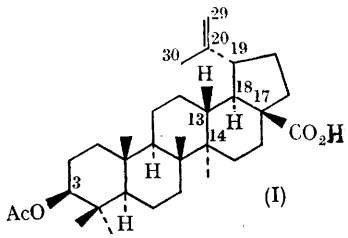
The Oxidation of Acetylbetulic Acid by Mercuric Acetate

By G. V. BADDELEY, R. A. EADE, J. ELLIS, P. HARPER, and J. J. H. SIMES*
(*School of Chemistry, University of New South Wales, Kensington, N.S.W., Australia*)

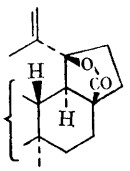
THE oxidation of acetylbetulic acid (I) by mercuric acetate gives the lactone (II).

This method of oxidation[1] has been exploited extensively for the structural elucidation of triterpenes biogenetically related to lup-20(29)-ene and possessing a free or lactonised carboxy-group at C-14 (*e.g.* melaleucic acid,[2] ceanothenic acid,[3] and emmolactone[4]). The γ-lactone obtained previously by Allison *et al.*,[1] from the mercuric acetate oxidation of acetylbetulic acid, was assigned structure (III). Since this assignment was based, in part, on the non-identity of the lactone with the acetate of thurberogenin, the recent revision of the structures of stellatogenin and thurberogenin[5] invalidates this feature of the argument. The assumed correctness of the formulation (III) was the foundation for experiments devised by Khastgri and Bose[6] to elucidate the stereochemistry of the isopropenyl group at C-19 in the products of oxidation by mercuric acetate in the lup-20(29)-ene series.

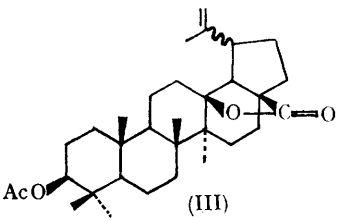
Acetylbetulic acid[7] (I) was oxidised by mercuric acetate under conditions identical with those described previously. The only detectable product, obtained in 55—70% yield in a series of experiments, was the γ-lactone (II), m.p. >350°,



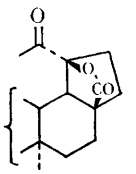
(I)



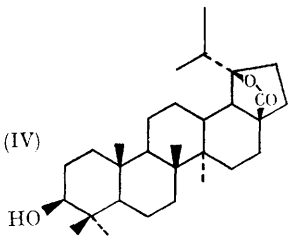
(II)



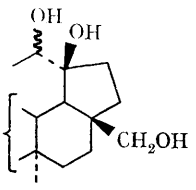
(III)



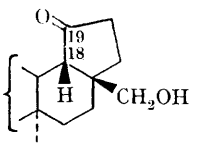
(V)



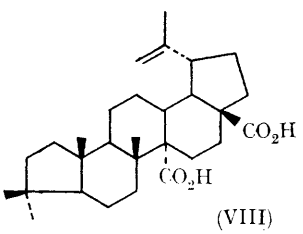
(IV)



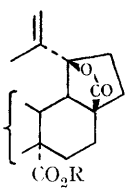
(VI)



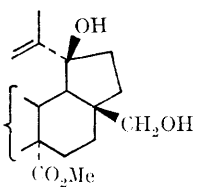
(VII)



(VIII)



(IX) R=H
(X) R=Me



(XI)

$[\alpha]_D$ + 55°. Successive hydrogenation and hydrolysis afforded the hydroxy-lactone (IV), m.p. 322—323° (*in vacuo*), $[\alpha]_D$ + 28°.

Ozonolysis of the γ-lactone (II) gave the norketo-lactone (V), m.p. >350°, $[\alpha]_D$ + 8°, which was recovered unchanged after treatment with alkali, (*i.e.* with reacetylation of the 3β-hydroxy-group where necessary) including the method described by Khastgir and Bose.[6] The norketo-lactone (V) was reduced by lithium aluminium hydride, to the tetra-ol (VI), m.p. 294—296°, $[\alpha]_D$ + 27°, which was cleaved by lead tetra-acetate in acetic acid at 90°. The partially acetylated product was hydrolysed by alkali to give the trisnorketone (VII), m.p. 254—256°, $[\alpha]_D$ + 40·5°. This ketone showed i.r. absorption at 1735 and 1414 cm.$^{-1}$ (Nujol), expected for a cyclopentanone possessing an α-methylene group. The derived di-acetate showed absorption at 1410 and carbonyl absorption at 1738 cm.$^{-1}$ only (CCl_4). The stereochemistry at C-18 in the trisnorketone (VII) follows from the strong positive Cotton effect in the o.r.d curve ($[\phi]_{328}$ + 4928°, $[\phi]_{284}$ −5178°; *a* + 101)[8,9] and from the high positive maximum of the c.d. curve ($[\theta]_{313}$ + 8250°).[9] These results are consistent with a *cis* D–E ring fusion.

Dreiding models reveal that only 18α-H stereochemistry is possible in the lactone (II). Since the tetra-ol (VI) must also have this stereochemistry, the formation of the trisnorketone (VII) must involve inversion at C-18 after formation of the C-19 ketone. Similar inversion has been noted in other series.[10] Clearly, 18β-H stereochemistry is thermodynamically more stable for C-19 ketones in the 20,29,30-trisnorlupane series. The foregoing results are compatible only with structure (II) for the lactone from acetylbetulic acid.

This lactone presumably arises through allylic oxidation at C-19 together with participation, across the β-face of ring E, by the carboxy-group at C-17. Competitive participation by a carboxy-group at C-14 would not, therefore, be expected and indeed the oxidation of dihydroceanothenic acid (VIII) by mercuric acetate gives exclusively the lactone (IX) involving the carboxy-group at C-17. Thus, the derived lactone-ester (X) was reduced by lithium aluminium hydride to give the diol (XI) which retained the methoxycarbonyl group at C-14 (i.r. and n.m.r.). This inertness towards reduction is known to distinguish between methoxycarbonyl groups at C-14 and C-17.[4]

The C-17,19-bridge can also explain the

resistance of the lactone (II) towards acid-catalysed expansion of ring E (*cf.* ref. 6).

In the absence of a free carboxy-group at C-17, the product of oxidation by mercuric acetate is the most stable C-13(18)-olefin.[6]

(*Received, June 10th,* 1968; *Com.* 744.)

[1] J. M. Allison, W. Lawrie, J. McLean, and G. R. Taylor, *J. Chem. Soc.*, 1961, **3353**.
[2] C. S. Chopra and D. E. White, *Tetrahedron*, 1966, **22**, 897.
[3] P. de Mayo and A. N. Starratt, *Canad. J. Chem.*, 1962, **40**, 1632.
[4] R. A. Eade, J. Ellis, and J. J. H. Simes, *Austral. J. Chem.*, 1967, **20**, 2737.
[5] M. Marx, J. Leclercq, B. Tursch, and C. Djerassi, *J. Org. Chem.*, 1967, **32**, 3150.
[6] H. N. Khastgir and S. Bose, *Tetrahedron Letters*, 1968, 39.
[7] J. L. Courtney, J. J. H. Simes, and W. Stern, *Austral. J. Chem.*, 1965, **18**, 591.
[8] A. R. Van Horn and C. Djerassi, *J. Amer. Chem. Soc.*, 1967, **89**, 651.
[9] P. Crabbe, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, San Francisco, 1965.
[10] G. V. Baddeley, T. G. Halsall, and E. R. H. Jones, *J. Chem. Soc.*, 1960, 1715.