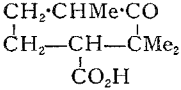
THE CONSTITUTION OF THE ACID FORMED BY THE ACTION OF SULPHURIC ACID ON CAMPHORQUINONE[1]

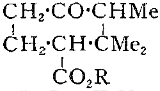
By Madhav Balaji Bhagvat and John Lionel Simonsen.

In a recent communication (J.C.S., 1925, **127**, 1294), evidence was advanced which appeared to prove that the keto-acid, $C_{10}H_{16}O_3$, first prepared by Manasse and Samuel (*Ber.*, 1897, **30**, 3157; 1902, **35**, 3831) by the action of sulphuric acid on camphorquinone, was *d*-2 : 2 : 4-trimethyl*cyclo*hexan-3-one-1-carboxylic acid (I). The assignment of this constitution to the acid was based essentially on two facts: (i) on oxidation with nitric acid it gave β-methylpentane-βγε-tricarboxylic acid (III), and (ii) on treatment with amyl nitrite and hydrochloric acid it did not yield an oximino-derivative, the formation of which might have been expected if the keto-acid had the alternative constitution (II) (compare footnote, *loc. cit.*, p. 1295), since in this case there is a methylene group adjacent to the carbonyl group.



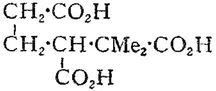
$$\begin{array}{l} CH_2\cdot CHMe\cdot CO \\ CH_2-CH-CMe_2 \\ \quad\quad CO_2H \end{array}$$

(I)



$$\begin{array}{l} CH_2\cdot CO\cdot CHMe \\ CH_2\cdot CH\cdot CMe_2 \\ \quad\quad CO_2R \end{array}$$

(II; R = H, Me.)

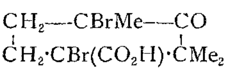


$$\begin{array}{l} CH_2\cdot CO_2H \\ CH_2\cdot CH\cdot CMe_2\cdot CO_2H \\ \quad\quad CO_2H \end{array}$$

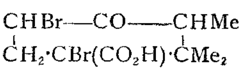
(III)

In deciding between these two formulæ, owing to the symmetry of the molecules, simple degradation products were unlikely to be of much assistance, but it seemed probable that, on bromination, a dibromo-acid would result of either formula (IV) or (V). It was further anticipated that this acid would, on removal of two molecules of hydrogen bromide, tend to lose simultaneously a methyl group and so pass into a phenolic acid (VI or VII) the identification of which would have offered little difficulty.

(IV)



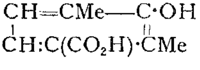
$$\begin{array}{l} CH_2-CBrMe-CO \\ CH_2\cdot CBr(CO_2H)\cdot CMe_2 \end{array}$$



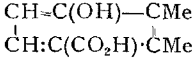
$$\begin{array}{l} CHBr-CO-CHMe \\ CH_2\cdot CBr(CO_2H)\cdot CMe_2 \end{array}$$

(V)

(VI)



$$\begin{array}{l} CH=CMe-C\cdot OH \\ CH:C(CO_2H)\cdot CMe \end{array}$$



$$\begin{array}{l} CH=C(OH)-CMe \\ CH:C(CO_2H)\cdot CMe \end{array}$$

(VII)

On bromination in acetic acid, the crystalline and the liquid methyl ester of the keto-acid each gave a *dibromo*-ester, $C_{11}H_{16}O_3Br_2$,

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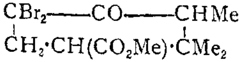
[1] Reprinted from the *Journal of the Chemical Society*, 1927, p. 77.

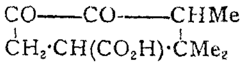
which reacted in an identical manner with alkali. In some experiments, under conditions which could not be exactly defined, the dibromo-ester was obtained crystalline. Since both the pure crystalline ester and the crude liquid ester yielded the same products, they were apparently stereoisomerides.

On treatment with a solution of barium or potassium hydroxide the dibromo-ester gave a complex mixture of acids, from which, with considerable difficulty, (A) a *hydroxyketo-acid*, $C_{10}H_{14}O_4$, m. p. 151–152°, (B) a dibasic *hydroxy-acid*, $C_{10}H_{16}O_5$, m. p. 191–192°, (C) and (D) unsaturated dibasic *acids*, $C_{10}H_{14}O_4$, m. p. 257° and 215–216°, respectively, were isolated.

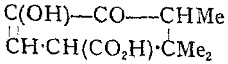
The formation of the hydroxyketo-acid, which also reacted as a diketo-acid, yielding a *dioxime* and a *disemicarbazone*, would appear to indicate that the dibromo-ester has two bromine atoms attached to the same carbon atom—a fact most simply explained if the original keto-ester has formula (II), the dibromo-ester then being represented by (VIII). An ester of this formula should yield on treatment with alkali a diketo-acid (IX); the acid obtained, however, and also its *methyl* ester, were colourless substances which gave intense colorations with ferric chloride, and the methyl ester was readily soluble in dilute potassium hydroxide solution and reprecipitated by carbon dioxide. Moreover, in alkaline solution, the acid was unstable to potassium permanganate and on treatment with acetyl chloride it yielded an *acetyl* derivative. There can be no doubt, therefore, that the hydroxyketo-acid is represented by (X) or (XI), the latter being the more probable, since the acid shows no tendency to yield a lactone. Owing to the small quantity of material available, the decison between these two formulæ could not be made.

(VIII)


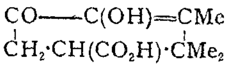
$$\begin{array}{l}\mathrm{CBr_2{-\!-\!-}CO{-\!-\!-}CHMe}\\ \mathrm{CH_2{\cdot}CH(CO_2Me){\cdot}CMe_2}\end{array}$$


(IX)

$$\begin{array}{l}\mathrm{CO{-\!-\!-}CO{-\!-\!-}CHMe}\\ \mathrm{CH_2{\cdot}CH(CO_2H){\cdot}CMe_2}\end{array}$$

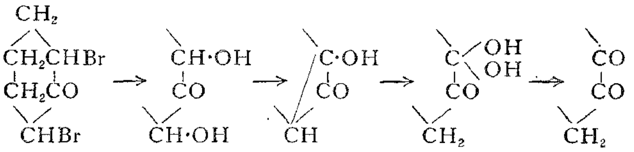
(X)


$$\begin{array}{l}\mathrm{C(OH){-}CO{-\!-}CHMe}\\ \mathrm{CH{\cdot}CH(CO_2H){\cdot}CMe_2}\end{array}$$


(XI)

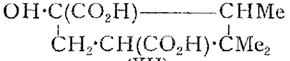
$$\begin{array}{l}\mathrm{CO{-\!-\!-}C(OH){=}CMe}\\ \mathrm{CH_2{\cdot}CH(CO_2H){\cdot}CMe_2}\end{array}$$

In its general properties this acid resembles the diketones or, more correctly, the hydroxy-ketones obtained by Wallach (*Annalen*, 1918, **414**, 296) in an analogous manner by the action of alkali on the dibromo-derivatives of various cyclic ketones. Wallach considered that the two bromine atoms were not attached to the same carbon atom and that the formation of the diketone proceeded in accordance with the scheme :



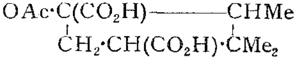
Our experiments do not furnish any evidence in support of this somewhat complicated series of reactions and we prefer for the present to assume that the dibromo-ester has formula (VIII).

The hydroxyketo-ester (or acid), on digestion with a strong solution of potassium hydroxide (50 per cent. KOH), behaves in a similar manner to Wallach's hydroxy-ketones, undergoing molecular rearrangement with addition of water and becoming converted into a dibasic hydroxy-acid identical with the acid (B) that forms the main product of the action of alkali on the dibromo-ester. There can be no doubt that this acid is *1-hydroxy-4 : 4 : 5-trimethyl*cyclo*pentane-1 : 3-dicarboxylic acid* (XII). It yields an unsaturated acid when heated above its melting point and gives an *acetyl* derivative (XIII) when digested with acetic anhydride. It is somewhat remarkable that the



$$\begin{array}{l}OH\cdot C(CO_2H)\text{————}CHMe\\ \quad CH_2\cdot CH(CO_2H)\cdot CMe_2\end{array}$$

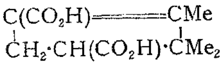
(XII)

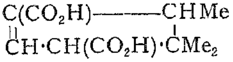


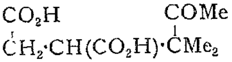
$$\begin{array}{l}OAc\cdot C(CO_2H)\text{————}CHMe\\ \quad CH_2\cdot CH(CO_2H)\cdot CMe_2\end{array}$$

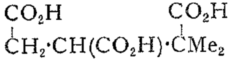
(XIII)

acid yields neither a lactone nor an anhydride, since either the carboxyl groups or the hydroxyl and one carboxyl group must be in the *cis*-position. We are of opinion that the carboxyl groups are in the *trans*-position, because the acetyl derivative of the hydroxy-acid, when heated to its melting point, loses acetic acid and is converted quantitatively into an unsaturated acid, $C_{10}H_{14}O_4$, m. p. 257°. This acid is identical with the unsaturated acid (C) referred to on p. 44 and must be represented by formula (XIV) or (XV) ; there can be no doubt that it is *4 : 4 : 5-trimethyl-*Δ^5-cyclo*pentene-1 : 3-dicarboxylic acid* (XIV). On oxidation with potassium permanganate, it yields a dibasic *keto-acid*, $C_9H_{14}O_5$, m. p. 125—126°, which, on further oxidation with sodium hypobromite, gives γ-methylbutane-αβγ-tricarboxylic acid (XVIII). The keto-acid must therefore be *γ-acetyl-γ-methylbutane-αβ-dicarboxylic acid* (XVII), γ-Methylbutane αβγ-tricarboxylic acid is also formed when 4 : 4 : 5-trimethyl-Δ⁵-*cyclo*pentene-1 : 3-dicarboxylic acid is oxidised with dilute nitric acid.

(XIV)

$$\begin{array}{l}\mathrm{C(CO_2H)\!=\!=\!=\!=\!=CMe}\\ \mathrm{\overset{|}{C}H_2\cdot CH(CO_2H)\cdot\overset{|}{C}Me_2}\end{array}$$


$$\begin{array}{l}\mathrm{C(CO_2H)\!-\!-\!-\!-\!-CHMe}\\ \mathrm{\overset{\|}{C}H\cdot CH(CO_2H)\cdot\overset{|}{C}Me_2}\end{array}$$
(XV)

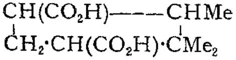
(XVII)

$$\begin{array}{l}\mathrm{CO_2H\qquad\qquad\quad COMe}\\ \mathrm{\overset{|}{C}H_2\cdot CH(CO_2H)\cdot\overset{|}{C}Me_2}\end{array}$$

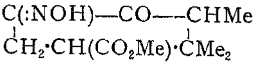

$$\begin{array}{l}\mathrm{CO_2H\qquad\qquad\quad CO_2H}\\ \mathrm{\overset{|}{C}H_2\cdot CH(CO_2H)\cdot\overset{|}{C}Me_2}\end{array}$$
(XVIII)

When 4 : 4 : 5-trimethyl-Δ⁵-*cyclo*pentene-1 : 3-dicarboxylic acid is oxidised with potassium permanganate at 0°, in addition to γ-acetyl-γ-methylbutane-αβ-dicarboxylic acid a second *keto-dicarboxylic* acid, $C_{10}H_{12}O_5$, m. p. 183–185°, is formed. This acid, which was characterised by the preparation of the *oxime* and *semicarbazone*, was unstable to potassium permanganate in alkaline solution. It was unfortunately not obtained in quantity and we are unable to suggest a satisfactory formula or account for its formation. The reaction would appear to be abnormal and recalls the conversion of Δ¹-*cyclo*hexeneacetic acid into 1-acetyl-Δ¹-*cyclo*pentene by an alkaline solution of potassium permanganate (Perkin and Wallach, *Ber.*, 1909, **42**, 145). On oxidation with dilute nitric acid, the keto-acid yielded γ-methylbutane-αβγ-tricarboxylic acid, whilst on treatment with sodium hypobromite solution, although carbon tetrabromide and bromoform separated, the product was a resin which could not be crystallised and contained an appreciable quantity of bromine.

4:4 : 5-Trimethyl-Δ⁵-*cyclo*pentene-1 : 3-dicarboxylic acid was somewhat resistant to reducing agents, but it was converted into the saturated *cyclo*pentane *acid* (XVI) by an excess of sodium and boiling amyl alcohol.

Unlike all the substances so far described, the unsaturated acid (D), m. p. 215–216° (p. 44) was optically active, the *sodium* salt being laevorotatory. Since the acid was racemised, with formation of the saturated cyclic acid (XVI), on reduction with sodium and amyl alcohol and yielded γ-methylbutane-αβγ-tricarboxylic acid on oxidation with nitric acid, there can be no doubt that it is the lævo-form of (XIV).

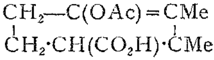
(XVI)

$$\begin{array}{l}\mathrm{CH(CO_2H)\!-\!-\!-\!-CHMe}\\ \mathrm{\overset{|}{C}H_2\cdot CH(CO_2H)\cdot\overset{|}{C}Me_2}\end{array}$$


$$\begin{array}{l}\mathrm{C({:}NOH)\!-\!CO\!-\!-CHMe}\\ \mathrm{\overset{|}{C}H_2\cdot CH(CO_2Me)\cdot\overset{|}{C}Me_2}\end{array}$$
(XIX)

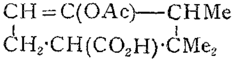
The foregoing results appear to us to establish definitely that the keto-acid first described by Manasse and Samuel must be d-2 : 2 : 3-*trimethyl*cyclo*hexan*-4-*one*-1-*carboxylic acid* (II), and it became necessary once more to attempt the preparation of an oximinoderivate. Although neither the acid nor the methyl ester could be induced to react with benzaldehyde or piperonal, the methyl ester reacted with amyl nitrite in the presence of sodium to yield an oil which was soluble in alkali and was evidently the crude *oximino-ester* (XIX). This ester could not be obtained crystalline, but on hydrolysis with formaldehyde and hydrochloric acid, followed by treatment with a dilute solution of potassium hydroxide, it gave an acid which partly crystallised on keeping. This acid, which was evidently somewhat impure 4-hydroxy-2 : 2 : 3-trimethyl-Δ^3-*cyclo*hexen-5-one-1-carboxylic acid (XI), was not purified, but was converted into the *cyclo*pentene acid by the reactions outlined above. The acid melted at 257° and was identical with that prepared from the dibromo-ester. The formation of 4 : 4 : 5-trimethyl-Δ^5-*cyclo*pentene-1 : 3-dicarboxylic acid in this manner would appear to eliminate definitely and possibility of molecular rearrangement during its formation from the bromo-ester.

The suggestion (*loc. cit.*, p. 1296) that the keto-acid can exist in keto- and enol-forms has been confirmed by Mr. Aswath Narain Rao, who has prepared the *acetyl* derivative of the enolic form by treating camphorquinone with acetic anhydride and zinc chloride. This acetyl derivative is lævorotatarory in chloroform solution and does not show mutarotation. It may be represented by formula (XX) or (XXI), and from analogy with the other unsaturated acids here referred to we are inclined to consider (XX) the more probable.

(XX)



$$\begin{array}{lll}\mathrm{CH_2}&\mathrm{{-}C(OAc){=}}&\mathrm{CMe}\\ |&&|\\ \mathrm{CH_2}&\mathrm{{\cdot}CH(CO_2H){\cdot}}&\mathrm{CMe_2}\end{array}$$

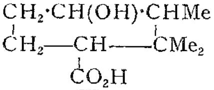


$$\begin{array}{lll}\mathrm{CH}&\mathrm{{=}C(OAc){-}}&\mathrm{CHMe}\\ |&&|\\ \mathrm{CH_2}&\mathrm{{\cdot}CH(CO_2H){\cdot}}&\mathrm{CMe_2}\end{array}$$

(XXI)

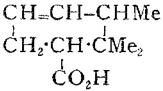
On hydrolysis, the acetyl derivative yields the ordinary ketonic form of the acid and all attempts to prepare it by direct acetylation have proved unsuccessful.

Since the acid previously considered to be *d*-2 : 2 : 4-trimethyl*cyclo*hexan-3-one-1-carboxylic acid has now been shown to be *d*-2 : 2 : 3-trimethyl*cyclo*hexan-4-one-1-carboxylic acid, the constitution of some of the compounds prepared from it require revision. *trans-d*-3-Hydroxy-2 : 2 : 4-trimethyl*cyclo*hexane-1-carboxylic acid should be *trans-d*-4-hydroxy-2 : 2 : 3-trimethyl*cyclo*hexane-1-carboxylic acid (XXII), and the unsaturated acid derived therefrom must be represented by formula (XXIII) or (XXIV.)



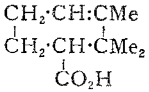
$$\begin{array}{ccc}\mathrm{CH_2}&\mathrm{{\cdot}CH(OH){\cdot}}&\mathrm{CHMe}\\ |&&|\\ \mathrm{CH_2}&\mathrm{{-}CH{-}}&\mathrm{CMe_2}\\ &|&\\ &\mathrm{CO_2H}&\end{array}$$

(XXII)



$$\begin{array}{ccc}\mathrm{CH}&\mathrm{{=}CH{-}}&\mathrm{CHMe}\\ |&&|\\ \mathrm{CH_2}&\mathrm{{\cdot}CH{\cdot}}&\mathrm{CMe_2}\\ &|&\\ &\mathrm{CO_2H}&\end{array}$$

(XXIII)



$$\begin{array}{ccc}\mathrm{CH_2}&\mathrm{{\cdot}CH{:}}&\mathrm{CMe}\\ |&&|\\ \mathrm{CH_2}&\mathrm{{\cdot}CH{\cdot}}&\mathrm{CMe_2}\\ &|&\\ &\mathrm{CO_2H}&\end{array}$$

(XXIV)

EXPERIMENTAL.

Bromination of Methyl 2 : 2 : 3-*Trimethyl*cyclo*hexan*-4-*one*-1-*carboxylate. Methyl* 5 : 5-*Dibromo*-2 : 2 : 3-*trimethyl*cyclo*hexan*-4-*one*-1-*carboxylate* (VIII).—To a well-cooled solution of the crystalline methyl ester (55 g.) in acetic acid (280 c.c.), bromine (91·4 g.), dissolved in acetic acid (91·4 c.c.), was added. The reaction mixture was poured on to ice and the viscid oil which separated was washed with dilute aqueous sodium carbonate solution and dried in ethereal solution. On evaporation of the ether, the *dibromo-ester* was usually obtained as a brown oil, but in one experiment this gradually crystallised in needles: these were collected, drained on porous porcelain, and recrystallised from methyl alcohol, the dibromoester thus being obtained in glistening prisms, m. p. 57–58° (Found: Br, 45·1. $C_{11}H_{16}O_3Br_2$ requiries Br, 44·9).

Action of Barium Hydroxide on Methyl 5 : 5-*Dibromo*-2 : 2 : 3-*trimethyl*cyclo*hexan*-4-*one*-1-*carboxylate*.—A mixture of the crystalline (or liquid) dibromo-ester (26 g.) with a hot solution of barium hydroxide (52 g. in 170 c. c. of water) was boiled with constant agitation during one hour. The hot solution was filtered from a little insoluble matter (from which a further quantity of the mixed acids was obtained after treatment with a boiling solution of potassium hydroxide) and acidified. The liberated acids, which were isolated as a viscid brown oil (15 g.) by means of ether and partly crystallised on keeping, were esterified with methyl alcohol in the usual manner, and the esters formed were dissolved in ether. The ethereal solution was washed with dilute aqueous sodium carbonate (A), and then with 5 per cent sodium hydroxide solution (B) until a test portion no longer gave a colour with ferric chloride. The ethereal solution was then dried and the solvent evaporated (C).

The sodium carbonate extract (A) on acidification yielded a small quantity of a resinous acid which was not further examined.

Methyl 4-*Hydroxy*-2 : 2 : 3-*trimethyl*-Δ^3-cyclo*hexen*-5-*one*-1-*carboxylate* (formula as XI).—The deep red sodium hydroxide extract (B) was saturated with carbon dioxide and the colourless crystalline solid that separated was collected (1·4 g.); the alkaline solution was then acidified and the viscid red oil produced was added to the mixture of acids obtained in later experiments and re-esterified.

The crystalline solid separated from light petroleum in rosettes of prismatic needles, m. p. 73–74° (Found : C, 61·9; H, 7·6. $C_{11}H_{16}O_4$ requires C, 62·3; H, 7·5 per cent.). The ester was appreciably soluble in hot water and dissolved readily in all the ordinary organic solvents except light petroleum, in which it was somewhat sparingly soluble. It gave with alcoholic ferric chloride a dirty green coloration, which was discharged by a trace of alkali.

The *dioxime*, which was obtained by heating the ester with hydroxylamine hydrochloride and sodium acetate in methyl-alcholic solution, crystallised from benzene in fine needles, m. p. 138–139° (Found: C, 54·1; H, 7·5; N, 11·9. $C_{11}H_{18}O_4N_2$ requires C, 54·5; H, 7·4; N, 11·6 per cent.). In alcoholic solution it gave with ferric chloride a deep brown coloration. The *disemicarbazone* separated from hot water, in which it was somewhat readily soluble, in prisms, m.p. 206–237° (Found: N, 25·9. $C_{13}H_{22}O_4N_6$ requires N, 25·8 per cent.).

4-Hydroxy-2 : 2 : 3-trimethyl-Δ^3-cyclo*hexen-5-one-1-carboxylic acid* (XI), obtained by hydrolysing the methyl ester on the water-bath with a slight excess of dilute potassium hydroxide solution, crystallised from hot water or toluene in prismatic needle, m.p. 151–152° (Found: C, 60·8, 60·7; H, 7·4, 7·2. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1 per cent. It was readily soluble in hot water, alcohol, acetone, or ether, but more sparingly soluble in chloroform, benzene, or toluene, and gave a dirty bluish-green coloration with aqueous or alcoholic ferric chloride. In alkaline solution it immediately decolorised potassium permanganate, but it did not react with bromine. The acid was readily oxidised by hydrogen peroxide, but the crystalline products were too small in quantity for identification. It condensed with *o*-phenylenediamine, and on treatment with phenylhydrazine it gave a mixture of the *mono-* and the *di-phenylhydrazone* as a yellow, amorphous solid, which was purified by solution in alkali and precipitation by acid (Found: N, 11·5. $C_{16}H_{20}O_3N_2$ requires N, 9·7 per cent. $C_{22}H_{26}O_2N_4$ requires N, 14·8 per cent.).

The *acetyl* derivative, prepared by digesting the acid with acetyl chloride, crystallised from water in irregular plates; these melted at 95° when air-dried and at 128° after being dried over sulphuric acid. They retained water of crystallisation ($\frac{1}{2}$ mol.) even after being kept for some months in a vacuum over phosphoric oxide (Found: C, 58·0; H, 6·7. $C_{12}H_{16}O_5, \frac{1}{2}H_2O$ requires C, 57·8; H, 6·8 per cent.).

Conversion of 4-Hydroxy-2 : 2 : 3-trimethyl-Δ^3-cyclo*hexen-5-one-1-carboxylic acid into 1-Hydroxy-4 : 4 : 5-trimethyl*cyclo*pentane-1 : 3-dicarboxylic Acid* (XII).—A mixture of the hydroxyketo-acid (1 mol.) and 50 per cent. potassium hydroxide solution (3 mols.) was boiled for one hour. The product, obtained in quantitative yield on cooling and acidification, melted at 191–192° after crystallisation from hot water and was identified with the following acid by the mixed melting-point method (Found: C, 55·1; H, 7·9 per cent.).

1-*Hydroxy*-4 : 4 : 5-*trimethyl*cyclo*pentane*-1 : 3-*dicarboxylic Acid* (XII).—The ester fraction (C) (p. 48) distilled almost entirely at 150–160°/10 mm. as a colourless oil, which was a mixture. The ester from one experiment (55 g.) was heated with an excess of methyl-alcoholic potassium hydroxide on the water-bath for 1 hour, and the solution kept at 0° for 12 hours. A somewhat sparingly soluble *potassium* salt separated in needles. This was well washed with ice-cold methyl alcohol (the filtrate, C_1, was reserved for later examination), dissolved in the minimum quantity of water, and acidified ; a precipitate (16 g.) separated, and a little more was extracted from the filtrate with ether, 1-*Hydroxy*-4 : 4: 5-*trimethyl*cyclo*pentane*-1 : 3-*dicarboxylic acid* thus obtained crystallised from hot water in glistening needles, m. p. 191–192° after softening at 184°, which contained $\frac{1}{2}H_2O$ (Found : C, 53·2 ; H, 7·8 ; H_2O, 4·0. $C_{10}H_{16}O_5$, $\frac{1}{2}H_2O$ requires C, 53·3 ; H, 7·6; H_2O, 4·0 per cent. Found in material dried at 110°: C, 55.5; H, 7·5. $C_{10}H_{16}O_5$ requires C, 55·5 ; H, 7·4 per cent. It was sparingly soluble in benzene, chloroform, or light petroleum, readily soluble in alcohol or acetic acid, gave no coloration with ferric chloride, was stable to potassium permanganate in alkaline solution, and was optically inactive.

The acid was treated with phosphorus pentachloride (3 mols.) and the product, after removal of the phosphorus oxychloride under diminished pressure, poured into formic acid. 4 : 4 : 5-Trimethyl-Δ^5-*cyclo*pentene-1 : 3-dicarboxylic acid, m. p. 257°, was thus obtained in poor yield; the other products of the reaction were not examined.

The *acetyl* derivative (XIII) formed when the hydroxy-acid was digested for 1 hour with an excess of acetic anhydride was obtained in needles on addition of water and concentration of the solution ; it was recrystallised from hot water, in which it was somewhat sparingly soluble (Found: C, 55·7 ; H, 7·5. $C_{12}H_{18}O_6$ requires C, 55·8 ; H, 7·0 per cent.) It decomposed at 207–208° and immediately resolidified to a product, m. p. 257°, which was 4 : 4 : 5-trimethyl-Δ^5-*cyclo* pentene-1 : 3-dicarboxylic acid ; the elimination, of acetic acid is quantitative and this is the simplest method for the preparation of the pure unsaturated acid.

4 : 4 : 5-*Trimethyl*-Δ^5-cyclo*pentene*-1 : 3-*dicarboxylic Acid* (XIV).—The methyl-alcoholic solution (C_1, above) from which the potassium salt of the hydroxy-acid had been separated was freed from alcohol on the water-bath and acidified ; the crystalline precipitate was collected (7 g.) and the filtrate (C_2) reserved. By recrystallising the former from methyl alcohol, 4 : 4 : 5-*trimethyl*-Δ^5-cyclo*pentene* : 1 : 3-*dicarboxylic acid* was obtained in glistening rhombohedra, m. p. 257–258° (Found : C, 60·5 ; H, 7·2 ; *M*, 197·8. $C_{10}H_{14}O_4$ requires C, 60·6 ; H, 7·1 per cent. ; *M*, 198). It was very sparingly soluble in water, ether, benzene,

or chloroform, and more readily soluble in hot methyl alcohol, acetic acid, or formic acid. It immediately decolorised an alkaline solution of potassium permanganate, but reacted neither with bromine in acetic acid, solution nor with sodium amalgam at the ordinary temperature. When heated above its melting point, it did not yield an anhydride, but sublimed in long needles with very little decomposition. The aqueous solution of the *sodium* salt was optically inactive. The *dianilide*, prepared from the acid chloride in the usual manner, crystallised from dilute alcohol in fine needles, m. p. 200–201° (Found : C, 75·7 ; H, 7·4. $C_{22}H_{24}O_{22}N_2$ requires C, 75·9 ; H, 6·9 per cent.)

4 : 4 : 5-*Trimethyl*cyclo*pentane*-1 : 3-*dicarboxylic Acid* (XVI) was obtained in an excellent yield when the unsaturated acid was reduced with sodium and amyl alcohol. It separated from hot water in soft, glistening prisms, m. p. 182–183°, and showed no tendency to yield an anhydride, small quantities distilling unchanged. It would appear, therefore, to be the *trans*-acid. It was readily soluble in hot water, alcohol, or ethyl acetate, and very sparingly soluble in benzene or chloroform (Found: C, 59·7 ; H, 8·3. $C_{10}H_{16}O_4$ requires C, 60·0 ; H, 8·0 per cent.)

1-4 : 4 : 5-*Trimethyl*-Δ^5-cyclo*pentene*-1 : 3-*dicarboxylic Acid.*—The filtrate (C_2), on extraction with ether, yielded a viscid yellow oil which could not be purified. Since it apparently contained a quantity of the hydroxy*cyclo*pentanedicarboxylic acid, it was digested with acetic anhydride and the crude acetyl derivative was heated at 200–210° until all evolution of acetic acid had ceased. The melt was dissolved in sodium carbonate solution, filtered from a little tar, and acidified. The solid which separated was collected, the filtrate (C_3) being reserved, and recrystallised from methyl alcohol, a further quantity of the *cyclo*pentene acid, m. p. 257°, being obtained. The methyl-alcoholic filtrate was evaporated, and the residue repeatedly crystallised from formic acid ; 1-4 : 4 : 5-*trimethyl*-Δ^5-cyclo*pentene*-1 : 3-*dicarboxylic acid* was thus obtained in irregular plates, m. p. 215–216° (Found : C, 60·5 ; H, 7·5. $C_{10}H_{14}O_4$ requires C, 60·6 ; H, 7·1 per cent.) This acid was very much more readily soluble in all the ordinary organic solvents than its inactive isomeride. On reduction with sodium and amyl alcohol, it yielded the inactive *cyclo*pentane acid (XVI). Under the conditions used for the oxidation of the racemic acid with nitric acid (see below), it gave γ-methylbutane-$\alpha\beta\gamma$-tricarboxylic acid, decomp. 154–155°, thus leaving no doubt as to its constitution. The sodium salt was lævorotatory in aqueous solution ; $[\alpha]_{D}^{25^\circ}-62^\circ$.

The *dianilide* crystallised from dilute alcohol in glistening cubes, m. p. 208–209° (Found : N, 8·4. $C_{22}H_{24}O_2N_2$ requires N, 8·0 per cent.)

The filtrate (C_3, above) gave on extraction with ether a viscid oil which on trituration with formic acid yielded a further small quantity of the *l*-unsaturated acid. The formic acid-mother-liquor contained an oil which was not examined.

Oxidation of 4 : 4 : 5-*Trimethyl*-Δ^5-cyclo*pentene*-1 : 3-*dicarboxylic Acid.*—(i) *With nitric acid.* The unsaturated acid (2 g.) was heated with nitric acid (*d* 1·2 ; 35 c.c.) on a water-bath for 8 hours and on a sand-bath for 8 hours ; nitric acid (*d* 1·4 ; 15 c.c.) was then added and the heating continued for a further 8 hours, a clear solution being obtained. The excess of mineral acid was removed on the water bath ; the viscid oily residue, on trituration with a little hydrochloric acid, crystallised almost completely. After draining on porous porcelain, it was recrystallised from a little hydrochloric acid, γ-methylbutane-βγ-tricarboxylic acid separating in rosettes of needles, decomp. 154–155° (Found : C, 47·2; H, 5·8; *M*, 205. Calc. : C, 47·1 ; H, 5·9 per cent; *M*, 204). The identity of this acid was confirmed by the preparation of the anhydride, m.p. 142°.

(ii) *With potassium permanganate.* To a solution, at 0–5° of the *cyclo*pentene acid (5 g.) in aqueous sodium carbonate through which a current of carbon dioxide was passing, 2·5 per cent. potassium permanganate solution (equiv. to 1 O_2) was added ; the colour then remained permanent for 5 minutes. The filtered solution was concentrated in a current of carbon dioxide, acidified, and repeatedly extracted with ether and the extracts were dried and evaporated ; a viscid brown oil remained which partly crystallised. This was triturated with concentrated hydrochloric acid, which removed a readily soluble brown oil (Z), and the residue was drained on porous porcelain and recrystallised from hydrochloric acid or from acetone-benzene ; a *ketodicarboxylic acid* was thus obtained in glistening prisms, m.p. 182–183°, softening at 177° (Found : C, 56·4, 56·9 ; H, 6·0, 5·8 ; *M*, 212·6. $C_{10}H_{12}O_5$ requires C, 56·6 H, 5·6, per cent. ; *M*, 212). This acid was readily soluble in water, alcohol, ethyl acetate, or acetone, and more sparingly soluble in benzene or chloroform. It was slowly attacked by hot chromic acid solution, did not absorb bromine in acetic acid solution, and rapidly decolorised an alkaline solution of potassium permanganate at room temperature. It was readily oxidised by sodium hypobromite with formation of bromoform and carbon tetrabromide ; the acid resulting from the oxidation was a gum which contained bromine and was not further examined. The salts of the keto-acid are readily soluble in water.

The *oxime* crystallised in small plates, decomp. 214°, containing apparently $\frac{1}{2}H_2O$ which it did not lose at 100° (Found : C, 50·6, 50·7 ; H, 5·8, 6·2. $C_{10}H_{13}O_5N, \frac{1}{2}H_2O$ requires C, 50·8 ; H, 5·9 per cent.).

The *semicarbazone* crystallised from dilute alcohol in microscopic prisms, decomp. 241° (Found: C, 48·8; H, 5·9. $C_{11}H_{15}O_5N_3$ requires C, 49·1; H, 5·6 per cent.

The keto-acid, on oxidation with nitric acid (*d* 1·2), gave an excellent yield of γ-methylbutane-αβγ-tricarboxylic acid.

γ-Acetyl-γ-methylbutane-αβ-dicarboxylic Acid (XVII).—The hydrochloric acid solution (Z, above) gave, after the removal of the solvent in a vacuum over potassium hydroxide, a viscid brown oil. This (7 g.) was oxidised in sodium carbonate solution with potassium permanganate at 15–20°. Repeated extraction of the filtered, concentrated, and acidified solution with ether yielded an oil which partly crystallised. The solid was collected and recrystallised from dry ether, in which it was only sparingly soluble, *γ-acetyl-γ-methylbutane-αβ-dicarboxylic acid* separating in fine, glistening prisms, m. p. 125–126°. This acid was readily soluble in water or alcohol, but sparingly soluble in benzene or light petroleum. It did not react with phenylhydrazine or semicarbazide (Found: C, 53·1; H, 7·2. $C_9H_{14}O_5$ requires C, 53·5, H, 6·9 per cent.).

When a solution of the sodium salt of the keto-acid was treated with the calculated quantity of a solution of sodium hypobromite, bromoform immediately separated. After 1 hour, this was removed and the alkaline solution was acidified and extracted with ether; the oil obtained on removal of the solvent immediately crystallised and was identified as γ-methylbutane-αβγ-tricarboxylic acid.

*Methyl 5-oximino-2:2:3-trimethyl*cyclo*hexan-4-one-1-carboxylate* (XIX).—Methyl *d*-2:2:3-trimethyl*cyclo*hexan-4-one-1-carboxylate (0·5g.) was dissolved in ether containing finely divided sodium (0·06 g.), and to the well-cooled mixture *iso*amyl nitrite (0·26 g.) in ether was added. After the mixture had been kept at 0° for 12 hours the sodium had completely dissolved and a flocculent, yellow precipitate had separated. Ice was then added and the yellow, aqueous solution was separated and acidified. The brown oil obtained (0·3 g.), which showed no tendency to crystallise, was analysed after being kept for some days in a vacuum over sulphuric acid. The first and the second analysis refer to specimens prepared from the crystalline and the liquid ester, respectively (Found: N, 6·5, 6·7. $C_{11}H_{17}O_4N$ requires N, 6·2 per cent.) The *oximino-ester* was soluble in all the ordinary organic solvents and in a solution of potassium hydroxide, but was insoluble in aqueous sodium carbonate; it gave with alcoholic ferric chloride a deep brown coloration.

The ester[1] was hydrolysed by treatment with formaldehyde and hydrochloric acid, followed by dilute aqueous potassium hydroxide; the viscid oil obtained gave with ferric chloride a dirty bluish-green coloration. On keeping, the oil partly crystallised, but, as the quantity of material available was small, no attempt was made at purification and the oil was converted directly into 4 : 4 : 5-trimethyl-Δ^5-*cyclo* pentene-1 : 3-dicarboxylic acid by the methods already described. The *cyclo*pentene acid prepared in this manner crystallised from methyl alcohol in the characteristic rhombohedra, m. p. 257–258°, and was identical in every way with the acid prepared from the dibromo-ester.

1-4-*Acetyl* 2 : 2 : 3-*trimethyl*-Δ^3-cyclo*hexene*-1-*carboxylic Acid* (XX [with ASWATH NARAIN RAO].—A mixture of camphorquinone (25 g.) acetic anhydride (75 c.c.), and freshly-fused zinc chloride (5 g.), was heated on a sand-bath, a vigorous reaction taking place with effervescence and evolution of heat. As soon as the reaction started, the source of heat was removed and the dark brown solution was allowed to cool, diluted with water (150 c.c.), and warmed on the water-bath for a short time to decompose the acetic anhydride. After 12 hours, the pale yellow precipitate of needles and tar was collected and washed with water (yield, 25·5 g.). The filtrate, on neutralisation of the excess of acetic acid with solid sodium carbonate, deposited a further quantity of solid (1 g.). The crude product was repeatedly extracted with dilute sodium carbonate solution until a test portion no longer gave a precipitate on acidification. The residue was extracted with dilute sodium hydroxide solution, which left undissolved camphorquinone (5·4 g.) and a little tar. The sodium hydroxide solution, on acidification, deposited a resinous mass which could not be purified. The deep brown sodium carbonate extract was carefully acidified with dilute sulphuric acid; after the addition of a small quantity of acid, the solution was extracted with ether to remove resinous impurities; on further addition of acid, an oil was deposited which, on evaporation of the dissolved ether, solidified. The crude acid (13·2 g.) was crystallised from hot water, dilute alcohol, or, preferably, light petroleum (b.p. 60–80°), 1-4-*acetyl*-2 : 2 : 3-*trimethyl*-Δ^3-cyclo*hexene*-1-*carboxylic acid* separating in colourless, transparent, glistening laminæ, m. p. 109–111° (Found: C, 63·2; H, 8·3; *M*, 224. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0 per cent.; *M*, 226). In chloroform solution (1·283 g. in 25 c.c.), it showed $[\alpha]_D$–66·3°, and this value did not alter during 48 hours. In carbon tetrachloride solution the acid absorbed an equivalent weight of bromine, hydrogen bromide being evolved, and on evaporation of the solvent a sharp-smelling oil remained. In

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[1] During the hydrolysis with potassium hydroxide amyl alcohol separated, indicating that 'alcoholysis' with partial formation of the amyl ester had taken place during the reaction with amyl nitrite.

alkaline solution, the acid was unstable to potassium permanganate; the products of the reaction could not be identified.

A solution of the acid (1 g.) in 15 per cent sodium hydroxide solution (8 c.c.) was heated on the water-bath for three hours. On acidification of the cooled solution, an oil was precipitated which partly solidified over-night. The solid was separated, drained on porous porcelain, and recrystallised from water; it was then obtained in needles, m. p. 69–70°. The anhydrous acid melted at 97–98°. It yielded a semicarbazone, m. p. 227–228°, and was identified as 2 : 2 : 3-trimethyl*cyclo*hexan-1-one-1-carboxylic acid by direct comparison with an authentic specimen. The oil extracted from the porous porcelain on which the keto-acid had been drained gave no colour with ferric chloride and evidently contained no hydroxy-acid. The enolic form, therefore, would appear to be incapable of existence. Attempts were made to acetylate the keto-acid directly, but in all cases the acid was recovered unchanged.

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