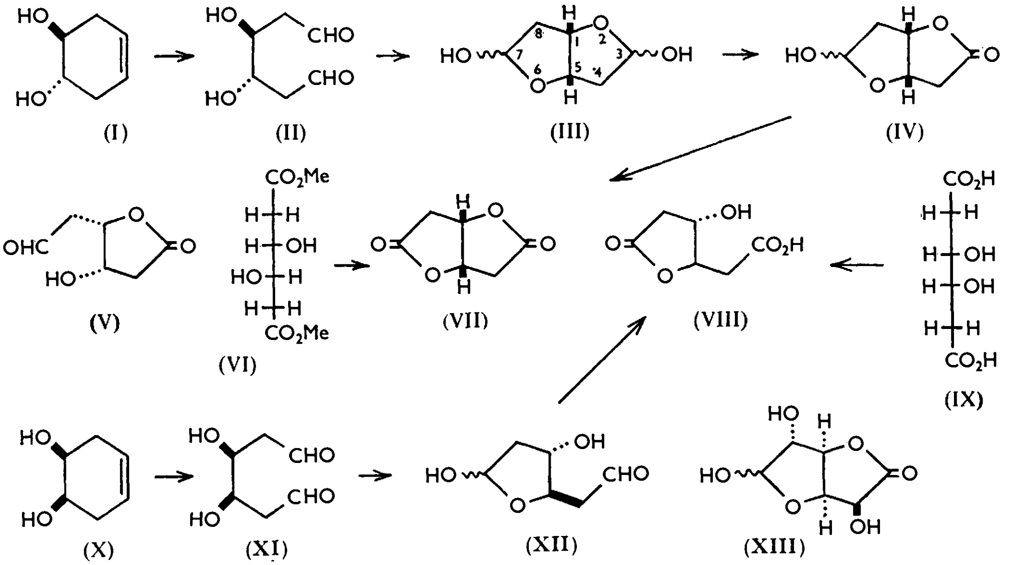
213. *Alicyclic Glycols. Part XV.*[1] *Some Lactols and Lactones Derived from the* cyclo*Hex-4-ene-1 : 2-diols.*

By Md. Erfan Ali and L. N. Owen.

Ozonolysis of *cyclo*hex-4-ene-*trans*- and -*cis*-1 : 2-diol, followed by further oxidation, yields respectively the $\gamma\gamma$-dilactone of ($\pm$)-$\beta\beta'$-dihydroxyadipic acid and the γ-lactone of the *meso*-acid. ($\pm$)-$\beta\beta'$-Dihydroxyadipdialdehyde exists as the crystalline bicyclic hemiacetal (III).

By treatment of *cis-cis*-muconic acid with aqueous hydrochloric or sulphuric acid, Linstead and his co-workers[2] obtained a compound which they suggested was probably the dilactone (VII) of ($\pm$)-$\beta\beta'$-dihydroxyadipic acid, on the assumption that a *cis*-fused bicyclic system would be preferred. Although it has subsequently been shown[3] that the *trans*-fusion of two five-membered rings can occur with unexpected ease, the structure (VII) was suported by the observation[4, 5] that the same dilactone was obtained by hydrolysis of a dimethyl $\beta\beta'$-dihydroxyadipate which, from its method of preparation (*cis*-hydroxylation of dimethyl *trans*-Δ^{β}-dihydromuconic acid with permanganate[4] or with hydrogen peroxide-*tert.*-butyl alcohol–osmium tetroxide[5]), could be assigned the ($\pm$)-configuration (VI). This conclusion has recently been confirmed[6] by resolution of the corresponding ($\pm$)-acid, which is also readily converted into the same dilactone (VII).



When *trans*-Δ^{β}-dihydromuconic acid was treated with performic acid it gave,[4] presumably *via meso*-$\beta\beta'$-dihydroxyadipic acid (IX), the hydroxy-lactonic acid (VIII), which showed no tendency to give a *trans*-fused dilactone. The experiments described below, which were in progress when the resolution of the ($\pm$)-acid was reported, provide independent proof of these configurations by correlation with the *cyclo*hex-4-ene-1 : 2-diols.[1]

Ozonolysis of *cyclo*hex-4-ene-*trans*-1 : 2-diol (I) furnished a crystalline product, $C_6H_{10}O_4$, which gave a bis-*p*-nitrophenylhydrazone and a dioxime, but it reacted only very slowly

---

[1] Part XIV, Ali and Owen, preceding paper.

[2] Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *J.*, 1950, 2228; Elvidge, Linstead, Sims, and Orkin, *ibid.*, p. 2235.

[3] Owen and Peto, *J.*, 1955, 2383.

[4] Linstead, Owen, and Webb, *J.*, 1953, 1225.

[5] Legrand, *Bull. Soc. chim. France*, 1953, 540.

[6] Posternak and Susz, *Helv. Chim. Acta*, 1956, **39**, 2032.

with Schiff's reagent and was devoid of carbonyl absorption in the infrared spectrum. The (±)-dialdehyde (II) therefore exists entirely as the bicyclic double hemiacetal, (±)-*cis*-2 : 6-dioxa*bicyclo*[3 : 3 : 0]octane-3 : 7-diol (III), in which the *cis*-fusion of the two rings follows from the *trans*-disposition of the hydroxyl groups in the original diol. There are three possible stereoisomers of (III), according to the configurations of the hydroxyl groups (*endo-cis*, *exo-cis*, and *trans*), but a choice is not possible on the evidence available. Only one of the potential aldehydic groups in (III) was oxidised by aqueous bromine at room temperature, the product being a crystalline monolactone, (±)-7-hydroxy-*cis*-2 : 6-dioxa*bicyclo*[3 : 3 : 0]octan-3-one (IV); its infrared spectrum showed absorption at 1779 cm.$^{-1}$, due to the presence of the carbonyl group in the γ-lactone ring, but ordinary carbonyl absorption was again absent. The hemiacetal ring in this compound was markedly more stable than those in its precursor (III), for it was quite unreactive towards Schiff's reagent; it did, however, react with *p*-nitrophenylhydrazine to give the derivative of *cis*-tetrahydro-3-hydroxy-5-oxo-2-furylacetaldehyde (V). More vigorous treatment of the monolactone (IV), with aqueous bromine at 70°, gave the γγ-dilactone (VII) of (±)-ββ'-dihydroxyadipic acid, identical with that obtained earlier.

Ozonolysis of *cyclo*hex-4-ene-*cis*-1 : 2-diol gave a non-crystalline aldehydic product which was probably mainly the monohemiacetal (XII) of *meso*-ββ'-dihydroxyadipdialdehyde (XI), though no satisfactory crystalline carbonyl derivatives could be prepared. On oxidation with an excess of aqueous bromine, however, it readily gave the crystalline lactonic acid (VIII).

The infrared spectra of the three lactones (IV), (VII), and (VIII) in chloroform solution showed a single absorption maximum near 1780 cm.$^{-1}$, consistent [7] with the γ-lactone structure. In paraffin mull the lactones (VII) and (VIII) still showed absorption at 1780 ± 10 cm.$^{-1}$, though the bands were complex; the absorption maximum of (IV), however, moved to 1756 and 1742 cm.$^{-1}$ (doublet), presumably owing to intermolecular bonding between the hydroxy- and the carbonyl group. This lactone is a simple analogue of glucurone (XIII), and for comparison the infrared absorption of the latter, which undoubtedly is a γ-lactone, was also measured in paraffin mull; it showed a maximum at 1751 cm.$^{-1}$. Since the quoted [7] range for the carbonyl absorption band in δ-lactones is 1750—1735 cm.$^{-1}$, misleading conclusions could clearly be reached when measurements are made, other than in dilute solution, on γ-lactones containing other functions capable of bonding to the carbonyl group.

Barker and Stephens [8] have reported that compounds containing a furanose or hydrofuranol ring, including those with two fused five-membered rings, show characteristic infrared absorption in the 1000—700 cm.$^{-1}$ range, the maxima being usually located within four distinct regions. The frequencies of the absorption maxima shown in that range by our compounds (III), (IV), (VII), and (VIII), however, cannot all be accommodated within the limits quoted for these four regions.

EXPERIMENTAL

Analyses were by Miss J. Cuckney and staff, and infrared spectra by Mr. R. L. Erskine, B.Sc., A.R.C.S. The absorption maxima refer to the regions 4000—1500 and 1000—700 cm.$^{-1}$ in paraffin mull, and 2000—1500 cm.$^{-1}$ in $CHCl_3$.

Ozonolysis of cyclo*Hex-4-ene-*trans-1 : 2-*diol*.—Ozonised oxygen was passed through a solution of the *trans*-diol (4·2 g.) in dry ethyl acetate (225 c.c.) at −20° until no more was absorbed. The solution was then hydrogenated over 2% palladium-calcium carbonate (0·5 g.), with cooling. After filtration, the solution was evaporated and the residue, m. p. 103—106°, was recrystallised from ethyl acetate to give (±)-*cis*-2 : 6-*dioxa*bicyclo[3 : 3 : 0]*octane*-3 : 7-*diol* (2·5 g., 47%), plates, m. p. 110° (Found: C, 49·2; H, 7·0. $C_6H_{10}O_4$ requires C, 49·3; H, 6·9%). It was very sparingly soluble in ether, light petroleum, and chloroform, but readily soluble

---

[7] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen and Co., London, 1954.

[8] Barker and Stephens, *J.*, 1954, 4550.

in water. With Schiff's reagent, a colour appeared after *ca.* 3 min. Infrared absorption in paraffin mull: $\nu_{max.}$ 3344 (O–H), 964, 907, 859, 825, 810 cm.$^{-1}$; no absorption in the 1600—1800 cm.$^{-1}$ region.

A mixture of the compound (0·07 g.), *p*-nitrophenylhydrazine (0·18 g.), and ethanol (3 c.c.), refluxed for 30 min. and then diluted with water, gave a precipitate which was washed with boiling methanol and then dissolved in boiling dioxan (15 c.c.). Dilution of the solution with light petroleum (b. p. 40—60°) gave (±)-3 : 4-*dihydroxyhexanedial bis*-p-*nitrophenylhydrazone* (0·19 g., 95%) as a yellow powder, m. p. 205° (Found: C, 52·0; H, 5·2; N, 19·6. $C_{18}H_{20}O_6N_6$ requires C, 51·9; H, 4·8; N, 20·2%).

Reaction of the *bicyclo*-compound (0·1 g.) with hydroxylamine hydrochloride (0·15 g.) and sodium acetate (0·25 g.) in water (2 c.c.) for 1 hr. at 40°, followed by 24 hr. at room temperature, gave a precipitate which on recrystallisation from methanol gave the slightly impure *dioxime*, m. p. 170° (decomp.), of (±)-3 : 4-dihydroxyhexanedial (Found: C, 41·9; H, 7·2; N, 15·1. $C_6H_{12}O_4N_2$ requires C, 40·9; H, 6·9; N, 15·9%).

(±)-7-*Hydroxy*-cis-2 : 6-*dioxa*bicyclo[3 : 3 : 0]*octan*-3-*one*. Bromine (2·2 g.) was added to a solution of the above dihydroxy*bicyclo*-compound (1 g.) in water (25 c.c.), and the mixture was shaken for 5 hr. and left overnight at room temperature. The remaining bromine was then removed in a current of nitrogen, and the colourless solution was neutralised with silver carbonate, filtered, then saturated with hydrogen sulphide and again filtered. The filtrate was continuously extracted with ether, to yield a solid (0·5 g.) which after three recrystallisations from ethyl acetate gave (±)-7-*hydroxy*-cis-2 : 6-*dioxa*bicyclo[3 : 3 : 0]*octan*-3-*one* (0·23 g., 22%), prisms, m. p. 100° (Found: C, 50·1; H, 5·65. $C_6H_8O_4$ requires C, 50·0; H, 5·6%). It gave no colour with Schiff's reagent even after several hours, and gave a neutral aqueous solution. Infrared absorption, in paraffin mull: $\nu_{max,}$ 3356 (O–H), 1756 and 1742 (C=O in lactone), 988, 923, 897, 864, 836, 824, 806, 778 cm.$^{-1}$; in $CHCl_3$: $\nu_{max.}$ 1779 cm.$^{-1}$.

Treatment of a portion (0·13 g.) with *p*-nitrophenylhydrazine (0·13 g.) in boiling ethanol (10 c.c.) for 30 min., followed by dilution with water and recrystallisation of the precipitate from methanol, gave *tetrahydro*-3-*hydroxy*-5-*oxo*-2-*furylacetaldehyde* p-*nitrophenylhydrazone* (0·24 g., 95%), yellow needles, m. p. 148° (Found: C, 51·45; H, 4·85; N, 15·0. $C_{12}H_{13}O_5N_3$ requires C, 51·6; H, 4·7; N, 15·05%).

(±)-2 : 6-*Dioxa*bicyclo[3 : 3 : 0]*octane*-3 : 7-*dione*.—A mixture of the above monolactone (0·2 g.), water (2 c.c.), and bromine (0·25 g.) was heated at 70° in a sealed tube for 7 hr. with occasional shaking. Next day, a trace of unchanged bromine was removed by a stream of nitrogen, and the solid (0·05 g.) which had separated from the solution in hard prisms, m. p. 132°, was collected. The m. p. was unchanged by recrystallisation of the compound from ethyl acetate, and the mixed m. p. with an authentic sample [4] of (±)-2 : 6-dioxa*bicyclo*[3 : 3 : 0]octane-3 : 7-dione, m. p. 130—131°, was undepressed. A further quantity (0·13 g.) was isolated by concentration of the aqueous mother-liquor (total yield, 66%). Infrared absorption, in paraffin mull: $\nu_{max.}$ 1789, 1774, and 1759 (C=O in γ-lactone), 929, 892, 841, 818 cm.$^{-1}$; in $CHCl_3$: $\nu_{max.}$ 1783 cm.$^{-1}$.

Ozonolysis of cyclo*Hex*-4-*ene*-cis-1 : 2-*diol* (with M. H. BENN).—A solution of the *cis*-diol (1·7 g.) in pure dry ethyl acetate (130 c.c.) was ozonised, and the solution subsequently hydrogenated, in the same way as described for the *trans*-isomer. Evaporation of the filtered solution gave a viscous acidic syrup (1·6 g.) which gave an immediate colour with Schiff's reagent and an amorphous precipitate with 2 : 4-dinitrophenylhydrazine sulphate; no crystalline carbonyl derivatives could be obtained.

trans-γ-*Carboxymethyl*-β-*hydroxybutanolide*.—A mixture of the above syrup (0·4 g.), bromine (1·2 g.), and water (10 c.c.) was kept at 45—50° for 3 hr. with occasional shaking. The excess of bromine was then removed in a stream of nitrogen, and sodium hydrogen carbonate was gradually added to the colourless solution to neutralise only the hydrogen bromide (*i.e.*, until only a dull blue colour was produced on Congo paper). The solution was evaporated to dryness under reduced pressure, and the residue was kept at 70°/15 mm. for 30 min. and then extracted with boiling ethyl acetate. Evaporation of the filtered extracts gave a pale yellow oil which partly crystallised. The solid (0·25 g.) was drained on porous tile and recrystallised from ethyl acetate, to give *trans*-γ-carboxymethyl-β-hydroxybutanolide, m. p. 98°. Infrared absorption, in paraffin mull: $\nu_{max.}$ 3472 (O–H), 2700—2600 (O–H in CO_2H, dimeric form), 1786 and 1770 (C=O in γ-lactone), 1709 (C=O in CO_2H), 980, 930, 908, 877, 832 cm.$^{-1}$; in $CHCl_3$: $\nu_{max.}$ 1777, 1715 cm.$^{-1}$.

The quoted[4] m. p. is 91°, but re-examination of the original specimen showed it to have m. p. 97°; a mixed m. p. with the acid now obtained was undepressed.

DEPARTMENT OF ORGANIC CHEMISTRY, IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
SOUTH KENSINGTON, LONDON, S.W.7.

[*Received, November 7th,* 1957.]