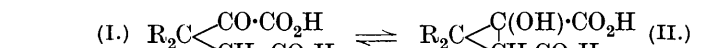
CCCXLIII.—*Experiments on the Synthesis of Certain γ-Ketonic Acids Closely Allied to Balbiano's Acid. Part I. Synthesis of α-Methylcyclopentane-1 : 1-diacetic Acid, of the Lactone of α-Hydroxy-α-methylcyclopentane-1 : 1-diacetic Acid, and of 1-Acetylcyclopentane-1-acetic Acid.*

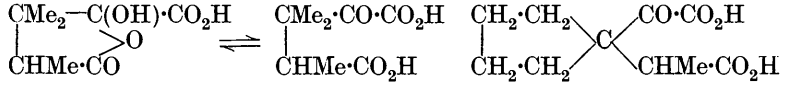
By JOGENDRA CHANDRA BARDHAN.

THE outcome of work which has been carried out in these laboratories during the past few years has been to show that in certain ββ-disubstituted ketoglutaric acids there exists a kind of tautomerism (keto-cyclol type) between the open-chain keto-form (I) and the hydroxy-ring form (II) (compare, *e.g.*, Deshapande and Thorpe, J., 1922, **121**, 1430; Bains and Thorpe, J., 1923, **123**, 1206). In



(I.) (II.)

the case of the corresponding acids containing an additional α-substituent, however, other factors come into play which considerably reduce the tendency to *cyclo*propane ring formation. The determining conditions are well illustrated in the case of an acid $C_8H_{12}O_5$ (Balbiano's acid), which has recently been dealt with by Kon, Stevenson, and Thorpe (J., 1922, **121**, 650), by Pandya and Thorpe (J., 1923, **123**, 2825), and by Rothstein, Stevenson, and Thorpe (J., 1925, **127**, 1072). Here, the usual keto-cyclol change is completely suspended, the substance exhibiting a marked tendency to pass into the lactol-form (III), which in the liquid state or in solution comes into equilibrium with the tautomeric parent (IV).



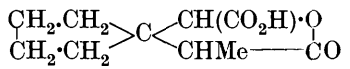
(III.) (IV.) (V.)

In view of the light which this phenomenon throws on the difficult question of the constitution of Balbiano's acid, it seemed desirable to ascertain the rôle played by the α-substituent, and, incidentally, to synthesise other keto-acids capable of exhibiting this kind of tautomerism.

In the course of an extended series of investigations on *spiro*- and associated alicyclic compounds, Thorpe and his co-workers have shown that the angle of the *cyclo*pentane ring is very close to that included between the *gem*-dimethyl groupings (Becker and Thorpe, J., 1920, **117**, 1579; Dickens, Kon, and Thorpe, J., 1922,

121, 1496; Lanfear and Thorpe, J., 1923, **123**, 1683; Ingold, Lanfear, and Thorpe, *ibid.*, p. 3140). It is to be expected, therefore, that the acid (V) would, if it could be synthesised, simulate the characteristic properties of Balbiano's acid. A general method of synthesis of α-ketoglutaric acids, indicated many years ago by Perkin and Thorpe (J., 1901, **79**, 737), consists in converting a substituted glutaric acid by means of the Hell–Volhard method into the dibromo-ester, from which the keto-acid is obtained either directly through the action of alkali or by further hydrolysis of the intermediate *cyclo*propane compounds through the agency of concentrated hydrobromic acid. Unfortunately, the above reaction breaks down in the case of the corresponding glutaric acids containing an additional α-substituent, owing to the occurrence of an abnormal decomposition, whereby the dibromo-ester is transformed into oxalic acid and an acid of the acrylic series (compare Pandya and Thorpe, *loc. cit.*, p. 2855; also Kon, Smith, and Thorpe, J., 1925, **127**, 567).

The necessity therefore arose of devising methods for the synthesis of αββ-trisubstituted ketoglutaric acids. A consideration of the conditions under which Balbiano's acid is produced showed that the synthesis of the *cyclo*pentane acid (V) might be attained through the oxidation of (i) the lactonic acid (VI) and (ii) the *spiro*-compound (VII) by means of alkaline permanganate, and a number of experi-



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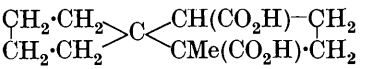
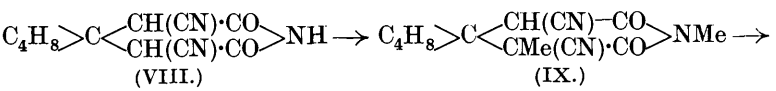


(VII.)

ments were made with this end in view. Although these attempts were unsuccessful, the results obtained led to the isolation of a number of substances of considerable interest.

The starting point in these attempts was α-*methyl*cyclo*pentane*-1 : 1-*diacetic acid* (X), which was prepared in quantity by methylating the imide (VIII) and hydrolysing the resulting *methylimide* (IX) with mineral acid. The *anhydride* of the acid (X) on treatment

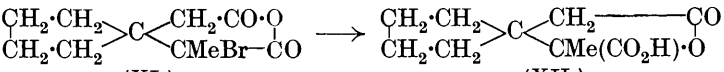


(VIII.) (IX.)

(X.)

with the calculated amount of bromine gave a monobromo-compound (XI), which on hydrolysis with alkali readily furnished a crystalline lactonic *acid* (XII). This acid is very resistant to oxidising and reducing agents, and in this respect resembles the corresponding

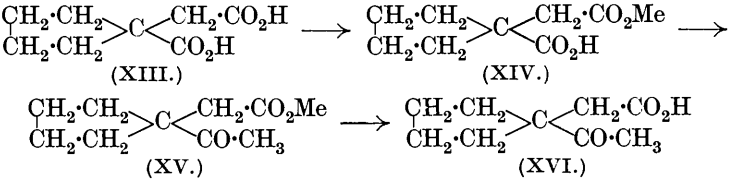
gem-dimethyl lactonic acid prepared by Blanc (*Bull. Soc. chim.*, 1901, **25**, 68).



(XI.) (XII.)

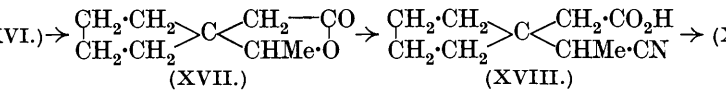
That the above scheme correctly represents the course of the bromination follows from the following synthesis of the lactonic acid (XII), which leaves no room for doubt as to its constitution.

1-*Acetylcyclopentane*-1-*acetic acid* (XVI) was first prepared in the following manner: *cyclo*Pentane-1-acetic-1-carboxylic acid (XIII), prepared by an extension of Lapworth and McRae's method (J., 1922, **121**, 2754), was successively converted into its *anhydride* and acid *ester* (XIV); the *acid chloride* of this ester was then allowed to react with zinc methyl iodide to give a product (XV), which on hydrolysis yielded 1-acetyl*cyclo*pentane-1-acetic acid.



(XIII.) (XIV.) (XV.) (XVI.)

This synthesis, although simple and convenient as a method of preparation, does not provide an adequate basis for the constitution assigned to the acid (XVI), since the acid ester (XIV) might have an alternative structure. To settle this point, the keto-acid (XVI) was reduced with sodium and alcohol, the lactone (XVII) was converted by potassium cyanide into the cyano-compound (XVIII), and hydrolysis then yielded the acid (X), the identity of which was established by direct comparison.

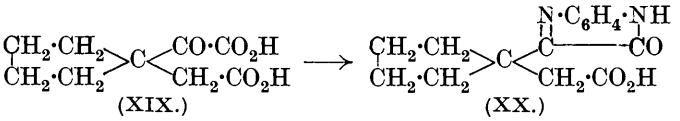


(XVI.) (XVII.) (XVIII.) (X.)

1-Acetyl*cyclo*pentane-1-acetic acid shows all the properties of a ketonic acid; its *methyl* ester readily yields a *semicarbazone* and in this respect differs from its *cyclo*hexane analogue (Rothstein and Thorpe, J., 1926, 2014).

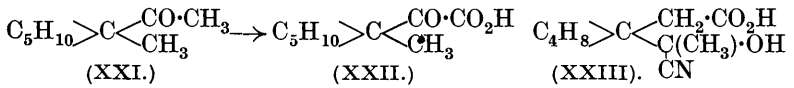
On oxidation with alkaline permanganate at the ordinary temperature the ketonic ester (XV) yielded an acid (XIX) which gave a condensation product (XX) with *o*-phenylenediamine. Although no authentic material was available for comparison, there can be no doubt that the acid is α-keto*cyclo*pentane-1 : 1-diacetic acid, previously obtained by Lanfear and Thorpe (J., 1923, **123**, 1688)

by the hydrolysis of the dibromo-ester of *cyclo*pentane-1 : 1-diacetic acid. Its formation in the present instance must have been due to



(XIX.) (XX.)

the oxidation of the methyl group, the reaction being precisely similar to the oxidation of the *cyclo*hexane ketone (XXI), which gives the keto-acid (XXII) as the sole product (Tarbourisch, *Compt. rend.*, 1910, **150**, 1606).



(XXI.) (XXII.) (XXIII).

The above reaction is very important, as it opens up a possibility of synthesising α-ketoglutaric acids, the preparation of which by the more obvious synthetical methods is either difficult or impossible. There can be no doubt, moreover, that the formation of trimethylpyruvic acid from pinacolin (Glucksmann, *Monatsh.*, 1889, **10**, 771) and of benzoylformic acid from acetophenone (Claus and Neukranz, *J. pr. Chem.*, 1891, **44**, 777) are instances of a very general reaction whereby an acetyl group attached to a quaternary carbon atom is similarly transformed into the corresponding oxalyl derivative.

In order to obtain the lactonic acid (XII), 1-acetyl*cyclo*pentane-1-acetic acid (XVI) was allowed to react with hydrocyanic acid, and under the prescribed conditions (p. 2602) combination readily took place with the formation of (XXIII), which on hydrolysis smoothly passed into the desired lactonic acid, which proved to be identical in all essential respects with that obtained in the bromination of α-methyl*cyclo*pentane-1 : 1-diacetic acid.

It therefore follows that in the bromination of the acid (X), the bromine atom has entered the carbon atom adjacent to the methyl group. It is somewhat remarkable that no trace of the isomeric bromo-derivative could be obtained, although Pandya and Thorpe (*loc. cit.*) succeeded in isolating both the possible lactonic acids from the products of the bromination of αββ-trimethylglutaric acid. On the other hand, Hariharan, Menon, and Simonsen (this vol., p. 432) obtained only one lactonic acid from the action of alkali on the monobromo-derivative of α-*iso*propylglutaric acid.

In order to avoid the formation of the lactonic acid (XII), it was next decided to brominate the monoethyl ester (prepared by partial hydrolysis of the normal ester) of α-methyl*cyclo*pentane-1 : 1-diacetic acid (XXIV), for in this case only the bromo-ester (XXV) could be formed, and on hydrolysis this should yield the desired

lactonic acid (VI). The bromination did not proceed very smoothly, however, and the crude product on treatment with alkali yielded a

$$C_4H_8{>}C{<}\begin{matrix}CH_2\cdot CO_2H\\CHMe\cdot CO_2Et\end{matrix} \longrightarrow C_4H_8{>}C{<}\begin{matrix}CHBr\cdot CO_2Et\\CHMe\cdot CO_2Et\end{matrix}$$

(XXIV.) (XXV.)

gummy acid from which no material of any definite composition could be obtained. On one occasion the impure acid was oxidised with alkaline permanganate and the resulting product was treated with *o*-phenylenediamine, but no trace of any quinoxaline derivative indicating the formation of the keto-acid (V) could be detected.

Finally, an attempt was made to prepare the lactonic acid (VI) by the hydrolysis of the *bromo*-compound (XXVI), which was readily prepared by direct bromination of the imide (IX); but on hydrolysis with concentrated hydrochloric acid the substance apparently lost bromine, the only isolable product being the acid (X), evidently derived from the original imide.

(XXVI.) $\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}{>}C{<}\begin{matrix}CBr(CN)\text{–}CO\\CMe(CN)\cdot CO\end{matrix}{>}NMe$

Several preliminary experiments have also been made with a view to synthesise the *cyclo*pentane analogue of camphoric acid (VII) by an extension of Komppa's method (*Annalen*, 1909, **370**, 209; **368**, 126), but these, together with a much easier method of preparing α-ketoglutaric acids which has now been discovered, are reserved for future communications.

During preliminary attempts to obtain the acid (X), a *ketone* was prepared from the acid (XXVII) (Wallach and Martins, *Annalen*, 1909, **365**, 272) by means of the Blaise reaction, and might therefore be expected to possess the αβ-structure (XXVIII). It readily yielded a mixture of two *semicarbazones*, one melting at 189° and the other at 169°; the regenerated ketones showed identical physical properties, and an exaltation characteristic of αβ-unsaturated ketones. Moreover, the corresponding *βγ-ketone* (XXX),

$$\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}{>}C{:}CMe\cdot CO_2H \longrightarrow \begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}{>}C{:}CMe\cdot COMe$$

(XXVII.) (XXVIII.)

$$\begin{matrix}CH_2\cdot CH_2\\CH_2\text{–}CH\end{matrix}{>}C\cdot CHMe\cdot CO_2H \longrightarrow \begin{matrix}CH_2\cdot CH_2\\CH_2\text{–}CH\end{matrix}{>}C\cdot CHMe\cdot COMe$$

(XXIX.) (XXX.)

prepared from the acid (XXIX) (Wallach and Martins, *loc. cit.*, p. 271), gave a *semicarbazone* melting at 144°, and was markedly different from the αβ-ketones in physical properties. It seems probable that the semicarbazones are stereoisomeric like those of mesityl oxide (Wilson and Heilbron, J., 1913, **103**, 378). It is

proposed to investigate the action of ultra-violet light on these semicarbazones with a view to determine whether and under what conditions they may be interconvertible.

EXPERIMENTAL.

A. *Synthesis of α-Methylcyclopentane-1 : 1-diacetic Acid* (X).

The imide of αα'-dicyano*cyclo*pentane-1 : 1-diacetic acid was prepared by condensing *cyclo*pentanone with cyanoacetic ester and alcoholic ammonia (Kon, J., 1921, **119**, 818; Kon and Thorpe, J., 1919, **115**, 686). The crude product (yield 60%), after having been dried in the steam-oven, was directly used in the experiments described below.

N-*Methyl-ω-imide of αα'-Dicyano-α-methylcyclopentane-1 : 1-diacetic Acid* (IX).—In the preparation of this substance by an extension of Kon and Thorpe's method (J., 1922, **121**, 1795), it was found essential to adhere to the following conditions: The above imide (108 g.), dissolved in absolute alcohol (300 c.c.), was gradually added with vigorous shaking to a solution of sodium ethoxide prepared from sodium (35 g.) and absolute alcohol (500 c.c.); the biscuit-coloured sodium salt which separated was cooled in ice, cautiously mixed with methyl iodide (100 c.c.), and the mixture allowed slowly to attain room temperature. After 12 hours, the clear solution was heated under reflux on the steam-bath until neutral. The greater part of the alcohol was then evaporated off, the residue mixed with water (2 l.), and slightly acidified with hydrochloric acid. The methylated imide which separated as a viscous gum was washed with hot water, and when left in contact with methylated spirit gradually solidified to a brittle resin. This was thoroughly ground in a mortar with alcohol and the solid collected, washed successively with sodium sulphite solution, water, and alcohol, and dried. The material (90 g.), m. p. 132—135°, is sufficiently pure for most purposes, but can be recrystallised from alcohol, from which it separates as minute, colourless prisms, m. p. 136—137° (Found: C, 63·6; H, 6·2; N, 17·4. $C_{13}H_{15}O_2N_3$ requires C, 63·7; H, 6·1; N, 17·1%). The *imide* slowly dissolves in alkali and is reprecipitated on the addition of dilute acids.

Hydrolysis of the Methylated Imide: Formation of α-Methylcyclopentane-1 : 1-diacetic Acid.—(i) *With sulphuric acid.* The imide (87 g.) was dissolved in sulphuric acid (400 c.c.; *d* 1·84), and after remaining over-night, the viscous liquid was cautiously mixed with water (365 c.c.) and boiled under reflux for 8—10 hours. The solution was cooled, diluted with water, saturated with ammonium sulphate, and exhaustively extracted with ether. The ethereal extract was washed with a moderately concentrated solution of

sodium carbonate, from which the acid (55 g.) was recovered in the usual way as a pale yellow oil which rapidly solidified when kept in an evacuated desiccator over sulphuric acid. The residue from the ethereal extract above consisted of a neutral liquid which partly solidified on keeping. The solid product on purification first from alcohol and then from glacial acetic acid was obtained in pearly plates, m. p. 223—224° (Found: C, 59·1; H, 6·1; N, 11·0. $C_{13}H_{16}O_4N_2$ requires C, 59·1; H, 6·1; N, 10·7%). Owing to the small amount available, the constitution of this *substance* could not be determined.

(ii) *With hydrochloric acid.* The imide (5 g.) was heated with concentrated hydrochloric acid (35 c.c.) at 160—180° in a closed tube for 5 hours, and the acid was isolated in the usual way in nearly quantitative yield and of a high degree of purity.

α-*Methyl*cyclo*pentane*-1 : 1-*diacetic acid* crystallises from benzene–light petroleum (b. p. 40—60°) in small, colourless prisms, m. p. 90—91° (Found: C, 60·0; H, 8·1; *M*, 200·2. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·0%; *M*, 200), readily soluble in acetone, alcohol, ethyl acetate, and ether, moderately soluble in benzene and water, and almost insoluble in hydrochloric acid and light petroleum. A neutral solution of the ammonium salt of the acid gives a bluish-green, crystalline precipitate with copper acetate, a white, crystalline precipitate on boiling with calcium chloride, and a heavy white precipitate with lead acetate. The *silver* salt, prepared in the usual manner, is a white, curdy, insoluble precipitate (Found: Ag, 51·9. $C_{10}H_{14}O_4Ag_2$ requires Ag, 52·2%).

The *anhydride*, prepared by boiling with excess of acetic anhydride, distils at 193°/24 mm. as a colourless liquid, and solidifies to a crystalline cake on cooling. It crystallises from light petroleum (b. p. 40—60°) and chloroform in colourless transparent plates, m. p. 48° (Found: C, 65·9; H, 7·7. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·7%), and dissolves in aqueous alkali when warmed, the acid (m. p. 90—91°) being deposited on acidification of the solution.

The β-*naphthylamic acid*,

$$C_{10}H_7\cdot NH\cdot CO\cdot CHMe\cdot C(:C_4H_8)\cdot CH_2\cdot CO_2H\ (?),$$

prepared from the anhydride, was obtained as a viscid oil, which solidified in contact with methyl alcohol and separated on recrystallisation in microscopic needles, m. p. 133—134° (Found: C, 73·9; H, 7·4. $C_{20}H_{23}O_3N$ requires C, 73·7; H, 7·1%). The corresponding derivatives of aniline and *p*-toluidine could only be obtained as oils.

The β-*naphthylimide*, obtained by heating the naphthylamic acid to 180° in a test-tube and cooling, was twice crystallised from dilute alcohol (charcoal), and separated in colourless, glistening plates,

m. p. 179° (Found : C, 78·3 ; H, 6·9. $C_{20}H_{21}O_2N$ requires C, 78·2 ; H, 6·8%). The *imide*, obtained on heating the dried ammonium salt of the acid in a sealed tube at 150° for 4 hours (Thorpe and Young, J., 1903, **83**, 358), crystallises from boiling water (charcoal) in long, colourless needles, m. p. 123—124° (Found : C, 66·7 ; H, 8·3 ; N, 7·9. $C_{10}H_{15}O_2N$ requires C, 66·3 ; H, 8·3 ; N, 7·7%) ; on boiling with a 30% solution of sulphuric acid, it was rapidly hydrolysed, and on extraction of the product with ether, the acid (m. p. 90—91°) was obtained in almost theoretical yield.

B. *Attempts to prepare the Lactone of α-Hydroxy-α'-methyl*cyclo*pentane*-1 : 1-*diacetic Acid* (VI).

*Bromination of α-Methyl*cyclo*pentane*-1 : 1-*diacetic Acid.*—Since the Hell–Volhard method did not give satisfactory results, the bromination was carried out as follows : The anhydride (6 g.) was treated with the calculated amount of bromine (5·3 g.) and heated in a sealed tube in a boiling water-bath for 5 hours ; the liquid was then kept in a desiccator over potash to remove the last traces of hydrobromic acid. The resinous product was dissolved in light petroleum (b. p. 40—60°), and the solution cooled in a freezing mixture. The *bromo-anhydride* (XI) separated in colourless prisms, m. p. 95° (Found : Br, 30·1. $C_{10}H_{13}O_3Br$ requires Br, 30·7%).

Hydrolysis. The crude bromination product was boiled with an excess of 2*N*-sodium carbonate for 10 hours, the solution concentrated, acidified with concentrated hydrochloric acid, and evaporated to dryness, and the residue extracted with ethyl acetate. On removal of the solvent, a thick syrup was obtained which, when kept over sulphuric acid in a vacuum desiccator, began to crystallise. In contact with porous porcelain the mother-liquor was slowly absorbed, and a colourless crystalline residue of the *lactone* of *α-hydroxy-α-methyl*cyclo*pentane*-1 : 1-*diacetic acid* remained ; it crystallised from ethyl acetate–light petroleum (b. p. 60—80°) (charcoal) in long, colourless needles, m. p. 140° (Found : C, 60·6 ; H, 7·0. $C_{10}H_{14}O_4$ requires C, 60·6 ; H, 7·1%), readily soluble in acetone, chloroform, and ethyl acetate, moderately soluble in benzene, and almost insoluble in light petroleum.

The *silver* salt was obtained from the ammonium salt as a rather soluble, white precipitate (Found : Ag, 35·7. $C_{10}H_{13}O_4Ag$ requires Ag, 35·4%). The *barium* salt, prepared from the lactonic acid by shaking with a suspension of barium carbonate, separated from a fairly concentrated solution in leaflets, which were dried at 110° [Found : Ba, 25·4. $(C_{10}H_{13}O_4)_2Ba$ requires Ba, 25·8%]. The *lead* salt is very soluble. The *ethyl* ester, obtained by saturating an alcoholic solution of the lactonic acid with hydrogen chloride, is a

mobile liquid, b. p. 197°/30 mm. (Found : C, 63·6; H, 8·2. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%).

*Bromination of Ethyl Hydrogen α-Methyl*cyclo*pentane*-1 : 1-*diacetate* (XXIV).—The *diethyl* ester, prepared by the esterification of the acid with alcohol and sulphuric acid, was obtained as a colourless oil, b. p. 165°/25 mm. (Found : C, 65·8; H, 9·3. $C_{14}H_{24}O_4$ requires C, 65·6; H, 9·4%). This was partly saponified as follows : The ester (25·6 g.) was boiled under reflux with potassium hydroxide (5·6 g.) in alcohol (30 c.c.) for ½ hour, the alcohol evaporated, the residue mixed with water, extracted with ether to remove any neutral product, and the aqueous solution acidified and again extracted with ether. The residual oil was kept in a vacuum desiccator for 2 days. The *silver* salt was obtained as a white precipitate (Found : Ag, 31·8. $C_{12}H_{19}O_4Ag$ requires Ag, 32·2%). The acid ester was warmed with excess of thionyl chloride for ½ hour, and the excess was removed under reduced pressure. The residue was mixed with the required amount of bromine and gently warmed (55°) until all the bromine had disappeared. It was then poured into an excess of ice-cold alcohol, and the mixture allowed to remain over-night. The product, *ethyl α-bromo-α′-methyl*cyclo*pentane*-1 : 1-*diacetate* (XXV), was then collected in ether after the addition of water. The residual oil was dried in a vacuum (Found : Br, 18·2. $C_{14}H_{23}O_4Br$ requires Br, 23·9%). The crude product was hydrolysed by boiling with an aqueous solution of sodium carbonate as described before. The brown oil did not show any tendency to solidify and all attempts to purify the product were fruitless. The oil was oxidised with alkaline permanganate and the resulting product warmed in acetic acid solution with an excess of *o*-phenylenediamine, but no quinoxaline derivative could be isolated.

Bromination of the Methylimide (IX).—A suspension of the methylimide in water was shaken with a slight excess of bromine for 24 hours (compare Gupta and Thorpe, J., 1922, **121**, 1900). The solid *methylimide* of *α-bromo-αα′-dicyano-α′-methyl*cyclo*pentane*-1 : 1-*diacetic acid* (XXVI), when collected and purified from alcohol, separated in colourless needles, m. p. 180° (decomp.) (Found : Br, 24·0. $C_{13}H_{14}O_2N_3Br$ requires Br, 24·7%). Hydrolysis with concentrated hydrochloric acid led to α-methyl*cyclo*pentane-1 : 1-diacetic acid, identified by its m. p. (90—91°) and by direct comparison with a known specimen.

C. *Synthesis of* 1-*Acetyl*cyclo*pentane*-1-*acetic Acid* (XVI) *and of the Lactone of α-Hydroxy-α-methyl*cyclo*pentane*-1 : 1-*diacetic Acid* (XII).

cyclo*Pentane*-1-*acetic*-1-*carboxylic Acid*.—This substance is obtained in excellent yield by the action of potassium cyanide on

ethyl *cyclo*pentylidenecyanoacetate (Harding and Haworth, J., 1910, **97**, 486) under the following conditions (compare Lapworth and McRae, *loc. cit.*). The ester (165 g.) was dissolved in rectified spirit (825 c.c.) to which was added a solution of potassium cyanide (115 g.) in water (260 c.c.). The clear solution was then allowed to stand at the ordinary temperature for about a week, during which a considerable amount of the potassium salt of the condensation product gradually separated. The mixture was evaporated on the steam-bath, and the dark residue then boiled with a large excess of concentrated hydrochloric acid for 6 hours. The solution was cooled and repeatedly extracted with ether, the extract dried, and the solvent removed. The residue of almost colourless solid (120 g.) consisted of nearly pure *cyclo*pentane-1-acetic-1-carboxylic acid, m. p. 156—156·5° (compare Norris and Thorpe, J., 1921, **119**, 1207) (Found : C, 55·8; H, 7·1. Calc. : C, 55·8; H, 7·0%). The *anhydride*, obtained by boiling the acid with acetyl chloride for 2 hours and fractionating under reduced pressure, was a colourless oil, b. p. 154°/20 mm., but it solidified in a freezing mixture and then had m. p. 30° (Found : C, 62·5; H, 6·6. $C_8H_{10}O_3$ requires C, 62·3; H, 6·5%). The *anilic acid*, prepared by mixing cold benzene solutions of the anhydride and aniline and crystallising the precipitated product from 84% alcohol, forms colourless plates, m. p. 167—167·5° (Found : C, 67·5; H, 6·8. $C_{14}H_{17}O_3N$ requires C, 68·0; H, 6·9%). The *anil*, prepared by heating the anilic acid, crystallises from alcohol in glistening prisms, m. p. 127—128° (Found : C, 73·4; H, 6·8. $C_{14}H_{15}O_2N$ requires C, 73·4; H, 6·6%). The *monomethyl* ester (XIV) was obtained by boiling the anhydride (46·2 g.) with methyl alcohol (24·4 c.c.) under reflux for 3 hours, removing excess of methyl alcohol in a vacuum, and crystallising the residue from light petroleum (b. p. 60—80°); it separated as magnificent transparent needles, m. p. 80—81° (Found : C, 58·0; H, 7·5; *M*, 185·5. $C_9H_{14}O_4$ requires C, 58·1; H, 7·5%; *M*, 186). The corresponding acid ethyl ester could not be solidified. The *acid chloride* was prepared by heating the acid ester (38 g.) with freshly distilled thionyl chloride (25 c.c.) at 50—60° in a glycerol-bath for 45 minutes; the excess of thionyl chloride was then removed in a vacuum, and the residue distilled under reduced pressure, giving a colourless oil, b. p. 132°/16 mm. The p-*toluidide* crystallises from dilute methyl alcohol in feathery needles, m. p. 111° (Found : C, 69·6; H, 7·6. $C_{16}H_{21}O_3N$ requires C, 69·8; H, 7·6%).

1-*Acetyl*cyclo*pentane*-1-*acetic Acid* (XVI).—The acid chloride described above was diluted with its own volume of dry benzene and gradually added during ¾ hour to a well-cooled solution of zinc methyl iodide prepared from zinc–copper couple (60 g.), methyl

iodide (25 c.c.), benzene (22 c.c.), and dry ethyl acetate (15 c.c.). After standing for an hour, the product was mixed with ice-cold dilute sulphuric acid, the benzene layer removed, washed successively with a 10% solution of potash, saturated ammonium sulphate solution, and water, dried, and distilled. The keto-ester boiled constantly at 121°/9 mm. as a colourless oil having a characteristic ethereal smell, but was not sufficiently pure for analysis; it was therefore hydrolysed to the acid by boiling with alcoholic potash, and this was converted into the sparingly soluble *semicarbazone*, which crystallised from boiling water in long, colourless needles, m. p. 197° (Found: C, 53·3; H, 7·8. $C_{10}H_{17}O_3N_3$ requires C, 52·9; H, 7·5%).

The semicarbazone was gently warmed with dilute hydrochloric acid, the solution extracted with ether, the extract dried with sodium sulphate, and evaporated; the solid residue was recrystallised from light petroleum (b. p. 60—80°) and 1-*acetyl*cyclo*pentane*-1-*acetic acid* was thus obtained in shining plates, m. p. 83—84° (Found: C, 63·5; H, 8·1; *M*, 171. $C_9H_{14}O_3$ requires C, 63·5; H, 8·2%; *M*, 170). The keto-acid, on oxidation with sodium hypobromite, gave an excellent yield of *cyclo*pentane-1-acetic-1-carboxylic acid. The *oxime* crystallised from water in flat needles, m. p. 124—125° (Found: C, 58·2; H, 8·2. $C_9H_{15}O_3N$ requires C, 58·4; H, 8·1%). The *methyl* ester, prepared from the acid in the usual way, was obtained as an oil, b. p. 131°/18 mm. (Found: C, 65·0; H, 8·9. $C_{10}H_{16}O_3$ requires C, 65·3; H, 8·7%); it readily yielded a *semicarbazone*, which separated from alcohol in shining scales, m. p. 152—153° (Found: C, 54·7; H, 7·8. $C_{11}H_{19}O_3N_3$ requires C, 54·8; H, 7·9%). On treatment with dry sodium methoxide (Rothstein and Thorpe, *loc. cit.*, p. 2016), the ester was transformed into a gummy product which readily dissolved in dilute alkali and gave a brownish-violet colour with an aqueous-alcoholic solution of ferric chloride. The substance could not, however, be obtained in a crystalline condition.

Reduction of 1-*Acetyl*cyclo*pentane*-1-*acetic Acid.*—Attempts to reduce the acid by means of sodium amalgam and by hydrogen in presence of platinum-black were unsuccessful, but reduction was ultimately effected as follows: The acid (5 g.) was dissolved in ethyl alcohol (15 c.c.), and sodium (4 g.) introduced in small lumps. The mixture was then heated at 112°, and alcohol (45 c.c.) gradually added during 2 hours. As soon as the last portions of sodium had disappeared, the excess of alcohol was removed in steam, the aqueous solution acidified, extracted with ether, the extract washed with sodium carbonate, dried, and evaporated. The *lactone* (XVII) was obtained on distillation under reduced pressure as a colourless oil, b. p. 132°/15 mm., having a characteristic smell

(Found : C, 69·6; H, 9·0. $C_9H_{14}O_2$ requires C, 70·1; H, 9·1%); $d_4^{15\cdot8°}$ 1·057645, $n_D^{15\cdot8°}$ 1·4742, $[R_L]_D$ 40·9 (calc., 41·0).

Conversion of the Lactone into α-*Methyl*cyclo*pentane*-1 : 1-*diacetic Acid*.—The lactone (5 g.) was heated with finely powdered 98% potassium cyanide (2·7 g.) in a sealed tube at 260° for 8 hours, and the resulting product acidified and repeatedly extracted with ether; the acidic product was washed out with an aqueous solution of sodium carbonate, and the alkaline solution evaporated to dryness. The residue was then boiled with an excess of 40% sulphuric acid for 3 hours; the acid isolated in the usual way melted at 90—91° and was identified as α-methyl*cyclo*pentane-1 : 1-diacetic acid by direct comparison and by the analysis of the silver salt (Found : Ag, 51·8. Calc. : Ag, 52·2%).

Oxidation of Methyl 1-*Acetyl*cyclo*pentane*-1-*acetate with Alkaline Permanganate : Formation of* α-*Keto*cyclo*pentane*-1 : 1-*diacetic Acid* (XIX).—The crude ester (6 g.) was stirred with water (400 c.c.), and to this was gradually added during 6 hours a solution of potassium permanganate (11 g.) and sodium hydroxide (4 g.) in 350 c.c. of water. The colour of the permanganate was slowly discharged, and after remaining for 12 hours, the solution became almost colourless. The filtrate and washings from the manganese precipitate were evaporated to small bulk, again filtered, and acidified with dilute hydrochloric acid. The liberated organic acids were dissolved in ether, and the semi-solid mass which remained on removal of the solvent was dissolved in glacial acetic acid, mixed with an excess of *o*-phenylenediamine, and slowly heated on the steam-bath for ½ hour. Excess of acetic acid was then removed, and the residue mixed with water. The brown, resinous product was collected and freed from impurities by rubbing with ether. The remaining solid was purified by two crystallisations from dilute acetone and thus obtained as a microcrystalline powder, m. p. 221° (Found : C, 66·3; H, 6·4. Calc. : C, 66·2; H, 5·9%). There can be no doubt, therefore, that the product consists of the quinoxaline derivative of α-keto*cyclo*pentane-1 : 1-diacetic acid (Lanfear and Thorpe, *loc. cit.*, p. 1688, give m. p. 222°).

Action of Hydrocyanic Acid on 1-*Acetyl*cyclo*pentane*-1-*acetic Acid : Synthesis of the Lactone of* α-*Hydroxy*-α-*methyl*cyclo*pentane*-1 : 1-*diacetic Acid* (XII).—The keto-acid (10 g.) was mixed with water (25 c.c.), and pure potassium cyanide (30 g.) was added in small quantities at a time, the whole being cooled in a freezing mixture. The clear solution was allowed to stand for about an hour and concentrated hydrochloric acid (44 c.c.) was gradually run in with constant shaking, the temperature being kept below −10°. After 24 hours, more hydrochloric acid was added, and the mixture left

for another day at the ordinary temperature; it was then warmed on the steam-bath for 10 minutes and extracted with ether. The ethereal solution was washed with a solution of sodium carbonate, dried, and evaporated. The residual oil, consisting of nearly pure cyano-lactone, was then hydrolysed with an excess of concentrated hydrochloric acid on the steam-bath. The clear solution was evaporated, and the solid extracted with chloroform or ethyl acetate; the residue which remained after the removal of the solvent crystallised from ethyl acetate and light petroleum (b. p. 60—80°) in long, colourless, flattened needles, m. p. 139—140°. The product was identified with the lactonic acid obtained in the bromination of α-methyl*cyclo*pentane-1 : 1-diacetic acid by direct comparison and by analysis (Found: C, 60·8; H, 7·3. Calc.: C, 60·6; H, 7·1%).

D. *Synthesis of* α-*Methyl*cyclo*pentylideneacetone* (XXVIII) *and of* α-*Methyl*-Δ^1-cyclo*pentenylacetone* (XXX).

α-*Methyl*cyclo*pentylideneacetic Acid* (XXVII).—The condensation of *cyclo*pentanone with ethyl α-bromopropionate and magnesium proceeded readily in benzene solution, giving a 50% yield of ethyl 1-hydroxy-α-methyl*cyclo*pentane-1-acetate, b. p. 130—140°/36 mm. The ester on hydrolysis with 50% alcoholic potash at the ordinary temperature yielded the hydroxy-acid as a viscous oil which showed no tendency to solidify; it was therefore boiled with acetic anhydride, and the mixture distilled in steam; the unsaturated acid, which separated from the distillate as a solid, crystallised from dilute methyl alcohol in needles, m. p. 108—109° (Found, for silver salt: Ag, 43·8. Calc.: Ag, 43·7%). The *acid chloride*, prepared in the usual way with thionyl chloride, distilled as a colourless liquid, b. p. 123°/30 mm.

α-*Methyl*cyclo*pentylideneacetone*.—This ketone was prepared in a good yield by the action of zinc methyl iodide on the foregoing acid chloride. With semicarbazide acetate it readily yielded a *semicarbazone*, of which two different forms were isolated by repeated crystallisation from methyl alcohol. The less soluble separated in rosettes of small crystals, m. p. 189° (Found: C, 61·6; H, 8·8; N, 21·7. $C_{10}H_{17}O_3N$ requires C, 61·5; H, 8·7; N, 21·5%), and the *ketone*, regenerated from it in the usual way, was obtained as a colourless oil, b. p. 108°/27 mm., $d_{4^\circ}^{19\cdot2^\circ}$ 0·960808, $n_D^{19\cdot2^\circ}$ 1·49642, $[R_L]_D$ 41·986 (calc., 41·106) (Found: C, 78·0; H, 10·2. $C_9H_{14}O$ requires C, 78·3; H, 10·1%). The more soluble semicarbazone crystallised from dilute alcohol in colourless, felted needles, m. p. 169° (Found: C, 61·8; H, 8·8; N, 21·6%), and the ketone regenerated from it had b. p. 109°/25 mm., $d_{4^\circ}^{20\cdot3^\circ}$ 0·958084, $n_D^{20\cdot3^\circ}$ 1·49528, $[R_L]_D$ 42·025 (Found: C, 77·9; H, 9·9%). The physical properties of the ketones corresponded well with their αβ-structure.

α-Methyl-Δ^1*-cyclopentenylacetic Acid.*—The ethyl ester was readily obtained by the dehydration of the hydroxy-ester (above) with the theoretical amount of phosphorus oxychloride in benzene solution; it distilled as a colourless oil with an agreeable smell, b. p. 108—110°/30 mm., $d_4^{17\cdot7°}$ 0·96668, $n_D^{17\cdot7°}$ 1·4583, $[R_L]_D$ 47·45 (calc., 47·37). The acid, prepared from this ester by hydrolysis with alcoholic potash, distilled as a colourless oil, b. p. 150°/28 mm., $d_4^{19\cdot7°}$ 1·050988, $n_D^{19\cdot7°}$ 1·4792, $[R_L]_D$ 37·79 (calc., 38·01) (Found, for Ag salt: Ag, 44·0. Calc.: Ag, 43·7%). A sample did not deposit any crystals during 14 months (compare Wallach, *loc. cit.*). The *acid chloride*, prepared in the usual way, had b. p. 86—88°/20 mm., and on treatment with zinc methyl iodide gave a good yield of the corresponding βγ-ketone. The crude ketone readily yielded a *semicarbazone*, which separated in lustrous plates, m. p. 144°, from dilute alcohol (Found: C, 61·8; H, 8·7; N, 21·8. $C_{10}H_{17}O_3N$ requires C, 61·5; H, 8·7; N, 21·5%), and *α-methyl-*Δ^1*-cyclopentenylacetone*, regenerated from it by means of oxalic acid, had b. p. 82°/17 mm., $d_4^{20°}$ 0·921922, $n_D^{20°}$ 1·4632, $[R_L]_D$ 41·24 (calc., 41·11) (Found: C, 78·7; H, 10·3. $C_9H_{14}O$ requires C, 78·3; H, 10·1%). The ketones could not be induced to react with ethyl sodiomalonate or sodiocyanoacetate.

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