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A PHORBOL DERIVATIVE FROM CROTON RHAMNIFOLIUS

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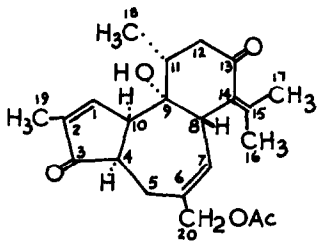
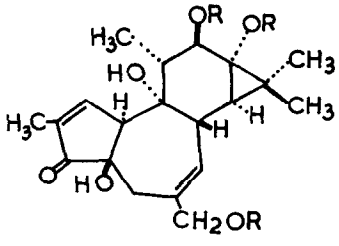
On the basis of spectral data and subsequent correlation studies, structure (I) has been established for the $C_{22}H_{28}O_5$ diterpene acetate, M^+ 372, m.p. 171-174°, $[\alpha]_D^{20}$ - 259° ($CHCl_3$), which has been isolated from C.rhamnifolius. The C-20-acetoxy group was introduced by acetylation during the isolation procedure, so this compound could exist in the plant as the parent alcohol or as a fatty acid ester.



I



II

Spectral data revealed common structural features with phorbol triacetate (II; R = Ac) (1). Several n.m.r. bands could be assigned by comparing the spectrum with that of phorbol triacetate: δ^{CDCl_3} 1.83 (3H, dd; C - 19) δ 7.15 (H - 1, m), δ 1.15 (3H, d, J = 6 Hz; C - 18), δ 4.46 (2H, C - 20), δ 5.10 (H - 7, d, J = 3 Hz), δ 3.40 (m, H - 8), δ 2.69 (1H, exchangeable by D_2O; C - 9 hydroxyl) and δ 2.08 (OAc). The i.r., $\nu_{max.}^{nujol}$ 3410, 1736, 1689, 1661, 1626 $cm.^{-1}$ demonstrated the presence of a hydroxyl group and two α,β-unsaturated carbonyl systems. The latter features were supported by u.v., $\lambda_{max.}^{EtOH}$ 205, 235 nm (ε 14,180, 12, 210).

The remaining n.m.r. spectral features could be readily accommodated by a β,β-dimethyl cisoid α,β-unsaturated ketone structure, easily derivable from the gem-dimethylcyclopropane system in phorbol, and also by the absence of hydroxyl groups at C-4 and C-12. The C-16 and C-17 methyl groups appeared at δ 1.58 and δ 1.87. The very intense i.r. band at 1626 cm^{-1} supported the presence of the cisoid α,β-unsaturated ketone, and all data was consistent with structure (I) (without stereochemical implications). The absolute configuration of phorbol (II; R=H) has recently been unequivocally established by X-ray studies (2,3), and Professor Hecker et al.(4) recently converted phorbol to 9-hydroxy-20-acetoxy-13,15-seco-4α-tiglia-triene-(1,6,14)-dione-(3,13) which was shown to be identical in all respects (t.l.c., m.p., i.r. mass spectrum) to the diterpene acetate (I) from C.rhamnifolius.

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