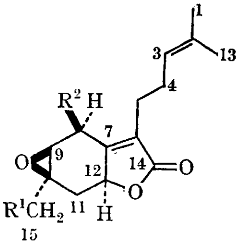
Paniculides A, B, and C, Bisabolenoid Lactones from Tissue Cultures of *Andrographis paniculata*‡

By A. J. ALLISON, D. N. BUTCHER,† J. D. CONNOLLY, and K. H. OVERTON*
(*Departments of Chemistry* and Botany†, The University of Glasgow, Glasgow, W.2*)

CALLUS cultures derived from hypocotyl and stem tissues of *Andrographis paniculata* Nees (Acanthaceae), grown in liquid-shake culture, have produced three new sesquiterpene lactones based on bisabolene: paniculide A (3–5 mg./l.) (I), $C_{15}H_{20}O_4$, m.p. 120—121°, ν_{max} (CCl_4) 1766, 1686 ($\Delta^{\alpha\beta}$-butenolide), 3618, and 3578 (OH) cm.$^{-1}$, λ_{max} (EtOH) 216 nm. (ϵ 15,500); paniculide B (20—25 mg./l.) (II), $C_{15}H_{20}O_5$, m.p. 145—146°, $[\alpha]_D + 4°$ (MeOH), ν_{max} ($CHCl_3$) 1755, 1680 ($\Delta^{\alpha\beta}$-butenolide) and 3600 (OH) cm.$^{-1}$, λ_{max} (EtOH) 217 nm. (ϵ 17,000); paniculide C (8—12 mg./l.) (III), $C_{15}H_{18}O_5$, $[\alpha]_D + 37°$ (MeOH), oil, ν_{max} (CCl_4) 1780 ($\Delta^{\alpha\beta}$-butenolide), 1709 ($\alpha\beta$-oxido-$\Delta^{\alpha'\beta'}$-cyclohexenone), 3633, and 3600 (OH) cm.$^{-1}$, λ_{max} (EtOH) 250 nm.(ϵ 4500). Andrographolide,[1] a major constituent of whole plants, or related substances, could not be detected.

	R^1	R^2
(I)	H	OH
(II)	OH	OH
(III)	OH	8-ketone
(IV)	OAc	OAc
(V)	H	OAc



The constitution of paniculide B diacetate (IV), $C_{19}H_{24}O_7$, m.p. 98—99°, is uniquely consistent with the following evidence: i.r. (CCl_4) 1773 ($\Delta^{\alpha\beta}$-butenolide), 1756 (acetates) cm.$^{-1}$; n.m.r. ($CDCl_3$, 100 and 220 MHz); the following assignments are in each case supported by double resonance: (a) τ 8·32 and 8·42 (3H each, diffuse s), 4·99 (1H, diffuse t) and 7·74 (2H, m) [H's attached to C-1, C-13, C-3, and C-4]; (b) 3·87 (1H, d), 6·55 (1H, d) [C-8, C-9]; (c) 5·30 (1H, t), 7·33 (1H, sharp q), 8·18 (1H, sharp q) [C-12, C-11]; (d) 5·90 (2H, sharp q) [C-15]; (e) 7·66 (2H, m) [C-5]; and (f) 7·84 and 7·97 (each 3H, s, acetate Me).

Selective oxidation of paniculide B (II) at the allylic secondary alcohol furnished paniculide C (III), whose n.m.r. spectrum shows H-9 at τ 6·64 (sharp s) and disappearance of the H-8 signal. Paniculide A acetate (V), $C_{17}H_{22}O_5$, m.p. 95—96°, ν_{max} (CCl_4) 1768 and 1751 cm.$^{-1}$ differs in its n.m.r. spectrum from B diacetate (IV) principally in replacement of its 2H quartet at τ 5·90 (-CH_2OAc) by a 3H singlet at τ 8·54 (-CH_3).

The high resolution (MS 9) mass spectra of the paniculides support the proposed structures, showing the following major ions: A: 264·13652 [P]; 196 [$P - C_5H_8$]; 178 [$P - (C_5H_8 + H_2O)$]. B: 280·13044 [P]; 262 [$P - H_2O$]; 249 [$P - CH_2OH$]; 244 [$P - 2H_2O$]; 231 [$P - (CH_2OH + H_2O)$]; 212 [$P - C_5H_8$]; 181 [$P - (C_5H_8 + CH_2OH)$]; 163 [$P - (C_5H_8 + CH_2OH + H_2O)$]. C: 278·11490 [$P$]; 260 [$P - H_2O$]; 245 [$P - (H_2O + CH_3)$].

The c.d. of paniculide C (III) [dioxan; 350 nm. ($\Delta\epsilon$ +1·68)] indicates[2] a β-epoxide. Arguments to be detailed elsewhere then favour the configurations indicated at C-8 and C-12 in paniculides A and B.

The paniculides are structurally related to bisabolangelone.[3] Preliminary tracer experiments show that the cultures efficiently incorporate DL-[2-^{14}C]mevalonolactone (1·3—1·4% based on DL) into paniculide B.

The production by tissue cultures of major secondary metabolites not found in the parent plant is of phytochemical interest.

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