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Structures of the Natural Products Blumenols A, B, and C

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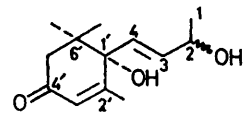
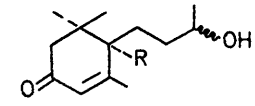
Summary Blumenols A, B, and C, new compounds from *Podocarpus blumei*, are shown to have structures (**1**), (**2**), and (**3**), respectively, with the opposite stereochemistry to that of abscisic acid (**4**) at the ring chiral centre.

Chromatography of the extract of the leaves of *Podocarpus blumei* Endl., afforded three new compounds, named blumenol A, B, and C, which showed strong u.v. absorption at 236 nm. Blumenol A, $C_{13}H_{20}O_3$ (microanalysis and M^+ ion at m/e 224), m.p. 114—115°, formed a monoacetate, $C_{15}H_{22}O_4$ m.p. 98·5—99·5°. The presence of a –CO–CH=C–CH_3 grouping was indicated by u.v. and i.r. absorptions [λ_{max} (EtOH) 236 nm (ϵ 13,100), ν_{max} (KBr) 1680 cm^{-1}] and an n.m.r. signal at δ1·92 (3H, doublet, J 2Hz) coupled to a broadened partially obscured signal at about δ5·90 (1H, sharp singlet on irradiation at δ1·92). A broad peak in the i.r. spectrum of blumenol A at 3400 cm^{-1} and the presence of a two-proton D_2O-exchangeable signal in the n.m.r. spectrum (δ2·45) indicated the presence of two hydroxy-functions. The presence of the grouping –CH=CH–CH(OH)CH_3 was established as follows: the n.m.r. spectrum contained signals (2H, *ca.* δ5·90), which were assigned, from a strong band in the i.r. spectrum at 978 cm^{-1} to the protons on a *trans*-distributed double bond. An n.m.r. signal at δ 1·30 (3H, doublet, J 6 Hz) was found to be coupled to a broad signal at *ca.* δ 4·42 (1H) also coupled to one of the ethylenic protons at δ 5·90. On addition of tris(dipivalomethanato)europium[1] the broad signal at δ 4·42 was shifted downfield to δ 9·6, the methyl doublet to δ 4·2 and the ethylenic protons clearly separated as a pair of signals at δ 8·8 and 9·0 (J 16 Hz) with the lower field proton showing further coupling to the carbinyl proton at δ 4·2 (J 5 Hz).

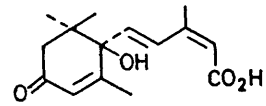
From the n.m.r. spectrum it was clear that the molecule also contained two tertiary methyl groups (δ 1·04 and 1·09) and a pair of isolated methylene protons at δ 2·32 and 2·39 (J 17 Hz) and this together with the above data permitted the formulation of blumenol A as (**1**) (stereochemistry undefined), a structure similar to that of abscisic acid (**4**). The n.m.r. spectra of blumenol A and abscisic acid[2] showed a close correspondence of analogous signals and further



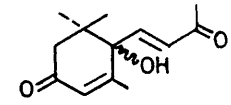
(**1**)



(**2**) R = OH
(**3**) R = H



(**4**)



(**5**)

similarities were observed in the mass spectra of blumenol A and abscisic acid.[3] The structural assignment was confirmed by a two-stage partial synthesis from α-ionone as follows: α-ionone was oxidized[4] to the keto-alcohol (**5**), reduction of which with $LiAlH(OBu^t)_3$ in tetrahydrofuran afforded the required product, m.p. 86—90°. The R_F of the synthetic material on t.l.c. and its u.v. and n.m.r. spectra were identical with those of blumenol A, but its i.r. spectrum showed minor differences in the finger print region, no doubt because it was a mixture of diastereoisomers.

Blumenol B (**2**) was isolated as an oil, but afforded a crystalline monoacetate, $C_{15}H_{24}O_4$, m.p. 101—102°, on mild acetylation. The i.r., u.v., and n.m.r. spectra of (**2**) were very similar to those of blumenol A, except for the absence of

the side-chain ethylenic proton signals in the n.m.r. spectrum, which showed instead methylene signals at δ 1·4—2·0. Blumenol B is accordingly assigned the dihydroblumenol A structure (**2**). This assignment was confirmed by preparing blumenol B by partially hydrogenating blumenol A using a platinum catalyst.

A small amount of a third compound, blumenol C, was isolated as an oil from a less polar chromatographic fraction than those that afforded blumenols A and B. Blumenol C showed u.v. absorption at 236 nm, and its lower polarity and molecular weight (M^+ *m/e* 208) indicated that it contained one less hydroxy-group than blumenol B. From its n.m.r. spectrum blumenol C was closely related to blumenol B. The appearance in the n.m.r. spectrum of a doublet at δ 1·23 (J 6 Hz) indicated the presence of a C-2 hydroxy-group, so that blumenol C is assigned structure (**3**). The absence of a ring OH was further confirmed by preparation of a (non-crystalline) mono-*p*-nitrobenzoate, which showed no OH absorption in its i.r. spectrum.

The o.r.d. spectra of blumenol A and blumenol B acetate both showed positive Cotton effects {blumenol A: $[\phi]_{381}$ + 1570° (peak), $[\phi]_{358}$ + 1530° (trough): blumenol B acetate: $[\phi]_{359}$ + 2180° (peak), $[\phi]_{301}$ − 6850° (infl.)} arising from the $n \rightarrow \pi^*$ transition of the αβ-unsaturated-ketone chromophore. The sign of this Cotton effect is the opposite of that assigned to the corresponding transition of the unsaturated-ketone chromophore in the c.d. spectrum of abscisic acid,[6] *i.e.* the stereochemistry at the ring chiral centre in blumenol A and B is the opposite to that of abscisic acid.[6] The o.r.d. spectrum of blumenol C also shows a positive Cotton effect centred at 330 nm {$[\phi]_{357}$ + 1580° (peak), $[\phi]_{309}$ − 330° (trough)}. If it is assumed that the side-chain is equatorial to the ring, and that the ring adopts a half-chair conformation, the sign of this Cotton effect indicates the 1′-*R* configuration shown for blumenol C (**3**), as in natural (+)-α-ionone[7] and in lutein,[8] a carotenoid with an end group of related structure. As blumenols A and B occur together with blumenol C it can be expected that they are biosynthesised from blumenol C, hydroxylation being accomplished as expected[9] with retention of configuration. By contrast, abscisic acid, which has the opposite stereochemistry, clearly arises by a different mechanism.[10] A recent report[11] of the isolation of 3-oxo-α-ionol (3,4-dehydroblumenol C) provides a close analogy with the blumenols.

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