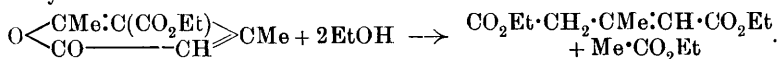


CLXXII.—*The Chemistry of the Glutaconic Acids.*  
*Part IX. A Method for Distinguishing Between*  
*the Esters of the Normal and Labile Acids.*

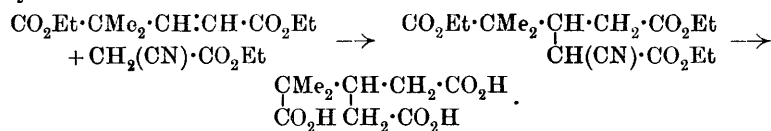
By JOCELYN FIELD THORPE and ARTHUR SAMUEL WOOD.

IN Part V of this series (T., 1912, **101**, 1565) a method was described by which the *cis*-labile ester of  $\beta$ -methylglutaconic acid,  $\text{CO}_2\text{H}\cdot\text{CH}_2\cdot\text{CMe}\cdot\text{CH}\cdot\text{CO}_2\text{H}$ , could be prepared in a yield of 75 per cent. by the action of alcoholic sodium ethoxide on ethyl *iso*-dehydracetate:



The ester of the normal acid,  $\text{CO}_2\text{H}\cdot\dot{\text{C}}\text{H}\cdot\text{CHMe}\cdot\dot{\text{C}}\text{H}\cdot\text{CO}_2\text{H}$ , can also be easily prepared by the esterification of the normal acid, and it is therefore a simple matter to obtain large quantities of these esters for the purpose of comparison.

It has been shown by Perkin (T., 1902, **81**, 246) that the ester of a substituted glutaconic acid in which the unsaturated structure is fixed, condenses with the sodium derivative of ethyl cyanoacetate to form a condensation product, for in this way he was enabled to synthesise *isocamphoronic* acid by condensing ethyl  $\alpha\alpha$ -dimethylglutaconate with ethyl sodiocyanoacetate and hydrolysing the cyano-ester formed:

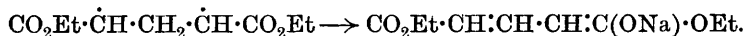


It is therefore to be expected that the esters of the labile acids would react in the same manner with the sodium compound of ethyl cyanoacetate to form a cyano-ester, which would hydrolyse to a homologue of *isocamphoronic* acid. On the other hand, if the structure of the esters of the normal acid is analogous to that of ethyl *isophthalate* (T., 1912, **101**, 871), it is to be expected that they would not enter into condensation with additive substances of the type of ethyl cyanoacetate.

Before investigating the two esters of  $\beta$ -methylglutaconic acid, it was thought advisable to experiment with several esters of the normal acids of this series in order to ascertain the extent to which they were capable of forming additive products, the first substance treated being ethyl glutaconate.

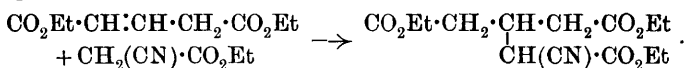
Glutaconic acid is certainly the most mobile acid of the series,

for although the normal acid is the only isolable form, the mobile hydrogen readily passes out of the three-carbon system, as is shown by the formation of the hydroxy-anhydride, as also by the formation of the yellow sodium derivative of the ester by the action of alcoholic sodium ethoxide:



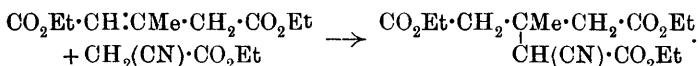
Both the yellow sodium derivative and the hydroxy-anhydride revert to the normal form on treatment with water, but it is to be expected that the amount of condensation product formed from ethyl glutaconate and ethyl sodiocyanoacetate would depend on the tendency for the ester to pass into the labile form under the experimental conditions employed.

Actually, under the experimental conditions which were subsequently found to give a yield of 60 per cent. in the case of a true labile ester, ethyl glutaconate was found to react to the extent of 5 per cent., in accordance with the scheme:



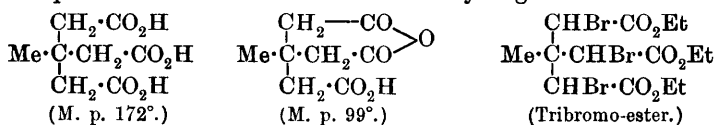
The esters of normal  $\alpha$ -methylglutaconic acid, normal  $\alpha$ -ethylglutaconic acid, and normal  $\alpha$ -benzylglutaconic acid were then tried, but no trace of condensation product could be isolated, and it is therefore evident that the normal esters, as such, do not form additive products.

A comparison was then made between the ester of normal  $\beta$ -methylglutaconic acid and that of the *cis*-labile acid, when it was found that, whereas the last-named formed a condensation product to the extent of 60 per cent., in accordance with the scheme:



no condensation product could be isolated in the case of the normal ester.

$\beta\beta$ -Dimethylpropanetricarboxylic acid, which is formed from this cyano-ester on hydrolysis, belongs to a series of which only one or two members are at present known. The acid readily yields an anhydro-acid, and the bromination of either the acid or the anhydro-acid leads to the formation of a tribromo-ester, from which quinoline removes the elements of hydrogen bromide:



The bromine-free product appears to belong to a new system

of ring compounds, and, as it is an easy matter to prepare large quantities of  $\beta\beta$ -dimethylpropanetricarboxylic acid, experiments on the structure of this and similar compounds are in progress.

### EXPERIMENTAL.

*Condensation of Ethyl Glutaconate and Ethyl Sodicyanoacetate.—*  
*Ethyl  $\alpha$ -Cyanoisobutane- $\alpha\gamma\gamma'$ -tricarboxylate,*  
 $\text{CO}_2\text{Et}\cdot\text{CH}(\text{CN})\cdot\text{CH}(\text{CH}_2\cdot\text{CO}_2\text{Et})_2$ .

In effecting this condensation, 28 grams of ethyl cyanoacetate were converted into the sodium compound by the aid of 5.8 grams of sodium dissolved in 70 grams of alcohol, and mixed with 46 grams of ethyl glutaconate, the mixture being heated on the water-bath for six hours. The product, worked up in the usual way, yielded a neutral ester boiling at  $208^\circ/28$  mm., mixed with much unchanged ethyl glutaconate:

0.2304 gave 0.4708  $\text{CO}_2$  and 0.1446  $\text{H}_2\text{O}$ .  $\text{C}=55.73$ ;  $\text{H}=6.98$ .

$\text{C}_{14}\text{H}_{21}\text{O}_6\text{N}$  requires  $\text{C}=56.2$ ;  $\text{H}=7.0$  per cent.

The yield of pure ester was only about 3 grams. A considerable quantity of acid ester was isolated from the mother liquors, and this was esterified by alcohol and sulphuric acid, and the neutral ester distilled. It consisted for the most part of ethyl glutaconate, but contained a small quantity of the ester boiling at  $208^\circ/28$  mm., mixed with a substance of higher boiling point. It was noticed that the neutral ester always possessed a fine blue colour, which disappeared during distillation.

*isoButane- $\alpha\gamma\gamma'$ -tricarboxylic Acid,  $\text{CH}(\text{CH}_2\cdot\text{CO}_2\text{H})_3$ .*

The cyano-ester is best hydrolysed by dissolving it in an equal volume of concentrated sulphuric acid, adding sufficient water to keep the solution clear, and then boiling for two hours. The acid is extracted by ether, and the ethereal residue allowed to crystallise. The acid crystallises from dry ether in small, colourless prisms, which melt at  $115^\circ$ :

0.1694 gave 0.2740  $\text{CO}_2$  and 0.0819  $\text{H}_2\text{O}$ .  $\text{C}=44.12$ ;  $\text{H}=5.37$ .

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

The acid is readily soluble in water and in concentrated hydrochloric acid. It reacts with acetyl chloride, forming an anhydro-acid, which could not be obtained crystalline; the quantity at our disposal was too small for further investigation.

An acid of this formula has been prepared by Coutelle (*J. pr. Chem.*, 1906, [ii], 73, 49) by the action of chloroform on ethyl sodiomalonate. It is described as an acid, difficult to purify, which

melts at about 95°. Coutelle's acid was characterised by the formation of a barium salt of the formula  $C_{14}H_{14}O_{12}Ba_3 \cdot 4H_2O$ , which was precipitated from its aqueous solution by the addition of alcohol. The acid prepared by us behaves in the same manner (Found, Ba = 48.05.  $C_{14}H_{14}O_{12}Ba_3$  requires Ba = 48.0 per cent.), and it is therefore probable that the two acids are identical.

*Normal Ethyl  $\alpha$ -Methylglutaconate*,  $CO_2Et \cdot \dot{C}H \cdot CH_2 \cdot \dot{C}Me \cdot CO_2Et$ .—Normal  $\alpha$ -methylglutaconic acid (m. p. 145–146°) is readily transformed into the above ester by esterification with alcohol and sulphuric acid. It is a mobile liquid, boiling at 165°/60 mm.:

0.1897 gave 0.4173  $CO_2$  and 0.1380  $H_2O$ . C = 59.98; H = 8.08.

$C_{10}H_{16}O_4$  requires C = 60.0; H = 8.0 per cent.

Twenty grams of this ester were treated with ethyl sodiocyanoacetate under the same conditions as in the experiment with ethyl glutaconate, but no condensation product was formed.

*Normal Ethyl  $\alpha$ -Ethylglutaconate*,  $CO_2Et \cdot \dot{C}H \cdot CH_2 \cdot \dot{C}Et \cdot CO_2Et$ .—This ester, prepared from normal  $\alpha$ -ethylglutaconic acid (m. p. 133–134°) by esterification with alcohol and sulphuric acid, is a mobile liquid, boiling at 171°/62 mm.:

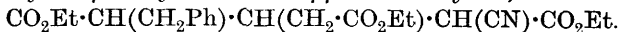
0.1939 gave 0.4383  $CO_2$  and 0.1495  $H_2O$ . C = 61.65; H = 8.57.

$C_{11}H_{18}O_4$  requires C = 61.7; H = 8.4 per cent.

This ester yields no condensation product with ethyl sodiocyanoacetate.

Ethyl  $\alpha$ -benzylglutaconate has already been described (T., 1912, 101, 886). It was prepared by the elimination of a carbethoxy-group from ethyl carbethoxy- $\alpha$ -benzylglutaconate by the action of alcoholic sodium ethoxide, and on account of its mode of formation was regarded as a mixture of the normal and labile esters.

An experiment with 28 grams of this ester, 11.3 grams of ethyl cyanoacetate, and 2.3 grams of sodium in alcohol yielded about 1 gram of a product, boiling at 253°/20 mm., which is evidently *ethyl  $\alpha$ -cyano- $\gamma$ -benzylisobutane- $\alpha\gamma\gamma'$ -tricarboxylate*,

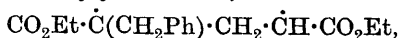


0.2103 gave 0.4982  $CO_2$  and 0.1331  $H_2O$ . C = 64.61; H = 7.03.

$C_{21}H_{27}O_6N$  requires C = 64.8; H = 6.9 per cent.

The ester is a viscid oil, which is hydrolysed by dilute sulphuric acid, but the amount at our disposal was too small to enable us to isolate the acid in a pure condition.

*Normal ethyl  $\alpha$ -benzylglutaconate*,



is formed in a pure condition by the esterification of normal

$\alpha$ -benzylglutaconic acid by means of alcohol and sulphuric acid. It is a mobile oil, which boils at  $181^{\circ}/21$  mm.:

0.1934 gave 0.4923  $\text{CO}_2$  and 0.1255  $\text{H}_2\text{O}$ .  $\text{C}=69.41$ ;  $\text{H}=7.21$ .

$\text{C}_{16}\text{H}_{20}\text{O}_4$  requires  $\text{C}=69.6$ ;  $\text{H}=7.2$  per cent.

This ester does not form any trace of a condensation product with ethyl cyanoacetate.

*Condensation of Labile Ethyl  $\beta$ -Methylglutaconate with Ethyl Sodicyanoacetate.*—*Ethyl  $\alpha$ -Cyano- $\beta\beta$ -dimethylpropanetricarboxylate*,  $\text{CO}_2\text{Et}\cdot\text{CH}(\text{CN})\cdot\text{CMe}(\text{CH}_2\cdot\text{CO}_2\text{Et})_2$ .

Ethyl  $\beta$ -methylglutaconate (84 grams) (for preparation, see T., 1912, 101, 1565) are added to the sodium compound of ethyl cyanoacetate prepared from 47 grams of the ester and 9.7 grams of sodium dissolved in 110 grams of alcohol, and the mixture is heated on the water-bath for six hours. The product consisted of about equal proportions of an acid and a neutral ester, which were separated by aqueous sodium carbonate in the usual manner. The neutral ester boiled at  $210^{\circ}/21$  mm. as a moderately viscid liquid:

0.1913 gave 0.4039  $\text{CO}_2$  and 0.1274  $\text{H}_2\text{O}$ .  $\text{C}=57.58$ ;  $\text{H}=7.40$ .

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

Although the acid ester evolved carbon dioxide on being heated, so much decomposition ensued that it was found advisable, in order to purify this substance, to esterify it by means of alcohol and sulphuric acid, and fractionate the neutral ester formed. In this way a further large amount of the cyano-ester was obtained.

*Ethyl  $\alpha$ -cyano- $\beta\beta$ -dimethylpropanedicarboxylate*,

$\text{CN}\cdot\text{CH}_2\cdot\text{CMe}(\text{CH}_2\cdot\text{CO}_2\text{Et})_2$ ,

can be prepared by the distillation of the acid ester. It is a fairly mobile liquid, which boils at  $181^{\circ}/22$  mm.:

0.1976 gave 0.4326  $\text{CO}_2$  and 0.1419  $\text{H}_2\text{O}$ .  $\text{C}=59.69$ ;  $\text{H}=7.98$ .

$\text{C}_{12}\text{H}_{19}\text{O}_4\text{N}$  requires  $\text{C}=59.8$ ;  $\text{H}=7.9$  per cent.

*$\beta\beta$ -Dimethylpropanetricarboxylic Acid*,  $\text{CMe}(\text{CH}_2\cdot\text{CO}_2\text{H})_3$ .

Either one of the above cyano-esters is converted into this acid on hydrolysis with dilute sulphuric acid, care being taken to allow the mixture of equal volumes of ester and concentrated acid to remain for one hour prior to being diluted with an equal volume of water and boiled until the hydrolysis is completed. The acid crystallises from the solution on cooling, but is best extracted by ether; it was recrystallised, for analysis, from dry ether:

0.1965 gave 0.3394  $\text{CO}_2$  and 0.1052  $\text{H}_2\text{O}$ .  $\text{C}=47.10$ ;  $\text{H}=5.95$ .

$\text{C}_8\text{H}_{12}\text{O}_6$  requires  $\text{C}=47.1$ ;  $\text{H}=5.9$  per cent.

Large quantities of the acid are best recrystallised by dissolving

in water and adding an equal volume of concentrated hydrochloric acid, when the characteristic branching needles, melting at  $172^{\circ}$ , are obtained. The acid is sparingly soluble in dry ether or benzene. Unlike *isocamphoronic* acid, it is unaltered by concentrated sulphuric acid at  $100^{\circ}$ . The *silver* salt is a white, microcrystalline powder:

0.2735 gave 0.1684 Ag. Ag = 61.57.

$C_8H_9O_6Ag_3$  requires Ag = 61.7 per cent.

From a neutral solution of the ammonium salt, the calcium salt is precipitated as a white, insoluble powder; the barium salt is soluble, but is precipitated by the addition of alcohol as a gelatinous mass; the lead salt is a heavy, white precipitate, and the copper salt separates as an insoluble, green, crystalline mass.

The *anhydro-acid*,  $CO_2H \cdot CH_2 \cdot CMe \begin{smallmatrix} \text{CH}_2 \cdot CO \\ \text{CH}_2 \cdot CO \end{smallmatrix} O$ , is best prepared by heating the acid in an open tube at  $200^{\circ}$  until water vapour ceases to be evolved. It separates from benzene in large plates, which melt at  $99^{\circ}$ :

0.2666 gave 0.5051  $CO_2$  and 0.1310  $H_2O$ . C = 51.66; H = 5.46.

$C_8H_{10}O_5$  requires C = 53.6; H = 5.4 per cent.

The *anhydro-acid* is sparingly soluble in dry ether; when boiled with water, it is converted into the acid from which it was derived.

The *double anhydride*,  $(O \begin{smallmatrix} \text{CO} \cdot \text{CH}_2 \\ \text{CO} \cdot \text{CH}_2 \end{smallmatrix} CMe \cdot CH_2 \cdot CO)_2 O$ .—This curious compound is formed in small amount when the acid is treated with excess of acetyl chloride for three hours at the temperature of the boiling reagent, and can be isolated from the *anhydro-acid*, which is formed at the same time, by treating the product, freed from acetyl chloride, with aqueous sodium hydrogen carbonate. The *anhydride* crystallises from ethyl acetate in small needles, which melt and decompose at  $185^{\circ}$ :

0.2131 gave 0.4221  $CO_2$  and 0.1003  $H_2O$ . C = 54.01; H = 5.23.

$C_{16}H_{18}O_9$  requires C = 54.2; H = 5.1 per cent.

The *double anhydride* is sparingly soluble in all organic solvents excepting ethyl acetate; when boiled with water it is transformed into the acid melting at  $172^{\circ}$ .

#### *The Aniline Derivatives of $\beta\beta$ -Dimethylpropanetricarboxylic Acid.*

The action of aniline on a benzene solution of the *anhydro-acid* leads to the formation of an oily substance, which could not be obtained in a crystalline condition. The acid may, however, be readily characterised by the formation of two aniline derivatives which are produced when it is heated with aniline. The acid

(2 grams) is heated with three molecular proportions of aniline (2·9 grams) at 180° until water vapour ceased to be evolved. The product was then rubbed with dry ether, and the solid collected. It was found to consist of two substances, which could be readily separated by boiling alcohol.

The *anil-anilide*,  $\text{NPh} \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{CMe} \begin{smallmatrix} \text{CH}_2 \cdot \text{CO} \\ \text{CH}_2 \cdot \text{CO} \end{smallmatrix} \text{NPh}$ , is insoluble in boiling alcohol. It crystallises from dilute acetic acid in small, colourless prisms, which melt at 220°:

0·1755 gave 0·4560  $\text{CO}_2$  and 0·0952  $\text{H}_2\text{O}$ .  $\text{C} = 70\cdot87$ ;  $\text{H} = 6\cdot03$ .

$\text{C}_{20}\text{H}_{20}\text{O}_3\text{N}_2$  requires  $\text{C} = 71\cdot4$ ;  $\text{H} = 6\cdot0$  per cent.

The *trianilide*,  $\text{CMe}(\text{CH}_2 \cdot \text{CO} \cdot \text{NPh})_3$ , is soluble in hot alcohol, and crystallises from this solvent in small, colourless needles, which melt at 197°:

0·1981 gave 0·5280  $\text{CO}_2$  and 0·1131  $\text{H}_2\text{O}$ .  $\text{C} = 72\cdot66$ ;  $\text{H} = 6\cdot34$ .

$\text{C}_{26}\text{H}_{27}\text{O}_3\text{N}_3$  requires  $\text{C} = 72\cdot7$ ;  $\text{H} = 6\cdot3$  per cent.

Both these compounds are insoluble in benzene or dry ether.

*Normal Ethyl  $\beta$ -Methylglutaconate*,  $\text{CO}_2\text{H} \cdot \dot{\text{C}}\text{H} \cdot \text{CHMe} \cdot \dot{\text{C}}\text{H} \cdot \text{CO}_2\text{H}$ . —The ethyl ester of this acid has been prepared by Genvresse (*Ann. Chim. Phys.*, 1891, [vi], **24**, 119) and by Feist (*Annalen*, 1906, **345**, 89), but it was obtained in both cases by the esterification of the crude mixture of the two modifications. We have therefore prepared this substance from the pure normal acid melting at 147°, by esterifying it with alcohol and sulphuric acid in the usual manner. It boils at 165°/70 mm. as a clear, mobile oil:

0·1872 gave 0·4112  $\text{CO}_2$  and 0·1362  $\text{H}_2\text{O}$ .  $\text{C} = 59\cdot91$ ;  $\text{H} = 8\cdot08$ .

$\text{C}_{10}\text{H}_{16}\text{O}_4$  requires  $\text{C} = 60\cdot0$ ;  $\text{H} = 8\cdot0$  per cent.

This ester was treated with ethyl sodiocyanoacetate in precisely the same manner as the labile ester, and although a small amount of a substance of high boiling point was isolated, no definite fraction could be obtained. The fraction boiling at 210—215°/20 mm. (about 2 grams from 42 grams of the ester) was hydrolysed, but no trace of  $\beta\beta$ -dimethylpropanetricarboxylic acid could be isolated.

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