CCCCI.—*Derivatives of Methyl* 2 : 2-*Dimethyl*cyclo*pentan*-3-*one*-1-*carboxylate*.

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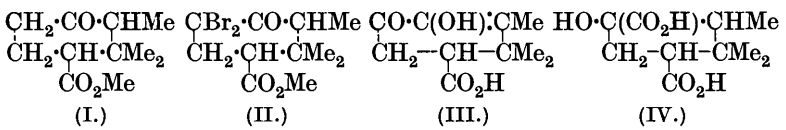
IT was shown recently that when methyl 2 : 2 : 3-trimethyl*cyclo*hexan-4-one-1-carboxylate (I) (J., 1925, **127**, 1294; this vol., p. 77) was brominated it yielded the dibromo-ester (II) and that this ester on treatment with alkali gave together with other products the hydroxyketo-acid (III) and the dibasic hydroxy-acid (IV).



(I.) (II.) (III.) (IV.)

It has appeared to us of interest to investigate whether *methyl* 2 : 2-*dimethyl*cyclo*pentan*-3-*one*-1-*carboxylate* (V) would on treatment with bromine and alkali behave in a similar manner, yielding the

dibromo-ester (VI), the hydroxyketo-acid (VII) and a dibasic hydroxy-acid (VIII). The latter acid would be of particular importance, being the hydroxy-acid related to norpinic acid (IX), the synthesis of which has still to be effected.

CMe_2--CO--CH_2 / $CH(CO_2Me)$·CH_2 (V.)

CMe_2--CO—CBr_2 / $CH(CO_2Me)$·CH_2 (VI.)

CMe_2—CO—CHBr / $CBr(CO_2Me)$·CH_2 (VIA.)

CMe_2--CO—C·OH / $CH(CO_2H)$·CH (VII.)

CMe_2———C(OH)·CO_2H / $CH(CO_2H)$·CH_2 (VIII.)

CMe_2———CH·CO_2H / $CH(CO_2H)$·CH_2 (IX.)

2 : 2-Dimethyl*cyclo*pentan-3-one-1-carboxylic acid was prepared by Perkin and Thorpe (J., 1904, **85**, 138), and by a modification of their process we have devised a method for obtaining it in excellent yield. When the *methyl* ester was brominated in acetic acid solution a crystalline *dibromo-ester* was obtained which is probably best represented by formula (VI); it is, however, not impossible that, in accordance with Wallach's views (*Annalen*, 1918, **414**, 296), the correct representation is by formula (VIA), and this will be further discussed below. This ester was readily acted upon by alkali, the main product of the reaction being a crystalline acid, $C_8H_{10}O_4$, m. p. 150—152°. There can be no doubt that this acid is represented by formula (X) for the following reasons: it gives a deep brown coloration with ferric chloride in aqueous solution and its alkaline solution is immediately oxidised by potassium permanganate; further, when oxidised with dilute nitric acid, it yields a mixture of dimethylmalonic acid and oxalic acid.

(X CMe_2·CO·CH·OH / $C(CO_2H)$:CH

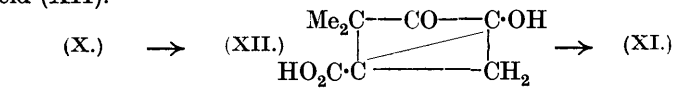
CMe_2–CO–CO / $CH(CO_2H)$·CH_2 (XI.)

4-*Hydroxy*-2 : 2-*dimethyl*-Δ^5-cyclo*penten*-3-*one*-1-*carboxylic acid* can, however, also react in its tautomeric form as the diketo-acid (XI), since on treatment with semicarbazide acetate it yields a *disemicarbazone* and with *o*-phenylenediamine a *quinoxaline* derivative. The ketohydroxy-acid showed no tendency to yield a lactone, giving with acetyl chloride a liquid acetyl derivative, and when it was distilled under diminished pressure, apart from the formation of an oil which was probably 3 : 3-*dimethyl*cyclo*pentane*-1 : 2-*dione*, the greater part of the acid was recovered unchanged. On titration, the acid behaved like a dibasic acid, the hydroxy-group being evidently activated by the adjacent carbonyl group.

Since the conversion of (XI) into (X) must proceed through the intermediate stage of (VII)—an example of $\alpha\beta$: $\beta\gamma$-tautomerism—an attempt was made to find the acid (VII) amongst the products

of the action of alkali on the dibromo-ester. An oil was separated which, unlike the Δ^5-acid, gave with ferric chloride a red coloration. This acid, which could not be obtained crystalline, gave on boiling with alkali a quantity of the crystalline Δ^5-acid, and on treatment with semicarbazide acetate and with *o*-phenylenediamine the disemicarbazone and the quinoxaline derivative of the diketo-acid were obtained. There seemed to be little doubt, therefore, that this liquid acid consisted essentially of 4-*hydroxy*-2 : 2-*dimethyl*-Δ^4-cyclo*penten*-3-*one*-1-*carboxylic acid*, and this view was confirmed by the formation of *as*-dimethylsuccinic acid on oxidation with dilute nitric acid.

The possibility that the constitution of the dibromo-ester should be represented by formula (VIA) remains to be investigated by studying the mechanism of the conversion of the Δ^5-acid (X) into the diketo-acid (XI), which may proceed by intramolecular tautomerism through the intermediate stage of the dicyclic ketohydroxy-acid (XII).



A large number of experiments were carried out with the object of converting both the Δ^4- and the Δ^5-acid into the dibasic hydroxy-acid (VIII), but no evidence of its formation has been obtained. Whether this is due to an actual inability of the *cyclo*pentane ring to pass into a *cyclo*butane ring or to the particular substituted ring used will form the subject of future experiments, which will also include the stereochemical investigation of the Δ^5-acid itself.

EXPERIMENTAL.

Ethyl $\beta\gamma$-*Dicyano*-β-*methylpentane*-$\gamma\varepsilon$-*dicarboxylate*.—To a solution of sodium (2·3 g.) in alcohol (30 g.), ethyl $\alpha\beta$-dicyano-β-methylbutyrate (18 g.) was added, the solution cooled, and ethyl β-iodopropionate (23 g.) gradually added, care being taken to avoid a rise of temperature (which produces a considerable quantity of ethyl acrylate). After remaining for 1 hour, during which time the temperature rose to about 40°, the reaction mixture was heated on the water-bath for 2 hours, water was then added, and the condensation product was isolated by extraction with ether and purified by distillation under diminished pressure. The whole distilled between 170° and 190°/5 mm. and on redistillation a large fraction was obtained, b. p. 184°/5 mm. (yield, 22 g.). *Ethyl* $\beta\gamma$-*dicyano*-β-*methylpentane*-$\gamma\varepsilon$-*dicarboxylate* is a faintly yellow, viscid oil with a somewhat unpleasant smell (Found: N, 9·8. $C_{14}H_{20}O_4N_2$ requires N, 10·0%).

β-*Methylpentane*-$\beta\gamma\varepsilon$-*tricarboxylic Acid*.—The dicyano-ester was

mixed with an equal volume of concentrated sulphuric acid, excessive rise of temperature being avoided, and when the mixture had cooled water was added until the solution was turbid. The hydrolysis was completed by boiling until evolution of carbon dioxide ceased and all the alcohol had evaporated, water being added from time to time to prevent charring (15 hrs.). From the cooled solution saturated with ammonium sulphate, the tricarboxylic acid was isolated by repeated extraction with ether. After crystallisation from hydrochloric acid it decomposed at 153—155°, but, as has been mentioned previously (*loc. cit.*, p. 1302), the m. p. is dependent on the rate of heating (Found: C, 49·8; H, 6·5. Calc.: C, 49·5; H, 6·4%).

The triethyl ester was obtained in a poor yield on esterification with alcohol and sulphuric acid; b. p. 161°/4 mm. (Found: C, 59·6; H, 8·6. Calc.: C, 59·6; H, 8·6%).

Ethyl 3 : 3-*Dimethylcyclopentan*-2-*one*-1 : 4-*dicarboxylate*.—Ethyl β-methylpentane-βγε-tricarboxylate (37 g.) was added to a suspension of finely divided sodium (5·6 g.) in benzene (100 c.c.), and the mixture warmed on the water-bath. A vigorous reaction took place and proceeded nearly to completion after removal of the source of heat; the last traces of sodium were dissolved by boiling for 1 hour. The deep brown solution was mixed with ice and made faintly acid with dilute sulphuric acid, and the benzene was separated, washed with sodium carbonate solution,* dried, and evaporated. The residual oil was distilled under diminished pressure; *ethyl* 3 : 3-*dimethylcyclopentan*-2-*one*-1 : 4-*dicarboxylate* was then obtained as a colourless oil, b. p. 145°/4 mm. (yield, 70%) (Found: C, 60·5; H, 8·1. $C_{13}H_{20}O_5$ requires C, 60·9; H, 7·8%). An alcoholic solution of the ester gave with ferric chloride a violet coloration.

2 : 2-*Dimethylcyclopentan*-3-*one*-1-*carboxylic Acid*.—The keto-ester was boiled with sulphuric acid (100 c.c.; 5%) under reflux for 6 hours. After addition of sodium carbonate sufficient to render the solution alkaline, the alcohol was removed on the water-bath and the solution was acidified and extracted with ether. On removal of the solvent the keto-acid crystallised immediately and had m. p. 108—109° as stated by Perkin and Thorpe (*loc. cit.*).

The *methyl* ester (V), prepared in the usual manner, had b. p. 158°/100 mm. (Found: C, 63·7; H, 7·9. $C_9H_{14}O_3$ requires C, 63·5; H, 8·2%).

Bromination of Methyl 2 : 2-*Dimethylcyclopentan*-3-*one*-1-*carboxylate*. *Methyl* 4 : 4-*Dibromo*-2 : 2-*dimethylcyclopentan*-3-*one*-1-*carboxylate* (VI).—A solution of the ester (17 g.) in acetic

* The sodium carbonate solution on acidification yielded a small quantity of a viscid oil which was not examined.

acid (17 c.c.) was kept at 5—10° while bromine (32 g.) in acetic acid (10 c.c.) was gradually added. The bromine was very rapidly absorbed with evolution of hydrogen bromide. When the addition was complete the mixture was poured on ice. A heavy oil was deposited which solidified. The *bromo*-ester crystallised from dilute methyl alcohol or dilute formic acid in long prisms, m. p. 76—77° (yield, 86%) (Found: Br, 48·8. $C_9H_{12}O_3Br_2$ requires Br, 48·8%).

Action of Barium Hydroxide on Methyl 4 : 4-*Dibromo*-2 : 2-*dimethyl*cyclo*pentan*-3-*one*-1-*carboxylate*.—To the bromo-ester (34 g.) a hot solution of barium hydroxide (96 g.) in water (250 c.c.) was added, and the reaction mixture boiled under reflux. A vigorous action ensued and in order to avoid loss of material it was necessary to remove the source of heat. The hydrolysis was completed by boiling for 45 minutes, and the pale yellow solution was then evaporated on the water-bath until free from alcohol, acidified, and repeatedly extracted with ether. On removal of the solvent a crystalline cake remained (17 g.). This was mixed with benzene (50 c.c.) and after digestion allowed to remain over-night in the ice-chest; the acid which was insoluble in benzene was then collected and the filtrate (A) reserved for later investigation.

The acid (m. p. 148—150°) crystallised from hydrochloric acid in glistening prisms, m. p. 150—152° (slight decomp.) (Found: C, 56·0; H, 5·9. $C_8H_{10}O_4$ requires C, 56·4; H, 5·9%).

4-*Hydroxy*-2 : 2-*dimethyl*-Δ^5-cyclo*penten*-3-*one*-1-*carboxylic acid* (X) was readily soluble in water, acetone, ethyl acetate and formic acid, very sparingly soluble in benzene, toluene, and light petroleum, somewhat more soluble in chloroform. It gave a brown coloration with ferric chloride and immediately decolorised alkaline potassium permanganate. In chloroform it rapidly absorbed bromine, but the bromo-acid decomposed with evolution of hydrogen bromide. From its deep yellow solution in concentrated sulphuric acid the acid could be recovered unchanged. On titration with alkali and phenolphthalein it behaved as a dibasic acid, but the end-point was not quite sharp (Found: *M*, 176. Calc.: *M*, 170). The acid decomposed when heated above its melting point, but it distilled under diminished pressure largely unchanged and showed no tendency to lactone formation. A small quantity of a neutral yellow oil was separated (b. p. 80—100°/4 mm.) which gave a deep red colour with ferric chloride and showed weakly acidic properties. The oil, which was readily soluble in water, yielded a resinous semicarbazone and a liquid phenylhydrazone. With *o*-phenylenediamine it gave an oil which appeared to be a quinoxaline derivative and it also gave a sparingly soluble, oily benzoyl deriv-

ative. Although, therefore, it was not possible to characterise the oil, there can be little doubt that it consisted of 3 : 3-*dimethyl*cyclo*pentane*-1 : 2-*dione* or its tautomerides.

When the ketohydroxy-acid (X) was digested with acetyl chloride it yielded an oil which was sparingly soluble in water but readily soluble in sodium bicarbonate solution. The oil was precipitated unchanged from the alkaline solution on acidification and doubtless consisted of 4-*acetoxy*-2 : 2-*dimethyl*-Δ^5-cyclo*penten*-3-*one*-1-*carboxylic acid*. On treatment with semicarbazide acetate it underwent hydrolysis, yielding the disemicarbazone described below.

The ketohydroxy-acid was recovered unchanged after prolonged digestion with potassium hydroxide solution (10%); on treatment with more concentrated alkali solutions or on fusion with potassium hydroxide at 200° some resinification took place with formation of deep red solutions, but the bulk of the acid was recovered unchanged.

The *disemicarbazone* of 2 : 2-*dimethyl*cyclo*pentane*-3 : 4-*dione*-1-*carboxylic acid* (XI) crystallised from dilute alcohol in needles, decomp. 200—201° (Found : C, 42·1; H, 5·5; N, 29·1. $C_{10}H_{16}O_4N_6$ requires C, 42·3; H, 5·6; N, 29·6%).

The *quinoxaline* derivative was prepared by boiling an alcoholic solution of the acid with an excess of *o*-phenylenediamine. It separated from benzene in pale yellow, irregular plates, m. p. 175—177° (Found : C, 69·2; H, 6·0. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8%).

Oxidation of 4-*Hydroxy*-2 : 2-*dimethyl*-Δ^5-cyclo*penten*-3-*one*-1-*carboxylic Acid with Nitric Acid*.—The ketohydroxy-acid (2 g.) was heated with nitric acid (*d* 1·2; 20 c.c.) on the water-bath for 12 hours, nitric acid (*d* 1·4; 5 c.c.) was added, and the mixture heated for a further 3 hours. After removal of the excess of mineral acid on the water-bath, during which process a small quantity of a volatile organic acid was evaporated with the steam, an oil remained which partly crystallised. An aqueous solution of the acid was treated with an excess of calcium chloride to remove oxalic acid and the filtrate was extracted with ether. On removal of the solvent, a solid cake remained which after crystallisation from hydrochloric acid decomposed at 187°. This acid was identified as dimethylmalonic acid by the method of mixed m. p. and by titration (Found : *M*, 133. Calc. : *M*, 132).

4-*Hydroxy*-2 : 2-*dimethyl*-Δ^4-cyclo*penten*-3-*one*-1-*carboxylic Acid* (VII).—The benzene solution (A) (see p. 3013) yielded on removal of the solvent a viscid brown oil which could not be induced to crystallise. It was readily soluble in water, gave a deep red coloration with ferric chloride, and immediately decolorised alkaline potassium permanganate. On treatment with semicarbazide acetate

and with *o*-phenylenediamine it yielded the derivatives of the diketo-acid described above. When it was boiled for some hours with a solution of potassium hydroxide (10%) partial conversion into the Δ^5-acid took place. It gave a liquid acetyl derivative and showed no tendency to lactone formation.

When the oil was oxidised with dilute nitric acid under the conditions used for the oxidation of the Δ^5-acid, *as*-dimethylsuccinic acid was obtained, m. p. 140—141°. This was identified by the method of mixed m. p. and by the preparation of the characteristic, sparingly soluble calcium salt.

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