CLXV.—*Note on the Formation of β -Methylglutaconic Acid and of $\alpha\beta$ -Dimethylglutaconic Acid.*

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THE research of which this note forms a part has for its object the determination of the conditions under which bromo-derivatives of substituted glutaric acids pass on eliminating hydrogen bromide into either (1) the corresponding glutaconic acid; (2) the corresponding trimethylenedicarboxylic acid; (3) the corresponding γ -lactone ethyl ester.

The conditions under which these changes take place have not as yet been clearly defined, although in one or two instances the products formed have been isolated and identified.

Thus, Perkin and Bowtell (*Proc.*, 1899, 15, 241) found that by eliminating hydrogen bromide from ethyl α -bromoglutarate,

by means of alcoholic potash they obtained only the corresponding *trans*-trimethylene-1 : 2-dicarboxylic acid, $\text{CH}_2 \begin{smallmatrix} \text{CH} \cdot \text{CO}_2\text{H} \\ | \\ \text{CH} \cdot \text{CO}_2\text{H} \end{smallmatrix}$, and no trace of either glutaconic acid or of the γ -lactone.

This question has recently formed the subject of a further communication by Perkin and Tattersall (this vol., p. 361), in which the formation of ethyl trimethylenedicarboxylate from ethyl α -bromoglutarate and diethylaniline is described, thus placing beyond question the formation of the trimethylene ring under both experimental conditions.

There would thus appear to be a very much greater tendency for a compound of this nature to pass into a trimethylene ring than into either the unsaturated acid or the γ -lactone, but that this is not

always the case is shown by the work of Perkin and Thorpe (Trans., 1899, 75, 56) on the elimination of hydrogen bromide from ethyl α -bromo- $\beta\beta$ -dimethylglutarate, $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CMe}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$.

In this instance, the formation of the corresponding glutaconic acid is impossible owing to the presence of the two methyl groups on the central carbon atom, but it was found that under certain conditions the trimethylene ring was formed, and that under others the γ -lactone was the chief product.

Thus on boiling the hydrogen ethyl salt of α -bromo- $\beta\beta$ -dimethylglutaric acid, $\text{CO}_2\text{H}\cdot\text{CHBr}\cdot\text{CMe}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, with dilute sodium carbonate solution, the lactone $\text{CMe}_2\left\langle\begin{array}{c}\text{CH}(\text{CO}_2\text{H}) \\ \text{CH}_2-\text{CO}\end{array}\right\rangle\text{O}$ alone is formed, whereas on boiling it with alcoholic potash, *trans*-caronic acid, $\text{CMe}_2\left\langle\begin{array}{c}\text{CH}\cdot\text{CO}_2\text{H} \\ \text{CH}\cdot\text{CO}_2\text{H}\end{array}\right\rangle$ is the chief product.

If, however, the normal ethyl ester, $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CMe}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, is treated with diethylaniline, a mixture of ethyl caronate,

and the lactone ethyl ester, $\text{CMe}_2\left\langle\begin{array}{c}\text{CH}(\text{CO}_2\text{Et}) \\ \text{CH}_2-\text{CO}\end{array}\right\rangle\text{O}$, is formed.

The two compounds chosen in this investigation as best calculated to attain the object in view were ethyl α -bromo- β -methylglutarate, $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, and ethyl α -bromo- $\alpha'\beta$ -dimethylglutarate, $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CHMe}\cdot\text{CHMe}\cdot\text{CO}_2\text{Et}$; in the first case, the constitution of the substance would cause one to expect it to behave in the same way as ethyl α -bromoglutarate, $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, and to be converted entirely into the corresponding trimethylenedicarboxylic acid on eliminating hydrogen bromide; in the second instance, the presence of the second methyl group might influence the nature of the products formed.

The experiments are not yet finished, but sufficient work has been done to indicate that a mixture of compounds is produced on eliminating hydrogen bromide from the two ethyl esters mentioned above, both by means of dimethylaniline and of alcoholic potash, and that the corresponding glutaconic acid is in each case formed.

Thus, from ethyl α -bromo- β -methylglutarate on treatment with diethylaniline, a mixture of ethyl esters is obtained, which on fractional distillation can be separated into two fractions boiling at constant temperatures; the higher one consists probably of the lactone ethyl ester, $\text{CHMe}\left\langle\begin{array}{c}\text{CH}(\text{CO}_2\text{Et}) \\ \text{CH}_2-\text{CO}\end{array}\right\rangle\text{O}$, whilst the lower fraction gives on hydrolysis a mixture of acids, from which β -methylglutaconic acid,

$\text{CO}_2\text{H}\cdot\text{CH}_2\cdot\text{CMe}\cdot\text{CH}\cdot\text{CO}_2\text{H}$, can be isolated by methods described in the experimental portion.

In the same way, $\alpha\beta$ -dimethylglutaconic acid,

can be isolated from the product of the interaction of ethyl α -bromo- $\alpha'\beta$ -dimethylglutarate and diethylaniline.

The constitution of these two acids is of importance in connection with the work described in the preceding papers, and we have therefore decided to publish an account of their formation, reserving a description of the other compounds formed for a future communication. Ethyl α -bromo- β -methylglutarate, $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, was prepared from β -methylglutaric anhydride by the usual methods.

β -Methylglutaric acid, from which this anhydride was produced, can be obtained in large quantities by the method indicated by Thorpe and Young (*Trans.*, 1903, **83**, 350), namely, by the condensation of ethyl β -methylacrylate with ethyl sodiocyanoacetate; the product, which consists for the most part of an acid ethyl ester, can be readily hydrolysed to the corresponding acid.

In the same way, $\alpha\beta$ -dimethylglutaric acid was prepared, only in this case the sodium compound of the condensation product was treated directly with methyl iodide (*loc. cit.*).

EXPERIMENTAL.

Formation of Ethyl α -Cyano- β -methylglutarate,

Ethyl cyanoacetate (113 grams) was added to the equivalent quantity (1 mol.) of sodium dissolved in alcohol, mixed with 114 grams of ethyl β -methylacrylate, and heated on the water-bath for twenty-four hours. Water was then added, and the oil which separated extracted by means of ether. On shaking the ethereal solution thus obtained with aqueous sodium carbonate, a considerable amount of oil, consisting of the hydrogen ethyl ester, is extracted, whilst the normal ethyl ester, which is formed in quantities depending on the length of heating, remains in the ether and can be obtained on evaporation.

The hydrogen ethyl ester is precipitated as an oil on acidifying the sodium carbonate extract; it was extracted by means of ether, and without further purification converted into the normal ethyl ester by mixing it with three times its volume of alcohol and an equal volume of concentrated sulphuric acid and heating on the water-bath for three hours. The mixture was then poured into water and extracted with ether, the ethereal solution being washed with aqueous sodium carbonate in order to separate any unesterified hydrogen ethyl ester.

The two specimens of normal ethyl ester, representing about 60 per cent. of the theoretical quantity, were then mixed together and fractionated under diminished pressure.

Ethyl α -cyano- β -methylglutarate is a colourless oil boiling at 190° (25 mm.).

0.2173 gave 0.4605 CO_2 and 0.1427 H_2O . $\text{C} = 57.79$; $\text{H} = 7.9$.

$\text{C}_{11}\text{H}_{17}\text{O}_4\text{N}$ requires $\text{C} = 58.1$; $\text{H} = 7.5$ per cent.

Hydrolysis of Ethyl α -Cyano- β -methylglutarate. Formation of β -Methylglutaric Acid, $\text{CO}_2\text{H}\cdot\text{CH}_2\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$.

In order to prevent the formation of the imide, a substance which, as previously mentioned (Trans., 1899, 75, 48), is difficult to hydrolyse, the ethyl ester was hydrolysed by means of dilute sulphuric acid. Equal volumes of the ethyl ester and concentrated sulphuric acid were mixed together and water added until the oil which was first precipitated no longer dissolved, the mixture being then heated until a test portion was completely soluble in water, a process which usually took about twelve hours. Crystals of β -methylglutaric acid usually separated from the hydrolysed mixture on cooling, but these were not isolated, the whole of the acid being extracted by means of ether after the solution had been saturated with ammonium sulphate.

The acid thus obtained was generally converted into the anhydride without further purification, but in order to be certain as to the nature of the product a small quantity was purified by recrystallisation from concentrated hydrochloric acid and analysed.

β -Methylglutaric acid formed in this way is identical with the acid prepared by Auwers (Ber., 1891, 24, 308); it melts at 86° .

0.2012 gave 0.3625 CO_2 and 0.1218 H_2O . $\text{C} = 49.13$; $\text{H} = 6.72$.

$\text{C}_6\text{H}_{10}\text{O}_4$ requires $\text{C} = 49.3$; $\text{H} = 6.9$ per cent.

Formation of β -Methylglutaric Anhydride, $\text{CHMe}\begin{matrix} \text{CH}_2\cdot\text{CO} \\ \text{CH}_2\cdot\text{CO} \end{matrix}\text{O}$.

β -Methylglutaric acid is converted into its anhydride on distillation, but in dealing with large quantities the following method was found more convenient. The crude acid was mixed with twice its volume of acetic anhydride and heated on the sand-bath for six hours; the product was then distilled under the ordinary pressure until most of the acetic anhydride and acetic acid had passed over, when the residue was subjected to distillation under diminished pressure. The anhydride passed over as a clear, colourless liquid at 180 — 182° (25 mm.), which on cooling solidified to a hard, crystalline cake. Recrystallised from

carbon disulphide it is obtained in the form of colourless prisms which melt at 46° ; it is in every way identical with the compound prepared by Kommenos (*Annalen*, 1883, 218, 150).

Formation of Ethyl α -Bromo- β -methylglutarate,
 $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}.$

In order to prepare this substance, 30 grams of the anhydride were mixed with 100 grams of phosphorus pentabromide and warmed on the water-bath until complete solution had been effected, 40 grams of bromine were then added and the whole gently warmed until the colour of the bromine had completely disappeared. This process requires about five hours. The product was then poured into well-cooled absolute alcohol and the solution allowed to stand for one hour, when water was added and the oil which separated extracted with ether. The ethereal solution was then washed with aqueous sodium carbonate in order to separate any acid ethyl ester, which in the case of the bromination of $\beta\beta$ -dimethylglutaric anhydride by similar means occurred in considerable quantities. The sodium carbonate extract in this case, however, gave, on acidifying, no deposition of oil, and therefore no acid ethyl ester could have been formed under the experimental conditions. The washed ethereal solution gave on evaporation a large quantity of the normal ethyl bromo-ester, which was purified by distillation under diminished pressure; it is a mobile oil boiling at $165\text{--}168^{\circ}$ (25 mm.).

0.1796 gave 0.1212 AgBr. $\text{Br} = 28.21$.

$\text{C}_{10}\text{H}_{17}\text{O}_4\text{Br}$ requires $\text{Br} = 28.46$ per cent.

Elimination of Hydrobromic Acid from Ethyl α -Bromo- β -methylglutarate by means of Diethylaniline. Formation of β -Methylglutaconic Acid, $\text{CO}_2\text{H}\cdot\text{CH}_2\cdot\text{CMe}\cdot\text{CH}\cdot\text{CO}_2\text{H}.$

Thirty grams of the ethyl bromo-ester were mixed with 45 grams of freshly-distilled diethylaniline and boiled on the sand-bath for four hours. The liquid was then poured into dilute hydrochloric acid, and the oil which separated extracted with dilute hydrochloric acid in order to remove the last traces of diethylaniline. The oil which was obtained on evaporating the ether was then distilled under diminished pressure and thus divided into two chief fractions, which were subsequently fractionally distilled under the ordinary pressure, and in this way two ethyl esters were isolated, one boiling at $269\text{--}272^{\circ}$, which gave on analysis numbers corresponding with the lactone ethyl ester:

0.1937 gave 0.3955 CO_2 and 0.1190 H_2O . $\text{C} = 55.69$; $\text{H} = 6.83$.

$\text{C}_8\text{H}_{12}\text{O}_4$ requires $\text{C} = 55.8$; $\text{H} = 7.0$ per cent.;

the other boiling at $240-243^\circ$ and giving numbers corresponding with the formula $C_{10}H_{16}O_4$:

0.2001 gave 0.4419 CO_2 and 0.1408 H_2O . $C=60.21$; $H=7.81$.

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

The nature of the first ethyl ester will be dealt with in a future communication, whereas the second, which is evidently a mixture of two or more compounds of the same empirical formula, gives, on hydrolysis with either alcoholic potash or hydrochloric acid, a gummy acid which does not become solid after standing for many days. It was therefore dissolved in hydrochloric acid, and the solution thus obtained, after being touched with a crystal of β -methylglutaconic acid produced in the manner described in the previous paper, allowed to stand for some time. Crystals slowly separated, and after the solution had stood for some days about three grams were obtained on filtration.

The acid was purified by recrystallisation from a little water, and proved to be identical with β -methylglutaconic acid obtained in the manner described in the previous paper. The pure acid melted at 149° .

0.2199 gave 0.4042 CO_2 and 0.1073 H_2O . $C=50.13$; $H=5.42$.

$C_6H_8O_4$ requires $C=50.0$; $H=5.6$ per cent.

β -Methylglutaconic acid prepared in this way was further identified with the acid from ethyl sodiocyanoacetate and ethyl acetoacetate by the fact that with acetyl chloride it gave an anhydride melting at 86° , and that the ammonium salt of the acid on distillation gave 4-methyl-2:6-dihydroxypyridine melting at 194° . The acid instantly decolorises permanganate in alkaline solution.

Formation of Ethyl α -Cyano- $\alpha\beta$ -dimethylglutarate and its Hydrolysis to $\alpha\beta$ -Dimethylglutaric Acid, $CO_2H \cdot CHMe \cdot CHMe \cdot CH_2 \cdot CO_2H$.

The method employed in preparing ethyl α -cyano- $\alpha\beta$ -dimethylglutarate was precisely the same as that described by Thorpe and Young (Trans., 1903, 83, 355), but since it was unnecessary for the purposes of the experiment to prepare the acid in its *cis*- and *trans*-forms, the ethyl ester was directly hydrolysed by means of dilute sulphuric acid. This operation is best effected by first mixing the oil with an equal volume of concentrated sulphuric acid, allowing the mixture to become as hot as it will ; water is then added until oily drops begin to separate, when the whole is heated on the sand-bath until a test portion is completely soluble in water. The hydrolysed solution is then saturated with ammonium sulphate and thoroughly

extracted with ether. The acid extracted in this way was then, without further purification, converted into the anhydride. For this purpose, it was mixed with an equal volume of acetic anhydride and boiled on the sand-bath for six hours, the product being freed as far as possible from acetic anhydride and acetic acid by distillation under the ordinary pressure, the residue being subsequently fractionated under diminished pressure. By these means, a large quantity of the pure anhydride can be conveniently and quickly prepared.

Formation of Ethyl α -Bromo- α' - β -dimethylglutarate,
 $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CHMe}\cdot\text{CHMe}\cdot\text{CO}_2\text{Et}.$

Thirty-three grams of the anhydride were mixed with 100 grams of phosphorus pentabromide and heated on the water-bath until dissolved, when 40 grams of bromine were added and the heating continued until the bromine had all been absorbed, the cooled mixture being then slowly poured into well-cooled absolute alcohol. Water was then added and the oil which separated extracted with ether, the ether washed, dried, and distilled off. The oil which remained was then fractionated under diminished pressure, and the main fraction boiling at $160-163^\circ$ (25 mm.) was analysed.

0.2177 gave 0.1379 AgBr. Br = 27.01.

$\text{C}_{11}\text{H}_{19}\text{O}_4\text{Br}$ requires Br = 27.11 per cent.

Action of Diethylaniline on α -Bromo- α' - β -dimethylglutarate. Formation of $\alpha\beta$ -Dimethylglutaconic Acid, $\text{CO}_2\text{H}\cdot\text{CHMe}\cdot\text{CMe}\cdot\text{CH}\cdot\text{CO}_2\text{H}.$

The purified ethyl bromo-ester was mixed with $1\frac{1}{2}$ times its weight of freshly-distilled diethylaniline and the mixture heated on the sand-bath for four hours; dilute hydrochloric acid was then added to the cooled product and the whole extracted with ether. The residue obtained on evaporating the ether, when fractionally distilled under diminished pressure, gave two chief fractions which were subsequently further purified by distillation under the ordinary pressure. In this way two ethyl esters were isolated, one, which is evidently the lactone ethyl ester, having the formula $\text{CHMe}\langle\begin{smallmatrix} \text{CH}(\text{CO}_2\text{Et}) \\ \text{CHMe}-\text{CO} \end{smallmatrix}\rangle\text{O}$ and boiling at $265-266^\circ$:

0.1972 gave 0.4173 CO_2 and 0.1315 H_2O . C = 57.71; H = 7.4.

$\text{C}_9\text{H}_{14}\text{O}_4$ requires C = 58.0; H = 7.5 per cent.;

and the other boiling at $239-240^\circ$, giving numbers corresponding with the formula $\text{C}_{11}\text{H}_{18}\text{O}_4$:

0.2102 gave 0.4741 CO_2 and 0.1570 H_2O . $\text{C} = 61.51$; $\text{H} = 8.29$.

$\text{C}_{11}\text{H}_{18}\text{O}_4$ requires $\text{C} = 61.7$; $\text{H} = 8.4$ per cent.

The more volatile fraction was hydrolysed by boiling with concentrated hydrochloric acid until all the oil had completely dissolved, when, on cooling, a considerable quantity of crystals separated, which after recrystallisation from water melted at 145°

0.2218 gave 0.4312 CO_2 and 0.1239 H_2O . $\text{C} = 53.02$; $\text{H} = 6.20$.

$\text{C}_7\text{H}_{10}\text{O}_4$ requires $\text{C} = 53.2$; $\text{H} = 6.3$ per cent.

The acid gives a liquid anhydride, and an anilic acid melting at 139° ; it instantly decolorises permanganate in alkaline solution, and is in every way identical with the acid prepared by the method described in the preceding paper. This acid is formed in much larger quantities than the corresponding β -methylglutaconic acid, and so far as the experiments have as yet gone, it does not appear as if the trimethylene ring is produced in any quantities under these conditions.

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