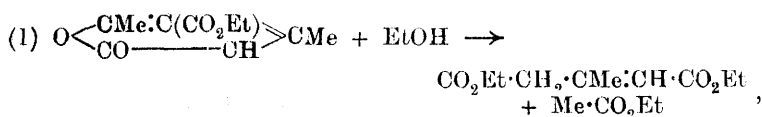


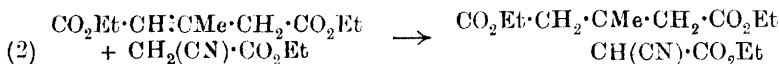
LVI.—*The Chemistry of the Glutaconic Acids.*
Part XI. The Occurrence of 1 : 3-Addition to the
Normal Form.

By JOCELYN FIELD THORPE.

IN Part IX of this series (T., 1913, **103**, 1579) it was shown that the *cis*-labile ester of β -methylglutaconic acid, which can be readily formed by the action of alcoholic sodium ethoxide on ethyl *iso*-dehydracetate,



condenses with the sodium compound of ethyl cyanoacetate, giving a 60 per cent. yield of a condensation product in accordance with the equation

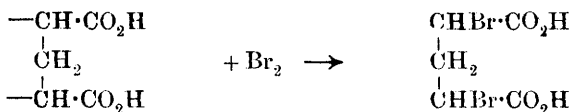


whereas the normal ester, $\text{CO}_2\text{Et}\cdot\dot{\text{C}}\text{H}\cdot\text{CHMe}\cdot\dot{\text{C}}\text{H}\cdot\text{CO}_2\text{Et}$, which can be prepared from the normal acid by etherification, yields no condensation product under the same experimental conditions.

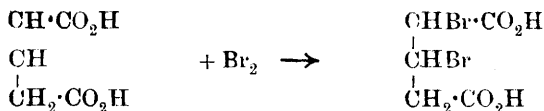
Several other esters of normal acids of the series were subjected to the same reaction, and the failure in each case to obtain a condensation product was regarded as evidence that substances possessing the normal structure which, in accordance with the

views put forward in this series, have constitutions best represented by the general formula $\text{CO}_2\text{R}\cdot\dot{\text{C}}\text{R}\cdot\text{CHR}\cdot\dot{\text{C}}\text{R}\cdot\text{CO}_2\text{R}$ ($\text{R}=\text{H}$ or alkyl), do not form additive products when treated with the usual additive reagents.

The evidence is, however, negative, and during the whole course of these researches on the glutaconic acids, frequent attempts have been made to obtain direct evidence of the structure of the normal forms by inducing them to form additive products in the 1:3-positions. If, for example, bromine could be made to unite with the terminal carbon atoms of the normal system, thus:



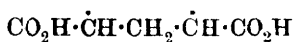
and if the isomeric compound produced from the labile modification were found to be formed in accordance with the scheme:



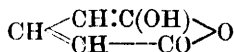
no reasonable doubt would then remain that the formulæ for the glutaconic acids suggested in this series must be a close approximation to the truth.

Unfortunately, the evidence obtained in this way is far from satisfactory. The stable normal acids of the type of β -methylglutaconic acid (the *cis*-acid of Feist, *Annalen*, 1906, **345**, 64, and of Fichter and Schwab, *Annalen*, 1907, **348**, 254, melting at 149°) do not react with the halogen to give any definite additive products, although the *cis*-labile acid (the *trans*-acid of Feist and Fichter, melting at $115\text{—}116^\circ$) readily forms $\alpha\beta$ -dibromo- β -methylglutaric acid, $\text{CO}_2\text{H}\cdot\text{CHBr}\cdot\text{CMeBr}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ (m. p. 145°), when treated with bromine in direct sunlight (Fichter and Schwab, *loc. cit.*).

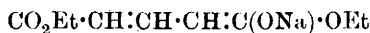
On the other hand, those acids, of which glutaconic acid itself is the best example, the labile forms of which are so unstable as to be incapable of isolation, yet readily pass, either through hydroxy-anhydride formation or through the formation of the sodium derivative of the esters, into derivatives of the labile forms (T.,



Glutaconic acid.



Hydroxy-anhydride.



Sodium derivative of ester.

1912, **101**, 863; 1913, **103**, 1757), react with bromine in a curious manner. For example, glutaconic acid readily absorbs the correct amount of bromine, but no one appears to have been able to isolate any definite product from the reaction mixture. Kiliani (*Ber.*, 1885, **18**, 2517) first studied the action of bromine on this acid. He noticed the rapid absorption of the halogen, but, without attempting to isolate the additive product, treated the crude reaction mixture with calcium carbonate and obtained a 10 per cent. yield of $\alpha\beta$ -dihydroxyglutaric acid,



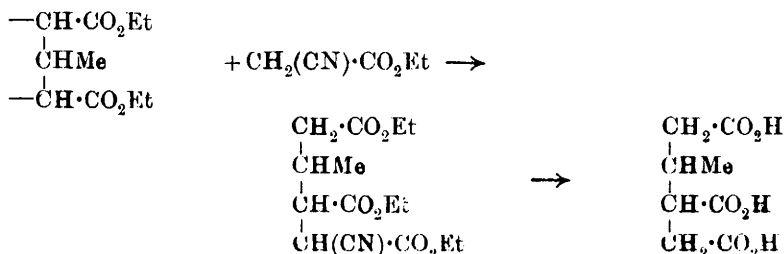
a yield which was subsequently increased to 14 per cent (*Ber.*, 1905, **38**, 3625). Ultimately, Feist (*Ber.*, 1911, **44**, 137) was able to obtain an 80—85 per cent. yield of the dibromo-ester,



by brominating ethyl glutaconate in sunlight.

It is evident, therefore, that the normal acids of this series do not react with bromine in the way one would expect an $\alpha\beta$ -unsaturated acid to react, and that they only form additive products under conditions which favour the transformation of the normal into the labile modifications. The labile acids, on the other hand, are easily converted into $\alpha\beta$ -dibromo-additive products in accordance with the properties of the structures assigned to them.

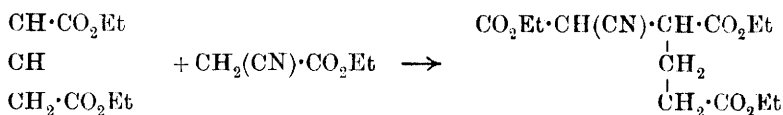
Direct evidence respecting the structure of the normal form can, however, be obtained from a study of the condensation products formed from the normal and labile esters of β -methylglutaconic acid with the sodium compound of ethyl cyanoacetate, for it is now found that whereas the *cis*-labile ester reacts in accordance with equation (2) and gives a yield, which has now been increased to 80 per cent., of the 1:2-additive product, the normal ester can, under special conditions described in the experimental portion, be made to yield a small quantity (approximately 6 per cent.) of a condensation product which, when hydrolysed, is converted into γ -methylbutane- $\alpha\beta\delta$ -tricarboxylic acid, in accordance with the scheme:



an acid which was found by direct comparison to be identical with that prepared by Hope and Perkin (T., 1911, **99**, 762) by the interaction of ethyl bromoacetate and the condensation product of ethyl sodiocyanoacetate with ethyl crotonate.

There can be no question, therefore, that in this reaction addition has been effected in the 1:3-positions, and although the yield is small, the formation of a condensation product having the above composition is direct evidence of the structure of the normal form.

A similar condensation tried with ethyl glutaconate failed to bring about addition in the 1:3-positions, and the product (about 5 per cent. yield) was found to have the structure assigned to it in the previous paper (T., 1913, **103**, 1580). It had therefore been formed in accordance with the scheme:



and it is evident that a small quantity of the normal ester is converted into the labile ester under the experimental conditions used. It is of interest to record at this stage a tendency that has been detected for the *cis*-labile ester to pass into the normal ester when kept. Hitherto, the *cis*-ester has been regarded as a comparatively stable substance. It distils without change, and can be hydrolysed to the corresponding *cis*-acid without conversion into the normal isomeride.

The following facts show, however, that, under certain conditions, the labile ester passes slowly into its normal form. About the middle of 1914, some 600 grams of the *cis*-labile ester had been accumulated for use in the preparation of the "enclosed" ring compound, an account of which is about to be published. It had all been prepared within the previous month, and some of it had already been used in condensation with the sodium compound of ethyl cyanoacetate, and found to give the usual yield of the condensation product. War then broke out, and the ester remaining over was laid aside until January of the present year, that is, for approximately four and a-half years. It happened that the larger quantity of the ester (about 450 grams) was placed in a deep yellow glass bottle, whereas the remaining amount (about 130 grams) was kept in a white glass bottle. Both bottles were placed side by side in a shallow cupboard with glass doors facing a strong north light. In January, 1919, the ester in the white glass bottle was noticed to have become deep brown, and when condensed with the sodium compound of ethyl cyanoacetate was found to give only 20 per

cent. of the usual condensation product. It was therefore distilled and hydrolysed, when the mixture of acids formed was found to consist of 75 per cent. of the normal acid melting at 149° and 25 per cent. of the labile acid melting at 115—116°. The ester in the yellow bottle, on the other hand, was found to have altered little in colour and to give the usual yield when condensed with ethyl sodiocyanoacetate. After distillation and hydrolysis, it was found to yield the *cis*-acid melting at 115—116° in an almost pure form, a small quantity, about 5 per cent. only, of the *trans*-acid being isolated. In order to check these results, a further quantity of the *cis*-labile ester was prepared from ethyl *isodehydracetate* and hydrolysed, when the product was found to be the pure *cis*-acid.

It is evident, therefore, that exposure to light for a considerable period of time leads to the partial conversion of the *cis*-labile form into the normal modification.

EXPERIMENTAL.

Condensation of Normal Ethyl β-Methylglutaconate with the Sodium Compound of Ethyl Cyanoacetate.

In the earlier attempt which was made to effect this condensation (T., 1913, **103**, 1580), molecular quantities of the ingredients were used, and the mixture was heated on the water-bath for twenty-four hours. As no condensation product could be isolated under these conditions, they were altered in the present instance so as to ensure that a large excess of ethyl cyanoacetate was present throughout the reaction. Forty-two grams of the normal ester, prepared by the etherification of the normal acid, were added to an alcoholic suspension of the sodium compound of ethyl cyanoacetate prepared from 94 grams of the ester and 9.7 grams of sodium dissolved in 110 grams of alcohol, and the mixture was heated for thirty-six hours on the water-bath. Water was then added, and the acidified liquid extracted with ether. Sodium carbonate solution failed to extract any appreciable quantity of acid ester from the ethereal solution, and the latter was therefore dried and freed from ether. The residual oil was then carefully fractionated under diminished pressure, when, besides the two fractions of lower boiling point, consisting of ethyl cyanoacetate and unchanged ethyl β-methylglutaconate, a small fraction (about 4 grams) of high boiling point was isolated.

Ethyl α-cyano-γ-methylbutane-αβδ-tricarboxylate,
 $\text{CH}_2(\text{CO}_2\text{Et})\cdot\text{CHMe}\cdot\text{CH}(\text{CO}_2\text{Et})\cdot\text{CH}(\text{CN})\cdot\text{CO}_2\text{Et},$

is a colourless, moderately viscid liquid which boils at $212^{\circ}/22$ mm.:

0.1932 gave 0.4081 CO_2 and 0.1293 H_2O . $\text{C}=57.66$; $\text{H}=7.41$.

$\text{C}_{15}\text{H}_{23}\text{O}_6\text{N}$ requires $\text{C}=57.5$; $\text{H}=7.4$ per cent.

γ -Methylbutane- $\alpha\beta\delta$ -tricarboxylic Acid,
 $\text{CO}_2\text{H}\cdot\text{CH}_2\cdot\text{CH}(\text{CO}_2\text{H})\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}.$

Hope and Perkin found it necessary, in order to obtain this acid in a crystalline condition, to hydrolyse their cyano-triethyl ester to the tribasic acid, to etherify this, and, after fractionation, to isolate the potassium salt by the aid of methyl-alcoholic potassium hydroxide. Apparently there is no need to use this method in order to obtain the crystalline acid from the isomeric cyano-triethyl ester described above, because the hydrolysis proceeded rapidly and smoothly through the agency of "50 per cent." aqueous sulphuric acid. Twelve grams of the cyano-triethyl ester were dissolved in an equal volume of concentrated sulphuric acid, care being taken to keep the mixture cool, and allowed to remain at the ordinary temperature for two hours. Water was then added until the solution became slightly turbid, when it was boiled under a reflux condenser for five hours, the alcohol formed during hydrolysis being removed from time to time by detaching the condenser tube from the flask. After the cooled product had been saturated with ammonium sulphate, it was extracted with ether, and the syrupy acid, which rapidly solidified, obtained by evaporating the dried ethereal solution. The crude acid was then purified by treatment with concentrated hydrochloric acid, filtering, and re-crystallising from this solvent. It melted sharply at 154° (Hope and Perkin give $153\text{--}154^{\circ}$) (Found: $\text{C}=46.95$; $\text{H}=6.13$. $\text{C}_8\text{H}_{12}\text{O}_6$ requires $\text{C}=47.1$; $\text{H}=5.9$ per cent.).

The acid was found to crystallise in nodular masses, as described by Hope and Perkin, and mixtures of it with Hope and Perkin's acid were found to have the same melting point (154°) as either constituent. It also gave a potassium salt insoluble in methyl-alcoholic potassium hydroxide. Unfortunately, the amount of acid available was insufficient for the purpose of preparing crystalline derivatives, because the anhydro-acid is apparently one of those intractable substances which are very difficult to obtain in a crystalline condition, similar properties being possessed by the aniline and toluidine derivatives of the anhydro-acid. All attempts to prepare these substances in a crystalline condition were

unsuccessful, and it is possible that the same difficulty was encountered by Hope and Perkin, since it will be noticed that no derivatives of this acid are described by them.

The evidence of the mixed melting point is, however, usually accepted as sufficient proof of identity. In the present instance, this is, of course, strengthened by the fact that the only other acid of this formula which could be produced in the reaction, namely, $\beta\beta$ -dimethylpropanetricarboxylic acid, $\text{CMe}(\text{CH}_2\cdot\text{CO}_2\text{H})_3$ (T., 1913, **103**, 1583), melts at 172° and readily gives a crystalline anhydro-acid, which can be converted into a crystalline anil-anilide and trianilide.

The Transformation of cis-Labile Ethyl β -Methylglutaconate into the Normal Form.

There is little to add to the general description of this change given in the introductory portion. The labile ester contained in the white glass bottle, which had previously given the usual yield of the condensation product with the sodium compound of ethyl cyanoacetate, was found at the end of four and a-half years to give a yield of only 20 per cent. under the same experimental conditions. It was therefore distilled, and was found to have the same boiling point as the original ester. When hydrolysed, it was found, however, that a mixture of acids was obtained, from which an insoluble, crystalline barium salt could be isolated in large quantities when the neutral ammonium salts of the mixed acids were treated with barium chloride solution and boiled. This was collected and converted into the acid, which was found to melt at 149° (Found: C=49.89; H=5.68. $\text{C}_6\text{H}_8\text{O}_4$ requires C=50.0; H=5.6 per cent.).

This acid, which was evidently, therefore, the normal acid, constituted approximately 75 per cent. of the mixture. The labile acid melting at 115 – 116° was isolated in the usual manner from the mother liquors of the barium salt precipitation.

The ester which had been kept in the deep yellow bottle, and had altered little in appearance, was found on conversion into the acids to yield only a small quantity of an insoluble barium salt, from which the acid melting at 149° was isolated. The amount constituted about 5 per cent. of the mixed acids obtained, the remainder being the *cis*-labile acid melting at 115 – 116° , which was isolated from the mother liquors. The original ester was also found to give approximately the normal yield of con-

densation product with the sodium derivative of ethyl cyanoacetate.

The change was further proved by preparing some fresh *cis*-labile ester from ethyl *isodehydracetate*, when the product was found to yield the pure labile acid on hydrolysis.

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