purified by preparative GLC on a 15-ft Carbowax 20M column at 160 °C: NMR δ 1.01 (d, $J = 7$ Hz, 6 H), absence of signal at δ 5.7; IR similar to that of **5**.

2,7-Dimethyl-2-(2-propynyl)-4-cycloheptenone (6). To 7.02 g (50.9 mmol) of 2,7-dimethyl-4-cycloheptenone (**5**) in 40 mL of DMF was added 2.9 g (60.4 mmol) of 50% NaH dispersion. The mixture was stirred until the slow bubbling stopped (ca. 2 h). Propargyl bromide (7.6 g, 63.8 mmol) was added slowly with external cooling (vigorous reaction), and the mixture was stirred overnight at room temperature. The reaction mixture was poured into ice–water and extracted with ether, and the ethereal solution was washed with $NaHCO_3$ solution and NaCl solution, dried over $MgSO_4$, and evaporated under reduced pressure. The crude oil was fractionally distilled to give unchanged **5** [2.8 g; bp 47–52 °C (2.5 mm)] and **6** (0.94 g; bp 83–90 °C (2.5 mm); 18%, 30% with allowance for recovered **5**]: NMR δ 1.00 (d, $J = 7$ Hz, each further split by 1 Hz, 3 H), 1.11 (s, 3 H), 1.8–2.8 (including $C{\equiv}CH$ and H α to carbonyl at ca. 2.4), 3.5 (m, 1 H), 5.62 (m, 2 H). There was evidence of a mixture of isomers in some later fractions: IR 3225 (s), 2990 (sh), 2970 (s), 2950 (s), 2095 (w), 1690 (s), 1440 (m), 1180 (w), 1140 (w), 990 (m) cm^{-1}.

2,7-Dimethyl-2-(2-oxopropyl)cyclohept-4-enone (7). Propargyl ketone **6** (9.99 g, 5.56 mmol) in 8 mL of glacial acetic acid, 0.8 mL of water, and 0.44 g of Dowex 50 impregnated with Hg^{2+} ion[7] was refluxed for 45 min. The solution was decanted, and the Dowex 50 was washed with ether (3 × 30 mL), which was added to the decanted solution. Remaining acid was neutralized by addition of $NaHCO_3$. The ether extract was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The pale yellow oil was distilled to give 0.61 g (56%) of **7**: bp 104–106 °C (2 mm); NMR δ 1.07 (d, $J = 7$ Hz, 3 H), 1.15 (s, 3 H), 1.8–3.0 (incld δ 2.00 (s) and δ 2.06 (s)), 5–6 (m, 2 H); IR 2950 (s), 1690 (s) with 1730 (sh), 1435 (m), and 1345 (m), 1145 (m), 1110 (m), 990 (m) cm^{-1}; mass spectrum, *m/e* 196 (M^+).

Cyclization of 2,7-dimethyl-2-(2-oxopropyl)cyclohept-4-enone (7). Diketone **7** (9.76 g, 3.88 mmol) in 5 mL of *tert*-butyl alcohol was added dropwise to 0.76 g (6.78 mmol) of potassium *tert*-butoxide in 30 mL of *tert*-butyl alcohol, and the mixture was stirred under nitrogen at room temperature for 2 h. The mixture was then poured into 60 mL of ice-cold 10% H_2SO_4 and extracted with 100 mL of dichloromethane. The dichloromethane solution was washed with $NaHCO_3$ and then with water, dried over Na_2SO_4, and evaporated under reduced pressure. GLC analysis showed one major and three minor components in the crude residue. Distillation yielded 0.57 g (87%) of **8**: bp 122–128 °C (4 mm); NMR δ 1.21 (d, $J = 9$ Hz, 3 H), 1.20 (s, 3 H), 1.8–2.8 (incld δ 2.2 (s), 6 H), 5.7 (d, $J = 1$ Hz, 1 H), 5.82 (m, 2 H); IR 3015 (sh), 2980 (s), 2965 (s), 1700 (s with sh at 1735), 1600 (m), 1450 (w), 1370 (w), 1250 (w) cm^{-1}. The semicarbazone of **8** was prepared and recrystallized from alcohol; mp 185–187 °C. Anal. Calcd for $C_{13}H_{19}N_3O_3$: C, 66.92; H, 8.21; N, 18.01. Found: C, 66.55; H, 8.18; N, 17.58.

Acknowledgment. We thank the Robert A. Welch Foundation for generous financial support.

Registry No. *cis*-4, 1476-11-5; **5**, 31333-42-3; **6**, 78109-59-8; **7**, 78109-60-1; **8**, 78109-61-2; **8** semicarbazone, 78109-62-3; 3-pentanone, 96-22-0; 2,7-dimethylcycloheptanone, 7272-19-7; propargyl bromide, 106-96-7.

Further Cembranoid Derivatives from the Red Sea Soft Corals *Alcyonium flaccidum* and *Lobophytum crassum*

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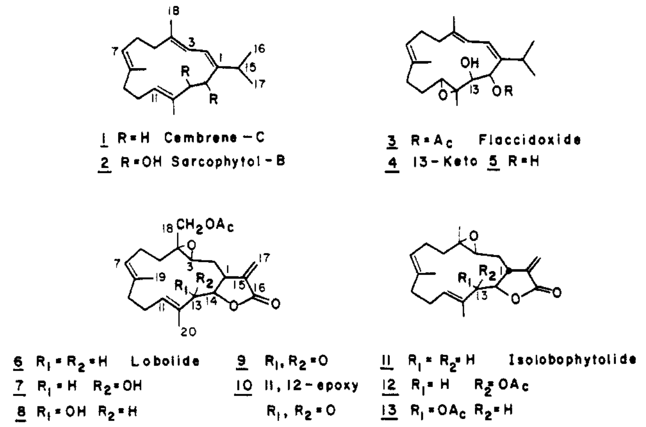
Received August 13, 1980

The cembranoid content of two soft corals has been investigated. Three compounds were isolated from *Alcyonium flaccidum* and were found to be cembrene-C (**1**), sarcophytol-B (**2**), and the as yet unreported 11,12-epoxy-13-hydroxy-14-acetoxycembrene-C (**3**), which was named flaccidoxide. From *Lobophytum crassum*, another soft coral whose chemical content was found to change remarkably with place of collection, were isolated two new 13-hydroxylobolides (**7** and **8**) in addition to lobolide (**6**), and their structures were characterized. The ^{13}C NMR spectra of all the above compounds were assigned.

Among the soft coral diterpenoids, the cembrane-type diterpenes form a large group of compounds which are widely distributed within the alcyonarian.[1,2] Of special interest are the observed, although not yet well understood, variations within a specific soft coral in the content of cembranes and other terpenoids.[2]

The case of *Sarcophyton glaucum* can serve as a good example for such variations as a function of location. Thus *S. glaucum* from the Red Sea yielded several cembranoids, the most prominent of which were the fish toxins sarcophine and sarcophytoxide (16-deoxysarcophine).[3] Tursch and co-workers,[4] on the other hand, found no sarcophine in *S. glaucum* specimens collected at Laing Island on the north coast of New Guinea but instead obtained sarcoglaucol, another new cembranoid fish toxin.[5] Most recently, Kobayashi and co-workers[6] reported isolation of

Chart I



1 R = H Cembrene-C
2 R = OH Sarcophytol-B
3 R = Ac Flaccidoxide
4 13-Keto **5** R = H
6 $R_1 = R_2 = H$ Lobolide
7 $R_1 = H$ $R_2 = OH$
8 $R_1 = OH$ $R_2 = H$
9 $R_1, R_2 = O$
10 11,12-epoxy $R_1, R_2 = O$
11 $R_1 = R_2 = H$ Isolobophytolide
12 $R_1 = H$ $R_2 = OAc$
13 $R_1 = OAc$ $R_2 = H$

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[1] A. J. Weinheimer, C. W. J. Chang, and J. A. Matson in *Fortscher. Chem. Org. Naturst.*, **36**, 286 (1979).

[2] For an up to date review, see B. Tursch, J. C. Braekman, D. Daloze, and M. Kaisin in "Marine Natural Products", Vol. 2, P. Scheuer Ed., Academic Press, New York, 1978, p 247.

[3] (a) J. Bernstein, U. Shmueli, E. Zadock, Y. Kashman, and I. Nēeman, *Tetrahedron*, **30**, 2817 (1974); (b) Y. Kashman, E. Zadock, and I. Nēeman, *ibid.*, **30**, 3615 (1974).

[4] M. Alberieci, J. C. Braekman, D. Daloze, and B. Tursch, *Bull. Soc. Chim. Belg.* 87, 487 (1978).

[5] Sarcoglaucol has been isolated recently by us also from *S. auritum* (unpublished results).

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Table I. ^1H NMR Chemical Shifts and Multiplicity Data (270 MHz, $CDCl_3$)

	compound														
	1[a]			2			3			4			5		
H at C	δ	mult	*J*, Hz	δ	mult	*J*, Hz	δ	mult	*J*, Hz	δ	mult	*J*, Hz	δ	mult	*J*, Hz
2	5.92	d	11	6.18	d	11.4	6.24	d	11.8	6.33	d	12	6.18	d	11.4
3	5.83	d	11	5.91	d	11.4	6.02	d	11.8	6.01	d	12	5.81	d	11.4
7	4.99	br t*		4.96	br t	5	5.15	m		5.14	m		5.10	m	
11	4.78	br t*		5.40	br t	5	3.17	dd	8.5, 2.6	3.06	dd		3.16	t	6
13				3.92	d	8	3.93	br d	9				3.74	d	7
14				4.73	d	8	5.66	d	9	6.19	s		4.48	d	7
15				2.56	m								2.59	m	
Me(16)	0.96	d	5.9	1.12	d	6.6	1.07	d	6.7	1.09	d	6.7	1.11	d	6.7
Me(17)	0.96	d	5.9	1.06	d	7.0	1.03	d	7.0	0.93	d	6.8	1.02	d	6.7
Me(18)	1.64	br s		1.74	br s		1.77	br s		1.78	br s		1.75	br s	
Me(19)	1.49	br s*		1.46	br s		1.47	br s		1.47	br s		1.51	br s	
Me(20)	1.42	br s*		1.63	br s		1.42	s		1.51	s		1.41	s	
CH_3CO_2							2.05	s		2.09	s				

[a] Asterisked values may be interchanged.

Table II. ^{13}C NMR Data of Cembrene-C and Derivatives (22.63 MHz, $CDCl_3$)

		shift, ppm					
C	mult[a]	1	2	3	5	A[e]	B[f]
1	s	146.2	144.1	140.4	145.1	147.0	146.8
2	d	118.6	121.5[d]	124.1[b]	120.4[b]	118.4	120.4[d]
3	d	122.1	121.9[d]	121.3[b]	121.7[b]	120.9	121.2[d]
4	s	134.7[d]	134.3[b]	139.1	137.7	135.8[c]	135.8[b]
5, 9	t	39.3,[b] 39.0[b]	39.8, 38.3	39.9, 36.5	39.3, 36.4	38.4,[b] 37.0[b]	39.6, 38.8
6, 10	t	25.3, 24.6	25.4, 24.5	25.9, 24.2	25.5, 24.1	25.3, 24.6	25.5, 24.5
7	d	125.0[c]	124.1[c]	126.1	126.4	127.1	125.2[c]
8	s	134.3	134.3[b]	134.3	134.0	133.8[c]	134.5[b]
11	d	124.6[c]	127.4[c]	60.9	60.5	60.4	124.5[c]
12	s	134.1[d]	136.2[b]	62.1	62.8	61.0	131.8
13	t, d	38.6[b]	77.5	73.4[c]	74.9	36.8[b]	44.5
14	t, d	28.1	73.2	71.3[c]	68.0		69.8
15	d	33.8	28.0	28.5	27.7	34.1	27.0
16, 17	q	22.4, 22.4	25.9, 23.7	25.1, 24.9	25.0, 24.6	22.3, 22.3	25.4, 24.5
18–20	q	17.2, 16.9, 15.7	16.4, 16.4, 15.9	16.3, 15.4, 17.3	16.2, 15.4, 16.7	17.4, 15.0, 18.1	16.3, 15.5, 18.2
$CH_3C{=}O$	s			170.3			
	q			21.1			

[a] Assignments of Multiplicities were made by off-resonance spin decoupling. [b-d] These signals may be interchanged. [e] 11,12-Epoxycembrene-C.[9] [f] 14-Hydroxycembrene-C (sarcophytol-A).[6]

still other previously unknown cembranoids from *S. glaucum* collected in Ishigaki Island, Okinawa Prefecture, but again found no sarcophine or sarcophytoxide.

We now report isolation from the petroleum ether extract of another soft coral, *Alcyonium flaccidum* (order Alcyonacea family Alcyoniidae), of three main cembrenoid constituents, all of which exhibited ^1H NMR signals and UV spectra characteristic of 1,4-tetrasubstituted dienes. Several dienes of this type, cembrene-C,[7] 7,8-epoxy-15-hydroxycembrene-C,[8] and 11,12-epoxycembrene-C,[9] have been previously isolated from soft corals.

The least polar diene was identified as cembrene-C (**1**). The diene next in polarity was identified as 13,14-dihydroxycembrene-C (**2**) and shown to be identical with sarcophytol-B of Kobayashi et al.[6] (See Chart I for various names and structures of compounds.)

The third compound which we named flaccidoxide (**3**) was deduced to be 11,12-epoxy-13-hydroxy-14-acetoxycembrene-C on the basis of its spectral properties. Like **1** and **2**, it had a UV maximum at 252 nm. The ^1H and ^{13}C NMR spectra summarized in Tables I and II point clearly to the common presence of the 1,4-tetrasubstituted diene (C-1 to C-4 and C-15 to C-18) in **1**–**3** (and **5** vide infra). The NMR spectra also revealed immediately that one of the two unconjugated double bonds present in compounds **1** and **2** was replaced in **3** by an epoxide [δ 60.9 (d) and 62.1 (s)]. Microozonolysis[10] of **3**, which resulted in levulinaldehyde and the presence of two vinyl methyl groups, further permitted extension of the 1,4-diene moiety into the same 13-carbon unit (C-1 to C-8) found in compounds **1** and **2**.

The second major functionality suggested by the spectroscopic data is $-CH_2\overline{CHOC}(CH_3)CH(OR)CH(OR)C<$ (R = H or Ac; see Tables I and II). This is the only combination which agrees with the observed δ values and multiplicites in the ^1H NMR spectrum; thus, the single epoxidic proton appears as a double doublet, split by the protons of a vicinal CH_2 group, while the two methins of the CHOH and CHOAc groups appear as doublets with only mutual coupling among themselves (see Table I). The above two units (accounting for 19 of the 20 skeleton C atoms) together with the remaining CH_2 group can be linked to each other in only two ways, with the un-

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(6) M. Kobayashi, T. Nakagawa, and H. Mitsuhashi, *Chem. Pharm. Bull.*, **27**, 2382 (1979).

(7) D. J. Vanderah, N. Rutledge, F. J. Schmitz, and L. S. Ciereszko, *J. Org. Chem.*, **43**, 1614 (1978).

(8) J. C. Coll, G. B. Hawes, N. Liyanage, W. Oberhansli, and R. J. Wells, *Aust. J. Chem.*, **30**, 1305 (1977).

(9) B. F. Bowden, J. C. Coll, W. Hicks, R. Kazlauskas, and S. J. Mitchell, *Aust. J. Chem.*, **31**, 2707 (1978).

(10) B. P. Moore and W. V. Brown, *J. Chromatogr.*, **60**, 157 (1971).

Table III. ^1H NMR Chemical Shifts and Multiplicity Data (270 MHz, $CDCl_3$)

	compound								
	6			7			8		
H at C	δ	mult	*J*, Hz	δ	mult	*J*, Hz	δ	mult	*J*, Hz
1	2.85	m	13.5, 3.8, 6.7, 2.8, 3.1	3.30	m	3.2, 9.1, 6.5, 3.2, 2.6	2.75	m	3.4, 13.0, 6.8, 3.2, 2.9
2	1.88	dt	14.5, 3.8	1.80	ddd	14.4, 3.2, 2.6	1.87	ddd	14.5, 3.4, 2.6
2	1.52	ddd	14.5, 13.5, 6.9	1.49	ddd	14.4, 9.1, 7.3	1.50	ddd	14.5, 13.0, 7.3
3	2.94	dd	6.9, 3.8	2.90	dd	7.3, 2.6	2.86	dd	7.3, 2.6
7	5.04	br t	6.5	5.04	br t	6.8	5.04	br t	7.4
11	5.18	br dd	8.2, 5.0	5.62	br d	9.8	5.46	br dd	9.7, 3.5
13				4.46	br s	7.5 ($\Delta w_{1/2}$)	4.04	d	8.5
14	4.17	ddd	9.7, 6.7, 2.9	4.22	dd	6.5, 1.5	4.09	dd	8.5, 6.8
17	5.93	d	2.8	6.24	d	3.2	6.31	d	3.2
17	6.28	d	3.1	5.96	d	2.6	6.03	d	2.9
18	3.93	d	12.0	3.87	br d	12.1	3.88	br d	12.3
18	4.34	d	12.0	4.35	d	12.1	4.38	d	12.3
19, 20	1.61, 1.72	br s		1.61, 1.71	br s		1.64, 1.73	br s	
OAc	2.12	s		2.13	s		2.13	s	

Table IV. ^{13}C NMR Chemical Shifts (22.63 MHz, $CDCl_3$)

		shift, ppm					
C	mult[a]	6	11[g]	7	12[g]	8	13[g]
1	d	45.0	44.5	37.2	38.4	42.1	42.1
2	t	31.8[b]	32.3	33.0[b]	33.5	31.5[b]	32.3
3	d	61.9	63.0	62.5	62.8	62.5	63.0
4	s	60.4	60.1	60.4	60.3	60.4	60.2
5	t	32.4[b]	37.8	32.6[b]	37.6	32.6[b]	37.8
6	t	23.2	24.2	23.5	24.0	23.7	24.3
7[f]	d	124.5	124.5	124.2	124.8	124.1	124.6
8	s	135.0	134.5	135.2	134.5	135.2	134.7
9	t	38.7	39.0	38.6	38.7	38.5	38.6
10	t	24.8	24.9	24.6	24.5	24.7	24.8
11[f]	d	130.2	130.3	127.6	128.9	132.1	129.1
12	s	129.5	129.3	131.4	129.3	132.1	133.7
13[c,d]	t, d	45.3	45.2	73.5	75.9	80.7	79.9
14	d	79.6	79.9	82.0	80.5	82.1	80.4
15	s	139.7	140.0	139.8	139.4	138.7	138.6
16	s	169.4	169.6	170.1	169.5	169.1	169.6
17	t	122.7	122.5	123.4	123.1	124.1	123.9
18[e]	t,q	64.3	17.0	64.2	15.0	64.0	15.7
19	q	15.6	15.5	15.9	17.1	15.9	16.8
20	q	17.0	17.0	15.3	15.5	12.5	13.2
OAc	q	20.5		20.8	20.9	20.8	21.1
	s	170.4		170.9	169.5	170.8	169.6

[a] Assignments of multiplets were made by off-resonance spin decoupling. [b] These signals may be interchanged. [c] The C-13 configuration mainly affects C-1, C-13 and to a lesser extent C-20. [d] The OH/OAc replacement affects C-1 > C-11, C-12 > C-14, C-15, C-17, and C-20. [e] The CH_3/CH_2OAc replacement affects C-5 > C-6 and C-3. [f] C-12 being affected by C(14)–O (a γ effect) appears at higher field than C-8; distinction between C-7 and C-11 is tentative and is based on the larger variations in the δ values suggested for C-11 due to changes in C-13. [g] Compounds **11–13** are the 18-desacetoxy analogues of **6–8**, respectively; see Chart I.

protonated carbon next to the CHOR–methine being either C-1 or C-8. Of the two possible structures, only one, the one possessing the C-9,C-10 unfunctionalized ethylene bridge (formula **3**, Chart I), obeys the isoprene rule and has a cembrenoid skeleton.

Oxidation of **3** with Jones reagent gave a ketone (ν_{max} 1710 cm^{-1}) with essentially the same UV spectrum as **3**; a small, but definite downfield shift of H-2 from δ 6.24 to 6.33 (rather than a ca. 1-ppm shift as expected from a β-proton of an α,β-unsaturated ketone) and the IR maximum at 1710 cm^{-1} indicated that the acetoxy group was located at C-14. The observation that the CHOAc signal is shifted from δ 5.66 in **3** to δ 6.19 in **4** is also in accordance with an α-acetoxy ketone. Basic hydrolysis of **3** gave compound **5** with the spectral data expected of a 1,2-diol (see Experimental Section). Unequivocal proof for the structure of flaccidoxide (**3**) was obtained by formation of sarcophytol-B (**2**) on Zn/Cu deoxygenation of alcohol **5**.

Lobophytum crassum is another example which illustrates the chemical variations in the content in soft corals. From *L. crassum* collected at Leti Island, the Brussels group has isolated crassolide[11] whereas isolobophytolide (**11**), another cembranoid, has been isolated by Coll and co-workers from *L. crassum* collected on the Great Barrier Reef.[12] Our group has isolated lobolide (**6**) several times from *L. crassum* (collected during the period 1976–1979) in the Gulf of Eilat near Na'ama.[13]

We now report the isolation of the two epimeric 13-hydroxylobolides **7** and **8** isolated together with lobolide (**6**) from the petroleum ether extract of *L. crassum* which was collected near Dahab ca. 100 km north of the previous collection spot. Compounds **7** and **8** possess the same functional groups as lobolide (see Tables III and IV and the Experimental Section) and in addition a secondary

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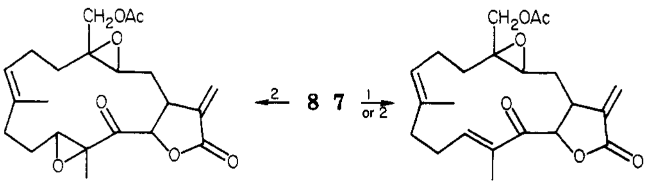
(11) B. Tursch, J. C. Braekman, D. Daloze, H. Dedeurwaerder, and R. Karlsson, *Bull. Soc. Chim. Belg.*, 87, 75 (1978).

(12) B. F. Bowden, J. A. Brittle, J. C. Coll, N. Liyanage, S. J. Mitchell, and G. J. Stokie, *Tetrahedron Lett.*, 3661 (1977).

(13) Y. Kashman and A. Groweiss, *Tetrahedron Lett.*, 1159 (1977).

Scheme I[a]



10 9

[a] 1. MnO_2, 2. Jones reagent.

hydroxyl group. Extensive decoupling and chemical shift studies, summarized in Table III, confirmed inter alia the H-3, H-2,2′, H-1, H-17,17′, H-14, and H-13 sequence and suggested a 13-hydroxylobolide structure. Most characteristic in this sequence are the H-17,17′ doublets which together with the IR absorption (1760 cm^{-1}) confirm the presence of the α-methylene γ-lactone group. The absence of a methyl next to the 3,4-epoxide [δ 60.4 (s), 62.5 (d)] was obvious from the absence of a signal in the 1.2–1.4 ppm region of the ^1H NMR spectrum and led to the positioning of the CH_2OAc group on C-4, the only tertiary carbon atom in the molecule. As H-13 is coupled only to H-14, one of the two trisubstituted double bonds has to be next to C-13. Proof for this relationship was obtained, in the case of 7, by MnO_2 oxidation to a corresponding α,β-unsaturated ketone (**9**) vide infra. Microozonolysis,[10] which as in the case of compound 3 gave levulinaldehyde, further extended the C-4 to C-12 segment up to C-7, with the remaining ethylenic fragment closing the macrocycle from C-7 to C-4.

The ^{13}C NMR spectra of 7 and 8, which are fully assigned (Table IV) supplied further evidence for the suggested structures. While 7 on oxidation with MnO_2 gave ketone 9, compound 8, on the other hand, was unchanged. Oxidation of 8 with Jones reagent, however, gave an 11,12-epoxy-13-keto derivative (**10**), while oxidation of 7 resulted in the same α,β-unsaturated ketone (**9**) as obtained with MnO_2 (see Scheme I). These observations, together with the different stability of 7 and 8 toward acid under which 8 polymerized rapidly, can be best explained by assuming different stereochemistries for the C-13 OH group of 7 and 8, a conclusion supported by the different chemical shifts in the ^1H NMR spectrum. The stereochemistry assigned to 7 would explain the lower susceptibility of the double bond toward epoxidation as compared with the rate of oxidation of the alcohol, a situation which would be reversed in the case of 8.[14]

In going from 7 and 8 to 9 and 10, the H-14 signal changes from a doublet of doublets with J = 6.5 or 6.8 Hz to a doublet with $J_{1,14}$ = 3.3 Hz, which illustrates the difficulty in deducing the nature of the ring fusion from the value of $J_{1,14}$.[15] The possibility that 7 and 8 differ in stereochemistry at another center apart from C-13 seems remote because the ^{13}C NMR spectra which are a delicate probe for the stereochemistry in these compounds seem otherwise so similar. The extreme flexibility of the cembrane ring, which permits large changes in the populations of the various conformers is evidenced by the observed shifts of the ^{13}C NMR lines of compound 9 and 10 compared with those of the alcohols (see Experimental Section).

Extracts of *L. crassospiculatum* collected northwest of Townsville were found by the James Cook University group to afford three cembranolides: isolobophytolide (**11**) and two epimeric 13-acetoxy derivatives **12** and **13**.[15] The NMR spectral data (for a ^{13}C NMR comparison see Table IV) support the conclusions that isolobophytolide is 18-desacetoxylobolide. Comparison of the ^1H NMR and ^{13}C NMR spectra (Table IV) shows that the data for compounds 7 and 8 are in excellent agreement with those reported for the 13-acetoxyisolobophytolides **12** and **13**, taking into consideration the fact that in **12** and **13** the 13-OH is acetylated and the 18-acetoxy is replaced by hydrogen.[16] This agreement indicates that 7 and 8 possess the same stereochemistry as **12** and **13** and that the lactone ring of lobolide and 7 and 8 is trans fused as in isolobophytolide and its 13-acetoxy derivatives. However, although $J_{13,14}$ for 7 and 8 differed considerably, just as in the case of **12** and **13**,[15] it was not possible to make a definite configurational assignment for these centers because of the extreme flexibility of the cembrane ring.

Noteworthy is the conclusion concerning the lactone ring fusion in cembranoids possessing the α-methylene γ-lactone moiety; all of the lactones from horny corals for which an X-ray analysis has been performed possess a cis lactone ring fusion while all the lactones reported from soft corals contain a trans junction.[2]

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 177 spectrophotometer. Ultraviolet spectra were recorded on a Varian Cary 219 spectrophotometer in methanol solutions. Optical rotations were measured with a Bellingham and Stanley polarimeter in $CHCl_3$ solutions. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Mass spectra were taken with a Du Pont 21-491B instrument. Parent peaks of the compounds were analyzed on a high-resolution mass spectrum Varian MAT 731 instrument. ^{13}C NMR spectra were measured with a Bruker WH-90 spectrometer (22.63 MHz) in $CDCl_3$ solutions. ^1H NMR spectra were recorded, unless stated otherwise, on a Bruker WH-270 spectrometer. Chemical shifts are reported in δ values downfield from internal Me_4Si, and the coupling constants are quoted in hertz. All solvents used were either spectral grade or freshly distilled ones.

Isolation of Cembranoids 1–3 from *Alcyonium flaccidum*. The soft coral was collected at Marsa-Hadamiya (the Gulf of Suez, the Red Sea) in April 1979. Freeze-dried material (220 g) was ground and extracted with hot petroleum ether in a Soxhlet apparatus for 48 h to give, after evaporation, 38.0 g of viscous brown oil. The crude extract (27 g) was chromatographed on a silica gel H short column under suction. The materials were eluted with solvent mixtures of increasing polarity, from petroleum ether to CH_2Cl_2 and then to ethyl acetate. The fractions, which were eluted with petroleum ether–CH_2Cl_2 mixtures (17.5 g) were found to contain mixtures of cembrene-C (1) with nonpolar glycerides. These mixtures were combined and later separated on a Sephadex LH-20 column (prepared and eluted with $CHCl_3$–petroleum ether, 7:3) to give ca. 7 g of pure 1 (4.5% based on dry material weight). The fraction, which was eluted with 3:17 ethyl acetate–CH_2Cl_2 (1.96 g), was also separated on Sephadex LH-20 to give compound 3 (1.2 g, ca. 75% pure) and then crystals of 2 (100 mg). Compound 3 was finally purified on a preparative TLC plate and even so contained traces of other accompanying materials.

Cembrene-C (1) and Sarcophytol-B (2). These compounds were identical in all respects (melting point, $[\alpha]_D$, UV, IR, ^1H NMR, and ^{13}C NMR) with the previously reported compounds.[6,7]

11,12-Epoxy-13-hydroxy-14-acetoxycembrene-C (3): an oil, ca. 95% pure; $[\alpha]^{24}_D$ +118° (c 2.4, $CHCl_3$); UV (methanol) 252 nm (ϵ 11 000); IR (neat) 3470, 2960, 2920, 2870, 1735, 1645 (w), 1455, 1370, 1240, 1035, 965, 870, 790, 760 cm^{-1}; mass spectrum (EI, 12 eV), m/e (relative intensity) 362 (M^+, $C_{22}H_{34}O_4$, 6), 347

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[14] J. Iriarte, J. N. Schoolery, and C. Djerassi, *J. Org. Chem.* 27, 1139 (1962).

[15] A. Ahond, B. F. Bowden, J. C. Coll, J. D. Fournerou, and S. J. Mitchell, *Aust. J. Chem.*, 32, 1273 (1979).

[16] Among the two pairs 7, 8 and 12, 13, 7 and 12 are the less polar compounds, an observation which points to similar conformations for 7 and 12 on the one hand and 8 and 13 on the other.

(1), 344 (1), 319 (3), 302 (M$^+$ – HOAc, 20), 285 (10), 191 (10), 163 (16), 137 (42), 109 (15), 84 (100). For the ^{1}H NMR see table I and for the ^{13}C NMR see table II.

Jones Oxidation of Compound 3. To a solution of compound **3** (36 mg) in acetone (20 mL) at 0 °C were added a few drops of Jones reagent. After 20 min the reaction mixture was worked up in the usual way to give, after chromatography on a Sephadex LH-20 column, compound **4** (the 13-keto derivative of **3**). Compound **4** is an oil: UV (methanol) 255 nm (ϵ 13 100), 245 (13 600); IR (neat) no OH absorption, 2950, 1730, 1370, 1030, 870, 760 cm^{-1}. For the ^{1}H NMR see table I.

Basic Hydrolysis of Compound 3. Compound **3** (40 mg) was dissolved in methanol (6 mL) at 0 °C and 2% KOH in methanol (4 mL) were added. After 30 min the solution was neutralized (HOAc) and the solvent removed under vacuo. Chromatography through a short silica gel column gave 11,12-epoxy-13,14-dihydroxycembrene-C (**5**) (28 mg). Lack of sufficient material prevented recrystallization: $[\alpha]^{24}{}_{\mathrm{D}}$ +124° (*c* 0.76, CHCl$_3$); UV (methanol) 252 nm (ϵ 15 600); IR (neat) 3430, 2940, 1645 (w), 1455, 1380, 1030, 868, 760 cm^{-1}; mass spectrum (CI), *m/e* 320 (C$_{20}$H$_{32}$O$_3$). For the ^{1}H NMR see table I, and for the ^{13}C NMR see table II.

Transformation of Compound 5 to Sarcophytol-B (2). A mixutre of **5** (50 mg) and freshly prepared Zn–Cu couple (2 g) in absolute methanol (5 mL) was heated under reflux for 16 h. The precipitate was filtered off, washed with ether, and the solution evaporated under reduced pressure to give an oil (35 mg). Chromatography on a silica gel column gave sarcophytol-B (5 mg) and another, yet unidentified, compound.

Isolation of Cembranoids 6–8 from *Lobophytum crassum*. The soft coral *Lobophytum crassum* (Margenzeller, 1886) was collected by hand at a depth of 2–5 m near Dahab in the Gulf of Eilat in March 1979. The soft coral was deep frozen immediately after collection and then freeze–dried to give the dry material (500 g). Dry, soft coral (250 g) was extracted with petroleum ether in a Soxhlet apparatus for 4 h. Evaporation of the extract gave a green gum (13.4 g, 5.4% dry weight).

The crude extract (8 g) was applied to a column of silica gel H (100 g), and material was eluted with solvents of gradually increasing polarity from petroleum ether through ethyl acetate. Fraction 4, eluted with 20% ethyl acetate in petroleum ether, gave lobolide (**6**).[13] Recrystallization from acetone petroleum ether gave pure **6** (220 mg, 0.15% dry weight). Fraction 6, eluted with 40% ethyl acetate in petroleum ether, contained a mixture of compounds **7** and **8**. Fraction 6 was rechromatographed on Sephadex LH-20 with chloroform–petroleum ether (65:35) as eluant to yield compound **7**, the less polar alcohol (190 mg, 0.13% dry weight). Fraction 7, eluted with 50% ethyl acetate in petroleum ether gave compound **8** (780 mg, 0.53% dry weight).

(7*E*,11*E*)-18-Acetoxy-3,4-epoxy-7,11,15(17)-cembratrien-16,14-olide; lobolide (6): mp 114–115 °C (acetone–petroleum ether); $[\alpha]^{24}{}_{\mathrm{D}}$ –58° (*c* 2.7, CHCl$_3$); IR (KBr) 2950, 2910, 2850, 1770, 1740, 1660, 1435, 1390, 1370, 1335, 1267, 1230, 1140, 1085, 1038, 997, 972, 965, 930, 900, 880, 845, 837, 820, 797, 695 cm^{-1}; UV (methanol) 209 nm (ϵ 7600); mass spectrum (EI, 20 eV), *m/e* (relative intensity) 374 (M$^+$, C$_{22}$H$_{30}$O$_5$, 5), 150 (5), 107 (15), 58 (100); mass spectrum (EI, 70 eV), *m/e* (relative intensity) 332 (M$^+$ – 42, 1), 316 (71), 287 (40), 259 (50), 245 (83), 202 (61), 115 (100), 91 (93). For ^{1}H and ^{13}C NMR spectra see Tables III and IV.

(7*E*,11*E*)-18-Acetoxy-3,4-epoxy-13-hydroxy-7,11,15(17)-cembratrien-16,14-olide (7): an oil; $[\alpha]^{24}{}_{\mathrm{D}}$ –81° (*c* 1.3, CHCl$_3$); IR (neat) 3450, 2930, 1760, 1740, 1655, 1430, 1370, 1270, 1235, 1145, 1125, 1035, 1005, 950, 860, 815, 730 cm^{-1}; mass spectrum (EI, 12 eV), *m/e* (relative intensity) 390 (M$^+$, C$_{22}$H$_{30}$O$_6$, 4), 329 (3), 311 (6), 306 (7), 283 (10), 282 (10), 254 (10), 246 (40), 238 (25), 228 (64), 178 (50), 132 (70), 83 (100). For ^{1}H and ^{13}C NMR spectra see Tables III and IV.

(7*E*,11*E*)-18-Acetoxy-3,4-epoxy-13-epihydroxy-7,11,15-(17)-cembratrien-16,14-olide (8): an oil; $[\alpha]^{24}{}_{\mathrm{D}}$ +16° (*c* 0.9, CHCl$_3$); IR (neat) 3500, 2985, 1770, 1745, 1660, 1440, 1380, 1275, 1250, 1150, 1050, 1000, 900, 865, 825, 805, 775 cm^{-1}; mass spectrum (EI, 12 eV), *m/e* (relative intensity) 390 (M$^+$, C$_{22}$H$_{30}$O$_6$, 2), 372 (1), 329 (2), 318 (3), 311 (3), 282 (6), 254 (6), 246 (33), 238 (14), 228 (34), 178 (22), 150 (37), 132 (57), 118 (91), 116 (100), 83 (59). For ^{1}H and ^{13}C NMR spectra see Tables III and IV.

Oxidation of Alcohol 7 with Manganese Dioxide. MnO$_2$ (150 mg) was added to a solution of **7** (24 mg) in dichloromethane (15 mL), and the reaction mixture was kept at room temperature for 40 h. The mixture was filtered and the manganese dioxide washed with dichloromethane (25 mL). Evaporation of the combined organic phase gave the α,β-unsatuated ketone **9**: 13 mg (55% theoretical); an oil, IR (CHCl$_3$) 2940, 1765, 1740, 1680, 1655, 1435, 1380, 1270, 1225, 1150, 1020, 950 cm^{-1}; mass spectrum (EI, 12 eV) *m/e* (relative intensity) 388 (M$^+$, C$_{22}$H$_{28}$O$_6$, 30), 328 (M$^+$ – AcOH, 100), 311 (5), 283 (3), 244 (7), 215 (5), 188 (10), 148 (15), 132 (17), 105 (25), 93 (40), 82 (12); ^{1}H NMR (270 MHz, CDCl$_3$) δ 3.02 (H-1, m), 3.04 (H-3, dd, J = 3.3, 7.2 Hz), 5.09 (H-7, br t, J = 7.0 Hz), 6.65 (H-11, br t, J = 8.0 Hz), 5.52 (H-14, d, J = 3.3 Hz), 5.63 (H-17, d, J = 2.0 Hz), 6.30 (H-17′, d, J = 2.0 Hz), 4.10 (H-18,18′, AB system, J = 12.0 Hz), 1.61 (19-CH$_3$, br s), 1.84 (20-CH$_3$, br s), 2.11 (COCH$_3$, s); ^{13}C NMR (22.63 MHz, CDCl$_3$) δ 195.3 (s), 170.4 (s), 170.1 (s), 151.9 (s), 145.4 (d), 136.9 (s), 134.1 (s), 127.0 (d), 123.1 (t), 77.0 (d), 65.5 (t), 61.2 (s), 58.0 (d), 42.5 (d), 37.6 (t), 35.1 (t), 30.4 (t), 26.0 (t), 21.3 (t), 20.7 (q), 15.4 (q), 11.6 (q).

Jones Oxidation of Alcohol 7. Jones reagent (5 drops) was added to a solution of **7** (118 mg) in acetone (25 mL), and the reaction mixture was kept at 0 °C for 30 min. The usual workup gave the same α,β-unsaturated ketone **9** (52 mg, 45% theoretical) as described above.

Jones Oxidation of Alcohol 8. Jones oxidation of alcohol **8** (28 mg) in the same manner as described above for **7**, gave the epoxy ketone **10**: 14 mg, 48% theoretical; an oil, IR (CHCl$_3$) 2920, 1770, 1735, 1725, 1660, 1440, 1370, 1205, 1105, 1040, 910 cm^{-1}; mass spectrum (EI, 15 eV), *m/e* 404 (M$^+$, C$_{22}$H$_{28}$O$_7$, 15), 344 (M$^+$ – AcOH, 40), 279 (15), 244 (20), 214 (12), 161 (55), 134 (80), 100 (77), 84 (100); ^{1}H NMR (270 MHz, CDCl$_3$) δ 2.96 (H-1, m), 2.90 (H-3, dd, J = 3.3, 7.9 Hz), 5.13 (H-7, br t, J = 5.5 Hz), 3.07 (H-11, dd, J = 3.0, 7.9 Hz), 5.07 (H-14, d, J = 3.3 Hz), 5.70 (H-17, d, J = 2.0 Hz), 6.30 (H-17′, d, J = 2.0 Hz), 4.10 (H-18,18′, A$_2$ s), 1.66 (19-CH$_3$, br s), 1.50 (20-CH$_3$, s), 2.10 (COCH$_3$, s); ^{13}C NMR (22.63 MHz, CDCl$_3$) δ 204.5 (s), 170.6 (s), 168.4 (s), 136.8 (s), 133.2 (s), 127.6 (d), 123.7 (t), 77.1 (d), 65.3 (t), 63.2 (s), 61.8 (s), 59.4 (d), 59.2 (d), 41.1 (d), 36.4 (t), 34.2 (t), 30.4 (t), 24.7 (t), 22.3 (t), 20.7 (q), 15.3 (q), 12.8 (q).

Acknowledgment. We express our appreciation to Professor Y. Loya and Mr. Y. Benayahu for collection and identification of the soft corals and the United States–Israel Binational Science Foundation for partial support (Grant 2201/80). The excellent technical assistance of Mrs. Y. Abudi is gratefully acknowledged.

Registry No. 1, 64363-64-0; **2**, 72629-68-6; **3**, 77965-78-7; **4**, 77965-79-8; **5**, 77965-80-1; **6**, 64180-71-8; **7**, 77965-81-2; **8**, 78037-40-8; **9**, 77965-82-3; **10**, 77965-83-4; 11, 66275-29-4; **12**, 78037-41-9; **13**, 78037-42-0.