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SEVERAL NEW CEMBRANOID DITERPENES FROM THREE SOFT CORALS OF THE RED SEA

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Abstract—Eight new diterpenoids have been isolated from three soft corals, *Alcyonium utinomii*, *Lobophytum pauciflorum* and *Lobophytum crassum*. The compounds were shown to be: 1,3,7,10-cembratetraen-12-ol(**4**); 1,3,6,11-cembratetraen-8-ol (**5**); 1,3,7,12(20)-cembratetraen-11-ol (**6a**); 2,7,11-cembratrien-4,15-diol(**8**); 3,7,10-cembratrien-12,15-diol(**9**); and the lobolide related deacetyldeepoxy lobolide (**15**), deepoxy lobolide (**16**) and deacetyl-13-hydroxy lobolide (**17**), by spectral data and chemical studies (mainly ozonolysis).

Among the diterpenes isolated from soft corals, the cembranes[1] so far are the largest and most abundant group of compounds. The biosynthesis of these C_{20}-isoprenoids is assumed to start from geranylgeraniol pyrophosphate leading through the initially obtained 3,7,11-cembratrien-15-carbonium ion intermediate, inter alia, to one or more of the following compounds: Nephthenol (**1**, the 3,7,11-trien-15-ol)[1], cembrene-A (**2**, the 3,7,11,15-tetraen) or cembrene-C (**3**, the 1,3,7,11-tetraene)[1] (see Chart 1) (for nomenclature of the cembranes see Ref. 1). The first compound (**1**) is assumed to be obtained by quenching of the C-15 carbonium ion by H_2O, the second by H-16 elimination and the third by a possible migration of H-1 to C-15 followed by elimination of H-2.

Each one of compounds **1–3** can of course undergo further secondary reactions such as epoxidation(s) or allylic oxidation(s) with or without double bond migration. Another common biosynthetic change is the $C_3{=}C_2{-}C_1 \rightarrow HOC_3{-}C_2{=}C_1$ transformation which is believed to take place in the biosynthesis of five of the new, herewith reported, compounds (**4–6**, **8**, **9**). It is suggested that an intermediate epoxide might be involved in the latter process; this process is similar to the Lewis acid opening of epoxides, leading to allyl alcohols as described by Dev[2] and has also been found by us in the case of sarcophine and some xenia diterpenes.[3]

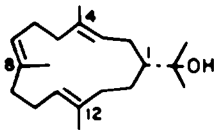
The above described transformations are not the only ones observed within the cembranes. Other more extensive ones involve new ring formations as well as skeletal rearrangements.[4] Many of the newly formed rings result from nucleophilic attacks of epoxide moieties by alkoxide or carboxylate anions[1] (originating from oxidation of one of the five cembrane methyl groups). In the formation of other compounds, where ethereal bridges are present,[5] transannular reactions seem to be involved.[1,6] Lobolide (**12**) and its newly reported derivatives (**15–17**), are good examples of such extensive changes within the cembranes.

Several dozen, of more than 150 reported species of soft corals of the Gulf of Eilat (the Red Sea), have been examined by us. The findings from three animals, *Alcyonium utinomii* and *Lobophytum pauciflorum* (both examined for the first time) and *Lobophytum crassum* (re-investigated),[8] follow.

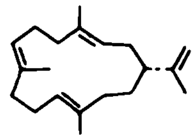
Repeated chromatography of the petroleum ether extract of *A. utinomii* on a column of silica gel yielded three major components designated alcyonol-A (**4**), alcyonol-B (**5**), and alcyonol-C (**6a**) (Chart 1). All three appeared as oils and corresponded to the same molecular formula of $C_{20}H_{32}O$, on the basis of their mass spectra (M^+, *m/e*288), containing five unsaturations. The ^1H and ^{13}C NMR spectra of **4** indicated the presence of three major segments: $-C(CH_3){=}CH{-}CH{=}C(iPr){-}$, $-CH_2CH{=}CH{-}C(OH)(CH_3){-}$ and $-CH_2CH{=}C(CH_3){-}$ (see Tables 1 and 2). Furthermore, the IR absorptions at 1600 and 1660 cm^{-1} and the UV maximum at 248 nm (ϵ 10000) confirmed the presence of the conjugated diene like the one found in cembrene-C (**3**). The above moieties, together with the only one double allylic methylene group agree with each one of the following two structures: the 1,3,6,11-tetraen-8-ol or the 1,3,7,10-tetraen-12-ol. The distinction between the two possible structures was achieved by ozonolysis. The microozonolysis[9] of **4** which gave levulinaldehyde, established its structure to be the 1,3,7,10-tetraen-12-ol isomer. Further support for this determination was obtained from the structure of alcyonol-B (**5**) as will be discussed below.

Alcyonol-B (**5**) contains exactly the same three segments as alcyonol-A (**4**), (Tables 1 and 2), however in a different sequence. Microozonolysis of **5** gave 2-methyl-2-hydroxypentan-1,5-dial (as obtained from thunbergol (**10**) and trocheliophorol (**11**)) but not levulinaldehyde as obtained from **4**. Irradiation of the double allylic methylene (H-5,5') changed the multiplicities of the double doublet at δ5.70 (H-6, Table 1) and the vinyl methyl at δ1.78, which is attributed to the diene methyl group (Me-18), thereby determining the structure of **5** to be the 1,3,6,11-tetraen-8-ol isomer. The fact that both **4** and **5** each contain a single chiral center, the carbinol C-atom, and that they are not enantiomers, but rather two possible position isomers, further supports the suggested structures.

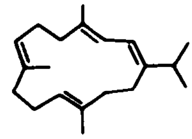
The third isomer, alcyonol-C (**6a**), contains the same conjugated diene as the former two compounds (**4**, **5**), as well as one trisubstituted double bond



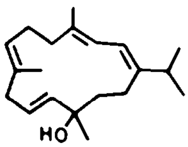
1 nephthenol



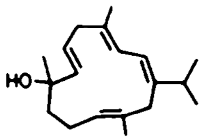
2 cembrene - A



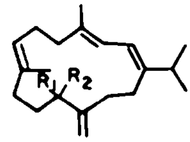
3 cembrene - C



4 alcyonol-A



5 alcyonol-B



6a R_1=H, R_2=OH alcyonol - C
6b R_1=H, R_2=OAc
7 R_1, R_2=O

Chart 1.

Table 1. 270 MHz ^{1}H NMR data (δ, ppm; multiplicity; J, Hz)

	4	5	6a	8	9
H_2	5.96 d, 10.7	6.03 d, 10.6	5.97 d, 11.1	5.25 dd, 15.9, 6.8	
H_3	5.90 d, 10.7	5.83 d, 10.6	5.90 d, 10.7	5.85 d, 15.9	5.06 bt, 6.0
H_5		2.78 d, 6.0			
H_6		5.70 dd, 15.5, 6.1			
H_7	5.17 bt, 6.5	5.62 d, 15.1	5.17 bt, 6.5	5.2 t, 6.8	4.98 bd, 10.0
$H_{9,9'}$	2.67 d, 6.4				2.63 m
H_{10}	5.75 dt, 15.9, 7.0				5.56 dt, 15.6, 7.7
H_{11}	5.58 d, 15.3	5.28 bt, 7.0	4.18 dd, 2.6, 9.0	4.99 bd, 6.8	5.46 d, 15.8
H_{15}	2.5 m	2.34 m, 6.8	2.35 m		
$Me_{16,17}$	1.03, 1.05 d, 6.6	1.02 d, 6.8	1.04 d, 6.9	1.19, 1.1 s	1.21, 1.23 s
Me_{18}	1.72 s	1.78 s	1.75 s	1.35 s	^{b}1.55 s
Me_{19}	1.65 s	1.31 s	1.59 s	^{a}1.62 s	^{b}1.64 s
Me_{20}	1.27 s	1.58 d, 1.0	5.05 s	^{a}1.52 s	1.29 s
			4.84 s		

a,b; These signals may be interchanged.

(-CH_2CH=$C(CH_3)$-). However, the third grouping is different and was found to be a -$CH_2CH(OH)\overset{|}{C}$=CH_2 moiety (Tables 1 and 2). Compound 6a undergoes acetylation (Ac_2O/Pyridine, rt) to give a monoacetate (6b). Obtaining levulinaldehyde following ozonolysis of 6a established the 1,3,7-triene sequence of the former two moieties in the compound. The fourth, exocyclic, double bond has to be in the 12(20) position. However, the distinction between the possible 11-ol and 13-ol, allyl alcohols, was not self evident. The distinction between the two structures became possible after compound 6a was oxidized to the corresponding α,β-unsaturated ketone (7). Obtaining this ketone following a Jones oxidation, confirmed the allyl alcohol which was previously suggested on the basis of the relatively large Δδ value between H-20 and 20', in compounds 6a and acetate 6b (see Experimental for the NMR data).

An 11-ketone was expected to give rise, in the ^{1}H-NMR spectrum, to a complex (ABMN) two proton signal (for H-10,10') in the 2.5–2.7 ppm region while a 13-ketone could have been expected to give rise to an A_2 singlet for the 14 proton pair (as no more chiral centers are left in the molecule). The latter pair being α to a carbonyl and in an allylic position could be expected to resonate around δ3.10. In the event, the former case was the observed one; an additional multiplet appeared at δ2.76, thus determined the 1,3,7,12(20)-tetraen-11-ol structure for 6a.

The second examined soft coral *Lobophytum pauciflorum*,[10] is one of the three most abundant soft

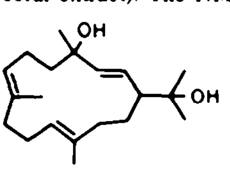
Table 2. 22.65 MHz ^{13}C NMR data

c	4	a[a]	5	6a	b[b]	8	9	10	3	1
1	147.1	151.8	149.2	146.5	150.6[c]	51.5	50.2	46.0	146.2	48.5
2	118.15	117.9	118.3	118.5	118.5	128.4	30.7	129.2	118.6	28.6[b]
3	121.6	121.9	121.5	121.9	122.4	141.3	125.7	138.2	122.1	126.2[c]
4	135.8	135.0	136.7	135.3[c]	134.9[d]	72.5[c]	134.8[c]	72.6	134.7[d]	134.1[d]
5	38.5	39.2	41.5[c]	39.4	40.3	43.1	39.4	43.0	39.3[f]	39.5
6	24.7[c]	25.1	124.6	25.4	26.0	22.5	23.8	22.6	25.3[e]	24.6[f]
7	125.8	125.3	141.2	125.6	125.3	125.9	125.7	125.2	125.0[c]	125.9[c]
8	134.4	135.0	72.8	134.2[c]	135.0[d]	132.6	134.2[c]	132.4[c]	134.3	133.2[d]
9	41.7[d]	38.5	42.0[c]	34.8[d]	35.5	36.9	41.1	36.9	39.0[f]	37.9[e]
10	127.1	126.4	23.3	33.7[d]	33.6	23.7	123.8	23.8	24.6[e]	24.0[f]
11	137.3	140.0	124.6	69.9	62.2[e]	126.7	138.4	125.2	124.6[c]	125.0
12	73.6	72.6	135.1	153.7	152.4[c]	131.8	73.5[d]	128.5[c]	134.1[d]	133.0
13	42.0[d]	50.9	41.5[c]	34.6[d]	43.6	39.1	43.5	39.2	38.6[f]	39.0[e]
14	24.9[g]	66.9	29.6	28.9	63.3[e]	27.7	23.8	27.7	28.1	28.4[h]
15	32.6	26.1	36.6	34.5	28.1	72.4[c]	74.2[d]	33.0	33.8	73.8
16	22.3[e]	28.2[c]	21.9	22.1[e]	24.0[f]	26.1[d]	27.0[e]	20.5[d]	22.4[g]	27.7[g]
17	21.9[e]	28.5[c]	21.9	21.8[e]	24.5[f]	25.5[d]	30.0[e]	19.5[d]	22.4[g]	29.8[g]
18	17.5[f]	16.7[d]	18.2[d]	19.8[f]	16.0[g]	27.9	15.3[f]	28.1	17.2[b]	15.6
19	17.0[f]	17.0[d]	28.7	16.6[f]	16.5[g]	15.0[e]	17.5[f]	15.2[e]	16.9[h]	15.6
20	28.7	24.5	15.7[d]	108.5	110.1	14.4[e]	28.9	14.7[e]	15.7[h]	15.6

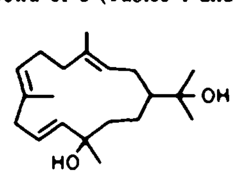
a; Sarcophytol-D[15]. b, Sarcophytol-E[15]. c-h; These signals may be interchanged.

corals which cover the coral reefs of the Gulf of Eilat.[11] The petroleum ether extract of this soft coral yielded, after repeated silica gel chromatography, two interesting new diterpenes (Chart 2) in addition to large amounts of nephthenol (1).

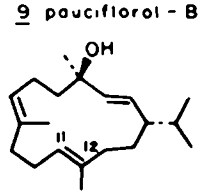
The less polar component (8), named pauciflorol-A, $C_{20}H_{34}O_2$ appeared as an oil (*ca.* 0.01% dry weight of the coral extract). The NMR spectra of 8 (Tables 1 and 2)



8 pauciflorol – A



9 pauciflorol – B



10 thunbergol

11 11α,12α-epoxide of 10: trocheliophorol

Chart 2.

showed the existence of a $-C(OH)(CH_3)_2$, $-C(OH)(CH_3)CH{=}CH{-}CH{<}$ and two $-CH_2CH{=}C(CH_3){-}$ groups. Comparisons of the NMR data of the C_1–C_8 segment of 8 with those reported for thunbergol (10) and trocheliophorol (11)[12] showed marked similarities suggesting the same carbocycle substitution pattern in 8 and thunbergol (10). Upon ozonolysis, obtaining levulinaldehyde and the same pentandial as from alcyonol-B (5), together with the NMR proved 2-hydroxy isopropyl group, established the structure of 8 to be the 2,7,11-cembratrien-4,15-diol.†

The more polar component (9) designated pauciflorol-*B*, was isolated in 0.01% yield. Mass spectral analysis indicated a formula $C_{20}H_{34}O_2$, four degrees of unsaturation as in the case of 8. The NMR spectra of 9 (Tables 1 and 2) supported a triene diol derivative of cembrane; two of the double bonds being E-trisubstituted and the third one being a trans disubstituted bond. Because of two tertiary carbinols ($-C(OH)(CH_3)-$ and $-C(OH)(CH_3)_2$) and the above mentioned three double bonds, it seemed most likely that pauciflorol-*A* and *B* were merely positional isomers. Obtaining levulinaldehyde upon ozonolysis of 9 confirmed a 7,8 double bond as well as a 1,5-diene moiety. The only structure which agrees with the NMR data and the ozonolysis experiment is the 3,7,10-trien-12,15-diol. All other possible isomers could be excluded; a 2,7,10-trien-4,15-diol and a 3,7,13-trien-12,15-diol on the basis of the H-2 and H-14 NMR signals, respectively (none being expected to give a double triplet with J = 15 and 7Hz), and a 5,7,11-

†A different NMR spectrum of a reported synthetic 2,7,11-cembratrien-4,15-diol[13] suggests this compound to be a stereoisomer of compound 8.

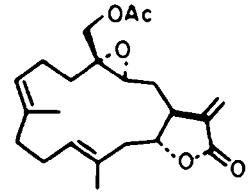
trien-4,15-diol, as no conjugated diene system (UV and NMR) does exist. Thus, the only possible structure is the 3,7,10-trien-12,15-diol. The NMR spectra of the C_7–C_{13} segment was also found to be in good agreement with the spectrum of the corresponding protons (H-7, Me-19, the double allylic pair H-9,9', H-10 and H-11) of alcyonol-*A* (4).

A further investigation of minor constituents of collections of *Lobophytum crassum*[8] afforded three new cembrane-type diterpenes (15, 16, 17), all three closely related to the previously reported lobolide (12)† and the epimeric 13-hydroxy lobolide pair (13, 14) (Chart 3). The first compound $C_{20}H_{28}O_3$ (15) possessed the same unsaturated γ-lactone, two E-trisubstituted double bonds and a methylenoxy group as in lobolide (12) (see Experimental and Table 3). However in contrast to 12, instead of an epoxide, an additional double bond was present in the molecule. We assumed that this compound is the biogenetic precursor of deacetyl lobolide as was proved by the ¹H NMR spectrum (see Experimental and Table 3).

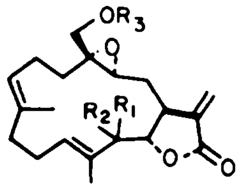
The second compound, 16, $C_{22}H_{30}O_4$, could be easily prepared from 15 by acetylation with Ac_2O/Pyridine at rt for 18 h. Compound 16 is, therefore, 3,4-deepoxy lobolide (see Table 3).

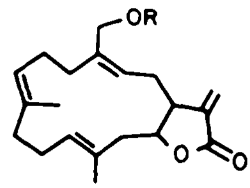
†The structure of lobolide was recently confirmed by an x-ray analysis.[14]

The third compound, 17, which was isolated from *L. crassum* was proved to be the deacetyl derivative of 14 as acetylation of 14 and 17 gave the same diacetate 18.



12 lobolide





13 R1 = H, R2 = OH, R3 = Ac
14 R1 = OH, R2 = H, R3 = Ac
17 R1 = OH, R2 = H, R3 = H
18 R1 = OAc, R2 = H, R3 = Ac

15 R = H
16 R = Ac

Chart 3.

Table 3. 22.65 MHz ¹³C NMR data

C	Multi-plicity	14	15	16	17
1	d	42.1	44.8	44.5	41.4
2	t	31.5[a]	30.9	33.9[a]	31.5[a]
3	d	62.5	125.6	128.5[c]	63.0
4	s	60.4	134.1	135.6[b]	61.9
5	t	32.6[a]	33.7	34.6[a]	32.7[a]
6	t	23.7	29.6	24.4	23.7
7	d	124.1	124.2	123.8	124.4[b]
8	s	135.2	129.5	134.1[b]	134.8
9	t	38.5	34.6	37.9	38.5
10	t	24.7	24.5	24.4	24.6
11	d	132.1	124.7	127.0[c]	131.5
12	s	132.1	128.5	129.1	131.8
13	d/t	80.7	38.0	45.1	80.1
14	d	82.1	81.2	81.1	82.5
15	s	138.7	142.0	142.1	138.9
16	s	169.1	169.2	169.3	169.5
17	t	124.1	122.8	122.8	123.8[b]
18	t	64.0	60.0	61.7	63.2
19	q	15.9	16.8	16.8	15.6
20	q	12.5	17.5	17.5	12.6
Ac-CH_3	q	20.8		20.9	
Ac-CO	s	170.8		170.8	

a-c; These signals may be interchanged.

EXPERIMENTAL

IR spectra were recorded on a Perkin–Elmer Model 177 spectrophotometer. Ultraviolet spectra were recorded on a Varian Cary 219 spectrophotometer in methanol solutions. Mass spectra were taken with a DuPont 21–491B instrument.

^{13}C NMR spectra were measured with a Bruker WH 90 spectrometer (22.63 MHz) in $CDCl_3$ solutions. ^{1}H 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 **3–6a** *from Alcyonium utinomii.* The soft coral was collected at the Gulf of Suez in July 1979. Freeze dried material (230g) was ground and extracted with hot petroleum ether in a Soxhlet apparatus for 24 h to give, after evaporation, 42g of viscous dark oil. The crude extract (5g) was chromatographed on a silica gel H column under suction. The materials were eluted with solvent mixtures in increasing polarity, from petroleum ether to ethyl acetate. Fractions 1–4 eluted with a petroleum ether–ethyl acetate 4 : 1 mixture, contained mixtures of cembrene C (**3**) and non-polar glycerides. The more polar fractions were combined and separated on a Sephadex LH-20 column (prepared and eluted with $CHCl_3$–petroleum ether 7 : 3), and then on a silica gel column (prepared and eluted with petroleum ether–ethyl acetate 20 : 1), to give compounds **4**, **5** and **6a**. Compound **6a** was finally purified on a preparative tlc plate (Silica gel, pentane–ether 2 : 1).

(1*E*,3*E*,7*E*,10*E*)-12-*Hydroxy*-1,3,7,10-*cembratetraene*(*alcyonol-A*, **4**). An oil, λ_{max}(EtOH) 248 nm (ϵ9980), ν_{max}^{neat} 3400, 1660, 1450, 1380 and 975 cm^{-1}, mass spectrum (EI, 15 eV; *m/e*, %): 288(2.5, M$^+$, $C_{20}H_{32}O$), 270(4, M$^+$-H_2O) 245(4.6, M$^+$-iPr), 227(22, M$^+$-H_2O-iPr) and 43(100). For ^{1}H and ^{13}C NMR spectra see Tables 1 and 2.

(1*E*,3*E*,6*E*,11*E*)-8-*Hydroxy*-1,3,6,11-*cembratetraene*(*alcyonol-B*, **5**). An oil, λ_{max}(EtOH) 252 nm(ϵ 13600), ν_{max}^{neat} 3400, 1660, 1450, 1380 and 975 cm^{-1}, mass spectrum (EI, 15 eV; *m/e*, %): 288(3.6, M$^+$, $C_{20}H_{32}O$), 270(12, M$^+$-H_2O), 245(3.5, M$^+$-iPr), 227(11, M$^+$-H_2O-iPr) and 43(100). For ^{1}H and ^{13}C NMR spectra see Tables 1 and 2.

(1*E*,3*E*,7*E*)-11-*Hydroxy*-1,3,7,12(20)-*cembratetraene*(*alcyonol-C*, **6a**). An oil, λ_{max} (EtOH) 248 nm (ϵ 10880), ν_{max}^{neat} 3400, 1450, 1380 and 910(s) cm^{-1}, mass spectrum (EI, 15 eV; *m/e*, %): 288 (1.3, M$^+$, $C_{20}H_{32}O$), 270(1.8 M$^+$-H_2O), 255(1.4), 245(2.2), 227(4.1) and 83(100). For ^{1}H and ^{13}C NMR spectra see Tables 1 and 2.

Acetylation of **6a** *to give compound* **6b**. Alcyonol-C (**6a**) (10 mg) was left overnight at rt in a mixture of acetic anhydride-pyridine (0.1 ml). The usual work-up gave a mono acetate (**6b**); an oil, ν_{max}^{neat} 2900, 1720, 1600, 1450, 1370, 1800, 1250 and 910 cm^{-1}, mass spectrum (EI, 15 eV; *m/e*, %): 330(3.5, M$^+$, $C_{22}H_{34}O_2$), 269(6), 254(6), 226(12), 186(10) and 43(100). ^{1}H NMR ($CDCl_3$ 270 MHz) δ 1.03 and 1.04(3H each, 16 and 17 Me's d, J = 6.7 Hz), 1.53(3H, 19–Me's, 1.75(3H, 18 Me's), 2.04(3H, Ac, s), 4.83 and 4.94(2H, H-20,20', brs), 5.14(1H, H-7, brt, J = 6.5 Hz), 5.26(1H, H-11, dd, J = 8.0 and 4.0 Hz), 5.93(1H, H-3, d, J = 9.4 Hz) and 6.08(1H, H-2, d, J = 9.4 Hz).

Jones oxidation of **6a** *to give compound* **7**. Jones reagent (2 drops) was added to a sol of **6a** (30 mg) in acetone (5 ml) and the reaction mixture was kept at 0°C for 30 min. The usual work-up gave the $\alpha\beta$-unsaturated ketone **7** (17 mg); an oil; λ_{max}(EtOH) 248(ϵ 13300) and 240 nm(ϵ 12560); ν_{max}^{neat} 1725, 1675, 1610, 1450, 1375 and 910 cm^{-1}; mass spectrum (EI, 15 eV; *m/e* %); 286(1, M$^+$, $C_{20}H_{30}O$), 243(1.5, M$^+$-iPr), 226(1), 212(1) and 43(100); ^{1}H NMR($CDCl_3$, 270 MHz) δ 1.04(6H, 16 and 17 Me's, d, J = 6.8 Hz), 1.59(3H, 19 Me's), 1.68(3H, 18 Me's) 2.44(1H, H-15, m), 2.76(2H, H-10,10', m), 5.0(1H, H-7, bt), 5.60(1H, H-3, d, J = 10 Hz), 5.51 and 5.99(2H, H-20,20', bs) and 6.01 (1H, H-2, d, J = 10 Hz).

Microozonolysis of compounds **4**, **5**, **6a**, **8** *and* **9**. Ozone in oxygen was bubbled, for a few minutes, through a sol of each one of the examined cembranoids (10 mg), in CH_2Cl_2 (2 ml) at −70°. The ozonide was decomposed by the addition of Ph_3P (20 mg) and the solution left to warm up to rt (*ca.* 5 min). The various oxo compounds were analyzed by GC on a capillary carbowax 20 M column (20 m, 0.25 mm) at 80°, 110° and 150°. The fragments of thunbergol (**10**), and cembrene-C (**3**) served as standard compounds (retention time, temperature); levulinaldehyde 7.7 min (80°) and 3.0 min (110°); 2-methyl-2-hydroxy-1,5-pentandial 10.5 min (150°) and 2-methyl-3,6-heptadione 13.5 min (80°) and (4.5 min (110°). The first aldehyde was observed in case of **4**, **6a**, **8** and **9**, the dial in case of **5** and **8** and the dione in case of **5**.

Isolation of cembranoids **8** *and* **9** *from Lobophytum pauciflorum.* The soft coral was collected at Dahab (Gulf of Eilat) in November 1979. Freeze-dried material (200 g) was ground and extracted with hot petroleum ether in a Soxhlet for 24 h to give, after evaporation, 3.5g of an oil. The crude extract was chromatographed on a Sephadex LH-20 column. The more polar fractions were then chromatographed on a silica gel column using solvent mixtures increasing in polarity from petroleum ether to ethyl acetate. Compound **8** was obtained from the fraction eluted with petroleum ether-ethyl acetate (3 : 7) and compound **9** from the one eluted with petroleum ether–ethyl acetate (2 : 8).

Compound **8** was further purified on a silica gel column (ethyl acetate–ether) and **9** on a 2% $AgNO_3$ impregnated silica gel column (benzene-ethyl acetate 3 : 7).

(2*E*,7*E*,11*E*)-4,15-*Dihydroxycembra*-2,7,11-*triene*(*pauciflorol-A*, **8**). An oil, ν_{max}^{neat} 3400, 2940 and 1660 cm^{-1}, mass spectrum (EI, 12 eV; *m/e*, %)): 288(4.8, M$^+$-H_2O), 273(3), 270(5), 255(4), 229(48), 214(29) and 93(100). For ^{1}H and ^{13}C NMR spectra see Tables 1 and 2.

(3*E*, 7*E*, 10*E*) - 12,15 - *Dihydroxycembra* - 3,7,10 - *triene* - (*pauciflorol-B*, **9**). An oil, ν_{max}^{neat} 3350, 2920, 1430 and 1360 cm^{-1}, mass spectrum (EI, 15 eV; *m/e*, %): 288(42, M$^+$-H_2O), 270(54), 255(33), 215(53), 189(22) and 93(100). For ^{1}H and ^{13}C NMR spectra see Tables 1 and 2.

Isolation of cembranoids **15**, **16** *and* **17** *from Lobophytum crassum.* The soft coral was collected near Dahab in November 1980. Freeze dried material (560 g) was ground and extracted with hot petroleum ether to give 38g of dark oil, and then extracted with ethyl acetate to give 3g of dark oil. Each crude extract was chromatographed on a silica H column under suction. The materials were eluted with solvent mixture of increasing polarity from petroleum ether to ethyl acetate. The more polar fractions from the petroleum ether extract were rechromatographed on silica gel columns. The fractions eluted with petroleum ether–ether 3 : 1 contained compound **16** and those eluted with petroleum ether–ether 1 : 1 contained compound **15**. Each compound was purified once again: compound **15** on a 2% $AgNO_3$ impregnated silica gel column eluted with petroleum ether–ethyl acetate 3 : 2, compound **16** on a silica gel column eluted with petroleum ether–ether 4 : 1.

(3*E*, 7*E*, 11*E*)-18-*Hydroxy*-3,7,11,15(17)-*cembratetraen*-16,14-*olide* (**15**). An oil, ν_{max}^{neat} 3400, 2920, 1750, 1660 cm^{-1}, mass spectrum (EI, 14 eV; *m/e*, %): 316(21, M$^+$ $C_{20}H_{28}O_3$): ^{1}H NMR($CDCl_3$, 270 MHz) 1.62, 1.67(3H each, 19 and 20 Me's), 2.76(1H, H-1, bdt, J = 10, 3 Hz), 4.12(2H, H-18, 18', s), 4.35(1H, H-14, dt, J = 9.6, 2.6 Hz), 4.91, 5.05(1H each, H-7 and -11, bt), 5.22(1H, H-3, bt), 5.70, 6.28(1H each, H-17, 17', d, J = 1.9 Hz).

(3*E*,7*E*,11*E*) - 18 - *Acetoxy* - 3,7,11,15(17) - *cembratetraen* - 16,14-*olide* (**16**). An oil, ν_{max}^{neat} 2910, 2840, 1755, 1730, 1650 cm^{-1}; mass spectrum (EI, 15 eV; *m/e*, %): 358(1.5, M$^+$, $C_{22}H_{30}O_4$), 315(7.5), 298(30), 282(28), 269(15), 254(12), 107(100); ^{1}H NMR($CDCl_3$, 270 MHz) δ 1.61, 1.66(3H each, 19 and 20 Me's), 2.72(1H, H-1, bdt, J = 10, 2 Hz), 4.31(1H, H-14, dt, J = 10, 2.5 Hz), 4.56(2H, H-18,18', s), 5.05, 4.90(1H each, H-7 and -11, bt), 5.30(1H, H-3, bt), 5.70, 6.29(1H each, H-17,17', d, J = 1.6 Hz). Fractions 5–6 from the ethyl acetate extract, eluted with petroleum ether–ethyl acetate 1 : 2 contained compound **17**.

(7*E*, 11*E*)-13,18-*Dihydroxy*-3,4-*epoxy*-7,11,15(17)-*cembratrien*-16,14-*olide* (**17**). An oil, ν_{max}^{neat} 3400, 2940, 1755, 1740, 1660 cm^{-1}; mass spectrum, (EI, 15 eV; *m/e*, %): 317(1, M^+-CH_2OH), 299(0.5), 284(0.5), 256(1), 237(1), 213(1.5), 83 (100); ^1H NMR($CDCl_3$ 270 MHz) δ 1.70, 1.63(3H each, 19 and 20 Me's), 1.85(1H, H-2, ddd), 2.77 (1H, H-1, m), 2.89(1H, H-3, dd, J = 7.5, 2.3 Hz), 3.82, 3.58(1H each, H-18, 18', d, J = 12 Hz), 4.04(1H, H-13, d, J = 8.5 Hz), 4.12(1H, H-14, dd, J = 8.5, 6.5 Hz), 5.03(1H, H-7, bt), 5.43(1H, H-11, bt), 6.01, 6.29(1H each, H-17, 17', d, J = 3 Hz).

Acetylation of compounds **14**, **17** *and* **15**. Acetylation of compounds **14** and **17** (10 mg) with a few drops of acetic anhydride-pyridine solution at room temperature overnight afforded after the usual work-up, the same product, **18**. Acetylation of **15** in the same manner gave product **16**. Compound **18**: An oil, ^1H NMR($CDCl_3$, 270 MHz) δ 1.70, 1.63(3H each, 19 and 20 Me's, s), 1.86(1H, H-2, dt, J = 15.0, 4.0 Hz), 2.13, 2.10(3H each, s, OAc), 2.80(1H, H-1, m), 2.88(1H,H-3,dd,J = 7.0, 3.2 Hz), 3.87, 4.36(1H each, H-18, 18', d, J = 12.0 Hz), 4.19(1H, H-14, dd, J = 8.8, 6.5 Hz), 5.04(1H, H-7, bt), 5.21(1H, H-13, d, J = 8.8 Hz), 5.55(1H, H-11, bt), 6.00, 6.31(1H each, H-17, 17', d, J = 2.6 Hz).

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