CXXXI.—*Syntheses of Cyclic Compounds. Part VIII. The Conversion of β-Methyladipic Acid into 3-Methyl*cyclo*pentanone and the Preparation of 3-Methyl*cyclo*pentane-*1 : 1-*diacetic Acid.*

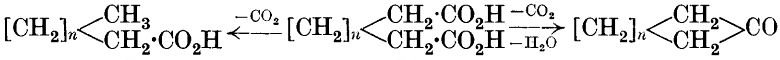
By Arthur Israel Vogel.

The numerous investigations undertaken during the last fifteen years on carbon ring formation and stability have been chiefly concerned with the spatial effect of substituents, more especially in connexion with the Thorpe–Ingold valency deflexion hypothesis :

the effect of polar factors seems to have been either overlooked or neglected.

The conversion of β-methyladipic acid into 3-methyl*cyclo*pentanone has now been studied in order to determine the effect of a methyl group on the formation of a 5-carbon ring. This case of ring formation was selected because (*a*) the situation of the methyl group is that furthest removed from the carboxyl group and steric effects are therefore reduced to a minimum, (*b*) the *cyclo*pentane ring is uniplanar and strainless and hence " strain " effects play little part.

The chief quantitative methods for the study of ring formation are (1) distillation of metallic salts of dibasic acids; (2) the action of 6*N*-potassium hydroxide on esters of α-monobromo-dibasic acids, which leads to the replacement of bromine by hydroxyl and the formation of a ring acid together with small quantities of unsaturated acid: the relative extents of ring formation and hydroxylation are taken as a measure of the ease of ring formation (Ingold, J., 1921, **119**, 305; 1922, **121**, 951, 2676; 1925, **127**, 387; Hassell and Ingold, J., 1926, 1465; Goss and Ingold, J., 1926, 1471); (3) the thermal decomposition of dibasic acids, which may be represented thus (Vogel, J., 1929, 721):



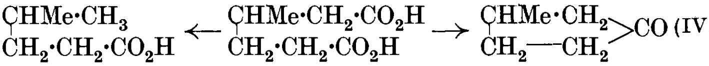
$$[CH_2]_n<{CH_3 \atop CH_2\cdot CO_2H} \xleftarrow{-CO_2} [CH_2]_n<{CH_2\cdot CO_2H \atop CH_2\cdot CO_2H} \xrightarrow[-H_2O]{-CO_2} [CH_2]_n<{CH_2 \atop CH_2}>CO$$

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

Method (1) is valueless, because not only does the yield of the cyclic compound vary with the metallic salt employed (Vogel, *loc. cit.*), but, as will be shown in a future communication, the actual character of the decomposition can be modified by suitable choice of the metal.

Ingold's method takes no account of the polar character of the bromine atom. The reactivity of the bromine atom will vary with the length of the polymethylene chain; this is well illustrated in the different rates of conversion of ethylene, trimethylene, tetramethylene, and pentamethylene dibromides into the corresponding glycols by treatment with aqueous alkali, and also by the difference in reactivity of these dibromides with aqueous-alcoholic potassium cyanide. For instance, the maximum yield of succinonitrile from ethylene dibromide is 46% (unpublished observation in collaboration with Mr. G. H. Jeffery), whereas a 77—80% yield of glutaronitrile is obtained from trimethylene dibromide under similar conditions (Roger Adams, " Organic Syntheses," 1925, **5**, 103). It would seem, therefore, that, pending a quantitative study of the relative reactivities of the bromine atoms in the various α-bromodibasic acids and esters, which will obviously affect the amount of hydroxylation, the results of Ingold and his co-workers must be accepted with reserve.

The third method was used in the present work.

(V.)  (IV.)

$$\begin{array}{l}\mathrm{CHMe{\cdot}CH_3}\\ \mathrm{CH_2{\cdot}CH_2{\cdot}CO_2H}\end{array} \longleftarrow \begin{array}{l}\mathrm{CHMe{\cdot}CH_2{\cdot}CO_2H}\\ \mathrm{CH_2{\cdot}CH_2{\cdot}CO_2H}\end{array} \longrightarrow \begin{array}{l}\mathrm{CHMe{\cdot}CH_2}\\ \mathrm{CH_2{-}CH_2}\end{array}\!\!>\mathrm{CO}$$

The ease of formation of carbon rings is usually regarded as being controlled by two factors, one related to the distance between the two carbon atoms at the ends of the chain, and the other dependent on the intrinsic stability of the ring and favouring the formation of strainless rings (Ruzicka, Brugger, Pfeiffer, Scinz, and Stoll, *Helv. Chim. Acta*, 1926, **9**, 499). In the conversion of β-methyladipic acid into 3-methyl*cyclo*pentanone (IV) the second effect may be neglected.

If the distance between two adjacent carbon atoms is taken as unity, by employing the normal tetrahedral angle 109° 28′ the distances between the various carbon atoms in a polymethylene chain, regarded as uniplanar, are calculated to be : C_1C_2 1·000 ; C_1C_3 1·633 ; C_1C_4 1·667 ; C_1C_5 1·088. A similar order is obtained by assuming Ingold's angular value of 115·3° for $CH_2<$ (J., 1921, **119**, 305), *viz.*, C_1C_2 1·000; C_1C_3 1·689; C_1C_4 1·854; C_1C_5 1·445. If one of the hydrogen atoms is replaced by methyl and Ingold's value of 112·5° for CHMe< (J., 1925, **127**, 387) is assumed, C_1C_5 is 1·368, from which one would expect a greater ease of formation of the *cyclo*pentane ring from β-methyladipic than from adipic acid, provided that steric effects only were operative. (All the values given above are computed trigonometrically.)

β-Methyladipic acid is obtained in quantity and in comparatively good yield by rapid distillation under reduced pressure from the other oxidation products of 4-methyl*cyclo*hexanol. When the acid is slowly distilled under the standard conditions, 3-methyl*cyclo*pentanone is obtained in 75·8 ± 0·4% yield, together with a small quantity of γ-methyl-n-valeric acid. This yield of ring compound is definitely smaller than that obtained from adipic acid (80%) and greater than that from pimelic acid (52%) (Vogel, J., 1929, 725). The difference (4·2%) in the yields of cyclic ketone obtained from adipic and β-methyladipic acids is not due to the slight difference in the temperatures of distillation of the two acids, because it persists when the temperatures are the same. If, as the author believes, the difference is due to a small decrease in the tendency to ring formation attributable to the polar effect of the methyl group, a third factor, the polar factor, in the formation of substituted carbon rings must be taken into account. Other substituted dibasic acids are being studied with this object in view.

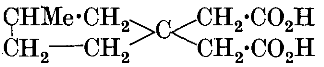
The view that the small difference in the magnitudes of the distances C_1C_5 in the unsubstituted and the substituted adipic acid chain may have an appreciable effect on the tendency to ring formation and other properties is supported by the facts that the distances between the two carboxyl groups in *cyclo*hexane- and *cyclo*heptane-1 : 1-diacetic acid are 1·04 Å. and 1·10 Å. respectively (Gane and Ingold, J., 1928, 2268) but only the former acid yields the corresponding *spirocyclo*butanone on distillation of the calcium salt (Kon, J., 1921, **119**, 810).

For the preparation of 3-methyl*cyclo*pentanone in quantity, the distillation of β-methyladipic acid may be carried out somewhat rapidly; a small quantity of the acid also distils but may be readily recovered. The addition of a small quantity of barium hydroxide, which lowers the decomposition temperature from 319—324° to 303—304° but gives a slightly decreased yield of less pure ketone (compare adipic acid; Part V, *loc. cit.*), is not recommended (contrast D.R.-P. 256,622).

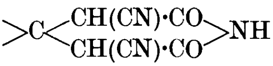
The catalytic decomposition of β-methyladipic acid, *i.e.*, its thermal decomposition in the presence of excess of iron filings and a little baryta, which probably involves the intermediate formation of an iron salt, gave a 55% yield of ketone : the corresponding yields for adipic and pimelic acids were 51% and 56% respectively (J., 1928, 723).

In connexion with the study of the influence of polar factors on ring stability 3-methyl*cyclo*pentane-1 : 1-diacetic acid (VI) and its anhydride were required. 3-Methyl*cyclo*pentanone condenses readily with ethyl cyanoacetate and ammonia in ethyl-alcoholic solution, giving a good yield of the *dicyano-imide* (VII). In contrast to the corresponding derivatives of *cyclo*pentanone and *cyclo*hexanone, the ammonium salt of (VII) is fairly readily soluble in alcohol and is therefore only partly precipitated from the solution. Treatment of (VII) with cold concentrated sulphuric acid results in partial hydrolysis to the *dicarbamyl-imide* (VIII), and complete hydrolysis with 85% sulphuric acid gives a satisfactory yield of 3-*methyl*cyclo*pentane*-1 : 1-*diacetic acid* (VI). This acid closely resembles its isomeride, *cyclo*hexane-1 : 1-diacetic acid (Thole and Thorpe, J., 1911, **99**, 422), and is characterised by the formation of the *anhydride* and its β-*naphthylamic acid*, and the *ethyl* ester.

(VI.)

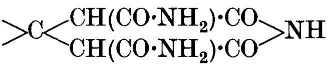


$$\begin{array}{l}CHMe\cdot CH_2\\ CH_2 — CH_2\end{array}\!>\!C\!<\!\begin{array}{l}CH_2\cdot CO_2H\\ CH_2\cdot CO_2H\end{array}$$



$$>C<\begin{array}{l}CH(CN)\cdot CO\\ CH(CN)\cdot CO\end{array}\!>\!NH$$

(VII.)



$$>C<\begin{array}{l}CH(CO\cdot NH_2)\cdot CO\\ CH(CO\cdot NH_2)\cdot CO\end{array}\!>\!NH$$

(VIII.)

EXPERIMENTAL.

Preparation of β-*Methyladipic Acid.*—(It is essential to adhere closely to the following experimental conditions, otherwise a product of low m. p., which cannot be easily raised by crystallisation from organic solvents, is obtained.) 1700 C.c. of nitric acid (*d* 1·42) are heated in a 5-litre Pyrex flask fitted with a cork carrying a 250-c.c. dropping-funnel and a 10-inch Davies double-surface condenser. When the acid is boiling vigorously (previous addition may result in a dangerous explosion), 500 g. of pure 4-methyl*cyclo*hexanol are added, at the rate of about one drop per second, during 5 hours. There is a torrential evolution of nitrous fumes, which slackens towards the end of the addition, the rate of which may then be slightly increased. The reaction is completed by heating for another 20 minutes. Contrary to Juéry's statement (*Bull. Soc. chim.*, 1915, **17**, 172), the oxidation product does not crystallise spontaneously or over-night. The reaction mixture is diluted with an equal volume of water, saturated with ammonium sulphate, and extracted in two portions twice with ether (4—5 litres are required), the extract dried with anhydrous sodium sulphate, and the ether distilled off. The residue, which largely crystallises, is distilled in two portions under diminished pressure (water-pump) until the pressure begins to rise rapidly (50—100 mm.), and the temperature rises to 160—180° ; the yellow mobile liquid then commences to darken. This process removes the more volatile products, but if the distillation is continued beyond this stage the acid carbonises. The two residues are dissolved in warm benzene and the acid is precipitated with light petroleum (b. p. 40—60°). It separates as an oil but changes almost completely over-night to a brown, slightly sticky solid, which is submitted to suction and well pressed during 12 hours on a *large* Buchner funnel to remove the adhering oil. (This method of removing the oil is more economical than the alternative one of spreading on porous plates.) The brown granular product is distilled as rapidly as possible, in order to minimise the attendant carbonisation, under diminished pressure in lots of 125—150 g. β-Methyladipic acid passes over at 220—223°/17—18 mm. or 223—226°/20 mm. as a pale yellow liquid which solidifies on cooling. It is advisable to interrupt the distillation about half way, and pass a little dilute sodium hydroxide solution, followed by water, through the connecting tubes to the pump, since the acid, being slightly volatile under the experimental conditions employed, may block the tap leading to the pump. The acid is then recrystallised from benzene–light petroleum (b. p. 40—60°) and air-dried; it has m. p. 92—93° after 2 days, and m. p. 96—97° after being dried in a vacuum over calcium chloride, which removes the last trace of solvent. Yield, 245 g. or 35% of the theoretical. The m. p.'s recorded in the literature are : Sabatier and Mailhe (*Compt. rend.*, 1914, **158**, 988), 88°; Wallach (*Annalen*, 1913, **397**, 193), 92—93°; Juéry (*loc. cit.*), 93·5°; Mannich and Hanen (*Ber.*, 1908, **41**, 569), and Pauly, Gilmour, and Will (*Annalen*, 1914, **403**, 157), 94°; Ciamician and Silber (*Ber.*, 1913, **46**, 3080), 97°.

(A) *Thermal decomposition of* β-*methyladipic acid.* 50·0 G. of the acid, m. p. 96—97°, were slowly heated during 5—6 hours. Distillation began after about an hour at 312° (thermometer in the liquid) and the main bulk passed over at 319—324°. There was a small carbonaceous residue. The almost colourless distillate was treated with excess of dilute ammonia solution and the upper layer of liquid was removed, dried with anhydrous calcium chloride, and distilled. 3-Methyl*cyclo*pentanone, b. p. 143—144·5°/756—764 mm., was obtained, together with an almost negligible quantity of high-boiling substance. The crude ketone had $d_{4^\circ}^{20^\circ}$ 0·9110, $n_D^{20^\circ}$ 1·433 (Abbé refractometer) (Wallach, *Annalen*, 1912, **394**, 371, gives for the pure ketone d^{22° 0·913, n_D 1·4329), and yielded a semicarbazone, m. p. 185° (slightly dependent on the rate of heating) after crystallisation from methyl alcohol and from rectified spirit. The yields in four experiments were 23·1 g., 23·3 g., 23·0 g., and 23·3 g. respectively, giving a mean yield of 75·8 ± 0·4% of ketone. The ammonia was evaporated from the washings, and from the neutral solutions the silver salts were precipitated, the yields and percentages of silver being 2·6 g. (54·5%), 2·6 g. (54·7%), 2·8 g. (54·9%), and 2·2 g. (54·2%). The combined silver salts were decomposed with dilute sulphuric acid, and from the filtered solution, saturated with ammonium sulphate, ether extracted about 1 g. of a liquid, b. p. 204—206°/770 mm., which had an odour reminiscent of *n*-hexoic acid and was only partially miscible with cold water (Found for the silver salt : Ag, 48·7. Calc. for $C_6H_{11}O_2Ag$: Ag, 48·4%. Calc. for $C_7H_{12}O_4Ag_2$: Ag, 57·8%). There was a dark residue consisting chiefly of β-methyladipic acid.

(B) *Decomposition in the presence of* 2·5% *by weight of baryta.* 50·0 G. of the acid were intimately mixed with 1·25 g. of crystallised baryta and similarly heated during 2 hours. The distillate passed over chiefly at 302—304°, and yielded the following fractions after being treated as described under (A) : (1) b. p. 143—145°/755 mm., 20·4 g.; (2) b. p. 146—150°/755 mm., 1·5 g.; and (3) a dark viscid residue, 2·4 g.

(C) *Decomposition in the presence of* 5% *by weight of baryta.* The following fractions were obtained from a mixture of 50·0 g. of the acid and 2·5 g. of crystallised baryta, treated as detailed under (B) : (1) b. p. 142—145° (chiefly 143—145°)/753 mm., 20·0 g.;

(2) b. p. 146—150°/753 mm., 3·2 g.; and (3) a dark, moderately viscid residue, 3·3 g.

(D) *Catalytic decomposition* (see J., 1929, 727). A mixture of 50·0 g. of the acid (m. p. 96—97°), 50 g. of iron filings, and 2·5 g. of crystallised baryta was slowly heated (5 hours) as described under the thermal decomposition. There was much frothing initially, the temperature rose to 257°, and the ketone began to pass over at 290°. The aqueous layer having been removed, the distillate was dried with anhydrous potassium carbonate and fractionated: (a) 12·7 g., b. p. 142—146°/761 mm., $d_{4^\circ}^{19^\circ}$ 0·9095, $n_D^{19^\circ}$ 1·434; (b) 4·2 g., b. p. 147—151°/761 mm., $d_{4^\circ}^{19^\circ}$ 0·9151, $n_D^{19^\circ}$ 1·437, representing a maximum yield of ketone of 55%; (c) a dark-coloured residue (5·8 g.), which was not investigated.

Condensation of 3-*Methyl*cyclo*pentanone with Ethyl Cyanoacetate and Ammonia in Ethyl Alcohol.*—49 G. (0·5 mol.) of the ketone, b. p. 143—143·5°, and 114 g. (1 mol.) of ethyl cyanoacetate at −5° were mixed with 250 c.c. of absolute alcohol saturated with dry ammonia at −5°, and kept in the ice-chest for 4 days. The solid which had separated dissolved on addition of 800 c.c. of water, and the solution was then extracted three times with ether and acidified (Congo-red) with concentrated hydrochloric acid. After 12 hours, the ω-*imide* (VII) produced was washed with water and dried in the steam-oven (yield, 58 g.). After recrystallisation from boiling water it had m. p. 189—190° (Found: C, 62·4; H, 5·8. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·6%).

ω-*Imide of* αα'-*Dicarbamyl*-3-*methyl*cyclo*pentane*-1 : 1-*diacetic Acid* (VIII).—A solution of the crude imide (2 g.) in concentrated sulphuric acid (20 g.) was kept for 24 hours and poured into water. The solid produced on cooling crystallised from hot water in prisms, which charred at 232—233° after softening at 228° (Found: C, 53·5; H, 6·3. $C_{12}H_{17}O_4N_3$ requires C, 53·9; H, 6·4%).

3-*Methyl*cyclo*pentane*-1 : 1-*diacetic Acid* (VI).—A solution of the dicyano-imide (56 g.) in concentrated sulphuric acid (224 c.c.) was kept for 48 hours and, after addition of water (48 c.c.), heated under reflux until the vigorous evolution of carbon dioxide slackened (30 minutes); water (150 c.c.) was then added to the cooled liquid, and the whole heated under reflux for 5 hours. When cold, the solution was diluted with 500 c.c. of water and extracted four times with ether, the extract dried with anhydrous sodium sulphate, and the ether evaporated. The residual crystalline acid (34 g.) was best purified through the anhydride (small quantities may be crystallised from dilute hydrochloric acid, an acid, m. p. 134·5—135°, being obtained). The anhydride (9 g.) was boiled for 30 minutes with aqueous potassium hydroxide (20 g. in 30 g.), the solution acidified with hydrochloric acid, and the *acid* (VI) recrystallised from hot water, giving thin prisms, m. p. 134—135° (Found : C, 60·1 ; H, 7·9. $C_{10}H_{16}O_4$ requires C, 60·1 ; H, 8·1%. Found for the *silver* salt : Ag, 52·1. $C_{10}H_{14}O_4Ag_2$ requires Ag, 52·2%), readily soluble in ether, acetone, and ethyl acetate, moderately easily soluble in benzene, and very sparingly soluble in concentrated hydrochloric acid. A neutral solution of the ammonium salt gives no precipitate with barium chloride, a white precipitate with calcium chloride only on boiling, and white and bluish-green precipitates with lead acetate and copper sulphate respectively.

The *anhydride*, prepared by refluxing the acid (10 g.) for 3 hours with acetic anhydride (25 g.) and removing the acetic acid and the excess of acetic anhydride under ordinary pressure, was a colourless viscid liquid, b. p. 192°/20 mm. or 185°/12 mm. (Found : C, 65·6; H, 7·6. $C_{10}H_{14}O_3$ requires C, 65·9 ; H, 7·7%).

The β-*naphthylamic acid*, obtained by boiling benzene solutions of the anhydride (1·4 g.) and β-naphthylamine for 30 minutes, pouring the mixture into excess of dilute hydrochloric acid, and allowing the benzene layer to evaporate spontaneously, separated from dilute alcohol in lustrous plates, m. p. 162—163° after softening at 153° (Found : C, 73·5 ; H, 6·9. $C_{20}H_{25}O_3N$ requires C, 73·8 ; H, 7·1%).

The *ethyl* ester was prepared by heating a mixture of 6·5 g. of the acid, 30 g. of absolute alcohol, 30 g. of sodium-dried benzene, and 3 g. of concentrated sulphuric acid for 7 hours, and was isolated after the addition of water from the benzene layer and an ethereal extract of the aqueous layer. It had b. p. 155·5°/15 mm., $d_{4^\circ}^{15^\circ}$ 1·0602, $n_{\mathrm{D}}^{15^\circ}$ 1·4485, whence $[R_L]_{\mathrm{D}}$ 67·58 (calc., 67·72) ; yield, 7·1 g. (Found : C, 65·3 ; H, 9·2. $C_{14}H_{24}O_4$ requires C, 65·5 ; H, 9·4%).

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