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THE STRUCTURES OF FOUR ISOMERIC DIHYDROFURAN-CONTAINING CEMBRANOID DITERPENES FROM SEVERAL SPECIES OF SOFT CORAL

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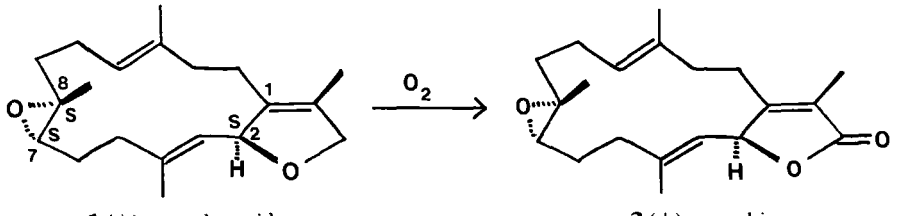
ABSTRACT.—The structures and absolute stereochemistry of four isomeric, cembranoid diterpenes derived from alcyoniid soft corals are reported. Two of these compounds, sarcophytoxide [**1**] and isosacrophytoxide [**6**], are known, but their diastereomeric counterparts [**3**] and [**7**] are here reported for the first time. High field nmr data are reported for all four compounds. The results of a single crystal X-ray structure determination of one of the isosarcophytoxides [**7**] permits unambiguous assignment of all four structures. A new cembranoid diterpene 15-hydroxycembra-1,3,7,11-tetraene [**5**] is reported.

The presence of cembranoid diterpenes in soft corals is well documented (1,2), although in some cases, the stereochemical detail with which the structures have been reported is often less than complete (3). Unless X-ray crystallographic data is available, it is often difficult to determine the relative, let alone the absolute stereochemistry of cembranoid diterpenes; this has only been achieved in a few cases by chemical degradation (4,5).

In 1974 Kashman (6) reported the isolation of a cembranoid diterpene from *Sarcophyton glaucum* Quoy and Gaimard. The same compound was referred to by Tursch (7) as sarcophytoxide [**1**]. Kashman's diterpene $[\alpha]_D+40°$ and Tursch's sarcophytoxide [**1**] $[\alpha]_D-137°$ were presumably enantiomers. We have subsequently reported (8) a compound corresponding to **1** with $[\alpha]_D-191°$. It is presumably also enantiomeric with Kashman's and identical with Tursch's diterpene. Faulkner (9) has reported the isolation of a sarcophytoxide [**1**] with $[\alpha]_D+102°$, which he converted to sarcophine [**2**], with properties identical with those reported by Kashman (10,11) (Scheme 1). Because the relative (10) (X-ray) and absolute (11) (cd) configuration of sarcophine [**2**] were known, the absolute stereochemistry of sarcophytoxide [**1**] was established. Kobayashi (12) has recently reported an X-ray structure determination of sarcophytoxide [**1**] $[\alpha]_D+157°$, which is consistent with the chemical correlations.

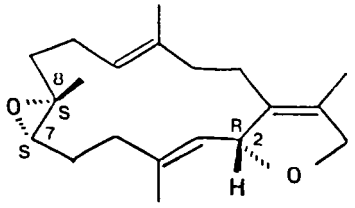
In this paper we describe the isolation and characterization of a diastereomer [**3**] of sarcophytoxide from *Lobophytum pauciflorum* Ehrenberg, samples of which also contained 14-hydroxycembra-1,3,7,11-tetraene [**4**] (13) and a new diterpene 15-hydroxycembra-1,3,7,11-tetraene [**5**] (Scheme 2).

The structure of isosarcophytoxide [**6**], a positional isomer of sarcophytoxide [**1**],

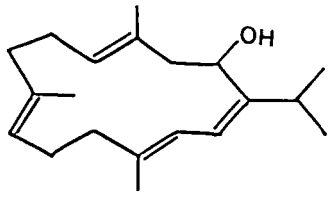


1 (+)-sarcophytoxide **2** (+)-sarcophine

SCHEME 1. Absolute configuration of sarcophytoxide [**1**] by chemical correlation of **1** and **2**



3 sarcophytoxide



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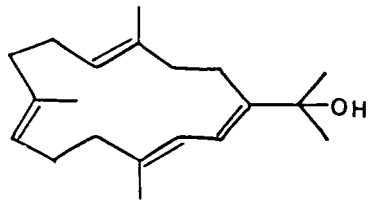

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SCHEME 2. Metabolites from *Lobophytum pauciflorum*

was first reported from a *Sarcophyton* species (14). The relative stereochemistry was not assigned for the epoxide and dihydrofuran rings; the compound was an oil. Recent investigations of *S. glaucum* from Guam (15) and *Sarcophyton* cf. *birklandi* Veseveldt from Australia provided an opportunity to determine the relative and absolute configuration of **6** and of its diastereomer [**7**] which could be obtained in crystalline form.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Reichert microscopic hot-stage apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ solutions with a Perkin-Elmer 141 polarimeter. Ir spectra were determined on KBr plates as films or nujol mulls using a Perkin-Elmer 297 ir spectrophotometer. Uv spectra were recorded in EtOH solutions using a Varian 634 spectrophotometer. ^{1}H- and ^{13}C-nmr spectra were recorded in $CDCl_3$ solution on a Bruker AM300 nmr spectrometer using $CHCl_3$ (δ 7.26) as reference. Eims spectra were recorded on a JEOL D100 mass spectrometer with a peak matching facility against PFK standards. Si gel, type 60 (Merck), was used for column chromatography, and plastic-backed plates coated with Si gel F254 (Merck) were used for tlc. Plates were visualized by spraying with vanillin-H_2SO_4 and warming.

LOBOPHYTUM PAUCIFLORUM METABOLITES.—Colonies of *L. pauciflorum* (0073)[1] were collected at Potter Reef off Innisfail, North Queensland, Australia, in July 1984. The coral was frozen on collection and freeze dried. Two separate collections of the coral were made, (a) colonies overgrown with algae and (b) colonies free from algal overgrowth. A voucher specimen is preserved at the Northern Territory Museum (C 5389).

(a) Freeze dried colonies with algal overgrowth (214 g) were extracted with CH_2Cl_2 (3×200 ml) to give a crude extract (8.3 g). Rapid chromatography on Si gel (16) afforded two major diterpenes: the known diterpene 14-hydroxycembra-1,3,7,11-tetraene [**4**] (1.2 g) identical with an authentic sample (13) by ^{1}H and ^{13}C nmr and the novel metabolite 15-hydroxycembra-1,3,7,11-tetraene [**5**] (0.8 g), crystals (hexane) mp 81-83°; uv λ max (EtOH) 245 sh (10500), 250 (11100), 260 sh (8800) nm; ir ν max (nujol) 3380 (broad), 1500, 1375, 1180 cm^{-1}; ^{1}H nmr δ (300 MHz, $CDCl_3$), 6.33 (d, 1H, J=11 Hz, H2); 5.84 (br d, 1H, J=11 Hz, H3), 4.95 (t, 2H, $J\sim$7 Hz, H7, H11), 2.3-2.0 (complex, 10H), 1.74 (s, 3H, 4-CH_3), 1.58, 1.52 (pr s, 3H, 3H, vinyl CH_3), 1.34 (s, 6H, isopropyl CH_3); ^{13}C nmr (75 MHz, $CDCl_3$) ppm 147.1 (s), 137.8 (s), 134.9 (s), 133.9 (s), 125.6 (d), 125.3 (d), 120.5 (d), 118.7 (d), 41.8 (t), 38.9 (t), 38.6 (t), 29.7 (q, 2C), 26.3 (t), 24.7 (t), 24.3 (t), 17.8 (q), 15.7 (q), 15.6 (q); eims *m/z* 288.235 ($M^{\cdot+}$, 50%, $C_{20}H_{32}O$ requires 288.245), 270 (50), 137 (60), 121 (75), 119 (100), 109 (70), 107 (55), 105 (60).

(b) Freeze dried colonies free from algal overgrowth (185 g) were extracted with CH_2Cl_2 (3×200 ml) to give a crude extract (7.5 g). Rapid chromatography on Si gel (16), and recrystallization from hexane af-

[1]Phil Alderslade, Northern Territory Museum, Darwin, Northern Territory, Australia, provided taxonomic identification.

TABLE 1. ^{13}C- and ^{1}H-nmr Assignments for the Two Sarcophytoxides **1** and **3**[a]

Carbon Atom	Compounds					
	1			**3**		
	^{13}C ppm	^{1}H δ, m, *J* Hz	^{1}H-^{13}C Correlation (*J* = 10 Hz)	^{13}C ppm	^{1}H δ, m, *J* Hz	^{1}H-^{13}C Correlation (*J* = 10 Hz)
1	133.5	—	—	133.9	—	—
2	83.8	5.53, m	83.8, 127.5, 133.5	85.3	5.30, m	85.3, 125.5
3	126.4	5.22, d, 10.2	15.6	125.5	5.17, d, 9.8	17.6, 35.1, 78.3, 125.5
4	139.2	—	—	140.2	—	—
5	37.6	2.3	—	35.1	2.25 2.05	27.4, 35.1, 125.5
6	25.4	1.9 1.3	—	27.4	1.75 1.65	27.4, 35.1, 62.3
7	61.9	2.71, t, 4.1	61.9	62.3	2.60, t, 5.6	16.4, 35.1, 38.8, 62.3
8	59.8	—	—	60.1	—	—
9	39.7	2.0 1.0, dt, 13.0, 2.9	— 17.0, 39.7, 61.9	38.8	1.90 1.05, dt, 12.8, 4.2	38.8, 62.3, 123.5
10	23.5	2.2 1.9	— —	23.1	2.25 1.85	23.1, 123.5
11	123.7	5.09, dd, 10.8, 5.1	—	123.5	5.03, t, 7.4	15.4, 23.1, 38.8, 123.5
12	136.7	—	—	135.8	—	—
13	36.7	1.9	—	38.4	2.1 1.8	15.4, 23.7, 38.4, 135.8
14	26.0	1.6 2.6	— —	23.7	2.25 1.60	23.7, 38.4, 133.9
15	127.5	—	—	128.1	—	—
16	78.4	4.49, "s"	—	78.3	4.43, d(ABq), 11.7, 5 4.37	78.3, 128.1, 133.9
17	10.1	1.64, s	10.1, 127.5, 133.5	10.3	1.57, s	10.3, 128.1, 133.9
18	15.6	1.81, s	15.6, 37.6, 126.4, 139.2	17.6	1.76, s	17.6, 125.5, 140.2
19	17.0	1.26, s	17.0, 59.8, 61.9, 39.7	16.4	1.17, s	16.4, 38.8, 60.1, 62.3
20	15.2	1.58, s	15.2, 36.7, 123.7, 136.7	15.4	1.49, s	15.4, 38.4, 123.5, 135.8

[a]All spectra were recorded in $CDCl_3$ containing $CHCl_3$ (δ 7.26) as internal standard, on a Bruker AM300 NMR spectrometer (300 MHz in ^{1}H, 75 MHz in ^{13}C). Assignments are based on one bond ^{1}H-^{13}C correlation (XHCORR, *J* = 125 Hz) for proton-bearing carbons and two or three bond ^{1}H-^{13}C correlations (XHCORR, *J* = 10 Hz) for quaternary carbons (25-27). All assignments are unambiguous.

forded (2*R*,7*S*,8*S*)-sarcophytoxide [**3**] (1.8 g), mp 52-56°; $[\alpha]_D$ − 64° (*c*, 0.6); ir ν max 2920, 2850, 1655, 1440, 1385, 1065, 935, 870 cm^{-1}; ^1H nmr δ (300 MHz, $CDCl_3$) see Table 1; ^{13}C nmr (75 MHz, $CDCl_3$) ppm, see Table 1; eims *m/z* 302.220 ($M^{\cdot+}$, 70%, $C_{20}H_{30}O_2$ requires 302.225), 228 (20), 230 (20), 177 (30), 175 (43), 163 (100), 149 (80), 135 (80), 109 (70), 95 (75).

Zn-Cu COUPLE REDUCTIVE CLEAVAGE OF **3**.—The epoxide **3** (100 mg) in absolute EtOH (20 ml) dried over Mg, was treated with a zinc-copper couple prepared from Zn dust (0.25 g) and 4% $CuSO_4$ solution (4). The mixture was heated under reflux for 72 h, filtered, and the solvent removed in vacuo. The less polar product was separated from unreacted epoxy compound **3** by rapid Si gel chromatography.

The product, (2*R*)-sarcophytonin [**8**] (60 mg) was identical with the literature report in all respects save $[\alpha]_D$ − 113.5° (*c*, 2.3); [lit. (14): − 210° (*c*, 0.1)].

Zn-Cu COUPLE REDUCTIVE CLEAVAGE OF (2*R*,7*R*,8*R*)-SARCOPHYTOXIDE [**1**].—Under conditions identical to the above, an authentic sample of (2*R*,7*R*,8*R*)-sarcophytoxide [**1**] (100 mg) afforded (2*R*-sarcophytonin [**8**] (85 mg) identical with the natural product in all respects save $[\alpha]_D$ − 198° (*c*, 0.7); [lit. (14): − 210° (*c*, 0.1)].

SARCOPHYTON cf. *BIRKLANDI* METABOLITES.—A small colony of *Sarcophyton* cf. *birklandi* was collected near Peloris Island, Palm Island group, 80 km northwest of Townsville, Australia, in November 1985; a voucher specimen is preserved at the Northern Territory Museum. It was frozen on collection and freeze dried. The freeze dried colony (7.6 g) was extracted with CH_2Cl_2 (3 × 100 ml) to give on concentration, a crude extract (0.9 g). Rapid Si gel chromatography afforded in order of increasing polarity, the known diterpenes: cembra-1,3,7,11-tetraene (20 mg), 11,12-epoxycembra-1,3,7-triene (35 mg) (8), (2*R*,11*R*,12*R*)-isosarcophytoxide [**6**] (23 mg), $[\alpha]_D$ − 128° [lit. (14): − 166°] and a new diterpene (2*S*,11*R*,12*R*)-isosarcophytoxide [**7**] (61 mg), mp 70-71°; $[\alpha]_D$ − 64° (*c*, 0.6); ir ν max 2920, 2850, 1440, 1380, 1040, 940 cm^{-1}; ^1H nmr δ (300 MHz, $CDCl_3$) see Table 2; ^{13}C nmr (75 MHz, $CDCl_3$) ppm, see Table 2; eims *m/z* 302.225 ($M^{\cdot+}$, 35%, $C_{20}H_{30}O_2$ requires 302.217), 187 (18), 285 (20), 177 (35).

Zn-Cu COUPLE REDUCTION OF (2*S*,11*R*,12*R*)-ISOSARCOPHYTOXIDE [**7**].—Under identical conditions to those earlier described, (2*S*,11*R*,12*R*)-isosarcophytoxide [**7**], $[\alpha]_D$ + 210°, (20 mg) was treated with a Zn-Cu couple to afford (2*S*)-sarcophytonin [**9**] (10 mg) $[\alpha]_D$ + 239° (*c*, 0.1) [lit. (14): $[\alpha]_D$ 210 − 210° (*c*, 0.1)] identical in all other respects with the literature report.

SARCOPHYTON GLAUCUM METABOLITES.—Samples of *S. glaucum* (450 g) (voucher specimen preserved at the University of Hawaii at Manoa Museum, Honolulu, Hawaii) collected in Guam in 1981 were frozen and blended with EtOH (1 liter). The homogenate was filtered through Whatman #1 filter paper, and the solvent removed in vacuo. The aqueous extract was frozen, freeze dried, and subjected to a Kupchan partition scheme (17). The CCl_4 portion (17 g) was shown by ^1H nmr to contain terpenes and was rapidly chromatographed in Si gel using hexane with increasing proportions of EtOAc as eluent. The fraction containing **6** and **7** by ^1H nmr was separated by hplc on Si gel using EtOAc-hexane (1:9). In this way (2*R*,11*R*,12*R*)-isosarcophytoxide [**6**] (60 mg), $[\alpha]_D$ − 156°, and (2*S*,11*R*,12*R*)-isosarcophytoxide [**7**] (100 mg), $[\alpha]_D$ + 196°, were isolated. The compounds isolated from *S. glaucum* (Guam) were identical in all respects with those from *Sarcophyton* cf. *birklandi* (Australia).

SINGLE CRYSTAL X-RAY DETERMINATION OF **7** (ex *S. glaucum*, Guam).—The ORTEP (18) perspective drawing of **7** appears as Figure 1. Atomic coordinates of all atoms in **7** appear in Table 3.[2]

CRYSTAL DATA.—$C_{20}H_{30}O_2$, M 302, orthorhombic space group $P2_12_12_1$, cell dimensions: a 10.736 (5), b 17.641 (9), c 9.862 (6)Å. A colorless, wedgeshaped crystal (0.7 mm × 0.3 mm × 0.3 mm) was mounted along the longest dimension and data collected on a Nicolet PI 4-circle diffractometer using MoK_α radiation from a graphite monochromator. The 2θ/θ scan mode was used with a scan "width" of − 1.2° to + 1.4°, a scan rate of 4°-24°/min, and a 2θ range of 3.0° to 50.0°. The 1512 reflections for which $I > 3\sigma$ (I) of the 3307 unique reflections were used in the structure solution. MULTAN 80 (19) did not yield a satisfactory solution in default operation, and many "solutions" were tried in the SHELX program (20) but gave R ≈ 50%. After the known crystal structure of sarcophine [**2**] (10) was input into MULTAN, the resulting solution with the highest figure of merit revealed the positions of 20 atoms. The remaining atoms were located in Fourier maps and refinement proceeded uneventfully to R = 3.68% (R = 0.037, Rw = 0.032).

The Hamilton R-value test (21) was applied to the structure (Figure 1) and its mirror image and indicated that the absolute configuration represented in the ORTEP diagram (Figure 1) was correct at the

[2]Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK.

TABLE 2. ^{13}C- and ^{1}H-nmr Assignments for the Two Sarcophytoxides **6** and **7**[a]

Carbon Atom	Compounds					
	6			**7**		
	^{13}C ppm	^{1}H δ, m, *J* Hz	^{1}H-^{13}C Correlation (*J*=10 Hz)	^{13}C ppm	^{1}H δ, m, *J* Hz	^{1}H-^{13}C Correlation (*J*=10 Hz)
1	132.7	—	—	132.6	—	—
2	84.6	5.33, m	84.6, 125.5	83.4	5.40, m	—
3	125.5	5.04, d, 11.1	15.1, 39.7, 125.5	126.6	5.05, d, 10.2	14.6, 38.9, 126.6
4	140.8	—	—	139.9	—	—
5	39.7	2.3	24.6, 39.7, 125.5, 140.8	38.9	2.3	24.3
		2.0	24.6, 39.7, 125.5		2.1	—
6	24.6	2.1	24.6, 39.7, 125.5	24.3	2.4	—
					2.0	
7	125.5	4.99, t, 6.8	15.1, 39.7, 125.5	125.7	5.0, m	14.7, 36.7, 125.7
8	133.1	—	—	133.2	—	—
9	37.0	2.0	37.0	36.7	2.3	23.6, 36.7, 133.2, 125.7
					2.0	
10	24.2	1.8	24.2, 60.7, 61.2	23.8	2.0	
		1.4			1.3	
11	61.2	2.75, dd, 9.2, 3.2	61.2	62.3	2.50, dd, 10.6, 2.5	62.3
12	60.7	—		61.4	—	
13	35.4	1.9	20.4, 35.4, 60.7	37.4	1.8	
		1.2			0.92, t, 11.1	22.5, 37.4, 61.4, 132.6
14	20.4	1.9	—	22.5	2.3	
					1.8	22.5, 37.4, 132.6
15	128.4	—		128.3	—	
16	78.3	4.41, "s"	78.3, 128.4, 132.7	78.3	4.49 ($AB^{1}\rightarrow A_2$)	78.3, 128.3, 132.6
17	10.2	1.58, s	10.2, 78.3, 128.4, 132.7	9.9	1.65, s	9.9, 78.2, 128.3, 132.6
18	15.1	1.70, s	15.1, 39.7, 125.5, 140.8	14.6	1.58, s	14.6, 38.9, 126.6, 139.9
19	15.1	1.58, s	15.1, 37.0, 125.5, 133.1	14.7	1.58, s	14.7, 36.7, 125.7, 133.2
20	7.7	1.18, s	15.1, 37.0, 125.5, 133.1	15.7	1.28, s	14.7, 36.7, 125.7, 133.2

[a]All spectra were recorded in $CDCl_3$ containing $CHCl_3$ (δ 7.26) as internal standard, on a Bruker AM300 NMR spectrometer (300 MHz in ^{1}H, 75 MHz in ^{13}C). Assignments are based on one bond ^{1}H-^{13}C correlation (XHCORR, *J*=125 Hz) for proton-bearing carbons and two or three bond ^{1}H-^{13}C correlations (XHCORR, *J*=10 Hz) for quaternary carbons (25-27). All assignments are unambiguous.

TABLE 3. Atomic Coordinates (see Figure 1 for numbering system)

Atom	*x*	*y*	*z*
C(1)	0.8117(4)	−0.1291(2)	1.0441(4)
C(2)	0.9180(4)	−0.1257(2)	1.1411(4)
C(3)	1.0334(4)	−0.1024(2)	1.1180(4)
C(4)	1.1283(4)	−0.1012(2)	1.2295(5)
C(5)	1.1924(4)	−0.0240(2)	1.2439(7)
C(6)	1.1040(3)	0.0393(2)	1.2650(4)
C(7)	1.1098(4)	0.1086(2)	1.2137(3)
C(8)	1.0121(5)	0.1662(2)	1.2466(5)
C(9)	0.9454(6)	0.2003(2)	1.1244(6)
C(10)	0.8735(6)	0.1416(2)	1.0422(4)
C(11)	0.7432(5)	0.1248(2)	1.0513(4)
C(12)	0.7041(6)	0.0451(2)	1.0113(4)
C(13)	0.7009(5)	−0.0081(2)	1.1326(3)
C(14)	0.6946(3)	−0.0913(2)	1.0966(3)
C(15)	0.6064(4)	−0.1410(2)	1.1129(3)
C(16)	0.6497(5)	−0.2162(3)	1.0723(5)
C(17)	0.4775(6)	−0.1276(5)	1.1659(8)
C(18)	1.0782(6)	−0.0780(3)	0.9793(6)
C(19)	1.2148(6)	0.1340(3)	1.1229(7)
C(20)	0.6564(6)	0.1673(3)	1.1418(5)
O(21)	0.7733(3)	−0.2070(1)	1.0233(3)
O(22)	0.7924(3)	0.1679(1)	0.9374(2)
H(1)	0.836(2)	−0.108(1)	0.955(2)
H(2)	0.901(2)	−0.141(1)	1.241(3)
H(4)	1.192(2)	−0.140(1)	1.211(3)
H(4)′	1.081(3)	−0.115(1)	1.323(3)
H(5)	1.242(3)	−0.025(2)	1.321(4)
H(5)′	1.249(3)	−0.012(2)	1.150(4)
H(6)	1.034(2)	0.033(1)	1.321(2)
H(8)	1.063(2)	0.208(2)	1.297(3)
H(8)′	0.937(3)	0.149(2)	1.297(3)
H(9)	0.882(2)	0.237(1)	1.135(3)
H(9)′	1.004(3)	0.222(2)	1.068(3)
H(10)	0.927(2)	0.103(1)	1.013(2)
H(12)	0.761(3)	0.030(2)	0.945(3)
H(12)′	0.623(3)	0.045(2)	0.965(4)
H(13)	0.631(2)	0.004(1)	1.195(3)
H(13)′	0.783(2)	0.000(1)	1.187(2)
H(16)	0.604(3)	−0.237(2)	1.003(4)
H(16)′	0.659(3)	−0.249(2)	1.163(3)
H(17)	0.461(5)	−0.071(2)	1.182(5)
H(17)′	0.474(5)	−0.158(2)	1.221(5)
H17″	0.421(4)	−0.139(2)	1.100(4)
H(18)	1.080(3)	−0.027(2)	0.971(4)
H(18)′	1.028(4)	−0.097(2)	0.897(4)
H18″	1.167(4)	−0.098(2)	0.964(4)
H(19)	1.167(6)	0.133(3)	1.020(7)
H(19)′	1.296(5)	0.112(3)	1.120(6)
H19″	1.223(4)	0.178(2)	1.140(4)
H(20)	0.650(4)	0.151(2)	1.249(5)
H(20)′	0.690(3)	0.212(2)	1.148(4)
H20″	0.578(8)	0.161(5)	1.120(9)

99.995% confidence limit. This finding was at odds with the chemical correlation, which devolved from Kashman's original assignment of the absolute configuration of sarcophine [**2**] (11). The chemical results favored the enantiomer of the ORTEP representation of **7**. Unfortunately, the X-ray results at this level of

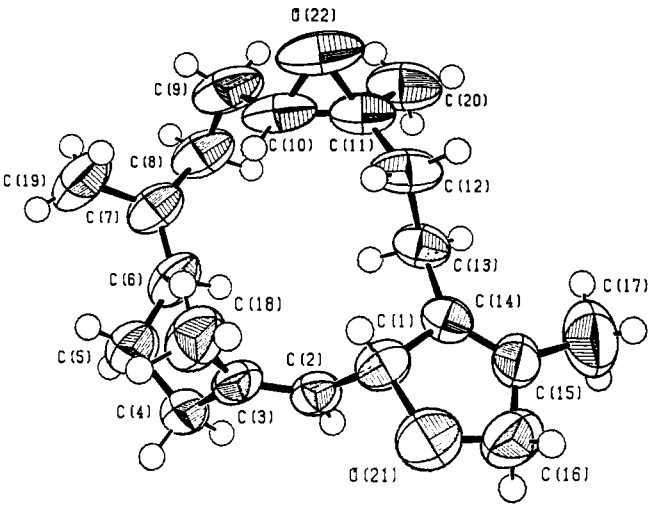


FIGURE 1. Perspective view of **7** with the non-hydrogen atoms shown as thermal ellipsoids at the 40% probability level (ORTEP Diagram). Crystallographers numbering scheme is indicated. (It differs from the chemists numbering scheme.)

resolution were not regarded as being sufficient per se to establish the absolute configuration of **7**. We have chosen to accept Kashman's assignment (11) for consistency throughout this paper.

RESULTS AND DISCUSSION

Our reinvestigation of the sarcophytoxides [**1** and **3**] and of the isosarcophytoxides [**6** and **7**] arose when we observed a monospecific clump of *L. pauciflorum* in which some colonies were overgrown by filamentous algae (especially *Ceramium gracillimum* and *Enteromorpha* sp.), while others appeared unaffected by this phenomenon. Investigation of the chemistry of the overgrown and non-overgrown colonies revealed significant differences. The overgrown colonies contained only (2*R*,7*S*,8*S*)-sarcophytoxide [**3**], while the non-overgrown colonies contained 14-hydroxycembra-1,3,7,11-tetraene [**4**] and 15-hydroxycembra-1,3,7,11-tetraene [**5**]. The biological implications of the phenomenon have been discussed elsewhere (22). A second study of overgrown and non-overgrown colonies again revealed differences in chemistry, but careful taxonomic evaluation[1] suggested that the two colonies in this case were probably different species. From *Sarcophyton birklandi*,[1] the overgrown colony of the two, we obtained (2*R*,7*R*,8*R*)-sarcophytoxide [**1**] and from the non-overgrown colonies identified as *Sarcophyton* cf. *birklandi*,[1] we obtained the two isosarcophytoxides [**6** and **7**] and the known diterpenes cembra-1,3,7,11-tetraene and 11,12-epoxycembra-1,3,7-triene (8,23). Because the nmr data on the four isomeric dihydrofurans had not been reported under identical conditions, Tables 1 and 2 contain ^{1}H- and ^{13}C-nmr data for the four isomers [**1**,**3**,**6**, and **7**] at 300 and 75 MHz, respectively. Schemes 1, 2, and 3 summarize the structural and stereochemical features of this investigation.

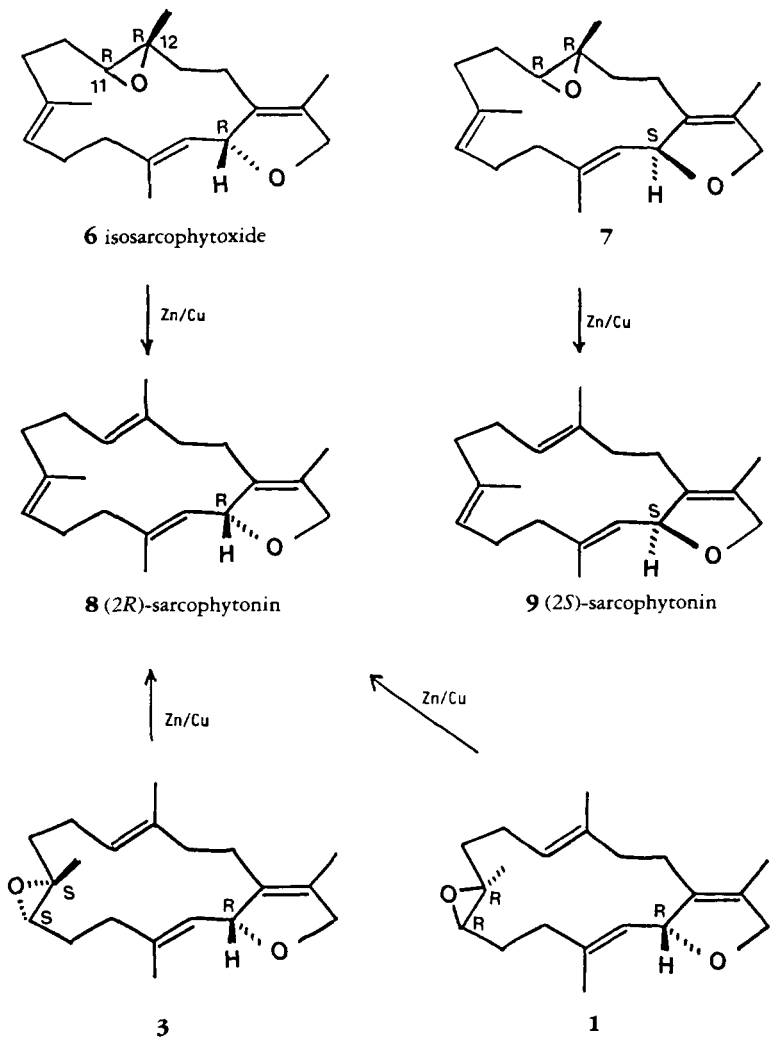
The two sarcophytoxides [**1** and **3**], $[\alpha]_D - 191°$ and $-64°$, respectively, were each converted to (2*R*)-sarcophytonin [**8**] ($[\alpha]_D - 156 \pm 42°$).[3] This confirmed the fact that each sarcophytoxide **1** and **3** had the same absolute configuration at the C-2 position and differed in the configuration of the 7,8-epoxide functionality. (2*R*,7*R*,8*R*)-Sarcophytoxide [**1**] is enantiomeric with compounds isolated by Kashman (6), Kobayashi

[3]Better agreement could not be obtained and lack of material precluded further purification. It is difficult to interpret the sign and order of magnitude in any other way.

(12), and Faulkner (9) and has the absolute configuration depicted in Scheme 3. (2*R*,7*S*,8*S*)-Sarcophytoxide [**3**] has the opposite absolute configuration at the 7,8-epoxide functionality (Scheme 3).

The two isosarcophytoxides [**6** and **7**] exhibited large specific rotations, $[\alpha]_D = -161 \pm 5°$ and $+203 \pm 7°$, respectively, which differed in the sign of rotation. Reductive elimination of the epoxide group in **6** with a Zn-Cu couple (4) afforded (2*R*)-sarcophytonin [**8**] (24) ($[\alpha]_D -210°$), while the same Zn-Cu couple mediated reaction (4) on **7** afforded (2*S*-sarcophytonin [**9**] ($[\alpha]_D +239°$). In this case the isosarcophytoxides [**6** and **7**] differed in absolute configuration at the C-2 position; the absolute configuration of the epoxide groups was the same in **6** and **7**. The single crystal X-ray structure determination of **7** (Figure 1) determined the relative configuration between the dihydrofuran and the 11,12-epoxide group in **7**. The absolute configuration of **6** and **7** was established by the reductive elimination reaction sequence and is as depicted in Scheme 3.

It is of interest that this latter finding is consistent with the notion advanced by Kashman (6) that the doubly allylic oxygenated position of the dihydrofuran ring may



SCHEME 3. Chemical correlation of absolute configuration for **1**,**3**,**6**, and **7**

epimerize under certain conditions. Thus, the isosarcophytoxides [**6** and **7**] co-occur within the same coral and differ in configuration only at the doubly allylic C-2 position. In our hands however, these compounds seem to be exceedingly configurationally stable when pure, and indeed, our samples of (2*R*,7*R*,8*R*)-sarcophytoxide [**1**] [enantiomeric with Kashman's (2*S*,7*S*,8*S*)-sarcophytoxide which may not have been pure] and the (2*R*,7*S*,8*S*)-sarcophytoxide [**3**] were both configurationally stable under all conditions to which they were subjected. We prefer the proposition that the formation of both 2-epimeric isosarcophytoxides [**6** and **7**] in *S. glaucum* and *S.* cf. *birklandi* was biologically mediated and not a reflection of configurational instability at C-2.

The structure of the diterpene **5** isolated from the non-overgrown colonies of *L. pauciflorum* follows from the spectroscopic data. The molecular formula, $C_{20}H_{32}O$, required five double bond equivalents. There were four double bonds present in the molecule (8 sp^2 carbon signals) and a cembrane ring. Three methyl groups were present on double bonds (δ 1.74, 1.58, 1.52), and two methyl groups were on oxygenated carbons (δ 1.34). Two of the double bonds were conjugated [λ max 245 (sh), 250, 260 sh nm (ε 10,500, 11,100 and 8,800); (δ 6.35, 5.84, ABq, $J \approx 11$ Hz)]. Only one structure [**5**] is compatible with these data, assuming that there are no doubly allylic protons. No signals were observed in ^{1}H-nmr spectrum of **5** between δ 3 and δ 2.5. The new diterpene **5** was, thus, 15-hydroxycembra-1,3,7,11-tetraene. All trisubstituted methyl bearing double bonds were *E* with respect to the continuous carbon chain (three methyl signals upfield of 20 ppm).

The relative and absolute stereochemistry of the four isomeric sarcophytoxides [**1**, **3**, **6**, and **7**] have been related to the absolute configuration assigned to (+)-sarcophine [**2**] by Kashman (11), and the structure of the new cembranoid diterpene **5** established. It should be noted that the results of the X-ray structure determination herein reported cast some doubt on Kashman's original assignment. Unfortunately, the nature of the X-ray experiment using Mo radiation is not sufficiently unambiguous per se to introduce such a major change to the literature.

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