LXXXVI.—CONTRIBUTIONS FROM THE LABORATORIES
OF THE HERIOT WATT COLLEGE, EDINBURGH.*New Synthesis of the Hexamethylenedicarboxylic Acids.*

By W. H. PERKIN, Jun., Ph.D., F.R.S., and BERTRAM PRENTICE.

IN the last number of this Journal (p. 798), it was shown that the sodium compound of ethyl pentanetetracarboxylate reacts with methylene iodide in alcoholic solution at 100°, with formation of ethyl hexamethylenetetracarboxylate, thus :—

On hydrolysis, this ethereal salt yields the corresponding hexamethylenetetra-carboxylic acid, and the latter, when heated at 200—220°, is decomposed with elimination of 2 mols. of CO₂ and formation of Γ^{cis} and $\Gamma^{\text{cis-trans}}$ hexamethylenemetadicarboxylic acids:—

As the amount of these interesting acids obtained by this method is small, numerous experiments were made, under very varying conditions, with the object of improving the yield, but without success. It then seemed probable that the same ethyl hexamethylene-tetra-carboxylate should result from the action of trimethylene bromide on the disodium compound of ethyl propanetetra-carboxylate, thus:—

On making the experiment, it was found that a considerable quantity of the ethereal salt may be prepared in this way, but the yield obtained, though better than that from ethyl pentanetetra-carboxylate, is far from good, and does not appear to be more than 10—12 per cent. of theoretical.

Preparation of Ethyl Propanetetra-carboxylate,
(COOC₂H₅)₂CH·CH₂·CH(COOC₂H₅)₂, and of Glutaric Acid.

Ethyl propanetetra-carboxylate was first prepared by Conrad and Guthzeit (*Annalen*, **222**, 253), afterwards by W. H. Perkin, jun. (*Ber.*, **19**, 1056), by the condensation of ethyl malonate with formaldehyde:

Subsequently, Guthzeit and Dressel (*Annalen*, **256**, 171) obtained the same substance by treating the sodium compound of ethyl malonate with methylene iodide, thus:—

This method gives a yield of 84 per cent. of the theoretical, and is, therefore, the most convenient method of preparation.

As, however, methylene iodide is an expensive substance, it occurred to us that it would be a great advantage if we could employ the cheaper methylene chloride in its place, and we, therefore, instituted a number of experiments on the action of methylene chloride on the sodium compound of ethyl malonate. 64 grams of ethyl malonate was dissolved in a solution of 9.2 grams of sodium in absolute alcohol, 17 grams of methylene chloride added, and the mixture heated in soda-water bottles at 100° for two hours; the product was then heated on a water-bath till free from alcohol, the residue mixed with water, and extracted three times with ether. During this operation, beautiful, yellow crystals separated from the ethereal solution; they contain sodium, and consist apparently of the sodium compound of a somewhat complicated ethereal salt; this substance, which seems to have very interesting properties, is at present under examination. The filtrate from this sodium compound, after drying over calcium chloride and evaporating the ether, deposited a thick oil, which was purified by fractional distillation under reduced pressure, and thus separated into unchanged ethyl malonate, and a substance boiling at 230—240° (80 mm.), which, after refractionation, boiled constantly at 234—236° (80 mm.), and was found to consist of pure ethyl propane-tetracarboxylate.

0.2016 gram substance gave 0.1354 gram H_2O and 0.4020 gram CO_2 .

	Theory. $C_{15}H_{24}O_8$.	Found.
C	54.21 per cent.	54.35 per cent.
H	7.23 ,,	7.46 ,,
O	38.55 ,,	38.19 ,,

The yield obtained was about 60 per cent. of the theoretical, without taking the recovered ethyl malonate into account.

The action of methylene chloride on the sodium compound of ethyl malonate has been already investigated by S. Tanatar (*Chem. Centralblatt*, 1891, i, 21, 22), but his results differ entirely from those described above, as he makes no mention of having obtained an ethereal salt, $C_{15}H_{24}O_8$. On this account it seemed necessary to prove that the ethereal salt, $C_{15}H_{24}O_8$, obtained by this reaction, really was ethyl propane-tetracarboxylate before employing it for synthetical experiments. This is readily done by converting it into the corresponding tetracarboxylic acid, and then decomposing this by heating it at 200°, when glutaric acid results (compare W. H. Perkin, jun., Guthzeit and Dressel, *loc. cit.*).

30 grams of the pure ethyl salt, $\text{C}_{15}\text{H}_{24}\text{O}_8$, was dissolved in methyl alcohol, mixed with a solution of 25 grams of potassium hydrate in methyl alcohol, and the whole heated for three hours on a water-bath, in a flask connected with a reflux apparatus. The product was then mixed with water, vigorously boiled till free from alcohol, evaporated to a small bulk, acidified with hydrochloric acid, and extracted 10 times with pure ether. The ethereal solution was dried over calcium chloride, evaporated, and the residual, yellowish, semi-solid mass heated at $200\text{--}220^\circ$ until the evolution of carbonic anhydride had entirely ceased.

In order to purify the crude acid thus obtained, the residual dark-brown syrup was dissolved in 10 times its weight of absolute alcohol, the solution mixed with $1/5$ th of the quantity of concentrated sulphuric acid, heated in a reflux apparatus for two hours, and the ethereal salt isolated by pouring the product into water and extracting with ether. The ethereal solution was well washed with water, dried over calcium chloride, evaporated, and the crude ethyl salt purified by fractional distillation. In this way a colourless oil was obtained, which boiled constantly at 234° , and showed all the properties of ethyl glutarate. Analysis:—

0.1104 gram substance gave 0.0864 gram H_2O and 0.2321 gram CO_2 .

	Theory. $\text{COOC}_2\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOC}_2\text{H}_5$.	Found.
C	57.44 per cent.	57.34 per cent.
H	8.51 ,,	8.68 ,,
O	34.05 ,,	33.98 ,,

The pure ethereal salt was hydrolysed by boiling with an excess of alcoholic potash for two hours, the solution mixed with water, boiled until free from alcohol, acidified with hydrochloric acid, and extracted five times with pure ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a crystalline cake of almost pure glutaric acid; this was washed with ether, dried on a porous plate over sulphuric acid, under reduced pressure, and then at 80° .

The acid melted at $97\text{--}98^\circ$, and on analysis gave numbers agreeing with those required for glutaric acid.

0.1702 gram substance gave 0.0950 gram H_2O and 0.2836 gram CO_2 .

	Theory. $\text{C}_5\text{H}_8\text{O}_4$.	Found.
C	45.45 per cent.	45.48 per cent.
H	6.06 ,,	6.20 ,,
O	48.48 ,,	48.32 ,,

The formation of this acid proves that the substance $C_{15}H_{24}O_8$, obtained by the action of methylene chloride on the sodium compound of ethyl malonate, is in reality ethyl propanetetra-carboxylate, $(COOC_2H_5)_2CH \cdot CH_2 \cdot CH(COOC_2H_5)_2$.

The method of preparation of glutaric acid given above is probably the simplest and cheapest way of preparing this important substance, and, with this object in view, it would not be necessary to purify the ethyl propanetetra-carboxylate by fractionation, the crude product of the action of methylene chloride on the sodium compound of ethyl malonate, might be freed from unchanged ethyl malonate by distillation in a current of steam, and the residual oil at once hydrolysed and treated as above.

Action of Trimethylene Bromide on the Disodium Compound of Ethyl Propanetetra-carboxylate. Formation of Hexamethylenetetra-carboxylic Acid.

In carrying out this synthesis, 70 grams of pure ethyl propanetetra-carboxylate was mixed with a solution of 9.7 grams of sodium in 120 grams of absolute alcohol, 43 grams of trimethylene bromide added, and the whole heated gently in a flask connected with a reflux apparatus. In a short time, the temperature rose rapidly, a vigorous reaction set in, and, after boiling for about one hour, the decomposition was completed. The product was gently evaporated till free from alcohol, mixed with water, extracted two or three times with ether, the ethereal solution evaporated, and the residual oil (78 grams) hydrolysed by boiling with $1\frac{1}{2}$ times the calculated quantity of alcoholic potash for three hours. After mixing with water, the alkaline solution was boiled until free from alcohol, evaporated to a small bulk, acidified with hydrochloric acid, and extracted 25 times with pure ether. The ethereal solution, after drying over calcium chloride and evaporating to a small bulk, deposited, on standing, a quantity of a white, crystalline substance; this was collected, washed with ether, and recrystallised from warm water.

In this way, beautiful, colourless, glistening crystals were obtained, which, on analysis, proved to be pure hexamethylenetetra-carboxylic acid:—

0.1418 gram substance gave 0.0620 gram H_2O and 0.2400 gram CO_2 .

	Theory. $C_{10}H_{12}O_8$.	Found.
C	46.15 per cent.	46.15 per cent.
H	4.61 "	4.85 "
O	49.23 "	49.00 "

This substance, when rapidly heated, decomposed at 218—220°, and was in all respects identical with the hexamethylenetetracarboxylic acid previously obtained. A quantity of the pure acid was heated at 220° until the evolution of carbonic anhydride had ceased, and the resulting, almost colourless oil which consists of a mixture of Γ^{cis} and Γ^{cistrans} hexamethylenemetadicarboxylic acids, digested with acetyl chloride, and thus converted into the anhydride of the Γ^{cis} acid (this vol., pp. 812, 816). The solid, crystalline mass which remained after distilling off the excess of the acetyl chloride and the acetic acid was purified by spreading on a porous plate, and subsequent recrystallisation from a mixture of benzene and light petroleum.

The magnificent, glistening crystals thus obtained, after drying at 110°, melted at 187°, and consisted of the pure anhydride of Γ^{cis} hexamethylenemetadicarboxylic acid, as is shown by the following analyses:—

- I. 0.1074 gram substance gave 0.0656 gram H_2O and 0.2451 gram CO_2 .
 II. 0.1599 gram substance gave 0.0958 gram H_2O and 0.3642 gram CO_2 .

	Theory. $\text{C}_8\text{H}_{10}\text{O}_3$.	Found.	
		I.	II.
C.	62.33 per cent.	62.24	62.11 per cent.
H.	6.50 „	6.79	6.65 „
O.	31.17 „	30.97	31.24 „

This anhydride was further identified by conversion into Γ^{cis} hexamethylenemetadicarboxylic acid by boiling with water.

The ethereal mother liquors from which the hexamethylenetetracarboxylic acid had separated, as described above, were evaporated, the residue heated at 200—220° until the evolution of carbonic anhydride had ceased, and then converted into the methyl salt by means of methyl alcohol and sulphuric acid (*loc. cit.*, p. 806).

On fractioning this salt, a small amount of crude methyl hexamethylenedicarboxylate was obtained, boiling at 170—185° (60 mm.), together with considerable quantities of high and low boiling fractions; of these, the former were not examined; the latter appear to contain methyl glutarate, which must have been produced by the hydrolysis of some unchanged ethyl propanetetracarboxylate.

The yield of pure hexamethylenetetracarboxylic acid obtained in the above reaction from 140 grams of ethyl propanetetracarboxylate was about 13.5 grams, or about 12 per cent. of the theoretical. The amount of hexamethylenedicarboxylic acids obtained by the hydrolysis of the methyl salt has not yet been accurately determined, but it is approximately 4 grams.

Further experiments on these interesting acids are in progress.