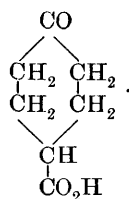
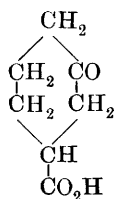
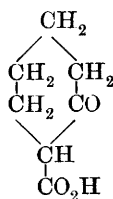


XLVIII.— δ -Ketohehexahydrobenzoic Acid.

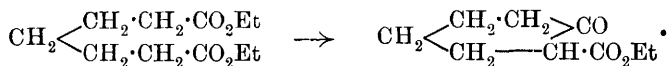
By WILLIAM HENRY PERKIN, jun.

OF the three possible (β -, γ -, and δ -)-ketohehexahydrobenzoic (*cyclohexanonecarboxylic*) acids,

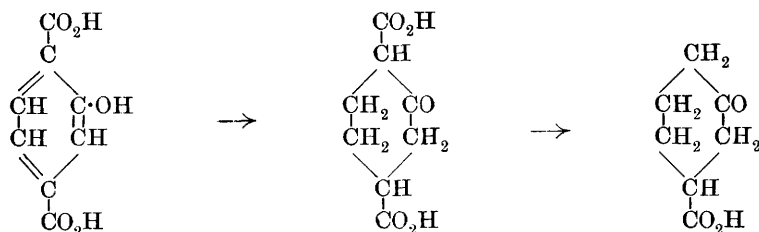


only the first two are known. The ester of the β -acid was synthesised

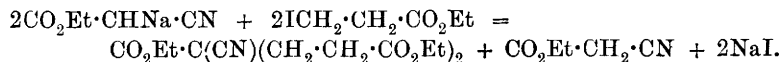
by Dieckmann (*Ber.*, 1894, 27, 103; 1900, 33, 2683) from ethyl pimelate by the action of sodium:



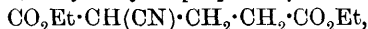
γ -Ketohehexahydrobenzoic acid was obtained by Baeyer and Tutein (*Ber.*, 1889, 22, 2182) by first reducing hydroxyterephthalic acid to ketohehexahydroterephthalic acid and then eliminating carbon dioxide by boiling with water:



Since the unknown δ -keto-acid might be expected to exhibit unusually interesting properties, the author has been engaged for some time in devising a method for its synthesis, and has ultimately succeeded in preparing it in considerable quantities by the following series of reactions. When ethyl β -iodopropionate and ethyl sodio-cyanoacetate are allowed to interact in molecular proportions at the ordinary temperature, a curious reaction takes place, which results in the formation of ethyl γ -cyanopentane- $\alpha\gamma\epsilon$ -tricarboxylate and regeneration of half of the ethyl cyanoacetate:

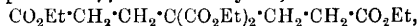


Under the conditions employed, it was to be expected that the mono-substitution product, ethyl α -cyanopropane- $\alpha\gamma$ -dicarboxylate,



would be formed, but no trace of this substance could be isolated, the reaction proceeding apparently quantitatively in the direction shown above.* Ethyl cyanopentane-tricarboxylate is hydrolysed by boiling with concentrated hydrochloric acid with the formation of pentane- $\alpha\gamma\epsilon$ -tricarboxylic acid, $\text{CO}_2\text{H} \cdot \text{CH}(\text{CH}_2 \cdot \text{CH}_2 \cdot \text{CO}_2\text{H})_2$, which

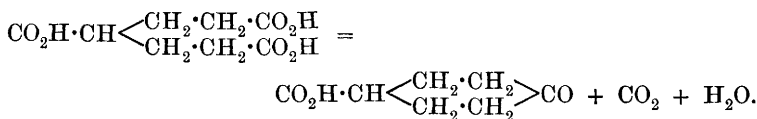
* In the case of the very similar action of ethyl β -bromopropionate on ethyl sodiomalonate, Emery (*Ber.*, 1891, 24, 282) showed that the principal product of the reaction was the normal mono-substitution product, namely, ethyl propane- $\alpha\alpha\gamma$ -tricarboxylate, $\text{CO}_2\text{Et} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{CO}_2\text{Et})_2$, but he also noticed that small quantities of ethyl pentane- $\alpha\gamma\gamma\epsilon$ -tetracarboxylate,



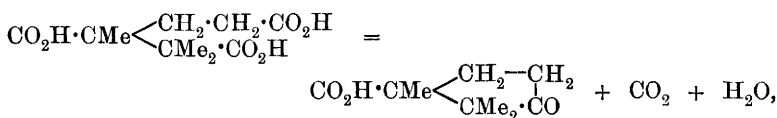
were produced at the same time.

melts at 116—118°, and has already been described by Emery (*Ber.*, 1891, 24, 384) and by Bottomley and Perkin (*Trans.*, 1900, 77, 299).

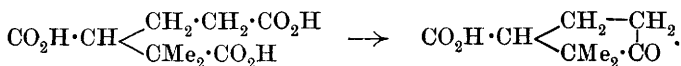
When the sodium salt of this acid is heated with acetic anhydride, or when the acid itself is digested with acetic anhydride and then distilled, a remarkable decomposition takes place with elimination of carbon dioxide and water and formation of δ -ketohehexahydrobenzoic acid (m. p. 68°):



Similar cases of ring formation from dibasic acids have already been observed on one or two occasions, thus Lapworth and Chapman (*Trans.*, 1900, 77, 464) showed that homocamphoronic acid, when slowly distilled, is converted into camphononic acid,



and Perkin and Thorpe (*Trans.*, 1904, 85, 138) recently obtained ketodimethylpentamethylenecarboxylic acid by heating the sodium salt of dimethylbutanetricarboxylic acid with acetic anhydride:

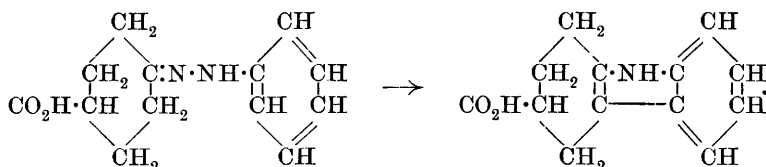


Experiments are in progress, which, it is hoped, will indicate to what extent this valuable method may be employed in the formation of closed chain compounds containing the keto-group.

δ -Ketohehexahydrobenzoic acid crystallises with 1 molecule of water and shows all the properties of a keto-acid; it yields the following derivatives, the preparation and properties of which are described in the experimental part of this paper: *methyl δ -ketohehexahydrobenzoate*, $\text{CO}(\text{CH}_2 \cdot \text{CH}_2)_2\text{CH} \cdot \text{CO}_2\text{Me}$ (b. p. 140°/20 mm.); *ethyl δ -ketohehexahydrobenzoate*, $\text{CO}(\text{CH}_2 \cdot \text{CH}_2)_2\text{CH} \cdot \text{CO}_2\text{Et}$ (b. p. 158°/40 mm.); *δ -ketoximehehexahydrobenzoic acid*, $(\text{OH})\text{N} \cdot \text{C}(\text{CH}_2 \cdot \text{CH}_2)_2\text{CH} \cdot \text{CO}_2\text{H}$ (m. p. 147°); the *semicarbazone*, $\text{NH}_2 \cdot \text{CO} \cdot \text{NH} \cdot \text{N} \cdot \text{C}(\text{CH}_2 \cdot \text{CH}_2)_2\text{CH} \cdot \text{CO}_2\text{H}$ (m. p. 194°).

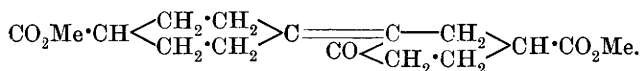
When treated with phenylhydrazine, δ -ketohehexahydrobenzoic acid yields a yellow oil, which is doubtless the hydrazone, and this, when boiled with hydrochloric acid, loses ammonia and is converted into a sparingly soluble crystalline substance having the formula $\text{C}_{13}\text{H}_{13}\text{O}_2\text{N}$. This decomposition is evidently analogous to the well-known conversion of phenylhydrazones into indole derivatives discovered by Emil

Fischer, and the substance $C_{13}H_{13}O_2N$ is obviously *tetrahydrocarbazole-p-carboxylic acid*, formed according to the scheme :



It is interesting to observe that Baeyer and Tutein (*Ber.*, 1889, **22**, 2184) had previously described the exactly similar conversion of γ -keto-hexahydrobenzoic acid into tetrahydrocarbazole-*m*-carboxylic acid by the action of phenylhydrazine and subsequent treatment with hydrochloric acid.

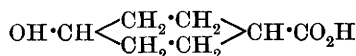
Carboxyhexamethenyl- δ -keto-hexahydrobenzoic Acid.—During a series of experiments on the preparation of the methyl and ethyl esters of δ -keto-hexahydrobenzoic acid (see above) it was noticed that, when the acid was boiled with methyl alcohol and sulphuric acid, a large quantity of an oil was formed which, on account of its high boiling point (255° under 20 mm. pressure), was evidently a condensation product. The examination of this oil proved that it was *methyl carboxyhexamethenyl- δ -keto-hexahydrobenzoate*, formed by the elimination of water from two molecules of methyl δ -keto-hexahydrobenzoate, and therefore its constitution is obviously that represented by the formula :



On hydrolysis, this methyl ester yields the free *carboxyhexamethenyl- δ -keto-hexahydrobenzoic acid*, a colourless, crystalline substance which melts at 170° . Although it is well known that ketopolymethylene ring compounds readily condense with substances containing the $>\text{CO}$ group, no case, like the above, seems to have been observed in which condensation of two molecules of the substance is brought about simply by boiling with methyl alcohol and sulphuric acid.

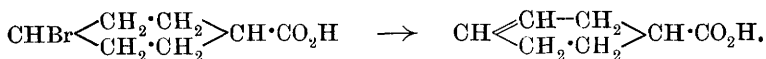
Reduction of δ -Keto-hexahydrobenzoic Acid. Formation of δ -Hydroxy-hexahydrobenzoic Acid and the Conversion of this Acid into Δ^3 -Tetrahydrobenzoic Acid.

δ -Keto-hexahydrobenzoic acid is readily reduced by sodium amalgam with formation of *δ -hydroxy-hexahydrobenzoic* (cyclohexanol-4-carboxylic) acid,

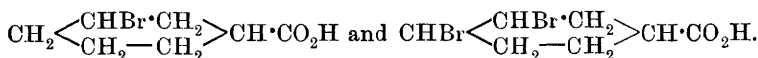


(m. p. 121°), and, since this acid shows no tendency to form a lactone, it is evidently the *trans*-modification. It was to be expected that both the *cis*- and *trans*-forms of this acid would be produced by the reduction of the keto-acid, but, although a careful search was made, no trace of the *cis*-acid could be isolated.

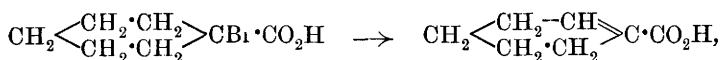
When the hydroxy-acid is heated with hydrobromic acid, it is converted into δ -bromohexahydrobenzoic (bromocyclohexane-4-carboxylic) acid (m. p. 167°), and this, when digested with sodium carbonate, readily loses hydrogen bromide with formation of Δ^3 -tetrahydrobenzoic (Δ^3 -cyclohexenecarboxylic) acid,



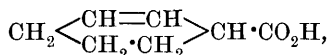
This new acid melts at about 13° and distils at 237° (748 mm.); it shows all the properties of an unsaturated acid, since it reduces permanganate, combines with hydrogen bromide yielding γ -bromohexahydrobenzoic acid (m. p. 122°), and at once decolorises bromine with formation of $\gamma\delta$ -dibromohexahydrobenzoic (3 : 4 dibromocyclohexanecarboxylic) acid (m. p. 86°),



The above synthesis of Δ^3 -tetrahydrobenzoic acid is a welcome addition to our knowledge of the chemistry of the tetrahydrobenzoic acids, since all the possible isomerides have now been prepared and carefully investigated. The Δ^1 -acid (m. p. 29° and b. p. 240 — 243°) was obtained by Aschan (*Annalen*, 1892, 271, 267) from bromohexahydrobenzoic acid by elimination of hydrogen bromide,



whereas the Δ^2 -acid (b. p. 235°),



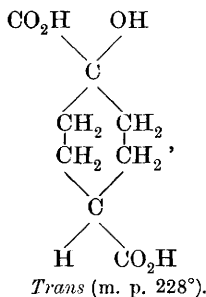
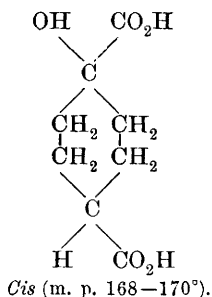
is formed by the direct reduction of benzoic acid with sodium amalgam (Hermann, *Annalen*, 1864, 132, 75; Aschan, *loc. cit.*, p. 236).

Action of Hydrogen Cyanide on δ -Ketohehexahydrobenzoic Acid. Formation of the cis- and trans-Modifications of α -Hydroxyhexahydroterephthalic Acid and of Δ^1 -Tetrahydroterephthalic Acid.

When δ -ketohehexahydrobenzoic acid is treated with hydrogen cyanide in the presence of potassium cyanide (compare Lapworth, *Trans.*, 1903,

83, 995), addition takes place readily with formation of an oil, which consists of the mixed nitriles of the *cis*- and *trans*-modifications of α -hydroxyhexahydroterephthalic acid, and from which the *trans*-nitrile (m. p. 140°) was isolated in a crystalline condition.

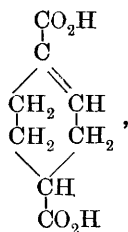
By hydrolysing the mixed nitriles under the conditions described in the experimental part of this paper (p. 435), the corresponding hydroxy-acids,



were easily separated in a state of purity. In the absence of definite proof of their configurations, the more sparingly soluble and less fusible isomeride was taken as being the *trans*-modification.

It is remarkable that when δ -ketohehexahydrobenzoic acid is reduced, that is, when the keto-group, $>\text{CO}$, is converted into $>\text{CH}\cdot\text{OH}$, only one modification of hydroxyhexahydrobenzoic acid should result, whereas, in the very similar addition of hydrogen cyanide converting the keto-group into $>\text{C}(\text{CN})\cdot\text{OH}$, both the *cis*- and *trans*-modifications of the nitrile of α -hydroxyhexahydroterephthalic acid should be formed. It is also interesting that in the latter case very much more of the *cis*-modification is produced than of the *trans*-modification.

Both the *cis*- and *trans*-modifications of hydroxyhexahydroterephthalic acid are decomposed on distillation, with loss of water and formation of Δ^1 -tetrahydroterephthalic acid,

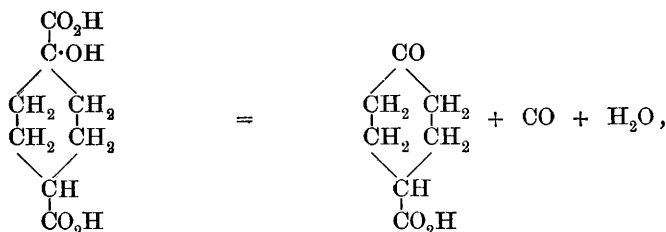


and the acid thus synthesised is identical with the Δ^1 -tetrahydroterephthalic acid which Baeyer (*Annalen*, 1888, 245, 160) obtained directly from terephthalic acid by reduction with sodium amalgam.

The *cis*- and *trans*-modifications of α -hydroxyhexahydroterephthalic

acid are readily acted on by concentrated sulphuric acid, decomposition taking place in both cases in two distinct directions.

Part of the acid is decomposed with elimination of carbon monoxide and water and formation of δ -keto-hexahydrobenzoic acid,



whereas the remainder is converted into Δ^1 -tetrahydroterephthalic acid by the simple elimination of water.

The investigation of δ -keto-hexahydrobenzoic acid and its derivatives is being continued in various directions.

EXPERIMENTAL.

Ethyl γ -Cyanopentane- $\alpha\gamma\epsilon$ -tricarboxylate, $\text{CO}_2\text{Et}\cdot(\text{CN})\text{C}(\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et})_2$.

In preparing this cyano-ester, the quantities usually employed were sodium (25 grams), alcohol (400 c.c.), ethyl cyanoacetate (125 grams), and ethyl β -iodopropionate* (250 grams).

The sodium is dissolved in the alcohol in a two-litre flask, and, after cooling, the ethyl cyanoacetate added all at once; the flask is then cooled again in running water and the ethyl β -iodopropionate added in three portions, care being taken that the temperature never rises above 25° , as otherwise some of the ethyl β -iodopropionate is liable to be decomposed with formation of ethyl acrylate (compare Trans., 1904, 85, 120). After being left overnight, the mixture is heated for half an hour on the water-bath, diluted with three times its volume of water, and extracted three times with ether.

The ethereal solution is washed until free from alcohol, dried over

* Owing to the costliness of β -iodopropionic acid, a number of comparative experiments were made with the object of discovering the best conditions for converting it into its ethyl ester, and the following process was found to give excellent results. The acid (500 grams) is dissolved in alcohol (400 c.c.) and mixed with a cold solution of sulphuric acid (150 grams) in alcohol (200 c.c.) and the whole allowed to remain for four days at the ordinary temperature. The product, which will have separated into two layers, is mixed with three volumes of water, extracted twice with ether, the ethereal solution washed with water containing a little sulphurous acid (to remove iodine), and fractionated under reduced pressure.

The boiling point is 136° under 100 mm. pressure, and the yield 525—535 grams, or 94 per cent. of that theoretically possible.

calcium chloride, and evaporated, and the residual oil fractionated under 20 mm. pressure. At first, unchanged ethyl cyanoacetate passes over, then the temperature rises rapidly to 220° , almost the whole of the residue passing over between this and 240° ; on repeating the fractionation, the pure substance is then easily obtained, distilling almost constantly at 228° (20 mm.).

0.1888 gave 0.3881 CO_2 and 0.1245 H_2O . $\text{C} = 57.0$; $\text{H} = 7.4$.

0.2880 „ 12.3 c.c. nitrogen at 15° and 756 mm. $\text{N} = 4.9$.

$\text{C}_{15}\text{H}_{23}\text{O}_6\text{N}$ requires $\text{C} = 57.5$; $\text{H} = 7.3$; $\text{N} = 4.5$ per cent.

Ethyl cyanopentanetricarboxylate is a viscid, colourless oil, which, when placed in a freezing mixture, showed no signs of solidifying.

It is formed apparently quantitatively, according to the equation, given in the introduction (p. 417), since on one occasion, when four of the above quantities were worked up together, the yields obtained were ethyl cyanoacetate (190 grams), and ethyl cyanopentanetricarboxylate (680 grams), whereas the theoretical quantities are 240 and 686 grams respectively.

Pentane- $\alpha\gamma\epsilon$ -tricarboxylic Acid, $\text{CO}_2\text{H}\cdot\text{CH}(\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{H})_2$.

Ethyl cyanopentanetricarboxylate is with difficulty completely hydrolysed by boiling with mineral acids, especially when the operation is carried out in a reflux apparatus, and the alcohol formed cannot escape. This behaviour caused great difficulties at first, and a number of experiments had to be made before the best conditions for hydrolysis were discovered; now that these have been determined, the yield of acid is almost quantitative.

The pure cyano-ester (100 grams) is mixed with concentrated hydrochloric acid (200 c.c.) in a litre flask fitted with a ground-in air condenser, and carefully heated just to boiling on a sand-bath.

In the course of about half an hour, the oil will have completely dissolved, and care is necessary at this stage to avoid loss owing to frothing due to the elimination of carbon dioxide. After 1 hour, the air-tube is removed and the alcohol allowed to escape, a further quantity of hydrochloric acid (50—100 c.c.) is added, and the boiling continued in the open flask for 8 hours. The crystals of pentanetricarboxylic acid mixed with ammonium chloride, which will have separated overnight, are collected at the pump, washed with concentrated hydrochloric acid, and the filtrate again boiled in an open flask, when a further crop of crystals will be obtained. These are treated in the same way as the first crop, and the boiling of the filtrate and the whole cycle of operations continued as long as crystals continue to separate. The last mother liquors, which have a brown colour, are evaporated on the water-bath and the viscid syrup set aside to crystal-

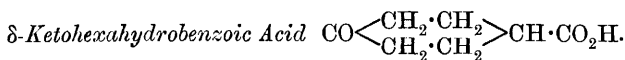
lise; the crude acid is then placed in contact with porous porcelain, when in the course of a few days it will have become almost white. The crops of crystals are combined, thoroughly dried on the water-bath, powdered, and extracted with pure ether,* preferably in a Soxhlet apparatus, by which means the acid is dissolved, and separated from the insoluble ammonium chloride. The concentrated ethereal solution deposits the pure acid in crystalline crusts, which are collected and washed with ether, and from the mother liquors the remainder of the acid is obtained by concentrating and recrystallising either from ether or from hydrochloric acid.

0.1627 gave 0.2801 CO_2 and 0.0874 H_2O . $\text{C} = 47.0$; $\text{H} = 6.0$.

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

Pentane- α - γ -tricarboxylic acid melts at 116 — 118° , and has already been prepared by Emery (*Ber.*, 1891, 24, 284) from ethyl pentane-tetracarboxylate, $(\text{CO}_2\text{Et})_2\text{C}(\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et})_2$, and by Bottomley and Perkin (*Trans.*, 1900, 77, 299) from ethyl pentanehexacarboxylate, $(\text{CO}_2\text{Et})_2\text{CH}\cdot\text{CH}_2\cdot\text{C}(\text{CO}_2\text{Et})_2\cdot\text{CH}_2\cdot\text{CH}(\text{CO}_2\text{Et})_2$, by hydrolysis, but the previously observed melting points were rather too low.

The process given in this paper is by far the most suitable for the preparation of large quantities of this acid.



This acid may be obtained in a variety of ways from pentanetricarboxylic acid, as, for example, by the distillation of the ammonium salt or, better, by heating the sodium salt with acetic anhydride under exactly the same conditions as those described in the preparation of ketodimethylpentamethylenecarboxylic acid from dimethylbutanedicarboxylic acid (*Trans.*, 1904, 85, 138), but, as the result of a large number of experiments, the following process, which should be followed exactly, was found to give by far the most satisfactory results. The pure tribasic acid, in quantities of not more than 15 grams, is heated with twice its weight of acetic anhydride for 6 hours, the acetic acid and excess of acetic anhydride are then distilled off, the heating being continued until a thermometer, immersed in the liquid, registers 180° .

The residue is then transferred to a distilling flask connected with the pump and heated in a metal-bath under 15 mm. pressure, the thermometer being in the liquid during the first stages of the opera-

* It is important that the acid should be heated until every trace of hydrogen chloride has been removed and the ether quite free from alcohol; otherwise, partial etherification takes place and the acid does not crystallise.

tion. Some acetic anhydride passes over, and when the temperature reaches $200-210^\circ$, at which it is kept for 10 minutes, carbon dioxide is evolved and the pressure rises. The operation is suspended until the pressure is again reduced to 15 mm., when the heating at 220° is continued and, as soon as the evolution of carbon dioxide is seen to slacken considerably, the thermometer is drawn up to the usual position and the contents of the flask rapidly distilled until the temperature rises to 250° , the considerable brown residue remaining in the flask being neglected.

The distillate, which from 15 grams of tribasic acid weighs about 7 grams, is dissolved in a little water, mixed with semicarbazide hydrochloride (5 grams) and sodium acetate (5 grams), and heated just to boiling. After remaining overnight, the sparingly soluble semicarbazone (p. 427) is collected, washed with water, dissolved in hot dilute hydrochloric acid, and repeatedly extracted with ether. On evaporating the ethereal solution, a pale yellow oil is obtained which solidifies completely on cooling and consists of practically pure δ -keto-hexahydrobenzoic acid.

This is the most direct way, if small quantities only of the keto-acid are required, but in preparing the large quantities employed in this research the following method of purification was found to be more convenient and economical.

The distillate from the decomposition of 50 grams of the tribasic acid is fractionated under reduced pressure (15 mm.), when a large fraction passes over at $200-225^\circ$, leaving a viscid, brown residue in the flask. On refractionating, practically the whole distills at $205-215^\circ$ under the same pressure and solidifies almost completely on cooling, and the acid thus obtained, after remaining in contact with porous porcelain for a few days, is pure enough for most purposes, and in this form* it was, unless otherwise stated, used in the experiments described in this paper. For the analysis, the acid was purified by conversion into the semicarbazone and then recrystallised from a mixture of benzene and light petroleum.

0.1711 gave 0.3689 CO_2 and 0.1092 H_2O . C = 58.8; H = 7.1.

0.1523 „ 0.3288 CO_2 „ 0.0960 H_2O . C = 58.8; H = 7.0.

$\text{C}_7\text{H}_{10}\text{O}_3$ requires C = 59.1; H = 7.0 per cent.

δ -Keto-hexahydrobenzoic acid melts at about $67-68^\circ$ with a slight previous softening, and is readily soluble in alcohol, ether, or benzene, but sparingly so in light petroleum; it dissolves readily in cold water, and is soluble in almost all proportions in hot water, from which it separates, on cooling, in magnificent groups of needles.

* When purified in this way, the yield of keto-acid from 1 kilo. of ethyl β -iodo-propionate varied, in different experiments, from 130—160 grams.

The crystals thus obtained were dried at 40° and found to contain one molecule of water of crystallisation.

0.1782 gave 0.3433 CO_2 and 0.1176 H_2O . $\text{C} = 52.5$; $\text{H} = 7.3$.

$\text{C}_7\text{H}_{10}\text{O}_3 \cdot \text{H}_2\text{O}$ requires $\text{C} = 52.5$; $\text{H} = 7.5$ per cent.

The direct determination of the water of crystallisation was difficult, owing to the fact that the acid is slightly volatile at 100° , but, after heating at 80° until practically constant, 0.5096 gram lost 0.0592 gram, or 11.5 per cent., whereas the formula $\text{C}_7\text{H}_{10}\text{O}_3 \cdot \text{H}_2\text{O}$ requires 11.3 per cent. of water. On titration, 0.2177 of the crystals neutralised 0.0539 NaOH , whereas this amount of an acid, $\text{C}_7\text{H}_{10}\text{O}_3 \cdot \text{H}_2\text{O}$, should neutralise 0.0544 of the alkali.

Formation of δ -Keto-hexahydrobenzoic Acid from the Sodium Salt of Pentane- $\alpha\gamma\epsilon$ -tricarboxylic Acid by the Action of Acetic Anhydride, and from the Ammonium Salt by Distillation.

In the first experiment, the pure tribasic acid (41 grams) was dissolved in water, mixed with sodium carbonate (33 grams), and evaporated to dryness; the dry salt was powdered and passed through a fine sieve and then heated with acetic anhydride at 165° for 4 hours, when large quantities of carbon dioxide were eliminated.

The product was dissolved in water, mixed with semicarbazide hydrochloride (20 grams), when, after two days, a cake of the semicarbazone of δ -keto-hexahydrobenzoic acid had separated, and this was found to weigh 7 grams.

In the second experiment, 14 grams of the pure acid were dissolved in excess of ammonia and evaporated to dryness. The viscid semi-solid mass was first heated under the ordinary pressure, when a quantity of ammonia and steam was given off and, as soon as the temperature of the liquid had risen to 150° , the whole was transferred to the vacuum distillation apparatus and the heating continued under 20 mm. pressure. The mass soon solidified completely, then melted again and gave off a quantity of gas, and much oil distilled over. The distillate, on treatment with semicarbazide hydrochloride and sodium acetate, yielded 3 grams of the semicarbazone of δ -keto-hexahydrobenzoic acid.

The Methyl and Ethyl Esters, the Oxime, and the Semicarbazone of δ -Keto-hexahydrobenzoic Acid.

Methyl δ -Keto-hexahydrobenzoate, $\text{CO}(\text{CH}_2 \cdot \text{CH}_2)_2 \text{CH} \cdot \text{CO}_2 \text{Me}$.—A quantity of this ester was prepared by digesting the keto-acid with methyl alcohol and sulphuric acid in the usual way, but the yield was

very poor owing to the formation of considerable quantities of methyl carboxyhexamethenylketo-hexahydrobenzoate (see p. 429).

It is a colourless oil which boils at 140° under 20 mm. pressure.

0.1824 gave 0.4089 CO_2 and 0.1295 H_2O . $\text{C} = 61.2$; $\text{H} = 7.9$.

$\text{C}_8\text{H}_{12}\text{O}_8$ requires $\text{C} = 61.5$; $\text{H} = 7.7$ per cent.

Ethyl δ -Keto-hexahydrobenzoate, $\text{CO}(\text{CH}_2 \cdot \text{CH}_2)_2\text{CH} \cdot \text{CO}_2\text{Et}$.—This ester may be obtained, in an almost quantitative yield, by digesting the keto-acid (10 grams) with 40 grams of a 3 per cent. solution of hydrogen chloride in absolute alcohol in a reflux apparatus for 6 hours. The product is mixed with 3 times its volume of ether, water is then added, and the ethereal solution separated and washed 3 times with water and once with dilute sodium carbonate.

After drying over calcium chloride and distilling off the ether, an oil is obtained which distils almost constantly at 158° (40 mm.), and consists of pure ethyl δ -keto-hexahydrobenzoate.

0.1417 gave 0.3279 CO_2 and 0.1061 H_2O . $\text{C} = 63.1$; $\text{H} = 8.3$.

$\text{C}_9\text{H}_{14}\text{O}_8$ requires $\text{C} = 63.5$; $\text{H} = 8.2$ per cent.

δ -Ketoxime-hexahydrobenzoic Acid, $(\text{OH})\text{N}:\text{C}(\text{CH}_2 \cdot \text{CH}_2)_2\text{CH} \cdot \text{CO}_2\text{H}$.—In preparing this oxime, the pure acid (2 grams) was dissolved in a little water, mixed with a strong solution of hydroxylamine hydrochloride (2 grams) and caustic potash (4 grams), and after remaining for 2 days, the product was acidified and extracted at least 15 times with ether. The ethereal solution was dried over calcium chloride and evaporated, and the viscid, oily residue, which gradually became semi-solid, left in contact with porous porcelain until quite dry. The substance was then dissolved in ether and the ethereal solution evaporated to a small bulk, when, on cooling, the oxime gradually separated in crystalline crusts.

0.1704 gave 0.3336 CO_2 and 0.1080 H_2O . $\text{C} = 53.4$; $\text{H} = 7.0$.

0.2014 „ 14.8 c.c. nitrogen at 11° and 748 mm. $\text{N} = 8.6$.

$\text{C}_7\text{H}_{11}\text{NO}_8$ requires $\text{C} = 53.5$; $\text{H} = 7.0$; $\text{N} = 8.9$ per cent.

δ -Ketoxime-hexahydrobenzoic acid, melts at about 147° and is sparingly soluble in dry ether, chloroform, light petroleum, or benzene, but readily so in hot water or methyl alcohol.

The Semicarbazone of δ -Keto-hexahydrobenzoic acid,
 $\text{NH}_2 \cdot \text{CO} \cdot \text{NH} \cdot \text{N}:\text{C}(\text{CH}_2 \cdot \text{CH}_2)_2\text{CH} \cdot \text{CO}_2\text{H}$.

When keto-hexahydrobenzoic acid is dissolved in a little water and mixed with a solution of semicarbazide hydrochloride and sodium

acetate, the semicarbazone separates at once as a sandy, crystalline powder.

0.1605 gave 28.7 c.c. nitrogen at 17° and 761 mm. $N = 20.8$.

$C_8H_{13}O_3N_3$ requires $N = 21.2$ per cent.

This semicarbazone softens at about 194° and decomposes at 200°; it is very sparingly soluble in water and in alcohol. It dissolves readily in hydrochloric acid with liberation of the keto-acid, which may then be extracted with ether (see p. 425).

*Action of Phenylhydrazine on δ -Ketohehexahydrobenzoic Acid. Formation of Tetrahydrocarbazole-p-carboxylic Acid.**

A solution of the pure keto-acid (1 gram) in water was mixed with freshly distilled phenylhydrazine (2 grams) dissolved in dilute acetic acid, when, in a short time, pale yellow drops separated which, doubtless, consisted of hydrazone of the keto-acid. The substance showed, however, no signs of crystallising, and therefore no attempts were made to analyse it; it is also evidently an unstable substance, since it rapidly became brown and gave off gas. The freshly prepared oily hydrazone dissolves in warm concentrated hydrochloric acid, and, if the solution is heated just to boiling and then poured into cold water, an ochre-coloured precipitate of crude tetrahydrocarbazolecarboxylic acid separates.

The precipitate was collected at the pump, washed well with water, and left in contact with porous porcelain until quite dry; it was then digested with benzene, filtered from a brown, amorphous impurity, and the benzene solution evaporated to a small bulk.

The concentrated solution gradually deposited a crust of warty crystals which was collected, washed with benzene, dried at 100°, and analysed.

0.1635 gave 0.4364 CO_2 and 0.0890 H_2O . $C = 72.8$; $H = 6.0$.

0.2184 „ 11.4 c.c. nitrogen at 15° and 749 mm. $N = 6.1$.

$C_{13}H_{13}O_2N$ requires $C = 72.6$; $H = 6.0$; $N = 6.5$ per cent.

Tetrahydrocarbazole-p-carboxylic acid melts at about 195° and is readily soluble in alcohol, but sparingly so in chloroform, light petroleum, or benzene. The solution in sodium carbonate decolorises permanganate instantaneously. The finely powdered substance dissolves readily in concentrated hydrochloric acid and is reprecipitated in flocks on dilution with water. When the acid is heated in a test-tube, it gives off gas and yields a crystalline sublimate which is only partially soluble in sodium carbonate and has a pronounced odour of indole.

* For the constitution of this acid, see p. 419.

Carboxyhexamethenyl- δ -keto-hexahydrobenzoic Acid.

As explained in the introduction (p. 419), the ester of this acid was accidentally obtained in the course of an experiment made with the object of preparing methyl δ -keto-hexahydrobenzoate from the acid by treatment with methyl alcohol and sulphuric acid in the usual way; the details of the experiment are as follows.

The acid (70 grams) was dissolved in methyl alcohol (200 c.c.), and concentrated sulphuric acid (50 c.c.) gradually added, the whole being well cooled during the addition. The mixture was digested for 4 hours in a reflux apparatus, and, when cold, mixed with 3 volumes of ether; water was then added and the ethereal solution separated and washed successively with water and dilute sodium carbonate. After drying over calcium chloride and evaporating, a viscid oil remained which, on fractionating under 20 mm. pressure, was readily separated into methyl δ -keto-hexahydrobenzoate boiling at 140° (see p. 426) and a yellow, viscid liquid boiling at 255° . The latter was analysed with the following results:

0.266 gave 0.6356 CO_2 and 0.178 H_2O . $\text{C} = 65.2$; $\text{H} = 7.4$.

$\text{C}_{16}\text{H}_{22}\text{O}_5$ requires $\text{C} = 65.3$; $\text{H} = 7.5$ per cent.

In order to obtain the free acid, this *methyl carboxyhexamethenyl- δ -keto-hexahydrobenzoate* was dissolved in methyl alcohol mixed with a methyl alcoholic solution of caustic potash (8 grams) and heated to boiling for half an hour. Water was then added and the solution evaporated until free from methyl alcohol; it was then acidified, when a viscid syrup separated which gradually solidified.

After remaining in contact with porous porcelain until quite free from oily impurity, the acid was dissolved in dry ether, the ethereal solution concentrated and allowed to remain, when the acid gradually separated as a hard, crystalline crust.

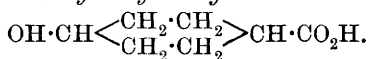
0.1508 gave 0.3474 CO_2 and 0.0958 H_2O . $\text{C} = 62.8$; $\text{H} = 7.0$.

$\text{C}_{14}\text{H}_{18}\text{O}_5$ requires $\text{C} = 63.1$; $\text{H} = 6.8$ per cent.

Carboxyhexamethenyl- δ -keto-hexahydrobenzoic acid melts at about 170° , but not sharply, since it softens a good deal below that temperature.

It is readily soluble in alcohol, but sparingly so in ether and cold water; it dissolves, however, in hot water, and separates on cooling, in colourless, microscopic needles. The solution in dilute sodium carbonate instantly decolorises permanganate, and when the aqueous solution of the acid is boiled with semicarbazide hydrochloride and sodium acetate, a very sparingly soluble semicarbazone is formed which was not further examined.

*Reduction of δ -Ketohehexahydrobenzoic Acid. Formation of
trans- δ -Hydroxyhexahydrobenzoic Acid,*



Sodium amalgam readily reduces δ -ketohehexahydrobenzoic acid to the above hydroxy-acid, and, in studying this reduction, the keto-acid, in quantities of 5 grams, was dissolved in a slight excess of dilute sodium carbonate solution and treated with 150 grams of 4 per cent. sodium amalgam. The reduction was carried out in a large porcelain beaker, fitted with a mechanical stirrer and cooled externally by ice, and the sodium amalgam was added in quantities of 30 grams, a stream of carbon dioxide being passed during the whole operation. The product from 5 of these operations was separated from the mercury, acidified and extracted 10 times with ether, and since, even then, 8 grams of the reduced acid remained in the mother liquor, the extraction was continued by shaking on the machine with large quantities of ether. The combined ethereal extracts were dried over calcium chloride and evaporated to a small bulk, when the hydroxy-acid (15 grams) gradually separated in colourless nodules, and was further purified by a second recrystallisation from ether.

0.1860 gave 0.3982 CO_2 and 0.1391 H_2O . C = 58.4; H = 8.3.

0.1676 „ 0.3574 CO_2 „ 0.1254 H_2O . C = 58.2; H = 8.3

$\text{C}_7\text{H}_{12}\text{O}_3$ requires C = 58.3; H = 8.3 per cent.

trans- δ -Hydroxyhexahydrobenzoic acid melts at 120—121°, and is readily soluble in water or alcohol, but sparingly so in cold dry ether, chloroform, or benzene. This acid shows no tendency to yield a lactone; when heated, it distils, and the oily distillate, which solidifies on rubbing, is completely soluble in cold sodium carbonate solution, and when the acid is boiled with 25 per cent. sulphuric acid, no signs of lactone formation could be detected.

The ethereal mother liquors of the *trans*-hydroxy-acid were evaporated to dryness and left for some days until the whole had become semi-solid. The mass was then spread on porous porcelain, and, when quite free from oil, recrystallised from ether, and in this way 5 grams of the pure *trans*-hydroxy-acid were obtained.

In order to see whether any *cis*-hydroxy-acid had been formed during the reduction of the keto-acid, the porous porcelain was broken up and extracted in a Soxhlet apparatus with ether, but only a small quantity of oil was obtained, and after distilling this under 30 mm. pressure the distillate was found to be completely soluble

in cold dilute sodium carbonate solution, showing that no trace of lactone was present, and thus proving that no *cis*-hydroxy-acid had been formed.

trans- δ -Bromohexahydrobenzoic Acid and its Conversion into Δ^3 -Tetrahydrobenzoic Acid,



and into γ -Bromohexahydrobenzoic Acid and $\gamma\delta$ -Dibromohexahydrobenzoic Acid.

When finely-powdered δ -hydroxyhexahydrobenzoic acid is mixed with hydrobromic acid (saturated at 0°), it dissolves, and even after several hours no separation takes place.

If, however, the solution is heated in a sealed tube at 100° for 30 minutes, a viscid, oily layer forms on the surface of the hydrobromic acid, and this gradually becomes semi-solid. After washing with water, contact with porous porcelain readily removes the oily impurity, and the residue crystallises readily from light petroleum (b. p. $70-80^\circ$) in colourless, glistening plates.

0.1388 gave 0.1254 AgBr. Br = 38.4.

$\text{C}_7\text{H}_{11}\text{O}_2\text{Br}$ requires Br = 38.6 per cent.

trans- δ -Bromohexahydrobenzoic acid softens at 160° and melts at about 167° , and is readily soluble in chloroform, benzene, or alcohol, but less so in cold light petroleum.

When the bromo-acid is boiled with water, hydrogen bromide is only slowly eliminated, and, indeed, the acid crystallises well from water if the operation is carried out moderately rapidly, and is then obtained in plates having a satiny lustre and exactly resembling benzoic acid, and, like this acid, the bromo-acid is also volatile in steam.

Δ^3 -Tetrahydrobenzoic Acid.—In preparing this acid, δ -bromohexahydrobenzoic acid was dissolved in a considerable excess of moderately concentrated sodium carbonate and the solution heated to boiling for half an hour. On acidifying, Δ^3 -tetrahydrobenzoic acid was precipitated as a colourless oil, and, after extracting with ether, the ethereal solution was dried over calcium chloride, evaporated, and the residue distilled under 25 mm. pressure.

With the exception of a small quantity of a higher boiling substance (probably δ -hydroxyhexahydrobenzoic acid, produced from the bromo-acid by hydrolysis), the whole passed over at $145-150^\circ$, and, on

subsequently distilling under the ordinary pressure, the acid was readily obtained pure as a colourless oil boiling constantly at 237° (748 mm.).

0.2348 gave 0.5700 CO_2 and 0.1686 H_2O . $\text{C} = 66.2$; $\text{H} = 8.0$.

0.1490 „ 0.3626 CO_2 „ 0.1064 H_2O . $\text{C} = 66.4$; $\text{H} = 7.9$.

$\text{C}_7\text{H}_{10}\text{O}_2$ requires $\text{C} = 66.6$; $\text{H} = 7.9$ per cent.

When placed in a freezing mixture, the distilled acid solidified completely, and the melting point, determined by placing a thermometer in the melting acid, was about 13° . Possibly, if the acid were left in contact with porous porcelain in order to remove any trace of oily impurity, a higher melting point than this might be observed, but the amount of material at my disposal did not allow of this being done. Δ^3 -Tetrahydrobenzoic acid has a most unpleasant odour, closely resembling that of allylacetic acid; it shows the properties of an unsaturated acid, since its solution in sodium carbonate decolorises permanganate instantly and the acid itself combines directly with both bromine and hydrogen bromide (see below). When the acid is exposed on a watch glass to the action of the air, very little change is noticed until after some days, and then a thin film of crystals forms on the surface, and these crystals appear to consist of benzoic acid, although this could not be established with certainty.

In any case, oxidation takes place only very slowly, and in this respect the Δ^3 -acid resembles the Δ^1 -acid and differs from the Δ^2 -acid, as the latter is rapidly oxidised to benzoic acid in contact with air. Δ^3 -Tetrahydrobenzoic acid shows no signs of being converted into a lactone when it is digested with dilute sulphuric acid.

γ -Bromohexahydrobenzoic Acid.— Δ^3 -Tetrahydrobenzoic acid dissolves readily and completely in four times its volume of aqueous hydrobromic acid (saturated at 0°) with evolution of heat, but the solution soon becomes cloudy, and in a short time a viscid oil separates on the surface of the hydrobromic acid. The oil gradually solidifies, and the aqueous layer becomes filled with colourless crystals.

After 12 hours, water is added, the pasty, crystalline mass collected at the pump, washed well, and left in contact with porous porcelain until quite dry. The residue crystallises from its warm dilute solution in light petroleum (b. p. 60 — 80°) in groups of flat needles, but from a hot concentrated solution the substance separates in glistening plates.

0.1712 gave 0.1552 AgBr . $\text{Br} = 38.6$.

$\text{C}_7\text{H}_{11}\text{O}_2\text{Br}$ requires $\text{Br} = 38.6$ per cent.

γ -Bromohexahydrobenzoic acid shrinks together at 110° and melts at about 122° , and repeated crystallisation did not alter this behaviour or make the melting point any sharper; it is practically insoluble in cold

light petroleum or cold water, but readily soluble in benzene, alcohol, or ether. It dissolves to a considerable extent in boiling water, and separates, on cooling, as a voluminous mass of glistening plates which closely resemble benzoic acid.

In its behaviour towards sodium carbonate, this γ -bromo-acid differs in a marked manner from the δ -bromo-acid (see above), since, after boiling for half an hour and acidifying, no sparingly soluble tetrahydrobenzoic acid separates. On extracting with ether, a very soluble oily acid is obtained, which rapidly becomes insoluble in sodium carbonate and develops the odour of a lactone. It is probable that the neutral oil produced in this way is the lactone of γ -hydroxyhexahydrobenzoic acid.

$\gamma\delta$ -Dibromohexahydrobenzoic Acid.—When the solution of tetrahydrobenzoic acid in chloroform is cooled to -10° and treated with bromine, the colour of the halogen disappears instantly, and only traces of hydrogen bromide are formed. As soon as the solution had acquired a permanent pale yellow tint, it was transferred to a large watch glass and left until the chloroform had evaporated. A viscid, colourless oil resulted which did not crystallise for some days, but ultimately solidified almost completely. The mass was rapidly washed with formic acid (sp. gr. 1.22) and recrystallised from this solvent, from which the dibromo-acid separates in small, glistening crystals.

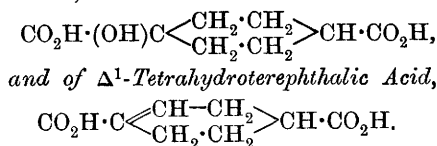
0.1444 gave 0.1888 AgBr. Br = 55.6.

$C_7H_{10}O_2Br_2$ requires Br = 55.9 per cent.

$\gamma\delta$ -Dibromohexahydrobenzoic acid melts at $84-86^\circ$, and is sparingly soluble in cold formic acid and light petroleum, but readily so in alcohol, ether, or chloroform. It dissolves readily in sodium carbonate, and, if the solution is boiled for 5 minutes and then acidified, nothing separates, but ether extracts a very readily soluble syrupy acid which, when kept, shows signs of crystallising.

Since this acid reduces ammoniacal silver solution, but does not decolorise permanganate, it is probably $\gamma\delta$ -dihydroxyhexahydrobenzoic acid produced from the dibromo-acid by hydrolysis.

Action of Hydrogen Cyanide on δ -Keto-hexahydrobenzoic Acid. Formation of the cis- and trans-Modifications of α -Hydroxyhexahydro-terephthalic Acid,



In the first experiments on the action of hydrogen cyanide on δ -keto-hexahydrobenzoic acid, the conditions recommended by Baeyer and Tutein (*Ber.*, 1889, 22, 2186) in the similar case of γ -keto-hexahydrobenzoic acid were employed, that is to say, the acid was mixed with potassium cyanide and the mixture treated with hydrochloric acid. The addition did not take place satisfactorily under these conditions, and, after several experiments, the following process, based on the observations of Lapworth (*Trans.*, 1903, 83, 995), was employed with excellent results. The pure acid (4 grams) was dissolved in a little warm water, cooled until crystallisation just commenced, and then mixed with pure potassium cyanide (5 grams) and 10 c.c. of a 15 per cent. solution of hydrocyanic acid. The liquid gradually darkened, and after 24 hours had become nearly black; it was mixed with a little hydrochloric acid and extracted 6 times with ether. After drying over calcium chloride and evaporating, a light brown syrup (5 grams) was obtained, which, on rubbing with a glass rod, rapidly became semi-solid. The mass was left in contact with porous porcelain until quite dry; the residue was dissolved in ether, the solution digested with animal charcoal, filtered, and concentrated. An equal volume of chloroform was then added and the ether distilled off, when a sandy, crystalline precipitate was soon deposited, which melted at 180° , and was easily identified as aminomalononitrile, $\text{NH}_2 \cdot \text{CH}(\text{CN})_2$, produced by the polymerisation of some of the hydrogen cyanide employed. The filtrate from this substance deposited, on spontaneous evaporation, a mass of crystals, which were collected and purified by re-dissolving in ether, adding chloroform, and distilling off the ether as before.

The glistening, pale yellow plates thus obtained consist of the nitrile of trans- α -hydroxyhexahydroterephthalic acid.

0.1805 gave 12.6 c.c. nitrogen at 14° and 774 mm. $\text{N} = 8.4$.

$\text{C}_8\text{H}_{11}\text{O}_3\text{N}$ requires $\text{N} = 8.3$ per cent.

The melting point of this nitrile is not sharp; it begins to shrink together at 125° and is completely melted at 140° . It is readily

soluble in water or methyl alcohol, but sparingly so in chloroform, benzene, or light petroleum. When heated in a test-tube, water is eliminated and an oil distils which does not solidify on cooling, and, since the solution of this oil in sodium carbonate does not decolorise permanganate, it may very probably be the corresponding cyano-lactone. When the nitrile is hydrolysed under the conditions stated below, it yields *trans*- α -hydroxyhexahydroterephthalic acid.

The chloroform mother liquors of this *trans*-nitrile contain the *cis*-modification, but, as this did not appear to crystallise readily, no attempt was made to isolate it in a condition suitable for analysis.

In preparing the *cis*- and *trans*-modifications of hydroxyhexahydroterephthalic acid in quantity, 20 grams of ketohexahydrobenzoic acid were converted into the mixed nitriles, and after extracting with ether, the oil was dissolved in 100 c.c. of concentrated hydrochloric acid and heated, first on the water-bath for three hours and then to boiling for one hour. The whole was evaporated to dryness, the crystalline cake was then ground up and digested with absolute alcohol, and after filtering from the ammonium chloride the alcoholic solution was evaporated almost to dryness. The residue, which still contained ammonium chloride, was dissolved in excess of dilute barium hydroxide and boiled until the evolution of ammonia had completely ceased, the barium was then exactly removed by sulphuric acid, and the filtrate from the barium sulphate evaporated almost to dryness.

After remaining for 24 hours, the crystalline crust was left in contact with porous porcelain until quite dry, dissolved in water, digested with animal charcoal, and evaporated considerably, when a mass of white, nodular crystals of the *trans*-hydroxy-acid gradually separated. These were collected and purified by crystallising twice from water, when the substance was obtained in hard crystals containing one molecule of water of crystallisation.

After being exposed to the air for 6 days, the following results were obtained on analysis:

0.1654 gave 0.2822 CO_2 and 0.1023 H_2O . $\text{C} = 46.5$; $\text{H} = 6.9$.

$\text{C}_8\text{H}_{12}\text{O}_5, \text{H}_2\text{O}$ requires $\text{C} = 46.6$; $\text{H} = 6.8$ per cent.

0.2416 gram, heated at 90° until constant, lost 0.0221 gram or 9.1 per cent., whereas $\text{C}_8\text{H}_{12}\text{O}_5, \text{H}_2\text{O}$ contains 8.8 per cent. of water. The anhydrous acid was also analysed.

0.1852 gave 0.3488 CO_2 and 0.1064 H_2O . $\text{C} = 51.3$; $\text{H} = 6.4$.

$\text{C}_8\text{H}_{12}\text{O}_5$ requires $\text{C} = 51.1$; $\text{H} = 6.4$ per cent.

On titration with decinormal caustic soda, 0.0956 gram required for

neutralisation 0.0408 NaOH, whereas this amount of a dibasic acid, $C_8H_{12}O_5$, should neutralise 0.0407 NaOH.

trans- α -Hydroxyhexahydroterephthalic acid melts at 228—230° with decomposition, and when heated in small quantities in a test-tube, water is eliminated and a crystalline sublimate of Δ^1 -tetrahydroterephthalic acid is obtained (p. 437). It is readily soluble in water or alcohol, but sparingly so in cold ether, chloroform, benzene, or concentrated hydrochloric acid. The neutral solution of the ammonium salt gives no precipitate with barium or calcium chloride, but a heavy caseous precipitate with lead acetate; with copper sulphate, a turbidity is produced, and, on warming, a pale blue, amorphous precipitate separates.

cis- α -Hydroxyhexahydroterephthalic Acid.—The aqueous mother liquors of the *trans*-acid yielded, on further concentration, first an additional small crop of the same acid, and afterwards the *cis*-hydroxy-acid separated in masses of irregularly shaped crystals. These were collected and purified by repeated crystallisation from water, the substance being dried at 100° before analysis.

0.1594 gave 0.2958 CO_2 and 0.0912 H_2O . C = 50.6; H = 6.4.

The substance was then recrystallised from ether and again analysed.

0.1832 gave 0.3428 CO_2 and 0.1052 H_2O . C = 51.0; H = 6.4.

$C_8H_{12}O_5$ requires C = 51.1; H = 6.4 per cent.

On titration, 0.1220 gram neutralised 0.051 gram NaOH, whereas this amount of a dibasic acid, $C_8H_{12}O_5$, should neutralise 0.052 NaOH.

cis- α -Hydroxyhexahydroterephthalic acid melts at 168—170°, and is readily soluble in water and alcohol, but sparingly so in chloroform, benzene, or ether. If, however, the finely-powdered substance is digested in a reflux apparatus with a large quantity of ether, it dissolves, and, after concentrating considerably, the pure acid gradually separates in hard, crystalline crusts. When crystallised from water, the hard nodules obtained do not, like the *trans*-acid, contain water of crystallisation, since the air-dried substance loses only very slightly in weight on drying at 90°.

If a small quantity of the dry acid is heated in a test-tube, it first melts and then gives off water, and a sublimate of Δ^1 -tetrahydroterephthalic acid forms on the cooler portions of the tube.

When the *cis*-hydroxy-acid is mixed with concentrated sulphuric acid and warmed to about 60°, carbon monoxide is evolved in quantity, and if, when the evolution has ceased, the pale yellow liquid is poured into water, a white, crystalline precipitate separates.

This was collected and found to consist of pure Δ^1 -tetrahydro-

terephthalic acid, and from the filtrate a quantity of δ -keto-hexahydrobenzoic acid was obtained by extraction with ether and identified by conversion into the semicarbazone.

The *cis*-hydroxy-acid shows a curious behaviour when heated with fuming hydrobromic acid (saturated at 0°) in a sealed tube in a boiling water-bath. The acid dissolves, and then a gas (presumably carbon dioxide) is slowly given off and, on diluting the yellow solution with water, a quantity of a very voluminous, white, amorphous precipitate separates. This substance, which contains bromine, seems to be formed quantitatively; it is practically insoluble in water, but dissolves in sodium carbonate. It separates from dilute formic acid apparently as a microcrystalline precipitate; this shrinks together at 160—165° and has no definite melting point. This substance was not further investigated, but it was noticed that the *trans*-hydroxy-acid also appeared to show the same behaviour on heating with hydrobromic acid.

The amount of the mixed hydroxyhexahydroterephthalic acids obtained by the addition of hydrogen cyanide to δ -keto-hexahydrobenzoic acid and subsequent hydrolysis was upwards of 70 per cent. of the theoretical, and it is interesting to note that in this way a very much larger amount of the *cis*-acid is produced than of the *trans*-acid.

Δ^1 -Tetrahydroterephthalic Acid.—As explained above, this acid is produced when either the *cis*- or *trans*-modification of α -hydroxyhexahydroterephthalic acid is heated. In investigating this decomposition, 5 grams of the pure *cis*-acid was distilled under 10 mm. pressure, the sublimate was dissolved in hot sodium carbonate, the solution decolorised with animal charcoal, concentrated, and acidified, when the tetrahydro-acid separated as a microcrystalline deposit.

This was collected and recrystallised from much water.

0.1406 gave 0.2894 CO₂ and 0.0764 H₂O. C = 56.2; H = 6.0.

C₈H₁₀O₄ requires C = 56.4; H = 5.9 per cent.

This acid melted above 300° and reduced permanganate, and was evidently identical with the Δ^1 -tetrahydroterephthalic acid described by Baeyer (*Annalen*, 1888, 245, 160). In order that there should be no doubt as to its identity, the acid was converted into its methyl ester by digesting with a five per cent. solution of hydrogen chloride in methyl alcohol. The methyl ester, thus obtained, crystallised from dilute methyl alcohol in needles and melted at 38—39°, whereas Baeyer gives 39° as the melting point of methyl Δ^1 -tetrahydroterephthalate.

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VOL. LXXXV. G G

438 KIPPING AND SALWAY: ARRANGEMENT IN SPACE OF THE

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