CXXXVII.—*The cis- and trans-Modifications of 1-Methyl-cyclohexan-2-ol-4-carboxylic Acid and their Conversion into 1-Methyl- Δ^1 -cyclohexene-4-carboxylic Acid.*

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1-METHYL- Δ^1 -CYCLOHEXENE-4-CARBOXYLIC acid has already been prepared synthetically (Trans., 1904, **85**, 418) by the following series of reactions :

Ethyl sodiocyanoacetate is converted by treatment with ethyl β -iodopropionate into ethyl γ -cyanopentane- $\alpha\gamma\epsilon$ -tricarboxylate,

which, when hydrolysed by hydrochloric acid, yields pentane- $\alpha\gamma\epsilon$ -tricarboxylic acid.

This acid is decomposed by boiling with acetic anhydride and

$$* \quad b=6087; \quad c= -43200; \quad d=134500.$$

subsequent distillation into *cyclohexanone-4-carboxylic acid* δ -keto-hexahydrobenzoic acid),

the ester of which reacts with magnesium methyl iodide and the product, on treatment with water, yields 1-methyl*cyclohexan-1-ol-4-carboxylic acid* (δ -hydroxyhexahydro-*p*-toluic acid) :

The yield of this acid was always most unsatisfactory, a fact which was subsequently (Trans., 1907, 91, 372) found to be largely due to the formation of considerable quantities of terpin and other neutral substances. The next step in the synthesis was the conversion of the hydroxy-methyl acid into 1-bromo-1-methyl*cyclohexane-4-carboxylic acid* (δ -bromohexahydro-*p*-toluic acid) by the action of hydrobromic acid, and, finally, the bromo-acid, when treated with weak alkalis or pyridine, yielded 1-methyl- Δ^1 -*cyclohexene-4-carboxylic acid* :

It will be readily understood that this method of preparation is most laborious, and, as the yield is so small, it was found to be practically impossible to obtain this acid, by this process, in quantities sufficient for a further series of synthetical experiments which are in contemplation. We therefore decided to attempt to devise a more convenient method of preparation, and in this we were ultimately successful.

The starting-point is *p*-toluic acid, which is converted by sulphonation into 2-sulpho-*p*-toluic acid, and then by fusion with potassium hydroxide into 2-hydroxy-*p*-toluic acid (I) :

This acid is readily reduced by sodium and alcohol, and converted into the corresponding 1-methyl*cyclohexan-2-ol-4-carboxylic acid* (II).

It is interesting to notice that this addition of six atoms of hydrogen to 2-hydroxy-*p*-toluic acid results in the formation of a hexahydro-acid containing three asymmetrical carbon atoms, which, therefore, should be capable of existing in four inactive modifications.

On carefully examining the product of reduction, we were only able, however, to isolate two acids, of melting points 132° and 161°

respectively, and there can hardly be a doubt that these are the *cis*- and *trans*-modifications corresponding with the formulæ:

Of these, the more soluble acid melting at 132° is evidently the *cis*-modification, since it yields a lactone (m. p. $30-33^\circ$) which, on hydrolysis, is again converted into the same acid.

On the other hand, the much more sparingly soluble acid melting at 161° distils under reduced pressure (20 mm.) almost without decomposition, but, when slowly heated under ordinary pressures, it is gradually converted into the lactone of the acid of melting point 132° . The *cis*- and *trans*-hydroxy-acids react readily with hydrobromic acid with formation of the corresponding *cis*- and *trans*-2-bromo-1-methylcyclohexane-4-carboxylic acids,

which are isomeric with the 1-bromo-acid previously prepared (p. 1417) and, like this acid, both yield 1-methyl- Δ^1 -cyclohexene-4-carboxylic acid,

by elimination of hydrogen bromide.

It was thought probable that one of the modifications of the bromo-acid might lose hydrogen bromide with formation of the Δ^2 -acid, but there was no evidence of this and the elimination apparently takes place entirely in the direction of the methyl group.

We have now been able to work out a method, based on the above facts, for the preparation of 1-methyl- Δ^1 -cyclohexene-4-carboxylic acid which is less laborious than that described at the beginning of this paper, and this method is described on p. 1425.

During the course of this investigation we studied the action of oxidising agents on the *cis*- and *trans*-modifications of 1-methylcyclohexan-2-ol-4-carboxylic acid and obtained interesting results which may be briefly summarised as follows.

The *cis*-acid is rather readily attacked by chromic acid mixture with formation of 1-methylcyclohexan-2-one-4-carboxylic acid (γ -keto-hexahydro-*p*-toluic acid),

which melts at $112-113^\circ$ and yields a sparingly soluble *semicarbazone* (m. p. 195°) and a sparingly soluble *oxime* (m. p. 186°). When this

acid is oxidised by chromic acid, it is converted into a new keto-dibasic acid, $C_8H_{12}O_5$, which melts at 120° and yields a *semicarbazone* which decomposes at 183° and a readily soluble *oxime* (m. p. about 140°).

There can be no doubt that this acid is β -carboxy- δ -acetylvaleric acid, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CH(CO_2H) \cdot CH_2 \cdot CO_2H$, and its formation is readily explained by the following scheme :

The *trans*-hydroxy-acid is attacked by chromic acid with much more difficulty than the *cis*-modification, and we were unable to isolate 1-methylcyclohexan-2-one-4-carboxylic acid as a product of oxidation. Under the conditions which had to be employed, this latter acid evidently undergoes further oxidation, since the product consisted entirely of β -carboxy- δ -acetylvaleric acid.

The sulphonation of *p*-toluic acid appears to have been first carried out by Fischli (*Ber.*, 1879, **12**, 616), who prepared 2-sulpho-*p*-toluic acid in this way and examined several of its salts.

Subsequently Weinreich (*Ber.*, 1887, **20**, 982) investigated this sulphonic acid and showed that, when fused with potassium hydroxide, it is converted into 2-hydroxy-*p*-toluic acid. In preparing large quantities of 2-sulpho-*p*-toluic acid we have found that the following process yields excellent results.

p-Toluic acid (200 grams) is heated with fuming sulphuric acid (monohydrate, 500 c.c.) in a strong flask on the sand-bath, the temperature being kept at 150° by a regulator placed in the mixture. The *p*-toluic acid dissolves in the sulphuric acid and is readily sulphonated, and, after eight hours, the cold product is mixed with water (650 c.c.), when the sulphonic acid crystallises at once. In order to obtain it in a better condition for filtering, the whole is heated until solution is complete and then allowed to cool slowly. The mass of crystals is then collected on glass wool or flannel by the aid of the pump, dissolved in hot water (600 c.c.), the solution filtered, concentrated, and allowed to crystallise, when the pure sulphonic acid is obtained in a yield of about 380 grams. Meyer and Baur

(*Annalen*, 1883, **220**, 19) state that this sulphonic acid has the composition $C_8H_7O_2SO_3H \cdot 2H_2O$, and that, when exposed over sulphuric acid in a vacuum desiccator, it loses water and becomes $C_8H_7O_2SO_3H \cdot H_2O$, but our analytical results do not confirm this statement. We crystallised two different specimens of the sulphonic acid from glacial acetic acid and, after allowing the crystals to remain in the air until free from acetic acid, the composition was determined by titration with standard sodium hydroxide.

I. 0.224 neutralised 0.077 NaOH. Equivalent = 116.1.

II. 0.628 „ 0.2147 NaOH. „ = 116.8.

The equivalent of $C_8H_7O_2SO_3H \cdot H_2O$ is 117.

Some of the acid was then crystallised from water, from which it separated in slender, colourless needles which, after drying in the air at the ordinary temperature, gave the following results on titration:

I. 0.5426 neutralised 0.1596 NaOH. Equivalent = 135.9.

II. 0.3016 „ 0.0895 NaOH. „ = 134.7.

The equivalent of $C_8H_7O_2SO_3H \cdot 3H_2O$ is 135.

It appears therefore that the sulphonic acid crystallises from water with $3H_2O$ and from acetic acid with $1H_2O$.

The *barium hydrogen* salt, $(C_8H_7O_5S)_2Ba \cdot 5H_2O$.—This characteristic salt is readily obtained when the solution of the sulphonic acid (5 grams) in water is digested with barium carbonate, filtered, and the hot filtrate mixed with 5 grams of the sulphonic acid. On cooling, the sparingly soluble salt separates in brilliant flat plates.

0.8972 gave 0.3190 $BaSO_4$. Ba = 20.9.

0.6918 neutralised 0.0842 NaOH. Equivalent = 328.3.

$(C_8H_7O_5S)_2Ba \cdot 5H_2O$ requires Ba = 20.82 per cent. and equivalent = 328.5.

Weinreich (*Ber.*, 1887, **20**, 982) prepared this acid from 2-sulpho-p-toluic acid by fusion with four times its weight of potassium hydroxide, but he gives no details of temperature and time of fusion.

In preparing large quantities of the hydroxy-acid, we have found the following process to give excellent results. Potassium hydroxide (1 kilo.) is moistened with very little water and heated in a large nickel crucible at 200° ; the sulphonic acid (356 grams) is then added in small quantities at a time, and the temperature gradually raised to 260° and maintained at this point until the fusion is perfectly fluid. The almost colourless product is dissolved in water, neutralised with sulphuric acid, the potassium sulphate removed by filtration, and the

filtrate acidified with hydrochloric acid, when the hydroxy-acid separates at once in a crystalline condition.

The mass is collected, washed, and recrystallised from water, from which it separates in colourless needles, melting at 206—207°, the yield being 187 grams. Weinreich (*loc. cit.*) states that this acid is volatile in steam, but we found that it was carried over only with great difficulty; he also obtained terephthalic acid as one of the products of the fusion, but none of this acid was formed during our experiments. Probably Weinreich's sulphonic acid contained some unchanged *p*-toluic acid, which would doubtless yield terephthalic acid on fusion with potassium hydroxide.

Reduction of 2-Hydroxy-p-toluic Acid.

The conversion of 2-hydroxy-*p*-toluic acid into the *cis*- and *trans*-modifications of 1-methylcyclohexan-2-ol-4-carboxylic acid by reduction with sodium and alcohol was carried out under the following conditions. The hydroxy-acid (40 grams) was dissolved in alcohol (1250 c.c.) in a large flask fitted with a long and efficient condenser, the solution heated to boiling, and then sodium (150 grams) added as quickly as possible. As soon as the sodium had dissolved, the product was mixed with water (300 c.c.), the solution nearly neutralised with hydrochloric acid, evaporated to a small bulk, acidified, and extracted many times with ether. The ethereal solution was dried, evaporated, and the residue, which on standing becomes semi-solid, was esterified by leaving it in contact with four times its weight of 4 per cent. alcoholic hydrogen chloride for forty-eight hours.*

The product was dissolved in ether, washed with water and dilute sodium carbonate, dried, and fractionated several times under reduced pressure, when a large fraction 157—163° (20 mm.) was obtained, which consisted of the esters of the mixed *cis*- and *trans*-acids. In order to hydrolyse this ester, it (90 grams) was dissolved in methyl alcohol (200 c.c.) and potassium hydroxide (45 grams) in the cold, and, after remaining for twenty-four hours, the crystals (27 grams), which had separated, were collected and washed with a little methyl alcohol. The colourless salt was dissolved in water, evaporated until free from methyl alcohol, and acidified, when a solid acid separated, which crystallised from water in short prisms, melted at 130—132°, and consisted of pure *cis*-1-methylcyclo-hexan-2-ol-4-carboxylic acid. The filtrate from the potassium salt was mixed with water, nearly neutral-

* An alternative method is to leave the semi-solid mass in contact with porous porcelain until free from oil and then to crystallise the residue fractionally from ether and then from water. The porous plates are extracted with ether and the crude syrupy acid purified by conversion into the ester, &c.

ised with hydrochloric acid, evaporated until free from methyl alcohol, acidified, and, after remaining for twenty-four hours, the crystalline acid was collected, drained on porous porcelain, and crystallised from ether, from which the pure *trans*-acid separated in rectangular plates melting at 160—161°. The mother liquors yield, on extraction with ether, a mixture of the *cis*- and *trans*-acids, which may be separated by repeated crystallisation, first from ether and then from water, or better by converting into the ester, fractionating this, and then hydrolysing with potassium hydroxide in the way described above. As far as could be determined from rough weighings, the *cis*- and *trans*-acids are produced in the above process in the proportion, approximately, of 3 : 2.

Cis-1-Methylcyclohexan-2-ol-4-carboxylic Acid.

The preparation of this acid is described in the preceding section. It is much more soluble both in ether and in water than the corresponding *trans*-acid, and separates from water in small, glistening prisms melting at 130—132°:

0.1546 gave 0.3430 CO₂ and 0.1216 H₂O. C = 60.5; H = 8.7.

0.1551 „ 0.3456 CO₂ „ 0.1233 H₂O. C = 60.7; H = 8.8.

C₈H₁₄O₃ requires C = 60.8; H = 8.8 per cent.

The Lactone.—In preparing this substance, the crude *cis*-acid was slowly distilled under 20 mm. pressure, when much water was eliminated and, after this had passed over, a quantity of a viscid syrup distilled at about 125—170°, leaving a considerable residue.

The distillate was twice fractionated, and yielded a quantity of a colourless oil, which distilled constantly at 128—130°/17mm., and solidified completely when it was left for twenty-four hours in the ice chest.

The crystals were freed from oil by contact with porous porcelain, and washed with a little light petroleum, in which the lactone is sparingly soluble:

0.1190 gave 0.2985 CO₂ and 0.0940 H₂O. C = 68.4; H = 8.8.

C₈H₁₂O₂ requires C = 68.6; H = 8.6 per cent.

This lactone melts at 30—33° and, especially when warm, has a pronounced odour of camphor. It dissolves in hot water, yielding an acid solution, but hydrolysis takes place only very gradually, since, even after boiling for several minutes, the addition of ammonium sulphate causes most of the lactone to separate. It was hydrolysed by boiling with sodium carbonate, and the solution acidified and extracted with ether. The ethereal solution was dried and evaporated, when a crystalline residue was obtained, which, after crystallisation from water, melted at 130—132°, and consisted of the pure *cis*-acid.

cis-2-Bromo-1-methylcyclohexane-4-carboxylic Acid and its Conversion into 1-Methyl- Δ^1 -cyclohexene-4-carboxylic Acid.

The *cis*-hydroxy-acid dissolves readily in fuming aqueous hydrobromic acid (saturated at 0°), but the formation of the bromo-acid does not appear to take place until the solution is heated on the water-bath, when it clouds and separates into two layers. On standing in the ice-chest, the upper layer gradually solidifies to a gelatinous solid, which is washed well, left in contact with porous porcelain until quite dry, and then crystallised from light petroleum (b. p. 60—70°):

0.2508 gave 0.2129 AgBr. Br = 36.1.

$C_8H_{13}O_2Br$ requires Br = 36.2 per cent.

This *cis*-bromo-acid becomes red at 105°, melts and decomposes at about 118°, and is very readily soluble in formic acid, chloroform, alcohol, or benzene. It separates, when its concentrated solution in formic acid is cooled in ice, in thin glistening plates.

When warmed with water it dissolves completely, but decomposition, with elimination of hydrogen bromide, takes place only gradually, even when the solution is boiled.

The *cis*-bromo-acid is readily decomposed by boiling with five times its weight of anhydrous pyridine, and, if the bulk of the pyridine is removed by evaporation on the water-bath and the residue mixed with hydrochloric acid, a solid acid separates which, after crystallisation from light petroleum, melts at 97—99°:

0.1817 gave 0.4559 CO_2 and 0.1421 H_2O . C = 68.5; H = 8.7.

$C_8H_{12}O_2$ requires C = 68.6; H = 8.6 per cent.

That this acid is 1-methyl- Δ^1 -cyclohexene-4-carboxylic acid was proved by mixing it with a specimen which had been prepared from δ -keto-hexahydrobenzoic acid (Trans., 1904, 85, 664), when the mixture melted at 98—99°.

trans-1-Methylcyclohexan-2-ol-4-carboxylic Acid.

When quite pure, this acid is sparingly soluble in ether or cold water, and separates from these solvents in glistening rectangular plates melting at 160—161°:

0.1466 gave 0.3276 CO_2 and 0.1152 H_2O . C = 60.8; H = 8.7.

0.1617 „ 0.3608 CO_2 „ 0.1287 H_2O . C = 60.8; H = 8.8.

$C_8H_{14}O_3$ requires C = 60.8; H = 8.8 per cent.

When this *trans*-hydroxy-acid is heated under 15 mm. pressure, it distils apparently without decomposition, but if distillation is conducted under the ordinary pressure, water is eliminated and an oil passes over at about 260°. The distillate was dissolved in ether, dried,

and twice refractionated, when a considerable quantity of oil distilled at about $138^{\circ}/25$ mm. and crystallised on cooling. After draining on porous porcelain the crystals melted at $28-30^{\circ}$, and consisted of the lactone of the *cis*-hydroxy-acid, since they yielded the *cis*-acid, melting at $129-132^{\circ}$, on hydrolysis. It is therefore possible in this way to convert the *trans*-hydroxy-acid into the corresponding *cis*-modification.

trans-2-Bromo-1-methylcyclohexane-4-carboxylic Acid and its Conversion into 1-Methyl- Δ^1 -cyclohexene-4-carboxylic Acid.

The *trans*-hydroxy-acid dissolves readily in fuming hydrobromic acid (saturated at 0°) and the solution remains clear for several hours, but when heated on the water-bath, separation into two layers readily takes place. The product, which showed no signs of crystallising, was mixed with water, extracted with ether, the ethereal solution dried and evaporated, and the viscid syrupy residue converted into the ester by dissolving in 10 per cent. alcoholic sulphuric acid in the cold. After twenty-four hours, the ester was precipitated by water, extracted with ether, the ethereal solution washed with dilute sodium carbonate, dried, evaporated, and distilled, when the crude bromo-ester passed over at about $170-175^{\circ}/100$ mm., but yielded, on analysis, only 19.6 instead of 32.2 per cent. of bromine. This low percentage of bromine is doubtless due to the presence of unsaturated ester, produced by the elimination of hydrogen bromide during the preparation and purification of the bromo-ester. The oil was now digested with diethylaniline (5 vols.) for one hour, the product dissolved in ether, washed thoroughly with dilute hydrochloric acid, and then with sodium carbonate, dried, and evaporated. The residual oil distilled almost constantly at about $148^{\circ}/100$ mm., and consisted of ethyl 1-methyl- Δ^1 -cyclohexene-4-carboxylate:

0.1221 gave 0.3181 CO_2 and 0.1045 H_2O . $\text{C} = 70.9$; $\text{H} = 9.5$.

$\text{C}_{10}\text{H}_{16}\text{O}_2$ requires $\text{C} = 71.4$; $\text{H} = 9.5$ per cent.

This ester was hydrolysed by leaving it in contact with alcoholic potash for twenty-four hours, water was then added, the solution saturated with carbon dioxide, evaporated until free from alcohol, and acidified, when a solid mass separated, which was collected and crystallised from dilute acetic acid:

0.1211 gave 0.3036 CO_2 and 0.0944 H_2O . $\text{C} = 68.4$; $\text{H} = 8.6$.

$\text{C}_8\text{H}_{12}\text{O}_2$ requires $\text{C} = 68.6$; $\text{H} = 8.6$ per cent.

This acid melted at $98-99^{\circ}$, and was 1-methyl- Δ^1 -cyclohexene-4-carboxylic acid, since, when mixed with a specimen which had been prepared on a previous occasion (Trans., 1904, 85, 664), there was no change in the melting point.

Preparation of 1-Methyl- Δ^1 -cyclohexene-4-carboxylic Acid,

The crude mixture of the esters of the *cis*- and *trans*-modifications of 1-methylcyclohexan-2-ol-4-carboxylic acid, obtained as described on p. 1421, is fractionated under 20 mm. pressure, and the fraction 150—170° hydrolysed by methyl-alcoholic potash. The syrupy hydroxy-acid is dissolved in five times its weight of fuming hydrobromic acid (saturated at 0°), and, after remaining overnight, the solution is heated for half an hour on a rapidly-boiling water-bath; the dark brown product is then poured into water and extracted with ether.

After drying and evaporating, the crude bromo-acid is dissolved in five times its volume of 10 per cent. alcoholic sulphuric acid, and left for two days. The ester is precipitated by water, extracted by ether in the usual way, and distilled under 20 mm. pressure, in order to separate it from a considerable quantity of resinous matter which is always produced.

The almost colourless distillate is boiled with four times its volume of diethylaniline, the product dissolved in ether, repeatedly extracted with a large excess of dilute hydrochloric acid, dried, evaporated, and fractionated, when almost the whole quantity passes over at 147—148°/100 mm., and consists of nearly pure ethyl 1-methyl- Δ^1 -cyclohexene-4-carboxylate.

When this ester is left in contact with half its weight of potash dissolved in methyl alcohol, hydrolysis rapidly takes place, and, after twelve hours the product is nearly neutralised with hydrochloric acid, evaporated until free from alcohol, cooled, and acidified, and the solid acid collected and washed with water. If the acid is now dissolved in a slight excess of dilute sodium carbonate, digested for a few minutes on the water-bath with purified animal charcoal, filtered, and reprecipitated, it is obtained perfectly colourless and pure enough for most purposes. In this condition it usually melts at 94—97°, but one crystallisation from light petroleum or dilute acetic acid at once raises the melting point to 98—99°. The yield of 1-methyl- Δ^1 -cyclohexene-4-carboxylic acid, obtained from 250 grams of *p*-toluic acid, is frequently as much as 70 grams.

1-Methylcyclohexan-2-one-4-carboxylic Acid,

This acid was prepared by the oxidation of *cis*-1-methylcyclohexan-2-ol-4-carboxylic acid under the following conditions:

The crude *cis*-acid (30 grams) was dissolved in water (150 c.c.), and oxidised by the gradual addition of potassium dichromate (40 grams) and sulphuric acid (30 c.c.) in water (150 c.c.), the temperature being kept at 75° during the operation. The product was saturated with ammonium sulphate, extracted with ether in a continuous extraction apparatus, the ethereal solution dried, evaporated, and the crude, syrupy residue (25 grams) esterified by leaving it in contact with 2·5 per cent. alcoholic hydrogen chloride (100 c.c.) for four days. After diluting with water, the ester was extracted with ether, the ethereal solution well washed with dilute sodium carbonate, dried, evaporated, and the oily residue repeatedly fractionated, when about 10 grams of oil were obtained, which distilled constantly at 146—148°/25 mm., possessed a rather pleasant fruity odour, and consisted of almost pure *ethyl 1-methylcyclohexan-2-one-4-carboxylate* :

0·1801 gave 0·4268 CO₂ and 0·1439 H₂O. C = 64·6 ; H = 8·8.

C₁₀H₁₆O₃ requires C = 65·2 ; H = 8·7 per cent.

This ester was digested with hydrochloric acid (10 c.c.) and water (60 c.c.) for four hours, the clear solution evaporated until free from alcohol, saturated with ammonium sulphate, and repeatedly extracted with ether. The ethereal solution was then dried and evaporated, when a colourless syrup was obtained, which gradually crystallised, and, after remaining in contact with porous porcelain until quite free from oil, the keto-acid was further purified by crystallisation from ether :

0·1520 gave 0·3430 CO₂ and 0·1030 H₂O. C = 61·5 ; H = 7·5.

C₈H₁₂O₃ requires C = 61·5 ; H = 7·7 per cent.

1-Methylcyclohexan-2-one-4-carboxylic acid melts at 112—113° with slight previous softening, and is readily soluble in water. It is sparingly soluble in cold ether, but dissolves rather readily in the boiling solvent, and separates from the concentrated solution in hard crusts.

The *oxime* was prepared by adding hydroxylamine hydrochloride and excess of potassium hydroxide to a saturated aqueous solution of the acid. After remaining for twenty-four hours, the product was acidified, and the crystalline oxime which separated extracted with large quantities of ether. The ethereal solution was dried, and concentrated until crystals began to separate from the boiling solution :

0·1777 gave 13·4 c.c. N₂ at 21° and 758 mm. N = 8·5.

C₈H₁₃O₃N requires N = 8·2 per cent.

When crystallised from ether, this oxime melts at about 186° and is characterised by being very sparingly soluble in ether ; it dissolves readily in boiling water, and separates from the concentrated solution in short prisms grouped together like cactus leaves and melting at about 193—195°.

The *semicarbazone* separates immediately, as a granular precipitate,

when the aqueous solution of the keto-acid is mixed with a strong solution of semicarbazide hydrochloride and sodium acetate.

It was collected, washed with water, followed by alcohol, and dried at 100°:

0.1060 gave 18.5 c.c. N_2 at 21° and 756 mm. $N = 19.7$.

$C_9H_{15}O_3N$ requires $N = 19.7$ per cent.

When purified in this way this semicarbazone melted at about 193—195° with slow decomposition. It is very sparingly soluble in water or alcohol, and separates from much boiling water as a glistening, microcrystalline powder.

It has been pointed out in the introduction (p. 1419) that, whilst *cis*-1-methylcyclohexan-2-ol-4-carboxylic acid is converted into 1-methylcyclohexan-2-one-4-carboxylic acid by oxidation with chromic acid mixture, the corresponding *trans*-acid is attacked by the oxidising agent with much greater difficulty, and then with formation of *β*-carboxy-δ-acetylvaleric acid. The pure *trans*-acid (6 grams) was dissolved in the least possible quantity of hot water, and oxidised on the water-bath by the gradual addition of potassium dichromate (9 grams) and sulphuric acid (8 c.c.) dissolved in water (50 c.c.).

As soon as oxidation was complete, the green solution was saturated with ammonium sulphate, extracted 10 times with ether, the ethereal solution dried and evaporated, when a syrup was obtained which gradually crystallised. After remaining in contact with porous porcelain until free from traces of oil, the colourless mass was crystallised from ether;

0.1492 gave 0.2800 CO_2 and 0.0890 H_2O . $C = 51.1$; $H = 6.6$.

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

The basicity of the acid was determined by titration with decinormal sodium hydroxide, when 0.1510 required 0.0644 NaOH for neutralisation, whereas this amount of a dibasic acid, $C_8H_{12}O_5$, should neutralise 0.0643 NaOH.

β-Carboxy-δ-acetylvaleric acid melts at 119—120°, is readily soluble in water, but sparingly so in ether, and separates in brilliant crusts when the solution, in much ether, is concentrated.

The presence of the $CH_3 \cdot CO$ group in the acid is indicated by the fact that it is readily attacked by potassium hypobromite with immediate separation of bromoform.

The *oxime* was prepared by mixing a strong solution of the potassium salt of the acid with hydroxylamine hydrochloride and potassium hydroxide; after twelve hours, the product was acidified

and repeatedly extracted with ether. The ethereal solution was dried and evaporated, when a readily soluble, colourless syrup was obtained which gradually crystallised and in fourteen days had become quite hard. The mass was ground with light petroleum, transferred to porous porcelain, and, when quite free from oil, dissolved in acetone, the solution mixed with benzene and the acetone evaporated. After some time, the benzene solution deposited the oxime as a hard crystalline crust :

0.1350 gave 7.9 c.c. N_2 at 23° and 770 mm. $N = 6.7$.

$C_8H_{13}O_5N$ requires $N = 6.9$ per cent.

This oxime has no definite melting point ; it softens at 130° and melts gradually between 135° and 140° , becoming orange red and evolving gas. It is readily soluble in alcohol, ether, or acetone, but sparingly so in benzene or light petroleum.

The *semicarbazone*.—A concentrated solution of the acid gives no immediate precipitate with semicarbazide hydrochloride and sodium acetate, but when the solution is warmed and the containing vessel rubbed with a glass rod, the semicarbazone soon separates as a colourless granular precipitate, which is collected, washed with water, and dried at 100° . On analysis :

0.1055 gave 15 c.c. N_2 at 18° and 760 mm. $N = 16.3$.

$C_9H_{15}O_5N_3$ requires $N = 17.1$ per cent.

When *cis*-1-methylcyclohexan-2-one-4-carboxylic acid is oxidised under the conditions observed in the case of the *trans*-acid, it yields a syrup which gradually crystallises. This was converted into the semicarbazone and the keto-acid regenerated by treatment with dilute hydrochloric acid and extraction with ether, when a colourless solid was obtained which, after crystallisation from ether, melted at 119 — 120° , and consisted of *β -carboxy- δ -acetylvaleric acid* :

0.1206 gave 0.2244 CO_2 and 0.0700 H_2O . $C = 50.8$; $H = 6.4$.

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

Since it is shown on p. 1425 that the first product of the oxidation of the *cis*-acid is 1-methylcyclohexan-2-one-4-carboxylic acid, it follows that *β -carboxy- δ -acetylvaleric acid* is produced from this keto-acid by the further action of the oxidising agent.

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