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DOLABELLANE DITERPENOIDS FROM THE LIVERWORT *ODONTOSCHISMA DENUDATUM*

AKIHIKO MATSUO,* KI-ICHIRO KAMIO, KATSUMI UOHAMA, KEN-ICHIRO YOSHIDA, JOSEPH D CONNOLLY† and GEORGE A. SIM†

Department of Chemistry, Faculty of Science, Hiroshima University, Naka-ku, Hiroshima 730, Japan, †Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, U K

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Key Word Index—*Odontoschisma denudatum*, Hepaticae, bryophyte, dolabellane diterpenoids, structural determination, absolute configuration, antifungal activity

Abstract—Five new dolabellane diterpenoids have been isolated from the liverwort *Odontoschisma denudatum*, and their structures and absolute configurations have been determined on the basis of ^{1}H and ^{13}C NMR evidence and chemical correlation.

INTRODUCTION

The less common diterpenoids of the Hepaticae include verrucosane and neoverrucosane derivatives from *Mylia verrucosa* [1, 2] and fusicoccane derivatives from *Anastrepta orcadensis* [3] and *Plagiochila acanthophylla* subsp. *japonica* [4] Such carbon skeletons and the tricyclic dolastane framework [5] may be biosynthesized by cyclization of dolabellane derivatives. Initially dolabellanes appeared to be restricted to marine algae and herbivorous molluscs [6, 7] but recently they have been reported from the liverworts *Odontoschisma denudatum* [8] and several *Barbilophozia* species [9].

In the present paper we describe the details of the structural elucidation of five dolabellane diterpenoids which we have isolated from the leafy liverwort *Odontoschisma denudatum* (Nees) Dum. which belongs to the Cephaloziaceae of the Jungermanniales and usually grows on decayed wood. The major compound, (+)-acetoxyodontoschismenol (**1**), which has been reported in a preliminary paper [8], has been shown to be (1*R*,6*R*,11*R*,12*R*)-6-acetoxy-12-hydroxydolabella-3*E*,7*E*-diene on the evidence presented below. The structures of the four minor constituents, (1*R*,6*R*,11*R*,12*R*)-6,12-dihydroxydolabella-3*E*,7*E*-diene (**2**), (1*R*,6*R*,11*R*,12*R*)-6-acetoxy-12,16-dihydroxydolabella-3*E*,7*E*-diene (**3**), (1*R*,-6*R*,11*R*,12*R*)-6,16-diacetoxy-12-hydroxydolabella-3*E*,-7*E*-diene (**4**) and (1*R*,3*S*,4*S*,6*R*,11*R*,12*R*)-6-acetoxy-3,4-epoxy-12-hydroxydolabell-7*E*-en-16-al (**5**) have been established by chemical correlation with compound **1**. The antifungal activity of these diterpenoids is discussed.

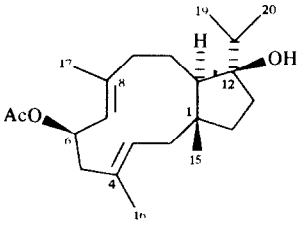
RESULTS AND DISCUSSION

The liverwort, *Odontoschisma denudatum*, was extracted with methanol, and the extract was then partitioned with ethyl acetate The ethyl acetate extract, obtained in 2.6% yield, was submitted to a combination of column chromatography (CC) and preparative thin layer chromatography over silica gel to yield five new dolabellane diterpenoids (**1**–**5**) in yields of 4.2, 0.4, 0 9, 1 4 and 0 6%, respectively, of the ethyl acetate extract

Structure of the major dolabellanoid (+)-acetoxyodontoschismenol (**1**)

The major compound, (+)-acetoxyodontoschismenol (**1**), $C_{22}H_{36}O_3$, mp 56–57°, $[\alpha]_D$ +66 2°, was a bicarbocyclic diterpenoid containing a secondary acetoxy [ν_{max} 1730, 1255 cm^{-1}; δ2.01 (3H, *s*), 5 60 (1H, *ddd*, *J* = 11 7, 11.2 and 5.3 Hz); δ170.4 (*s*), 69 5 (*d*), 21.3 (*q*)], a tertiary hydroxy [ν_{max} 3635, 3519 cm^{-1}; δ87.3 (*s*)] and two trisubstituted double bonds [ν_{max} 855 cm^{-1}; δ1.55 (3H, *t*, *J* = 1.0 Hz), 1.76 (3H, *d*, *J* = 1 1 Hz), 5 09 (1H, *br d*, *J* = 10.2 Hz), 5.21 (1H, *br d*, *J* = 12.3 Hz); δ139 9 (*s*), 127.4 (*d*), 125.4 (*d*), 131.7 (*s*), 17 9 (*q*), 16 6 (*q*)] as well as a tertiary methyl [δ1 03 (3H, *s*); δ44.2 (*s*), 23.7 (*q*)] and an isopropyl group [ν_{max} 1390, 1380 cm^{-1}; δ0 90 (3H, *d*, *J* = 6.8 Hz), 0 96 (3H, *d*, *J* = 6.7 Hz); δ35.0 (*d*), 19.8 (*q*), 18.9 (*q*)]. In addition the ^{13}C NMR spectrum exhibited the presence of six methylene carbons [δ45 5, 43.4, 40 8, 36 0, 30.4, 25.9 (each *t*)] and one methine carbon [δ 46.2 (*d*)] The ^{13}C NMR shifts are shown in Table 1 together with those of the other dolabellanoids (**2**–**5**). The existence of the above functional groups in compound **1** was confirmed by the following chemical reactions (i) by alkaline hydrolysis the acetate (**1**) was converted into the 6β,12β-diol (**2**), $C_{20}H_{34}O_2$ [ν_{max} 3620, 3450 cm^{-1}; δ4 62 (1H, *ddd*, *J* = 10, 10 and 5 Hz)] (ii) Dehydration of **1** with thionyl chloride in pyridine gave the 3,7,12-triene (**6**), $C_{22}H_{34}O_2$ [ν_{max} 859 cm^{-1}; δ5.01 (1H, *br d*, *J* = 10 Hz), 5 23 (1H, *br s*, $W_{1/2}$ = 6 Hz) and 5 36 (1H, *br d*, *J* = 11 Hz)] (iii) The diene (**1**) was oxidized exclusively to the 3*S*,4*S*-monoepoxide (**7**), $C_{22}H_{36}O_4$ [δ1.22 (3H, *s*), 2.88 (1H, *dd*, *J* = 10 and 2 Hz); δ62.6 (*d*), 60.4 (*s*)] with one equivalent of *m*-chloroperbenzoic acid (MCPBA) in chloroform at room temperature, although under reflux with two equivalents of the peracid in chloroform the diene (**1**) produced the 3*S*,4*S*; 7*S*,8*S*-bisepoxide (**8**),

*Author to whom correspondence should be addressed



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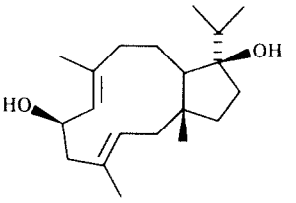

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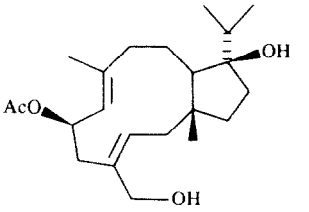

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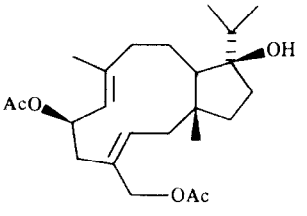

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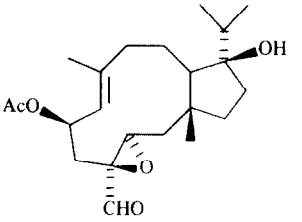

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Table 1 The ^{13}C NMR chemical shifts of the dolabellane diterpenoids

Compound	1	2	3	4	5	6	7	8
C								
1	44.2 *s*	44.3 *s*	44.2 *s*	43.8 *s*	43.1 *s*	46.3 *s*	42.9 *s*	43.6 *s*
2	40.8 *t*[a]	40.8 *t*[a]	40.9 *t*[a]	40.7 *t*[a]	42.1 *t*[a]	41.8 *t*[a]	42.1 *t*[a]	41.8 *t*[a]
3	127.4 *d*	129.6 *d*	131.1 *d*	133.7 *d*	63.9 *d*	128.7 *d*	62.6 *d*	63.0 *d*
4	131.7 *s*	132.7 *s*	135.4 *s*	130.0 *s*	63.6 *s*	132.3 *s*	60.4 *s*	58.4 *s*
5	45.5 *t*	49.0 *t*[a]	40.9 *t*[a]	40.7 *t*[a]	37.4 *t*[a]	45.9 *t*[a]	44.2 *t*[a]	43.4 *t*[a]
6	69.5 *d*	66.3 *d*	70.2 *d*	69.8 *d*	67.6 *d*	69.6 *d*	68.0 *d*	69.1 *d*
7	125.4 *d*	126.3 *d*	125.5 *d*	125.2 *d*	123.7 *d*	127.7 *d*	123.9 *d*	60.9 *d*
8	139.9 *s*	137.1 *s*	140.3 *s*	140.3 *s*	142.1 *s*	139.6 *s*	141.5 *s*	63.7 *s*
9	36.0 *t*[a]	35.7 *t*[a]	36.1 *t*[a]	36.0 *t*[a]	36.3 *t*[a]	38.1 *t*[a]	35.7 *t*[a]	36.9 *t*[a]
10	25.9 *t*[a]	25.9 *t*[a]	25.7 *t*[a]	25.4 *t*[a]	24.2 *t*[a]	25.7 *t*[a]	24.3 *t*[a]	23.4 *t*[a]
11	46.2 *d*	46.0 *d*	46.3 *d*	46.0 *d*	47.2 *d*	47.5 *d*	46.8 *d*	48.3 *d*
12	87.3 *s*	87.5 *s*	87.8 *s*	87.4 *s*	87.8 *s*	153.9 *s*	87.7 *s*	86.4 *s*
13	30.4 *t*[a]	30.4 *t*[a]	30.6 *t*[a]	30.2 *t*[a]	32.2 *t*[a]	118.9 *d*	31.6 *t*[a]	32.4 *t*[a]
14	44.4 *t*[a]	43.3 *t*[a]	42.8 *t*[a]	42.7 *t*[a]	42.2 *t*[a]	48.5 *t*[a]	43.5 *t*[a]	43.2 *t*[a]
15	23.7 *q*	23.6 *q*	23.5 *q*	23.1 *q*	22.5 *q*	23.4 *q*	23.3 *q*	21.7 *q*
16	16.6 *q*	16.7 *q*	59.8 *t*	62.0 *t*	199.8 *d*	15.9 *q*	17.1 *q*[b]	17.6 *q*[b]
17	17.9 *q*	17.9 *q*	17.9 *q*	17.6 *q*	17.6 *q*	17.3 *q*	17.8 *q*[b]	17.6 *q*[b]
18	35.0 *d*	34.9 *d*	35.0 *d*	34.6 *d*	36.0 *d*	27.3 *d*	35.7 *d*	36.5 *d*
19	18.9 *q*	18.8 *q*	18.9 *q*	18.4 *q*	18.3 *q*	21.5 *q*[b]	18.6 *q*	18.6 *q*[b]
20	19.8 *q*	19.5 *q*	19.6 *q*	19.3 *q*	18.4 *q*	22.3 *q*[b]	19.0 *q*	21.0 *q*[c]
Ac-Me	21.3 *q*	—	21.3 *q*	20.7 *q*	21.2 *q*	21.3 *q*[b]	21.3 *q*	21.2 *q*[c]
Ac-Me	—	—	—	20.7 *q*	—	-	—	—
Ac-CO	170.4 *s*	—	170.8 *s*	170.3 *s*	169.9 *s*	170.6 *s*	170.3 *s*	170.0 *s*
Ac-CO	—	—	—	170.7 *s*				

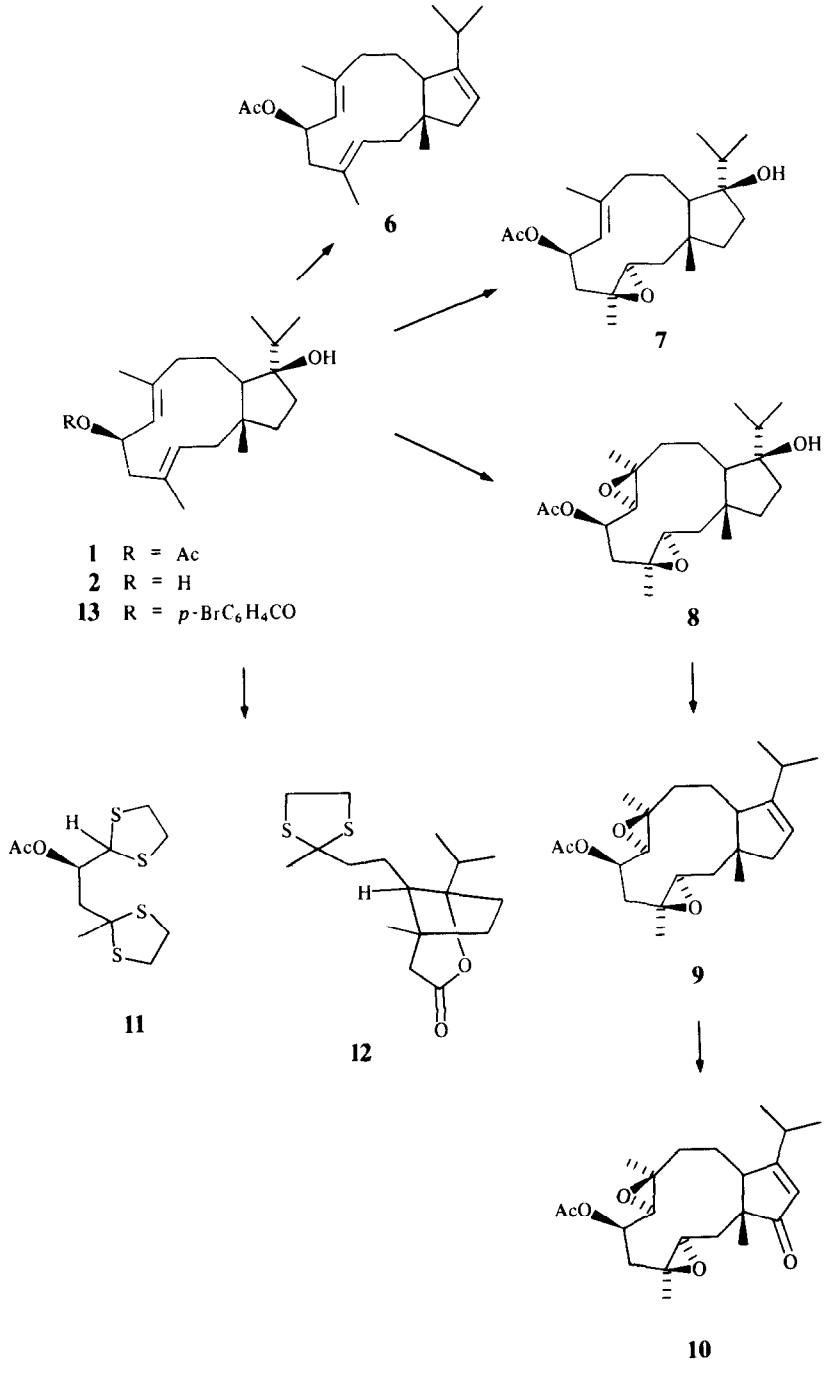
[a,b,c] Assignments may be interchanged

$C_{22}H_{36}O_5$ [δ1.36 (3H, *s*), 1.55 (3H, *s*), 2.89 (1H, *d*, J = 9.5 Hz), 3.07 (1H, *dd*, J = 8.8 and 1.1 Hz), δ63.7 (*s*), 63.0 (*d*), 60.9 (*d*), 58.4 (*s*)], accompanying a minor isomer, the structure of which will be described elsewhere

In an attempt to determine the size of the ring to which the tertiary hydroxy group is attached, the major bisepoxide (**8**) was first treated with $POCl_3$ in pyridine to give the dehydrated product **9**, $C_{22}H_{34}O_4$ [δ5.28 (1H, *br s*, $W_{1/2}$ = 4 Hz)], which was then submitted to allylic oxidation with Collins reagent to afford the enone **10**, $C_{22}H_{32}O_5$. The IR and UV spectra [ν_{max} 1706, 1621 cm^{-1}, λ_{max} 230 nm] suggested the presence of an

α,β-unsaturated cyclopentenone structure. Moreover, the failure of any protons to move downfield, apart from the vinyl proton [δ 5.90 (1H, *s*)] suggested that the ketonic carbonyl was flanked by a fully substituted carbon atom

Certain significant information about the other ring was obtained by ozonolysis of the original diene (**1**) in methanol followed by reductive cleavage of the ozonide with dimethyl sulphide to give unstable products which were immediately treated with 1,2-ethanedithiol and boron trifluoride etherate to give the two components as the thioketal derivatives **11** and **12** The structure of the smaller fragment (**11**), $C_{11}H_{18}O_2S_4$, was elucidated by analysis of the ^1H NMR and ^{13}C NMR spectral data as the bisthioketal derivative of 2-acetoxylevulinic aldehyde (**11**) (see Experimental). This revealed the presence of a 1,5-diene partial structure in the parent molecule (**1**) The spectroscopic properties of the larger fragment (**12**), $C_{17}H_{28}O_2S_2$, suggested it was a δ-lactone [ν_{max} 1728 cm^{-1}] containing the original cyclopentane ring substituted by an isopropyl and a tertiary methyl together with a newly formed (2-thioketal)-butyl group (see Experimental) The formation of this lactone suggested



that the C-12 hydroxy group of **1** was in the α-configuration and *trans* to the C-1 methyl group

The above chemical and spectroscopic evidence in conjunction with the biogenetic isoprene rule [10] indicated that acetoxyodontoschismenol (**1**) was a dolabellane diterpenoid containing two double bonds (Δ^3 and Δ^7), a 12-hydroxy group and a 6β-acetoxy moiety The structure **1**, excluding the configuration of the 12-hydroxy group, was supported by extensive decoupling experiments at 360 MHz. In addition, difference NOE experiments [1-Me and 3-H (13%), 4-Me and 6-H (10%), 8-Me and 6-H (10%)] and the ^{13}C NMR chemical shifts of the C-4 and C-8 methyl groups [δ 16 6 and 17 9 (each *q*)] revealed that both double bonds had the *E*-configuration The complete structure, including the configuration of the C-12 hydroxy group, was determined unequivocally by X-ray analysis of the *p*-bromobenzoate (**13**), $C_{27}H_{37}O_3Br$ A computer-generated perspective drawing is shown in Fig 1 The details of this crystal structure analysis appear in reference [8] Since the C-12 hydroxy group has a β-configuration and has a *cis*-relationship to the C-1 methyl group, the formation of the δ-lactone (**12**) must be accompanied by inversion of configuration at C-12

The conformation of **1** in the crystalline state (X-ray analysis) [8] and the major conformer in solution (^1H NMR spectrum) [11] correspond to the CC conformer of the sesquiterpene humulene [12] The absolute configuration of (+)-acetoxyodontoschismenol as in **1** was determined by the exciton chirality method [240 nm ($\Delta\varepsilon$ −8 36)] on the allylic *p*-bromobenzoate (**13**) This result was confirmed by anomalous dispersion in the X-ray analysis [8] Accordingly, the structure and absolute configuration of the major dolabellanoid (+)-acetoxyodontoschismenol is represented as (1*R*,6*R*,11*R*,12*R*)-6-acetoxy-12-hydroxydolaballa-3*E*,7*E*-diene (**1**)

Structures of the four minor dolabellanoids (**2**–**5**)

Four dolabellanoids (**2**–**5**) were subsequently isolated in minor amount from the same liverwort, and their structures were correlated chemically with 6β-acetoxy-12β-hydroxydolabella-3*E*,7*E*-diene (**1**) as follows The spectral data of the diol (**2**), $C_{20}H_{34}O_2$, mp 139–140°, $[\alpha]_D$ +56 2°, suggested it was a bicyclic diterpenoid containing tertiary and secondary hydroxy groups, two trisubstituted double bonds, a tertiary methyl and an isopropyl group This compound was found to be identical in all respects including the optical rotation with the diol obtained by alkaline hydrolysis of **1** Acetylation of the natural diol (**2**) afforded the major dolabellanoid (**1**) The third compound (**3**), $C_{22}H_{36}O_4$, mp 103 5–104 5 °, $[\alpha]_D$ +36 0°, and the fourth compound (**4**), $C_{24}H_{38}O_5$, mp 76–77 °, $[\alpha]_D$ +2 9°, had spectral data similar to those of **1**, except for the resonance of a primary hydroxy group [δ 3 93 and 4 21 (each 1H, *d*, *J* = 12 Hz), δ 59 8 (*t*) in **3**] and a primary acetoxy group [δ 4 42 and 4 68 (each 1H, *d*, *J* = 12 Hz), δ 62 0 (*t*) in **4**] replacing those of the vinyl methyl group at C-16 Acetylation of **3** with acetic anhydride in pyridine gave the hydroxy-diacetate (**4**) When the acetoxy-diol (**3**) was treated with the pyridine sulphur trioxide complex followed by lithium aluminium hydride to reduce the allylic hydroxymethyl to a methyl group, the diol **2** was obtained. The structure and stereochemistry of **3** were confirmed by X-ray analysis [13] The ^1H NMR and ^{13}C NMR data of the most oxygenated compound (**5**), $C_{22}H_{34}O_5$, $[\alpha]_D$ −23 3 °, revealed that it was a dolabellane diterpenoid with a secondary acetytoxy, a tertiary hydroxy, a trisubstituted double bond, an epoxy group [δ 3 27 (1H, *dd*, *J* = 10 and 3 Hz), δ 63 9 (*d*), 63 6 (*s*)] and an aldehyde [δ 9 34 (1H, *d*, *J* = 1 Hz), δ 199 8 (*d*)] These data suggested that this epoxy-aldehyde was the 16-oxo derivative (**5**) of the monoepoxide (**7**) Confirmation of this proposal was obtained as follows The allylic alcohol (**3**) was oxidized with *m*-chloroperbenzoic acid to give the 3*S*,4*S*-monoepoxide which was transformed by PDC oxidation into the epoxy-aldehyde (**5**), identical in all respects with the natural compound

From the above chemical and spectroscopic evidence the structures and absolute configurations of the four minor diterpenoids (**2**–**5**) were deduced to be (1*R*,6*R*,11*R*,12*R*)-6,12-dihydroxydolabella-3*E*,7*E*-diene (**2**), (1*R*,6*R*,11*R*,12*R*)-6-acetoxy-12,16-dihydroxydolabella-3*E*,7*E*-diene (**3**), (1*R*,6*R*,11*R*,12*R*)-6,16-diacetoxy-12-hydroxydolabella-3*E*,7*E*-diene (**4**) and (1*R*,3*S*,4*S*,6*R*,11*R*,12*R*)-6-acetoxy-3,4-epoxy-12-hydroxydolabell-7*E*-en-16-al (**5**)

Biological activity

Since the liverwort *Odontoschima denudatum* usually grows on decayed wood, it seemed likely that the plant contains some antimicrobial compounds. The growth-inhibitory activity on these plant pathogenic fungi of the dolabellane diterpenoids, 6β-acetoxy-12β-hydroxy- (**1**), 6β,12β-dihydoxy- (**2**), 6β-acetoxy-12β,16-dihydroxydolaballa-3*E*,7*E*-diene (**3**), and the 3*S*,4*S*-monoepoxide (**7**) and the 3*S*,4*S*,7*S*,8*S*-diepoxide (**8**), was tested The percent inhibition of the dolabellanoids determined at the concentration of 100 ppm is shown in Table 2

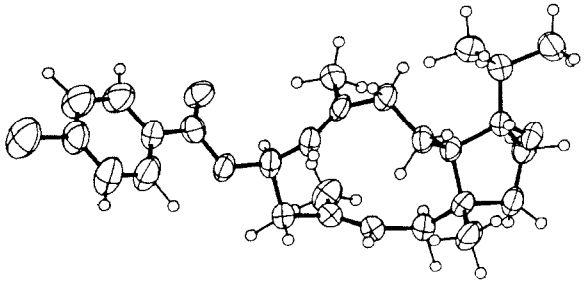


Fig 1 A perspective view of the *p*-bromobenzoate (**13**).

Table 2 Growth-inhibitory activity of the dolabellane diterpenoids (at 100 ppm) on the pathogenic fungi

	1	**2**	**3**	**7**	**8**
B cinerea	39%	44	13	10	35
R solani	38	24	20	30	38
P debaryanum	22	28	5	11	14

EXPERIMENTAL

General procedure Mps uncorr IR and $[\alpha]_D$ $CHCl_3$ at room temp ^1H NMR (90, 360 or 400 MHz) and ^{13}C NMR (22 63 MHz) $CDCl_3$ with TMS as int standard, EIMS 70 eV, UV EtOH, CC Merck kieselgel 60, TLC and prep TLC Merck kieselgel 60 PF_{254}, Analytical plates were visualized under UV radiation, iodine vapour or spraying with 10% H_2SO_4 in EtOH followed by heating at 120°

Material and its extraction The liverwort, *Odontoschisma denudatum*, which grows on decayed wood, was collected in a forest at Motoyama-cho, in Kochi-ken, Shikoku The whole plant (1 71 kg) was separated carefully from the decayed wood, washed with H_2O, dried in the shade for several days, and extracted × 3 with MeOH for 1 week at room temp The solvent was distilled off under red pres and the oily material obtained was extracted with EtOAc. Removal of the solvent under red pres. gave a viscous oil (43 7 g)

Isolation of the constituents (**1**–**5**) The EtOAc extract (23 0 g) was firstly chromatographed on a column of silica gel (600 g), using hexane containing increasing amounts of EtOAc as eluant. The separated fractions were then subjected to a combination of CC and prep TLC on silica gel to isolate the following compounds in order of elution (1*R*,6*R*,11*R*,12*R*)-6-acetoxy-12-hydroxydolabella-3*E*,7*E*-diene, (+)-acetoxyodontoschismenol (**1**) (970 mg), (1*R*,6*R*,11*R*,12*R*)-6,16-diacetoxy-12-hydroxydolabella-3*E*,7*E*-diene (**4**) (210 mg), (1*R*,3*S*,4*S*,6*R*,11*R*,12*R*)-6-acetoxy-3,4-epoxy-12-hydroxydollabell-7*E*-en-16-al (**5**) (140 mg), (1*R*,6*R*,11*R*,12*R*)-6-acetoxy-12,16-dihydroxydolabella-3*E*,7*E*-diene (**3**) (320 mg) and (1*R*,6*R*,11*R*,12*R*)-6,12-dihydroxydolabella-3*E*,7*E*-diene (**2**) (90 mg). The physical constants and spectroscopic properties of these compounds are listed below

(1R,6R,11R,12R)-6-*Acetoxy*-12-*hydroxydolabella*-3E,7E-*diene* [(+)-*acetoxyodontoschismenol*] (**1**) $C_{22}H_{36}O_3$ (Found C, 75 98, H, 10 48, requires C, 75 81, H, 10.41%), mp 75–76°, $[\alpha]_D$ +66 2° (*c*, 0 9), IR ν_{max} cm^{-1}. 3635, 3510, 2985, 1730, 1680, 1390, 1380, 1255, 1030, 970, 850; ^1H NMR (360 MHz) δ0 90 (3H, *d*, *J* = 6 8 Hz, isopro-Me), 0 96 (3H, *d*, *J* = 6 7 Hz, isopro-Me), 1 03 (3H, *s*, 1-Me), 1.47 (1H, *ddd*, *J* = 9 6, 4 0 and 1 0 Hz, 11-H), 1.54 (1H, *dddd*, *J* = 14 5, 11 3, 4 0 and 3 7 Hz, 10-H), 1 55 (3H, *t*, *J* = 1 0 Hz, 4-Me), 1.69 (1H, *d*, *J* = 13 0 Hz, 2-Hβ), 1.69 (1H, *dddd*, *J* = 14 5, 9 6, 6 1 and 4 8 Hz, 10-Hβ), 1 76 (3H, *d*, *J* = 1 1 Hz, 8-Me), 1 86 (1H, *dddd*, *J* = 14 5, 11 3, 4 8 and 1 0 Hz, 9-Hβ), 2 01 (3H, *s*, Ac-Me), 2.10 (1H, *dd*, *J* = 11 5 and 10 7 Hz, 5-Hβ), 2 16 (1H, *dd*, *J* = 13 0 and 12 3 Hz, 2-Hα), 2 32 (1H, *ddd*, *J* = 14 5, 6 1 and 3 7 Hz, 9-Hα), 2.50 (1H, *dd*, 11 5 and 5.3 Hz, 5-Hα), 5 09 (1H, *br d*, *J* = 10 2 Hz, 7-H), 5 21 (1H, *br d*, *J* = 12 3 Hz, 3-H), 5 60 (1H, *ddd*, *J* = 11 7, 11.2 and 5.3 Hz, 6-H), MS *m/z* (rel int) 348 $[M]^+$ (1), 330 (4), 288 (23), 270 (5), 245 (14), 227 (10), 219 (9), 201 (7), 159 (9), 135 (14), 121 (13), 107 (20), 93 (24), 81 (19), 71 (25), 55 (24), 43 (100)

(1R,6R,11R,12R)-6,12-*Dihydroxydolabella*-3E,7E-*diene* (**2**). $C_{20}H_{34}O_2$ (Found: C, 78 41, H, 11 45, requires C, 78 38, H, 11 18%), mp 139–140°, $[\alpha]_D$ +56 2° (*c*, 1.3), IR ν_{max} cm^{-1} 3625, 3450, 2975, 1670, 1445, 1390, 1230, 1010, ^1H NMR (400 MHz): δ0 91 (3H, *d*, *J* = 7.0 Hz, isopro-Me), 0.98 (3H, *d*, *J* = 6 6 Hz, isopro-Me), 1 06 (3H, *s*, 1-Me), 1.55 (3H, *s*, 4-Me), 1.71 (3H, *d*, *J* = 0 7 Hz, 8-Me), 2 03 (1H, *dd*, *J* = 11.0 and 10 3 Hz, 5-Hβ), 2 17 (1H, *dd*, *J* = 13.2 and 12 5 Hz, 2-Hα), 2 34 (1H, *dt*, *J* = 14 7 and 4 4 Hz, 9-Hα), 2 55 (1H, *dd*, *J* = 11 0 and 5 5 Hz, 5-Hα), 4 62 (1H, *ddd*, *J* = 10 3, 9.9 and 5 5 Hz, 6-H) 5 14 (1H, *dd*, *J* = 9.9 and 1 5 Hz, 7-H), 5 20 (1H, *br d*, *J* = 12 5 Hz, 3-H), MS *m/z* (rel. int.) 306 $[M]^+$ (3), 288 (29), 270 (14), 245 (12), 227 (20), 219 (36), 178 (28), 172 (26), 159 (27), 149 (26), 135 (53), 123 (52), 107 (64), 93 (67), 55 (75), 43 (100)

(1R,6R,11R,12R)-6-*Acetoxy*-12,16-*dihydroxydolabella*-3E,7E-*diene* (**3**) $C_{22}H_{36}O_4$ (Found C, 72.28, H, 10 05, requires C, 72 49, H, 9 96%), mp 103 5–104 5°, $[\alpha]_D$ +36 0° (*c*, 1 4), IR ν_{max} cm^{-1} 3630, 3470, 2980, 1720, 1445, 1370, 1250, 1025, 960; ^1H NMR (90 MHz): δ0.91 and 0 98 (each 3H isopro-Me_2), 1 09 (3H, *s*, 1-Me), 1 73 (3H, *s*, 8-Me), 2.03 (3H, *s*, Ac-Me), 2 87 (1H, *dd*, *J* = 10 and 5 Hz, 5-Hα), 3 93 and 4 21 (each 1H, *d*, *J* = 12 Hz, 16-H_2), 5 11 (1H, *br d*, *J* = 10 Hz, 7-H), 5 38 (1H, *dd*, *J* = 12 and 4 Hz, 3-H), 5 63 (1H, *ddd*, *J* = 10, 10 and 5 Hz, 6-H), MS *m/z* (rel int) 364 $[M]^+$ (1), 346 (19), 304 (15), 286 (9), 261 (13), 243 (18), 219 (14), 201 (14), 159 (23), 133 (19), 123 (22), 105 (21), 97 (26), 81 (32), 71 (44), 55 (30), 43 (100)

(1R,6R,11R,12R)-6,16-*Diacetoxy*-12-*hydroxydolabella*-3E,7E-*diene* (**4**) $C_{24}H_{38}O_5$ (Found M^+, 406 2743, requires M, 406 2720), mp 76–77°, $[\alpha]_D$ +2 9° (*c*, 1 1), IR ν_{max} cm^{-1} 3600, 3510, 2960, 1730, 1450, 1375, 1250, 1030, 1020, 960, ^1H NMR (90 MHz) δ0 91 and 0 97 (each 3H, *d*, *J* = 7 Hz, isopro-Me_2), 1 11 (3H, *s*, 1-Me), 1 76 (3H, *d*, *J* = 1 Hz, 8-Me), 2.03 and 2 10 (each 3H, *s*, Ac-Me_2), 2 68 (1H, *dd*, *J* = 13 and 5 Hz, 5-Hα), 4 42 and 4 68 (each 1H, *d*, *J* = 12 Hz, 16-H_2), 5 11 (1H, *br d*, *J* = 10 Hz, 7-H), 5 48 (1H, *dd*, *J* = 11 and 3 Hz, 3-H) 5.65 (1H, *ddd*, *J* = 10, 10 and 5 Hz, 6-H), MS *m/z* (rel. int.) 406 $[M]^+$ (1), 388 (12), 346 (7), 286 (14), 243 (16), 159 (18), 133 (11), 119 (12), 195 (14), 93 (16), 83 (23), 71 (31), 55 (18), 43 (100)

(1R,3S,4S,6R,11R,12R)-6-*Acetoxy*-3,4-*epoxy*-12-*hydroxydolabell*-7E-en-16-al (**5**) $C_{22}H_{34}O_5$ (Found: M^+, 378 2398, requires M, 378 2407), $[\alpha]_D$ −23 3° (*c*, 2 2), IR ν_{max} cm^{-1} 3635, 3510, 2985, 1735, 1680, 1450, 1375, 1250, 1145, 1030, 1020, 970, ^1H NMR (90 MHz) δ0 83 and 0 94 (each, 3H, *d*, *J* = 7 Hz, isopro-Me_2), 1 24 (3H, *s*, 1-Me), 1 80 (3H, *d*, *J* = 1 Hz, 8-Me), 2.01 (3H, *s*, Ac-Me), 2 71 (1H, *dd*, *J* = 12 and 6 Hz, 5-Hα), 3.27 (1H, *dd*, *J* = 10 and 3 Hz, 3-H), 5 17 (1H, *brd*, *J* = 10 Hz, 7-H), 6 12 (1H, *ddd*, *J* = 10, 10 and 6 Hz, 6-H), 9 34 (1H, *d*, *J* = 1 Hz, 16-H), MS *m/z* (rel int) 378 $[M]^+$ (1), 360 (2), 335 (4), 318 (6), 300 (3), 289 (5), 275 (15), 257 (8), 201 (10), 165 (14), 147 (16), 135 (15), 123 (24), 109 (24), 93 (26), 81 (42), 71 (53), 55 (33), 43 (100)

Alkaline hydrolysis of the acetoxy-alcohol (**1**) The acetate (**1**) (25 0 mg) was added to 5% methanolic KOH soln (2 ml), and the mixture was refluxed for 3 hr The reaction mixture was poured into H_2O, acidified with dil HCl and extracted with CH_2Cl_2 The crude product, after drying with Na_2SO_4 and evapd the solvent, was subjected to prep TLC to isolate the diol (**2**) (19 3 mg)

Dehydration of the acetoxy-alcohol (**1**) To a cooled soln of the alcohol (**1**) (32.6 mg) in pyridine (1 ml) was added $SOCl_2$ (15 mg) in pyridine (2 ml), and the mixture stirred for 6 hr at 70° The mixture was poured into ice-H_2O and extracted with $CHCl_3$ The $CHCl_3$ soln was washed with 5% aq H_2SO_4, 5% aq $NaCO_3$, dried with Na_2SO_4, and the solvent was evapd to leave the crude product This was purified by prep TLC, yielding the triene (**6**) (11 0 mg) as a gum

(1R,6R,11R,12R)-6-*Acetoxydolabella*-3E,7E,12-*triene* (**6**) $[\alpha]_D$ 0° (*c* 2 0), IR ν_{max} cm^{-1}. 1725, 1385, 1373, 1250, 1023, 959, 859, ^1H NMR (90 MHz): δ0 98 (3H, *d*, *J* = 7 Hz, isopro-Me), 1 09 (3H, *d*, *J* = 6 Hz, isopro-Me), 1 19 (3H, *s*, 1-Me), 1.56 (3H, *br s*, 4-Me), 1 77 (3H, *br s*, 8-Me), 2 03 (3H, *s*, Ac-Me), 2 56 (1H, *dd*, *J* = 11 and 5 5 Hz 5-Hα), 5 01 (1H, *br d*, *J* = 10 Hz, 7-H), 5 23 (1H, *br s*, $W_{1/2}$ = 6 Hz, 13-H), 5 36 (1H, *br d*, *J* = 11 Hz, 3-H), 5.65 (1H, *ddd*, *J* = 11, 10 and 5.5 Hz, 6-H), MS *m/z* (rel int) 330 $[M]^+$ (7), 315 (2), 287 (3), 270 (34), 255 (8), 227 (17), 201 (8), 191 (55), 175 (6), 159 (13) 149 (25), 135 (100), 121 (56), 107 (52), 93 (54), 83 (50), 69 (21), 55 (27), 43 (62)

Epoxidation of the diene (**1**) (i) Formation of the monoepoxide (**7**). To a soln of the diene (**1**) (27 1 mg) in $CHCl_3$ (1 ml) was added MCPBA (14 mg) in $CHCl_3$ (1 ml) with stirring for 30 min After decomposition of the peracid with KI and drying with Na_2SO_4 the solvent was evapd to obtain the crude product

which was purified by prep TLC to isolate the monoepoxide (**7**) (24 0 mg)

(1R,3S,4S,6R,11R,12R)-6-*Acetoxy*-3,4,-*epoxy*-12-*hydroxydolabell*-7E-*ene* (**7**) $C_{22}H_{36}O_4$ (Found C, 72 32, H, 10 15, requires C, 72 49, H 9 95%), mp 104–104 5°, $[\alpha]_D$ +63 5 (*c* 1 2), IR ν_{max} cm^{-1} 3625, 3420, 1727, 1675, 1618, 1387, 1371, 1245, 1137, 1023 960, 890, 825, ^{1}H NMR (90 MHz) δ0 90 and 0 97 (each 3H, *d*, *J* = 7 Hz, isopro-Me$_2$), 1 19 (3H, *s*, 1-Me), 1 22 (3H, *s*, 4-Me), 1 86 (3H, *s*, 8-Me), 2 00 (3H, *s*, Ac-Me), 2 47 (1H, *dd*, *J* = 12 and 5 Hz 5-Hα), 2 88 (1H, *dd*, *J* = 10 and 2 Hz, 3-H), 5 23 (1H, *br d*, *J* = 10 Hz, 7-H), 5 59 (1H, *ddd*, *J* = 10, 10 and 5 Hz, 6-H), MS *m z* (rel int)' 364 [M]$^+$ (2), 346 (1), 332 (2), 321 (3), 304 (8), 286 (23), 261 (21), 244 (7), 225 (19), 215 (8) 203 (10), 185 (16), 175 (13) 159 (23) 145 (24), 135 (33), 121 (30), 107 (30), 93 (32), 81 (30), 71 (34), 55 (23), 43 (100)

(ii) Formation of the diepoxide (**8**) To a soln of the diene (**1**) (94 8 mg) and $NaHCO_3$ (57 mg) in $CHCl_3$ (5 ml) was added MCPBA (117 mg) in $CHCl_3$ (3 ml), and the mixture was refluxed for 5 hr The reaction mixture was worked up in the same way as that of the monoepoxide to afford the crude product The major 3*S*,4*S*,7*S*,8*S*-diepoxide (**8**) (59 7 mg) was isolated by prep TLC together with an unknown diepoxide (12 3 mg)

(1R,3S,4S,6R,7S,8S,11R,12R)-6-*Acetoxy*-3,4,7,8-*diepoxy*-12-*hydroxydolabellane* (**8**) $C_{22}H_{36}O_5$ (Found M$^+$, 380 2554, requires M, 380 2653), mp 109–110 °, $[\alpha]_D$ +31 9 (*c* 1 3), IR ν_{max} cm^{-1} 3635, 3540, 1750, 1390, 1375, 1240, 1040, 960, ^{1}H NMR (400 MHz) δ0 95 (3H, *d*, *J* = 7 0 Hz, isopro-Me), 1 00 (3H, *d*, *J* = 6 6 Hz, isopro-Me), 1 15 (3H, *s*, 1-Me), 1 36 (3H, *s*, 4-Me), 1 55 (3H, *s*, 8-Me), 2 08 (3H, *s*, Ac-Me), 2 50 (1H, *dd*, *J* = 13 2 and 3 7 Hz, 5-Hα), 2 89 (1H, *d*, *J* = 9 5 Hz, 7-H), 3 07 (1H, *dd*, *J* = 8 8 and 1 1 Hz 3-H), 4 91 (1H, *ddd*, *J* = 12 1, 9 5 and 3 7 Hz, 6-H), MS *m/z* (rel int) 380 [M]$^+$ (1), 362 (1), 337 (2), 320 (1), 302 (2), 259 (6), 193 (7), 175 (5), 149 (5), 135 (12), 121 (11), 109 (13), 105 (14), 81 (14), 71 (28), 55 (28), 43 (100)

Dehydration of the diepoxy-alcohol (**8**) A mixture of a cooled soln of the alcohol (**8**) (64 5 mg) in pyridine (1 ml) and a soln of $POCl_3$ (50 mg) in pyridine (0 5 ml) was stirred for 44 hr at room temp and then for 3 hr at 70 The reaction mixture was poured into ice-H_2O and the $CHCl_3$ extract was washed 5% aq HCl, dried with Na_2SO_4, and the solvent evapd to yield a crude product. The cyclopentene (**9**) (34 3 mg), was purified by prep TLC

(1R,3S,4S,6R,7S,8S,11R)-6-*Acetoxy*-3,4,7,8-*diepoxydolabell*-12-*ene* (**9**) $C_{22}H_{34}O_4$, mp 132–133 °, $[\alpha]_D$ +35 2° (*c* 0 9), IR ν_{max} cm^{-1} 1737, 1391, 1375, 1242, 1143, 1127, 1094, 1034, 976, 943, 919, 907, 877, 840 cm^{-1}, ^{1}H NMR (90 MHz) δ1 01 and 1 12 (3H, *d*, *J* = 6 Hz, isopro-Me$_2$), 1 28 (3H, *s*, 1-Me), 1 31 (each 3H, *s*, 4-Me), 1 51 (3H, *s*, 8-Me), 2 07 (3H, *s*, Ac-Me), 2 51 (1H, *dd*, *J* = 13 and 5 Hz, 5-Hα), 2 86 (1H, *d*, *J* = 9 Hz 7-H), 3 08 (1H, *dd*, *J* = 10 and 5 Hz 3-H), 5 28 (1H, *br s*, $W_{1/2}$ = 4 Hz 13-H), MS *m/z* (rel. int) 362 [M]$^+$ (3), 347 (1), 344 (1), 302 (6), 284 (6), 268 (3), 259 (5), 241 (6), 202 (10), 175 (19), 161 (14), 149 (21), 135 (100), 121 (53), 107 (50), 107 (50), 105 (26), 81 (28), 69 (41), 55 (61), 41 (32)

Collins oxidation of the cyclopentene (**9**) The CrO_3–(pyridine)$_2$ complex was prepared by the usual manner from dry pyridine (10 ml) and dry CrO_3 (0 9 g) To a mechanically stirred soln of the cyclopentene (30 2 mg) in dry CH_2Cl_2 (1 ml) was added the above complex as a slurry in dry CH_2Cl_2 (1 ml) at 0 After 30 hr of stirring at 60 , the CH_2Cl_2 soln was passed through a Florisil column and was then washed with 5% aq HCl The crude product was subjected to prep TLC affording the cyclopentenone (**10**) (7 3 mg) as a gum

(1R,3S,4S,6R,7S,8S,11R)-6-*Acetoxy*-3,4,7,8-*diepoxydolabell*-12-*en*-14-*one* (**10**) $C_{22}H_{32}O_5$, $[\alpha]_D$ −53 3 (*c* 0 2), IR ν_{max}cm^{-1} 1742, 1706, 1621, 1394, 1381, 1368, 1333, 1240, 1157, 1145, 1092, 1037, 966, 928, 886, 841, 822, UV λ_{max} nm 230 (ε 12000), ^{1}H NMR (90 MHz) δ1 15 (3H, *d*, *J* = 8 Hz, isopro-Me), 1 22 (3H, *d*, *J* = 6 Hz, isopro-Me), 1 28 (3H, *s*, 1-Me), 1 30 (3H, *s*, 4-Me), 1 56 (3H, *s*, 8-Me), 2 08 (3H, *s*, Ac-Me), 2 36 (1H, *dd*, *J* = 13 and 5 Hz, 5-Hα), 2 87 (1H, *d*, *J* = 9 Hz, 7-H), 3 07 (1H, *dd*, *J* = 11 and 2 Hz, 3-H), 5 05 (1H, *ddd*, *J* = 13, 9 and 5 Hz, 6-H), 5 90 (1H, *s*, 13-H), MS *m/z* (rel int) 376 [M]$^+$ (2), 316 (1), 283 (2), 254 (2), 191 (17), 151 (12), 135 (11), 121 (21), 109 (21), 95 (14), 81 (15), 71 (14), 55 (17), 43 (100)

Ozonolysis of the diene **1** *followed by thioketalization with ethanedithiol* Ozonized O_2 gas was passed through a soln of the diene (**1**) (87 5 mg) in MeOH (10 ml) at −78° for 40 min After bubbling N_2 gas into the mixture to remove excess O_3, Me_2S (70 mg) was added at −78 and the mixture stirred for 1 hr at 0°, for 3 hr at room temp The reaction mixture was poured into H_2O and extracted with CH_2Cl_2 The soln was dried with Na_2SO_4 and evapd to afford a crude product To the crude reaction mixture in CH_2Cl_2 (2 ml) was added 1,2-ethanedithiol (300 mg) and a drop of BF_3–Et_2O and the mixture was stirred in the dark for 16 hr under N_2 gas The reaction product was washed with 5% aq NaOH, H_2O and dried with Na_2SO_4 The solvent was evapd under red pres to obtain crude products which were purified by prep TLC to give the levulinic aldehyde derivative (**11**) (26 4 mg) and the δ-lactone (**12**) (20 4 mg)

(2R)-2-*Acetoxypentane*-1,4-*bisethanethioketal* (**11**) $C_{13}H_{18}O_2S_4$, $[\alpha]_D$ +27 3° (*c* 1 1), IR ν_{max}cm^{-1} 1740, 1425, 1368, 1274, 1227, 1080, 1012, 910, ^{1}H NMR (90 MHz) δ1 77 and 2 08 (each 3H, *s*), 2 39 (1H, *d*, *J* = 7 Hz), 2 43 (1H, *d*, *J* = 4 Hz), 3 23 and 3 34 (each 2H, *s*), 4 58 (1H, *d*, *J* = 7 Hz), 5 23 (1H, *ddd*, *J* = 7 7 and 4 Hz), ^{13}C NMR δ21 3 (*q*), 32 5 (*q*), 37 8 (*t*), 38 6 (*t*), 39 0 (*t*), 39 7 (*t*), 45 8 (*t*), 56 6 (*d*), 64 3 (*s*), 73 6 (*d*), 170 1 (*s*), MS *m. z* (rel. int.) 310 [M]$^+$ (1), 259 (4), 196 (8), 134 (13), 119 (100), 105 (64), 61 (15), 43 (54)

(3R,4R,5S)-5-*Isopropoyl*-3,5-*ethano*-4-(3,3-*ethanedithio*-*butyl*)-3-*methyl*-5-*pentanolide* (**12**) $C_{17}H_{28}O_2S_2$ (Found C, 62 36, H, 8 83, requires C, 62 15, H, 8 59%), mp 45 5–46 °, $[\alpha]_D$ −69 1° (*c* 1 7), IR ν_{max}cm^{-1} 1728, 1422, 1395, 1380, 1322, 1290, 1258, 1163, 1078, 1007, 988, 948, 932, 865, ^{1}H NMR (90 MHz) δ0 91 and 1 03 (each 3H, *d*, *J* = 7 Hz), 1 11 (3H, *s*), 1 76 (3H, *s*), 2 26 (1H, *d*, *J* = 19 Hz), 2 53 (1H, *dd* *J* = 19 and 3 Hz), 3 31 (4H, *s*), ^{13}C NMR 17 0 (*q*), 17 2 (*q*), 20 1 (*t*), 20 3 (*q*), 24 6 (*t*), 31 0 (*d*), 32 3 (*q*), 36 9 (*t*), 39 8 (*t*), 39 8 (*t*), 41 4 (*t*), 41 4 (*s*), 45 5 (*t*), 49 2 (*d*), 66 5 (*s*), 96 2 (*s*), 171 4 (*s*), MS *m/z* (rel. int.) 328 [M]$^+$ (14), 313 (3), 269 (11), 235 (7), 225 (5), 194 (16), 175 (14), 159 (8), 135 (19), 119 (100), 105 (29), 95 (19), 79 (19), 71 (38), 59 (65), 43 (77), 41 (78)

Preparation of the p-*bromobenzoate* (**13**) *p*-BrC_6H_4COCl (46 0 mg) was added to the diol (**2**) (27 8 mg) in dry pyridine (2 ml) The mixture was refluxed in the dark at 70 for 11 hr with stirring under N_2 gas The product, recovered in the usual way (dild with $CHCl_3$ washed with 5% aq HCl, dried with Na_2SO_4 and evapd the solvent), was purified by prep TLC to give the *p*-bromobenzoate (**13**) (36 4 mg)

(1R,6R,11R,12R)-6-p-*Bromobenzoyl*-12-*hydroxydolabella*-3E,7E-*diene* (**13**) $C_{27}H_{37}O_3Br$, mp 80 5–82 5°, $[\alpha]_D$ −54 6° (*c* 1 3), UV λ_{max}nm 244 (ε 9760), CD λ_{ext} 240 nm (Δε −8 36), IR ν_{max}cm^{-1} 3620, 3540, 1706, 1586, 1478, 1390, 1382, 1270, 1224, 1176, 1116, 1061, 1012, 937, 846, ^{1}H NMR (90 MHz) δ0 94 and 0 99 (each 3H, *d*, *J* = 7 Hz, isopro-Me$_2$), 1 10 (3H, *br* s, 1-Me), 1 63 (3H, *br* s, 4-Me) 1 87 (3H, *br* s, 8-Me), 2 67 (1H, *dd*, *J* = 11 and 6 Hz, 5-Hα), 5 86 (1H, *ddd*, *J* = 10, 10 and 5 Hz, 6-H), 7 52 (2H, *dd*, *J* = 9 and 1 Hz), 7 88 (1H, *dd*, *J* = 9 and 1 Hz), MS *m/z* (rel int) 490 [M]$^+$ (2) 488 [M]$^+$ (1), 473 (5), 472 (5), 470 (5), 403 (2), 401 (2), 288 (35), 202 (32), 200 (32), 185 (97), 183 (100), 134 (38), 93 (45), 80 (44), 71 (49), 55 (46)

Acetylation of the diol (**2**) The mixture of the diol (**2**) (30 2 mg), dry pyridine (1 ml) and Ac_2O (0 2 ml) was allowed to stir for 1 hr at room temp The reaction mixture was extracted with Et_2O,

washed with 5% aq NaCl, dried with Na_2SO_4 and the solvent was evapd under red. pres. to yield a crude product which was purified by prep TLC to give the hydroxy-acetate (**1**) (25 5 mg)

Acetylation of the acetoxy-diol (**3**) The acetoxy-diol (**3**) (32 0 mg) was treated with Ac_2O (0 2 ml) in dry pyridine (1 ml) as above for 1 hr. The diacetate (**4**) (22 0 mg) was purified by prep TLC

Reduction of the primary alcohol (**3**) *with pyridine–SO_3 complex and* $LiAlH_4$. Pyridine–SO_3 complex (167 mg) was added to the primary alcohol (**3**) (183 mg) in dry THF (3 ml) and the suspension was stirred at 0° for 5 hr under N_2 gas Addition of $LiAlH_4$ (185 mg) in dry THF (5 ml) was followed by stirring for 11 5 hr at room temp After decomposition of excess hydride by addition of H_2O and 15% aq. NaOH, the crude reaction product was extracted with Et_2O, dried with Na_2SO_4 and the solvent was evapd The diol (**2**) (9 0 mg) was isolated by prep TLC together with a second diol which was not identified

Epoxidation of the diene (**3**) To a soln of the acetoxy-diol (**3**) (42 0 mg) in dry CH_2Cl_2 (2 ml) was added MCPBA (18 7 mg) in dry CH_2Cl_2 (1 ml) and the mixture stirred for 30 min Normal work-up afforded a crude product which was purified by prep. TLC to give the 3*S*,4*S*-epoxide (26 4 mg).

Oxidation of the epoxy-alcohol with PDC To a slurry of PDC (170 mg) in CH_2Cl_2 the above epoxide (26 4 mg) in CH_2Cl_2 (1 ml) was added and the mixture was stirred for overnight at room temp The CH_2Cl_2 soln was passed through a Florisil column and evapd to give a crude product which was purified by prep TLC and yielded the aldehyde (**5**) (18.2 mg)

Test of the antifungal activity The growth inhibitory effect of the dolabellane diterpenoids **1**, **2**, **3**, **7** and **8**, on the plant pathogenic fungi, *Botrytis cinerea*, *Rhizoctonia solani* and *Phythium debaryanum*, was tested by the following manner Mycelia discs (5 mm in diameter) of each of the pathogenic fungi were placed on a potato-sucrose-agar medium with or without each of the test compounds, and cultured for 5 days at 25° The inhibition percentage was obtained by measuring the diameter of mycelia colonies.

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REFERENCES

1 Matsuo, A, Nozaki, H, Nakayama, M, Hayashi, S and Takaoka, D (1978) *J Chem. Soc Chem Commun* 198
2 Matsuo, A, Nozaki, H, Nakayama, M, Takaoka, D and Hayashi, S. (1980) *J Chem Soc Chem Commun* 822
3 Huneck, S, Baxter, G, Cameron, A. F, Connolly, J D and Rycroft, D S (1983) *Tetrahedron Letters* **24**, 3787
4 Hashimoto, T., Tori, M, Taira, Z and Asakawa, Y (1985) *Tetrahedron Letters* **26**, 6473
5. Pettit, G R., Ode, R H, Herald, C L, Von Dreele, R B and Michel, C (1976) *J Am Chem Soc* **98**, 4677
6 Faulkner, D J (1977) *Tetrahedron* **33**, 1421
7 Faulkner, D J (1984) *Natural Product Reports* **1**, 251.
8 Matsuo, A, Yoshida, K, Uohama, K, Hayashi, S, Connolly, J D and Sim, G A (1985) *Chem Letters* 935
9 Huneck, S., Baxter, G A, Cameron, A F, Connolly, J D, Harrison, L J, Phillips, W R., Rycroft, D. S and Sim, G. A. (1986) *J Chem Soc Perkin Trans I* 2652
10 Ruzicka, L (1959) *Experienta* **9**, 357
11 Matsuo, A, Yoshida, K, Fukazawa, Y, Nakayama, M and Kuriyama, K. (1987) *Chem Letters* 369
12 Shirahama, H., Osawa, E and Matsumoto, T (1980) *J Am Chem Soc* **102**, 3280.
13 Connolly, J D, Sim, G A and Matsuo, A (1987) *Acta Crystallogr* **C43**, 1422