920. *Olefinic Acids. Part VIII.** α-*Bromo*cyclo*hexylideneacetic Acid.*

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Dehydrobromination of 1 : α-dibromo*cyclo*hexylacetic acid with pyridine or aqueous alkali gives mainly ω-bromomethylene*cyclo*hexane, but with sodium ethoxide α-bromo*cyclo*hexylideneacetic acid is obtained. The main product of the reaction of the latter acid with sodium methoxide is *cyclo*hex-1-enyl-α-methoxyacetic acid, the structure of which is rigidly proved; it shows anomalous light absorption. A very small amount of *cyclo*hexylidene-α-methoxyaceticacid is probably also formed. The effect of the methoxy-group on the αβ–βγ-equilibrium appears to be anomalous.

Syntheses of *cyclo*hexyl-α-methoxyacetic, *cyclo*hexyl-α-ketoacetic, and 1-hydroxy-2-methoxy*cyclo*hexylacetic acid are described; dehydration of the last with acetic anhydride gives a mixture of αβ- and βγ-unsaturated lactones.

In Part IV (Owen and Sultanbawa, *J.*, 1949, 3089) it was shown that the formation of α-methoxy-ββ-dimethylacrylic acid (IV) by treatment of α-bromo-ββ-dimethylacrylic acid (I) with methanolic sodium methoxide occurred, not by direct nucleophilic replacement of the bromine atom, but by a succession of prototropic changes *via* the βγ-unsaturated acids (II) and (III). The final product consisted mainly of (IV), and the equilibrium mixture (III) $\rightleftharpoons$ (IV), approached from either side, contained about 90% of (IV). Although no

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* Part VII, *J.*, 1949, 3109.

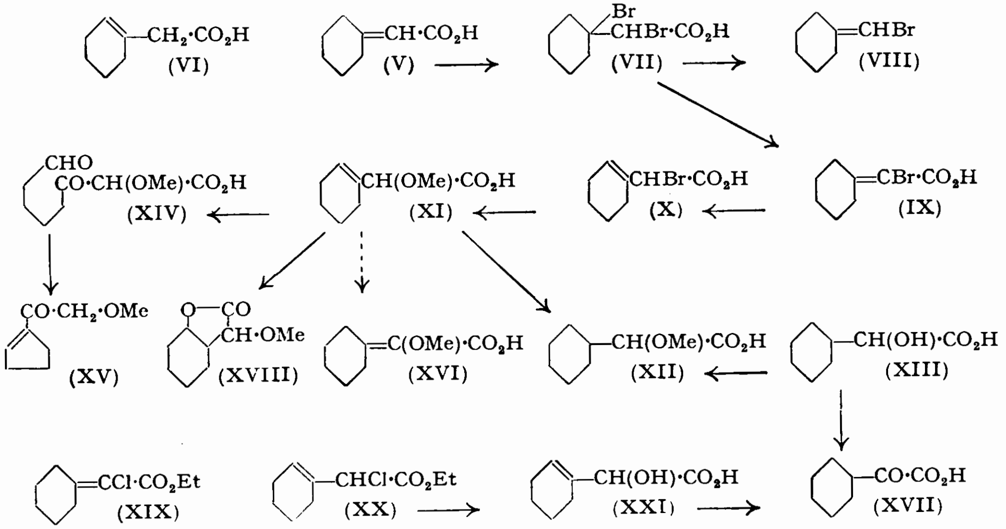
such direct proof has been obtained in the corresponding reaction with α-bromocrotonic acid (Part I; Owen, *J.*, 1945, 385), there can be little doubt that a similar series of changes occurs, the only difference being that the mobility is probably greater, and the final

$$\underset{(I)}{CMe_2{:}CBr{\cdot}CO_2H} \longrightarrow \underset{(II)}{CH_2{:}CMe{\cdot}CHBr{\cdot}CO_2H} \longrightarrow \underset{(III)}{CH_2{:}CMe{\cdot}CH(OMe){\cdot}CO_2H} \longrightarrow \underset{(IV)}{CMe_2{:}C(OMe){\cdot}CO_2H}$$

equilibrium lies even more on the αβ-side, so that no α-methoxy-βγ-unsaturated isomer is isolated. In both of these cases, the alkali-catalysed equilibria of the parent unbrominated compounds (ββ-dimethylacrylic and crotonic acids) are entirely in favour of the αβ-unsaturated forms (Kon and Linstead, *J.*, 1925, **127**, 616; Linstead and Noble, *J.*, 1934, 614), and it was therefore of interest to examine the behaviour of an α-bromo-αβ-unsaturated acid the unbrominated parent of which showed a greater tendency towards isomerisation into the βγ-unsaturated form. α-Bromo-γ-methoxycrotonic acid, which fulfils such a requirement, had already been investigated (Owen and Sultanbawa, *J.*, 1949, 3105), but owing to its very high reactivity and its tendency to polymerise, the results were not clearly defined. α-Bromo*cyclo*hexylideneacetic acid was therefore chosen, since the equilibrium mixture of *cyclo*hexylideneacetic acid (V) and *cyclo*hex-1-enylacetic acid (VI) contains about 88% of the latter (Linstead, *J.*, 1927, 2579).

The dehydrobromination of 1 : α-dibromo*cyclo*hexylacetic acid (VII) has not previously been studied, although Wallach (*Annalen*, 1907, **353**, 289) and Ingold, Oliver, and Thorpe (*J.*, 1924, **125**, 2136) reported that with aqueous alkali it underwent profound decomposition. Bromo-olefins are often formed in such reactions (Farrell and Bachmann, *J. Amer. Chem. Soc.*, 1935, **57**, 1281) and we found that treatment of (VII) with cold dilute sodium hydroxide or with pyridine results in dehydrobromination and decarboxylation, to give mainly ω-bromomethylene*cyclo*hexane (VIII); the structure of this was confirmed by oxidation with potassium permanganate to *cyclo*hexanone. With cold ethanolic sodium ethoxide, however, (VII) gave the required α-bromo*cyclo*hexylideneacetic acid (IX) in 85% yield; this showed light-absorption maxima at 2260 and 2500 Å of roughly equal intensity (ε *ca.* 4000), in marked contrast to the parent acid (V), which has a high-intensity band at 2260 Å (ε 13,200).

Preliminary experiments showed that the bromo-acid (IX) was much less reactive towards methanolic sodium methoxide than any of the α-bromo-αβ-unsaturated acids previously studied. Complete liberation of bromide ion was complete in 15 hours with the boiling 5N-reagent, and *cyclo*hex-1-enyl-α-methoxyacetic acid (XI) was isolated in good yield. The methoxy-group was shown to be in the α-position by hydrogenation of the product to *cyclo*hexyl-α-methoxyacetic acid (XII), which was independently synthesised by



methylation of *cyclo*hexyl-α-hydroxyacetic acid (XIII) (prepared by a new route, the hydrolysis of ethyl α-bromo*cyclo*hexylacetate) with methyl iodide and silver oxide, followed by hydrolysis of the resulting methyl ester. Attempts to synthesise (XII) by reaction of ethyl α-bromo*cyclo*hexylacetate with sodium methoxide gave mixtures of methoxy- and unsaturated ester, from which, after hydrolysis, (XII) could be isolated only in an impure state. The fact that the methoxy-acid (XI) gave no ketonic derivative on prolonged treatment with 2 : 4-dinitrophenylhydrazine in aqueous sulphuric acid showed that the double bond could not be in the αβ-position, and this was confirmed by ozonolysis to carbon dioxide and, in poor yield, an unsaturated ketone. This was isolated as the semicarbazone, the analysis and light-absorption properties of which agreed with its formulation as a derivative of methoxymethyl *cyclo*pent-1-enyl ketone (XV), formed by intramolecular aldol-type condensation of the initial keto-aldehyde (XIV). Oxidation of (XI) was also performed with cold aqueous permanganate, adipic acid being formed; since *cyclo*hexanone is unaffected under these conditions (Fraser and Kon, *J.*, **1934**, 606) this confirms the endocyclic position of the double bond.

The light-absorption of (XI), however, is anomalous in that it shows a low-intensity maximum at 2260 Å (ε 1000); since the band persists with the same intensity in samples of the methoxy-acid prepared as above or exhaustively recrystallised or regenerated from the crystalline sodium or *S*-benzylthiuronium salts, the absorption is a genuine property of the acid. The methyl ester, prepared with diazomethane, showed similar light-absorption properties.

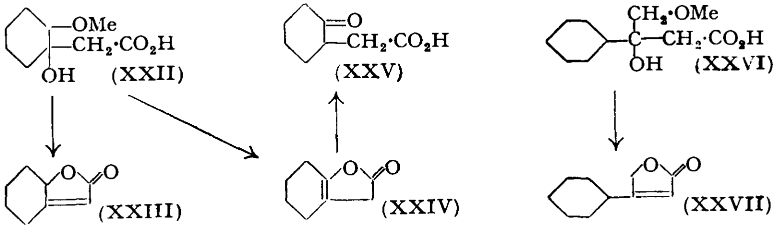
Although the α-methoxy-βγ-unsaturated acid (XI) is undoubtedly the main product in the reaction of (IX) with sodium methoxide, indirect evidence has been obtained for the formation, in small proportion, of the αβ-unsaturated isomer (XVI). The crude distilled acid, before recrystallisation, showed a light-absorption maximum at 2640 Å (ε 100—350 in various experiments), which was also present in the oily acid obtained by evaporation of the mother-liquors from the crystallisation; this is approximately the wavelength expected for the structure (XVI). In order to concentrate this component, the reaction mixture from (IX) was evaporated to dryness, and the residue dissolved in water, and cautiously acidified; the sparingly soluble acid salt, $C_9H_{14}O_3,C_9H_{13}O_3Na$, of (XI) was precipitated and removed; the residual solution was further acidified, and the liberated acid was converted into the methyl ester. Fractional distillation failed to separate the αβ- and βγ-unsaturated esters, but the distillate, which gave correct analyses for $C_{10}H_{16}O_3$, had a considerably higher refractive index than that of the methyl ester of the pure βγ-unsaturated acid (XI), and showed a light absorption maximum at 2640 Å (ε 2500); this affords strong evidence for the presence of some αβ-unsaturated ester, though the amount corresponded to a proportion of only about 5% in the original reaction product. Attempts were made to confirm the formation of (XVI) by acid hydrolysis, and detection as *cyclo*hexyl-α-ketoacetic acid (XVII), which was synthesised for comparison by oxidation of *cyclo*hexyl-α-hydroxyacetic acid (XIII) and characterised as the 2 : 4-dinitrophenylhydrazone. However, apart from unchanged *cyclo*hex-1-enyl-α-methoxyacetic acid, the only substance obtained by treatment of a reaction product with cold N-hydrochloric acid was the corresponding lactone (XVIII). Acid hydrolysis of the enriched methyl ester, described above, did result in the formation of a keto-acid, since a small amount of a 2 : 4-dinitrophenylhydrazone was isolated which was soluble in sodium hydrogen carbonate solution, but the presence of other decomposition products made purification impracticable.

Prolonged treatment of the pure βγ-unsaturated acid (XI) with sodium methoxide at 100° failed to isomerise it appreciably to (XVI). This can hardly be due to low mobility, since the presence of the methoxy-group (—*I*) would be expected to increase the mobility relative to the unsubstituted acid (VI), which is readily equilibrated under such conditions. The equilibrium between (XI) and (XVI) must therefore lie almost entirely in favour of (XI), and since the equilibrium (V) $\rightleftharpoons$ (VI) contains about 88% of the βγ-form it appears that the presence of the methoxy-group in the α-position results in an *increased* proportion of that form. In the crotonic acid series the presence of a methoxy-group in the γ-position resulted in a very large shift in equilibrium to the βγ-side (Part V; Owen and Sultanbawa, *J.*, **1949**, 3098) and this was attributed to the +*M* effect; in the present case this should favour the αβ-form, and the behaviour of the methoxy-group therefore appears to be anomalous. It is cognate that an α-methyl group, which normally favours the αβ-form (because hyperconjugation is then possible), apparently favours the βγ-form in certain *cyclo*hexylidene derivatives, though not in the acids (Kon and Thakur, *J.*, 1930, 2217). Consideration of our earlier results in the dimethylacrylic acid series (Part IV, *loc. cit.*) reveals a similar anomaly in that relatively to the parent acid (100% αβ-form at equilibrium) the α-methoxy-acid contained a greater equilibrium proportion (*ca.* 10%) of βγ-unsaturated isomer.

Although the present experiments do not prove chemically that the unsaturated methoxy-acid is derived, not by the route (IX) ⟶ (XVI) ⟶ (XI), but from the intermediate α-bromo-βγ-unsaturated acid (X), the second-order rate constants, calculated from the liberation of bromide ion, provide some confirmation that the direct substitution of halogen in (IX) does not occur. During the reaction, sodium bromide gradually crystallised from the solution, thus resulting in a diminution in ionic strength; such a change should result in a slight increase in the rate of a bimolecular substitution reaction, whereas the reverse was found. In the mechanism proposed, the rate-controlling stage would certainly be the isomerisation (IX) ⟶ (X), which in the transition state (attack by OMe^-) would show a concentration of charge and would therefore be affected by change of ionic strength in the way actually found (cf. Beste and Hammett, *J. Amer. Chem. Soc.*, 1940, **62**, 2481; Cooper, Dhar, Hughes, Ingold, MacNulty, and Woolf, *J.*, 1948, 2043).

The liberation of bromide ion from α-bromo*cyclo*hexylideneacetic acid with aqueous 4N-sodium hydroxide was slow (11% in 2 hours at 100°; cf. Parts I and IV, *locc. cit.*, for curves showing the reactivities of α-bromocrotonic and α-bromo-ββ-dimethylacrylic acid). Prolonged heating, or the use of more concentrated alkali, resulted in extensive polymerisation and no identifiable product. This is interesting in view of Darzens and Lévy's claim (*Compt. rend.*, 1937, **204**, 272) that aqueous alkali hydrolyses ethyl α-chloro*cyclo*hexylideneacetate (XIX) to *cyclo*hexyl-α-ketoacetic acid (XVII) (the latter was not isolated, but was decarboxylated to *cyclo*hexylformaldehyde, identified as the semicarbazone). The reaction was assumed by them to proceed directly, but it is clear from our work that the only reasonable course would involve rearrangement to give the βγ-isomer (XX), or the corresponding acid, followed by hydrolysis to (XXI) and a further prototropic change. Nevertheless, in view of the low reactivity of the bromo-acid (IX) towards hydrolysis with aqueous alkali, such a reformulation seems inadequate, since the corresponding chloro-compound would probably be even less reactive. Darzens and Lévy, however, recorded no yields, and gave no proof that the material hydrolysed had the structure (XIX); it was prepared by dehydration of ethyl α-chloro-1-hydroxy*cyclo*hexylacetate with phosphoric oxide, and it is probable that under these conditions (cf. Kon and Nargund, *J.*, 1932, 2461) the main product would be ethyl α-chloro*cyclo*hex-1-enylacetate (XX), from which the keto-acid would readily be formed by the route outlined above.

With the object of synthesising 2-methoxy*cyclo*hexylideneacetic acid, an analogue of γ-methoxycrotonic acid (Part V, *loc. cit.*), 2-methoxy*cyclo*hexanone was condensed with ethyl bromoacetate in the Reformatsky reaction to give ethyl 1-hydroxy-2-methoxy*cyclo*hexylacetate. Hydrolysis then gave the free acid (XXII) which was dehydrated by



heating with acetic anhydride, but instead of the expected αβ-unsaturated acid the lactones (XXIII) and (XXIV) were obtained. These were separated by virtue of the difference in their behaviour towards regeneration from the salts of the corresponding acids. By heating the mixture with 2N-sodium hydroxide for just sufficient time (so as to avoid extensive αβ–βγ-isomerisation) to dissolve the lactones, and then acidifying the solution, some of the αβ-unsaturated lactone (XXIII) was regenerated, whilst the βγ-unsaturated isomer (XXIV) was entirely converted into 2-keto*cyclo*hexylacetic acid (XXV), identified as the semicarbazone and 2 : 4-dinitrophenylhydrazone. The light-absorption properties of (XXIII) were very similar to those of *cyclo*hexylideneacetic acid. The formation of the lactone (XXVII) from the β-hydroxy-γ-methoxy-acid (XXVI) (Rubin, Paist, and Elderfield, *J. Org. Chem.* 1941, **6**, 260) provides an analogy for the above transformations.

The reaction of 2-methoxy*cyclo*hexanone with 2 : 4-dinitrophenylhydrazine has been the subject of controversy. In our hands, reaction with 1·1 mols. of the reagent gave as the major product the red 2 : 4-dinitrophenylosazone of *cyclo*hexane-1 : 2-dione, m. p. 220—221° (Adkins and Rossow, *J. Amer. Chem. Soc.*, 1949, **71**, 3836), accompanied by a very small amount of the yellow 2 : 4-dinitrophenylhydrazone, m. p. 135°, of 2-methoxy*cyclo*hexanone (Ferrante and Bloom, *Amer. J. Pharm.*, 1933, **105**, 381).

EXPERIMENTAL

*cyclo*Hexylideneacetic acid, prepared by the dehydration of 1-hydroxy*cyclo*hexylacetic acid (from the ethyl ester; *Org. Reactions*, 1942, **1**, 17) with acetic anhydride (Wallach, *Annalen*, 1909, **365**, 261), separated from light petroleum (b. p. 60—80°) in needles, m. p. 90—91°. Light absorption in ethanol : max. 2260 Å (ε 13,200).

*cyclo*Hexanone and keten in the presence of boron trifluoride (cf. U.S.P. 2,382,464) gave *cyclo*hex-1-enylacetic acid, m. p. 36—37°, as the only acidic product (Found : equiv., 142. Calc. for $C_8H_{12}O_2$: equiv., 140) (1 : 2-dibromide, m. p. 119—120°).

1 : *α-Dibromo*cyclo*hexylacetic Acid.*—Bromine (15·9 g.) in glacial acetic acid (30 c.c.) was added during 1 hour to *cyclo*hexylideneacetic acid (13·5 g.) in glacial acetic acid (80 c.c.), at 15° (cooling). Acetic acid was removed at 50°/15 mm. and the crushed solid residue was washed twice with light petroleum (30 c.c.). Recrystallisation from light petroleum (b. p. 80—100°) gave large prisms of the dibromo-acid (19 g., 65%), m. p. 136—137°.

Action of Aqueous Sodium Hydroxide on 1 : *α-Dibromo*cyclo*hexylacetic Acid.*—The acid (2·0 g.) was shaken vigorously in 0·12N-sodium hydroxide (200 c.c.) for 1 hour. The turbid alkaline solution was then extracted thrice with ether. After evaporation of the dried ($CaCl_2$) ethereal extracts, the residual oil was fractionally distilled to give *ω-bromomethylene*cyclo*hexane* (0·88 g.), a colourless liquid with a characteristic odour, b. p. 75—76°/15 mm., n_D^{19} 1·5165 (Found : C, 48·3; H, 6·2; Br, 45·3. $C_7H_{11}Br$ requires C, 48·0; H, 6·3; Br, 45·6%). A faint turbidity only was produced when the bromo-olefin was warmed with alcoholic silver nitrate.

The alkaline solution remaining after extraction with ether was acidified with N-hydrochloric acid; no material was extracted with ether.

Action of Pyridine on 1 : *α-Dibromo*cyclo*hexylacetic Acid.*—The acid (1·0 g.) in pyridine (5 c.c.) was heated at 60—65° for an hour; carbon dioxide was evolved and pyridine hydrobromide was gradually precipitated. The cooled product was diluted with water and was extracted with ether. The extracts were washed successively with dilute hydrochloric acid, water, and aqueous sodium carbonate, and then dried (Na_2SO_4) and evaporated, to give crude ω-bromomethylene*cyclo*hexane (0·24 g.), n_D^{15} 1·5420.

Acidification of the sodium carbonate washings, followed by extraction with ether, gave no acidic material.

*Oxidation of ω-Bromomethylene*cyclo*hexane.*—ω-Bromomethylene*cyclo*hexane (0·21 g.) was shaken with potassium permanganate (0·38 g.) in water (20 c.c.) for 2 hours at room temperature and the whole distilled in steam, 10 c.c of distillate being collected. This had a strong odour of *cyclo*hexanone, and on treatment with aqueous 2 : 4-dinitrophenylhydrazine sulphate gave the 2 : 4-dinitrophenylhydrazone (0·17 g.), yellow plates, m. p. and mixed m. p. 160° from ethanol.

*α-Bromo*cyclo*hexylideneacetic Acid.*—To a well-stirred solution of 1 : α-dibromo*cyclo*hexylacetic acid (12·5 g.) in absolute ethanol (50 c.c.), at −15°, was added ice-cold ethanolic sodium ethoxide (from sodium, 2·15 g., and absolute ethanol, 30 c.c.). The stirred mixture was allowed to attain room temperature during 16 hours. The ethanol was then removed at <50° and the residue was dissolved in water, filtered, and extracted thrice with ether to remove decarboxylated material. Acidification of the aqueous layer (from which dissolved ether had been removed) with 2N-sulphuric acid gave a white precipitate of *α-bromo*cyclo*hexylideneacetic acid* (7·8 g.) which was washed free from inorganic salts with water. The acid crystallised from light petroleum (b. p. 60—80°) in colourless prisms, m. p. 120° (Found : C, 44·2; H, 5·2; Br, 36·2%; equiv., 219. $C_8H_{11}O_2Br$ requires C, 43·9; H, 5·1; Br, 36·5%; equiv., 219). Light absorption in ethanol : max. 2260, 2420, 2470, 2510 Å (ε 3700, 3300, 4100, and 4100 respectively).

The p-*bromophenacyl* ester crystallised from ethanol in needles, m. p. 113° (Found : C, 46·5; H, 4·0. $C_{16}H_{16}O_3Br_2$ requires C, 46·2; H, 3·9%).

*Rate of Reaction of α-Bromo*cyclo*hexylideneacetic Acid with Methanolic Sodium Methoxide.*—A known weight of the acid (0·0005—0·001 mole) was heated with 3 equivs. of 3·0N-methanolic sodium methoxide in a sealed glass tube immersed in boiling methylated spirit (80°) for a known time (3—100 hours). The tube was then broken under water (30 c.c.). The solution was made slightly acid (Congo-red) with dilute nitric acid and extracted with ether. The aqueous solution was neutralised with calcium carbonate and titrated with 0·1N-silver nitrate, 1 c.c. of 5% aqueous potassium chromate being used as indicator.

Wt. of acid, g.	3·0N-NaOMe–MeOH (c.c.)	Time (hours)	0·1013N-AgNO$_3$ (c.c.)	Reaction (%)	10^4k_2 (mole l.$^{-1}$ min.$^{-1}$)
0·2132	0·97	3	0·74	8	2·4
0·1868	0·85	16	2·53	30	2·0
0·1476	0·67	27	2·85	43	2·0
0·1642	0·75	52	4·46	60	1·8
0·2051	0·94	95	7·22	78	1·8

Blank determinations with 0·0005—0·001 mole of potassium bromide and 0·1 g. of benzoic acid indicated an accuracy of ±2% for the estimation of bromide ion.

*Products of the Reaction of α-Bromo*cyclo*hexylideneacetic Acid with Methanolic Sodium Methoxide.*—(i) α-Bromo*cyclo*hexylideneacetic acid (0·99 g.) and 5N-methanolic sodium methoxide (10 c.c.) were boiled under reflux for 24 hours; after ½ hour the clear solution began to deposit sodium bromide. Methanol was then removed under reduced pressure. The residue was dissolved in water (200 c.c.), extracted with ether to remove any decarboxylated material (evaporation of the extracts left no residue), acidified with dilute nitric acid, and immediately extracted with ether. The aqueous layer was separated, diluted to 500 c.c., neutralised with calcium carbonate, and titrated against silver nitrate solution by the Mohr method; 50 c.c. required 4·93 c.c. of 0·0935N-AgNO$_3$, corresponding to 102% of bromide ion.

Evaporation of the dried (Na_2SO_4) ethereal extracts gave a liquid which on distillation afforded a waxy solid (0·62 g.), b. p. 130° (bath)/0·2 mm., m. p. 40—53° (Found : C, 62·9; H, 8·35%). Light absorption in ethanol : max. 2260, 2580, and 2640 Å (ε 1150, 340, and 340 respectively). Several recrystallisations from light petroleum (b. p 40—60°) gave cyclo*hex-1-enyl-α-methoxyacetic acid* (0·4 g. after one crystallisation), m. p. 59—60° (Found : C, 63·4; H, 8·3%; equiv., 172. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%; equiv., 170). Light absorption in ethanol : max. 2260 Å (ε 1100). The m. p. and light-absorption properties were unchanged after repeated recrystallisation. Evaporation of the mother-liquors gave an oily acid, which showed light absorption max. at 2260 and 2640 Å (ε 1200 and 1400 respectively), suggesting the presence of some αβ-unsaturated material.

The crystalline acid gave an S-*benzylthiuronium* salt, plates (from ethanol), m. p. 179° (Found : C, 60·8; H, 7·3. $C_{17}H_{24}O_3N_2S$ requires C, 60·7; H, 7·2%).

The *methyl* ester, prepared by diazomethane in ether, had b. p. 125°/16 mm., 90°/0·5 mm., n_D^{15} 1·4712 (Found : C, 64·9; H, 8·75. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·75%). Light absorption : max. 2260 Å (ε 1300).

(ii) α-Bromo*cyclo*hexylideneacetic acid (5·14 g.) was treated with methanolic sodium methoxide as above, and after removal of methanol under reduced pressure the residue was dissolved in water (100 c.c.). Careful acidification with 6N-hydrochloric acid, with cooling, precipitated the *sodium acid* double salt, $C_8H_{13}O{\cdot}CO_2H,C_8H_{13}O{\cdot}CO_2Na$, which separated from water in feathery needles, m. p. 201—202° (Found : Na, 6·9. $C_{18}H_{27}O_6Na$ requires Na, 6·35%), soluble in excess of water to give an acid solution, but insoluble in ether. It dissolved readily in dilute alkalis and with dilute hydrochloric acid was converted into *cyclo*hex-1-enyl-α-methoxyacetic acid, which after isolation in the usual manner had m. p. 59—60° (Yield, 2·15 g.). Light absorption in ethanol : max. 2260 Å (ε 1100).

The aqueous filtrate which remained after removal of the precipitated acid sodium salt was further acidified and extracted with ether. Evaporation of the dried (Na_2SO_4) extracts gave an oil which was treated with ethereal diazomethane. Distillation of the product gave a middle fraction (0·3 g.), b. p. 120°/15 mm., n_D^{16} 1·4767; light absorption max., 2260 and 2650 Å (ε 2200 and 2500 respectively) (Found : C, 65·0; H, 8·5. Calc. for $C_{10}H_{16}O_3$: C, 65·2; H, 8·75%), which was probably a mixture of methyl *cyclo*hex-1-enyl-α-methoxyacetate and methyl *cyclo*hexylidene-α-methoxyacetate, containing *ca.* 40% (=3% yield) of the latter.

(iii) α-Bromo*cyclo*hexylideneacetic acid (4·5 g.) was heated under reflux for 24 hours with 5N-methanolic sodium methoxide (45 c.c.). The mixture was cooled, diluted with water (200 c.c.), and extracted with ether. Evaporation of the dried (Na_2SO_4) extracts left no residue. Sufficient 6N-hydrochloric acid was added to the aqueous portion to make it approximately a N-acid solution, and it was set aside for 16 hours to hydrolyse any enol-ether. It was then extracted with ether and the dried (Na_2SO_4) extract was evaporated to give an oily residue which was fractionally distilled. The first fraction (0·5 g.), b. p. 60—63°/0·1 mm., on redistillation gave the *lactone* of 2-hydroxy*cyclo*hexyl-α-methoxyacetic acid, b. p. 120°/30 mm., n_D^{16} 1·4710 (Found: C, 64·4; H, 8·65. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%), insoluble in aqueous sodium hydrogen carbonate solution, but soluble in warm 2N-sodium hydroxide. The second fraction, b. p. 90—100°/10^{-3} mm., was *cyclo*hex-1-enyl-α-methoxyacetic acid. No ketonic compounds were detected in the products.

Ozonolysis of cyclo*Hex-*1*-enyl-α-methoxyacetic Acid.*—The acid (2·17 g.) was ozonised in dry carbon tetrachloride (20 c.c.) at 0° until ozone was no longer absorbed. Removal of the solvent at 20°/15 mm. gave an oily yellow ozonide which was decomposed by heating it at 100° with 2N-sulphuric acid (25 c.c.) for ¼ hour; considerable evolution of carbon dioxide occurred. The solution was then distilled in steam and the distillate (200 c.c.) was extracted with ether. Evaporation of the dried (Na_2SO_4) extracts gave an oil; this gave a deep red 2 : 4-dinitrophenylhydrazone which could not be purified and a biscuit-coloured semicarbazone. Recrystallisation from benzene gave the *semicarbazone* of methoxymethyl *cyclo*pentenyl ketone, m. p. 192—193° (decomp.) (Found: C, 55·0; H, 7·8; N, 21·3. $C_9H_{15}O_2N_3$ requires C, 54·8; H, 7·7; N, 21·3%). Light absorption in ethanol: max. 2740 Å (ε 36,000).

Permanganate Oxidation of cyclo*Hex-*1*-enyl-α-methoxyacetic Acid.*—Potassium permanganate (2·51 g.) in water (150 c.c.) was added during 1 hour to a vigorously stirred suspension of the acid (0·81 g.) in water (50 c.c.) at 0°. The mixture was kept at 0° for 72 hours and filtered from manganese dioxide. The colourless filtrate was made more strongly alkaline by the addition of 2N-sodium hydroxide, and extracted with ether. Evaporation of the dried (Na_2SO_4) extracts left no residue. The aqueous layer was acidified and continuously extracted with ether. Evaporation of the dried (Na_2SO_4) extracts left a solid, which when crystallised from ethyl acetate gave adipic acid (0·21 g.), m. p. and mixed m. p. 151°.

Hydrogenation of cyclo*Hex-*1*-enyl-α-methoxyacetic Acid.*—*cyclo*Hex-1-enyl-α-methoxyacetic acid (1·0 g.) was suspended in water (15 c.c.) and brought to pH 9 by the addition of sodium carbonate. A 10% palladium–charcoal catalyst (0·4 g.) was added, and the mixture was completely hydrogenated at room temperature and pressure (6 hours). After filtration, the solution was acidified and extracted with ether. Evaporation of the dried (Na_2SO_4) extracts gave a crystalline residue which was crushed on a porous tile to remove some oil. The residue (0·9 g.), m. p. 60—62°, recrystallised four times from pentane, gave needles of cyclo*hexyl-α-methoxyacetic acid*, m. p. and mixed m. p. 67° with a specimen obtained as below (Found: C, 62·7; H, 9·3. $C_9H_{16}O_3$ requires C, 62·8; H, 9·3%).

*Ethyl α-Bromo*cyclo*hexylacetate.*—Ethyl *cyclo*hexylacetate, b. p. 42—43°/0·2 mm., n_D^{15} 1·4470, was prepared in 86% yield by hydrogenation (Raney nickel) of ethyl phenylacetate at 150°/200 atm.; hydrolysis with alcoholic sodium hydroxide gave *cyclo*hexylacetic acid, b. p. 75°/0·3 mm., m. p. 26—27°, which was converted into the α-bromo-ester, b. p. 86—87°/0·4 mm., n_D^{19} 1·4848, by Braun's method (*Ber.*, 1923, **56**, 2183).

cyclo*Hexyl-α-hydroxyacetic Acid.*—Ethyl α-bromo*cyclo*hexylacetate (12·5 g.) was heated on the steam-bath for 16 hours with 2·5N-sodium hydroxide (100 c.c.) and pure dioxan (50 c.c.). Dioxan was then removed under reduced pressure and the residual solution was treated with a slight excess of 2N-hydrochloric acid. The precipitated *cyclo*hexyl-α-hydroxyacetic acid was recrystallised from hot water (yield, 5·7 g.; m. p. 135°). Freudenberg, Brauns, and Siegel (*Ber.*, 1923, **56**, 197) give m. p. 134—135°. The aqueous mother-liquors were extracted with ether and after evaporation of the dried (Na_2SO_4) extracts the residual crystalline mass was heated for 1 hour at 100°/0·2 mm., to remove unsaturated products. Recrystallisation of the residue from hot water gave a further 0·6 g. of hydroxy-acid, m. p. 135° (total yield, 80%).

Methyl cyclo*Hexyl-α-methoxyacetate.*—Freshly prepared dry silver oxide (12 g.) was added in small portions to *cyclo*hexyl-α-hydroxyacetic acid (2·05 g.) and dry methyl iodide (20 g.) with shaking. Finally the mixture was heated under reflux at 65° for 2 hours, and the product was extracted with ether and filtered. After evaporation, benzene was added and water was removed by azeotropic distillation. The residue was then re-methylated with half the above quantities of methyl iodide and silver oxide. The product was distilled, to give *methyl* cyclo*hexyl-α-methoxyacetate* (1·48 g.), b. p. 120°/30 mm., n_D^{16} 1·4520 (Found : C, 64·4; H, 9·9. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·7%).

cyclo*Hexyl-α-methoxyacetic Acid.*—The above methyl ester (1·32 g.) was hydrolysed for 2 hours with 2·5N-sodium hydroxide (20 c.c.) in boiling ethanol (15 c.c.). The cooled solution was extracted with ether and acidified with 2N-sulphuric acid. Extraction with ether and evaporation of the dried (Na_2SO_4) extracts gave a crystalline residue which was distilled at 80° (bath)/0·1 mm. The product (1·12 g., 92%), recrystallised from light petroleum (b.p. 40—60°), gave needles, m. p. 67°, of *cyclo*hexyl-α-methoxyacetic acid, identical with the material described above.

The p-*bromophenacyl* ester separated from ethanol as needles, m. p. 70° (Found : Br, 21·6. $C_{17}H_{21}O_4Br$ requires Br, 21·6%).

*Reaction of Ethyl α-Bromo*cyclo*hexylacetate with Methanolic Sodium Methoxide.*—Ethyl α-bromo*cyclo*hexylacetate (6·4 g) was refluxed for 16 hours with 2N-methanolic sodium methoxide (50 c.c.). The solution was then poured into water (500 c.c.) and immediately extracted with ether. Distillation of the dried (Na_2SO_4) ethereal extracts gave fractions of continually decreasing refractive index (n_D^{17} 1·4643—1·4568), the last of which showed the least unsaturation towards neutral potassium permanganate. This liquid ester (0·4 g.), b. p. 97—98°/15 mm., was hydrolysed to the free acid which was stirred with 1% aqueous potassium permanganate at −10° for 3 hours to destroy the unsaturated material. Isolation of the product gave a solid acid which softened below 50° and had m. p. 55—62°, raised to 58—65° on admixture with *cyclo*hexyl-α-methoxyacetic acid.

cyclo*Hexyl-α-ketoacetic Acid.*—*cyclo*Hexyl-α-hydroxyacetic acid (1·30 g.) was neutralised with 2N-sodium hydroxide, and potassium permanganate (0·87 g.) in water (50 c.c.) was added slowly with vigorous stirring at −15°. The solution was then allowed to attain room temperature, stirring being continued, and then stored for 12 hours at 0° and filtered from manganese dioxide. After acidification the colourless filtrate was continuously extracted with ether. Distillation of the dried (Na_2SO_4) extracts gave impure *cyclo*hexyl-α-ketoacetic acid (0·30 g.), b. p. 98°/10 mm., m. p. 45—49°, probably contaminated with some *cyclo*hexylformaldehyde (Found : C, 62·3; H, 8·2. Calc. for $C_8H_{12}O_3$: C, 61·5; H, 7·75%). The 2 : 4-*dinitrophenylhydrazone* separated from aqueous ethanol in pale yellow needles, m. p. 211—212° (Found : N, 16·5. $C_{14}H_{16}O_6N_4$ requires N, 16·7%).

Attempted Isomerisation of cyclo*Hex-*1*-enyl-α-methoxyacetic Acid.*—The acid (0·14 g.) was heated with 5N-methanolic sodium methoxide (1 c.c.) at 100° for 48 hours. Isolation of the product by careful acidification and ether-extraction gave a viscous liquid which on slow distillation gave unchanged *cyclo*hex-1-enyl-α-methoxyacetic acid (0·11 g.), m. p. 54—59°, mixed m. p. 56—59°, which gave no precipitate on treatment with aqueous 2 : 4-dinitrophenylhydrazine for 1 week. The product showed no absorption maximum above 2260 Å.

*Reaction of α-Bromo*cyclo*hexylideneacetic Acid with Aqueous Sodium Hydroxide.*—(i) The bromo-acid (0·1135 g.) was heated with 3·74N-sodium hydroxide (1 c.c.) at 100° in a sealed tube for 2¼ hours. The liberated bromide ion (estimated by the method used in the experiments with sodium methoxide) required 0·60 c.c. of 0·0960N-$AgNO_3$, equiv. to 11% reaction.

(ii) The bromo-acid (1·04 g.) was heated in an autoclave with 2N-sodium hydroxide (15 c.c.) at 125° for 2½ days. The solution was diluted with water (300 c.c.), filtered, acidified with 2N-nitric acid, and extracted with ether. Bromide ion in the aqueous portion corresponded to complete reaction. The ethereal extracts gave on evaporation a residue of mainly polymeric material from which no recognisable product could be isolated.

2-*Methoxy*cyclo*hexanone.*—This was prepared as an oil, b. p. 76°/15 mm., n_D^{20} 1·4535, by methylation of 2-hydroxy*cyclo*hexanone (Bloink and Pausacker, *J.*, 1950, 1328) by the method of Bergmann and Gierth (*Annalen*, 1926, **448**, 64). The *semicarbazone* separated from ethanol in plates, m. p. 178—179° (Found : N, 22·3. $C_8H_{15}O_2N_3$ requires N, 22·7%).

Reaction of 2-*Methoxy*cyclo*hexanone with* 2 : 4-*Dinitrophenylhydrazine.*—2-Methoxy*cyclo*hexanone (0·79 g.) in ethanol (25 c.c.) was added to a solution of 2 : 4-dinitrophenylhydrazine (1·35 g., 1·1 mol.) and concentrated sulphuric acid (10 c.c.) in ethanol (100 c.c.). After 16 hours the dark red precipitate was collected and washed with methanol (yield, 0·37 g.; m. p. 215—218°). Recrystallisation from acetic anhydride gave the red bis-2 : 4-dinitrophenylhydrazone of *cyclo*hexane-1 : 2-dione, m. p. 220—221° (Adkins and Rossow, *loc. cit.*, give m. p. 218—219°).

The filtrate was diluted with water (180 c.c.) and a bright yellow turbidity was produced which quickly gave place to a red precipitate. After 12 hours the precipitate was collected (0·73 g.; m. p. 150—180°) (the filtrate was a clear yellow solution which gave no precipitate with acetone, showing that no 2 : 4-dinitrophenylhydrazine remained). This solid was extracted with boiling ethanol (50 c.c.) for 2 hours and left a residue of bis-2 : 4-dinitrophenylhydrazone (0·38 g.), m. p. 218—219°. The total yield of bis-derivative was 0·75 g. (26% based on ketone; 37% is possible).

The alcoholic extract was evaporated to dryness at 40°/15 mm. and the residue was purified by chromatography in benzene on alumina. The eluate yielded 2-methoxy*cyclo*hexanone 2 : 4-dinitrophenylhydrazone (20 mg.), needles (from methanol), m. p. 135° (Ferrante and Bloom, *loc. cit.*, give m. p. 135°).

Ethyl 1-*Hydroxy*-2-*methoxy*cyclo*hexylacetate.*—2-Methoxy*cyclo*hexanone (4·43 g.), activated zinc (2·26 g.), ethyl bromoacetate (5·8 g.), dry benzene (14 c.c.) and toluene (12 c.c.) were heated on the steam-bath. After 2 minutes a vigorous reaction set in and continued for an hour. Heating was continued for 16 hours, whereafter almost all the zinc had dissolved. After filtration, the product was decomposed with ice-cold 2N-hydrochloric acid. The organic layer was separated and washed with saturated sodium hydrogen carbonate solution until free from acid. After evaporation of the dried (Na_2SO_4) solution, the product was fractionally distilled, to give *ethyl* 1-*hydroxy*-2-*methoxy*cyclo*hexylacetate* (2·30 g., 31%) b. p. 79—82°/0·5 mm., n_D^{20} 1·4590 (Found : C, 61·2; H, 9·1. $C_{11}H_{20}O_4$ requires C, 61·1; H, 9·3%).

Hydrolysis and Dehydration of Ethyl 1-*Hydroxy*-2-*methoxy*cyclo*hexylacetate.*—The ester (1·09 g.) was heated under reflux for 2 hours with 2N-sodium hydroxide (10 c.c.). The cooled solution was extracted with ether, acidified with 2N-sulphuric acid, and again extracted with ether. The latter extracts were dried (Na_2SO_4) and evaporated to an acidic oil (0·81 g.), n_D^{14} 1·4736, which slowly decolorised neutral potassium permanganate solution. It was therefore impure 1-hydroxy-2-methoxy*cyclo*hexylacetic acid.

This acid (0·72 g.) was heated under reflux with acetic anhydride (3 g.) for 3 hours. Distillation then gave a higher-boiling fraction (0·35 g.), b. p. 90° (bath temp.)/0·5 mm., n_D^{35} 1·4945, which was insoluble in sodium hydrogen carbonate solution and was strongly unsaturated to neutral permanganate. It was a mixture of the lactones of 2-hydroxy*cyclo*hexylideneacetic and 2-hydroxy*cyclo*hex-1-enylacetic acids containing *ca.* 25% of the former (Newman and VanderWerf, *J. Amer. Chem. Soc.*, 1945, **67**, 236, give n_D^{35} 1·5064 for the αβ- and n_D^{35} 1·4903 for the βγ-unsaturated lactone).

The mixed lactones were dissolved in 2N-sodium hydroxide (1 c.c.) by warming for 10 minutes, and the alkaline solution was diluted with water (10 c.c.) and extracted twice with ether to remove non-acidic material. The aqueous layer was made just acid with 2N-hydrochloric acid and excess of saturated sodium hydrogen carbonate solution was added. The solution was then extracted four times with ether and the dried (Na_2SO_4) extracts were evaporated, to give the lactone of 2-hydroxy*cyclo*hexylideneacetic acid, m. p. 21—24°. Light absorption in ethanol : max. 2260 Å (ε 9500) (Kuehl, Linstead, and Orkin, *J. Amer. Chem. Soc.*, 1950, **72**, 2217, give m. p. 24°).

The remaining aqueous layer was acidified with 2N-hydrochloric acid and extracted four times with ether. Evaporation of the dried (Na_2SO_4) ethereal extracts gave an oily residue of impure 2-keto*cyclo*hexylacetic acid [semicarbazone, m. p. 192—193° (decomp.); 2 : 4-dinitrophenylhydrazone, m. p. 191—193°. Newman and VanderWerf (*loc. cit.*) give m. p. 197—198° (decomp.) for the semicarbazone. Cocker and Hornsby (*J.*, 1947, 1164) give m. p. 193—194° for the 2 : 4-dinitrophenylhydrazone].

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