VI.—*The Bromination of Trimethylsuccinic Acid and the Interaction of Ethyl Bromotrimethylsuccinate and Ethyl Sodiocynoacetate.*

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IN connection with our investigations on the synthesis of alkyltricarballic acids, we have recently studied the bromination of trimethylsuccinic acid, and the interaction of ethyl bromotrimethylsuccinate and ethyl sodiocynoacetate. Some years ago, one of us, in conjunction with Professor W. H. Perkin, jun., unsuccessfully attempted the synthesis of *i*-camphoronic ($\alpha\alpha\beta$ -trimethyltricarballic) acid by a method involving this reaction, which is expressed by the following equation :

As a matter of fact, a crystalline acid melting at 137° and quite different from *i*-camphoronic acid was finally isolated from the hydrolytic products of the resulting cyano-ester, but the quantity obtained was too small to allow of a satisfactory investigation of its properties being made. The study of the subject was for the time being abandoned, partly on account of the difficulty experienced in preparing a sufficient quantity of trimethylsuccinic acid by any method then known, and also because Perkin and Thorpe succeeded in synthesising *i*-camphoronic acid by another method in 1897 (*Trans.*, **71**, 1169). Since, however, the preparation of large quantities of pure trimethylsuccinic acid is no longer a difficult matter, we decided to reinvestigate the subject, and, if possible, to ascertain the cause of the earlier failure to synthesise camphoronic acid.

In 1898, Gustav Komppa (*Acta Soc. Scient. Fenn.*, **24**, 1; also *Abstr.*,

1899, i, 419) tried to prepare bromotrimethylsuccinic acid by the action of phosphorus pentabromide on the corresponding hydroxy-acid. He was, however, unable to isolate any pure product from the complex mixture of substances obtained, and his experiments indicated that the three methyl groups in hydroxytrimethylsuccinic acid greatly hinder the replacement of hydroxyl by bromine.

The results of our experiments may be briefly stated as follows :

(1) When trimethylsuccinic acid is heated with the calculated quantity of bromine under pressure at 130° , it is quantitatively converted into the characteristic white crystalline *bromotrimethylsuccinic anhydride* melting at $197-198^{\circ}$; it is not possible to obtain the pure bromotrimethylsuccinic acid by dissolving this anhydride in hot water, since partial decomposition, with loss of hydrogen bromide, occurs during the process.

(2) If the bromination of trimethylsuccinic acid be carried out according to the Hell-Volhard-Zelinsky (phosphorus and bromine) method and the product poured into alcohol, a mixture of bromo-anhydride and ethyl bromotrimethylsuccinate results, from which it is very difficult to obtain the latter substance in a tolerably pure state.

(3) Both the bromo-anhydride and ethyl bromotrimethylsuccinate readily lose hydrogen bromide under the influence of an alkali. By heating the bromo-anhydride with diethylaniline and subsequently pouring the liquid into a solution of potassium hydroxide, we obtained the potassium salt of *methylenedimethylsuccinic acid*, $C_7H_{10}O_4$. The ethyl ester of this acid very readily combines with hydrogen bromide, forming a bromo-ester, $C_7H_{11}O_4Br$, which, so far as we have been able to ascertain, seems to be identical with the ethyl bromotrimethylsuccinate, $(CH_3)_2C(CO_2Et) \cdot CBr(CH_3) \cdot CO_2Et$, prepared directly from trimethylsuccinic acid.

We would point out in this connection that Vincenzo Paolini (*Gazzetta*, 1900, 30, ii, 497), by acting on ethyl hydroxytrimethylsuccinate with phosphorus pentachloride, has obtained the ethyl ester of an acid, $C_7H_{10}O_4$, melting at $153-154^{\circ}$. Since this acid neither absorbed bromine or hydrogen bromide at the ordinary temperature, nor decolourised cold alkaline permanganate, he concluded that its molecule was not unsaturated, and described it as *dimethyltrimethylenedicarboxylic acid*. The formation of such an acid he explained by supposing that the ethyl chlorotrimethylsuccinate formed in the first instance by the action of phosphorus pentachloride on the ester of the hydroxy-acid at once loses hydrogen chloride, the elimination of which takes place between the chlorine and a hydrogen atom of a methyl group attached to the other carbon atom, so that 'ring-formation' occurs thus,

His acid certainly appears to have properties quite different from those of methylenedimethylsuccinic acid, and we are therefore led to the interesting conclusion that the elimination of hydrogen bromide from a bromotrimethylsuccinic derivative and of hydrogen chloride from a chlorotrimethylsuccinic molecule may occur in two entirely different ways. This is a point which certainly deserves further investigation.

(4) Ethyl bromotrimethylsuccinate reacts with ethyl sodiocyanoacetate, yielding the cyano-ester of a tribasic acid, $\text{C}_9\text{H}_{14}\text{O}_6$, melting at $137\text{--}138^\circ$, and isomeric with *i*-camphoronic acid (m. p. $169\text{--}172^\circ$). The formation of such an acid can be explained on the supposition that ethyl bromotrimethylsuccinate loses hydrogen bromide, forming ethyl methylenedimethylsuccinate, which at once condenses with the ethyl cyanoacetate as follows :

If this interpretation of the matter be correct, the acid, $\text{C}_9\text{H}_{14}\text{O}_6$, obtained on hydrolysing the product with hydrochloric acid would be *aa-dimethylbutane- $\alpha\beta$ -tricarboxylic acid*,

the results of a 'potash fusion' of the acid, which yielded acetic and trimethylsuccinic acids, are consistent with this view of its constitution.

EXPERIMENTAL.

Bromination of Trimethylsuccinic Acid. Formation of Bromotrimethylsuccinic Anhydride and Ethyl Bromotrimethylsuccinate.

(1) *Hell-Volhard-Zelinsky Method*.—We have at various times carried out experiments in which rather more than the calculated quantity of dry bromine was slowly dropped on a well cooled mixture of trimethylsuccinic acid and the theoretical amount of dry amorphous phosphorus. In each case, a vigorous reaction ensued accompanied by a strong evolution of hydrogen bromide, which only ceased after the mixture had been heated on the water-bath in a reflux apparatus for 6 or 8 hours.

On dropping the resulting brown liquid into an excess of alcohol (well cooled in ice) and afterwards pouring the alcoholic solution into a large excess of water, a heavy brown oil separated, which was

extracted with ether in the usual manner. After washing the ethereal solution with dilute (5 per cent.) sodium carbonate solution, then drying it over anhydrous sodium sulphate, and finally distilling off the ether, there remained a heavy reddish-brown oil which appeared to decompose when we tried to distil it under reduced pressure.

Analyses showed, however, that samples prepared at different times invariably contained from 30 to 33 per cent. of bromine, or considerably more than that required for ethyl bromotrimethylsuccinate, $C_{11}H_{19}O_4Br$, namely, 27.12 per cent.

Bromotrimethylsuccinic Anhydride.—After the oil had stood for some weeks in an exhausted desiccator over sulphuric acid, yellowish crystals began to separate; these were removed from time to time, and after being pressed on a porous plate were recrystallised from hot benzene. When quite pure, they melted sharply at 197–198°. The substance was insoluble in cold water or a cold solution of sodium carbonate, but readily dissolved in a warm solution of potassium hydroxide without, however, any formation of alcohol. It was, therefore, neither an acid nor an ester; the following analysis showed that it had a composition corresponding to that of bromotrimethylsuccinic anhydride, and a further study of its properties showed it to be this substance.*

0.1691 gave 0.2368 CO_2 and 0.0600 H_2O . $C = 38.19$; $H = 3.95$.

0.2364 „ 0.2036 AgBr. $Br = 36.64$.

$C_7H_9O_3Br$ requires $C = 38.06$; $H = 4.07$; $Br = 36.20$ per cent.

Ethyl Bromotrimethylsuccinate.—The crude oil was kept for several months until no further separation of bromoanhydride occurred: on analysing the residual oil, we obtained, for two different preparations, the following numbers:

(1) 0.5202 gave 0.3525 AgBr. $Br = 28.82$ per cent.

(2) 0.2528 „ 0.1713 AgBr. $Br = 28.83$ „

It, therefore, still contained 1.7 per cent. more bromine than that

* Assuming that the dibromide of bromotrimethylsuccinic acid is produced by the action of phosphorus and bromine on trimethylsuccinic acid, the formation of this bromoanhydride can only be accounted for on the supposition that when the bromo-dibromide is dropped into alcohol, only part of it is decomposed, yielding ethyl bromotrimethylsuccinate, and that the other part reacts with the alcohol somewhat as follows:

required for ethyl bromotrimethylsuccinate, an indication that there remained a fair quantity of the bromo-anhydride in solution (a mixture of 81.3 parts of bromo-ester and 18.7 of bromo-anhydride would contain 28.8 per cent. of bromine). With a view to the complete esterification of this bromo-anhydride, the oil was repeatedly heated with an excess of ethyl alcohol containing 5 per cent. of hydrogen chloride ; by this means, the bromine was reduced to 28.0 per cent. As we subsequently found, however, that the bromo-anhydride, when treated with alcohol and hydrogen bromide, forms only the monoethyl salt, it was evident that the oil now consisted of a mixture of neutral and acid esters. We therefore dissolved it in pure ether and extracted the solution with a 5 per cent. sodium carbonate solution. On distilling off the ether, we found that the residual oil could now be fractionated under reduced pressure without undergoing any appreciable decomposition. Under 20 mm., the greater portion of it distilled over between 160° and 170° as a faint yellow oil having a very pungent odour. The following analysis indicated that it was practically pure ethyl bromotrimethylsuccinate :*

0.2934 gave 0.1846 AgBr. Br = 26.76.

$C_{11}H_{19}O_4Br$ requires Br = 27.12 per cent.

(2) *Action of Bromine on Trimethylsuccinic Acid at 120—130°.*—Bromotrimethylsuccinic anhydride may be most conveniently prepared in quantity by the following method.

Five grams of trimethylsuccinic acid are heated with an equal weight of dry bromine in a sealed tube at 120—130° for 6 to 8 hours. The careful regulation of the temperature is important, since below 120° the bromination is not complete, and above 140° the contents of the tube are liable to char. Great care should be taken in opening such tubes after the heating, for the pressure in them is very great, and since dense clouds of hydrogen bromide are evolved it is advisable to carry out the operation in the open air. A solid with a slight orange colour remains after the pressure has been relieved ; sometimes it swells up considerably during the escape of gas, and may occasionally froth over out of the tube, and it is therefore advisable to have a large beaker at hand in which to receive any that may be so forced out. The solid should be washed with a cold dilute solution of sodium carbonate, dried on a porous plate, and recrystallised from hot benzene. The yield is quantitative.

* The preparation of this ester is best carried out by dropping the brominated trimethylsuccinic acid into excess of ice-cold ethyl alcohol containing 5 per cent. of hydrogen bromide, heating the solution for about three hours on the water-bath to convert the bromo-anhydride into the monoethyl salt, and subsequently removing the latter by means of a cold 5 per cent. solution of sodium carbonate.

When pure, the bromo-anhydride melts at $197-198^{\circ}$; it is quite insoluble in cold water or a cold dilute solution of sodium carbonate. We endeavoured to prepare bromotrimethylsuccinic acid by dissolving the anhydride in warm water and evaporating the solution until, on cooling, crystals appeared. In this way, colourless needles were obtained which, however, melted indefinitely between 120° and 130° , and contained only 31.1 per cent. of bromine; since the bromo-acid, $C_7H_{11}O_4Br$, requires 33.5 per cent. of bromine, it was evident that some decomposition had occurred during the solution of the bromo-anhydride, and a subsequent careful examination showed that hydrogen bromide is slowly liberated during the process.

Action of Alcohol and Sodium Ethoxide on the Bromo-anhydride.—On heating the bromo-anhydride with a molecular proportion of sodium ethoxide in ethyl alcohol, the liquid became neutral in about half an hour without, however, any separation of sodium bromide. On passing dry hydrogen chloride into the resulting liquid, sodium chloride separated, and as soon as the whole of the sodium had been thus eliminated the liquid was filtered and the clear filtrate evaporated in a vacuum over sulphuric acid. There finally remained a colourless, semi-solid mass containing 30.3 per cent. of bromine, which exhibited all the properties of an acid ester (ethyl hydrogen bromotrimethylsuccinate, $C_9H_{15}O_4Br$, requires $Br = 30.0$ per cent.).

The same substance was obtained by heating the bromo-anhydride with an excess of ethyl alcohol in sealed tubes at 160° and afterwards distilling off the excess of alcohol on the water-bath. In neither of these experiments were we able to detect the formation of any neutral ester, and in each case the product instantly and completely dissolved in a cold solution of sodium carbonate with evolution of carbon dioxide. Our attempts to purify the substance by distillation under reduced pressure were unsuccessful, since decomposition began at temperatures below the boiling point.

We also made several unsuccessful attempts to prepare the silver salt of this acid ester, but as soon as silver nitrate was added to its aqueous solution neutralised with dilute ammonia, a copious yellow precipitate of silver bromide appeared, and we were not more successful in experiments in which freshly prepared silver carbonate was added to the aqueous solution.

Action of Diethylaniline on the Bromo-anhydride. Methylene-dimethylsuccinic Acid, $C_7H_{10}O_4$.

As bromotrimethylsuccinic anhydride showed a tendency to lose hydrogen bromide on being boiled with water, we decided to study the action of diethylaniline on it with the view of preparing the corresponding unsaturated acid.

Accordingly, a solution of 10 grams of the bromo-anhydride in 15 grams of diethylaniline was heated in a reflux apparatus on a sand-bath for 10 hours, after which it was poured into a hot concentrated solution of potassium hydroxide. After the diethylaniline had been extracted with ether, the alkaline liquor was acidified, saturated with ammonium sulphate, and again extracted with ether. In this way a solid acid was obtained which was purified by dissolving it in excess of sodium carbonate solution, extracting resinous matter with chloroform, then boiling the solution with animal charcoal, finally acidifying and extracting it with pure ether. The pure acid was thus obtained as perfectly white crystals which melted at $140-141^{\circ}$. On analysis :

0.2063 gave 0.4010 CO_2 and 0.1290 H_2O . $\text{C} = 52.9$; $\text{H} = 6.51$.

$\text{C}_7\text{H}_{10}\text{O}_4$ requires $\text{C} = 53.16$; $\text{H} = 6.33$ per cent.

Methylenedimethylsuccinic acid, $\begin{matrix} (\text{CH}_3)_2\text{C}\cdot\text{CO}_2\text{H} \\ | \\ \text{CH}_2\cdot\text{C}\cdot\text{CO}_2\text{H} \end{matrix}$, melts at $140-141^{\circ}$, is

fairly soluble in cold water, and, like other succinic acids, gives an insoluble calcium salt when a solution of its neutral ammonium salt is boiled with calcium chloride solution. Its aqueous solution instantly decolorises alkaline permanganate and rapidly absorbs bromine in the cold. The acid is readily esterified, and its liquid diethyl ester boils at $173-176^{\circ}$ under 755—760 mm.

Action of Bromine on the Diethyl Ester.—On adding a solution of bromine in chloroform to the diethyl ester, the halogen at once disappeared ; as soon as no more of it was absorbed, the chloroform was distilled off and the residual oil at once hydrolysed with hydrochloric acid. On cooling, a white crystalline dibromo-acid separated, which after recrystallisation from hydrochloric acid melted at $178-179^{\circ}$. On analysis :

0.3027 gave 0.3529 AgBr . $\text{Br} = 49.6$.

$\text{C}_7\text{H}_{10}\text{O}_4\text{Br}_2$ requires $\text{Br} = 50.0$ per cent.

Action of Hydrogen Bromide on the Diethyl Ester.—Ten grams of the diethyl ester were mixed with an aqueous solution of hydrogen bromide (saturated at 0°). Much heat was evolved, the bromide being very quickly absorbed. The product was extracted with ether, and the ethereal solution washed with dilute sodium carbonate solution and afterwards dried over anhydrous sodium sulphate. On distilling off the ether there remained a liquid diethyl ester of a bromo-acid which contained an amount of bromine corresponding to that required for the empirical formula $\text{C}_{11}\text{H}_{19}\text{O}_4\text{Br}$. Thus :

0.4165 gave 0.2650 AgBr . $\text{Br} = 27.07$.

$\text{C}_{11}\text{H}_{19}\text{O}_4\text{Br}$ requires $\text{Br} = 27.12$ per cent.

Most probably, therefore, this oil was ethyl bromotrimethylsuccinate, $(\text{CH}_3)_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\cdot\text{C}(\text{CH}_3)\text{Br}\cdot\text{CO}_2\text{C}_2\text{H}_5$, although it is just possible that it was the isomeric ethyl α -methyl- δ -bromobutane- $\beta\gamma$ -dicarboxylate, $(\text{CH}_3)_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\cdot\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\cdot\text{CH}_2\text{Br}$. On comparing the action of the oil with that of the ethyl bromotrimethylsuccinate obtained by the direct bromination of trimethylsuccinic acid (see p. 54) on ethyl sodiocyanoacetate (see next section), identical products were obtained in the two experiments. We afterwards found that the identity of these products does not necessarily imply the identity of the two bromo-esters in question, so that which of the two foregoing formulæ represents the constitution of the oil obtained by the action of hydrogen bromide on diethyl methylenedimethylsuccinate is a point we have not yet definitely established.

Interaction of Ethyl Bromotrimethylsuccinate and Ethyl Sodiocyanacetate.

(1) To a solution of 1.5 grams of sodium in 20 grams of alcohol were added 7.5 grams of ethyl cyanoacetate and 19 grams of ethyl bromotrimethylsuccinate; much heat was developed, sodium bromide separated, and the liquid became neutral after being heated for 3 hours on the water-bath. The product was extracted with ether and fractionated under 20 mm. pressure. A fair proportion of it passed over between 130° and 150° , the temperature then rose rapidly to above 200° , and about half of the oil distilled between 210° and 215° . This higher fraction was hydrolysed by boiling it with strong hydrochloric acid for 24 hours. On cooling the liquid, no crystals separated, so it was saturated with ammonium sulphate and thoroughly extracted with ether.

In this way, a white crystalline acid was isolated which, after recrystallisation from strong hydrochloric acid, melted sharply at 137 — 138° . This, it will be observed, is the same melting point as that of the acid obtained by one of us and Professor Perkin some years ago by the same series of reactions. The acid was therefore not *i*-camphoronic acid (m. p. 169 — 172°), and, further, all attempts to isolate any camphoronic acid from the hydrolytic products by means of its characteristic barium salt entirely failed, so we can only conclude that none had been formed. Analysis of our acid, however, indicated that it was tribasic and isomeric with camphoronic acid, $\text{C}_9\text{H}_{14}\text{O}_6$, thus:

0.1364 gave 0.2500 CO_2 and 0.0813 H_2O . C = 49.87; H = 6.62.

0.1095 silver salt gave 0.0657 Ag. Ag = 60.0.

$\text{C}_9\text{H}_{14}\text{O}_6$ requires C = 49.53; H = 6.42 per cent.

$\text{C}_9\text{H}_{11}\text{O}_6\text{Ag}_3$ „ Ag = 60.10 per cent.

(2) In another experiment, 11 grams of the bromo-ester obtained by the action of hydrogen bromide on ethyl methylenedimethylsuccinate were added to the calculated quantity of ethyl sodiocyanoacetate suspended in alcohol. Sodium bromide at once separated and on continuing the experiment as described in the preceding paragraph, we finally obtained a cyano-ester boiling at 230—240° under 40 mm. pressure. This on hydrolysis with hydrochloric acid yielded the same acid, $C_9H_{14}O_6$, melting at 137°.

Fusion of the Acid, $C_9H_{14}O_6$, with Potassium Hydroxide.

In order to obtain evidence as to the constitution of the acid, 5 grams of the substance were fused with a paste of 30 grams of potassium hydroxide at 180—200°. A vigorous decomposition ensued. After being cooled, the fused product was dissolved in water, acidified with dilute sulphuric acid, and the liquid then distilled with steam. The distillate contained a fatty acid, the analysis of whose silver salt showed it was acetic acid.

0.2021 silver salt gave 0.1303 Ag. $Ag = 64.47$.

$C_2H_3O_2Ag$ requires $Ag = 64.67$ per cent.

On extracting the residual liquor with ether, a solid acid melting at 147° and in other respects identical with trimethylsuccinic acid was obtained. (An analysis of the silver salt of this acid was made, but the results have, unfortunately, been mislaid; they agreed well with the calculated numbers for silver trimethylsuccinate.)

These results are quite consistent with the view that the acid $C_9H_{14}O_6$ is *aa-dimethylbutane- $\alpha\beta\delta$ -tricarboxylic acid*, and indeed it is difficult to see what other constitution could be assigned to it. The further investigation of its properties has, for the time being, been stopped on account of lack of material, but will be resumed in the near future.

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