Podolactones C and D, Terpene Sulphoxides from *Podocarpus neriifolius*

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Summary The structures of podolactones C and D, the first terpenes known to contain a sulphoxide grouping, are shown to be (**3**) and (**4**) respectively.

EARLIER[1] we reported that the bark from a *Podocarpus* species (*cf., P. neriifolius* D. Don ex Lamb.) contained two norditerpenoid dilactones, podolactones A (**1**) and B (**2**), with plant growth inhibitory activity. Further fractionation of the extract yielded two other compounds of the same type, podolactones C and D, which have lower inhibitory activity than podolactone A and which are shown to have structures (**3**) and (**4**) respectively.

Podolactone C (**3**), m.p. 288—290° (decomp.), has the formula $C_{20}H_{24}O_8S$ from microanalysis. U.v. and i.r. spectra show the presence of the αβ-unsaturated δ-lactone [λ_{max} (EtOH) 218 nm (ε 12,500), ν_{max} (KBr) 1720 and 1645 cm^{-1}] and γ-lactone (ν_{max} 1780 cm^{-1}) groups found in podolactones A and B, and a hydrogen-bonded hydroxy-group (ν_{max} 3150 cm^{-1}). In the n.m.r. spectrum (Table) of podolactone C there are peaks corresponding closely in chemical shifts and coupling constants to those in the spectrum of podolactone A for the ring protons and the three methyl groups. The only significant differences in the spectra are in the chemical shift of the signals assigned to the C-16 protons, and the appearance of an extra methyl signal. The C-16 protons give rise to a pair of doublets (*J* 14 Hz) at δ 3·39 and 3·76 p.p.m., while the methyl signal is found at δ 2·66 p.p.m. The presence of a sulphur atom in the molecule and the above chemical shifts (*cf.* dimethyl sulphoxide, δ 2·49 p.p.m. in pyridine) suggest the presence of a $-CH_2 \cdot SOMe$ group in place of the $-CH_2 \cdot OH$ group of podolactone A. Also, the i.r. spectrum of podolactone C, while very similar to that of podolactone A, shows a strong band at 1015 cm^{-1}, which can be assigned to the S=O stretching vibration of a hydrogen-bonded sulphoxide group.[2a]

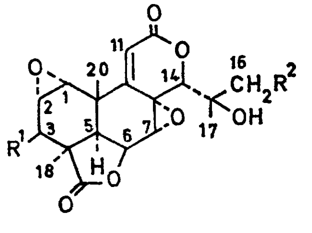
TABLE

^1H *n.m.r. data in* [$^2H_5$]*pyridine*; δ/p.p.m. (*J*/H_z)

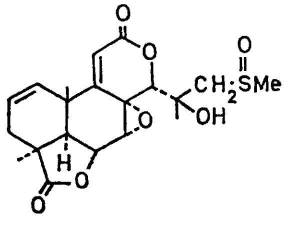
	Podolactone A	Podolactone C	Podolactone D
1-H	3·23d (4·5)	3·26d (4·0)	5·88d (10·5)
2-H	3·36m (4·5, 2·0, 1·0)	3·37m (4·0, 2·0, 1·0)	5·75m (10·5, 3·5, <1)
3α-H	2·17dd (2·0, 15·0)	2·21dd (2·0, 15·0)	2·03 broad s
3β-H	1·70dd (1·0, 15·0)	1·73dd (1·0, 15·0)	
5-H	1·77d (5·0)	1·80d (5·0)	2·05d (5·0)
6-H	5·07dd (5·0, 1·5)	5·03dd (5·0, 1·2)	5·06dd (5·0, 1·3)
7-H	5·18d (1·5)	5·23d (1·2)	5·25d (1·3)
11-H	6·11s	6·19s	6·19s
14-H	4·97s	4·83s	4·89s
16-H_2	4·25d (11·5) 4·48d (11·5)	3·39d (14·0) 3·76d (14·0)	3·40d (13·5) 3·76d (13·5)
17-H_3	1·80s	1·85s	1·86s
18-H_3	1·45s	1·43s	1·29s
20-H_3	1·41s	1·39s	1·15s
SOMe		2·66s	2·67s

Confirmation of this structure was obtained by oxidation of podolactone C with *m*-chloroperoxybenzoic acid to the corresponding sulphone in quantitative yield. This compound, $C_{20}H_{24}O_9S$, m.p. 330° (decomp.), shows in its n.m.r. spectrum the expected downfield shifts of the C-16 proton resonances (from δ 3·39 and 3·76 to 3·70 and 4·48 p.p.m. respectively), the C-17 methyl (from 1·85 to 2·00), and the extra methyl signal (from 2·66 to 3·23, *cf.* dimethyl sulphone, 3·07 in pyridine). The remainder of the spectrum was similar to that of the parent compound. The i.r. spectrum of the sulphone shows strong bands, not present in the spectrum of the parent compound, at 1315 and 1140 cm^{-1}, characteristic of sulphones.[2b]

Attempts to reduce the sulphoxide to a sulphide, to effect a Pummerer rearrangement, or to desulphurize the molecule were not successful.



(**1**) R^1 = H, R^2 = OH
(**2**) R^1 = R^2 = OH
(**3**) R^1 = H, R^2 = SOMe



(**4**)

The n.m.r. spectrum (Table) of podolactone D (**4**), $C_{20}H_{24}O_7S$, m.p. 261—266° (decomp.), is very similar to that of podolactone C, but indicates the presence of a Δ^1-double bond. The signals assigned to 1- and 2-H appear as a doublet and a multiplet centred at δ 5·88 and 5·75 p.p.m. respectively, with the latter signal coupled to the C-3 protons, which appear as a broad singlet at δ 2·03 p.p.m. These assignments were established by double irradiation. U.v. and i.r. spectra [λ_{max} 217 nm (ε 13,500), ν_{max} 3200, 1770, 1720, 1645, and 1020 cm^{-1}], together with the formation of a sulphone, m.p. 258—263° (decomp.), $C_{20}H_{24}O_8S$ (ν_{max} 1315 and 1140 cm^{-1}) on oxidation with *m*-chloroperoxybenzoic acid, confirm the similarity in structure of the two lactones, and podolactone D is assigned structure (**4**).

The mass spectra of (**3**) and (**4**) show weak molecular ion peaks at *m/e* 424 and 408 respectively, and the base peak in each spectrum is that resulting from side-chain fission (*m/e* 304 and 288), as for podolactones A and B. In addition there are small peaks at *m/e* 361 and 345 due to loss of SOMe from the molecular ion. The o.r.d. spectra of podolactones A, B, C, and D are alike, and similar in sign and shape to that of inumakilactone B,[3] though of somewhat greater amplitude. The absolute configurations can thus be assigned as shown in (**3**) and (**4**).

The presence of a sulphoxide group in a terpene molecule is unique among known natural products. Biogenesis of these compounds can be expected to take place *via* the corresponding 16-thiols.

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[1] M. N. Galbraith, D. H. S. Horn, J. M. Sasse, and D. Adamson, *Chem. Comm.*, 1970, 170.

[2] (a) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 357; (b) *ibid.*, p. 360.

[3] S. Ito, M. Sunagawa, M. Kodama, H. Honma, and T. Takahashi, *Chem. Comm.*, 1971, 91.