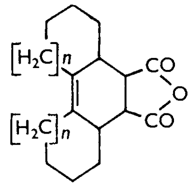
296. *Alicyclic Studies. Part XVIII.* Homologous Cyclic Lactone-acids.*

By Jacob Strumza and David Ginsburg.

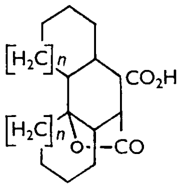
The formation of lactone-acids of type (II) and various reactions of these compounds are described.

When the Diels–Alder adduct (Ic) of bicyclodec-1-enyl and maleic anhydride was saponified under acidic conditions a lactone-acid (IIc) was obtained. This type of lactonisation has been reported for other systems.[1]

Since the six- and eight-membered ring homologues were more readily available we studied their analogous behaviour. Bicyclohex-1-enyl[2] and bicyclo-oct-1-enyl[3] gave with maleic anhydride the corresponding anhydrides (Ia and b). Both anhydrides afforded lactone-acids (IIa and b) on saponification in acid medium. Alkaline saponification of the anhydrides (Ia and b) permitted isolation of the unlactonised dicarboxylic acids (IIIa and b).



(I) a: $n = 1$
b: $n = 3$
c: $n = 5$



(II) a: $n = 1$
b: $n = 3$
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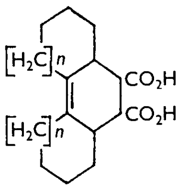
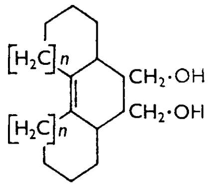


(III) a: $n = 1$
b: $n = 3$



(IV) a: $n = 1$
b: $n = 3$
c: $n = 5$

Reduction of the anhydride (Ic) with lithium aluminium hydride gave a diol (IVc). Similar diols (IVa and b) were obtained by reducing the diacid (IIIa) or the anhydride (Ib) with lithium aluminium hydride. The same reagent converted the lactone-acids (IIa and b) into the triols (VIa and b).

Dehydration of the triol (VIa) gave a diol (V), isomeric with (IVa), in which the double bond is presumed to be in the 4a,10a-position, by analogy with the behaviour of condensed six-membered alicyclic systems.

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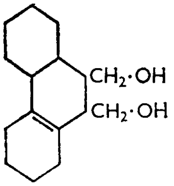
* Part XVII, preceding paper.

[1] Mousseron and Mousseron-Canet, *Compt. rend.*, 1957, **245**, 2156; Mousseron, Mousseron-Canet, and Graner, Colloque Internat. Stereochimie, Montpellier, Septembre, 1959; Klein, *J. Org. Chem.*, 1958, **23**, 1209; Barton and Holness, *J.*, 1952, 78.

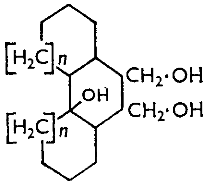
[2] Gruber and Adams, *J. Amer. Chem. Soc.*, 1935, **57**, 2555.

[3] Greidinger and Ginsburg, *J. Org. Chem.*, 1957, **22**, 1406.

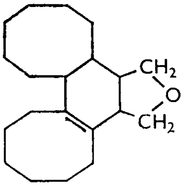
It is believed that an analogous shift of the double bond may occur during acidic dehydration of the triol (VIb). This would lead to a cyclic ether (VII) identical with the



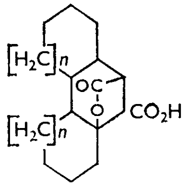
(V)



(VI) a: $n = 1$
b: $n = 3$



(VII)



(VIII)

product of acidic dehydration of the diol (IVb) in which the double bond also rearranges from the position exocyclic with respect to the two eight-membered rings to a position inside one of them (also inside the six-membered ring).[4]

It must be noted that although the structures (II) have been formulated as shown above, an alternative structure (VIII) has not been ruled out unequivocally. The products obtained from the lactone (II) by various interconversions could also be explained on the basis of (VIII), and a study of Dreiding models does not show an appreciable difference in steric interactions in the two formulations.

EXPERIMENTAL

10,18a-*Lactone* (IIc) *of Perhydro*-18a-*hydroxydicyclodeca*[a,c]*benzene*-9,10-*dicarboxylic Acid*.—A solution of the anhydride [5] (Ic) (1 g.) in 95% acetic acid (30 ml.) and concentrated hydrochloric acid (10 ml.) was heated under reflux for 5 hr. and left overnight. The solution was then poured into ice-water and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogen carbonate and water. Drying ($MgSO_4$), removal of the ether, and trituration with ethanol gave the *lactone-acid* (240 mg.) as colourless prisms, m. p. 249° (from methanol), $\nu_{max.}$ (in KBr) 1770 (γ-lactone), 1710 cm.$^{-1}$ (CO_2H) (Found: C, 73·8; H, 9·7; O, 16·5%; equiv., 391. $C_{24}H_{38}O_4$ requires C, 73·8; H, 9·8; O, 16·4%; equiv., 391).

$\Delta^{18a(18b)}$*Eicosahydro*-9,10-*di*(*hydroxymethyl*)*dicyclodeca*[a,c]*benzene* (IVc).—Reduction of the anhydride (Ic) (1·5 g.) with lithium aluminium hydride (3 g.) in dry ether (500 ml.) gave, after the usual working-up, the *diol* (IVc) (1·4 g., 96%) as colourless prisms, m. p. 155° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3650 cm.$^{-1}$ (OH) (Found: C, 79·6; H, 11·6; O, 9·0. $C_{24}H_{42}O_2$ requires C, 79·5; H, 11·7; O, 8·8%).

$\Delta^{4a(4b)}$*Dodecahydrophenanthrene*-9,10-*dicarboxylic Acid* (IIIa).—A solution of the anhydride [2] (Ia) (1 g.) in ethanol (84 ml.) and 30% aqueous potassium hydroxide (16 ml.) was heated under reflux for 1 hr. Most of the ethanol was removed at the water-pump, and saturated salt solution (50 ml.) added. After acidification with dilute hydrochloric acid and ether-extraction, the extract was dried ($MgSO_4$) and the solvent was removed. Trituration with hexane gave colourless prisms of the *diacid* (700 mg., 66%), m. p. 206° (decomp.) (from acetic acid), $\nu_{max.}$ (in KBr) 1710 cm.$^{-1}$ (CO_2H) (Found: C, 68·6; H, 7·7; O, 23·8. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0; O, 23·0%).

The *dimethyl ester*, obtained by treatment with diazomethane in ether, formed colourless prisms, m. p. 109° (from 2,2,4-trimethylpentane), $\nu_{max.}$ (in $CHCl_3$) 1740 cm.$^{-1}$ (ester C=O) (Found: C, 70·6; H, 8·6; O, 20·85. $C_{18}H_{26}O_4$ requires C, 70·6; H, 8·55; O, 20·9%).

10,4a-*Lactone of* 4a-*Hydroxyperhydrophenanthrene*-9,10-*dicarboxylic Acid* (IIa).—A solution of the anhydride (Ia) (5 g.) in 95% acetic acid (100 ml.) and concentrated hydrochloric acid (33 ml.) was heated under reflux for 5 hr. After the working-up described for (Ic), the *lactone-acid* was obtained as slender colourless needles (3·5 g., 69%), m. p. 247—248° (from xylene), $\nu_{max.}$ (in KBr) 1780 (γ-lactone), 1690 cm.$^{-1}$ (CO_2H) (Found: C, 69·0; H, 8·3; O, 22·7%; equiv., 278·5. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0; O, 23·0%; equiv., 278·3).

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[4] Cf. Cope, Ambros, Ciganek, Howell, and Jacura, *J. Amer. Chem. Soc.*, 1959, **81**, 3153.

[5] Strumza and Ginsburg, preceding paper.

The *methyl ester* obtained by treatment with ethereal diazomethane formed plates, m. p. 140° (from aqueous methanol) (Found: C, 69·8; H, 8·4; O, 21·75. $C_{17}H_{24}O_4$ requires C, 69·8; H, 8·3; O, 21·8%), $\nu_{\text{max.}}$ (in $CHCl_3$) 1770 (γ-lactone), 1730 cm.$^{-1}$ (ester C=O).

The identical (mixed m. p.) lactone-acid (0·9 g., 45%) was obtained by heating the dicarboxylic acid (IIIa), m. p. 206° (2 g.), in 98% formic acid (40 ml.) at 80° for 2 hr. Pouring into ice-water and ether-extraction, etc., gave needles, m. p. 247° (from xylene). It is possible that the compound, m. p. 242°, described [2] as the diacid is actually the lactone-acid, m. p. 247° in impure form.

$\Delta^{4a(4b)}$*Dodecahydro*-9,10-*di*(*hydroxymethyl*)*phenanthrene* (IVa).—Reduction of the diacid (IIIa), m. p. 206° (800 mg.), in dry ether (250 ml.) with lithium aluminium hydride (2 g.) in dry ether (200 ml.) gave the *dialcohol* (400 mg., 64%) as colourless prisms, m. p. 136—137° (from methylcyclohexane), $\nu_{\text{max.}}$ (in KBr) 3250 cm.$^{-1}$ (OH) (Found: C, 76·8; H, 10·45; O, 12·7. $C_{16}H_{26}O_2$ requires C, 76·75; H, 10·5; O, 12·8%). The same dialcohol (1·3 g.) was obtained by reducing the anhydride (Ia) (2 g.) in dry ether (250 ml.) with lithium aluminium hydride (4 g.) in dry ether (250 ml.).

Perhydro-9,10-*di*(*hydroxymethyl*)*phenanthren*-4a-*ol* (VIa).—Reduction of the lactone-acid (IIa) (2 g.) in dry ether (300 ml.) with lithium aluminium hydride (4 g.) in dry ether (200 ml.) gave the *triol* as colourless rhombs (1 g., 52%), m. p. 200° (from ethanol), $\nu_{\text{max.}}$ (in KBr) 3180 cm.$^{-1}$ (broad; OH) (Found: C, 71·6; H, 10·6; O, 18·1. $C_{16}H_{28}O_3$ requires C, 71·6; H, 10·5; O, 17·9%).

The *diacetate* formed colourless platelets, m. p. 112° (from methanol), $\nu_{\text{max.}}$ (in $CHCl_3$) 3600 (OH), 1725 cm.$^{-1}$ (ester C=O) (Found: C, 68·3; H, 9·15; O, 22·5. $C_{20}H_{32}O_5$ requires C, 68·15; H, 9·15; O, 22·7%).

When the triol (0·5 g.) was heated under reflux with dry benzene (100 ml.) in the presence of naphthalene-β-sulphonic acid (0·25 g.) for 5 hr., dehydration occurred with migration of the double bond. Concentration of the neutralised benzene solution gave plates (0·3 g., 64%) of a *diol* (V) believed to be the $\Delta^{4a(10a)}$-isomer. It had m. p. 153° (from methylcyclohexane), $\nu_{\text{max.}}$ (in $CHCl_3$) 3640 cm.$^{-1}$ (OH) (Found: C, 76·3; H, 10·4; O, 13·5. $C_{16}H_{26}O_2$ requires C, 76·75; H, 10·5; O, 12·8%).

The diol (IV) rearranged to this diol (V) when heated with naphthalene-β-sulphonic acid in benzene.

8,14a-*Lactone* (IIb) *of* $\Delta^{14a(14b)}$-*Octadecahydro*-14a-*hydroxydicyclo-octa*[a,c]*benzene*-7,8-*dicarboxylic Acid*.—The anhydride (Ib) (4 g.) was dissolved in 95% acetic acid (120 ml.) containing concentrated hydrochloric acid (5 ml.) and refluxing was maintained for 3 hr. The solvent was removed at the water-pump and the residue was triturated with benzene (100 ml.). The cooled solution deposited needles of the *lactone-acid* (950 mg.), m. p. 274° (decomp.) (from ethanol), $\nu_{\text{max.}}$ (in KBr) 1770 (γ-lactone), 1708 cm.$^{-1}$ (CO_2H) (Found: C, 71·5; O, 19·1; H, 9·3%); equiv., 335·0. $C_{20}H_{34}O_4$ requires C, 71·8; H, 9·0; O, 19·1%; equiv., 334·4). Concentration of the benzene solution gave starting material (3 g.).

The *methyl ester*, obtained (82%) by Fischer esterification, formed colourless cubes, m. p. 137° (from 2,2,4-trimethylpentane), $\nu_{\text{max.}}$ (in $CHCl_3$) 1770 (γ-lactone), 1730 cm.$^{-1}$ (ester) (Found: C, 72·2; H, 9·3; O, 18·3. $C_{21}H_{32}O_4$ requires C, 72·4; H, 9·3; O, 18·4%).

$\Delta^{14a(14b)}$-*Hexadecahydrodicyclo-octa*[a,c]*benzene*-7,8-*dicarboxylic Acid* (IIIb.)—A solution of the anhydride (Ib) (2 g.) in ethanol (10 ml.) and 30% aqueous potassium hydroxide (30 ml.) was heated under reflux for 1 hr. Most of the ethanol was removed at the water-pump, and the basic solution was diluted with water (30 ml.). The potassium salt of the diacid was separated by filtration, purified by crystallisation from ethanol (3·9 g., 75%), and dried by washing with ether. It was then dissolved in ice-water (50 ml.) and shaken with ether (100 ml.) and dilute hydrochloric acid (10 ml.). The aqueous layer was extracted with ether, the combined ether extracts were washed with water, dried ($MgSO_4$), and the solvent was removed at 40°. Trituration of the oily residue with pentane gave the diacid as a colourless amorphous solid (2 g., 48%), m. p. 178—180° with formation of the anhydride, $\nu_{\text{max.}}$ (in KBr) 1710 cm.$^{-1}$ (CO_2H).

The *dimethyl ester*, prepared with diazomethane in cold ether, formed prisms, m. p. 97° (from pentane), $\nu_{\text{max.}}$ (in $CHCl_3$) 1740 cm.$^{-1}$ (ester C=O) (Found: C, 72·65; H, 9·4; O, 17·5. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·45; O, 17·7%).

Perhydro-14a-*hydroxy*-7,8-*di*(*hydroxymethyl*)*dicyclo-octa*[a,c]*benzene* (VIb).—Reduction of the lactone-ester, m. p. 137° (1·4 g.), in dry ether (100 ml.) with lithium aluminium hydride (2 g.)

in dry ether (100 ml.) gave the *triol* (VIb) (1·2 g., 91%) as colourless rhombs, m. p. 117° (from benzene), $\nu_{max.}$ (in $CHCl_3$) 3650 cm.$^{-1}$ (OH) (Found: C, 74·1; H, 11·1; O, 14·9. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2; O, 14·8%).

$\Delta^{14a(14b)}$-*Hexadecahydro-7,8-di(hydroxymethyl)dicyclo-octa*[a,c]*benzene* (IVb).—Reduction of the anhydride (Ib) (2·7 g.) in dry ether (200 ml.) with lithium aluminium hydride (5·4 g.) in dry ether (250 ml.) gave, in the usual way, colourless prisms of the *diol* (IVb) (1·6 g., 61%), m. p. 128—130° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3330 cm.$^{-1}$ (OH) (Found: C, 78·6; H, 10·85; O, 10·7. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·2; O, 10·4%).

$\Delta^{3b(9a)}$-*Hexadecahydrodicyclo-octa*[e,g]*isobenzofuran* (VII).—The diol (IVb) (0·5 g.) was heated under reflux in benzene (50 ml.) containing naphthalene-β-sulphonic acid (0·3 g.) for 2 hr. The usual working-up gave prisms (160 mg.) of the cyclic *ether* (VII), m. p. 190° (from methanol) (Found: C, 83·1; H, 11·0; O, 5·6. $C_{20}H_{32}O$ requires C, 83·3; H, 11·2; O, 5·55%).

The identical ether (70 mg.) was obtained by dehydration of the triol (VIb) (200 mg.) with naphthalene-β-sulphonic acid (200 mg.) in boiling benzene during 2 hr.

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