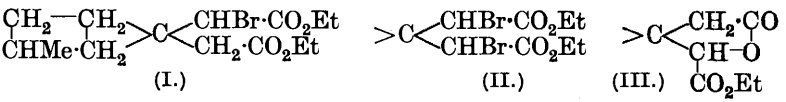
136. *The Chemistry of Alkyl*cyclo*pentanones. Part II. The Effect of the Methyl*cyclo*pentane Ring on the Carbon Tetrahedral Angle.*

By RANCHHODJI DAJIBHAI DESAI.

IN Part I (J., 1931, 1216) the synthesis of 3-methyl*cyclo*pentane-1 : 1-diacetic acid was described. Its mono- and di-bromo-derivatives and the products of their hydrolysis have now been studied with the object of ascertaining the effect of the methyl*cyclo*pentane ring on the carbon tetrahedral angle on the basis of Thorpe and Ingold's valency deflexion hypothesis.

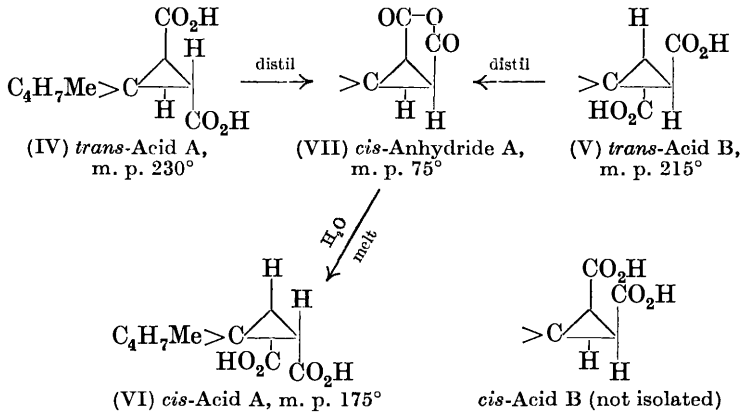
Monobromination.—The neutral *monobromo*-ester (I) prepared from the acid by the usual method of bromination was accompanied by the *dibromo*-ester (II) and unbrominated ester. It was obtained pure by bromination of *ethyl hydrogen* 3-*methyl*cyclo*pentane*-1 : 1-*diacetate*, though the *monobromo-acid ester* was always formed (15—20%). The monobromo-ester (I) could be distilled under reduced pressure, but distillation under ordinary pressure converted

it into the *lactone* of ethyl hydrogen α-hydroxy-3-methyl*cyclo*pentane-1 : 1-diacetate (III).



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

The neutral monobromo-ester was hydrolysed by 64% caustic potash solution at 150° to a mixture of *cyclo*propane-*spiro*-acids (40%) and lactonic acids. 3-Methyl*cyclo*pentane*spirocyclo*propane-2′ : 3′-dicarboxylic acid can exist in four *dl*-forms, two *cis* and two *trans*. The two trans-*acids* (IV and V) and one of the *cis*-acids (VI) were isolated from the hydrolysis product. The *cis*- was separated from the *trans*-forms by means of acetyl chloride, and the mixture of *trans*-acids was separated into its components by fractional crystallisation from acetone–benzene. On distillation, the *trans*-acids both gave the *anhydride* (VII) of the cis-*acid* (VI).



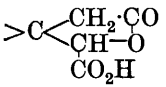
(IV) *trans*-Acid A, m. p. 230° (VII) *cis*-Anhydride A, m. p. 75° (V) *trans*-Acid B, m. p. 215°

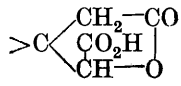
(VI) *cis*-Acid A, m. p. 175° *cis*-Acid B (not isolated)

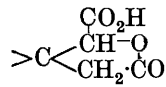
The two *trans-spiro*-acids are stable to 5% hydrochloric acid at 200°, but are completely decomposed by it at 240° after prolonged heating, and rapidly at 200° by 10% hydrochloric acid. The parent diacetic acid remains unaffected under identical conditions. The *spiro*-acids are thus slightly more stable than caronic acid or the *cyclo*pentane analogue, but considerably less so than the *cyclo*hexane acid.

The *lactone* of α-hydroxy-3-methyl*cyclo*pentane-1 : 1-diacetic acid should exist in eight stereoisomeric modifications, giving four *dl*-forms (VIIIA, B, C, and D); two of these have been isolated. The hydrolysis of the neutral monobromo-ester with sodium carbonate solution gave a mixture of lactonic acids, from which the *lactonic acid A* (VIII) was isolated. The *lactonic acid B* was prepared by

similar hydrolysis of the monobromo-acid ester. The lactonic acid A was also identified among the products of hydrolysis of the neutral


(VIIIA)


(B)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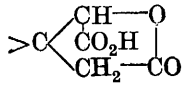
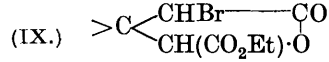
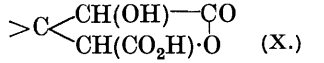

(D)

monobromo-ester with concentrated potash solution. As their configurations could not be determined, they have been called A and B forms.

Dibromination.—3-Methyl*cyclo*pentane-1 : 1-diacetic acid was smoothly brominated by the Hell–Volhard–Zelinsky method in 72 hours. The yield of monobromo- and *dibromo*-acid ester was 10—15%. The neutral dibromo-ester (II) was converted by distillation into the *lactone* of *ethyl hydrogen α-bromo-α'-hydroxy-3-methyl*cyclo*pentane*-1 : 1-*diacetate* (IX).

Hydrolysis of the neutral dibromo-ester with 64% potash solution at 150° gave mainly *α-keto-3-methyl*cyclo*pentane*-1 : 1-*diacetic acid* (45%), 3-*methyl*cyclo*pentylideneacetic acid* (5%), and a stereoisomeric mixture of hydroxy-lactonic acids from which the lactone of αα'-dihydroxy-3-methyl*cyclo*pentane-1 : 1-diacetic acid (X) was isolated in small amount.

(IX.) 

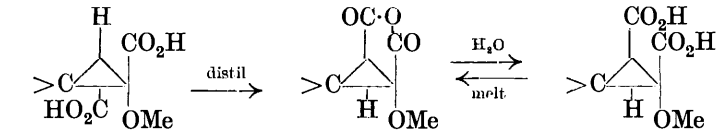

(X.)

The keto-acid was oxidised by hydrogen peroxide to 1-carboxy-3-methyl*cyclo*pentane-1-acetic acid, the constitution of which was proved by a rational synthesis from 3-methyl*cyclo*pentanone by Higson and Thorpe's method (J., 1906, **89**, 1455).

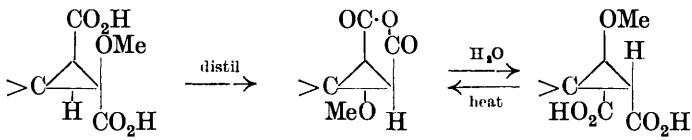
The formation of 3-methyl*cyclo*pentylideneacetic acid in the hydrolysis of the dibromo-ester probably involved the removal of the side chain as glyoxylic acid, which might have been oxidised to oxalic acid, as this was identified among the hydrolysis products. The unsaturated acid was proved to be the αβ-form by its reactions, and by its synthesis by the condensation of 3-methyl*cyclo*pentanone with bromoacetic ester in presence of zinc; the hydroxy-ester formed was accompanied by a considerable amount of 4-methyl-2-(3'-methyl*cyclo*pentylidene)*cyclo*pentanone (Wallach, *Ber.*, 1896, **29**, 2965), which gave 3-methyl*cyclo*pentanone and β-methyl-glutaric acid on oxidation. Wallach's liquid hydroxy-acid (*Annalen*, 1901, **314**, 160) was found to be a mixture of a liquid and a solid isomeride. The latter, C_5H_{10}>C(OH)·CH_2·CO_2H, on dehydration with acetic anhydride, gave a mixture of αβ-unsaturated acids, from which an acid identical with the one mentioned above was obtained by fractional crystallisation.

Hydrolysis of the dibromo-ester (II) with methyl-alcoholic potash gave a mixture of *cis-* and *trans*-methoxy-*spiro*-acids, together with small amounts of *α-hydroxy-α'-methoxy-3-methyl*cyclo*pentane*-1 : 1-*diacetic acid* and its *lactone*.

Two *trans-* (XIA and B) and two *cis*-forms (XIIA and B) of 3-*methyl*cyclo*pentane*spiro-2'(or 3')-*methoxy*cyclo*propane*-2' : 3'-*dicarboxylic acid* were isolated. The *trans*-acids were converted by distillation into the anhydrides of the *cis*-acids. All the methoxy-*spiro*-acids gave α-keto-3-methyl*cyclo*pentane-1 : 1-diacetic acid and a small amount of 1-carboxy-3-methyl*cyclo*pentane-1-acetic acid when heated with hydrobromic acid. The cyclic hydroxy-acid, 3-methyl*cyclo*pentane*spiro*-2'-hydroxy*cyclo*propane-2' : 3'-dicarboxylic acid, was probably formed, but owing to its instability changed into its open-chain isomeride, the keto-acid, the stability of which was shown by its recovery unchanged after 8 hours' heating with 64% potash solution at 150°.



(XIA) *trans*-Acid A, m. p. 190° — Anhydride A, m. p. 87° — (XIIA) *cis*-Acid A, m. p. 175°

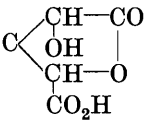


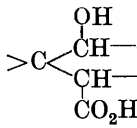
(XIB) *trans*-Acid B, m. p. 178° — Anhydride B, m. p. 60° — (XIIB) *cis*-Acid B, m. p. 162°

These results may be compared with those obtained by the hydrolysis of the dibromo-ester containing the *cyclo*hexane or the *cyclo*pentane ring. An unsaturated acid is formed in all three cases. On hydrolysis with aqueous potash, the *cyclo*hexane compound gives mainly the hydroxy-ring acid, whereas the *cyclo*pentane and the methyl*cyclo*pentane compound each give a keto-acid which is stable to 64% potash solution. When methyl-alcoholic potash is used, ring-hydroxy-acids are obtained from the *cyclo*hexane compound, methoxy-*spiro*-acids and a *cis*-ring-hydroxy-acid from the *cyclo*pentane compound, and methoxy-*spiro*-acids, but no ring-hydroxy-acids, from the methyl*cyclo*pentane compound.

As the dibromo-ester (II), owing to its insolubility, gave only a small amount of acid product on hydrolysis with sodium carbonate solution, the dibromo-acid ester was used. The products were α-keto-3-methyl*cyclo*pentane-1 : 1-diacetic acid (in small amount)

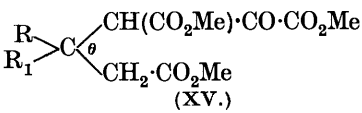
and the cis- (XIII) and the trans-*lactone* (XIV) of *αα'-dihydroxy*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic acid*. The lactone (XIV) reacted readily with acetyl chloride, forming the acetyl derivative, and hence must have the *trans*-configuration. The formation of the keto-acid in the hydrolysis must have involved simultaneous ring formation and hydroxylation. The former reaction would lead to the intermediate formation of a bromo- and a hydroxy-ring-acid $C_5H_{10}>C<\begin{matrix}CR\cdot CO_2H\\CH\cdot CO_2H\end{matrix}$ (R = Br or OH), which could not be isolated owing to their instability (compare Ingold, J., 1921, **119**, 314; Rao, J., 1930, 1170; Kandiah, J., 1931, 958).

(XIII.) 

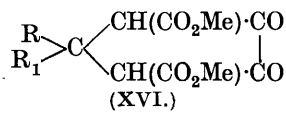
 (XIV.)

The above results obtained in the decomposition of the mono- and di-bromo-esters of 3-methyl*cyclo*pentane-1 : 1-diacetic acid show that the methyl*cyclo*pentane ring bears the closest similarity to the *cyclo*pentane ring and differs fundamentally from the *cyclo*hexane nucleus. If the effect of this ring were due to polar factors, it should be similar to that of the *gem*-ethylpropyl group. The effect is, however, more in harmony with that of the *gem*-dimethyl group and is due to valency deflexion (Becker and Thorpe, J., 1920, **117**, 1580; Lanfear and Thorpe, J., 1923, **123**, 1683). The evidence is strengthened by two other types of reaction.

(1) A series of cyclic diketones (XVI) was obtained by Dickins, Kon, and Thorpe (J., 1922, **121**, 1496) by condensing methyl oxalate with various substituted glutaric esters by the Dieckmann–Komppa method. The diketone was obtained in greatest yield from glutaric ester itself (RR_1 = H, H), and its non-formation from the *cyclo*hexane analogue was explained on the suppositions that the reaction took place through the intermediate formation of the compound (XV) and that the angle θ between the two acetic acid residues was diminished by the attachment of the oxalyl group to the α-carbon atom : in the case of *cyclo*hexane, the diminution was so great that there was actual overlapping of the carbethoxy- and the oxalyl group and consequently no reaction.



(XV.)



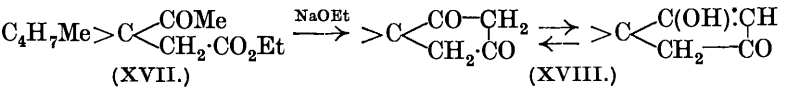
(XVI.)

When *methyl* 3-*methyl*cyclo*pentane*-1 : 1-*diacetate* was condensed with methyl oxalate, *methyl* 3-*methyl*cyclo*pentane*spiro-3' : 4'-*di*-

*keto*cyclo*pentane*-2′ : 5′-*dicarboxylate* (XVI; $RR_1 = C_4H_7Me$) was obtained in 45% yield. This diketonic ester was easily converted into 3-*methyl*cyclo*pentane*spirocyclo*pentane*-3′ : 4′-*dione* by dilute sulphuric acid.

(2) By the direct ring-closure of substituted lævulic esters to the corresponding *cyclo*pentanediones by Vorländer's method (*Annalen*, 1896, **294**, 270) Rothstein and Thorpe (J., 1926, 2011) found that ββ-dimethyllævulic ester and its *cyclo*hexane analogue gave 20—25% and 48% yields, respectively, of *cyclo*pentanedione. The increased yield in the latter case was ascribed to the ease of ring-closure owing to the proximity of the terminal acetyl and carbethoxy-groups due to the greater deflexion of the tetrahedral angle by the *cyclo*hexane ring in comparison with the dimethyl group.

Ethyl 1-*acetyl*-3-*methyl*cyclo*pentane*-1-*acetate* (XVII) was prepared by the action of methylzinc iodide on the acid chloride of ethyl 1-carboxy-3-methyl*cyclo*pentane-1-acetate. The crude acid obtained by hydrolysis of the resulting ester gave two *semicarbazones*, one in too small amount for further investigation. When the ester of the *acid* regenerated from the other semicarbazone was treated with dry sodium ethoxide, a 20% yield of 3-*methyl*cyclo*pentane*-spirocyclo*pentane*-2′ : 4′-*dione* (XVIII) was obtained. This gave a red colour with ferric chloride solution, and a solid *bromide*.



(XVII.) (XVIII.)

EXPERIMENTAL.

Ethyl Hydrogen 3-*Methyl*cyclo*pentane*-1 : 1-*diacetate*.—Absolute-alcoholic solutions of 3-methyl*cyclo*pentane-1 : 1-diacetic anhydride (180 g. in 125 c.c.) and of sodium (23 g. in 300 c.c.) were gradually mixed and then heated for ½ hour on the water-bath. The alcohol was evaporated, and the residue diluted with water and extracted with ether before and after acidification. The *ester* was obtained from the second extract as a viscous colourless liquid, which was changed to the anhydride by distillation (Found: equiv., 227. $C_{12}H_{20}O_4$ requires equiv., 228).

Monobromination.—Phosphorus pentachloride (120 g.) was added to the acid ester (114 g.) in portions, the mixture heated on the steam-bath for 1 hour, and dry bromine (28 c.c.) added slowly at 50—60°. After 8 hours, the product was poured into cooled absolute alcohol (450 c.c.) and heated on the water-bath for 4 hours. The oil precipitated on dilution was extracted, washed with 5% sodium carbonate solution, and dried in ether and recovered (yield, 80%); on distillation *ethyl* α-*bromo*-3-*methyl*cyclo*pentane*-1 : 1-*diacetate* (I) was

obtained as a colourless liquid, b. p. 163°/7 mm. (Found : Br, 23·8. $C_{14}H_{23}O_4Br$ requires Br, 23·9%).

The *lactonic* ester (III) was obtained as a colourless viscous syrup, b. p. 188°/20 mm. after three distillations (Found : C, 63·5; H, 8·0. $C_{12}H_{18}O_4$ requires C, 63·7; H, 7·9%).

The *monobromo-acid ester* obtained on acidification of the sodium carbonate extract was a dark yellow, viscid oil (Found : Br, 25·8. $C_{12}H_{19}O_4Br$ requires Br, 26·1%).

Hydrolysis of the Neutral Monobromo-ester (I) *with Potassium Hydroxide Solution at* 150°.—The bromo-ester (100 g.) was added as rapidly as possible to a boiling solution of the alkali (300 g.) in water (170 c.c.), and the mixture heated for 20 minutes. The solution was diluted with water, extracted with ether, and acidified with hydrochloric acid. The precipitated acids were removed by three extractions with ether, dried, recovered (46 g.), kept in a vacuum for a week, and triturated with benzene. The residual solid was removed (15 g.); the filtrate deposited a further quantity of *spiro*-acids (5 g.) when mixed with light petroleum (M). The solid was refluxed for 12 hours with acetyl chloride (50 c.c.), the excess of this removed, and the residue dissolved in ether and extracted with dilute sodium carbonate solution. Acidification of the alkaline extract gave a solid, which was extracted with ether, partly dried, and recovered. It melted at 198—205° and on fractional crystallisation from acetone–benzene gave a sparingly soluble acid, m. p. 225—227°; the more soluble fraction by further treatment gave an acid, m. p. 210—212°.

trans-3-*Methyl*cyclo*pentane*spirocyclo*propane*-2′ : 3′-*dicarboxylic acid A* (IV), obtained in small needles, m. p. 230° (Found : C, 60·4; H, 7·3; equiv., 99. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 99), by recrystallisation of the acid of m. p. 225—227° from acetone, formed a *dianilide*, which crystallised from alcohol in silky needles, m. p. 295° (Found : C, 75·6; H, 7·0. $C_{22}H_{24}O_2N_2$ requires C, 75·9; H, 6·9%). The trans-spiro-*acid B* (V), obtained in plates, m. p. 215° (Found : C, 60·3; H, 7·2%; equiv., 99), by recrystallisation of the acid of m. p. 210—212° from aqueous acetone, formed a *dianilide*, which crystallised from alcohol in needles, m. p. 275° (Found : C, 75·6; H, 7·1%); mixed m. p. with the isomeride A, 255—260°.

The ethereal solution from which the *trans*-acids had been removed gave a gum, which solidified in a vacuum after 2 weeks and was completely soluble in petroleum (b. p. 60—80°). The solution slowly deposited cis-3-*methyl*cyclo*pentane*spirocyclo*propane*-2′ : 3′-*dicarboxylic anhydride A* (VII) in plates, m. p. 75° (Found : C, 66·5; H, 7·0. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

The cis-spiro-*acid A* (VI), obtained from the anhydride, crystallised

from water in plates, m. p. 175° (Found: C, 60·3; H, 7·2%; equiv., 99). The *anilic acid*, precipitated from benzene solution, crystallised from alcohol in needles, m. p. 190° (Found: C, 70·1; H, 7·2. $C_{16}H_{19}O_3N$ requires C, 70·3; H, 7·0%).

The benzene–petroleum mother-liquor (M; p. 1071) was evaporated; the residual gum, esterified with ethyl alcohol, gave two fractions on distillation, (1) 170—171°/12 mm. (10 g.), (2) 178—180°/12 mm. (20 g.). The first fraction on hydrolysis with concentrated hydrochloric acid yielded an oily mixture of *spiro*-acids (4 g.), which solidified after some weeks; m. p. 180—190°. Fraction (2) was hydrolysed by hydrochloric acid to a mixture of lactonic acids which set to a gum after 6 months; trituration with benzene–petroleum gave a solid crystalline lactonic acid A (1 g.), m. p. 87° (see below).

Stereoisomeric Lactones of α-Hydroxy-3-methylcyclopentane-1 : 1-diacetic Acid.—Lactonic acid A (VIIIA). The monobromo-ester (I) (25 g.) was heated with a solution of sodium carbonate (50 g.) in water (150 c.c.) for 72 hours: much remained unchanged. The solution was diluted with water, extracted with ether, and acidified. The oil precipitated was extracted and dried in ether, recovered, and esterified with ethyl alcohol. Small low- and high-boiling fractions being rejected, a fraction, b. p. 178—180°/12 mm., was obtained (8 g.) which on hydrolysis with concentrated hydrochloric acid gave an acid; this, after being kept in a vacuum for months and then triturated with benzene–petroleum, gave the *lactonic acid A* as a crystalline solid, m. p. 87° (Found: C, 60·5; H, 7·2; equiv., 200. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 198). The *aniline* salt, which separated from a mixture of the lactonic acid and aniline in benzene, crystallised in needles, m. p. 95° (Found: C, 65·8; H, 7·3. $C_{10}H_{14}O_4,C_6H_5\cdot NH_2$ requires C, 66·0; H, 7·2%).

Lactonic acid B (VIIIB). The monobromo-acid ester (15 g.) was similarly treated (sodium carbonate, 10 g.; water, 100 c.c.; heating, 12 hours). The main ester fraction, b. p. 175—177°/15 mm., on hydrolysis, gave the *lactonic acid B*, which was ultimately obtained in plates (0·5 g.), m. p. 75°; mixed m. p. with its stereoisomeride, 60—63° (Found: C, 60·4; H, 7·3%; equiv., 199).

Dibromination of 3-Methylcyclopentane-1 : 1-diacetic Acid.—A mixture of phosphorus pentachloride (425 g.) and the acid (200 g.) was heated on the steam-bath for 3—4 hours, dry bromine (100 c.c.) then added during 24 hours, and after 72 hours the whole was poured into cooled absolute ethyl alcohol (750 c.c.) and refluxed for 4 hours. The oil precipitated on dilution was extracted with ether, washed with 5% sodium carbonate solution, dried, and recovered (yield, 80—85%). *Ethyl αα′-dibromo-3-methylcyclopentane-1 : 1-diacetate*

(II) was obtained as a reddish-yellow viscid liquid (Found : Br, 37·2. $C_{14}H_{22}O_4Br_2$ requires Br, 38·6%). From the alkaline washings, after acidification, a viscous mass was obtained, treatment of which with benzene–petroleum gave 5 g. of a solid : recrystallisation from benzene yielded plates, m. p. 128°, of *ethyl hydrogen* αα′-*dibromo*-3-*methyl*cyclo*pentane*-1 : 1-*diacetate* (Found : Br, 41·3; equiv., 384. $C_{12}H_{18}O_4Br_2$ requires Br, 41·5%; equiv., 386). The benzene–petroleum mother-liquor contained the monobromo-acid ester (Found : Br, 25·7. Calc. : Br, 26·1%).

The *lactone* of *ethyl hydrogen* α-*bromo*-α′-*hydroxy*-3-*methyl*cyclo*pentane*-1 : 1-*diacetate* (IX), obtained as a viscous oil when the neutral dibromo-ester (II) was distilled slowly at 15 mm., had b. p. 195—196°/15 mm. after redistillation (Found : Br, 26·7. $C_{12}H_{17}O_4Br$ requires Br, 26·2%).

αα′-*Dibromo*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic Acids*.—The dibromo-acid chloride was poured into anhydrous formic acid, and the mixture warmed on the steam-bath for 2 hours. The solid that separated on spontaneous evaporation was crystallised from chloroform. The less soluble *acid* crystallised from chloroform–petroleum in plates, m. p. 195° (decomp.) (Found : Br, 44·5; equiv., 177. $C_{10}H_{14}O_4Br_2$ requires Br, 44·7%; equiv., 179). The more soluble *acid* crystallised from benzene in cubes, m. p. 163° (Found : Br, 44·2%; equiv., 178).

Hydrolysis of the Dibromo-ester (II) *with* 64% *Potassium Hydroxide Solution*.—The dibromo-ester (100 g.) was added as rapidly as possible to a boiling solution of potassium hydroxide (300 g.) in water (170 c.c.); after 15—20 minutes' heating, a potassium salt separated. The diluted solution was acidified and the precipitated acids were thrice extracted with ether, dried, and recovered (42 g.) as a gum, which was esterified with ethyl-alcoholic sulphuric acid. On distillation, three fractions were collected : (1) 105—110°/15 mm. (4 g.); (2) 170—172°/15 mm. (25 g.); (3) 180—183°/15 mm. (20 g.).

Fraction (1) was hydrolysed with 10% aqueous methyl-alcoholic potash, and the resulting oily acid distilled; crystallisation from petroleum (b. p. 40—60°) then gave 3-methyl*cyclo*pentylideneacetic acid in prismatic needles, m. p. 112°.

Fraction (2) was hydrolysed with concentrated hydrochloric acid and the resulting gum was left in a vacuum for 3 months and then triturated with benzene; the solid obtained (12 g.), on recrystallisation from benzene, gave α-*keto*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic acid* in short needles, m. p. 121°, soluble in all solvents except petroleum (Found : C, 56·0; H, 6·5; equiv., 107. $C_{10}H_{14}O_5$ requires C, 56·1; H, 6·5%; equiv., 107).

Fraction (3) was hydrolysed with concentrated hydrochloric acid

and the oily acids formed were kept in a vacuum desiccator for 6—8 months; a small amount of the *trans*-lactone of αα'-dihydroxy-3-methyl*cyclo*pentane-1 : 1-diacetic acid (XIV), m. p. 146°, was obtained on trituration with benzene.

The keto-acid formed a *quinoxaline* derivative (with *o*-phenylenediamine in hot glacial acetic acid), which crystallised from dilute alcohol (charcoal) in short colourless needles, m. p. 226—227° (Found: C, 66·9; H, 6·5. $C_{16}H_{18}O_3N_2$ requires C, 67·1; H, 6·3%), a 2 : 4-*dinitrophenylhydrazone* (in hot alcohol), which crystallised in sulphur-yellow needles, m. p. 185° (decomp.) (Found: C, 48·5; H, 4·7. $C_{16}H_{18}O_8N_4$ requires C, 48·7; H, 6·7%), and a *methyl* ester (with boiling methyl-alcoholic sulphuric acid), b. p. 169°/19 mm. (Found: C, 59·2; H, 7·6. $C_{12}H_{18}O_5$ requires C, 59·5; H, 7·4%), the *phenylhydrazone* of which crystallised from benzene in plates, m. p. 163° (Found: C, 64·8; H, 7·5. $C_{18}H_{24}O_4N_2$ requires C, 65·0; H, 7·2%). Oxidation of the keto-acid in warm 10% sodium carbonate solution with hydrogen peroxide and acidification of the cooled solution gave 1-carboxy-3-methyl*cyclo*pentane-1-acetic acid, m. p. 120°.

Synthesis of 1-*Carboxy*-3-*methyl*cyclo*pentane*-1-*acetic Acid.*—3-Methyl*cyclo*pentanone (20 g.) was added with constant stirring to a cooled solution of sodium bisulphite (34 g.) in water (28 c.c.), and after 2 hours potassium cyanide (18 g. in 25 c.c. of water) was introduced. After 12 hours, the oil was taken up in ether, washed with saturated sodium chloride solution, dried, and distilled, 3-*methyl*cyclo*pentanonecyanohydrin* passing over as a colourless liquid, b. p. 128—130°/25 mm. (slight decomp.) (Found: C, 67·0; H, 9·0. $C_7H_{11}ON$ requires C, 67·2; H, 8·8%).

The cyanohydrin was gradually added to a cooled solution of ethyl sodiocyanoacetate (5 g. of sodium, 28 g. of ethyl cyanoacetate, and 75 c.c. of absolute ethyl alcohol) and kept at 0° for 24 hours. The dicyano-ester precipitated on dilution and acidification was extracted and dried in ether and distilled; b. p. 180°/11 mm. When hydrolysed with 50% hydrochloric acid, it gave 1-carboxy-3-methyl*cyclo*pentane-1-acetic acid, m. p. 120° (erroneously printed as 125° in J., 1931, 1224).

Synthesis of 3-*Methyl*cyclo*pentylideneacetic Acid.*—The reaction started by heating a mixture of zinc (70 g.), methyl*cyclo*pentanone (98 g.), and ethyl bromoacetate (110 c.c.) in dry benzene (400 c.c.) for ½ hour was allowed to proceed, and was completed by a further ½ hour's heating. The zinc compound was decomposed with ice-cold dilute sulphuric acid, and the benzene layer dried and distilled. Ethyl 3-methyl*cyclo*pentan-1-ol-1-acetate boiled at 121°/20 mm. (yield, 25—30%) (Found: C, 64·2; H, 9·9. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%).

A considerable quantity of the ketone was recovered and could be used again, but 20—25% of it underwent self-condensation, giving 4-methyl-2-(3′-methyl*cyclo*pentylidene)*cyclo*pentanone, which boiled at 132—133°/12 mm. and had $d_4^{20°}$ 0·9552, $n_D^{20°}$ 1·4964, whence $[R_L]_D$ 54·46 (calc., 52·76) (Found: C, 80·7; H, 10·3. Calc. for $C_{12}H_{18}O$: C, 80·9; H, 10·1%). Its *semicarbazone* crystallised from dilute alcohol in needles, m. p. 142—143° (Found: C, 66·1; H, 9·1. $C_{13}H_{21}ON_3$ requires C, 66·4; H, 8·9%). The substance (5 g.) was oxidised with cold 5% potassium permanganate solution (180 c.c.), the excess of permanganate destroyed, and the mixture steam-distilled. 3-Methyl*cyclo*pentanone was identified (as its semicarbazone) in the distillate, and from the residue ether extracted β-methylglutaric acid, which was identified by comparison with a genuine specimen (Day and Thorpe, J., 1920, **117**, 1469).

3-*Methyl*cyclo*pentan*-1-*ol*-1-*acetic acid*, obtained from the ester by hydrolysis with 10% methyl-alcoholic potassium hydroxide at the ordinary temperature, and subsequent acidification, partly solidified in a vacuum after 3 days; trituration with benzene–petroleum (b. p. 40—60°) gave a solid which crystallised in plates, m. p. 56° (Found: C, 60·6; H, 9·0. $C_8H_{14}O_3$ requires C, 60·8; H, 8·8%).

A solution of the hydroxy-acid (25 g.) in acetic anhydride (75 c.c.) was heated for 4 hours, the excess of anhydride distilled off, and the residue decomposed with water. On steam-distillation, an oil came over which solidified. The solid was fractionally crystallised from light petroleum (b. p. 60—80°), two acids, m. p. 112° and 81° (small amount) being obtained. The former was 3-*methyl*cyclo*pentylidene-acetic acid*, identified with the unsaturated acid, formed during the hydrolysis of the dibromo-ester (II) with concentrated potassium hydroxide solution, by m. p. and mixed m. p. (Found: C, 68·5; H, 8·8; equiv., 139. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%; equiv., 140).

Hydrolysis of the Dibromo-ester (II) *with Methyl-alcoholic Potash.*—The dibromo-ester (100 g.) was added as rapidly as possible to a boiling solution of potassium hydroxide (200 g.) in methyl alcohol (600 c.c.), heating continued for 20 minutes, the alcohol removed, and the residue dissolved in water, extracted with ether, and strongly acidified with concentrated hydrochloric acid. The precipitated acids were dried in ether, recovered (47 g.), and heated for 12 hours with acetyl chloride (150 c.c.); the excess of this was then removed, the residue dissolved in ether, and the unchanged acids extracted with 5% sodium bicarbonate solution. The ethereal solution on evaporation left the anhydrides (30 g.) (this is termed the neutral extract). The alkaline solution on acidification gave oily acids, which were dried in ether, recovered, and kept in a vacuum for 2 weeks (15 g.). Trituration with benzene gave a solid (7 g.); the oil

left after the removal of the solvent was esterified with ethyl alcohol and sulphuric acid. The esters were fractionally distilled : (1) b. p. 164—166°/15 mm. (7 g.); (2) 185—187°/15 mm. (3 g.).

The solid (7 g.) was boiled with benzene, and the insoluble portion fractionally crystallised from acetone–benzene. The sparingly soluble acid, m. p. 185—187°, was recrystallised from aqueous acetone, and trans-3-*methyl*cyclo*pentane*spiro-2′-*methoxy*cyclo*propane*-2′ : 3′-*dicarboxylic acid A* (XIA) obtained in plates, m. p. 190° (Found : C, 57·7; H, 7·2; equiv., 114. $C_{11}H_{16}O_5$ requires C, 57·9; H, 7·0%; equiv., 114). The more soluble acid, m. p. 165—170°, was recrystallised four times from acetone–benzene, the sparingly soluble acid being rejected, and finally from dilute aqueous acetone, the trans-*methoxy*-spiro-*acid B* (XIB) being obtained in thick plates (small amount), m. p. 178° (Found : C, 57·8; H, 7·1%; equiv., 114).

When hydrolysed with concentrated hydrochloric acid, the ester fraction (1) gave a mixture of the *trans*-methoxy-*spiro*-acids A and B (4 g.), and fraction (2) yielded a gum which partly solidified after 6 months. The solid (0·5 g.) was obtained by trituration with benzene–petroleum (b. p. 40—60°) and recrystallised from the same mixture, the *lactone* of α-*hydroxy*-α′-*methoxy*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic acid* being obtained in thick plates, m. p. 150° (previous sintering) (Found : C, 57·6; H, 7·2; equiv., 228. $C_{11}H_{16}O_5$ requires C, 57·9; H, 7·0%; equiv., 228).

The neutral extract (p. 1075) was dissolved in petroleum (b. p. 60—80°). The crystals deposited after some time were recrystallised thrice from the same solvent, giving silky needles, m. p. 87°, of cis-3-*methyl*cyclo*pentane*-spiro-2′-*methoxy*cyclo*propane*-2′ : 3′-*dicarboxylic anhydride A* (Found : C, 62·6; H, 6·9. $C_{11}H_{14}O_4$ requires C, 62·8; H, 6·7%). The cis-*methoxy*-spiro-*acid A* (XIIA) obtained from the anhydride crystallised from water in needles, m. p. 175° (Found : C, 57·8; H, 7·3%; equiv., 114). The petroleum mother-liquor after concentration deposited thick plates, and recrystallisation from petroleum (b. p. 40—60°) gave cis-*anhydride B*, m. p. 60° (Found : C, 62·5; H, 7·0%). The cis-*methoxy*-spiro-*acid B* (XIIB) crystallised from water in plates, m. p. 162° (Found : C, 57·6; H, 7·3%; equiv., 114).

The residue of oily anhydride from which the anhydrides of the methoxy-*spiro*-acids A and B were removed was decomposed with dilute potash solution, and the resulting acids were treated with benzene : the insoluble portion gave a mixture of the *cis*-acids A and B; the soluble portion, thrice recrystallised from benzene–petroleum (b. p. 60—80°), gave α-*hydroxy*-α′-*methoxy*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic acid* in small needles, m. p. 145° (Found : C, 53·5; H, 7·5; equiv., 122. $C_{11}H_{18}O_6$ requires C, 53·7; H, 7·3%; equiv., 123).

Action of Fuming Hydrobromic Acid on the cis-*Methoxy*-spiro-*acid A*.—The acid (5 g.) was heated under reflux for 6 hours with fuming hydrobromic acid (50 c.c.); the solution was then cooled, diluted with water, saturated with ammonium sulphate, and extracted four times with ether. The residual gum was esterified with ethyl alcohol and two fractions of ester were collected, (1) 140—142°/15 mm. (1 g.) and (2) 170—172°/15 mm., and hydrolysed. The first fraction gave 1-carboxy-3-methyl*cyclo*pentane-1-acetic acid, m. p. and mixed m. p. 120°; The second fraction furnished α-keto-3-methyl*cyclo*pentane-1 : 1-diacetic acid, m. p. 121°.

cis- *and* trans-*Lactones of αα′-Dihydroxy*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic Acid* (XIII and XIV).—A solution of ethyl hydrogen αα′-dibromo-3-methyl*cyclo*pentane-1 : 1-diacetate (10 g.) in saturated aqueous sodium carbonate (100 c.c.) was heated for 12 hours, the acidified solution extracted four times with ether, the gum esterified, and the esters distilled. Fraction (1), b. p. 170—175°/15 mm. (small amount) gave the keto-acid (XVIII) on acid hydrolysis. Fraction (2), b. p. 187—190°/15 mm. (5 g.), was hydrolysed with concentrated hydrochloric acid, and the resulting acid left in a vacuum for 6 months; the solid (0·5 g.) then obtained by trituration with benzene was recrystallised, giving the trans-*lactone* of *αα′-dihydroxy*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic acid* in small plates, m. p. 146° (Found: C, 55·8; H, 6·7; equiv., 215. $C_{10}H_{14}O_5$ requires C, 56·1; H, 6·5%; equiv., 214). The *acetyl* derivative, crystallised from benzene, had m. p. 151° (Found: C, 56·0; H, 6·5. $C_{12}H_{16}O_6$ requires C, 56·3; H, 6·3%).

The benzene mother-liquor was evaporated to dryness, and the residual syrup kept in a vacuum for 2 weeks and then dissolved in benzene–light petroleum (b. p. 40—60°). The cis-*lactone* (XIII), which slowly separated, crystallised from the same solvent in tiny leaflets, m. p. 125° (Found: C, 55·9; H, 6·8%; equiv., 214); mixed m. p. with the *trans*-isomeride, 112—115°.

Condensation of Methyl 3-*Methyl*cyclo*pentane*-1 : 1-*diacetate with Methyl Oxalate*.—To an ethereal suspension (350 c.c.) of the sodio-derivative of methyl oxalate (76 g. of methyl oxalate, 29 g. of sodium, 40·3 g. of methyl alcohol), *methyl* 3-*methyl*cyclo*pentane*-1 : 1-*diacetate* (b. p. 137°/15 mm. Found: C, 63·0; H, 8·9. $C_{12}H_{20}O_4$ requires C, 63·2; H, 8·8%) (23 g.) was cautiously added with cooling and shaking till the mass became nearly homogeneous. Ether was removed after 12 hours, and the residue heated at 110—120° for 2—3 hours, most of the alcohol distilling off, and at 140° for 8 hours. The dried mass was ground and added to ice-cold dilute sulphuric acid. The precipitated solid (25 g.) was a mixture of (XVI; RR_1 = C_4H_7Me) and the diacetic acid, from which the former and a small

quantity of the latter were extracted by light petroleum (b. p. 60—80°). After two crystallisations from petroleum, *methyl* 3-*methyl*cyclo*pentane*spiro-3′:4′-*diketo*cyclo*pentane*-2′:5′-*dicarboxylate* was obtained in needles, m. p. 125°. It gave a red coloration with ferric chloride and was soluble in sodium bicarbonate solution (Found: C, 59·3; H, 6·7. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%). Its *semicarbazone* crystallised from alcohol in needles, m. p. 182° (decomp.) (Found: C, 52·8; H, 6·2. $C_{15}H_{21}O_6N_3$ requires C, 53·1; H, 6·2%).

When the above *spiro*-compound was heated with an excess of 20% sulphuric acid for 3 hours, 3-*methyl*cyclo*pentane*spirocyclo*pentane*-3′:4′-*dione* was obtained. This crystallised from petroleum in flat needles, m. p. 108°, and gave a red coloration with ferric chloride (Found: C, 72·1; H, 8·5. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%). The *disemicarbazone* was a microcrystalline solid, m. p. 245° (decomp.) (Found: C, 51·2; H, 7·1. $C_{12}H_{20}O_2N_6$ requires C, 51·4; H, 7·1%).

Ethyl 1-*Acetyl*-3-*methyl*cyclo*pentane*-1-*acetate* (XVII).—The anhydride of 1-carboxy-3-methyl*cyclo*pentane-1-acetic acid (56 g.) was decomposed by a solution of sodium ethoxide (8 g. of sodium in 100 c.c. of absolute alcohol), and the resulting acid ester heated with thionyl chloride (35 c.c.). The crude chloride, diluted with benzene (50 c.c.), was slowly added to a cold solution of methylzinc iodide in toluene. The resulting keto-ester (35 g.), b. p. 142—145°/19 mm., which was not pure, was hydrolysed with 50% aqueous-alcoholic potash, and the keto-acid converted into its *semicarbazone*, which crystallised from alcohol in needles, m. p. 200° (decomp.) (Found: C, 57·8; H, 8·0. $C_{11}H_{19}O_3N_3$ requires C, 54·8; H, 7·9%). Another semicarbazone, m. p. 177° (decomp.), was obtained in a small amount (Found: C, 57·6; H, 8·0%).

1-*Acetyl*-3-*methyl*cyclo*pentane*-1-*acetic acid*, regenerated from the semicarbazone (m. p. 200°), crystallised from petroleum (b. p. 40—60°) in thick plates (10 g.), m. p. 83° (Found: C, 65·0; H, 9·0; equiv., 183·5. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%; equiv., 184). It was oxidised to α-keto-3-methyl*cyclo*pentane-1:1-diacetic acid by dilute alkaline potassium permanganate solution. The *ethyl* ester boiled at 135°/11 mm., had $d_4^{16°}$ 1·008 and $n_D^{16°}$ 1·45723, whence $[R_L]_D$ 57·27 (calc., 57·08) (Found: C, 67·6; H, 9·5. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·4%), and formed a *semicarbazone*, which crystallised from dilute alcohol in needles, m. p. 105° (Found: C, 57·7; H, 8·6. $C_{13}H_{23}O_3N_3$ requires C, 58·0; H, 8·5%).

3-*Methyl*cyclo*pentane*spirocyclo*pentane*-2′:4′-*dione* (XVIII).—The ketonic ester (XVII) (8 g.) was warmed with dry sodium ethoxide in ether for 12 hours, and the mixture diluted with water and extracted

with 5% sodium bicarbonate solution. The oil obtained by acidification of the alkaline extract was isolated and extracted with petroleum (b. p. 40—60°). The insoluble portion set to a gum in a vacuum after 6—8 months and gave, on trituration with dry ether–light petroleum, the spiro-*compound* (XVIII), which crystallised from benzene–light petroleum in needles (20%), m. p. 101° (Found : C, 72·0; H, 8·5. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%). The *bromo*-compound, prepared in chloroform solution, crystallised from benzene in clusters of plates, m. p. 185° (Found : Br, 32·2. $C_{10}H_{13}O_2Br$ requires Br, 32·7%).

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