Tetrahedron Letters No.36, pp. 3897-3899, 1968. Pergamon Press. Printed in Great Britain.

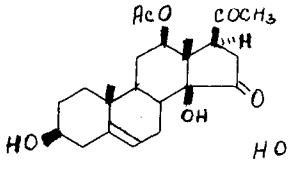
# THE STRUCTURE OF DIGACETIGENIN

C. W. Shoppee, N. W. Hughes, and Ruth E. Lack

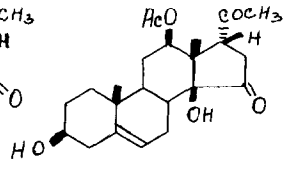
Department of Organic Chemistry, The University of Sydney, Australia

(Received in UK 5 June 1968; accepted for publication 11 June 1968)

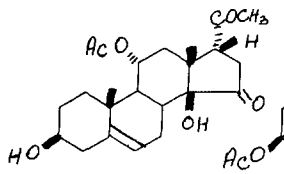
The assertion of Chandler, Coombe, and Watson (1) that the structure (I) for digacetigenin (2, 3, 4) is incorrect and should be replaced by one or other of the 17-iso-structures (II, III) requires a formal reply in order to avoid confusion in the literature. The structure (I) is based on n.m.r. spectroscopy and a chemical correlation with purprogenin (4), and a detailed mass spectrometric study of related 15-carbonyl compounds (3).



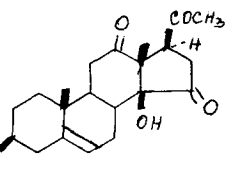

(I)




(II)




(III)




(IV)

Chandler, Coombe, and Watson (1) based their structure (II or III) on a single mass spectrum, and comparison of the fragmentation pattern observed with those reported (1, 5) for various steroids devoid of a 15-carbonyl group. They assumed that the large M-18 peak observed in the mass spectrum of digacetigenin was due to elimination of the 14β-hydroxyl group in a 17α-acetyl compound (II or III), and that this would be inhibited by hydrogen bonding to the 20-carbonyl group if digacetigenin had the 17β-acetyl configuration (I). However, Tschesche et al. (3) found that 5α, 6-dihydrodigacetigenin and other 5α, 6-dihydro steroids show only a low intensity M-18 peak, whilst in digacetigenin and other $\Delta^5$-compounds, preferential elimination of the 3-substituent was observed. Large M-18 peaks have previously

been observed (6) in $\Delta^5$-steroid-3β-ols, but not in their 5α,6-dihydroderivatives. Elimination of the 17-acetyl side chain (m/e 43) is large in most 17-acetyl steroids (1,3,5) and appears to bear little relation to the configuration of the side chain. Tschesche et al. (3) have established by mass spectrometric analysis, that the mass spectrum of dihydrodigacetigenin is consistent with a 12β-acetoxy-14β-hydroxypregnan-20-one structure (I), after comparison with suitable model compounds containing a 15-carbonyl group. The configuration of the 17β-acetyl group in (I) has been confirmed by circular dichroism (3) and by n.m.r. spectroscopy (2,3,4) since the 13β-Me signal appears at τ 8.9 (Cal. I, 8.83) (Cal. II, 8.54, III, 8.56) (7). Digacetigenin (I) is epimerised by hydroxyl ions to give (after reacetylation) the 3-acetate of 17α-digacetigenin (II) with the required shift downfield of the 13β-methyl group signal (2,3,4), and the characteristic large decrease in $[M]_D$ (4, 8, 9, 10), e.g. (I ⟶ II: $\Delta[M]_D$ -539), (12-deacetyl-I ⟶ 12-deacetyl II: $\Delta[M]_D$ -401); in conformity with the established greater thermodynamic stability of 14β-hydroxy-17α-pregnan-20-ones (as II) (11, 12, 13 cf. 14), the equilibrium (I ⟷ II) involves ~25% (I) and 75% (II) (3).

The equatorial acetoxyl group is excluded from the 11α-position since the n.m.r. signal for the proton attached to the same carbon appears as a quartet at τ 5.6, $J_{12\alpha, 11\alpha}$ 5 c./sec. $J_{12\alpha, 11\beta}$ 11 c./sec. (3) and since the triketone (IV) obtained by Jones oxidation at 0° of deacetyldigacetigenin 3-acetate is not identical with "γ"-digiprogenin acetate (2,4), and has identical mass spectrum and infrared spectrum with the triketone (IV) obtained from purprogenin under mild conditions of brief acetylation and Jones oxidation at 0° under nitrogen (4).

Thus digacetigenin has the structure (I) (2, 3, 4) and not either of the structures (II) and (III) (1).

## REFERENCES


1 R. I. Chandler, R. G. Coombe and T. R. Watson, Tetrahedron Letters, 1729 (1968).

2 C. W. Shoppee, N. W. Hughes, R. E. Lack and B. C. Newman, Tetrahedron Letters, 3171 (1967).

3 R. Tschesche, H. G. Bercheid, H. W. Fehlhaber and G. Snatzke, Chem. Ber., 100, 3289 (1967).

4 C. W. Shoppee, N. W. Hughes, and R. E. Lack, J. Chem. Soc., (C), 786 (1968).

5 R. Tschesche and H. W. Fehlhaber, Tetrahedron, 21, 1797 (1965).

6 S. S. Friedland, C. H. Lane, R. T. Longman, K. E. Train and M. J. O'Neal, Anal. Chem., 31, 169 (1959).

7 N. S. Bhacca and D. H. Williams, "Applications of N. M. R. Spectroscopy in Organic Chemistry", Holden Day Inc., 22 (1964); A. I. Cohen and S. Rock, Steroids, 3, 245 (1964).

8 H. Mitsuhashi and T. Nomura, Chem. and Pharm. Bull. (Japan), 11, 1333 (1963).

9 R. Tschesche, G. Brügmann, and G. Snatzke, Tetrahedron Letters, 473 (1964).

10 R. Tschesche, P. Welzel, and G. Snatzke, Tetrahedron, 21, 1777 (1965).

11 P. A. Plattner, L. Ruzicka, H. Heusser and E. Anglicker, Helv. Chim. Acta, 30, 385 (1947).

12 A. Lardon, Helv. Chim. Acta, 32, 1517 (1949).

13 N. Danieli, J. Mazur, and F. Sondheimer, J. Amer. Chem. Soc., 84, 875 (1962).

14 C. W. Shoppee, J. Chem. Soc., 1671 (1949).