CXII.—*The Condensation of Ethyl Sodiomalonate with Ethyl Citraconate and the Synthesis of β -Methyltricarballic Acid.*

By EDWARD HOPE.

DURING the course of his investigations on the addition of ethyl sodioacetoacetate and ethyl sodiomalonate to unsaturated esters, Michael (*J. pr. Chem.*, 1887, [ii], **35**, 354; 1891, [ii], **43**, 395 (with Freer); 1892, [ii], **45**, 57 (with Schulthess); 1894, [ii], **49**, 20; *Ber.*, 1900, **33**, 3757) studied the condensation of ethyl citraconate with ethyl sodiomalonate in alcoholic solution, and obtained a substance, $C_{14}H_{20}O_7$, which he stated was ethyl 1-methylcyclobutan-3-one-1:2:4-tricarboxylate, formed according to the scheme:

In view of the very limited number of methods available for synthesising cyclobutane compounds, the present work was undertaken (compare Proc., 1911, **27**, 281) in order to see how far the method described by Michael was capable of extension. The result of the investigation of the simplest case described by Michael—the condensation of ethyl citraconate with ethyl sodiomalonate in alcoholic solution—showed that this investigator was mistaken in his conclusions, and that the cyclic substance produced in this reaction is not a methyl cyclobutanone derivative, but a cyclopentanone derivative, namely, ethyl cyclopentan-2-one-1:3:4-tricarboxylate:

This is proved by the fact that when this ester is hydrolysed, cyclopentanone-4-carboxylic acid (m. p. 62—64°) is formed, the identity of this acid being established by comparison with the cyclopentanone-4-carboxylic acid described by Kay and Perkin (*Trans.*, 1906, **89**, 1646).

The first suggestion of the formation of a cyclopentane compound in a reaction similar to the above, would appear to emanate from Svoboda (*Monatsh.*, 1902, **23**, 842), who condensed the sodium

derivative of ethyl isosuccinate with ethyl citraconate, and stated that the reaction proceeded as follows:

No rigid proof was adduced to show that the substance formed was a *cyclopentane* derivative, and, moreover, the reaction is represented as proceeding by the elimination of alcohol from a carbethoxyl group and a methyl group—obviously an improbable assumption.

The same reaction had been carried out by Michael (*Ber.*, 1900, **33**, 3756), a fact overlooked by Svoboda, and Michael in pointing this out (*Ber.*, 1903, **36**, 576) again stated that in this case also a *cyclobutane* derivative is produced. No further investigations of reactions of this kind seem to have been carried out. In attempting to elucidate the mechanism of a reaction like the above, as large a variety of conditions as possible must necessarily be employed, and, although the variations so far used by the present author are comparatively few, yet they are sufficient to offer an explanation of the production of *cyclopentane* compounds in this type of reaction. Among the conditions which were varied, the most important were the solvent employed and the temperature. It became apparent at an early stage in the work that the whole of the previous investigations on the condensation of ethyl citraconate with sodium compounds would have to be repeated, and, incidentally, it has been found necessary carefully to examine the corresponding condensations with ethyl mesaconate and ethyl itaconate.

The condensation of ethyl citraconate with the sodium compound of ethyl malonate in ethereal solution has been already described by Michael and Schulthess (*J. pr. Chem.*, 1892, [ii], **45**, 57) and by Michael (*Ber.*, 1900, **33**, 3759). It has always been assumed, and never proved, that the reaction proceeds in agreement with Michael's positive-negative rule (*J. pr. Chem.*, 1888, [ii], **37**, 522; 1899, [ii], **60**, 286, 409), according to which ethyl β -methylpropane- $\alpha\alpha\beta\gamma$ -tetracarboxylate should be formed thus:

On hydrolysing the ester actually produced with hydrochloric acid, Michael obtained an acid melting at 168–173°. This he assumed to be β -methyltricarballic acid, identical with, but somewhat purer than, the acid melting at 164° prepared by Auwers,

Köbner, and v. Meyenburg (*Ber.*, 1891, **24**, 2893). The present author finds that ethyl citraconate condenses with ethyl sodiomalonate in solvents like ether and benzene (which do not react with sodium) in a manner quite different from that assumed by Michael to be the case, and the substance actually formed is ethyl butane- $\alpha\alpha\beta\gamma$ -tetracarboxylate:

The proof of this is that, on hydrolysing the tetrabasic ester thus formed, a practically quantitative yield of the isomeric α -methyltricarballic acids (m. p. 185° and 139—142°) was obtained. The identity of these acids was fully established by direct comparison with the α -methyltricarballic acids prepared by other methods. There is no reason to suppose that, in the above condensation, two reactions had gone on side by side leading, in the one case, to the formation of ethyl butane- $\alpha\alpha\beta\gamma$ -tetracarboxylate, and in the other, to ethyl β -methylpropane- $\alpha\alpha\beta\gamma$ -tetracarboxylate, for the hydrolysis of the latter with hydrochloric acid would have given β -methyltricarballic acid, an acid which, as was proved by subsequent synthesis, is easily isolated.

As a matter of fact, no trace of β -methyltricarballic acid could be isolated from the product of the hydrolysis of the condensation product. It is clear therefore that the acid (m. p. 168—173°) described by Michael (and, without doubt, also that of Auwers, Köbner, and v. Meyenburg) cannot have been β -methyltricarballic acid, and it was doubtless impure α -methyltricarballic acid.

The question as to why the reaction between ethyl citraconate and ethyl sodiomalonate takes a course exactly opposed to that which was to be expected from a consideration of the views held by Michael (*loc. cit.*) is one of some interest. Michael assumes that, owing to the presence of the methyl group, the carbon atom (+) in ethyl citraconate,

is more positive in character than the carbon atom (—), and consequently the negative portion of the ethyl sodiomalonate, —CH(CO₂Et)₂, should add itself to the carbon (+). As a matter of fact, the addition actually takes place at the carbon (—). In the opinion of the present author, there appears to be little use in discussing, for the present, at all events, any general theory of additive reactions of this kind, because it seems probable that the predominating factor in condensations of this type is that of steric influence. That there is almost always great resistance to the formation of a quaternary carbon atom (that is, a carbon atom

the four valencies of which are engaged by four other carbon atoms) is a well-known fact, and this resistance is the greater the larger the molecular magnitude of the groups involved. Thus, for example, it has not been found possible to condense ethyl teraconate, $\text{CMe}_2\cdot\text{C}(\text{CO}_2\text{Et})\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, and ethyl diphenylitaconate,

with the sodium derivative of ethyl malonate, the reason evidently being that quaternary compounds such as

would have to result. From this point of view, there is nothing surprising in the addition of ethyl citraconate to ethyl sodiomalonate leading to the formation of ethyl butane- $\alpha\beta\gamma$ -tetracarboxylate.

The condensation of ethyl sodiomalonate with ethyl citraconate in alcoholic solution is a reaction of great complexity. It was therefore considered advisable first to investigate the behaviour of these substances when mixed in cold alcoholic solution, and avoiding any elevation of temperature as far as possible. In this way, it was found possible to isolate, in good yield, an ester boiling at $207\text{--}209^\circ/15\text{ mm.}$, which, on hydrolysis, gave at once, in an almost pure condition, butane- $\alpha\beta\delta$ -tricarboxylic acid (m. p. 122°). The ester must therefore be ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate, $\text{CO}_2\text{Et}\cdot\text{CH}_2\cdot\text{CH}(\text{CO}_2\text{Et})\cdot\text{CH}_2\cdot\text{CH}(\text{CO}_2\text{Et})_2$. This ester is doubtless the intermediate product in the formation of ethyl *cyclopentan-2-one-1:3:4*-tricarboxylate from ethyl citraconate and ethyl sodiomalonate, and the mechanism of this ring formation is probably as follows.

In a series of papers (Trans., 1881, **39**, 348; 1885, **47**, 865; 1893, **63**, 229; 1895, **67**, 960) Purdie and his co-workers have shown that alkyloxysuccinic esters are produced by the action of sodium alkyloxides on ethyl fumarate; thus ethyl fumarate reacts with sodium ethoxide in alcoholic solution to form ethyl ethoxysuccinate,

Using the same conditions, the chief feature of which is the employment of $1/25\text{th}$ of an atom of sodium for each molecule of unsaturated ester, the present author has prepared from ethyl citraconate, ethyl methoxy- and ethoxy-methylsuccinates (boiling points $113\text{--}116^\circ/13\text{ mm.}$ and $133\text{--}137^\circ/15\text{ mm.}$ respectively), and from these by the action of alcoholic potassium hydroxide, methoxy- and ethoxy-methylsuccinic acids (m. p. $90\text{--}92^\circ$ and $83\text{--}85^\circ$ respectively). These substances and others similar to them are still under investigation, but their ready formation from ethyl citraconate by means of traces of sodium alkyloxides offers a clue to the pro-

duction of ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate from this ester by condensation with ethyl sodiomalonate. Traces of sodium ethoxide may, of course, always be assumed to be present in an alcoholic solution of ethyl sodiomalonate, and these small quantities are without doubt sufficient to transform the ethyl citraconate into ethyl ethoxymethylsuccinate. The latter substance has, in all probability, the constitution $\text{CO}_2\text{Et}\cdot\text{CMe}(\text{OEt})\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, and it may, in certain circumstances, lose the elements of alcohol in such a way that ethyl itaconate, $\text{CH}_2\cdot\text{C}(\text{CO}_2\text{Et})\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, is produced. If, now, the latter is assumed to condense with ethyl sodiomalonate in the normal manner (avoiding temperature elevation), ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate results:

Strong evidence in favour of the above explanation is to be found in the fact that ethyl itaconate may be substituted for ethyl citraconate in this condensation without the slightest effect on the ultimate result.

The process of ring-formation from ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate may possibly be explained thus, but at the same time the mechanism is by no means clear. When ethyl citraconate or ethyl itaconate react with the sodium derivative of ethyl malonate in cold alcoholic solution, the sodium compound,

results. This sodium compound is produced by the action of ethyl itaconate on ethyl sodiomalonate in benzene solution, and also by the interaction of metallic sodium and ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate. That the same sodium compound is produced in all these ways is proved by the action of methyl iodide. In all four cases the same ester (b. p. 205—208°/14 mm.) is obtained, and when this is hydrolysed with hydrochloric acid it gives, in each case, pentane- $\alpha\beta\delta$ -tricarboxylic acid (m. p. 157—158°),

This acid was identical with the pentane- $\alpha\beta\delta$ -tricarboxylic acid of that melting point described by Hope and Perkin (*Trans.*, 1911, **99**, 773), who prepared it by condensing ethyl methylacrylate with the sodium compound of ethyl cyanoacetate, and then treating the sodium compound thus formed with ethyl bromoacetate. This reaction was represented by them as proceeding in the following stages:

Although this is the most probable course of the reaction, still there are other possibilities, so that it was desirable to obtain more conclusive evidence for the above constitution. This has been done by condensing ethyl itaconate with the sodium derivative of ethyl isosuccinate in ethereal solution. The reaction proceeds in the following manner:

The ethyl pentane- $\alpha\beta\delta\delta$ -tetracarboxylate thus formed boils at 204—208°/14 mm., and on hydrolysis gives pentane- $\alpha\beta\delta$ -tricarboxylic acid (m. p. 157—158°) identical with the acid obtained by the five methods just described. The yield of ethyl pentane- $\alpha\beta\delta\delta$ -tetracarboxylate in the above experiment is far from good, but this does not affect the value of the proof of the constitution of pentane- $\alpha\beta\delta$ -tricarboxylic acid, since the explanation of the small yield is that ethyl 1-methylcyclopentan-2-one-1:3:4-tricarboxylate* (b. p. 190—195°/14 mm.) is the main product of the reaction,†

The sodium atom in ethyl sodiobutane- $\alpha\beta\delta\delta$ -tetracarboxylate (as produced in alcoholic solution from ethyl citraconate and ethyl sodiomalonate) is therefore proved to occupy the δ -position, but it is very doubtful if it remains in that position during ring-formation, and it is the opinion of the author that ring-formation occurs through the sodium first occupying the α -position. It is not asserted that the δ -sodio-compound is transformed completely into the α -sodio-compound, but rather that small amounts of the α -compound are successively formed from the large amount of the δ -compound, and, as soon as formed, are converted into the cyclic substance. The reasons for this opinion are as follows: (1) The elimination of sodium ethoxide from the δ -sodio-compound in the manner represented thus:

* This ester is, without doubt, identical with the so-called ethyl dimethylcyclobutanetricarboxylate of Michael (*Ber.*, 1900, **33**, 3756), and also the ethyl 1-methylcyclopentan-3-one-1:5:5-tricarboxylate of Svoboda (*Monatsh.*, 1902, **23**, 846), prepared, in both cases, by the action of ethyl citraconate on ethyl sodioisoscinate in hot alcoholic solution. The explanation of the formation of a cyclopentane derivative in this case is, no doubt, the same as that advanced in the present communication to account for the production of ethyl cyclopentanetricarboxylate from ethyl citraconate and ethyl sodiomalonate.

† The remarkable ease with which a cyclopentane derivative is formed in this reaction makes it important to investigate analogous cases, and it is the author's intention to extend his work in this direction.

is exceedingly improbable, because the resulting substance does not contain a hydrogen atom replaceable by sodium. (2) The striking ease with which ethyl itaconate and ethyl sodioisobutyrate yield a *cyclopentanone* derivative (p. 908) is further evidence in support of the point, because the condensation product,

cannot have the sodium atom in the δ -position. Returning now to the process of ring-formation from ethyl sodiobutane- $\alpha\beta\delta\delta$ -tetracarboxylate, it is probable that this must be represented thus:

the latter ester forming a mono- and probably to some extent a di-sodium compound.

Although the above scheme, in conjunction with that on p. 895, probably represents the main course of the reaction between ethyl citraconate and ethyl sodiomalonate in alcoholic solution, other changes occur, the nature of which is difficult to understand, and will form the subject of future investigation.

A series of experiments with ethyl mesaconate in the place of ethyl citraconate revealed the remarkable fact that this ester does not react with sodium ethoxide to form an ethoxy-derivative. Consequently ethyl mesaconate reacts normally with the sodium derivative of ethyl malonate, yielding ethyl butane- $\alpha\alpha\beta\gamma$ -tetracarboxylate whether the reaction is carried out in alcoholic solution (hot or cold) or in neutral solvents like benzene, the proof of this being that hydrolysis of the ester produced by any of these methods gives only a mixture of the isomeric α -methyltricarballic acids. This behaviour suggests a possible explanation of the fact that Auwers, Köbner, and v. Meyenburg obtained an acid melting at 164° (doubtless impure α -methyltricarballic acid) as a result of condensing ethyl citraconate with ethyl sodiomalonate in alcoholic solution. If, as seems probable, the ethyl citraconate employed by them was prepared through the ammonium salt and the silver salt, the citraconic acid may have been partly converted into mesaconic acid (a change well known to occur in alkaline solution), and the ethyl citraconate may therefore possibly have been largely contaminated with ethyl mesaconate.

Synthesis of β -Methyltricarballic Acid,

For the purpose of this investigation (compare p. 894) it was necessary to find a method for the preparation of β -methyltricarballic acid (which does not appear to have been previously made), and after a number of unsuccessful attempts had been made, it was finally obtained by the hydrolysis of the ester produced when potassium cyanide reacts with ethyl α -cyano- β -methylglutaconate, $\text{CO}_2\text{Et}\cdot\text{CH}(\text{CN})\cdot\text{CMe}\cdot\text{CH}\cdot\text{CO}_2\text{Et}$.

This reaction was first applied to the synthesis of polybasic acids by Bredt and Kallen (*Annalen*, 1896, **293**, 338), who investigated the addition of potassium cyanide and hydrocyanic acid (in aqueous alcoholic solution) to esters of the type $\text{R}\cdot\text{CH}\cdot\text{C}(\text{CO}_2\text{Et})_2$; thus, ethyl benzylidenemalonate and potassium cyanide yield ethyl β -cyano- β -phenylpropionate:

The present author has not, as yet, fully investigated the mechanism of the addition in the case of ethyl α -cyano- β -methylglutaconate, but purposes doing so both in this case and in the cases of other derivatives of glutaconic acid. Potassium cyanide appears to unite normally with ethyl cyanomethylglutaconate in absolute alcoholic solution, and the product, on hydrolysis with sulphuric acid, gives a moderate yield of β -methyltricarballic acid, which, when purified through the triethyl ester (boiling point $163\text{--}164^\circ/15$ mm.), melts, after crystallisation from hydrochloric acid, at $165\text{--}166^\circ$. It will be observed that the melting point is remarkably near to that (164°) given by Auwers, Köbner, and v. Meyenburg for the so-called β -methyltricarballic acid prepared by them, but their method of preparation cannot possibly have led to the formation of β -methyltricarballic acid (compare p. 894).

β -Methyltricarballic acid is scarcely distinguishable from the α -methyltricarballic acids in its general properties. It exhibits the same behaviour towards solvents, and a neutral solution of its ammonium salt gives precipitates with the same reagents. When heated under low pressures, it loses water, forming an anhydro-acid, which distils undecomposed at $220\text{--}224^\circ/15$ mm. This crystallises exceedingly well from ethyl acetate, and melts at $139\text{--}140^\circ$. On treatment with water, it regenerates the tribasic acid (m. p. $165\text{--}166^\circ$).

EXPERIMENTAL.

*Condensation of Ethyl Sodiomalonnate with Ethyl Citraconate in Ether and Benzene.**Formation of Ethyl Butane- $\alpha\alpha\beta\gamma$ -tetracarboxylate,*

$$\text{CH}(\text{CO}_2\text{Et})_2 \cdot \text{CH}(\text{CO}_2\text{Et}) \cdot \text{CHMe} \cdot \text{CO}_2\text{Et}.$$

The ethyl citraconate used in all the experiments described in this paper was prepared in the following way. Citraconic anhydride (Kahlbaum) was dissolved in six times its weight of absolute alcohol, to which had been added one-tenth of its volume of concentrated sulphuric acid. The solution was immediately heated for about ten minutes on a steam-bath, and allowed to remain overnight. After gently heating for half an hour next day on the steam-bath, water was added, and the ester extracted in the usual way. The ethereal solution requires careful washing with sodium carbonate, and it is advisable to use dilute alkali to remove traces of unchanged anhydride. The ester was thus obtained in a yield of about 80 per cent. of that theoretically possible. It boiled constantly at $116\text{--}117^\circ/15$ mm., also at $120^\circ/20$ mm. Its specific gravity at 16.5° was 1.046, compared with water at the same temperature.

When mixed with alcoholic potassium hydroxide in the cold, some considerable heat was generated (the temperature rising to 32°), and it was converted quantitatively into the potassium salt of mesaconic acid, which, on acidifying, gave mesaconic acid, melting at 202° .

The condensation with ethyl sodiomalonate was carried out in the following manner. 5.9 Grams of sodium were melted under boiling toluene and shaken vigorously until in the form of a coarse powder. The toluene was poured off, and the sodium washed with dry ether. Then a solution of 43 grams of ethyl malonnate in 200 c.c. of dry ether was poured on the sodium, and the sodium compound allowed to form for about five hours; 48 grams of ethyl citraconate were then added, and the mixture was gently heated for about five hours. At the end of that time the white sodium compound had entirely disappeared, and water was added. The ethereal layer contained the whole of the reaction-product, the sodium compound of which is readily decomposed by water. On evaporating the ether, a viscid oil remained, which distilled completely at $208^\circ/22$ mm. and $198^\circ/14$ mm.

The yield was 65 grams, or about 72 per cent. of that theoretically possible.

On acidifying the alkaline, aqueous layer, a small amount of an

oil was precipitated and extracted, but the amount was so small that it was not further investigated.

If benzene is employed instead of ether in this reaction, the same behaviour is observed throughout. Further, the course of the reaction is the same whether heated at the temperature of the steam-bath or allowed to remain at the ordinary temperature.

Butane- $\alpha\alpha\beta\gamma$ -tetracarboxylic Acid, $C_8H_{10}O_8$.—When the above ester is treated with alcoholic potassium hydroxide, it is readily hydrolysed, and a small quantity of a sparingly soluble potassium salt separates. On adding water, evaporating off the methyl alcohol, and acidifying the aqueous solution, an acid is set free, which can be readily extracted with pure ether. On evaporating the solvent, the acid crystallises, and can be purified by recrystallisation from a mixture of ethyl acetate and chloroform. After two crystallisations, the melting point remained constant at 154 – 156° (with effervescence). (Found, $C=41.1$; $H=4.6$. Calc., $C=41.0$; $H=4.3$ per cent.)

There is little doubt that two isomeric acids are produced in this reaction, for although the ester which was hydrolysed was of constant boiling point, an acid of constant melting point could only be obtained by an exceedingly wasteful crystallisation.

Hydrolysis of Ethyl Butane- $\alpha\alpha\beta\gamma$ -tetracarboxylate with Hydrochloric Acid. The Isomeric α -Methyltricarballic Acids, $C_7H_{10}O_6$.

Twenty grams of the pure ester were boiled with 150 c.c. of concentrated hydrochloric acid during eight hours. The homogeneous, slightly yellow liquid thus formed was evaporated to small bulk, and set aside in an ice-chest to crystallise. After several hours, the acid had crystallised to a solid, white mass. This first crop of crystals was collected, dried, and weighed. The weight was 3.6 grams, and the melting point 159 – 165° . Recrystallisation from dilute hydrochloric acid raised the melting point to 185 – 186° . Further recrystallisation from the same solvent or from organic solvents did not raise the melting point. (Found, $C=44.3$; $H=5.5$. Calc., $C=44.2$; $H=5.3$ per cent.)

The acid was evidently α -methyltricarballic acid. It was compared directly with α -methyltricarballic acid prepared according to Bone and Sprankling (Trans., 1902, **81**, 39), and also with a specimen obtained by condensing ethyl fumarate with ethyl sodiois succinate. The melting point was not changed by admixture with these acids; moreover, the same characteristic crystals (hexagonal plates) were observed under the microscope when any of the above acids were crystallised from dilute hydrochloric acid.

The aqueous filtrate from the acid, melting at 159—165°, was evaporated gradually over sulphuric acid in an exhausted desiccator, four further fractions of acid being thus obtained. The first of these fractions weighed 4.5 grams, and melted at 142—145°. Frequent crystallisation from water did not appreciably alter the melting point:

0.1427 gave 0.2324 CO₂ and 0.0687 H₂O. C=44.4; H=5.3.

C₇H₁₀O₆ requires C=44.2; H=5.3 per cent.

The other fractions all consisted of the variety of α -methyltricarballic acid of low melting point, and weighed in all 1 gram. The total yield of crystalline acid from 20 grams of pure ester was therefore 9.1 grams, or 83 per cent. of the theoretical.

The purest specimens of maleinoid α -methyltricarballic acid melted at 139—142°. On mixing with a specimen of this acid prepared by the action of ethyl fumarate on ethyl sodiois succinate, the melting point was unaltered. The difficulty of obtaining a satisfactory melting point is probably to be attributed to a conversion of minute amounts into the isomeride of higher melting point.

Ethyl α -methyltricarballylate (which does not appear to have been previously described) is readily prepared by esterifying the crude acid, as obtained in the previous experiment, by means of alcohol and sulphuric acid. It is a colourless oil, practically odourless, and boils constantly at 180—181°/24 mm. When hydrolysed by means of alcoholic potassium hydroxide, a mixture of the potassium salts of fumaroid and maleinoid α -methyltricarballic acids is formed.

Action of Sodium and Methyl Iodide on Ethyl Butane- $\alpha\beta\gamma\gamma$ -tetracarboxylate. Formation of Ethyl Pentane- $\beta\gamma\delta\delta$ -tetracarboxylate.

When finely divided metallic sodium (0.77 gram) is allowed to act on ethyl butane- $\alpha\beta\gamma\gamma$ -tetracarboxylate (24 grams) in ethereal solution, the latter readily forms a sodium compound which remains dissolved. If excess of methyl iodide is now added, and the mixture gently boiled for one hour, on adding water and extracting, a good yield (20 grams) of a new substance is obtained, which boils constantly at 196°/15 mm.

This ester, on hydrolysis with hydrochloric acid, gives a complex mixture of acids from which one was isolated melting at 202°. This acid crystallised magnificently from dilute hydrochloric acid, and was without doubt the $\alpha\alpha'$ -dimethyltricarballic acid described by Zelinsky and Tschernoswitoff (*Ber.*, 1896, **29**, 617). The mixture of acids obtained in the above experiment probably also

contains one of the other two isomeric $\alpha\alpha'$ -dimethyltricarballic acids described by the same authors.

It is of interest to note that when ethyl citraconate is condensed with ethyl sodiomalonate in ethereal solution and methyl iodide added directly to the mixture, a vigorous reaction occurs, but, on hydrolysing the resulting ester (which boils at 194—196°/13 mm.), only the isomeric α -methyltricarballic acids could be isolated.

Condensation of Ethyl Citraconate with Ethyl Sodiomalonate in Alcoholic Solution at the Ordinary Temperature.

Formation of Ethyl Butane- $\alpha\beta\delta\delta$ -tetracarboxylate,
 $\text{CO}_2\text{Et}\cdot\text{CH}_2\cdot\text{CH}(\text{CO}_2\text{Et})\cdot\text{CH}_2\cdot\text{CH}(\text{CO}_2\text{Et})_2$.

This reaction was carried out at follows: 5.85 Grams of sodium were dissolved in 150 c.c. of absolute alcohol, 42 grams of ethyl malonate then added, and the solution was cooled to the ordinary temperature. After the separation of the solid sodium derivative, 48 grams of ethyl citraconate were added all at once, and the temperature prevented from rising (as it will do if the reaction is left to itself for about twenty minutes) by cooling under the tap. Next day the cloudy alcoholic solution was poured into water. A colourless oil separated, and was extracted with ether. After drying the ethereal solution, the solvent was distilled off, and the residual ester distilled under diminished pressure. It boiled at 207—209°/13 mm., and was produced in about 50 per cent. yield. This ester gave no coloration in alcoholic solution with ferric chloride, and when hydrolysed with hydrochloric acid gave butane- $\alpha\beta\delta$ -tricarboxylic acid, $\text{C}_7\text{H}_{10}\text{O}_6$, melting at 122°. (Found, $\text{C}=44.1$; $\text{H}=5.4$. Calc., $\text{C}=44.2$; $\text{H}=5.3$ per cent.)

The acid was compared directly with a specimen of butane- $\alpha\beta\delta$ -tricarboxylic acid prepared by condensing ethyl itaconate with ethyl sodiomalonate in ethereal solution. The ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate obtained in this way, in 85 per cent. yield, boiled constantly at 209—211°/15 mm., and on hydrolysis gave butane- $\alpha\beta\delta$ -tricarboxylic acid, melting at 122°.

The aqueous solution into which the alcoholic solution was originally poured deposits an oil when acidified. For the sake of brevity, this oil will be referred to as "acid" oil. The "acid" oil, the sodium compound of which is presumably soluble in water without being decomposed, increases in amount (while the neutral oil decreases correspondingly) when the temperature of the reaction is raised. In the above case the "acid" oil is only produced in about one-fifth the quantity of the neutral oil. If the reaction is carried out at the temperature of the water-bath, the quantity

of "acid" oil increases to about five times the quantity of the neutral oil.

Action of Ethyl Citraconate on Ethyl Sodiomalonate in Hot Alcoholic Solution. Formation of Ethyl cyclopentan-2-one-1:3:4-tricarboxylate.

The relative amounts of substances used in these experiments were exactly those described in the last section, where the reaction was conducted at the ordinary temperature. The only difference was that, in the present case, the temperature employed was that of a steam-bath, the duration of each experiment being four hours. In examining the products of the reaction, the following process was adopted. The alcoholic solution was poured into water, and the oil extracted with ether. This oil was ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate (b. p. 214—216°/20 mm.), which is produced by the series of reactions already indicated. The fact that this small amount of an open-chain compound remains is no doubt attributable to the fact that the cyclic ester produced as the main product of this reaction can form a disodium derivative, thereby fixing a part of the sodium which would otherwise cause ring-formation.

After the removal of the neutral oil, carbon dioxide was passed through the aqueous solution for a long period until no further precipitation of oil took place. This oil having been extracted, the aqueous solution was finally treated with hydrochloric acid and again extracted.

The Oil Precipitated by Carbon Dioxide.—This substance gave an intense purple coloration with ferric chloride in alcoholic solution, and could be distilled under diminished pressure, although with considerable decomposition (195—200°/11 mm.). Without doubt this ester is identical with the tribasic ester of boiling point 217—219°/20 mm. described by Michael (*Ber.*, 1900, **33**, 3758). No subsequent attempt was made to distil the ester in quantity, the crude oil from the carbon dioxide being hydrolysed directly with 8 per cent. sulphuric acid. The hydrolysis was very rapid, and was complete at the end of two and a-half hours, after which the acid solution was saturated with ammonium sulphate and extracted six times with ether. After removing the ether and distilling under diminished pressure, a fraction passed over constantly at 172—174°/16 mm., and solidified in the receiver. An equal amount of an acid remained in the distillation flask, and showed no sign of distilling even at much higher temperatures. The distilled acid melted at 50—55°, but on recrystallisation from light petroleum the melting point rose to 62—64°. This acid

was compared directly with a specimen of the *cyclopentanone-4-carboxylic acid*,

described by Kay and Perkin (Trans., 1906, **89**, 1641), whose method of synthesis leaves no doubt as to its constitution, and the formula receives further corroboration from the subsequent work of Haworth and Perkin (Trans., 1908, **98**, 573).

An intimate mixture of the acid prepared in the above experiment with Kay and Perkin's acid melted at 61—63°. The oximes of the two specimens were prepared by allowing to remain overnight, a mixture of the acid, hydroxylamine hydrochloride, and potassium hydroxide in aqueous solution. The oximes in both cases were extracted with much ether, in which they are sparingly soluble. Both the specimens melted, after recrystallisation from ether, at 177—179°. The oxime, $\text{C}_6\text{H}_9\text{O}_3\text{N}$, of the acid prepared from ethyl citraconate was analysed. (Found, N=10.0. Calc., N=9.8 per cent.)

The semicarbazones of the same acids were prepared, and both found to melt at 197—198°, decomposing at that temperature.*

The Oil Precipitated by Hydrochloric Acid.—This oil, obtained by the addition of hydrochloric acid to the alkaline liquid into which carbon dioxide had previously been passed, was found to decompose vigorously when heated even at very low pressure. No attempt was therefore made to distil it, and it was hydrolysed at once with 8 per cent. sulphuric acid. The acid thus produced was extracted many times with ether, and then esterified by means of alcohol and sulphuric acid. The resulting ester was a complex mixture, and on distillation gave an ill-defined fraction, boiling between 110° and 140°/13 mm. (which probably contained a quantity of ethyl *cyclopentanone-4-carboxylate*), and later, a constant fraction at 235—242°/13 mm. The latter ester was also obtained by esterifying the residue in the flask from the distillation of the *cyclopentanonecarboxylic acid* (p. 904):

0.1244 gave 0.2614 CO_2 and 0.0808 H_2O . C=57.3; H=7.2.

0.1164 „ 0.2467 CO_2 „ 0.0714 H_2O . C=57.8; H=6.8.

The above analyses were carried out with material from two different preparations.

When boiled with methyl-alcoholic potassium hydroxide, solution of the ester takes place, with the immediate production of a deep brown colour, and in a few moments a viscous, brown potassium

* Michael gives 192—193° as the melting point of the semicarbazone of his cyclic acid. He does not appear to have prepared the oxime. The melting point of the acid itself is given as 62—64° (Ber., 1900, **33**, 3758).

salt separated. After twelve hours, water was added, and the whole of the alcohol evaporated. After extracting the alkaline solution with pure ether, the liquid was acidified and extracted many times with pure ether. On evaporating the ether, a viscid acid remained, which was boiled with water, and filtered. The solution was evaporated on the steam-bath, and the residue set aside in an ice-chest. After about a week, crystallisation took place. The crystals were pressed on porous porcelain, and re-crystallised from hydrochloric acid. The acid then melted at $103\text{--}106^\circ$, but the quantity was so small that no further purification could be attempted, nor could any derivatives be made:

0.1475 gave 0.2555 CO_2 and $0.0737\text{ H}_2\text{O}$. $\text{C}=47.2$; $\text{H}=5.5$.
 0.1662 required for neutralisation $25.53\text{ c.c. } N/10\text{-NaOH}$ (0.1022 gram of NaOH).

As already stated (p. 896), ethyl itaconate may be substituted for ethyl citraconate in the experiments just described without materially affecting the result. Both ethyl *cyclopentanone*-tricarboxylate and also the unidentified by-products are formed in the same relative quantities.

Ethyl *cyclopentan-2-one-1:3:4*-tricarboxylate is also produced in good yield when molecular quantities of sodium ethoxide and ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate are heated for five hours in alcoholic solution. In this case the formation of the above-mentioned by-products is almost entirely avoided.

Action of Sodium Ethoxide on Ethyl Citraconate in Alcoholic Solution. Formation of Ethyl Ethoxymethylsuccinate.

Twenty-five grams of ethyl citraconate were mixed with a solution of 0.2 gram of sodium in 120 c.c. of absolute alcohol (distilled from calcium). The mixture became yellow, and was left overnight at the ordinary temperature. It was then poured into water, and the precipitated ester extracted with ether. On distilling under diminished pressure, practically the whole quantity passed over at $133\text{--}137^\circ/15\text{ mm.}$, and on re-distillation the fraction $132\text{--}134^\circ/14\text{ mm.}$ was collected:

0.1240 gave 0.2564 CO_2 and $0.0955\text{ H}_2\text{O}$. $\text{C}=56.4$; $\text{H}=8.5$.
 $\text{C}_{11}\text{H}_{20}\text{O}_5$ requires $\text{C}=56.9$; $\text{H}=8.6$ per cent.

Ethyl ethoxymethylsuccinate is readily hydrolysed by alcoholic potassium hydroxide, yielding a crystalline potassium salt, sparingly soluble in methyl alcohol. After adding water, evaporating free from methyl alcohol, and acidifying, the acid was extracted with pure ether, and the ethereal solution evaporated. The residue was dissolved in water, boiled for five minutes, filtered, and evaporated

to small bulk, but the acid crystallised with difficulty from the aqueous solution, and melted at 78—82°. It was recrystallised from a mixture of ether and light petroleum, the melting point being thereby raised to 81—83°:

0.0905 gave 0.1578 CO₂ and 0.0563 H₂O. C=47.5; H=6.9.

C₇H₁₂O₅ requires C=47.7; H=6.8 per cent.

When the ester is heated in a sealed tube with concentrated hydrochloric acid for five hours at 140°, much ethyl chloride is produced, together with a considerable amount of mesaconic acid (m. p. 202°).

A similar series of substances is produced when methyl alcohol is substituted for ethyl alcohol in the above experiment. *Ethyl α-methoxy-α-methylsuccinate* boils at 113—116°/13 mm., and on hydrolysis with methyl-alcoholic potassium hydroxide yields *α-methoxy-α-methylsuccinic acid*, which melts at 90—92°.

The behaviour of ethyl itaconate and ethyl mesaconate under similar conditions is being investigated.

Action of Methyl Iodide on the Sodium Derivative of Ethyl Butane-αβδδ-tetracarboxylate. Formation of Ethyl Pentane-αβδδ-tetracarboxylate,

When ethyl citraconate (or ethyl itaconate) reacts with ethyl sodiomalonate in alcoholic solution at the ordinary temperature (compare p. 903), the sodium compound of the condensation product remains dissolved in the alcohol, and when this is boiled for half an hour with methyl iodide, an excellent yield of an ester boiling at 202—207°/13 mm. is obtained. On boiling with hydrochloric acid, this ester is readily hydrolysed, giving a mixture of acids, one of which, pentane-αβδ-tricarboxylic acid (m. p. 157—158°),

is readily isolated on account of its sparing solubility in hydrochloric acid. The other acid present, which was not isolated in a pure condition, is without doubt the *cis*-modification of the same pentanetricarboxylic acid. The acid melting at 157—158° was proved to be identical with that melting at the same temperature, prepared by Hope and Perkin (Trans., 1911, 99, 773) in the manner referred to on p. 896. Ethyl pentane-αβδδ-tetracarboxylate (which, of course, yields the acid of melting point 157—158° on hydrolysis) is also produced in almost quantitative yield by the two following methods:

(1) Ethyl itaconate is condensed with ethyl sodiomalonate in ethereal solution, and the resulting clear solution of the sodium

compound of the condensation product boiled for half an hour with methyl iodide. The resulting ester boiled constantly at $207^{\circ}/15$ mm.

(2) Ethyl butane- $\alpha\beta\delta\delta$ -tetracarboxylate is treated with finely divided sodium in ethereal solution. The solution of the sodium compound thus produced is boiled with methyl iodide, as in the previous experiment. The resulting ester boiled at $205^{\circ}/14$ mm. In all cases, the identity of the esters was proved by hydrolysis with hydrochloric acid.

The constitution of the above pentanetricarboxylic acid was finally determined by condensing ethyl itaconate with ethyl sodiois succinate in ethereal solution. The reaction was carried out as follows. Finely divided sodium (2.9 grams) was suspended in ether, and ethyl isosuccinate (22 grams) added. The sodium compound was produced with great vigour, the reaction being complete in about ten minutes. Ethyl itaconate (23.5 grams) was then added, in small quantities at a time, and the mixture allowed to remain for three hours at the ordinary temperature. On adding water, a portion of the reaction-product passed into solution in the ether. After washing the ethereal solution with water and dilute potassium hydroxide, the solvent was distilled off, and the residual oil fractionated under diminished pressure. The only constant fraction was one which passed over at $203\text{--}207^{\circ}/16$ mm. A quantity of some substance of higher boiling point remained in the distillation flask, and showed signs of decomposition on further heating. The ester boiling at $203\text{--}207^{\circ}/16$ mm. was without doubt the normal additive product of ethyl itaconate and ethyl isosuccinate. On hydrolysis with hydrochloric acid, it gave an acid melting at $157\text{--}158^{\circ}$ identical with the acid of that melting point prepared by the several methods just described.

The main product of the reaction between ethyl itaconate and ethyl sodiois succinate remained dissolved in the aqueous layer when water was added to the reaction mixture. On acidifying the red-coloured aqueous solution with acetic acid and extracting with ether, a considerable amount of an oil was obtained, which gave an intense red coloration with ferric chloride. It distilled fairly constantly at $190\text{--}195^{\circ}/15$ mm., but after a short time signs of decomposition showed themselves. A residue of very high boiling point remained in the flask.

In a further experiment, using the conditions just described, no attempt was made to distil the ester after liberation by means of acetic acid, but it was immediately hydrolysed with 8 per cent. sulphuric acid. The acid formed in the hydrolysis was extracted several times with ether, and distilled under diminished pressure.

Almost the whole quantity passed over at 172—175°/16 mm. This acid was 1-methylcyclopentan-2-one-4-carboxylic acid, identical with that prepared by Hope and Perkin (Trans., 1911, **99**, 774). It gave an oxime, which melted and decomposed at 176—177°. Its ethyl ester boiled at 126—127°/20 mm., and gave a semicarbazone melting at 137—139°.

Condensation of Ethyl Meseaconate with Ethyl Sodiomalonate in Alcoholic Solution. Formation of Ethyl Butane- $\alpha\beta\gamma\gamma$ -tetracarboxylate.

This condensation was carried out, both at the ordinary temperature and at the temperature of the steam-bath, exactly as described in the experiments with ethyl citraconate (pp. 903 and 904). Under both conditions a 60—70 per cent. yield of ethyl butane- $\alpha\beta\gamma\gamma$ -tetracarboxylate, boiling at 198—202°/14 mm., was produced. Hydrolysis of the ester gave a mixture of the fumaroid and maleinoid forms of α -methyltricarballic acid, the latter preponderating in quantity. No trace of any cyclic substance could be found in the products of these reactions.

In benzene solution, ethyl meseaconate behaves towards ethyl sodiomalonate exactly as does ethyl citraconate. A 75 per cent. yield of ethyl butane- $\alpha\beta\gamma\gamma$ -tetracarboxylate is produced. Hydrolysis of the condensation product with hydrochloric acid gave a mixture of the isomeric α -methyltricarballic acids, which were separated by fractional crystallisation from water.

Synthesis of β -Methyltricarballic Acid.

Ethyl α -cyano- β -methylglutaconate was prepared as described by Rogerson and Thorpe (Trans., 1905, **87**, 1669), by the action of ethyl acetoacetate on the sodium derivative of ethyl cyanoacetate. The product thus obtained (20 grams) was heated gently on the water-bath with finely powdered potassium cyanide (12 grams) and absolute alcohol (70 c.c.) for about twelve hours. At the end of that time the deep brown solution was poured into water, and, as no oil was precipitated, the whole was acidified and extracted with ether. The ester thus obtained was hydrolysed by boiling with 40 per cent. sulphuric acid, and the resulting acid was extracted several times with ether. After distilling off the ether, the residue was esterified by contact for three days with alcoholic sulphuric acid (20 c.c. of acid in 100 c.c. of absolute alcohol). On pouring into water and extracting with ether, about 8 grams of an oil were obtained, which boiled constantly at 163—164°/15 mm.:

0.1152 gave 0.2382 CO₂ and 0.0816 H₂O. C = 56.4; H = 7.8.

C₁₃H₂₂O₆ requires C = 56.9; H = 8.0 per cent.

The smallness of the yield is doubtless largely assignable to the difficulty of extracting polybasic acids of this kind with ether and of esterifying them in the way described.

When this ester (6 grams) was boiled for one hour with an alcoholic solution of potassium hydroxide (11 grams), hydrolysis took place readily. After adding water and evaporating off the alcohol, the alkaline solution was extracted with ether, then acidified, and again extracted several times with pure ether. After evaporation of the ether an acid remained in an almost pure condition, and readily solidified. It was purified by boiling with water, and filtering the solution. On cooling the filtrate, the acid was deposited, and melted at 162—164°. After another crystallisation from hydrochloric acid, the melting point rose to 165—166°, and was not altered on recrystallisation:

0.1529 gave 0.2506 CO_2 and 0.0747 H_2O . $\text{C} = 44.7$; $\text{H} = 5.4$.

$\text{C}_7\text{H}_{10}\text{O}_6$ requires $\text{C} = 44.2$; $\text{H} = 5.3$ per cent.

0.1382 Gram required for neutralisation 0.0871 gram NaOH , whereas a tribasic acid of the above formula should require 0.0874 gram.

β -Methyltricarballic acid is exactly similar to the isomeric α -methyl derivative in almost all its properties. A neutral solution of the ammonium salt gives a white, crystalline precipitate with solutions of silver nitrate, mercuric chloride, and lead acetate; a green precipitate with copper acetate; a white, gelatinous precipitate with cerium nitrate; and a brown, gelatinous precipitate with ferric chloride. It gives no precipitate with barium, calcium, magnesium, and manganese salts.

β -Methyltricarballic acid is insoluble in light petroleum, benzene, or chloroform, and fairly readily soluble in ethyl acetate acetone, acetic acid, or formic acid. It crystallises well from formic acid, aqueous hydrochloric acid, and from a mixture of acetone and benzene.

When heated strongly under low pressure, *β -methyltricarballic acid* loses water, forming the *anhydro-acid*, and the latter distils at 220—223°/15 mm. At first a viscous liquid, the anhydro-acid, soon solidifies, and can be readily crystallised from ethyl acetate, from which it separates in short, rectangular prisms melting at 139—140°.

The anhydro-acid is practically insoluble in light petroleum or benzene, sparingly soluble in chloroform (from which it readily crystallises), and readily so in ethyl acetate, acetone, or ether. When boiled with water and the solution allowed to cool, *β -methyltricarballic acid* separates (m. p. 165—166°). When an ethereal

solution of anhydro- β -methyltricarballic acid is mixed with an ethereal solution of *o*-toluidine (calculated amount), combination takes place, but the resulting *o*-toluidide is a gum. If α -naphthylamine is used instead of *o*-toluidine, the resulting compound is more crystalline, and separates from the ethereal solution, on keeping overnight, as a pure white crust melting at 98–100°. As it was found impossible to effect any purification by recrystallising the product, it was analysed in its original condition:

0.1295 gave 5.6 c.c. N_2 at 13° and 732 mm. $N=4.9$.

$C_{17}H_{15}O_4N$ requires $N=4.7$ per cent.

0.1076 gram required for neutralisation 0.024 gram NaOH, whereas a dibasic anhydride of the above formula requires 0.029 gram NaOH.

β -Methyltricarballic acid, prepared by the method just described, is identical in all respects with the acid prepared by an exceedingly convenient method suggested to the author by Dr. R. Robinson. Twenty-six grams of potassium cyanide, 26 grams of ethyl acetoacetate, 23 grams of ethyl cyanoacetate, and 100 c.c. of absolute alcohol are placed in a flask fitted with an air condenser, and maintained at the temperature of the water-bath for twelve hours, the whole being shaken up from time to time. The mixture turns dark brown very rapidly, and, if allowed to remain at the ordinary temperature after the heating is finished, sets to a solid mass, which probably consists largely of a potassium compound of ethyl $\beta\gamma$ -dicyano- β -methylpropane- $\alpha\gamma$ -dicarboxylate,

The yield of condensation products (for there is more than one formed in the reaction) is about 55–60 per cent. of that theoretically possible. The procedure adopted to obtain pure β -methyltricarballic acid was that already described (p. 909).

If the condensation is effected in a somewhat different manner from that just described, and only 1 molecule of potassium cyanide (instead of two in the experiment above) used, for each molecule of ethyl cyanoacetate, then, on pouring into water at the end of the reaction, instead of obtaining a clear solution, an oil is precipitated which distils at 180–200°/13 mm. On redistillation the fraction 200–205°/20 mm. was collected, and found to consist of ethyl $\beta\gamma$ -dicyano- β -methylpropane- $\alpha\gamma$ -dicarboxylate:

0.1350 gave 13.2 c.c. N_2 at 14° and 750 mm. $N=11.3$.

$C_{12}H_{16}O_4N_2$ requires $N=11.1$ per cent.

The crude oil obtained in this experiment contained other substances, and their nature will be investigated when the author

applies the methods described in this paper to the synthesis of other substituted tricarballic acids.

In conclusion, the author desires to express his indebtedness to Prof. W. H. Perkin for the interest which he has taken in this work.

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