## The Structure of Calodendrolide, a Novel Terpenoid from Calodendrum capense Thunb.

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Summary The structure and stereochemistry of calodendrolide, isolated from Calodendrum capense Thunb., has been established on the basis of spectroscopic evidence and by chemical transformation into pyroangolensolide.

The seeds of Calodendrum capense (fam. Rutaceae) have been reported to contain limonin (I) and the more highly oxygenated limonoids, limonin diosphenol, and rutaevin. Concentration of the n-hexane extract of the root bark of this plant led to a precipitate which on crystallization from ethanol gave calodendrolide, the first naturally occurring  $C_{15}$  degraded limonoid, for which we suggest structure (II).

Calodendrolide (II), m.p.  $111-111\cdot 5^{\circ}$ , has the formula  $C_{15}H_{16}O_4$  on the basis of microanalysis and mass spectrometry ( $M^+$  260) and gave positive Ehrlich (indicating the presence of the limonoid furan ring²), Dragendorff, and antimony trichloride tests.

The presence of the furan ring in (II) was further supported by the strong end-absorption in the u.v. spectrum,  $\lambda_{\max}$  (EtOH) calc. at 206 nm ( $\epsilon$  10,600). A strong absorption in the i.r. spectrum at 1751 cm<sup>-1</sup> was consistent with the strained  $\delta$ -lactone ring in the suggested structure.<sup>3</sup> The molecular formula and u.v. and i.r. data are also suggestive of sesquiterpene lactones of the type found in numerous Compositae.<sup>4</sup> However, the analysis of the n.m.r. spectrum eliminated this possibility† and gave further evidence for structure (II).

The n.m.r. spectrum (CDCl<sub>3</sub>) showed signals at  $\delta$  0.95 (s, 3H; C·CH<sub>3</sub>), 1.55 (br s, 3H, C=C·CH<sub>3</sub>), 3.9 (s, 1H, O-CH, epoxide), 5.45 (s, 1H, H on C-bearing lactone oxygen), 5.94 (m, 1H, C=CH), 6.31 (br s, 1H,  $\beta$ -furan H), 7.35 (br s, 2H,  $\alpha$ -furan H). These data confirmed the presence of the  $\beta$ -substituted furan ring, and the  $\alpha$ -epoxy- $\delta$ -lactone group. The signals at  $\delta$  1.55 (3H) and 5.94 (1H) were assigned to a methyl group attached to a double bond bearing one hydrogen on the adjacent carbon (CH<sub>3</sub>·C=CH). This structural unit was confirmed by epoxidation of (II) with m-chloroperbenzoic acid which gave epoxycalodendrolide (III). The n.m.r. spectrum of (III) showed the expected change with loss of the signal for the vinyl proton at  $\delta$  5.94 and a new

signal at  $\delta$  3·2 assigned to H on carbon-bearing epoxide oxygen and a shift of the signal for the methyl group from  $\delta$  1·55 to 1·25.

$$(III)$$

$$m-ci\cdot c_6H_4\cdot co_2OH$$

$$(III)$$

$$(III)$$

Treatment of (II) with hydriodic acid gave a deoxy-derivative (IV), which exhibited u.v. and n.m.r. data identical with those reported for pyroangolensolide and proved to be identical (t.l.c., i.r., m.p., mixed m.p.) with an authentic sample of pyroangolensolide. The c.d. curve of (IV) showed a positive Cotton effect, similar in profile and position ( $\Delta_{\max}\epsilon + 10.64$  at 282 nm) to pyroangolensolide, thus indicating that the chirality of calodendrolide is the same as that of other limonoids at the corresponding centres.

SCHEME. Suggested biosynethtic pathway

† The occurrence of C. capense in the Rutaceae would also argue against this suggestion.

Calodendrolide is apparently derived biosynthetically from a limonoid by loss of rings A and B, and is the logical precursor of fraxinellone (V) a C14 degraded limonoid isolated from Dictamnus albus L.5c,8 It has been suggested that fraxinellone arises from a limonoid by loss of rings A and B and of C-16. We suggest that fraxinellone could be formed by loss of C-16 of calodendrolide which would involve basecatalysed decarboxylation to give a lactol which on oxidation and double-bond isomerization would give (V) as shown in the Scheme. This sequence has been accomplished in the

laboratory in the conversion of gedunin into the corresponding y-lactone.9

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