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

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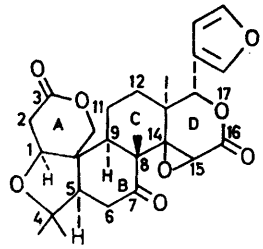
Summary The structure and stereochemistry of calodendrolide, isolated from *Calodendrum capense* Thunb., has been established on the basis of spectroscopic evidence and by chemical transformation into pyroangolensolide.

THE seeds of *Calodendrum capense* (fam. Rutaceae) have been reported to contain limonin (I) and the more highly oxygenated limonoids, limonin diosphenol, and rutaevin.[1] 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).

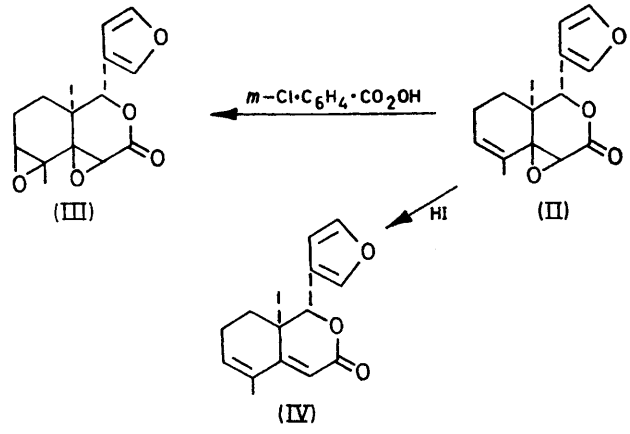
Calodendrolide (II), m.p. 111—111·5°, has the formula $C_{15}H_{16}O_4$ on the basis of microanalysis and mass spectrometry (M^+ 260) and gave positive Ehrlich (indicating the presence of the limonoid furan ring[2]), Dragendorff, and antimony trichloride tests.



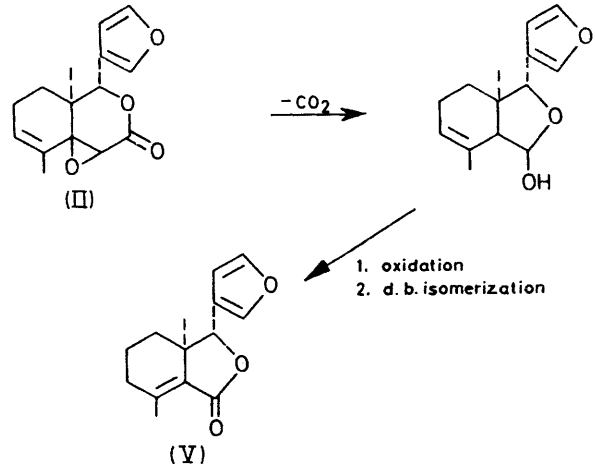
(I)

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

The n.m.r. spectrum ($CDCl_3$) showed signals at δ 0·95 (s, 3H; C·CH_3), 1·55 (br s, 3H, C=C·CH_3), 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, β-furan H), 7·35 (br s, 2H, α-furan H). These data confirmed the presence of the β-substituted furan ring,[5] and the α-epoxy-δ-lactone group.[6] The signals at δ 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_3·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 δ 5·94 and a new signal at δ 3·2 assigned to H on carbon-bearing epoxide oxygen and a shift of the signal for the methyl group from δ 1·55 to 1·25.



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.[7] 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.[7]



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 C_{14} 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 base-catalysed 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 γ-lactone.[9]

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[1] D. L. Dreyer, *Phytochemistry*, 1966, **5**, 372.
[2] D. L. Dreyer, *J. Org. Chem.*, 1965, **30**, 749.
[3] S. Takeuchi, Y. Ogawa, and H. Yonehara, *Tetrahedron Letters*, 1969, 2737.
[4] R. Hegnauer, "Chemotaxonomie der Pflanzen", Vol. III, Birkhauser Verlag, Basel, 1964, p. 448.
[5] (a) N. S. Ohochuku and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1969, 864; (b) D. L. Dreyer, *J. Org. Chem.*, 1967, **32**, 3442; (c) M. Pailer, G. Sehaden, G. Spiteller, and W. Fenzl, *Monatsh.*, 1965, **96**, 1330.
[6] D. L. Dreyer, *J. Org. Chem.*, 1966, **31**, 2279.
[7] We are grateful to Dr. K. Jewers for this sample. J. B. Davis, V. M. Godfrey, K. Jewers, A. H. Manchanda, F. V. Robinson, and D. A. H. Taylor, *Chem. and Ind.*, 1970, 301.
[8] P. Coggon, A. T. McPhail, R. Storer, and D. W. Young, *Chem. Comm.*, 1969, 828.
[9] A. Akisanya, E. O. Arene, C. W. L. Bevan, D. E. U. Ekong, M. N. Nwaji, J. I. Okogun, J. W. Powell, and D. A. H. Taylor, *J., Chem. Soc.* (*C*), 1966, 506.