = 5.02.

$\text{C}_6\text{H}_6\text{O}_3$ requires C = 57.14; H = 4.76 per cent.

The compound is insoluble in benzene and chloroform, readily soluble in alcohol and acetone.

The molecular weight of the compound, dried at 100° , was determined in solution in acetone with the following result.

1390 RUHEMANN AND WOLF: THE β -KETONIC ACIDS.

0.5788 gram dissolved in 34.365 grams of acetone increased the boiling point by 0.19° .

	Calculated for $C_6H_6O_3$.	Found.
M	126	148

The solution of the coumalin derivative in absolute alcohol only slightly reddens blue litmus paper; on addition of water, however, it becomes strongly acid. A solution of the compound in absolute alcohol, when mixed with sodium alcoholate dissolved in alcohol, becomes deep red; the colour grows paler as water is added. These facts point to the conclusion that the product formed by hydrolysis of the furfuran derivative, when dried at 100° , is not an acid, but becomes such in the presence of water. The acid, $C_6H_6O_4$, is not stable, and readily changes into its anhydride, $C_6H_6O_3$, and this transformation partially takes place in aqueous solution and reaches an equilibrium, corresponding with the composition $3C_6H_6O_4, C_6H_6O_3$, which is maintained in the air-dried crystals.

We are indebted to Dr. A. Hutchinson for the following crystallographic examination.

"System. Asymmetric.

$$a : b : c = 1.1925 : 1 : 1.2369.$$

$$\alpha = 94^\circ 8', \beta = 104^\circ 44', \gamma = 79^\circ 3'$$

"Forms observed:

$$a\{100\}, b\{010\}, c\{001\}, m\{110\}, q\{011\}, d\{012\}, x\{\bar{1}02\}.$$

"Table of angles:

Angle.	Measured (mean).	Calculated.
100 : 010	*100° 15'	—
100 : 001	*75 46	—
010 : 001	*88 34	—
100 : 110	*55 5	—
001 : 011	*49 46	—
001 : 012	31 15	30° 57½'
001 : $\bar{1}02$	30 13	30 24
110 : 001	78 35	78 35
110 : 011	48 27	48 30½
001 : 101	—	39 3

"The axial planes are well developed on these crystals which are often elongated in the direction of the Z axis.

"The form $\{110\}$ is nearly always present, and is sometimes large, the remaining faces, though of frequent occurrence, are small, and give poor reflections.

"There is no well marked cleavage.

"The extinction on $b(010)$ in the obtuse angle β is inclined 12° to the edge ab .

"The extinction on $a(100)$ in the obtuse angle α is inclined $36\frac{1}{2}^\circ$ to the edge ab ."

The substance gives off the whole of the water at 100° , no further loss occurring at 110° .

The following determinations of the water were made with specimens of different preparations of the air-dried substance.

0.2098	gram lost on drying at 100°	0.0202	gram	=	9.63	per cent.
0.3000	"	"	0.0290	"	=	9.66 "
0.2446	"	"	0.0236	"	=	9.65 "
0.3666	"	"	0.0360	"	=	9.55 "
0.4054	"	"	0.0398	"	=	9.81 "

$4C_6H_6O_3 \cdot 3H_2O$ requires for transformation into $4C_6H_6O_3$ a loss of 9.67 per cent.

On titration of three different preparations of the substance, it was found that a solution of 0.3766 gram of the air-dried compound was neutralised by 20.7 c.c. of a solution containing 0.0037 gram NaOH in 1 c.c., which corresponds to 20.34 per cent. of NaOH.

0.3704 gram of the air-dried compound was neutralised by 21 c.c. of the same solution, which corresponds to 20.98 per cent. NaOH.

0.2766 gram was neutralised by 16.8 c.c. of a solution containing 0.0036 gram NaOH in 1 c.c., which corresponds to 21.93 per cent. NaOH.

$4C_6H_6O_3 + 3H_2O$ requires for neutralisation 21.46 per cent. NaOH.

The acid does not form a stable salt with ammonia, for, on warming, dissociation of the salt takes place, and the liquid becomes acid. A silver salt is not formed, as on addition of silver nitrate to the solution, rendered neutral with ammonia, reduction sets in, a silver mirror being deposited on the glass on warming. The acid decolorises potassium permanganate and also reduces Fehling's solution, as does coumalic acid. The solution in alcohol turns deep red with sodium alcoholate, and, on adding ether, a reddish precipitate is thrown down, which is extremely hygroscopic. No precipitate is formed in aqueous solution by barium, lead, or zinc salts.

The properties of this compound are interesting enough to deserve further investigation, which is in progress.

Action of Ethylic Sodioacetoacetate on Ethylic α -Chlorocrotonate.

This reaction was studied with a view of ascertaining whether the grouping $\begin{array}{c} \text{C} \cdot \text{COOC}_2\text{H}_5 \\ || \\ \text{CH} \cdot \text{CH}_3 \end{array}$ of ethylic α -chlorocrotonate is negative enough

to cause a condensation similar to that brought about by the interaction of ethylic sodioacetoacetate and the ethereal salts of chloro-, fumaric and chloromaleic acids, thus giving rise to the formation of a compound of the formula

It was found, indeed, that an ethereal salt of the composition $\text{C}_{12}\text{H}_{18}\text{O}_5$ is produced, the behaviour of which, however, seems to indicate that it does not possess the above constitution. Of the two formulæ,

which may be taken into consideration, the symbol (3) best explains the properties of the compound described below. The formation of such a substance would lead to the conclusion that the negative grouping of ethylic α -chlorocrotonate is not sufficient to transform the ketone group of ethylic acetoacetate into the ethenol group.

The action may be regarded as proceeding first with formation of $\text{CH}_3 \cdot \text{CO} \cdot \text{CH} \cdot \text{COOC}_2\text{H}_5$, which, in the second phase of the reaction, suffers a molecular transformation, accompanied by a condensation to the ring compound, ethylic methylidihydrofurfurandicarboxylate.

The ethereal salt is prepared as follows. 29.6 grams of ethylic α -chlorocrotonate are added to a solution of ethylic sodioacetoacetate, obtained by mixing 26 grams of ethylic acetoacetate with 4.6 grams of sodium in 100 grams of absolute alcohol. The mixture is boiled on the water bath in a flask with a reflux condenser until it shows only a slight alkaline reaction to litmus; this point is reached after three or four hours' heating. The alcohol is then evaporated, water is added to the residue, the oil which is thrown down is extracted with ether, and, after removal of the ether, distilled in a vacuum. It boils at $160\text{--}162^\circ$ under a pressure of 16 mm., and has the density $d_{19^\circ/19^\circ} = 1.0986$.

The following analytical numbers agree with the formula $\text{C}_{12}\text{H}_{18}\text{O}_5$.

0.2296 gave 0.5024 CO_2 and 0.1538 H_2O . C = 59.62; H = 7.43.

$\text{C}_{12}\text{H}_{18}\text{O}_5$ requires C = 59.50; H = 7.43 per cent.

The molecular refraction does not enable us to decide between formula (1) or (3), on the one hand, and (2) on the other, as the values lie close together. They are for the expression $\text{C}_{12}\text{H}_{18}\text{O}''_2\text{O} < |^- = 60.76$ and for $\text{C}_{12}\text{H}_{18}\text{O}''_3\text{O}_2 < |^- = 60.88$.

Mr. A. S. Hemmy, of St. John's College, had the kindness to determine the refractive index of the compound, and found it to be $n_{Na} = 1.464$ at 22° .

The molecular refraction, $M \frac{n^2 - 1}{(n^2 + 2)d}$, amounts, therefore, to 60.78.

The chemical behaviour of the compound, however, points to the formula (3). The ethereal salt is insoluble in alkalis; it does not react with phenylhydrazine; it evolves hydrogen bromide on the addition of bromine, as does ethylic methylidihydrofurfurantricarboxylate. The action of the halogen on the ethereal salt is accompanied by an evolution of heat which renders the use of carbon tetrachloride as a diluting agent advisable. The yellow oil which remains after removal of the carbon tetrachloride, suffers partial decomposition on distillation in a vacuum. A bromine determination of the product, which had been heated to 150° under reduced pressure and allowed to stand in a vacuum over potash and sulphuric acid, gave 26.14 per cent. of Br. This value indicates that the formula of the bromo-derivative is $C_{12}H_{11}BrO_6$, which requires 24.92 per cent. Br. These properties of the compound seem to exclude the constitution represented by the symbol (2), and the behaviour towards ammonia points to formula (3).

Action of Ammonia.—The ethereal salt, when allowed to remain in contact with a concentrated aqueous solution of ammonia, gradually disappears, while crystals separate. The reaction is almost complete after three to four days, when the solid is collected. This dissolves in boiling water, and, on cooling, separates in colourless plates, which melt at 169 — 170° , and have the formula $C_{10}H_{15}NO_4$.

0.1999 gave 0.4134 CO_2 and 0.1276 H_2O . C = 56.40; H = 7.09.

0.2680 „ 16.0 c.c. moist nitrogen at 25° and 758 mm. N = 6.64.

$C_{10}H_{15}NO_4$ requires C = 56.24; H = 7.04; N = 6.57 per cent.

From the composition of this substance, it follows that the action of ammonia on the ethereal salt yields a monamide, which may be represented by one of the following two expressions.

The behaviour of ammonia towards the product resulting from the action of ethylic sodioacetoacetate on ethylic α -chlorocrotonate differs, therefore, from that of ammonia on the compounds formed from ethyl α -chlorofumarate and the sodium derivatives of ethylic acetoacetic acid and ethylic benzoylacetate. In these cases we have to assume the opening of the furfuran ring with accompanying condensation to

1394 RUHEMANN: FORMATION OF PYRAZOLONE DERIVATIVES

pyridine derivatives, which we should also expect if the compound $C_{12}H_{18}O_5$ had the constitution (1).

These considerations lead, thus, to the formula

for the ethereal salt.

The reason why this compound shows a greater stability is most probably to be found in the positive character of the groups with which the $-\text{O}-$ atom of the furfuran ring is united. The product formed on hydrolysis of the ethereal salt is still under examination.

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