LXXXIX.—*Experiments on the Synthesis of Camphoric Acid. Part II.**

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In 1896, the view was first expressed by one of us (Perkin, *Proceedings*, 1896, 12, 191) that most of the decompositions of camphoric acid might readily be explained with the aid of the formula

and this formula for camphoric acid was afterwards independently suggested by Bouveault (*Bull. Soc. Chim.*, 1897, [iii], 17, 990), and is now generally known on the continent as "Bouveault's formula." In view of the unusual difficulties which have been found to attend the determination of the constitution of camphoric acid by analytical methods, it was decided some years ago to undertake a long series of experiments with a view of preparing this acid synthetically. The present paper deals with the results which were obtained in an attempt to prepare an acid of the formula given above, and although this result so far has not been realised, our experiments have nevertheless led to the preparation and characterisation of a number of substances of considerable interest which are described in the following pages.

In attempting the synthesis, we proposed in the first place to prepare *αα*₁-methylisomethyl-α-hydroxysuccinic acid,

as it was thought that it might be found possible to eliminate water at the points marked *, in which case the acid represented by the formula at the commencement of this paper would be obtained. It will be seen that this research is very much on the same lines as that carried out by Bentley and Perkin (*Trans.*, 1898, 73, 45), who prepared isobutylmethylhydroxyglutaric acid,

* Part I., *Trans.*, 1898, 73, 45.

with a view of removing water at the points *, and of thus obtaining an acid of the formula

which may possibly be camphoric acid.

The latter change could, however, not be brought about, principally on account of the great tendency which the hydroxy-acid shows to pass into a lactone by the elimination of water between the COOH and OH groups situated in the γ -position, a possibility which is not present in the case of the hydroxy-acid which we are considering in this paper. After many unsuccessful attempts, we have ultimately succeeded in preparing *methylisoamylhydroxysuccinic acid* by the following series of reactions. Ethylic isoamylacetoacetate,

was first caused to combine with hydrogen cyanide by treating its solution in ether at a low temperature with potassium cyanide and hydrochloric acid, and in this way a good yield of *ethylic α -isoamyl- $\beta\beta$ -hydroxycyanobutyrate*, $\text{CH}_3 \cdot \text{C}(\text{OH})(\text{CN}) \cdot \text{CH}(\text{C}_5\text{H}_{11}) \cdot \text{COOC}_2\text{H}_5$, was obtained.

When this substance is treated with alcohol and hydrochloric acid, the two most important products are *methylisoamylhydroxysuccinimide*,

a solid, crystalline substance melting at 104° , and an oil which is doubtless ethylic methylisoamylhydroxysuccinate,

The imide, on boiling with sodium carbonate, yields, in the first place, the corresponding amide, and this is then very slowly further decomposed with elimination of ammonia and formation of the methylisoamylhydroxysuccinic acid,

which was required for our experiments. This interesting acid crystallises well, melts at 66° , and yields a silver salt of the formula $\text{C}_{10}\text{H}_{16}\text{Ag}_2\text{O}_5$, and its method of formation and the study of its properties leave no doubt that it has the constitution assigned to it here. When this acid is distilled, it readily loses water, and an oil passes over at about 260° , which, after careful investigation, has been found

to consist of *methylisoamylmaleic anhydride*, formed according to the equation

that is to say, the anhydride of an unsaturated acid is formed, and not of the saturated acid containing a ring of five atoms which we had hoped to obtain.

Methylisoamylmaleic anhydride dissolves in potash solution, but on acidifying, the anhydride and not the acid separates, and, in this respect, the substance behaves exactly like xeronic acid,

which, when set free from solutions of its salts, is obtained in the form of its anhydride.

When treated with aniline, methylisoamylmaleic anhydride yields an *anil*, $\text{C}_{16}\text{H}_{19}\text{NO}_2$ (m. p. 70°), and when boiled with hydriodic acid and phosphorus, it is readily reduced, with formation of a mixture of *cis*- and *trans*-methylisoamylsuccinic acids,

the former of which melts at 92° and the latter at 142° (compare W. Trevor Lawrence, *Proc.*, 1899, 15, 163).

In continuation of our experiments, we next investigated the action of reducing agents on ethylic isoamylacetoacetate in order to determine whether the α -isoamyl- β -hydroxybutyric acid, $\text{CH}_3 \cdot \text{CH}(\text{OH}) \cdot \text{CH}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$, which is formed in this way would, on distillation, lose water with formation of a ring compound,

or whether, as in the case of methylisoamylhydroxysuccinic acid, an unsaturated acid, $\text{CH}_3 \cdot \text{CH} : \text{C}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$, would be formed.

If the ring compound were formed, the synthesis would be most important, since, on the supposition that the formula for camphoric acid represented at the commencement of this paper is correct, the product would be *dihydroisolauronic acid* (compare *Trans.*, 1898, 73, 810).

On investigating the matter, it was found that the hydroxy-acid, on distillation, yields the unsaturated acid, and that apparently no trace of the ring acid is formed in this way.

The α -isoamylcrotonic acid, $\text{CH}_3 \cdot \text{CH} : \text{C}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$, thus obtained

is a colourless oil which distils at 240° , and its constitution is proved by the fact that it yields isobutylacetic acid, $C_4H_9 \cdot CH_2 \cdot COOH$, on oxidation.

Lastly, we investigated the action of hydrogen cyanide on isoamylacetone, $C_5H_{11} \cdot CH_2 \cdot CO \cdot CH_3$, and after hydrolysing the product we obtained in this way small quantities of *α-hydroxy-β-isoamylisobutyric acid*, $C_5H_{11} \cdot CH_2 \cdot C(OH)(CH_3) \cdot COOH$, which melts at 66° and is isomeric with the isoamylhydroxybutyric acid mentioned above. Unfortunately, the yield is scarcely more than 1 per cent. of the theoretical, and therefore we were unable to investigate it as completely as we could have wished.

Preparation and Hydrolysis of Ethylic α-Isoamyl-β-hydroxycyanobutyrate, $CH_3 \cdot C(CN)(OH) \cdot CH(C_5H_{11}) \cdot COOC_2H_5$.

In endeavouring to prepare this substance by the addition of hydrogen cyanide to ethylic isoamylacetoacetate, experiments were made under the most varied circumstances, in order to determine the best conditions, and ultimately it was found that the following method, which is very similar to that described by Haller and Held (*Ann. Chim. Phys.*, 1891, [vi], 23, 145), gave the most satisfactory result. Ethylic isoamylacetoacetate (50 grams) is dissolved in ether (50 grams), finely powdered potassium cyanide (25 grams) added, and then the calculated quantity of hydrochloric acid (about 40 c.c. of the ordinary concentrated acid) gradually run in with constant shaking, the temperature being kept below -10° during the whole operation. After standing for 24 hours at the ordinary temperature, the ethereal solution is washed with water, dried over calcium chloride, and the ether distilled off, when a thick, yellow oil is obtained, which consists of crude *ethylic isoamylhydroxycyanobutyrate*, and in this form it was used in all subsequent experiments. The hydrolysis of this crude ethereal salt was carried out by two methods which give different results, namely, (a) by means of hydrochloric acid, and (b) by means of sulphuric acid.

(a) *Hydrolysis by means of Hydrochloric Acid*.—The crude cyano-ethereal salt (100 grams) was dissolved in absolute alcohol (150 grams), and the whole saturated with hydrogen chloride, the temperature being kept below 20° by cooling with water. After standing overnight, the product was heated in a reflux apparatus on the water-bath for 2 hours, hydrogen chloride being passed through during the whole time, when large quantities of ammonium chloride separated. The alcoholic solution was poured into water and the oil, which separated, extracted with ether; the ethereal solution was washed with water and very dilute sodium carbonate solution and distilled in steam, in order to remove isoamylacetone, $C_5H_{11} \cdot CH_2 \cdot CO \cdot CH_3$. This substance, which

is always formed, and sometimes in considerable quantity, is evidently produced by the hydrolysis of the unchanged ethylic isoamylacetate present in the crude ethylic isoamylhydroxycyanobutyrate employed in these experiments. The oil remaining in the distillation flask may be treated in two ways: (a) it is shaken with dilute ammonia, and the aqueous solution, after filtering from the undissolved oil, is rapidly acidified, when a crystalline precipitate separates, which consists for the most part of *methylisoamylhydroxysuccinimide* (p. 914), or (b) the oil is boiled for about an hour with dilute sodium carbonate, when, after filtering and acidifying, a precipitate of *methylisoamylhydroxysuccinamide* is obtained (p. 914). In either case, the oil remaining undissolved, which still contains much nitrogen, is heated in a sealed tube with alcoholic hydrogen chloride for 5 hours at 150°.

After diluting with water and extracting with ether in the usual way, the oil which is obtained on distilling off the ether is fractionated under reduced pressure (20 mm.), and is thus easily separated into three fractions boiling at 30—90°, 120—130°, and 155—175° respectively. The first fraction, on distillation under ordinary conditions, yields a quantity of an oil boiling at 162—163°, and which was found to be *isoamylacetone*.

0.1783 gave 0.4899 CO₂ and 0.2015 H₂O. C = 74.93; H = 12.56.

C₈H₁₁·CH₂·CO·CH₃ requires C = 75.0; H = 12.50 per cent.

The second fraction was redistilled, when the greater portion passed over at 120° under 18 mm. pressure, and on analysis was found to consist of ethylic isoamylacetate.

0.2095 gave 0.5049 CO₂ and 0.1863 H₂O. C = 65.73; H = 9.88.

CH₃·CO·CH(C₅H₁₁)·COOC₂H₅ requires C = 66.0; H = 10.0 per cent.

On repeatedly fractionating the highest fraction, a large quantity of an oil was obtained which boiled remarkably constantly at 163° under 20 mm. pressure, and on analysis gave numbers agreeing fairly well with those required for the ethereal salt of an acid of the same composition as camphoric acid.

0.2173 gave 0.5130 CO₂ and 0.1870 H₂O. C = 64.38; H = 9.56.

0.2029 „ 0.4803 CO₂ „ 0.1726 H₂O. C = 64.55; H = 9.45.

C₈H₁₄(COOC₂H₅)₂ requires C = 65.62; H = 9.37 per cent.

It will be shown later that this oil, although boiling so constantly, is a mixture of the ethereal salts of methylisoamylmaleic acid and methylisoamylhydroxysuccinic acid, the latter predominating.

(b) *Hydrolysis by means of Sulphuric Acid*.—After a considerable

quantity of ethylic isoamylhydroxycyanobutyrate had been hydrolysed by means of hydrochloric acid, experiments were made with sulphuric acid in the hope that the hydrolysis could, in this way, be completed without the necessity of using sealed tubes, and this was found to be the case. The cyano-ethereal salt (100 grams) was dissolved in alcohol (200 grams), concentrated sulphuric acid (300 grams) was slowly added, and the mixture, after standing for 12 hours, heated for 8 hours on the water-bath; water was then added and the ethereal salt extracted with ether in the usual way. On fractionating the product under reduced pressure, isoamylacetone first passed over, but in less quantity than in the case of the hydrochloric acid hydrolysis; the greater portion of the residue then distilled between 155° and 175° under 20 mm. pressure, and, on examination, was found to have the same composition as the oil of this boiling point obtained in the case of the hydrochloric acid hydrolysis. A small quantity which distilled above 175° deposited, on standing, some crystals of methylisoamylhydroxysuccinimide. If, then, the object is to prepare this imide, the hydrochloric acid hydrolysis should be employed; but if, on the other hand, methylisoamylmaleic anhydride (p. 916) is required, then the sulphuric acid hydrolysis is much to be preferred as being less laborious.

It was stated in the previous section, that when ethylic isoamylhydroxycyanobutyrate is hydrolysed with alcohol and hydrochloric acid and the product extracted with ammonia, a solid substance separates on acidifying, which, on examination, has been found to be

methylisoamylhydroxysuccinimide, $\begin{array}{c} \text{CH}_3 \cdot \text{C}(\text{OH}) \cdot \text{CO} \\ \text{C}_5\text{H}_{11} \cdot \text{CH} - \text{CO} \end{array} > \text{NH}$. This substance crystallises from light petroleum in colourless needles, melts at 104° , and is readily soluble in alcohol, ether, and benzene, but only sparingly so in cold, light petroleum and water. When heated in small quantities, it distils, apparently without decomposition.

0.1631 gave 0.3610 CO_2 and 0.1280 H_2O . $\text{C} = 60.36$; $\text{H} = 8.72$.

0.2482 „ 14.65 c.c. nitrogen at 20° and 766 mm. $\text{N} = 6.88$.

$\text{C}_{10}\text{H}_{17}\text{NO}_3$ requires $\text{C} = 60.30$; $\text{H} = 8.54$; $\text{N} = 7.04$ per cent.

When methylisoamylhydroxysuccinimide is boiled with sodium carbonate solution, it gradually dissolves and, on acidifying, the corresponding *methylisoamylhydroxysuccinamide* is obtained as a white, sparingly soluble precipitate which crystallises from water in plates and melts at 183° .

0.1682 gave 0.3395 CO_2 and 0.1377 H_2O . $\text{C} = 55.04$; $\text{H} = 9.09$.

0.1606 „ 9.4 c.c. nitrogen at 17° and 748 mm. $\text{N} = 6.72$.

$\text{C}_{10}\text{H}_{19}\text{NO}_4$ requires $\text{C} = 55.29$; $\text{H} = 8.75$; $\text{N} = 6.45$ per cent.

The amide is readily soluble in alcohol, sparingly so in cold water, ether, or benzene, and almost insoluble in light petroleum. When heated in a test tube, it gives off water and an oil distills which only partially solidified.

Methylisoamylhydroxysuccinamide is readily decomposed by boiling with potash solution and ammonia is evolved, but even when the potash is only in slight excess, some secondary decomposition takes place, and the resulting acid is difficult to obtain in a crystalline form. If, however, the amide is boiled with strong sodium carbonate solution, ammonia is only very slowly evolved, and even after 24 hours much of the compound remains unchanged and is precipitated on acidifying the alkaline liquid. The filtrate made alkaline with ammonia gives, on boiling with calcium chloride, a white, crystalline precipitate of calcium methylisoamylhydroxysuccinate, which is collected by the aid of a vacuum pump and washed with hot water, this salt being less soluble in hot than in cold water.

In order to obtain the free acid, the calcium salt was dissolved in dilute hydrochloric acid and the solution extracted several times with pure ether; the ethereal solution, after drying over calcium chloride and evaporating, yielded a thick oil which, on standing over sulphuric acid in a vacuum desiccator, completely solidified. For the analysis, this acid was further purified by recrystallisation from a mixture of benzene and light petroleum.

I. 0.1896 gave 0.3863 CO_2 and 0.1430 H_2O . $\text{C} = 55.56$; $\text{H} = 8.38$.

II. 0.1701 „ 0.3441 CO_2 „ 0.1269 H_2O . $\text{C} = 55.17$; $\text{H} = 8.29$.

$\text{C}_{10}\text{H}_{18}\text{O}_5$ requires $\text{C} = 55.04$; $\text{H} = 8.26$ per cent.

Methylisoamylhydroxysuccinic acid melts at 66° and is very readily soluble in water, forming a strongly acid solution. It also dissolves readily in alcohol, and moderately so in benzene, but is almost insoluble in light petroleum.

The *silver* salt, $\text{C}_{10}\text{H}_{16}\text{Ag}_2\text{O}_5$, is obtained as a white precipitate on adding silver nitrate to a neutral solution of the ammonium salt.

0.2076 gave 0.2141 CO_2 and 0.0708 H_2O . $\text{C} = 28.12$; $\text{H} = 3.78$.

0.2380 „ 0.1181 Ag. $\text{Ag} = 49.64$.

$\text{C}_{10}\text{H}_{16}\text{Ag}_2\text{O}_5$ requires $\text{C} = 27.91$; $\text{H} = 3.72$; $\text{Ag} = 50.0$ per cent.

A neutral solution of the ammonium salt of the acid shows the following behaviour with reagents. *Barium chloride* gives a white, amorphous precipitate which becomes crystalline on boiling, and is

very sparingly soluble, even in boiling water. *Calcium chloride* forms no precipitate in the cold, but, on boiling, a very sparingly soluble, crystalline calcium salt separates. *Copper sulphate* gives a pale blue, amorphous precipitate, and *lead acetate*, a white, amorphous precipitate.

It was stated on p. 913 that the principal product of the hydrolysis of ethylic isoamylhydroxycyanobutyrate with alcoholic hydrochloric or sulphuric acid was an oil boiling constantly at 163° under 20 mm. pressure, which, on analysis, gave numbers agreeing approximately with those required by the formula $\text{C}_8\text{H}_{14}(\text{COOC}_2\text{H}_5)_2$.

This oil was hydrolysed by boiling with alcoholic potash for 2 hours, when, on adding water, a small quantity of oil separated, which, on examination, was found to consist of isoamylacetone. This oil was removed by extraction with ether, the alkaline solution was then acidified and repeatedly extracted with pure ether when, after drying over calcium chloride and evaporating, a thick, yellow oil was obtained which, even after long standing over sulphuric acid in a vacuum desiccator, showed no signs of crystallising. Ultimately, it was found that this product contained a small quantity of an acid which formed a sparingly soluble barium salt, and therefore the whole quantity was dissolved in a slight excess of ammonia and boiled with barium chloride. The insoluble barium salt was collected, washed with water, and dissolved in dilute hydrochloric acid, when, on extracting with ether, an acid was obtained which, on standing, solidified. The solid mass was spread on porous porcelain to remove traces of oily mother liquor, and recrystallised from a mixture of benzene and light petroleum. In this way glistening needles were obtained which melted at 66° and evidently consisted of methylisoamylhydroxysuccinic acid, as the following analysis and a careful comparison with a specimen of this acid, prepared as explained on p. 915, conclusively showed:

0.1346 gave 0.2708 CO_2 and 0.1 H_2O . $\text{C} = 54.87$; $\text{H} = 8.25$.

$\text{C}_{10}\text{H}_{18}\text{O}_5$ requires $\text{C} = 55.04$; $\text{H} = 8.26$ per cent.

The filtrate from the sparingly soluble barium salt was acidified, extracted with ether, and, after drying over calcium chloride and distilling off the ether, the residual oil fractionated under reduced pressure. After several distillations, an oil was obtained which boiled constantly at 142° under 16 mm. pressure, and which, on careful investigation, was found to consist of methylisoamylmaleic anhydride.

0.1856 gave 0.4460 CO_2 and 0.1348 H_2O . $\text{C} = 65.54$; $\text{H} = 8.07$.

$\text{C}_{10}\text{H}_{14}\text{O}_3$ requires $\text{C} = 65.93$; $\text{H} = 7.69$ per cent.

This anhydride is insoluble in cold sodium carbonate solution, but on warming with caustic soda it rapidly dissolves, and on acidifying and extracting with ether, an oil is obtained which is not the free acid, but the anhydride, since it is insoluble in sodium carbonate and, after standing for some time over sulphuric acid in a vacuum desiccator, it yielded the following results on analysis:

0.1860 gave 0.4436 CO_2 and 0.1333 H_2O . $\text{C} = 65.04$; $\text{H} = 7.96$.

Methylisoamylmaleic anhydride requires $\text{C} = 65.93$; $\text{H} = 7.69$ per cent.

„ acid requires $\text{C} = 60.0$; $\text{H} = 8.0$ per cent.

In order to obtain further evidence as to the mode of formation of methylisoamylmaleic anhydride, experiments were made with the object of determining whether this substance is formed when methylisoamylhydroxysuccinic acid is distilled at the ordinary pressure. On cautiously heating about 5 grams of the pure hydroxy-acid in a small fractionating flask, water was first given off and then the temperature rapidly rose to 255° , nearly the whole distilling between this temperature and 265° ; on refractionating, an oil was obtained boiling constantly at $260\text{--}262^\circ$, which was insoluble in sodium carbonate solution.

That this oil was methylisoamylmaleic anhydride was shown by converting it into the anil which melted at 70° , and was identical in properties with the anil of methylisoamylmaleic acid described below. An equation representing the formation of the anhydride from methylisoamylhydroxysuccinic acid is given in the introduction.

When a solution of methylisoamylmaleic anhydride in benzene is mixed with aniline, there is very little rise of temperature and no anilic acid separates on standing; if, however, the benzene is removed by evaporation on the water-bath and the residue then stirred with dilute hydrochloric acid, it gradually solidifies. The crystalline mass is spread on porous porcelain until quite free from oily mother-liquor, and then purified by crystallisation from dilute alcohol, from which it separates in glistening plates which melt at 70° .

0.1556 gave 0.4246 CO_2 and 0.1046 H_2O . $\text{C} = 74.42$; $\text{H} = 7.47$.

0.2412 „ 12.3 c.c. nitrogen at 20° and 757 mm. $\text{N} = 5.87$.

$\text{C}_{16}\text{H}_{19}\text{NO}_2$ requires $\text{C} = 74.71$; $\text{H} = 7.39$; $\text{N} = 5.44$ per cent.

This anil is readily soluble in ether, benzene, warm alcohol, or light petroleum (b. p. $80\text{--}90^\circ$), sparingly so in water, and insoluble in sodium carbonate solution. When heated in small quantities, it distils apparently without decomposition.

Reduction of Methylisoamylmaleic Anhydride. Formation of cis- and trans-Methylisoamylsuccinic Acids, $\text{CH}_3 \cdot \underset{\text{C}_5\text{H}_{11}}{\underset{|}{\text{CH}}} \cdot \text{COOH}$.

When methylisoamylmaleic anhydride (4 grams) is heated in a reflux apparatus on the sand-bath with fuming hydriodic acid (20 grams) and amorphous phosphorus (2 grams), reduction readily takes place, and after boiling for 8 hours and allowing to cool, a quantity of a crystalline substance separates. The product is diluted with twice its bulk of water, repeatedly extracted with ether, and the ethereal solution, after washing with dilute sodium bisulphite to remove iodine, dried over calcium chloride and evaporated, when a solid residue is obtained which consists of a mixture of the *cis*- and *trans*-acids. When this is stirred with light petroleum (b. p. 70—90°), the *cis*-acid dissolves, and leaves the almost pure *trans*-acid which, after recrystallising from water, is obtained in colourless prisms melting at 142°.

0.1686 gave 0.3676 CO_2 and 0.1337 H_2O . C = 59.46; H = 8.81.

$\text{C}_{10}\text{H}_{18}\text{O}_4$ requires C = 59.40; H = 8.91 per cent.

The light petroleum mother liquors of this acid, on evaporation, give a solid residue which crystallises from hydrochloric acid in plates melting at 92°, and consists of the *cis*-modification.

0.1534 gave 0.3328 CO_2 and 0.124 H_2O . C = 59.16; H = 8.98.

$\text{C}_{10}\text{H}_{18}\text{O}_4$ requires C = 59.40; H = 8.91 per cent.

These acids agree in all their properties with the *cis*- and *trans*-modifications of methylisoamylsuccinic acid which W. Trevor Lawrence has obtained by another process (Proc., 1899, 15, 163).

Reduction of Ethylic Isoamylacetoacetate. Formation of α-Isoamyl-β-hydroxybutyric Acid, $\text{CH}_3 \cdot \text{CH}(\text{OH}) \cdot \text{CH}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$.

In investigating this reduction, ethylic isoamylacetoacetate (50 grams) was dissolved in alcohol (250 c.c.) and water (100 c.c.), and then treated in flat dishes with 3 per cent. sodium amalgam (2 kilos.) at ordinary temperatures, small quantities of water being added from time to time to facilitate the decomposition of the amalgam. After standing for 2 days and pouring into water, very little oil separated, showing that hydrolysis, as well as reduction, had taken place, and, in order to isolate the hydroxy-acid, the product was evaporated on the water-bath until free from alcohol, acidified, and extracted several times with pure ether. The ethereal solution was dried over calcium chloride and evaporated, when a thick oil was obtained, which, even on long standing, showed no signs of crystallising, but which can be

readily purified by conversion into the characteristic crystalline copper salt. In order to prepare this, the acid is dissolved in a slight excess of ammonia, and the moderately* dilute solution mixed with excess of copper sulphate and allowed to stand, when a beautifully crystalline, dark blue copper salt separates, which is collected, decomposed by hydrochloric acid, and the acid again extracted with ether. The oily acid thus obtained, after standing for some days over sulphuric acid in a vacuum desiccator, gave the following numbers on analysis :

0.1820 gave 0.4125 CO_2 and 0.1655 H_2O . $\text{C} = 61.81$; $\text{H} = 10.10$.
 $\text{CH}_3 \cdot \text{CH}(\text{OH}) \cdot \text{CH}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$ requires $\text{C} = 62.07$; $\text{H} = 10.34$ per cent.

Isoamylhydroxybutyric acid is a thick, colourless oil, sparingly soluble in water, which, as shown below, distils under reduced pressure unchanged, but at the ordinary pressure decomposes on distillation into isoamylcrotonic acid and water.

The *silver* salt, $\text{C}_9\text{H}_{17}\text{AgO}_3$, was prepared by adding silver nitrate to a neutral solution of the ammonium salt. It is a white, amorphous precipitate, which, on analysis, gave the following result :

0.1233 gave 0.0477 Ag. $\text{Ag} = 38.68$.
 $\text{C}_9\text{H}_{17}\text{AgO}_3$ requires $\text{Ag} = 38.43$ per cent.

A neutral and moderately strong solution of the ammonium salt gives a white, gelatinous precipitate with *barium chloride*, but no precipitate with *calcium chloride*.

α -Isoamylcrotonic Acid, $\text{CH}_3 \cdot \text{CH} : \text{C}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$.

When isoamylhydroxybutyric acid is distilled under reduced pressure (50 mm.), it passes over at about 195° without decomposition, as the following analysis of the distillate shows :

0.1755 gave 0.4 CO_2 and 0.1587 H_2O . $\text{C} = 62.16$; $\text{H} = 10.04$.
 $\text{CH}_3 \cdot \text{CH}(\text{OH}) \cdot \text{CH}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$ requires $\text{C} = 62.07$; $\text{H} = 10.34$ per cent.

If, however, the distillation is conducted under the ordinary pressure, water is eliminated, and an oil passes over at $235\text{--}250^\circ$; this consists of crude isoamylcrotonic acid, and by repeatedly refractionating an oil is obtained boiling fairly constantly at about 240° . The analysis gave rather low results, due to some slight impurity, which could not be removed by fractionation.

0.1832 gave 0.4577 CO_2 and 0.1593 H_2O . $\text{C} = 68.13$; $\text{H} = 9.66$.
 0.1336 „ 0.3337 CO_2 „ 0.1182 H_2O . $\text{C} = 68.12$; $\text{H} = 9.83$.
 $\text{CH}_3 \cdot \text{CH} : \text{C}(\text{C}_5\text{H}_{11}) \cdot \text{COOH}$ requires $\text{C} = 69.23$; $\text{H} = 10.25$ per cent.

* It is important that the solution should not be too concentrated, otherwise the copper salt is apt to separate in resinous clumps.

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Isoamylcrotonic acid is sparingly soluble in water, but dissolves readily in sodium carbonate, and the solution decolorises permanganate at once at the ordinary temperature.

The *silver salt*, obtained in the usual way, is a white, sparingly soluble, amorphous precipitate.

0.1956 gave 0.0815 Ag. $\text{Ag} = 41.66$.

$\text{C}_9\text{H}_{15}\text{AgO}_2$ requires $\text{Ag} = 41.06$ per cent.

Oxidation of Isoamylcrotonic Acid. Formation of Isobutylacetic Acid.—In investigating this oxidation, about 20 grams of the acid, in quantities of 5 grams at a time, were dissolved in a slight excess of very dilute sodium carbonate, and treated with potassium permanganate at 0° until the pink colour remained permanent for some hours; the excess of permanganate was then destroyed by sodium sulphite, and the filtrate from the manganese precipitate evaporated to a small bulk. On acidifying, an oily acid was precipitated, which was extracted with ether; the ethereal solution was very carefully dried over calcium chloride, evaporated, and the residual oil several times fractionated. In this way an acid was obtained boiling constantly at 202° , and showing all the properties of isobutylacetic acid, which, according to Lieben and Rossi (*Annalen*, 1871, 159, 76), boils at 199.7° under 732 mm. pressure. The silver salt of this acid, prepared in the usual way, gave the following results on analysis:

0.2129 gave 0.2510 CO_2 and 0.0936 H_2O . $\text{C} = 32.15$; $\text{H} = 4.88$.

0.2021 „ 0.0974 Ag. $\text{Ag} = 48.19$.

$\text{C}_6\text{H}_{11}\text{AgO}_2$ requires $\text{C} = 32.28$; $\text{H} = 4.93$; $\text{Ag} = 48.43$ per cent.

β -Isoamyl- α -hydroxyisobutyric Acid, $\text{C}_6\text{H}_{11} \cdot \begin{array}{c} \text{CH}_2 \\ \text{CH}_3 \end{array} > \text{C}(\text{OH}) \cdot \text{COOH}$.

This acid, which is isomeric with the α -isoamyl- β -hydroxybutyric acid described on p. 919, was obtained in small quantities in the following way:

Isoamylacetone (40 grams) was dissolved in dry ether (40 grams), finely-powdered potassium cyanide (30 grams) added, and then the calculated quantity of hydrochloric acid run in drop by drop, the whole being kept at -10° during the operation. After standing for 24 hours, the ethereal solution was washed and evaporated, and the residual oil hydrolysed by means of alcoholic hydrochloric acid, the method employed being exactly the same as that described on p. 912. On fractionating the product under reduced pressure (20 mm.), much unchanged isoamylacetone first passed over, then the temperature rose rapidly to 150° , most of the oil passing over between this and 170° , and on refractionating this, an oil was obtained boiling almos

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constantly at 156° under 20 mm. pressure. Analysis showed that the composition of this oil varies, two different preparations giving respectively $C=79\cdot27$, $H=12\cdot41$, and $C=76\cdot27$, $H=11\cdot97$, whereas if the oil had consisted entirely of ethylic isoamylhydroxyisobutyrate, $C_5H_{11}\cdot CH_2\cdot C(OH)(CH_3)\cdot COOC_2H_5$, as was expected, the percentages would have been $C=65\cdot34$, $H=10\cdot89$.

The substance therefore contains some compound very rich in carbon and hydrogen, possibly produced by the condensation of two mols. of isoamylacetone under the influence of the reagents employed. On hydrolysing the oil with alcoholic potash, a large quantity of isoamylacetone was produced; this was removed by extracting with ether, the alkaline solution was then evaporated until free from alcohol, acidified, and repeatedly extracted with ether. After drying over calcium chloride and distilling off the ether, a small quantity of an oily acid was obtained, which soon solidified, and crystallised from light petroleum in glistening plates melting at 76° .

0.1318 gave $0\cdot3$ CO_2 and $0\cdot1253$ H_2O . $C=62\cdot07$; $H=10\cdot56$.

$C_9H_{18}O_3$ requires $C=62\cdot07$; $H=10\cdot34$ per cent.

The *silver* salt, $C_9H_{17}AgO_3$, was prepared from the neutral solution of the ammonium salt by adding silver nitrate. It is a white, amorphous precipitate, which, on analysis, gave the following result:

0.0937 gave $0\cdot0364$ Ag. $Ag=38\cdot84$.

$C_9H_{17}AgO_3$ requires $Ag=38\cdot43$ per cent.

There can be no doubt that this interesting acid is *β -isoamyl- α -hydroxyisobutyric acid*, but as the yield obtained by the method described above is only 1 per cent. of the isoamylacetone employed, it could not be investigated in more detail.

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