LXXIV.—*Condensation of Ethylic Salts of Acids of the Acetylene Series with Ketonic Compounds.*

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As shown before (this vol., 245, 411), the ethylic salts of β -ketonic acids—for example, ethylic acetoacetate and ethylic benzoylacetate—condense with ethylic phenylpropionate to α -pyrone derivatives under the influence of sodium ethoxide. The behaviour of β -diketones, such as acetylacetone and benzoylacetone, towards the ethylic salts of the unsaturated acid is similar, and leads to the formation of the corresponding cyclic compounds of the general formula :

We have undertaken the further study of the interaction of ethylic salts of acids of the acetylene series with those of β -ketonic acids, in order to ascertain whether they also yield α -pyrone derivatives, and find that, on using substitution products of ethylic phenylpropionate and ketonic compounds of the types $\text{R} \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOC}_2\text{H}_5$ or $\text{R} \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{CO} \cdot \text{R}'$, such cyclic compounds are produced ; the reaction, however, takes a different course if ethylic acetylenedicarboxylate is used instead of ethylic phenylpropionate. The union of this salt with ethylic benzoylacetate is readily effected by means of sodium ethoxide ; it is not accompanied, however, by the loss of alcohol and condensation to an α -pyrone compound. The product does not dissolve in alkali, does not give a colour reaction with ferric chloride, and does not condense with ammonia to a pyridine derivative.

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These facts lead to the view that the reaction does not take place in the following manner :

and indicate that both hydrogen atoms of the CH_2 -group of the ketonic compound play a part in the union of the two ethylic salts. For the constitution of the additive compound, there remains a choice between the two formulæ :

Either of these formulæ would correspond with the above-mentioned behaviour, yet we are inclined to prefer formula II, which represents the substance as ethylic benzoyltrimethylenetricarboxylate, since, on treatment with alcoholic ammonia, a monamido-compound is produced, whilst, in the light of the researches on the action of ammonia on the ethylic salts of aconitic acid and its homologues, it would be expected that a compound of the constitution I would condense to a pyridine derivative.

We are at present engaged in the study of the acid which is obtained by the hydrolysis of the ethereal salt, with the object of confirming the conclusion as to its constitution derived from the above considerations.

One of the authors (*loc. cit.*) has shown that the α -pyrone compounds, which are produced by the condensation of ethylic phenylpropionate with ethylic acetoacetate and ethylic benzoylacetate, can readily be changed into pyridine derivatives. This is effected by the substitution of the ethyl radicle for the ammonium group in the additive compounds of the α -pyrone derivatives with 2 mols. of ammonia, and distillation of the ethylic salts thus formed. These salts had not been isolated, and it is therefore of interest that such a compound can readily be obtained from the α -pyrone derivative which is produced by the condensation of benzoylacetone with ethylic phenylpropionate. This salt, which is most probably to be represented by the formula,

loses alcohol on distillation in a vacuum, and is quantitatively transformed into the pyridine derivative.

It may further be pointed out that the α -pyrone compounds also form additive products with 2 mols. of primary bases, such as ethyl-

amine. These we hope to be able to transform into derivatives of pyridine which contain an alkyl group united with the nitrogen atom.

The present paper contains, besides a record of the work indicated above, the description of some experiments on the behaviour of sodium ethoxide towards a mixture of ethylic phenylpropiolate and alkyl derivatives of ethylic acetoacetate. We found that the reaction was incomplete and that a mixture of substances was produced which we were unable to separate by fractional distillation.

EXPERIMENTAL.

On adding a small quantity of sodium ethoxide (0.5 gram) to the mixture of ethylic phenylpropiolate and acetylacetone, an oil is obtained which, as mentioned before, yields ethylic γ -diaceto- β -phenylcrotonate and γ -phenyl- α' -methyl- β' -aceto- α -pyrone on distillation. The formation of the latter is, however, accompanied by that of ethylic acetate and γ -phenyl- α' -methyl- α -pyrone if the mixture is digested with an excess of sodium ethoxide (several grams) for one to two days on the water-bath. The separation is effected by adding dilute sulphuric acid to the product and submitting the oil thus precipitated to fractional distillation in a vacuum; phenylmethylaceto- α -pyrone passes over between 210° and 220° under about 12 mm. pressure, and γ -phenyl- α' -methyl- α -pyrone at 270 — 280° . The latter crystallises from alcohol in faintly yellow, prismatic plates which soften at 172° and melt at 180° .

0.2040 gave 0.5798 CO_2 and 0.0988 H_2O . $\text{C} = 77.51$; $\text{H} = 5.38$.

$\text{C}_{12}\text{H}_{10}\text{O}_2$ requires $\text{C} = 77.41$; $\text{H} = 5.37$ per cent.

This compound owes its formation undoubtedly to the decomposition which the corresponding aceto-derivative undergoes under the influence of sodium ethoxide as expressed by the equation:

Action of Ethylamine on Ethylic α' -Methyl- γ -phenyl- α -pyrone- β' -carboxylate.

Ethylamine, just like ammonia, yields additive products with α -pyrone derivatives. We have studied this reaction more particularly in the case of the compound which is formed by the condensation of ethylic phenylpropiolate and ethylic acetoacetate. The additive product

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dissolves in alcoholic ethylamine and the solution does not deposit a solid after standing for two days; on evaporating the yellow solution under diminished pressure, a solid residue remains which almost completely dissolves in water containing a little ethylamine.

This compound is undoubtedly the ethylammonium salt, and is probably represented by the formula :

The aqueous solution yields, with silver nitrate, a yellowish precipitate of the corresponding silver salt, which, after washing with water and then with alcohol, is dried in a vacuum.

0.2680 left, on ignition, 0.0710 Ag. Ag = 26.49.

$\text{C}_{17}\text{H}_{20}\text{NO}_4\text{Ag}$ requires Ag = 26.34 per cent.

We hope to transform this silver salt into the pyridine derivative containing the ethyl group united with the nitrogen.

γa'-Diphenyl-β'-acetyl-α-hydroxypyridine.

Benzoylacetone and ethylic phenylpropionate, as shown by one of us (*loc. cit.*), under the influence of sodium ethoxide, condense to an α-pyrone derivative, which most probably is to be represented by the formula :

Its additive compound with 2 mols. of ammonia yields a silver salt of the formula $\text{C}_{19}\text{H}_{16}\text{AgNO}_3$ on treatment with silver nitrate. This, after drying in a vacuum, is digested with ethylic iodide on the water-bath for two hours; the excess of the iodide is evaporated and the residue extracted with boiling alcohol. The alcoholic filtrate from the silver iodide, on cooling, deposits faintly yellow plates, which melt at 161—162°, dissolve sparingly in cold, but readily in boiling alcohol, and are insoluble in alkali. This substance is the ethylic salt corresponding with the silver compound, and on analysis gave the following results :

0.2031 gave 0.5595 CO_2 and 0.1157 H_2O . C = 75.16; H = 6.33.

0.3060 ,, 10.8 c.c. nitrogen at 14° and 776mm. N = 4.23.

$\text{C}_{21}\text{H}_{21}\text{NO}_3$ requires C = 75.22; H = 6.26; N = 4.22 per cent.

From a consideration of the mode of transformation of α-pyrone compounds into pyridine derivatives (*loc. cit.*), the constitution of this substance is most probably expressed by the following formula :

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This view explains also the change which the ethylic salt suffers when heated in a vacuum. It first melts, then ebullition takes place, accompanied by the formation of white clouds which indicate the elimination of alcohol, and at a temperature above 300° a yellowish oil distils without decomposition which at once solidifies. This dissolves readily in glacial acetic acid, but only sparingly in alcohol, and crystallises from the latter in colourless needles which melt at 225° .

Diphenylacetopyridone, $C_6H_5 \cdot C \begin{smallmatrix} \text{CH} \\ \text{C}(\text{CO} \cdot \text{CH}_3) \end{smallmatrix} \text{C}(\text{OH}) \text{N}$, has acid properties, since it is soluble in dilute caustic potash, especially on warming, and is precipitated unchanged on the addition of a mineral acid to the alkaline solution; it is not dissolved in hydrochloric acid, however, and therefore does not exhibit the properties of a base.

0.2007 gave 0.5800 CO_2 and 0.0942 H_2O . $\text{C} = 78.81$; $\text{H} = 5.21$.

0.3192 „ 13.5 c.c. nitrogen at 15° and 776 mm. $\text{N} = 5.05$.

$C_{19}H_{15}NO_2$ requires $\text{C} = 78.89$; $\text{H} = 5.19$; $\text{N} = 4.84$ per cent.

Formation of α -Pyrone Compounds from Ethylic Paranitrophenylpropiolate and the Ethylic Salts of β -Ketonic Acids.

The ethylic salts of phenylpropionic acid with substituents in the nucleus, as mentioned above, combine with those of acetoacetic and benzoylactic acids, under the influence of sodium ethoxide, as readily as does ethylic phenylpropiolate itself. As an example of such a derivative, we have chosen ethylic paranitrophenylpropiolate.

Ethylic γ -Paranitrophenyl- β' -methyl- α -pyrone- β' -carboxylate,

is produced by digesting equivalent quantities of ethylic paranitrophenylpropiolate and acetoacetate with 0.5 gram of sodium ethoxide on the water-bath for 3 hours; the dark product is acidified with dilute sulphuric acid and repeatedly extracted with ether.

The α -pyrone compound, being sparingly soluble in ether, separates from this solvent in yellowish prisms, which, when recrystallised from boiling alcohol, melt at $131-132^{\circ}$.

0.2330 gave 0.5070 CO_2 and 0.0895 H_2O . $\text{C} = 59.34$; $\text{H} = 4.26$.

0.3030 „ 12.5 c.c. nitrogen at 17° and 762 mm. $\text{N} = 4.80$.

$C_{15}H_{13}NO_6$ requires $\text{C} = 59.40$; $\text{H} = 4.29$; $\text{N} = 4.62$ per cent.

Ethylic γ -Paranitrophenyl- α' -phenyl- α -pyrone- β' -carboxylate,

—This compound is obtained by mixing ethylic benzoylacetate (11 grams) with sodium ethoxide (0.5 gram), and then adding ethylic para-

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nitrophenylpropiolate (12 grams). The mixture is warmed over a flame until it melts, and finally digested on the water-bath for 2 hours. The red product thus obtained is treated with dilute sulphuric acid and extracted with ether; the ethereal solution, on standing, deposits yellowish plates which dissolve sparingly in alcohol and melt at 150°.

0.2288 gave 0.5505 CO₂ and 0.0850 H₂O. C = 65.61; H = 4.12.

0.3270 „ 11 c.c. nitrogen at 16° and 764 mm. N = 3.94.

C₂₀H₁₅NO₆ requires C = 65.75; H = 4.11; N = 3.83 per cent.

Ethylic γ-Phenyl-α-pyrone-α'-β'-dicarboxylate,

—The preparation of this substance from ethylic oxaloacetate and ethylic phenylpropiolate requires care, on account of the ease with which the ethylic salt of the ketonic acid decomposes. The method which in the former cases led to the formation of α-pyrone compounds cannot be used, since evolution of gas occurs on digesting the mixture of the two ethylic salts with sodium ethoxide.

The condensation, however, can be effected in the following manner. Ethylic oxaloacetate is gradually mixed with an equivalent quantity of dry sodium ethoxide suspended in absolute ether, and ethylic phenylpropiolate is slowly added; the green solution thus produced, after standing for 2 to 3 days at the ordinary temperature, is treated with dilute sulphuric acid, and, after removal of the ether, yields a very viscous oil which does not deposit crystals, and decomposes on distillation in a vacuum. When digested with a small quantity of sodium ethoxide on the water-bath and then treated with dilute sulphuric acid, this product forms an oil which deposits crystals after some time; these are collected by the aid of a pump, and dissolved in ether. On allowing the ether to evaporate slowly, yellowish, prismatic plates separate which melt at 94—95°, are very soluble in alcohol, and are not decolorised by treatment with animal charcoal. The compound was dried in a vacuum and analysed.

0.1963 gave 0.4620 CO₂ and 0.0905 H₂O. C = 64.28; H = 5.12.

C₁₇H₁₆O₆ requires C = 64.55; H = 5.06 per cent.

The yield is very small, and this circumstance prevented us from studying the α-pyrone compound further.

Action of Ethylic Phenylpropiolate on Ethylic Alkyl Acetoacetates in the presence of Sodium Ethoxide.

On examining the action of sodium ethoxide on a mixture of ethylic phenylpropiolate, and of β-diketones, or the ethylic salts of β-ketonic

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acids, which contain the CH_2 -group, it was found that the resulting oils, when distilled, yielded, besides α -pyrone derivatives, fractions with lower boiling points which probably consist of unsaturated ketonic compounds, forming the intermediate products of the reaction.

In one case, a substance of this type has been isolated (this vol., 415); this fact led to the view that the formation of the additive products preceded that of the pyrone derivative, and induced us to study the action of sodium ethoxide on a mixture of ethylic phenylpropiolate, and ethylic alkylacetoacetates, in the hope of preparing unsaturated ketonic compounds of the general formula,

In using ethylic acetoacetate, the reaction proceeds with marked evolution of heat, but scarcely any rise of temperature is observed on adding 0.5 gram of sodium ethoxide to the mixture of the ethylic salt of the unsaturated acid and that of the alkylated acetoacetic acid. Our experiments led to the conclusion that the reaction is complicated whether the mixture is heated on the water-bath for a longer or a shorter time, or whether the relative amount of sodium ethoxide is increased or not. In all cases, oils are obtained which boil through wide ranges of temperature.

We have repeatedly tried to separate pure substances from the mixtures by fractional distillation, but in vain. In one instance only, namely, in using ethylic propylacetoacetate, have we been able to obtain a definite substance of the expected type from the product of the reaction; this boiled at $203\text{--}206^\circ$ under 10 mm. pressure, and on analysis gave numbers agreeing with those required for the formula,

0.2345 gave 0.5975 CO_2 and 0.1595 H_2O . $\text{C} = 69.49$; $\text{H} = 7.55$.

$\text{C}_{20}\text{H}_{26}\text{O}_5$ requires $\text{C} = 69.36$; $\text{H} = 7.57$ per cent.

Additive Compounds of Ethylic Salts of β -Ketonic Acids and Ethylic Acetylenedicarboxylate.

We have already mentioned in the introduction that, under the influence of sodium ethoxide, the action of ethylic salts of β -ketonic acids on ethylic acetylenedicarboxylate differs from that on ethylic phenylpropiolate, giving rise to compounds which most probably are to be considered as trimethylene derivatives. Since on adding dry sodium ethoxide to the mixture of the ethylic salts, the action is

accompanied by a great evolution of heat, we have modified the method by using absolute ether as diluent.

Triethylic Benzoyltrimethylenetricarboxylate,

—Absolute ether, containing 3·4 grams of sodium ethoxide in suspension, is gradually mixed with 9·6 grams of ethylic benzoylacetate, and, when solution is effected, 8·5 grams of ethylic acetylenedicarboxylate are added; a reaction immediately sets in, and a yellow precipitate is formed. After standing for a day, the mixture is shaken with dilute sulphuric acid, when the solid dissolves and the colour disappears. The ethereal layer is separated, and after removal of the ether, leaves an oil which distils almost completely at 236—237° under 11 mm. pressure; the yellow oil thus obtained has a beautiful green fluorescence, does not dissolve in dilute caustic potash, and gives no coloration with ferric chloride.

0·2226 gave 0·5140 CO₂ and 0·1215 H₂O. C = 62·97; H = 6·06.

0·2360 „ 0·5445 CO₂ „ 0·1295 H₂O. C = 62·92; H = 6·09.

C₁₉H₂₂O₇ requires C = 62·98; H = 6·07 per cent.

The constitution indicated above accords with the behaviour of the substance towards alcoholic ammonia, in which it dissolves, producing a red solution. This, after standing for 2 days, yields, on evaporation, a solid residue which is very soluble in alcohol, and crystallises from dilute alcohol in silky needles melting at 137°. The following analytical data, and the fact that the compound, on warming with alkali, evolves ammonia, indicate that it is the *monamide* derived from triethylic benzoyltrimethylenetricarboxylate.

0·2155 gave 0·4845 CO₂ and 0·1108 H₂O. C = 61·31; H = 5·71.

0·2795 „ 10·5 c.c. nitrogen at 18° and 761 mm. N = 4·34.

C₁₇H₁₉NO₆ requires C = 61·26; H = 5·70; N = 4·20 per cent.

Triethylic Acetyltrimethylenetricarboxylate,

—Ethylic acetoacetate reacts with ethylic acetylenedicarboxylate and sodium ethoxide in a similar manner to the benzoylacetate, yielding a faintly yellow oil, the greater part of which distils at 186—187° under 13 mm. pressure.

0·2312 gave 0·4750 CO₂ and 0·1410 H₂O. C = 56·03; H = 6·77.

C₁₄H₂₀O₇ requires C = 56·0; H = 6·66 per cent.

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and of ethylic malonate and its homologues with the ethylic salts of the acids of the acetylene series, we add the result of an experiment which is closely connected with the above research. It is based upon the following consideration. Since the substances with the $-C\equiv C-$ group readily form additive products under the influence of sodium ethoxide, it might be expected that a similar reaction would occur with compounds containing the $N\equiv C-$ group. Such a compound, which might be compared with the ethylic salts of acids of the acetylene series, would be ethylic cyanoformate, $N\equiv C\cdot COOC_2H_5$. This we prepared according to Weddige's method (*J. pr. Chem.*, 1874, [ii], 10, 193) by distilling a mixture of ethylic oxamate and phosphoric anhydride, which we found to be much more convenient, and to give a better yield than that recommended by Wallach (*Annalen*, 1877, 184, 12).

Ethylic cyanoformate readily reacts with ethylic sodiomalonate suspended in absolute ether, but not in the manner we anticipated. The product, which smells strongly of hydrogen cyanide, gives, on acidifying with dilute sulphuric acid, an almost quantitative yield of triethylic methanetricarboxylate. A similar decomposition occurs on using ethylic salts of β -ketonic acids, such as ethylic acetoacetate or ethylic benzoylacetate. Ethylic cyanoformate therefore reacts in an analogous manner to ethylic chlorocarbonate.

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