Tetrahedron Letters No.47, pp. 4143-4146, 1969. Pergamon Press. Printed in Great Britain.

NOVEL PRODUCTS FROM THE OZONOLYSIS OF 9β,19-CYCLOLANOSTANES

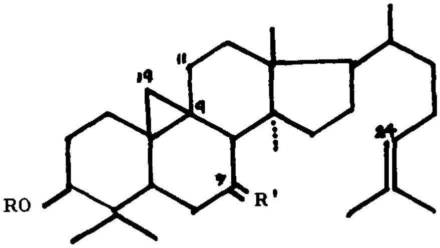
W. Lawrie, J. McLean and O. O. Olubajo

Department of Pure and Applied Chemistry
The University of Strathclyde, Glasgow, C.1.

(Received in UK 22 August 1969; accepted for publication 11 September 1969)

In order to show the presence of cycloartenol (Ia) and 24-methylenecycloartanol (IIa) in a mixture of these alcohols occurring in balata resin it was decided to ozonise the derived mixture of acetates and obtain the easily separable mixture of the trisnor acid III and the C_{24}-ketone IIb[1]. Ozonolysis was conducted in chloroform solution at -60°, the mixed ozonides reductively cleaved with zinc-acetic acid, and the resulting crude mixture of aldehyde and ketone oxidised at room temperature with chromic acid. The expected products, namely the trisnor acid (III) and the C_{24}-ketone (IIb) were obtained, but in addition to these, 7,24-dioxocycloartanyl acetate (IIc) was isolated, m.p. 224-225°, $[\alpha]_D$ + 31.2°, which on alkaline hydrolysis afforded 7,24-dioxocycloartanol (IId) m.p. 147-148°, $[\alpha]_D$ + 43.6°. The constitution of the dioxo-compound (IIc) was established by its conversion to the known[2] 7-oxolanost-8-enyl acetate (IV) as follows. The diketo-acetate (IIc) with ethanedithiol and BF_3-etherate gave the thioketal (IIe), m.p. 238-242°, $[\alpha]_D$ + 35°, which, when reduced with Raney nickel in refluxing ethanol, afforded 7-oxocycloartanyl acetate (IIf), m.p. 210°, $[\alpha]_D$ + 34.5°. Cleavage of the cyclopropane ring in the latter compound (IIf) was effected by refluxing in acetic acid - conc.hydrochloric acid (20:1) for 3 hours when 7-oxolanost-8-enyl acetate (IV) was obtained, and identified by comparison with an authentic specimen.

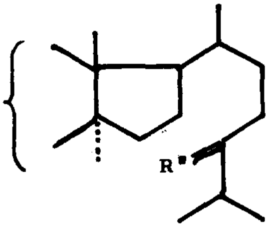
That the oxidation at C_7 had been accomplished by ozone and not by the chromic acid used in the oxidation of the unisolated trisnoraldehyde to the trisnoracid (III) was shown by subjecting 24-oxocycloartanyl acetate to chromic acid oxidation in acetic acid when the starting material was



I a, $R = H$; $R' = H_2$

b, $R = Ac$; $R' = H_2$

c, $R = Ac$; $R' = O$



II a, $R = H$; $R' = H_2$; $R'' = CH_2$

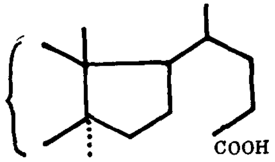
b, $R = Ac$; $R' = H_2$; $R'' = O$

c, $R = Ac$; $R' = O$; $R'' = O$

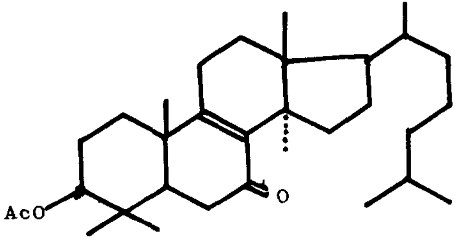
d, $R = H$; $R' = O$; $R'' = O$

e, $R = Ac$; $R' = O$; $R'' = \Big\langle\begin{matrix}S\\S\end{matrix}\Big]$

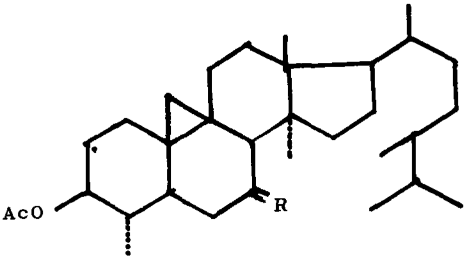
f, $R = Ac$; $R' = O$; $R'' = H_2$



III $R = Ac$; $R' = H_2$



IV



V a, $R = H_2$

b, $R = O$

recovered. On the other hand, ozonolysis of 24-oxocycloartanyl acetate (IIb) in chloroform at -60° until the solution became blue, followed by washing with ferrous sulphate, drying, and removal of solvent afforded 7,24-dioxocycloartanyl acetate (IIc) in good yield.

This novel oxidation of 24-oxocycloartanyl acetate at C_7 by means of ozone was extended to cycloartanyl acetate[3] (24,25-dihydro Ib) and resulted in a mixture, separable by chromatography on alumina, of starting material and 7-oxocycloartanyl acetate (IIf) (60% yield) identical with the product described above. Hydrolysis of the oxo-acetate (IIf) with ethanolic KOH afforded 7-oxocycloartanol, m.p. 124°, $[\alpha]_D$ + 41.3°.

The ozonolysis of cycloeucalanyl acetate (Va)[4] in chloroform at -60°

gives a compound, $C_{32}H_{52}O_3$, (from mass measurement) which we tentatively regard as 7-oxocycloeucalanyl acetate (Vb), m.p. 196°, $[\alpha]_D$ + 40° $\nu_{max.}$ 1690. (CO group in six-membered ring) 1739 and 1237 cm.$^{-1}$ (acetate). N.m.r. resonances show a pair of doublets centred at τ 9.48 and 9.62 (CH_2 protons on cyclopropane ring).

The oxidation of the above 9β,19-cyclolanostane derivatives at C_7 would appear to result from the presence of the cyclopropane ring as lanostanyl acetate is unaffected under the same conditions of ozonolysis. Presumably the strain caused in the molecule by the presence of the three membered ring is relieved by the introduction of a carbonyl group at C_7 whereby C_7 becomes sp^2 hybridised. Whereas cycloartanyl acetate is stable towards chromic acid-acetic acid at room temperature,[5] Corsano et al. have recently shown[6] that oxidation with Jones reagent in benzene leads to the 11-oxo derivative in poor yield. We find that oxidation with Jones reagent in methylene chloride affords the 7-oxo- and 11-oxo derivatives - each in *ca* 5% yield, while attempts to oxidise cycloartanyl acetate with oxygen either in the presence of potassium t-butoxide, or photolytically, were unsuccessful.

A typical experimental procedure for the isolation of a 7-oxo-derivative is given below:

Oxidation of 24-oxocycloartanyl acetate to 7,24-dioxocycloartanyl acetate. - A solution of 24-oxocycloartanyl acetate (0.2 g.) in chloroform (100 ml.) was treated with ozonised oxygen at -60° until the solution turned blue (1 hr.). After washing several times with aqueous ferrous sulphate and water, the solution was dried (Na_2SO_4) and the solvent removed *in vacuo*. The residual gum (0.156 g.) was crystallised from chloroform-methanol to give 7,24-dioxocycloartanyl acetate, needles, m.p. 224-225°, $[\alpha]_D$ + 31.2°; $\nu_{max.}$ (CS_2) 3040 (CH_2 on cyclopropane ring), 1733 and 1240 cm.$^{-1}$ (acetate) 1710 (side chain carbonyl), 1690 (six membered ring carbonyl) and 1020 cm.$^{-1}$ (cyclopropane ring). N.m.r. absorptions at τ 5.4 (3αH), 7.25 (CH_2 adjacent to carbonyl), 7.95 (acetate methyl), 9.5 and 9.75 (CH_2 on cyclopropane ring).

All new compounds described gave satisfactory elemental analysis and spectroscopic data.

The authors wish to thank the University of Ife for study leave to O. O. Olubajo.

References

[1] G. Ohta, Chem. Pharm. Bull. Japan, 8, 5 (1960).

[2] D. H. S. Horne and D. Ilse, J. Chem. Soc., 2280 (1957).

[3] H. R. Bentley, J. A. Henry, D. S. Irvine and F. S. Spring, ibid. 3673 (1953)

[4] J. S. G. Cox, F. E. King and T. G. King, ibid. 1384 (1956); 514 (1959).

[5] D. H. R. Barton, ibid, 1444 (1951).

[6] S. Corsano and G. Nicita, Ricerca Sci. 351 (1967).