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STRUCTURES OF SECOSPATANE-TYPE DITERPENES WITH FEEDING-DETERRENT ACTIVITY FROM THE BROWN ALGA DILOPHUS OKAMURAI

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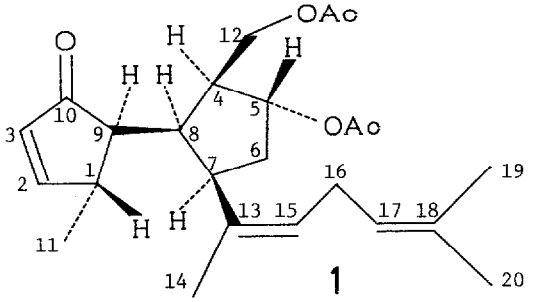
ABSTRACT: Structures of two new diterpenoids with feeding-deterrent activity isolated from the brown alga Dilophus okamurai Dawson have been determined on the basis of spectroscopic evidence.

During our survey of the biologically active metabolites from marine organisms, we have recently reported[1,2] the isolation of spatane-type and spatane-related diterpenoids, which showed feeding-deterrent activity against the young abalone Haliotis discus hannai Ino, from the brown alga Dilophus okamurai Dawson. Further studies on feeding-deterrent substances[3] have led to the isolation of two active compounds with a secospatane skeleton, **1** and **2**, in the yields of 0.9% and 0.8% of the extract. We wish to describe herein the structural elucidation of these two active compounds **1** and **2**.

Compound **1**, $C_{24}H_{34}O_5$ (m/z 402; M^+),[4] $[\alpha]_D$ -46.0° (c 1.30; $CHCl_3$), revealed in its IR[5] [ν_{max} 1704 cm^{-1}] and UV [λ_{max} 205 nm (ε 17000)] spectra the presence of an αβ-unsaturated ketone (probably a cyclopentenone[6]) moiety. In addition, the presence of two acetoxyl groups was indicated by



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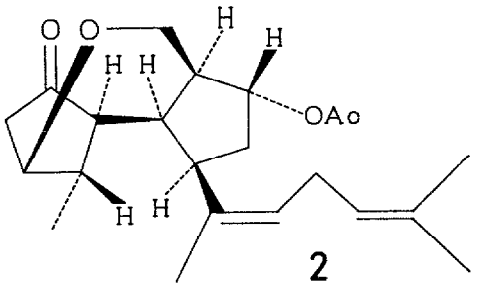

2

the IR [ν_{max} 1741 and 1245 cm^{-1}] and ^1H NMR [δ 2.01 and 2.04 (each 3H, s)] spectra. The ^1H NMR spectrum showed signals due to a secondary methyl group, three olefinic methyl groups and four olefinic protons. A combination of the ^1H-^1H and ^{13}C-^1H 2D-COSY spectra together with partial spin decoupling

Table 1. ^{13}C and ^1H NMR data for compounds **1** and **2**

	1		**2**	
Carbon[a]	^{13}C δb)	^1H δc)	^{13}C δ	^1H δ
1	40.9 (d)	3.0 (m)	42.1 (d)	2.3 (m)
2	167.0 (d)	7.50 (dd, J=5.8,2.2)	79.9 (d)	4.37 (d, J=5.5)
3	132.8 (d)	6.10 (dd, J=5.8,1.8)	39.7 (t)	2.39 (br d, J=19.8) Hβ
				2.54 (dd, J=19.8,5.5) Hα
4	50.0 (d)	2.68 (m)	51.6 (d)	2.35 (m)
5	76.8 (d)	5.2 (m)	75.7 (d)	5.52 (br t, J=6.8)
6	36.5 (t)	1.65 (m) Hα	35.8 (t)	1.75 (m) Hα
		2.35 (ddd, J=14.1,13.9,8.4) Hβ		2.5 (m) Hβ
7	44.2 (d)	3.32 (ddd, J=13.9,6.9,6.9)	44.2 (d)	3.41 (ddd, J=13.2,8.4,8.4)
8	43.8 (d)	3.0 (m)	49.8 (d)	2.69 (dd, J=8.4,8.4)
9	52.4 (d)	2.0 (m)	54.6 (d)	1.97 (br s)
10	209.4 (s)		220.1 (s)	
11	19.4 (q)	1.18 (d, J=7.3)	20.0 (q)	0.98 (d, J=7.3)
12	63.4 (t)	4.05 (dd, J=11.3,9.8)	60.9 (t)	3.54 (d, J=14.3) Hα
		4.26 (dd, J=11.3,5.9)		3.87 (dd, J=14.3,4.0) Hβ
13	132.7 (s)		132.8 (s)	
14	25.8 (q)	1.72 (br s)	25.8 (q)	1.72 (br s)
15	128.9 (d)	5.2 (m)	128.9 (d)	5.37 (br t, J=7.0)
16	27.8 (t)	2.77 (br t, J=7.3)	27.6 (t)	2.7 (m)
17	123.4 (d)	5.12 (br t, J=7.3)	123.3 (d)	5.16 (br t, J=7.3)
18	131.7 (s)		131.8 (s)	
19	17.8 (q)	1.66 (br s)	17.8 (q)	1.65 (br s)
20	23.1 (q)	1.58 (br s)	22.7 (q)	1.67 (br s)
	169.8 (s)	2.01 (s) Ac	170.1 (s)	2.04 (s) Ac
	169.9 (s)	2.04 (s)	20.8 (q)	
	20.4 (q)			
	20.8 (q)			

a) The numbering system corresponds to those used for spatane diterpenes.[8])

b) Measured at 67.9 MHz in C_6D_6 (TMS=0, INEPT).

c) Measured at 270 MHz in $CDCl_3$ (TMS=0, J in Hz).

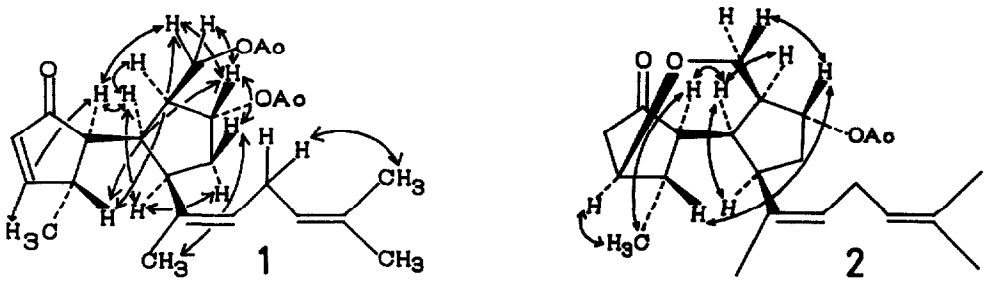

Fig. 1. NOEs (↷).

studies allowed a complete assignment of all proton and carbon resonances as shown in Table 1, leading to a planar formula **1** for compound **1**.

The relative stereochemistry of **1** was determined by the extensive NOE difference experiments, the results of which are depicted in Fig. 1. Since no NOE was observed between the C_{14}-H_3 and C_{16}-H_2 and the signal due to the C_{14}-CH_3 in the ^{13}C NMR spectrum appeared at δ 25.8,[7] the stereochemistry of the C-13 double bond was assigned as Z. It seemed to be reasonable that the secospatane diterpenes are derived, biosynthetically, from the spatane diterpenes and this assumption was supported by coexistence of spatane and secospatane derivatives in the same alga. However, the relative configuration at C_9-H (trans to the C_1-H) in **1** is different from that (cis to the C_1-H) in spatane derivatives.[8] When the secospatane skeleton of **1**, in which the C-9 position is adjacent to carbonyl group, has been formed, the proton at C-9 in **1** seems to be isomerized into more stable trans orientation. The relative configuration between C-8 and C-9 could not be assigned by the above NOE experiments and is discussed later.

Compound **2**, $C_{22}H_{32}O_4$ (m/z 360; M^+),[4] $[\alpha]_D$ -69.0° (c 0.860; $CHCl_3$), has an acetoxyl group [δ 2.04 (3H, s) and δ 170.1 (s) and 20.8 (q)] and a cyclopentanone moiety [δ 220.1 (s) and ν_{max} 1739 cm^{-1}] in the molecule. The IR spectrum[9] showed the absence of hydroxyl group and hence one of the four oxygen atoms in **2** was assumed to be involved as an ether link. The ^1H-^1H and ^{13}C-^1H COSY spectra of **2** coupled with a comparison of the spectral data of **1** and **2** indicated that a planar formula **2** can be assigned for compound **2**. The relative stereochemistry could be determined by NOE difference spectra as depicted in Fig. 1. The small coupling constants between C_1-H/C_2-H and C_1-H/C_9-H reflect trans configuration of these protons whose dihedral angles are nearly 90°. Moreover, the configuration between C-8 and C-9 can be represented by that shown in formula **2**. Therefore, the relative stereochemistry between C-8 and C-9 in **1** would also be the same as that of **2**.

The secospatane diterpenoids, whose stereochemistries were apparently different from those of our compounds **1** and **2**, have previously been isolated from the Australian Dilophus marginatus.[10]

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3) Feeding-deterrent activity was evaluated by comparing the number of biting traces left on the cellulose plates with that of the standard phosphatidylcholine.[2] Compound **1** exhibited strong feeding-deterrent activity, which is comparable to that of spatane diterpenes,[2] and compound **2** moderate activity. Results of the biological tests will be reported in near future.[11]

4) HR-MS; **1**: m/z 402.2424 (calcd for $C_{24}H_{34}O_5$, 402.2407), **2**: m/z 360.2303 (calcd for $C_{22}H_{32}O_4$, 360.2300).

5) **1**: IR (neat), ν_{max} 1741, 1704, 1591, 1245, 1172, 1143, 1105, 1035, 916, 871, 835, 799 and 735 cm^{-1}; ^1H NMR (C_6D_6), δ 1.84 (1H, dd, J=2.6, 2.6 Hz; C_9-H), 2.56 (1H, m; C_1-H), 3.11 (1H, m; C_8-H) and 5.52 (1H, dd, J=8.0, 8.0 Hz; C_5-H); LR-MS (70 eV), m/z (rel. intensity) 402 (3; M^+), 342 (25; M^+-AcOH), 282 (37; M^+-AcOHx2), 213 (22), 187 (26), 186 (25), 173 (24), 171 (23), 145 (28), 143 (35), 135 (20), 131 (22), 119 (21), 109 (100), 107 (23), 105 (26), 93(28), 91 (25), 69 (34), 67 (23), 55 (21), 43 (76) and 41 (29).

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9) **2**: IR (neat), ν_{max} 1739, 1405, 1297, 1245, 1194, 1154, 1104, 1084, 1067, 1027, 967, 949 and 747 cm^{-1}; ^1H NMR (C_6D_6), δ 1.85 (1H, br s; C_9-H), 1.91 (1H, br q, J=7.3 Hz; C_1-H), 2.28 (1H, ddd, J=15.0, 13.2, 8.8 Hz; C_6-Hβ), 2.73 (1H, br t, J=8.4, 8.4 Hz; C_8-H) and 2.83 (2H, br t, J=7.0 Hz; C_{16}-H_2); LR-MS (70 eV), m/z 360 (1; M^+), 300 (40; M^+-AcOH), 244 (17), 189 (13), 175 (16), 173 (21), 159 (15), 119 (25), 109 (67), 107 (22), 105 (27), 95 (20), 93 (34), 91 (28), 82 (58), 81 (30), 79 (25), 69 (37), 67 (32), 55 (35), 43 (100) and 41 (54).

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