LXXXI.—*Hexamethylenecarboxylic Acid and the cis- and trans-Modifications of Hexamethylenetetracarboxylic Acid (Hexahydropyromellitic Acid).*

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DURING the course of a series of experiments on the condensation of ethyl malonate with formaldehyde (Haworth and Perkin, *Trans.*, 1898, **73**, 330; Bottomley and Perkin, 1900, **77**, 294; compare Knoevenagel, *Ber.*, 1894, **27**, 2345), the observation was made that ethyl propanetetracarboxylate, which, in certain circumstances, is the principal product of the reaction

is readily acted on by bromine with the formation of *ethyl dibromopropanetetracarboxylate*, $(\text{CO}_2\text{Et})_2\text{CBr}\cdot\text{CH}_2\cdot\text{CBr}(\text{CO}_2\text{Et})_2$.

When this ester is digested with the disodium compound of ethyl propanetetracarboxylate, sodium bromide is immediately eliminated and an almost quantitative yield of *ethyl hexamethylenecarboxylate* is obtained,

This interesting ester is a beautifully crystalline substance which melts at 46° and which, when boiled with concentrated hydrochloric acid, is almost quantitatively hydrolysed with the formation of the corresponding *hexamethylenecarboxylic acid*,

That this acid should be formed in this way is certainly remarkable, because esters which contain the grouping $\text{:C}(\text{CO}_2\text{Et})_2$, when digested with concentrated hydrochloric acid, are not only hydrolysed but also lose carbon dioxide, the above group becoming $\text{:CH}\cdot\text{CO}_2\text{H}$. It is difficult to understand why, in the case of this ester, which contains no less than four of these $\text{:C}(\text{CO}_2\text{Et})_2$ groupings, there should be no elimination of carbon dioxide on hydrolysis with boiling hydrochloric acid.

Hexamethylenecarboxylic acid melts at 218° with rapid evolution of carbon dioxide and formation of a mixture of the *trans*-

modification of *hexamethylenetetracarboxylic acid* (hexahydropyromellitic acid) and the double anhydride of the *cis*-modification of the same acid. Since this acid contains two pairs of asymmetric carbon atoms, it may, of course, exist in the following modifications :

The above mentioned double anhydride of the *cis*-acid, which has the constitution

melts at 60° and behaves normally on treatment with aniline, yielding a double anilic acid from which the corresponding double anil is obtained by the action of heat. It is readily converted into the *cis*-acid (m. p. 139—140°) by boiling with water. Experiments which were instituted with the object of converting this *cis*-acid into the *trans*-modification by heating with hydrochloric acid were unsuccessful owing to decomposition taking place before the temperature necessary for the isomeric change had been reached.

On the other hand, the *trans*-acid, when heated with acetic anhydride at 200° and then distilled, yields large quantities of the anhydride of the *cis*-acid, and there can thus be no doubt that these two acids are stereoisomeric modifications of hexamethylenetetracarboxylic acid. It would have been interesting to have isolated the *cis-trans*-modification of this acid which is represented above, but, although many experiments were carried out with the object of obtaining this form, it was found impossible to isolate it in a pure condition. Attempts were also made to remove the six hydrogen atoms from the anhydride of the *cis*-acid by treatment first with bromine and then with caustic potash, in the hope of thus synthesising pyromellitic acid, but the decomposition proceeded in another direction and we were unable to isolate even traces of this acid.

Ethyl Dibromopropanetetra-carboxylate,
 $(\text{CO}_2\text{Et})_2\text{CBr}\cdot\text{CH}_2\cdot\text{CBr}(\text{CO}_2\text{Et})_2$.

In order to obtain a satisfactory yield of this bromo-ester, it is essential that the ethyl propanetetra-carboxylate employed shall be carefully purified by repeated fractionation, as small quantities of impurity very much hinder the solidification of the bromo-ester. The pure ester (30 grams) is dissolved in three times its volume of chloroform and mixed with rather more than the calculated quantity of bromine (35 grams), a trace of iodine is then added, and the whole heated on the water-bath in a reflux apparatus until hydrogen bromide has almost ceased to be evolved, which is usually the case after 6 or 8 hours. Substitution takes place very slowly, especially at first, and is considerably hastened if the flask containing the mixture is exposed to direct sunlight. The product, when washed with dilute sulphurous acid in order to remove hydrogen bromide and excess of bromine, dried over calcium chloride and evaporated, yields an oily residue, which slowly solidifies. The crystals are freed as far as possible from oily mother liquor by contact with porous porcelain, and then recrystallised from dilute methyl alcohol, from which the substance separates in colourless prisms. On analysis:

0.1819 gave 0.1392 AgBr. $\text{Br} = 32.6$.

$\text{C}_{15}\text{H}_{22}\text{O}_8\text{Br}_2$ requires $\text{Br} = 32.7$ per cent.

Ethyl dibromopropanetetra-carboxylate melts at $54-55^\circ$, and is readily soluble in most organic solvents with the exception of light petroleum, in which it dissolves very sparingly. It is readily acted on by alcoholic potash with the formation of a deep yellow salt, which is at present under investigation. When it is boiled with diethylaniline, a vigorous reaction takes place, the solution rapidly becoming black.

In preparing this ester, pure ethyl propanetetra-carboxylate (14 grams) is mixed with a solution of sodium (2 grams) in 30 grams of absolute alcohol, and then treated all at once with powdered ethyl dibromopropanetetra-carboxylate (20 grams), the temperature being kept below 30° by cooling with water. The reaction takes place immediately, and quantities of sodium bromide separate in the cold; after a few minutes, the decomposition is completed by heating the mixture for 10 minutes on the water-bath.

When the product is poured into four times its volume of water an

oil separates which quickly solidifies; after about an hour, the precipitate is collected, washed thoroughly with water, spread on porous porcelain, and dried over sulphuric acid. It is then purified by recrystallisation from light petroleum, from which it gradually separates in needles which greatly resemble crystals of sublimed phthalic anhydride and are often several inches in length:

0.1439 gave 0.2870 CO_2 and 0.0868 H_2O . $\text{C} = 54.4$; $\text{H} = 6.7$.

0.1581 „ 0.3152 CO_2 „ 0.0946 H_2O . $\text{C} = 54.4$; $\text{H} = 6.5$.

$\text{C}_{30}\text{H}_{44}\text{O}_{16}$ requires $\text{C} = 54.5$; $\text{H} = 6.6$ per cent.

Ethyl hexamethyleneoctocarboxylate melts at 46° , and is readily soluble in alcohol, chloroform, acetic acid, and benzene; it dissolves readily in boiling light petroleum (b. p. $70-80^\circ$), but is sparingly soluble in this solvent in the cold. The ester crystallises best from light petroleum or dilute methyl alcohol, but even from these media it is obtained in crystals with some difficulty, owing to its tendency to separate from warm solvents in the form of an oil. When a small quantity is heated in a test-tube, it distils without any residue and apparently without decomposition, as the colourless distillate solidifies on cooling.

In preparing this acid, the pure ester was heated to boiling in a reflux apparatus with concentrated hydrochloric acid until the oil had entirely dissolved. The solution, when evaporated to a small bulk, slowly deposited a crystalline crust which was collected at the pump, and washed with hydrochloric acid. On concentrating the filtrate, a further crop of crystals was obtained and the concentration of the mother liquors was repeated several times until crystals ceased to separate. Finally, the mother liquors were evaporated nearly to dryness and the semi-solid residue left in contact with porous porcelain until dry. In a quantitative experiment, the total yield of acid obtained from 50 grams of ester was 29 grams, whereas the calculated yield is 33 grams. For analysis, the acid was again crystallised from hydrochloric acid and thus obtained in colourless, glistening crystals:

0.1382 gave 0.1940 CO_2 and 0.0368 H_2O . $\text{C} = 38.3$; $\text{H} = 2.9$.

0.2073 „ 0.2911 CO_2 „ 0.0540 H_2O . $\text{C} = 38.3$; $\text{H} = 2.8$.

$\text{C}_{14}\text{H}_{12}\text{O}_{16}$ requires $\text{C} = 38.5$; $\text{H} = 2.7$ per cent.

Hexamethyleneoctocarboxylic acid melts at about $218-220^\circ$ with rapid decomposition, due to the escape of carbon dioxide and steam. It is sparingly soluble in dry ether, benzene, chloroform, and light

petroleum, but readily soluble in alcohol. It dissolves to almost any extent in water, from which it readily crystallises, if the strong solution is saturated with hydrogen chloride.

Salts of Hexamethyleneoctocarboxylic Acid.—The silver salt, $C_6H_4(CO_2Ag)_8$, is obtained as a white, caseous, very insoluble precipitate on adding silver nitrate to a slightly alkaline solution of the ammonium salt. This salt explodes on heating, giving a very voluminous mass of carbon, and for this reason considerable difficulty was experienced in obtaining satisfactory results on analysis. The silver was determined by heating the salt with hydrochloric and nitric acids in a sealed tube at 180° , and in determining the carbon and hydrogen, the substance was mixed in the combustion tube with powdered copper oxide:

0.2694 gave 0.1284 CO_2 and 0.0154 H_2O . $C = 13.0$; $H = 0.6$.

0.2910 „ 0.2571 $AgCl$. $Ag = 66.4$.

$C_{14}H_4Ag_8O_{16}$ requires $C = 13.0$; $H = 0.3$; $Ag = 66.9$ per cent.

A slightly alkaline solution of the ammonium salt immediately gives, in the cold, caseous precipitates with barium or calcium chloride. When titrated with decinormal caustic soda, using phenolphthalein as the indicator, hexamethyleneoctocarboxylic acid does not neutralise quite the theoretical amount of alkali. Three experiments made with three different preparations of the acid gave the following results:

I. 0.1947 neutralised 0.1394 $NaOH = 71.5$ per cent.

II. 0.2107 „ 0.1504 $NaOH = 71.4$ „

III. 0.1956 „ 0.1368 $NaOH = 70.0$ „

The amount of caustic soda neutralised by an octocarboxylic acid having the formula $C_{14}H_{12}O_{16}$ is theoretically 73.4 per cent.

When hexamethyleneoctocarboxylic acid, in quantities of not more than 5 grams, is heated in a wide test-tube in a sulphuric acid bath at 230° , much steam and carbon dioxide are given off, and in about ten minutes the frothing has ceased and the decomposition is complete.

The residue, which solidifies on cooling, consists of *trans*-hexamethylenetetra-carboxylic acid and the anhydride of the *cis*-modification of the same acid, the latter being present in by far the larger

quantity. In order to separate these two substances, the brown mass is powdered and digested with toluene in which the anhydride dissolves, but in which the *trans*-acid is almost insoluble.

After collecting at the pump and washing with toluene, the grey residue is dried at 100° until free from toluene, dissolved in water, and the solution decolorised by boiling with animal charcoal.

The pure *trans*-acid gradually separates in colourless, glistening plates when the concentrated aqueous solution is mixed with an equal volume of hydrochloric acid :

0.1531 gave 0.2593 CO₂ and 0.0677 H₂O. C = 46.2 ; H = 4.9.

0.1537 „ 0.2599 CO₂ and 0.0675 H₂O. C = 46.1 ; H = 4.8.

C₁₀H₁₂O₈ requires C = 46.2 ; H = 4.6 per cent.

trans-Hexamethylenetetra-carboxylic acid melts at 175°, and immediately solidifies again a few degrees below this temperature. It is sparingly soluble in benzene, chloroform, and light petroleum, but dissolves readily in alcohol and ether. It is very soluble in water, although to a less extent than the *cis*-acid, and crystallises well from hydrochloric acid, but the crystals are, as a rule, not well defined.

On titration with decinormal caustic soda, using phenolphthalein as the indicator, 0.1977 required, for neutralisation, 0.1214 NaOH, whereas this amount of a tetrabasic acid, C₁₀H₁₂O₈, should neutralise 0.1216 NaOH.

The slightly alkaline solution of the ammonium salt of this acid gives no precipitates with barium or calcium chloride, even on boiling, and in this respect the *trans*-acid differs from the *cis*-acid (p. 787). Zinc sulphate also gives no precipitate in the cold, but, on boiling, a very sparingly soluble salt separates in globular masses resembling starch granules. Mercuric chloride gives no precipitate at first, but the solution soon becomes cloudy, and, on warming, a very sparingly soluble, apparently crystalline, salt separates.

Conversion of trans-Hexamethylenetetra-carboxylic Acid into the cis-Modification.—When heated by itself, the *trans*-acid distils almost without decomposition and shows only little tendency to pass into the anhydride of the *cis*-acid. If, however, the *trans*-acid is heated in a sealed tube with acetic anhydride at 200° for three hours, and the product, after distilling off the acetic acid and excess of acetic anhydride, is distilled under reduced pressure (15 mm.), a considerable quantity of oil passes over, leaving a carbonaceous mass in the retort. The distillate solidifies on cooling, and, after removing the oily mother liquor by contact with porous porcelain and crystallisation from toluene, colourless crystals are obtained which melt at 60° and consist of the pure anhydride of the *cis*-acid :

0.1003 gave 0.1967 CO_2 and 0.0344 H_2O . $\text{C} = 53.3$; $\text{H} = 3.8$.

$\text{C}_{10}\text{H}_8\text{O}_6$ requires $\text{C} = 53.5$; $\text{H} = 3.6$ per cent.

The identity of this anhydride was further established by converting it into the *cis*-acid, which melted at $138-140^\circ$.

The dark brown toluene mother liquors from the purification of the *trans*-acid contain the anhydride of the *cis*-acid.

These were in the first instance digested for an hour with animal charcoal, and after filtering, evaporated to a small bulk, when, on remaining over-night, thick, curiously-shaped, light brown, crystalline masses had separated, and a further crop was obtained from the mother liquors by again treating with animal charcoal and evaporating to a small bulk. This crude anhydride was purified by recrystallising several times from toluene, traces of the *trans*-acid, if present, being always carefully removed by filtration before the anhydride was allowed to separate:

0.1827 gave 0.3558 CO_2 and 0.0637 H_2O . $\text{C} = 53.2$; $\text{H} = 3.8$.

0.1646 „ 0.3219 CO_2 „ 0.0573 H_2O . $\text{C} = 53.3$; $\text{H} = 3.8$.

$\text{C}_{10}\text{H}_8\text{O}_6$ requires $\text{C} = 53.5$; $\text{H} = 3.6$ per cent.

The *anhydride* of *cis*-hexamethylenetetra-carboxylic acid melts at about 60° , and is readily soluble in ether but sparingly so in benzene, light petroleum, and chloroform; it is insoluble in cold water, but slowly dissolves in sodium carbonate with effervescence. When heated with resorcinol and a drop of sulphuric acid at 130° , it yields a dark brown mass from which water precipitates an orange-coloured substance exactly like fluorescein in appearance. This dissolves in caustic soda, and if the dark brown solution is thrown into a large quantity of water, an intense fluorescence, indistinguishable from that of fluorescein, is produced.

When warmed with water, the anhydride first melts and then rapidly dissolves, and if the solution is evaporated nearly to dryness, the *cis*-acid separates on cooling in crystalline flakes and sometimes in flat prisms. These were collected on the pump, and purified by recrystallisation from hydrochloric acid:

0.1877 gave 0.3174 CO_2 and 0.0794 H_2O . $\text{C} = 46.1$; $\text{H} = 4.7$.

0.1325 „ 0.2235 CO_2 „ 0.0560 H_2O . $\text{C} = 46.0$; $\text{H} = 4.7$.

$\text{C}_{10}\text{H}_{12}\text{O}_8$ requires $\text{C} = 46.1$; $\text{H} = 4.6$ per cent.

cis-Hexamethylenetetra-carboxylic acid, when quite pure, melts at about 139—140°, but the exact temperature is ascertained with difficulty owing to the fact that the acid melts to a thick syrup, which only gradually becomes clear. It is excessively soluble in water, and dissolves readily even in concentrated hydrochloric acid; it is, however, sparingly soluble in chloroform, benzene, and light petroleum. On titration with decinormal caustic soda, using phenolphthalein as the indicator, 0.2042 required for neutralisation 0.1245 NaOH, whereas this amount of a tetrabasic acid, $C_{10}H_{12}O_8$, should neutralise 0.1256 NaOH.

The salts of the *cis*-acid differ very considerably in solubility from those of the corresponding *trans*-acid (p. 785).

The slightly alkaline solution of the ammonium salt gives no precipitate with calcium chloride in the cold, but, on boiling, a beautifully crystalline and very sparingly soluble calcium salt separates in six-sided plates. Barium chloride also gives no precipitate, in the cold, and, on boiling, the insoluble barium salt gradually crystallises in slender needles. Copper sulphate gives no precipitate, but, on gently warming, a bluish-green, amorphous salt separates; zinc sulphate gives no precipitate, but mercuric chloride and lead acetate immediately produce white precipitates.

cis-Hexamethylenetetra-carboxydianilic Acid,

On adding aniline to a solution of the anhydride in benzene, this substance separates at once as a thick syrup which gradually solidifies. It is readily purified by recrystallisation from methyl alcohol, from which it separates, either as a sandy powder consisting apparently of truncated octahedra, or in glistening plates. It melts at about 172°, softening at a slightly lower temperature, and then decomposing vigorously into water and the dianil:

0.2128 gave 13.2 c.c. nitrogen at 20° and 752 mm. $N = 7.0$.

$C_{22}H_{22}O_6N_2$ requires $N = 6.8$ per cent.

This *dianilic acid* is sparingly soluble in benzene, light petroleum, chloroform, and methyl alcohol in the cold, but dissolves moderately readily in the latter solvent on boiling; it dissolves in dilute aqueous caustic potash, and is reprecipitated on the addition of acid.

cis-Hexamethylenetetra-carboxydianil,

At 200°, the dianilic acid decomposes rapidly with evolution of steam, and the residue solidifies at once on cooling. By recrystallising from benzene or dilute methyl alcohol, the dianil is readily obtained pure in the form of long, thin needles which melt at 98° :

0.1474 gave 10 c.c. nitrogen at 18° and 757 mm. $\text{N} = 7.7$.

$\text{C}_{22}\text{H}_{18}\text{O}_4\text{N}_2$ requires $\text{N} = 7.5$ per cent.

Attempts to convert cis-Hexamethylenetetra-carboxylic Acid into the trans-Modification.—When the *cis*-acid dissolved in a small quantity of water is heated with hydrochloric acid at 175° for 1 hour, the solution remains nearly colourless, and, on evaporating to a small bulk, the unchanged acid separates. Several additional experiments were then made at gradually increasing temperatures up to 195°, but at the latter temperature decomposition took place with elimination of carbon dioxide and separation of carbonaceous flocks. On examining the contents of the tubes, which had been heated between 170° and 195°, no indication was observed of any conversion of the *cis*- into the *trans*-modification. The reverse change, namely, the conversion of the *trans*- into the *cis*-modification, is described on p. 785.

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