

Dolabellane Diterpenoids from the Liverworts *Barbilophozia floerkei*, *B. lycopodioides*, and *B. attenuata*: Spectroscopic and X-ray Studies of Structure, Stereochemistry, and Conformation. X-Ray Molecular Structure of 3*S*,4*S*;7*S*,8*S*-Diepoxy-10*R*,18-dihydroxydolabellane, 18-Acetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane, and 10*R*,18-Diacetoxy-3*S*,4*S*-epoxydolabell-7*E*-ene

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The dolabellane diterpenoids 10*R*,18-diacetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane (barbilycopodin) (1), 10*R*,18-diacetoxy-3*S*,4*S*-epoxydolabell-7*E*-ene (12), 18-acetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane (4), and 18-hydroxydolabell-7*E*-en-3-one (14) have been isolated from the liverworts *Barbilophozia floerkei*, *B. lycopodioides*, and *B. attenuata*. The ¹H and ¹³C n.m.r. spectroscopic properties of the compounds and some of their transformation products are described. The structures, relative stereochemistries, and conformations of compounds (4), (12), and 3*S*,4*S*;7*S*,8*S*-diepoxy-10*R*,18-dihydroxydolabellane (2) were defined by X-ray crystallographic studies. The eleven-membered ring has essentially the same conformation in compounds (2), (4), and (12), a conformation which has been characterised as a low-energy form of cycloundeca-1,5-diene by molecular-mechanics calculations.

In 1971 Huneck and Overton¹ reported the isolation of a diterpenoid, barbilycopodin, from the liverworts *Barbilophozia floerkei* (Web. et Mohr) Loeske and *B. lycopodioides* (Wallr.) Loeske. In a continuation of our investigations of the constituents of European, including Scottish, liverworts² we have also examined *B. attenuata* (Mart.) Loeske and describe in this paper the structural elucidation of barbilycopodin (1) and three related diterpenoids (4), (12), and (14) from these *Barbilophozia* species. The structures of the compounds, proposed on the basis of their ¹H and ¹³C n.m.r. spectroscopic properties and chemical transformations, have been confirmed by X-ray crystal structure analyses of (2) [a hydrolysis product of (1)], (12), and (4), which also revealed their relative configurations and conformations.

Barbilycopodin (1) C₂₄H₃₈O₆ [(M - H)⁻ 421; m/z 362 (M⁺ - AcOH)], m.p. 197–198 °C; [α]_D²⁴ -37.8° (c 1.54 in CHCl₃); ν_{max}(CCl₄) 1735 cm⁻¹, isolated from *B. floerkei* collected in the Thuringian Forest, Ore Mountains and the Hercynian Mountains in the German Democratic Republic (G.D.R.), and near Loch Doon, Ayrshire, Scotland, has proton and carbon resonances for five tertiary methyl groups [δ_H 1.29, 1.36, 1.42, 1.48, and 1.54], two acetates [δ_H 1.99 and 2.06; δ_C 170.3, 170.2, 21.3, and 22.7], one secondary [δ_H 5.38 (ddd, J 12, 6, and 2 Hz, 10-H); δ_C 75.5 (d, C-10)], and the other tertiary [δ_C 84.0 (s, C-18)], and two trisubstituted epoxides [δ_H 3.04 (dd, J 9 and 5 Hz, 3-H), 2.87 (d, J 8 Hz, 7-H); δ_C 58.8 and 6.13 (both s) and 62.4 and 65.6 (both d)]. The molecule is therefore bicarbocyclic. Alkaline hydrolysis of (1) afforded the diol (2),† C₂₀H₃₄O₄ [m/z 338 (M⁺)], m.p. 224–225 °C, in which 10-H, the proton associated with the secondary hydroxy group, resonates at δ_H 4.13 (ddd, J 12, 6, and 2 Hz). Double-irradiation experiments revealed that 10-H is coupled to an isolated methylene group [δ_H 2.29 (dd, J 14 and 6 Hz) and 1.76 (dd, J 14 and 12 Hz) (9-H₂)] and to one other proton. On oxidation the diol (2) was transformed into the ketol (3), C₂₀H₃₂O₄ [m/z 336 (M⁺)], m.p. 161–162 °C, whose i.r. spectrum [ν_{max}(CCl₄)

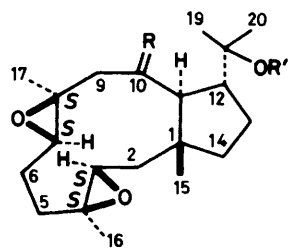
3 610, 3 595, and 1 687 cm⁻¹] suggested the presence of a medium-ring ketone [δ_C 211.9]. In the ¹H and ¹³C n.m.r. spectra of ketol (3) the C-9 methylene group is readily identified [δ_H 3.47 and 2.13 (ABq, J 16 Hz); δ_C 36.7 (dd, C-9)]. The Eu(fod)₃-shifted ‡ ¹H n.m.r. spectrum of ketol (3), in conjunction with double-resonance experiments, permitted the identification of the structural units (5) which can be satisfactorily accommodated in a dolabellane framework. Confirmation of this suggestion was obtained by direct X-ray analysis of the diol (2), which defined its structure and relative stereochemistry as 3*S**,4*S**;7*S**,8*S**-diepoxy-10*R**,18-dihydroxydolabellane (2). The c.d. spectrum of the ketol (3) [Δε₂₈₉ -0.97] suggests the absolute configuration shown in structure (2). Application of the Octant Rule using the molecular conformation derived from the X-ray results predicts a negative Cotton Effect for this absolute configuration. Thus barbilycopodin (1) is 10*R*,18-diacetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane. The same absolute configuration has been assigned to acetoxyodontoschismenol (8), a dolabellane diterpenoid from the liverwort *Odontoschisma denudatum*,³ on the basis of the benzoate chirality rule and X-ray analysis of a heavy-atom derivative, and to dolabellane derivatives from marine sources.^{4–6}

Mild base treatment of the ketol (3) resulted in the formation of the enone (6), C₂₀H₃₂O₄ [m/z 336 (M⁺)], 218–220 °C, ν_{max}(CHCl₃) 3 615 and 1 670 cm⁻¹, λ_{max} 235 nm (ε 8 000), which presumably arises by β-elimination of the C-8 oxygen function followed by transannular opening of the 3,4-epoxide. The ¹H and ¹³C data of compound (6) confirm the presence of the enone [δ_H 6.13 (brs, 9-H), 1.67 (d, J 2 Hz, 17-H₃); δ_C 214.9 (C-10), 138.9 (s, C-8), and 130.7 (d, C-9)], the cyclic ether [δ_H 4.25 (t, J 8 Hz, 7-H); δ_C 86.5 (s, C-4) and 80.3 (d, C-7)], and the new secondary hydroxy function [δ_H 3.65 (brs, 3-H); δ_C 72.2 (d, C-3)]. Oxidation of compound (6) afforded the diketone (7), C₂₀H₃₀O₄ [m/z 334 (M⁺)], m.p. 134–136 °C, ν_{max}(CHCl₃) 3 600, 1 710, 1 675, and 1 640 cm⁻¹.

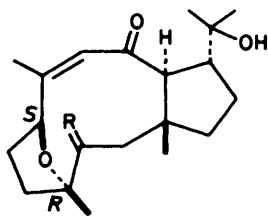
The epoxide groups of barbilycopodin (1) proved resistant

† This diol is described as floerkein B in ref. 1.

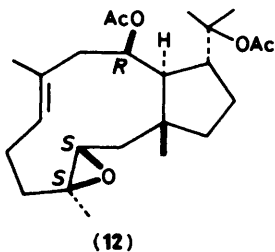
‡ Eu(fod)₃ = europium tris-(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionate).

(1) R = H, β -OAc, R' = Ac(2) R = H, β -OH, R' = H

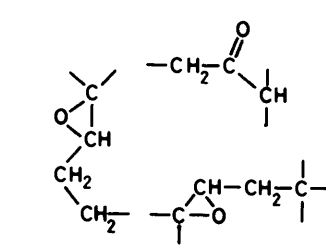
(3) R = O, R' = H

(4) R = H₂, R' = Ac(6) R = H, β -OH (S)

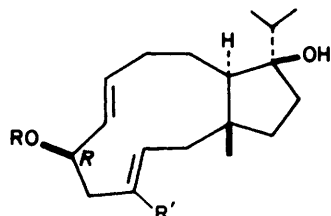
(7) R = O



(12)



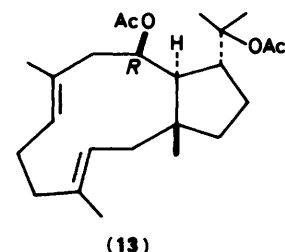
(5)



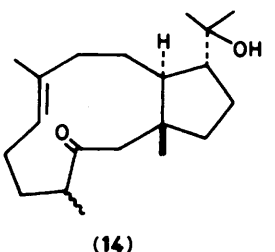
(8) R = Ac, R' = Me

(9) R = Ac, R' = CH₂OH(10) R = *p*-BrC₆H₄CO, R' = Me

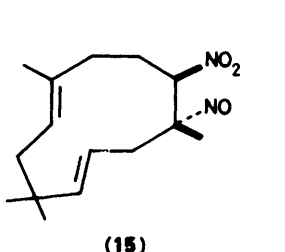
(11) R = Ac, R' = Me, 3S, 4S-epoxy



(13)



(14)



(15)

to reduction with LiAlH₄ but were successfully removed by treatment with Zn-Cu couple to give 10*R*,18-diacetoxylolabellane-3*E*,7*E*-diene (13), m.p. 83–85 °C [δ_{H} 5.13 (brdd, *J* 11.8 and 3.5 Hz, 3-H), 4.93 (brd, *J* 11.4 Hz, 7-H); δ_{C} 133.3 and 129.8 (both s, C-4 and C-8) and 130.9 and 124.7 (both d, C-7 and C-3)]. The high shielding of the olefinic methyl groups [δ_{C} 16.4 and 15.7] supports the *E* configurations assigned to the double bonds.

The monoepoxide (12), m.p. 165–166 °C, was obtained as a minor product in the Zn-Cu couple reduction of compound (1). It was also isolated as a natural product from a G.D.R. sample of *B. floerkei*. Its spectroscopic properties revealed the presence of a trisubstituted double bond [δ_{H} 5.20 (br d, *J* 12.0 Hz, 7-H); δ_{C} 130.4 (s, C-8) and 128.6 (d, C-7)], an olefinic methyl [δ_{H} 1.69 (17-H₃)], and a trisubstituted epoxide [δ_{H} 2.98 (dd, *J* 10.0 and 3.4 Hz, 3-H); δ_{C} 62.3 (s, C-4) and 63.8 (d, C-3)] in addition to four tertiary methyl groups and two acetates, one secondary and one tertiary. The 3,4-position of the epoxide follows from

comparison of the chemical shift of 3-H with literature values^{5,6} for 3*S*,4*S*-epoxydolabell-7*E*-ene and 7*S*,8*S*-epoxydolabell-3*E*-ene derivatives. Confirmation of the structure of the monoepoxide as 10*R*,18-diacetoxy-3*S*,4*S*-epoxydolabell-7*E*-ene (12) was obtained by *X*-ray analysis.

From a Scottish sample of *B. floerkei*, collected near Loch Doon, we isolated, in addition to barbilycopodin (1), a second diterpenoid, 10-deacetoxybarbilycopodin (4), C₂₂H₃₆O₄ [*m/z* 364.2636 (*M*⁺), m.p. 89–91 °C, ν_{max} (CCl₄) 1730 cm⁻¹. It has resonances for a tertiary acetate [δ_{H} 1.96; δ_{C} 21.9, 170.3, and 84.9 (s, C-18)] in addition to five tertiary methyls and two trisubstituted epoxides. Comparison of the ¹H and ¹³C n.m.r. spectra of (4) and barbilycopodin (1) suggested that compound (4) is 10-deacetoxybarbilycopodin. A single-crystal *X*-ray analysis of compound (4) confirmed its structure as 18-acetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane. The absolute configuration is assumed to be the same as that of barbilycopodin (1).

The fourth new dolabellane derivative was isolated from a second sample of *B. floerkei* collected in the Hercynian Mountains. The extract, surprisingly, lacked barbilycopodin (1) but contained the monoepoxide (12) as a minor component. The major component was the non-crystalline 18-hydroxydolabell-7*E*-en-3-one (14), C₂₀H₃₄O₂ [*m/z* 306.2594 (*M*⁺), ν_{max} (CCl₄) 3610 and 1703 cm⁻¹, which has resonances for a ketone [δ_{C} 214.6 (C-3)], a trisubstituted double bond [δ_{H} 5.03 (dd sextets, *J* 7.0, 8.0, and 1.0 Hz, 7-H); δ_{C} 136.7 (s, C-8) and 126.1 (d, C-7)], an isolated methylene group [δ_{H} 2.41 and 2.26 (ABq, *J* 18.6 Hz, 2-H₂)], a secondary methyl group [δ_{H} 1.11 (d, *J* 6.8 Hz, 16-H₃) and 2.28 (ddq, *J* 8, 7, and 4 Hz, 4-H); δ_{C} 24.2 (C-16)], an olefinic methyl [δ_{H} 1.63 (d, *J* 1.5 Hz, 17-H₃); δ_{C} 16.6 (C-17)], a dimethyl carbinol group [δ_{H} 1.26 and 1.25 (19- and 20-H₃); δ_{C} 26.6 and 29.3 (C-19 and -20) and 74.0 (s, C-18)], and a tertiary methyl group [δ_{H} 0.85 (15-H₃); δ_{C} 17.8 (C-15)]. These data are readily accommodated in the dolabellane structure (14). The presence of the isolated methylene group served to locate the ketonic carbonyl at C-3. The alternative position at C-13 in the cyclopentane ring is excluded by the value of the i.r. carbonyl frequency (ν_{max} 1703 cm⁻¹). Definitive evidence for the position of the trisubstituted double bond is lacking but biogenetic analogy suggests a preference for 7,8 rather than 8,9. The ¹³C chemical shift of the olefinic methyl [δ_{C} 16.6] supports the *E* configuration of the double bond [cf. compounds (12) and (13)]. The configuration of the secondary methyl group remains in doubt. Although 4-H can be clearly observed, uncertainty about the conformation of the molecule renders unsafe the use of coupling constants for configurational assignment.

Barbilycopodin (1) was also isolated from *B. lycopodioides*¹ collected in Lappland, Sweden, and from *B. attenuata* collected in the Hercynian Mountains.

Dolabellane diterpenoids are common metabolites of marine organisms and have been isolated from the molluscs *Dolabella californica*^{7,8} and *Aplysia dactylomela*,⁹ from marine algae of the genus *Dictyota*,^{4,5,10,11} from the brown algae *Glossophora galapagensis*¹² and *Dilophus fasciola*,¹³ and from the sea whip *Eunicea calyculata*.⁶ It is interesting that they also occur in the Hepaticae. There are no reports of dolabellane diterpenoids from higher plants.

Crystal Structures.—The crystal structures were elucidated by direct phasing procedures and the atomic parameters adjusted by least-squares calculations that converged at *R* 0.041 for compound (2), 0.041 for compound (12), and 0.032 for compound (4). The molecular structures are illustrated in Figures 1–3.

The torsion angles around the carbon-carbon bonds of the eleven-membered ring are given in Table 1 and show that the ring has essentially the same conformation in all three compounds (2), (4), and (12). The related compound 6 β -acetoxy-

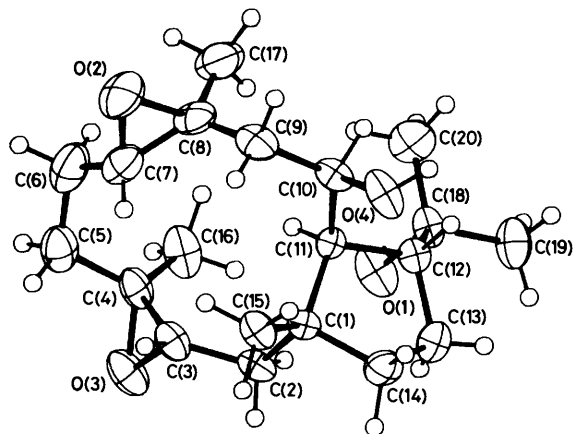


Figure 1. Molecular structure of 3*S*,4*S*;7*S*,8*S*-diepoxy-10*R*,18-dihydrodolabellane (**2**). The thermal ellipsoids of the C and O atoms are drawn at the 50% probability level and the H atoms are represented by spheres of radius 0.1 Å.

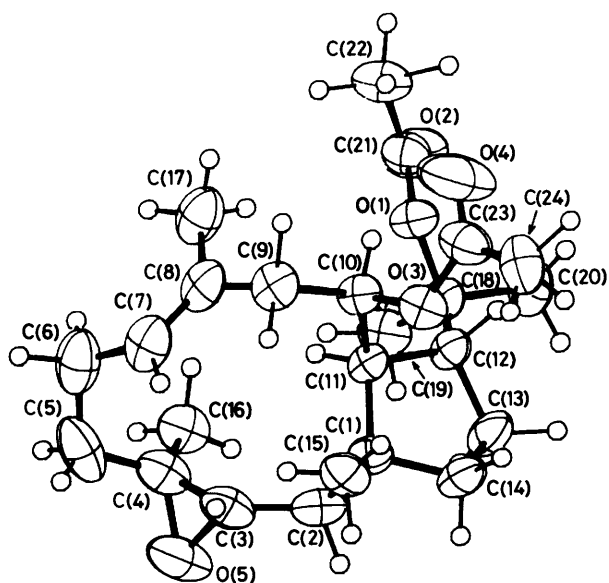


Figure 2. Molecular structure of 10*R*,18-diacetoxy-3*S*,4*S*-epoxydolabell-7*E*-ene (**12**). The thermal ellipsoids of the C and O atoms are drawn at the 50% probability level and the H atoms are represented by spheres of radius 0.1 Å.

12 β ,16-dihydrodolabella-3,7-diene (**9**)¹⁴ also adopts this conformation whereas 6 β -(*p*-bromobenzoyloxy)-12 β -hydroxydolabella-3,7-diene (**10**) and 6 β -acetoxy-3,4-epoxy-3,4-dihydroodontoschismenol (**11**) adopt an alternative conformation.¹⁵ These conformations have previously been observed in the two crystalline forms of humulene nitrosite (**15**).^{16,17}

The results in Table 1 show that substitution of an epoxide group for a C=C double bond has little effect on the molecular conformation. Moreover, X-ray studies of the bis(silver nitrate) adduct of humulene¹⁸ and of humulene di-¹⁹ and tri-epoxide²⁰ found a common conformation for the eleven-membered rings in these compounds. Accordingly, we chose cycloundeca-1,5-diene as the appropriate hydrocarbon for conformational comparison with compounds (**2**), (**4**), and (**12**).

Molecular-mechanics calculations for cycloundeca-1,5-diene using the force field developed by White and Bovill²¹ characterised a number of low-energy conformations.²² The

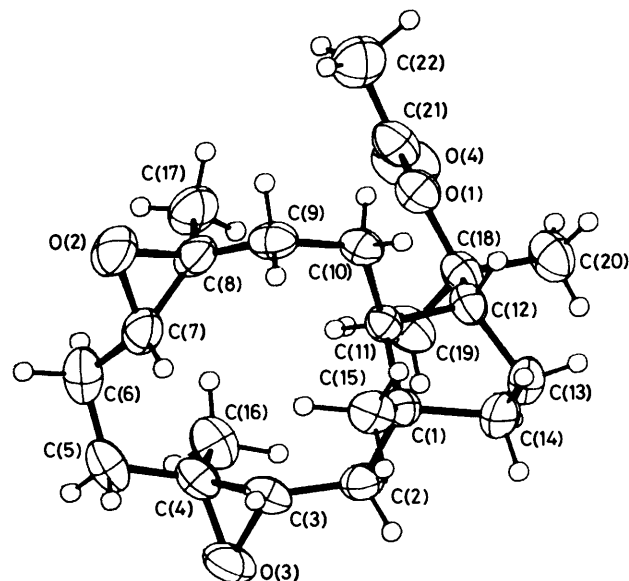


Figure 3. Molecular structure of 18-acetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane (**4**). The thermal ellipsoids of the C and O atoms are drawn at the 50% probability level and the H atoms are represented by spheres of radius 0.1 Å.

Table 1. Conformational details of the eleven-membered rings.

Torsion angle (°) about bond	Compound					
	(2)	(12)	(4)	(9)	(10)	(11)
1-2	-81	-81	-81	-68	-62	-65
2-3	103	111	107	120	132	114
3-4	-157	-156	-157	-173	-175	-160
4-5	96	91	95	88	103	95
5-6	-57	-55	-59	-55	-62	-45
6-7	123	127	122	116	110	130
7-8	-156	-170	-158	-166	-167	-174
8-9	109	116	112	122	64	34
9-10	-54	-49	-49	-45	71	65
10-11	-68	-70	-73	-75	-147	-154
11-1	145	139	141	131	96	117

three conformations with lowest energy are listed in Table 2 and comparison with Table 1 shows that compounds (**2**), (**4**), (**9**), and (**12**) adopt the cycloundeca-1,5-diene conformation of second lowest energy, 3.1 kJ mol⁻¹ above the global minimum-energy form which is seen in compounds (**10**) and (**11**).

In compounds (**2**), (**4**), (**9**), and (**12**), the highly substituted bond C(1)–C(11) has a length of 1.561–1.578, mean 1.572 Å, whereas the equally highly substituted bond C(12)–C(18) has a length of 1.535–1.555, mean 1.543 Å. The distinct lengthening of the former bond is a result of torsional strain, the torsion angle C(14)–C(1)–C(11)–C(12) [11–23°, mean 17°] deviating appreciably from the ideal staggered value of 60°, whereas the angle C(11)–C(12)–C(18)–C(19) [54–58°, mean 57°] is close to the ideal value. The torsional strain associated with a five-membered ring is also apparent in the length of bond C(11)–C(12) [1.563–1.566, mean 1.565 Å]; the associated torsion angle C(1)–C(11)–C(12)–C(13) [0–15°, mean 8°] deviates appreciably from the ideal value of 60°.

Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were recorded in CCl₄ solution, unless

Table 2. Torsion angles ($^{\circ}$) and calculated strain energies ($E_s/\text{kJ mol}^{-1}$) for low-energy conformations of cycloundeca-1,5-diene^a

	Conformation		
	I	II	III
	-57	-78	79
	119	103	79
	-177	-172	-172
	104	94	95
	-56	-46	-56
	100	110	95
	-171	-171	-172
	78	127	79
	64	-43	79
	-151	-71	-68
	100	146	-68
E_s	32.1	35.2	38.7

^a The torsion angles are listed in the order required for comparison with the X-ray results in Table 1.

otherwise stated, on a Perkin-Elmer 580 instrument. U.v. spectra were measured for ethanolic solutions using a Pye Unicam SP 800 spectrophotometer. Optical rotations were measured on an Optical Activity AA-100 polarimeter for CHCl_3 solution. N.m.r. spectra were recorded for CDCl_3 solutions, unless otherwise stated, using a Perkin-Elmer R32 instrument (^1H ; 90 MHz) or a Varian XL-100 instrument (^{13}C ; 25.16 MHz) with tetramethylsilane as internal standard. High-field n.m.r. spectra were recorded using either a Bruker WH 360 instrument (^1H ; 360.13 MHz) or a Bruker WP 200SY instrument (^1H ; 200.13 MHz; ^{13}C ; 50.32 MHz) using CHCl_3 at δ_{H} 7.25 and CDCl_3 at δ_{C} 77.0 as internal standards. Light petroleum refers to the fraction boiling in the range 60–80 $^{\circ}\text{C}$.

Extraction.—The dried and powdered liverwort was extracted with ether. The crude extract was subjected to preliminary chromatographic separation on a column of silica gel followed by preparative t.l.c. (p.l.c.).

(a) *Barbilophozia lycopodioides*. The extraction is described in ref. 1. Crystallisation from MeOH afforded barbilycopodin (1), 10*R*,18-diacetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane, m.p. 197–198 $^{\circ}\text{C}$; δ_{C} 17.0, 17.5, 21.3, 22.7, 23.6, 23.6, 26.0 (q), 23.2, 25.5, 37.2, 40.4, 41.6, 45.2 (t), 45.2, 55.5, 62.4, 65.6, 75.4 (d), 44.3, 58.8, 61.3, 84.4, 170.2, and 170.3 (s).

(b) *B. floerkei* (300 g) (*Loch Doon*). Crystallisation from hexane gave 10-deacetoxybarbilycopodin (4) (43 mg), 18-acetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane, m.p. 89–91 $^{\circ}\text{C}$; $[\alpha]_{\text{D}} - 16.8^{\circ}$ (c 1.43); δ_{H} (200 MHz) 1.19, 1.31, 1.39, 1.49, 1.55 (t-Me), 1.96 (OAc), 2.78 (d, *J* 8 Hz, 7-H), and 3.05 (dd, *J* 4 and 8 Hz, 3-H); δ_{C} 17.1, 18.3, 21.9, 23.1, 24.1, 26.1 (q), 22.8, 25.8, 30.9, 37.1, 37.1, 41.5, 43.2 (t), 43.2, 59.7, 61.6, 64.9 (d), 44.1, 61.1, 61.5, 84.9, and 170.3 (s) [Found: M^+ , 364.2636. $\text{C}_{22}\text{H}_{36}\text{O}_4$ requires M , 364.2613].

(c) *B. floerkei* (*Hercynian mountains*). Crystallisation from CHCl_3 -light petroleum yielded the monoepoxide (12), 10*R*,18-diacetoxy-3*S*,4*S*-epoxydolabell-7*E*-ene, m.p. 161–162 $^{\circ}\text{C}$; $[\alpha]_{\text{D}} - 75^{\circ}$; δ_{H} (360 MHz) 1.21, 1.45, 1.51, 1.53 (t-Me), 1.69 (brs, 17- H_3), 1.99, 2.09 (OAc), 2.98 (dd, *J* 10.0 and 3.4 Hz, 3-H), 5.20 (brd, *J* 12.0 Hz, 7-H), and 5.42 (ddd, *J* 11.2, 7.2, and 1.8 Hz, 10-H); δ_{C} 16.2, 16.8, 21.5, 22.8, 23.0, 23.9, 25.8 (q), 24.3, 25.7, 38.6, 42.0, 42.2, 45.7 (t), 44.4, 54.8, 63.8, 76.6, 128.6 (d), 44.4, 62.3, 84.6, 130.4, 170.4, and 170.8 (s) [Found: m/z 364.2636. $\text{C}_{22}\text{H}_{36}\text{O}_4$ ($M^+ - \text{C}_2\text{H}_2\text{O}$) requires m/z 364.2613]. The second compound isolated from the extract was the non-crystalline 18-hydroxydolabell-7*E*-enone (14) (30 mg), $[\alpha]_{\text{D}} + 52.9^{\circ}$ (c 1.43); δ_{H} (360

MHz) 1.25, 1.26 (19- and 20- H_3), 1.11 (d, *J* 6.8 Hz, 16- H_3), 0.85 (15- H_3), 1.63 (d, *J* 1.5 Hz, 17- H_3), 2.28 (ddq, *J* 4, 8, and 7 Hz, 4-H), 2.26, 2.41 (ABq, *J* 18.6 Hz, 2- H_2), and 5.03 (dd sextets, *J* 7.0, 8.0, and 1.0 Hz, 7-H); δ_{C} 16.6, 17.8, 24.2, 26.6, 29.3, 34.1 (q), 25.6, 25.6, 29.3, 37.7, 39.5, 43.3, 49.0 (t), 43.6, 58.4, 126.1 (d), 44.5, 74.0, 136.7, and 214.6 (s) (Found: M^+ , 306.2594. $\text{C}_{20}\text{H}_{34}\text{O}_2$ requires M , 306.2559).

(d) *B. attenuata* (*Hercynian mountains*). Barbilycopodin (1), identical with an authentic sample, was the only compound isolated from this extract.

Diol (2).—Barbilycopodin (1) (100 mg) was refluxed for 2 h in methanolic aqueous KOH (2*M*; 50 ml). Normal work-up and crystallisation from MeOH afforded the diol (2) (70 mg); m.p. 232–233 $^{\circ}\text{C}$; m/z 338 (M^+ for $\text{C}_{20}\text{H}_{34}\text{O}_4$); $[\alpha]_{\text{D}}^{24} - 52.6^{\circ}$ (c 0.805); δ_{H} (CDCl_3 - CD_3OD ; 90 MHz) 1.20, 1.26, 1.37, 1.39, 1.43 (C-Me), 1.76 (dd, *J* 12 and 14 Hz, 9-H), 2.29 (dd, *J* 6 and 14 Hz, 9-H), 2.94 (d, *J* 9 Hz, 7-H), 3.10 (dd, *J* 10 and 4 Hz, 3-H), and 4.13 (ddd, *J* 12, 6, and 2 Hz, 10-H); δ_{C} (CD_3OD) 17.6, 18.5, 24.1, 29.0, 31.1 (q), 24.8, 26.8, 38.4, 42.4, 46.2, 46.9 (t), 47.1, 57.3, 65.0, 67.0, 74.6 (d), 45.3, 61.3, 63.6, and 72.6 (s).

Ketol (3).—The diol (2) (80 mg) was dissolved in acetone (5 ml) and treated with excess of Jones' reagent at 15 $^{\circ}\text{C}$ for 5 min. Addition of water, extraction with CHCl_3 , and crystallisation of the crude product (72 mg) from CHCl_3 -light petroleum afforded the ketol (3), as plates, m.p. 161–162 $^{\circ}\text{C}$; m/z 336 (M^+ for $\text{C}_{20}\text{H}_{32}\text{O}_4$); $[\alpha]_{\text{D}}^{24} - 129.4^{\circ}$ (c 0.92); c.d. (MeOH) $\Delta\epsilon_{289} - 0.97$; o.r.d. (MeOH) $[\alpha]_{400} - 280$, $[\alpha]_{350} - 480$, $[\alpha]_{306} - 1260$, $[\alpha]_{270} - 240$, and $[\alpha]_{230} - 1620$; δ_{H} (90 MHz) 1.20, 1.22 (6 H), 1.33, 1.62 (t-Me), and 2.13 and 3.47 (ABq, *J* 16 Hz, 9- H_2); δ_{C} 16.7, 19.3, 21.8, 23.9, 31.4 (q), 24.3, 26.2, 36.7, 41.5, 43.9, 57.4 (t), 57.1, 58.3, 60.3, 63.6 (d), 46.0, 58.0, 60.4, 72.3, and 211.9 (s).

Enone (6).—A solution of the ketol (3) (72 mg) in CHCl_3 (15 ml) and MeOH (30 drops) was stirred with aqueous KOH (2%; 15 ml) at room temperature for 48 h. Normal work-up followed by p.l.c. (5% MeOH- CHCl_3) afforded the enone (6) (37 mg), m.p. 218–220 $^{\circ}\text{C}$ (from CHCl_3 -light petroleum); m/z 336 (M^+ for $\text{C}_{20}\text{H}_{32}\text{O}_4$); δ_{H} (90 MHz) 1.13, 1.16, 1.18, 1.32 (t-Me), 1.67 (d, *J* 2 Hz, 17- H_3), 2.99 (d, *J* 10 Hz, 11-H), 3.65 (brs, 3-H), 4.25 (t, *J* 8 Hz, 7-H), and 6.13 (brs, 9-H); δ_{C} 19.6, 20.9, 21.8, 22.5, 30.8 (q), 25.7, 33.2, 37.0, 42.6, 48.5 (t), 59.4, 60.0, 72.2, 80.3, 130.7 (d), 49.0, 73.0, 86.5, 138.9, and 214.9 (s) [Found: m/z 318.2196. $\text{C}_{20}\text{H}_{30}\text{O}_3$ ($M^+ - \text{H}_2\text{O}$) requires m/z 318.2195].

Diketone (7).—The enone (6) (20 mg) was dissolved in acetone (10 ml) and treated with Jones' reagent (10 drops) at 0 $^{\circ}\text{C}$ for 10 min. Normal work-up and p.l.c. gave the diketone (7) (10 mg), m.p. 134–136 $^{\circ}\text{C}$; m/z 334 (M^+ for $\text{C}_{20}\text{H}_{30}\text{O}_4$); λ_{max} 229 nm; δ_{H} (90 MHz) 1.20 (6 H), 1.28 (6 H) (t-Me), 1.73 (brs, 17- H_3), 2.95 (d, *J* 10 Hz, 11-H), 2.40 and 3.46 (ABq, *J* 10 Hz, 2- H_2), 4.56 (t, *J* 7 Hz, 7-H), and 6.15 (br, 9-H) [Found: m/z 316.2039. $\text{C}_{20}\text{H}_{28}\text{O}_2$ ($M^+ - \text{H}_2\text{O}$) requires m/z 316.2038].

Zn-Cu Couple Reduction of Barbilycopodin (1).—A solution of barbilycopodin (1) (100 mg) in absolute EtOH (10 ml) was refluxed with freshly prepared Zn-Cu couple (4 g) for 11 h. Filtration and removal of the solvent under reduced pressure yielded a crude product which was chromatographed over silica gel. Elution with hexane-ether (95:5) afforded 10*R*,18-diacetoxydolabella-3*E*,7*E*-diene (13) (60 mg) as an oil which crystallised after a time, m.p. 83–85 $^{\circ}\text{C}$; m/z 390 (M^+ for $\text{C}_{24}\text{H}_{38}\text{O}_4$); $[\alpha]_{\text{D}}^{22} - 32.2^{\circ}$ (c 2.385); ν_{max} (KBr) 1722 cm^{-1} ; δ_{H} (360 MHz) 1.35, 1.47, 1.52 (t-Me), 1.52 (16- H_3), 1.56 (17- H_3), 1.99, 2.05 (OAc), 4.93 (brd, *J* 11.4 Hz, 7-H), 5.13 (brdd, *J* 11.8 and 3.5 Hz, 3-H), and 5.43 (ddd, *J* 11.4, 6.8, and 1.7 Hz, 10-H); δ_{C} 15.7, 16.4, 22.6, 23.7, 26.0 (q), 21.3, 22.7 (OCOMe), 24.1, 26.0,

Table 3. Fractional atomic co-ordinates for 10*R*,18-dihydroxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane (2) (e.s.d.s in parentheses)

Atom	x	y	z
O(1)	0.357 5(5)	0.042 1(3)	0.430 6(3)
O(2)	0.952 0(6)	-0.254 9(2)	0.320 8(3)
O(3)	0.509 7(4)	-0.015 0(2)	0.156 7(2)
O(4)	1.014 3(4)	0.005 9(3)	0.486 4(2)
C(1)	0.797 7(5)	0.066 0(3)	0.338 2(3)
C(2)	0.653 2(7)	0.067 0(3)	0.272 1(3)
C(3)	0.652 8(6)	-0.008 9(3)	0.214 9(3)
C(4)	0.538 3(6)	-0.086 0(3)	0.215 1(3)
C(5)	0.602 6(8)	-0.168 2(4)	0.173 6(4)
C(6)	0.685 3(10)	-0.233 3(4)	0.231 2(4)
C(7)	0.837 3(7)	-0.195 7(4)	0.279 2(4)
C(8)	0.854 3(7)	-0.192 4(3)	0.369 2(3)
C(9)	0.969 6(6)	-0.124 8(3)	0.408 3(3)
C(10)	0.878 8(5)	-0.050 0(3)	0.454 8(3)
C(11)	0.740 6(5)	0.004 8(3)	0.410 1(2)
C(12)	0.648 3(5)	0.065 1(3)	0.474 1(3)
C(13)	0.653 2(7)	0.157 3(3)	0.438 6(4)
C(14)	0.805 2(7)	0.156 3(3)	0.380 0(4)
C(15)	0.974 4(6)	0.049 9(4)	0.296 1(3)
C(16)	0.395 1(7)	-0.097 3(5)	0.276 0(4)
C(17)	0.724 8(11)	-0.235 3(4)	0.424 5(5)
C(18)	0.462 9(5)	0.039 1(3)	0.502 7(2)
C(19)	0.397 2(7)	0.105 1(4)	0.565 3(4)
C(20)	0.457 7(8)	-0.051 1(4)	0.540 3(4)

Table 4. Fractional atomic co-ordinates for 10*R*,18-diacetoxy-3*S*,4*S*-epoxydolabell-7*E*-ene (12) (e.s.d.s in parentheses)

Atom	x	y	z
O(1)	-0.970 01(19)	-0.161 05(18)	-0.164 87(8)
O(2)	-0.752 8(2)	-0.270 3(2)	-0.153 5(1)
O(3)	-1.365 8(2)	-0.006 3(2)	-0.199 2(1)
O(4)	-1.321 3(5)	-0.189 2(4)	-0.245 0(1)
O(5)	-1.214 1(4)	0.230 0(3)	0.028 2(1)
C(1)	-1.254 9(3)	0.188 4(3)	-0.118 5(1)
C(2)	-1.193 6(4)	0.235 8(3)	-0.066 2(1)
C(3)	-1.269 4(4)	0.182 1(4)	-0.020 4(1)
C(4)	-1.213 5(4)	0.085 3(4)	0.017 1(1)
C(5)	-1.322 9(5)	0.001 8(5)	0.048 0(1)
C(6)	-1.359 2(4)	-0.135 9(5)	0.023 7(2)
C(7)	-1.414 0(3)	-0.118 4(4)	-0.029 5(2)
C(8)	-1.366 7(3)	-0.176 2(3)	-0.071 2(1)
C(9)	-1.419 9(3)	-0.128 2(3)	-0.121 8(1)
C(10)	-1.295 7(3)	-0.066 5(3)	-0.154 8(1)
C(11)	-1.193 4(3)	0.040 8(3)	-0.131 2(1)
C(12)	-1.056 6(3)	0.066 1(3)	-0.166 4(1)
C(13)	-1.029 9(4)	0.221 3(3)	-0.166 9(1)
C(14)	-1.185 9(4)	0.276 9(3)	-0.159 8(1)
C(15)	-1.424 1(3)	0.208 9(3)	-0.119 8(1)
C(16)	-1.060 6(4)	0.025 0(4)	0.013 7(2)
C(17)	-1.255 3(4)	-0.291 2(4)	-0.072 3(2)
C(18)	-0.915 2(3)	-0.019 7(3)	-0.156 8(1)
C(19)	-0.852 3(3)	-0.007 3(4)	-0.104 5(1)
C(20)	-0.798 6(4)	0.011 4(4)	-0.197 2(2)
C(21)	-0.881 8(3)	-0.271 3(3)	-0.164 2(1)
C(22)	-0.966 1(5)	-0.397 4(4)	-0.177 3(2)
C(23)	-1.373 3(4)	-0.077 6(4)	-0.241 3(1)
C(24)	-1.457 3(5)	-0.005 2(6)	-0.281 5(2)

40.0, 41.0, 42.6, 44.0 (t), 43.6, 54.4, 77.5, 124.7, 130.9 (d), 47.8, 84.9, 129.8, 133.3 (s), 170.5, and 170.8 (OCOMe). Further elution of the column with hexane-ether (9:1) yielded the monoepoxide (12) (5 mg), m.p. 165–166 °C (from MeOH), identical with the natural product described above.

Crystal Data.—10*R*,18-Dihydroxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane (2), C₂₀H₃₄O₄, *M* = 338.52, orthorhombic,

Table 5. Fractional atomic co-ordinates for 18-acetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane (4) (e.s.d.s in parentheses)

Atom	x	y	z
O(1)	-0.851 89(18)	-0.335 14(21)	-0.948 91(16)
O(2)	-0.870 0(2)	0.036 1(2)	-0.554 1(2)
O(3)	-0.544 9(2)	-0.297 4(2)	-0.248 9(2)
O(4)	-0.030 6(2)	-0.462 1(3)	-0.969 4(2)
C(1)	-0.458 3(2)	-0.2327	-0.645 4(2)
C(2)	-0.464 7(2)	-0.296 3(3)	-0.501 4(2)
C(3)	-0.532 0(3)	-0.238 1(3)	-0.382 7(2)
C(4)	-0.677 9(3)	-0.255 7(3)	-0.328 8(2)
C(5)	-0.746 3(3)	-0.164 3(3)	-0.251 9(2)
C(6)	-0.855 0(3)	-0.097 4(3)	-0.349 0(3)
C(7)	-0.786 4(3)	-0.047 2(3)	-0.474 2(3)
C(8)	-0.831 6(3)	-0.059 9(3)	-0.631 3(3)
C(9)	-0.719 0(3)	-0.037 7(3)	-0.737 5(2)
C(10)	-0.666 4(3)	-0.133 3(2)	-0.821 4(2)
C(11)	-0.613 6(2)	-0.236 2(2)	-0.739 4(2)
C(12)	-0.600 3(2)	-0.326 8(3)	-0.854 5(2)
C(13)	-0.450 3(3)	-0.381 9(3)	-0.812 3(3)
C(14)	-0.356 2(3)	-0.293 7(3)	-0.740 8(3)
C(15)	-0.392 6(3)	-0.121 0(3)	-0.611 9(3)
C(16)	-0.784 2(3)	-0.340 1(3)	-0.390 6(3)
C(17)	-0.964 4(3)	-0.126 1(4)	-0.687 7(4)
C(18)	-0.730 0(3)	-0.405 6(2)	-0.885 9(2)
C(19)	-0.775 5(4)	-0.461 3(3)	-0.750 7(3)
C(20)	-0.694 7(4)	-0.486 2(3)	-1.002 1(3)
C(21)	-0.989 5(3)	-0.371 7(3)	-0.987 1(2)
C(22)	-0.086 4(4)	-0.285 8(4)	-0.057 5(4)

a = 7.713(2), *b* = 15.306(5), *c* = 16.242(4) Å, *V* = 1917 Å³, *D*_c = 1.17 g cm⁻³, *Z* = 4, *F*(000) = 744, μ(Mo-*K*_α) = 0.86 cm⁻¹, space group *P*2₁2₁2₁.

10*R*,18-Diacetoxy-3*S*,4*S*-epoxydolabell-7*E*-ene (12), C₂₄H₃₈O₅, *M* = 406.60, orthorhombic, *a* = 9.015(3), *b* = 9.739(2), *c* = 26.488(9) Å, *V* = 2326 Å³, *D*_c = 1.16 g cm⁻³, *Z* = 4, *F*(000) = 888, μ(Mo-*K*_α) = 0.86 cm⁻¹, space group *P*2₁2₁2₁.

18-Acetoxy-3*S*,4*S*;7*S*,8*S*-diepoxydolabellane (4), C₂₂H₃₆O₄, *M* = 364.56, monoclinic, *a* = 9.040(1), *b* = 12.487(2), *c* = 9.228(1) Å, β = 95.90(1)°, *V* = 1036 Å³, *D*_c = 1.17 g cm⁻³, *Z* = 2, *F*(000) = 400, μ(Mo-*K*_α) = 0.84 cm⁻¹, space group *P*2₁.

Crystallographic Measurements.—Cell dimensions were derived from least-squares analysis of the setting angles of 25 reflections measured on an Enraf-Nonius CAD4 diffractometer with Mo-*K*_α radiation. For compound (2), reflections *hkl* were surveyed in the range θ < 30° and 1279 satisfied the criterion *I* > 2σ(*I*). For compound (12), reflections *hkl* were surveyed in the range θ < 26° and 2052 satisfied the criterion *I* > 2.5σ(*I*). For compound (4), reflections *hkl* and *hk̄l* were surveyed in the range θ < 27°, and after averaging 132 pairs of equivalent reflections (*R*_{merge} = 0.022), 1931 independent reflections satisfied the criterion *I* > 2.5σ(*I*).

Structure Analysis.—The crystal structures were elucidated by the direct phasing program MITHRIL.²³ After preliminary least-squares adjustment of the co-ordinates and thermal parameters of the C and O atoms, the H atoms were located in difference electron-density distributions. The H atoms were included in the least-squares calculations with isotropic thermal parameters. The weighting scheme used was *w* = 1/σ²(*F*). The calculations converged at *R* 0.041, *R*_w = 0.044 for (2), *R* = 0.041, *R*_w = 0.053 for (12), and *R* 0.032, *R*_w 0.040 for (4). The calculations were performed on an SEL 32/27 computer with the GX programs.²⁴

Atomic co-ordinates are listed in Tables 3–5. Full details

of the molecular geometries, together with observed and calculated structure amplitudes, thermal parameters, and hydrogen atom positions are included in the Supplementary Publication No. SUP 56471 (31 pp).*

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* For details of the Supplementary Publications Scheme, see Instructions for Authors (1986), *J. Chem. Soc., Perkin Trans. 1*, 1986, Issue 1. Structure factors are available from the editorial office on request.

References

- 1 S. Huneck and K. H. Overton, *Phytochemistry*, 1971, **10**, 3279.
- 2 J. D. Connolly, *Rev. Latinoam. Quim.*, 1981, **12**, 121.
- 3 A. Matsuo, K. Uohama, S. Hayashi, and J. D. Connolly, *Chem. Lett.*, 1984, 599.
- 4 C. Tringali, G. Oriente, M. Piattelli, and G. Nicolosi, *J. Nat. Prod.*, 1984, **47**, 615.
- 5 V. Amico, G. Oriente, M. Piattelli, C. Tringali, E. Fattorusso, S. Magna, and L. Mayol, *Tetrahedron*, 1980, **36**, 1409.
- 6 S. A. Look and W. Fenical, *J. Org. Chem.*, 1982, **47**, 4129.
- 7 C. Ireland, D. J. Faulkner, J. Finer, and J. Clardy, *J. Am. Chem. Soc.*, 1976, **98**, 4664.
- 8 C. Ireland and D. J. Faulkner, *J. Org. Chem.*, 1977, **42**, 3157.
- 9 A. G. González, J. D. Martin, M. Norte, R. Pérez, V. Weyler, S. Rafii, and J. Clardy, *Tetrahedron Lett.*, 1983, **24**, 1075.
- 10 V. Amico, R. Currenti, G. Oriente, M. Piattelli, and C. Tringali, *Phytochemistry*, 1981, **20**, 848.
- 11 C. Tringali, M. Piattelli, and G. Nicolosi, *Tetrahedron*, 1984, **40**, 799.
- 12 H. H. Sun and W. Fenical, *Phytochemistry*, 1979, **18**, 340.
- 13 S. De Rosa, S. De Stefano, E. Trivellone, and N. Zavodnik, 14th IUPAC Symposium on the Chemistry of Natural Products, Posnan, 1984, Abstracts, p. 120.
- 14 A. Matsuo and G. A. Sim, unpublished results.
- 15 A. Matsuo, K. Uohama, K. Yoshida, M. Nakayama, S. Hayashi, J. D. Connolly, and G. A. Sim, *Chem. Lett.*, 1985, 935.
- 16 D. K. MacAlpine, A. L. Porte, and G. A. Sim, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1385.
- 17 Z. F. Khan, D. K. MacAlpine, A. L. Porte, and G. A. Sim, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1259.
- 18 A. T. McPhail, R. I. Reed, and G. A. Sim, *Chem. Ind. (London)*, 1964, 976; J. A. Hartsuck and I. C. Paul, *ibid.*, p. 977; A. T. McPhail and G. A. Sim, *J. Chem. Soc. B*, 1966, 112.
- 19 M. E. Cradwick, P. D. Cradwick, and G. A. Sim, *J. Chem. Soc., Perkin Trans. 2*, 1973, 404.
- 20 P. Murray-Rust and J. Murray-Rust, *Acta Crystallogr., Sect. B*, 1977, **33**, 3931.
- 21 D. N. J. White and M. J. Bovill, *J. Chem. Soc., Perkin Trans. 2*, 1977, 1610.
- 22 M. A. Russell, G. A. Sim, and D. N. J. White, unpublished results.
- 23 C. J. Gilmore, *J. Appl. Crystallogr.*, 1984, **17**, 42.
- 24 P. R. Mallinson and K. W. Muir, *J. Appl. Crystallogr.*, 1985, **18**, 51.

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