Pergamon

0031-9422(95)00637-0

Phytochemistry, Vol. 41, No. 2, pp. 575 580, 1996

0031 9422/96 $15.00 + 0.00

TERPENOID CONSTITUENTS OF THE LIVERWORT *HETEROSCYPHUS COALITUS*

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(*Received* 26 *June* 1995)

Key Word Index—Bryophytes; Hepaticae; Jungermanniales; *Heteroscyphus coalitus*; *H. bescherellei*; halimane- and 3,4-seco-halimane-type diterpenoids; aromadendrane-type sesquiterpene.

Abstract—Two new diterpenoids and a new sesquiterpenoid have been isolated from the ether extract of *Heteroscyphus coalitus* and their structures and relative configurations were established by spectral methods. They were shown to be halimane- and 3,4-seco-halimane-type diterpenoids and an aromadendrane-type sesquiterpenoid. This is the first report of the isolation of a 3,4-seco-halimane-type diterpenoid from liverworts.

INTRODUCTION

The stem-leafy liverwort *Heteroscyphus coalitus* (=*Heteroscyphus bescherellei*) grows on deciduous plants or moist rock. In the genus *Heteroscyphus*, seven species are known in Japan. The Jungermanniales order is the largest of the liverworts, containing 75–80% of all species. There are *ca* 250 genera in 40 families [1]. The liverworts, including the Jungermanniales, are rich sources of terpenoids with a variety of carbon skeletons [2]. A previous phytochemical study of the genus *Heteroscyphus* led to the isolation of (+)-junceic acid and *ent*-spathulenol as the major constituents from *H. coalitus* [3]. In addition, clerodane-type diterpenoids and 2,3-secoaromadendrane-type sesquiterpenoids were isolated from *H. planus* [4], and clerodane-type diterpenoids and cadinane-type sesquiterpenoids from cultured cells of *H. planus* [5, 6].

The classification of liverworts belonging to the Jungermanniales is extremely difficult morphologically and thus a study of their chemical constituents is necessary in order to investigate the chemosystematics of liverworts. During the chemical investigation of liverworts, it has been found that they occasionally produce their own unique constituents, which have not been found in higher plants, fungi or marine organisms. The natural product chemistry of liverworts is thus of considerable interest. Furthermore, liverworts contain biologically active compounds which have antifungal, anticancer, insect antifeedant, pungent taste, bitterness and other interesting biological activities [7]. Here, we report on the isolation and structural elucidation of two new diterpene lactones and a new sesquiterpenoid from *H. coalitus*.

RESULTS AND DISCUSSION

The ether extract of *H. coalitus* was repeatedly chromatographed on silica gel and Sephadex LH-20 to give two new diterpenoids (**1**) and (**2**) and a new aromadendrane-type sesquiterpenoid (**3**).

The EI mass spectrum of **1** gave a molecular ion peak at *m/z* 390. A quasi-molecular ion peak at *m/z* 389 in the negative FAB mass spectrum of **1** provided further evidence for the M_r. The IR spectrum of **1** showed the presence of an acetyl group (1724 and 1250 cm^{-1}) and a lactone carbonyl group (1757 cm^{-1}). Compound **1** gave signals in its ^1H and ^{13}C NMR spectra (Tables 1 and 2) for three ester carbonyl groups (δ_C174.0, 177.5 and 170.6), four methyl groups [δ_H0.94 (*d*, $J = 6$ Hz), 0.99 (*s*), 1.09 (*s*) and 2.07 (*s*)], a methylene group bearing an oxygen [δ_H4.81 (*br s*) and δ_C70.4], a trisubstituted double bond [δ_H7.18 (*t*, $J = 2$ *Hz*), δ_C133.5 and 144.1] and an oxygenated methine [δ4.74 (*t*, $J = 3$ Hz) and δ76.0] group. The DEPT spectra of **1** indicated the presence of 30 protons. Hence, the molecular formula of **1** was found to be $C_{22}H_{30}O_6$. Thus, **1** has eight degrees of unsaturation and this, together with the spectral data, indicates that **1** is a tetracyclic compound. Further determination of the structure was obtained from the HMBC spectrum (Table 3). The signal for the methyl group at δ2.07 correlated with the carbonyl carbon at δ170.6, which further correlated with the oxygenated methine proton at δ4.74, thus suggesting the presence of a secondary acetyl group. The proton signal at δ4.74 (H-3) correlated with two tertiary methyl groups (δ23.9 and 20.1, C-18 and 19). Further correlations were observed between the tertiary methyl protons and an oxygenated quaternary at δ86.4 (C-5), which further correlated with the proton signals at δ1.47 (H-1), 4.74 (H-3), 1.86 (H-7) and 2.02 (H-10). Other correlations were observed as described in Table 3. The above spectral data are consistent with the planar structure shown for **1**, which possesses the halimane-type diterpene skeleton. The stereochemistry of **1** was deduced by difference NOE, NOESY (Table 4) and decoupling experiments. Irradiation of the secondary methyl proton

Table 1. ¹H NMR spectral data for compounds 1–3

	1*	2†		3*
1	1.47 (*m*) *ax*	1.61 (*m*)		
	1.56 (*ddd*, 10, 4, 6.6) *eq*	1.67 (*m*)		
2	1.75 (2H, *m*)	2.19 (*m*)		5.93 (*d*, 1)
		2.30 (*ddd*, 16, 9, 9)		
3	4.74 (*t*, 3)			
4				2.55 (*q*, 7)
6	1.51 (*ddd*, 12, 12, 6) *ax*	1.46 (*br d*, 14) *eq*		1.06 (*d*, 9)
	2.02 (*m*) *eq*	1.34 (*m*) *ax*		
7	1.30 (*dddd*, 12, 12, 14, 6) *ax*	1.21 (*ddd*, 14, 14, 14, 4) *ax*		1.12 (*ddd*, 9, 9, 6)
	1.86 (*m*) *eq*	1.35 (*m*) *eq*		
8	1.85 (*m*)	1.26 (*m*)		1.27 (*m*) *ax*
				2.16 (*ddd*, 16, 9, 7, 1) *eq*
9				1.96 (*dddd*, 13, 13, 12, 1) *ax*
				1.71 (*dddd*, 13, 7, 5, 1) *eq*
10	2.02 (*dd*, 6, 2)	1.61 (*m*)		2.93 (*m*)
11	1.72 (*ddd*, 14, 14, 3)	1.61 (*m*)		
	2.03 (*m*)	2.14 (*m*)		
12	2.10 (*br t*, 14)	2.06 (*br d*, 14)		0.91 (*s*)
	2.32 (*br t*, 14)	2.14 (*m*)		
13				1.03 (*s*)
14	7.18 (*t*, 2)	6.07 (*s*)	7.23 (*br s*)*	1.27 (*d*, 7)
15	4.81 (*br s*)	3.87 (*br s*)	4.82 (*br s*, 2H)*	1.15 (*d*, 7)
17	0.94 (*d*, 6)	0.84 (*d*, 6)	0.97 (*d*, 6)*	
18	0.99 (*s*)	4.80 (*s*)	4.99 (*br s*)*	
		5.30 (*br s*)	5.23 (*br s*)*	
19	1.09 (*s*)	1.52 (*br s*)	1.80 (*br s*)*	
$CO_2C\underline{H}_3$		3.35 (*s*)	3.66 (*s*)*	
Ac	2.07 (*s*)			

* Measurement in chloroform-d_1, 400 MHz.
† Measurement in benzene-d_6, 400 MHz.

at δ0.94 (H-17) led to a double doublet signal (*dd*, $J = 12$ and 6 Hz) for the methine proton at δ1.85 (H-8), confirming the presence of an axial–axial coupling between H-8 and the H-7 axial proton. Hence, the stereochemistry of the secondary methyl group at C-8 was confirmed to have an equatorial orientation. Moreover, the above was clarified by an X-ray crystallographic analysis of **1** crystallized from ether solution. The stereoscopic view for the crystal of **1** is shown in Fig. 1. All the above mentioned features showed that the structure and relative configuration of **1** are as shown.

The halimane-type diterpenoids are very rare in nature, but they have been isolated from the higher plants *Halimium viscosum* (Cistaceae) [8, 9] and *Polyalthia longifolia* (Annonaceae) [10], and the liverwort *Pleurozia gigantea* (Pleuroziaceae) [11].

The structure of **2** was deduced by comparing its spectral data with those of **1**. The IR spectrum of **2** ($[\alpha]_D$ + 43.3) suggested the presence of a carbonyl group (1759 cm^{-1}). The negative FAB mass spectrum of **2** gave a quasi-molecular ion peak at m/z 375. The ^{13}C NMR data (Table 2) indicated the presence of three ester carbonyl groups (δ173.1, 173.7 and 176.3 in C_6D_6), a trisubstituted double (δ133.3 and 143.9), a prenyl group (δ19.4, 111.8 and 142.6) and an oxygenated quaternary carbon (δ88.0). The ¹H NMR (Table 1) spectrum showed that **2** contained three methyl groups with signals at δ0.84 (*d*, $J = 6$ Hz, H-17), 1.52 (*br s*, H-19) and 3.35 (*s*, $COOC\underline{H}_3$), an olefinic proton in an α, β-unsaturated lactone ring at δ6.07 (*s*, H-14), two olefinic protons in an exocyclic moiety at δ4.80 (*s*) and 5.30 (*br s*), and two methylene protons at δ3.87 (2H, *br s*, H-15). The ^{13}C NMR spectrum of **2** indicated the presence of the same side chain including an α,β-unsaturated lactone ring as in **1**. In the HMBC spectrum of **2** correlations were observed between the methyl proton at δ3.35 and the carbonyl carbon at δ173.1, which was further correlated with four mutually coupled protons (δ1.61, 1.67, 2.19 and 2.30). The vinyl methyl proton correlated with C-4 (δ142.6), C-18 (δ111.8) and C-5 (δ88.0). Interpretation of NMR spectral data is consistent with a 3,4-seco-halimane-type diterpenoid with structure **2**. The 3,4-seco-halimane-type diterpenoids are rare in general. A few examples are known, such as the diterpene isolated from the higher plant *Chiliotrichium rosmarinifolium* [12].

The EI mass spectrum of **3** gave a molecular ion peak at m/z 234. The IR spectrum of **3** showed the presence of a hydroxyl group (3330 cm^{-1}) and an α,β-unsaturated carbonyl (1682 cm^{-1}), the latter being further supported by the UV spectrum (229 nm; $\log\varepsilon$ 3.85). The ¹H and ^{13}C NMR spectra of **3** (Tables 1 and 2) exhibited the signals for two protons on a cyclopropane ring

[δ1.06 (*d*, $J = 9$ Hz) and 1.12 (*ddd*, $J = 9$, 9 and 6 Hz)], two tertiary methyls (δ0.91 and 1.03), two secondary methyls (δ1.27 and 1.15) and an olefinic proton (δ5.93). The DEPT spectra of **3** indicated the presence of 21 protons, and the ^{1}H NMR spectrum showe!d an exchangeable hydroxyl proton at δ4.96 (1H, *s*, in DMSO-d_6), which disappeared upon addition of D_2O. Hence, the molecular formula of **3** was found to be $C_{15}H_{22}O_2$. This indicates five degrees of unsaturation and, from the spectral data, **3** must be a tricyclic compound. The ^{1}H NMR data, including a COSY spectrum and spin–spin ^{1}H decoupling, were used to deduce the partial structures of **3**. In a subsequent HMBC (Table 3) analysis the carbon at δ83.1, bearing the hydroxyl group, correlated with a secondary methyl proton (H-15), which showed a NOE with the doublet proton (δ_H1.06, H-6) of the cyclopropane ring. The carbonyl carbon correlated with the olefinic proton, quartet methine proton (δ2.55, $J = 7$ Hz) and the secondary methyl proton. Further correlations were observed as described in Table 3. The above spectral data are consistent with the planar structure of **3** which possesses an aromadendrane-type sesquiterpene skeleton. NOEs were observed between the hydroxyl proton and H-6, H-15 and H-14 (in DMSO-d_6), indicating that the tertiary hydroxyl group on C-5 and the secondary methyl group on C-10 are β-oriented as shown. Further NOEs observed are shown in Table 4. Further confirmation of the structure was provided by chemical transformation of **3**. Lithium aluminium hydride reduction of **3** yielded mainly the alcohol **4** and only a small amount of the C-4β isomer (C-4α:β = 11:1). The ^{1}H NMR spectral data for **4** gave the signals for two secondary methyls (δ1.16 and 1.18), two tertiary methyls (δ1.03, 6H) and a carbinyl methine proton at δ4.32. The observation of a NOE between H-12 and H-2 (δ5.93) in the NOE difference spectrum of **3** provided evidence for its conformation. A LIS experiment using Eu(FOD)$_3$ with **3** and **4** indicated that the two secondary methyls

Table 2. The ^{13}C NMR spectral data for compounds **1–3**

	1*	**2***	**2†**	**3‡**
1	18.3	21.4	21.9	184.4
2	23.7	31.2	31.5	132.3
3	76.0	173.4	173.1	209.3
4	37.9	141.7	142.6	53.8
5	86.4	88.5	88.0	83.1
6	29.7	34.2	34.3	36.5
7	28.9	28.9	29.1	27.7
8	33.4	34.7	34.3	22.3
9	55.3	53.9	54.0	32.2
10	46.3	50.2	49.9	40.1
11	24.2	24.8	25.2	18.8
12	19.5	19.3	19.9	15.1
13	133.5	133.4	133.3	30.2
14	144.1	144.4	143.9	25.6
15	70.4	70.4	69.9	11.1
16	174.0	174.0	173.7	
17	16.0	16.2	16.3	
18	23.9	112.0	111.8	
19	20.1	19.6	19.4	
20	177.5	177.1	176.3	
Ac	170.6			
	21.1			
CO_2CH_3		51.7	51.2	

* Measurement in chloroform-d_1, 50 MHz.
† Measurement in benzene-d_6, 100 MHz.
† Measurement in chloroform-d_1, 100 MHz.

Table 3. ^{1}H–^{13}C long-range correlations for compounds **1–3***

	1	**2**	**3**
C-1	H-3		H-2, 4, 6, 9, 10, 14
2		H-1	H-10
3	H-18, 19	$COOCH_3$, H-1, 2	H-2, 4, 15
4	H-18, 19	H-19	H-2, 15
5	H-1, 3, 7, 10, 18, 19	H-6, 18, 19	H-4, 6, 10, 15
6	H-10		H-4, 8, 12, 13
7	H-17	H-6, 17	H-8, 9, 12, 13
8	H-10, 11, 17	H-11, 17	H-9
9	H-7, 10, 11, 17	H-1, 7, 11, 12, 17	H-8, 10, 14
10	H-6		H-2, 8, 9, 14
11			H-6, 7, 12, 13
12			H-13
13	H-11, 12, 15	H-5, 12	H-6, 7, 12
14	H-12, 15	H-12, 15	H-10
15	H-14	H-14	H-4
16	H-14	H-12, 14	
18	H-19	H-19	
19	H-18		
20	H-10, 11	H-11	
$OCOCH_3$	H-3, $OCOCH_3$		

* Observed by HMBC spectrum.

Table 4. NOE correlations for compounds **1–3***

^{1}H	**1** (Observed ^{1}H)	**2** (Observed ^{1}H)	**3** (Observed ^{1}H)
H-2		1	10, 12, 14
6			15
8		10	
12			4
13			4
14		15	
17		12	
18	2β, 3β, 6β, 10	2, 19	
19	3β, 6α		
OH			6†, 14†, 15†

* Observed by NOESY spectrum.
† Measured in DMSO-d_6.

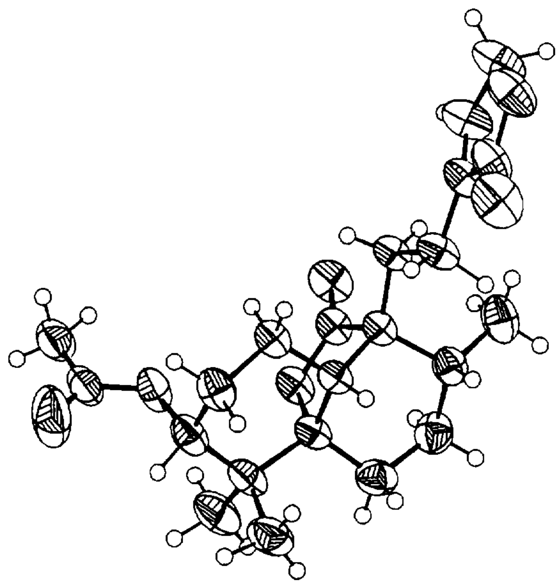


Fig. 1. A computer generated drawing of the final X-ray model of compound **1**.

and the tertiary hydroxyl (C-5) groups are β-oriented. The above data was clarified by an X-ray crystallographic analysis on crystals of **3** obtained from ether solution. The stereoscopic view of the crystal of **3** is shown in Fig. 2. All the above mentioned features show that the structure and relative configuration of **3** are as shown.

The classification of *H. coalitus* and *H. planus* is very difficult. Both species contain clerodane-type diterpenoids. The former species also contains halimane- and seco-halimane-type diterpenoids while the latter species also contains 2,3-seco-aromadendrane-type sesquiterpenoids, which are widely distributed in *Plagiochila* species. The *Plagiochila* species distributed in the world are classified into two types by using chemical markers, one of which is plagiochiline A, which possesses an intense pungent taste and insect antifeedant activity [13]. The other type does not have the pungent taste, but contains

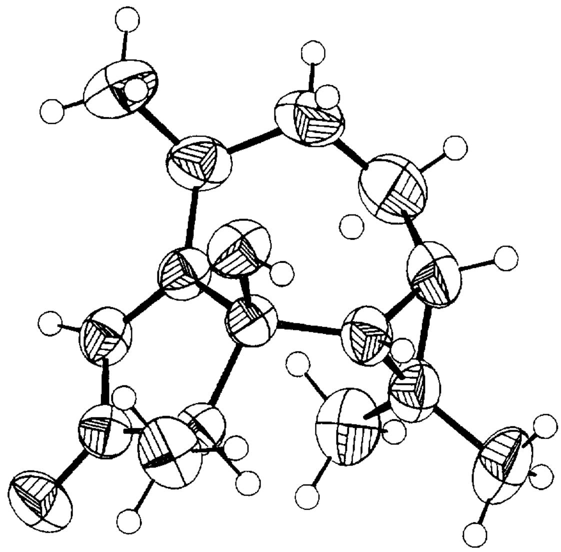


Fig. 2. A computer generated drawing of the final X-ray model of compound **3**.

large amounts of aromadendrane- maaliane- and/or 2,3-seco-aromadendrane-type sesquiterpenoids [14, 15] as chemical markers. Although the terpenoid contents of both species of *H. coalitus* and *H. planus* are clearly different, *H. planus* belongs to the latter type of *Plagiochila* species chemosystematically.

EXPERIMENTAL

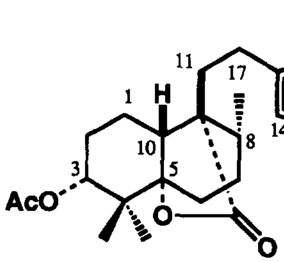
General. TLC: silica gel precoated glass plates with *n*-hexane–EtOAc (1:1 and 4:1). Detection was with Godin reagent [16]. CC: Silica gel 60 (40–63 μm) and Sephadex LH 20; with the latter CH_2Cl_2–MeOH (1:1) was used as solvent.

Spectral data. NMR: 100 MHz for ^{13}C and 400 MHz for ^{1}H; EIMS: 70 eV; FAB-MS: matrix using *m*-nitrobenzyl alcohol.

Plant material. Heteroscyphus coalitus (= *H. bescherellei*) (430.3 g) was collected in August, 1993, at Shishikui-cho, Kaifu-gun, Tokushima, Japan. A voucher specimen (# 93036) is deposited at the Faculty of Pharmaceutical Sciences, Tokushima Bunri University. The liverwort was dried for 2 days, the impurities removed, ground mechanically and then extracted with Et_2O for 1 month.

Extraction and isolation. The Et_2O extract (8.3 g) was chromatographed on silica gel using a *n*-hexane–EtOAc gradient, giving 10 frs (I–X). Fraction III (710 mg) was rechromatographed on Sephadex LH-20 to give **3** (68.7 mg; 0.8% of total extract) and a mixt. containing **1** and **2**. The mixt. was further purified by MPLC on silica gel using *n*-hexane–EtOAc (1:1), affording **1** (118.2 mg; 1.4%) and **2** (48.8 mg; 0.6%).

Compound **1**. $[\alpha]_D$ + 19.7 (MeOH; *c* 1.2); IR ν_{max} (neat) cm^{-1}: 1757, 1724, 1657, 1444, 1371, 1250, 1138, 1060, 966, 833, 733, 646, 606; Negative FABMS: *m/z* 389 $[M - H]^-$; EIMS *m/z* (rel. int.): 390, $[M]^+$ (1.6), 330 $[M - AcOH]^+$ (6), 286 (29), 284 (11), 274 (12), 273 (15),



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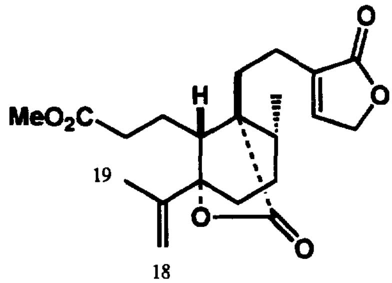

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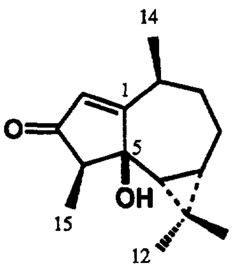

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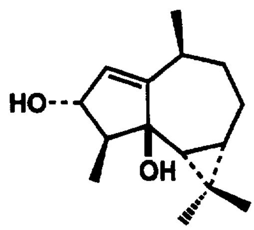

4

271 (11), 243 (13), 190 (17), 189 (100), 176 (19), 175 (34), 173 (40), 133 (16), 120 (10), 119 (28), 112 (10), 107 (10), 105 (34), 91 (13), 69 (10), 55 (13), 43 (25); UV λ_{max} (EtOH) (log ε): 207 (4.03).

Crystal data for compound **1**. Orthorhombic space group $P2_12_12_1$, $a = 12.320$ (5), $b = 25.934$ (7), $c = 6.520$ (2) Å; $V = 2083$ (1) Å; $Z = 4$, $D_c = 1.30\ \mathrm{g\,cm^{-3}}$, $\mu_{Cu} = 6.50\ \mathrm{cm^{-1}}$. Crystal size: $0.5 \times 0.5 \times 0.40$ mm. Reflection data were measured with a Mac Science MXC18 diffractometer using copper radiation Cu K_α ($\lambda = 1.54178$). Final residuals R and R_w were 0.043, 0.059.

Compound **2**. $[\alpha]_D + 43.3$ ($CHCl_3$, *c* 2.0); IR (neat) $\mathrm{cm^{-1}}$: 1759, 1651, 1439, 1346, 1263, 1177, 1067, 966, 939, 910, 833, 735; Negative FABMS: *m/z* 375 $[M - H]^-$; UV λ_{max} (EtOH) (log ε): 211 (3.9).

Compound **3**. $[\alpha]_D + 119.9$ ($CHCl_3$, *c* 1.7); IR (neat) $\mathrm{cm^{-1}}$: 3330, 1682, 1611, 1453, 1354, 1310, 1213, 1128, 1098, 993; CD ($CHCl_3$): $\Delta\varepsilon - 1.68$ (283 nm), $+1.84$ (210 nm); UV ν_{max} (EtOH) (log ε): 229 (3.85); EIMS *m/z* (rel. int.): 234 $[M]^+$ (68), 219 (100), 191 (66), 163 (32), 161 (22), 152 (63), 149 (20), 145 (22), 139 (41), 138 (28), 109 (23), 107 (21), 105 (21), 96 (29), 93 (28), 91 (24), 81 (21), 69 (28), 67 (23), 55 (31).

Crystal data for compound **3**. $C_{15}H_{24}O_2$, $M_r = 236.00$, orthorhombic space group $P2_12_12_1$, $a = 14.241$ (4), $b = 14.900$ (3), $c = 6.465$ (1) Å; $V = 1371.7$ (5) Å; $Z = 4$, $D_c = 1.20\ \mathrm{g\,cm^{-3}}$; $\mu_{Cu} = 5.03\ \mathrm{cm^{-1}}$. Cu K_α ($\lambda = 1.54178$), Crystal size $0.5 \times 0.5 \times 0.10$ mm. Reflection data were measured with a Mac Science MXC18 diffractometer using copper radiation Cu K_α ($\lambda = 1.54178$). Final residuals R and R_w were 0.045, 0.052.

Reduction of compound **3** *with* $LiAlH_4$. Compound **3** (22 mg) in dry Et_2O was added dropwise to a suspension of $LiAlH_4$ (47 mg) in dry Et_2O (2 ml) and stirred for 1 hr at room temp. An alcohol (5 mg) was obtained, **4**; ^1H NMR (400 MHz in $CDCl_3$): δ 1.03 (6H, *s*), 1.16 (3H, *d*, $J = 7$ Hz), 1.19 (3H, *d*, $J = 7$ Hz), 1.98, 2.12, 2.58, (each, 1H, *m*), 4.32 (*br s*), 5.63 (*t*, $J = 1$ Hz).

Acknowledgements—We thank Dr M. Mizutani (Hattori Botanical Laboratory, Nichinan, Miyazaki, Japan) for identification of the liverworts. This work was supported in part by the Grant-in-Aid for Cancer Research (04-01) from the Ministry of Health and Welfare of Japan.

REFERENCES

1. Gradstein, S. R. (1990) in *Proceeding of the Phytochemical Society of Europe* (Zinsmeister, H. D. and Meus, R., eds), Vol. **29**, p. 3. Oxford Science Publications, Oxford, U.K.
2. Asakawa, Y. (1982) in *Progress in the Chemistry of Organic Natural Products* (Herz, W., Grisebach, H. and Kirby, G. W., eds), Vol. **42**, p. 1. Springer, Vienna.
3. Asakawa, Y., Toyota, M. and Ueda, A. (1990) *Phytochemistry* **32**, 117.
4. Hashimoto, T., Nakamura, I., Tori, M., Takaoka, S. and Asakawa, Y. (1995) *Phytochemistry* **38**, 119.
5. Nabeta, K., Oohata, T., Izumi, N. and Katoh, K. (1994) *Phytochemistry* **37**, 1263.
6. Nabeta, K., Katayama, K., Nakagawara, S. and Katoh, K. (1993) *Phytochemistry* **32**, 117.

7. Asakawa, Y. (1982) in *Proceeding of the Phytochemical Society of Europe*, (Zinsmeister, H. D. and Mues, R., eds), Vol. **29**, p. 369. Oxford Science Publications, Oxford, U.K.
8. Urones, J. G., Marcos, I. S., Guadrado, M. J. S., Basabe, P. and Lithgow, A. M. (1990) *Phytochemistry* **29**, 1247.
9. Urones, J. G., Marcos, I. S., Guadrado, M. J. S., Basabe, P. and Lithgow, A. M. (1990) *Phytochemistry* **29**, 3597.
10. Hara, N., Asaki, H., Fujimoto, Y., Gupta, Y. K., Singh, A. K. and Sahai, M. (1995) *Phytochemistry* **38**, 189.
11. Asakawa, Y., Lin, X., Tori, M. and Kondo, K. (1990) *Phytochemistry* **29**, 2597.
12. Jakupovic, J., Banerjee, S., Bohlmann, F., King, R. M. and Robinson, H. (1986) *Tetrahedron* **42**, 1305.
13. Asakawa, Y., Toyota, M., Takemoto, T., Kubo, I. and Nakanishi, K. (1980) *Phytochemistry* **19**, 2147.
14. Asakawa, Y., Inoue, H., Toyota, M. and Takemoto, T. (1980) *Phytochemistry* **19**, 2623.
15. Spörle, J., Becker, H., Allen, N. S. and Gupta, M. P. (1991) *Phytochemistry* **30**, 3043.
16. Godin, P. (1954) *Nature* **174**, 134.