Isoprenoids of the Soft Coral *Sarcophyton glaucum*: Nyalolide, a New Biscembranoid, and Other Terpenoids†

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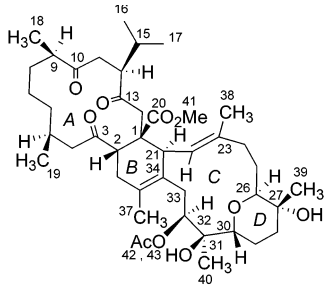
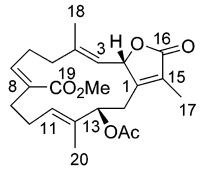
The chemical content of *Sarcophyton glaucum*, one of the more abundant soft corals on many coral reefs, collected from many seas, was thoroughly explored, resulting in the discovery of a large number of cembranoids, biscembranoids, sterols, and other secondary metabolites. The presently investigated Kenyan specimens of *S. glaucum* yielded three new metabolites, i.e., nyalolide (**15**), a biscembranoid, 16-oxosarcoglaucol acetate (**16**), a cembranoid, and the sesquiterpene guaiacophine (**17**). Nyalolide was also isolated from the Kenyan soft coral *Sarcophyton elegans*. The structures of the new compounds were elucidated by interpretation of their MS and 1D and 2D NMR experiments and, in the case of nyalolide, possessing 11 chiral centers, secured by X-ray diffraction analysis.

Soft corals are well known for their high content of diterpenes and particularly cembranoids.[1] Among the most abundant soft coral genera on many coral reefs are Sacrophyton, which tend to form large monospecific "carpets" of up to several square meters.[2,3] *Sarcophyton glaucum* is one of the more chemically investigated soft corals, with 55 reports[4] following our first report[5] on the isolation of the ichthiotoxic cembranoid sarcophine (**1**) in remarkable concentration (3% dry wt) from a specimen collected in the northern Red Sea near Eilat. As long ago as 1974 we demonstrated that the cembranoid content of the soft coral varies notably with the place of collection and other unknown factors.[6] Thus, the major cembranoid isolated from *S. glaucum*, collected ca. 100 km south of Eilat, was 16-deoxysarcophine (**2**) (4−5% dry wt), accompanied by only traces of sarcophine and several other cembranoids.[6] A whole variety of cembranoids were isolated from *S. glaucum* collected from all over the world,[4] starting from lowly oxygenated cembranes such as the potent antitumor promoter sarcophytol A (**3**)[7] to highly oxygenated ones where even one or more of the methyl groups oxidized to a $-CH_2OH$ group or carboxylic acid. The latter group appears as methyl esters or closes to five- to seven-membered lactones,[4] as, for example, in sarcophine (**1**),[5] sarcoglaucol (**4**),[8] or the polyfunctional cembranoid emblide (**5**)[9] and methyl sarcoate (**6**),[10] isolated from specimens collected in Hawaii and Okinawa, respectively (Figure 1). Interestingly, *S. glaucum* collected in Sodwana Bay, South Africa, did not contain any cembranoid but rather a completely different diterpene, sarcoglane (**9**), possessing a tricyclo-[7.5.0.0^{10,14}]tetradecane ring system.[11] In addition to the cembranoids, several *S. glaucum* specimens were found to contain biscembranoids such as methyl sarcophytoate (**10**).[12] A second major group of metabolites isolated from *S. glaucum* are the sterols,[4] representatives of which are the C_{31}-trimethylcyclopropane-bearing sterol **7**[13] and the tetrahydroxyandrostanone **8**.[14] Dimethylfuranoic acid (**11**) is an additional interesting compound that was isolated from *S. glaucum*.[15]

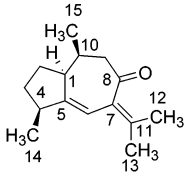
S. glaucum, like many other soft corals, contains a variety of sesquiterpenes. Whether these C_{15} terpenoids are produced by the soft corals themselves or by host symbiotic unicellular algae, the zooxanthellae, is unknown. It was previously suggested by us that the GC spectra of the volatile soft coral terpenoids may serve as an additional possible means for identification of soft corals.[16] It is important to stress that freeze-drying of soft corals results in the loss of part or all of these relatively volatile sesquiterpenes from the tissues. They can, however, be regained from the lypophilizer/ice. Several sesquiterpenes were isolated from *S. glaucum* such as alloaromadendrene (**12**)[16] and in the present work (+)-viridiflorol (**13**),[17] *trans*-calamanene (**14**)[18] (first here reported from a soft coral), and the new compound guaiacophine (**17**).



15 Nyalolide



16 16-Oxysarcoglaucol acetate



17 Guaiacophine

† Dedicated to the late Dr. D. John Faulkner (Scripps) and the late Dr. Paul J. Scheuer (Hawaii) for their pioneering work on bioactive marine natural products.

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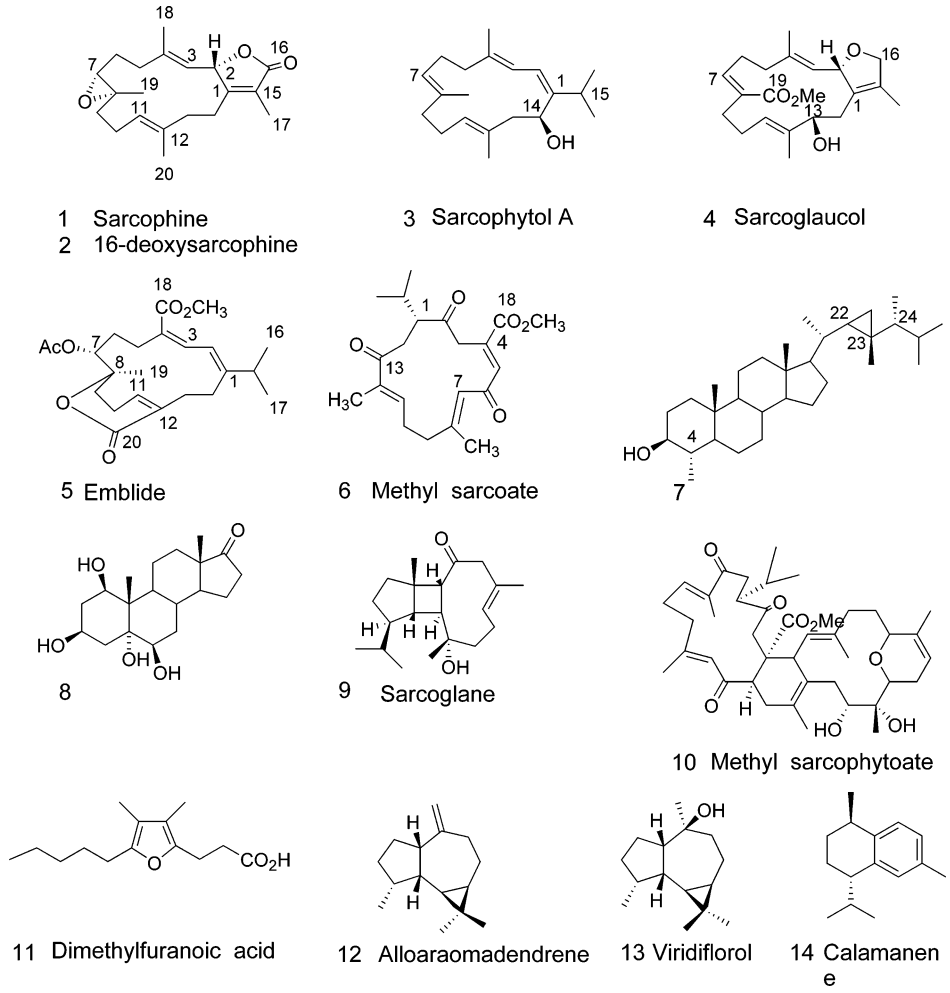

Figure 1. Representative secondary metabolites from *Sarcophyton glaucum*.

Results and Discussion

Hereafter we report the investigation of two specimens of *S. glaucum* collected near Nyali, Mombasa, and at Kitugamwe Reef, south of Kisiti National Marine Park, Kenya, and a specimen of *Sarcophyton elegans* collected near Shelly Beach, off Likoni, Kenya. Compound **15**, nyalolide, was obtained from the Nyali *S. glaucum* and from the Shelly Beach *S. elegans* specimens as a highly viscous colorless oil, representing 0.02% of the dried coral, which analyzed for $C_{43}H_{66}O_{10}$ by EIMS at *m/z* 742 (M^+) and ^{13}C NMR spectra. The NMR data clearly pointed to three ketones (δ_C 210.3 qC, 212.8 qC, and 213.4 qC), one methyl ester [δ_C 173.7 qC and 51.0 CH_3 and δ_H 3.52 s (3H)], one secondary acetate [δ_C 170.2 qC, 20.3 CH_3, and 75.6 CH and *m/z* 682 ($M^+ - 60$)], two double bonds, one tri- and one tetrasubstituted (δ_C 124.7 CH, 140.1 qC, 125.0 qC, and 126.4 qC), two vinyl methyl groups (δ_H 1.63 s and 2.00 d, $J = 2$ Hz), two methyl groups attached to oxygen-carrying C atoms (δ_H 1.11 and 1.13 s), two secondary CH_3 groups (δ_H 1.14 and 0.84 d), one isopropyl group (δ_H 0.83 and 0.93 d), and an additional five oxygen-carrying C atoms (δ_C 85.0 CH, 75.6 qC+CH (two overlapping C atoms), 69.7 qC, and 69.2 CH). Note that the overlapping C atom C-31 differs from C-32 in d_6-DMSO (Table 1). MS fragments at *m/z* 724 ($M^+ - H_2O$) and 706 ($M^+ - 2H_2O$) together with IR absorption at 3200−3600 cm^{-1} suggest two hydroxy groups. The above functionalities account for seven of the 11 degrees of unsaturation of **15**, suggesting a tetracyclic structure. The above evidence suggested that **15** may be a dimeric cembranoid.

The appearance of a broad C*H*-OAc methine signal (δ_H 4.94) in the NMR spectrum at room temperature and the absence of its $^1J_{CH}$ correlation in the HMQC experiment suggested that **15** may exist in an equilibrium of more than a single conformer. Indeed, repeating the measurements at 320 K caused a sharpening of the C*H*-OAc doublet, the appearance of the missing CH-correlation with the carbon atom resonating at 75.6 CH, and additional chemical shift changes of several protons ($\Delta\delta \geq 0.1$ was measured for H-6, -8, -21, -28, and -29). 2D NMR experiments, COSY, HMQC, HSQC-TOCSY, and ROESY in $CDCl_3$ at 297 and 320 K as well as in d_6-DMSO (Table 1) established the structure of **1** unequivocally as a biscembranoid composed from a tetrahydro methyl sarcoate dienophile (**6**)[10] and the proper unknown $\Delta^{1,3,15}$-cembratriene derivative. In the absence of O*H* signals in $CDCl_3$, the NMR spectra were taken again in d_6-DMSO, where, indeed, the two missing signals appeared and enabled the determination of their placement at C-26 and C-31 and hence also the position of the ethereal bridge between C-26 and C-30. The suggested quaternary position of the above two hydroxyls was further corroborated by both remaining intact under acetylation conditions (Ac_2O/pyridine, room temp). Moreover, in d_6-DMSO there seemed to be only a single major conformer, probably due to a solvation effect. Therefore, the d_6-DMSO was chosen for the detailed planar and spatial structure determination.

The relative chirality of C-1,2 and -21 was suggested on the basis of the stereochemistry of the Diels−Alder reaction

Table 1. ^{13}C and ^{1}H NMR Data of **1** in $CDCl_3$ at 297 and 320 K and in d_6-DMSO at 297 K (100 and 500 MHz)

	δ_C[a]	δ_H (J, Hz)[a] $T = 297$ K $CDCl_3$	δ_H (J, Hz)[c] $T = 320$ K $CDCl_3$	δ_H (J, Hz)[b] $T = 297$ K DMSO-d_6	HMBC (H to C)	COSY	ROESY DMSO-d_6	HSQC-TOCSY
1	47.9 qC *47.4*							
2	46.4 CH *46.0*	3.84 dd 7.3, 2.1	**3.86 dd (9.0; 2.0)**	*3.67 bd (9.0)*	14a, 14b, 36a, **36b,** 2, 4a, 4b, 36a	36a, 36b	*4a*	**36a,b**
3	210.3 qC *209.8*							
4	48.9 CH_2 *48.0*	a 2.3 m b 2.1 m	**a 2.40 d (8.2)** **b 2.14 m**	*2.24 dd (6.4; 18.1)* *2.14 dd (5.7; 18.1)*	19, **2**	4b, **19** 4a	*2*	**9,19**
5	26.2 CH *25.7*	2.12 m	**2.12 m**	*1.94 m*	4a, 4b, 19	6, 19		**6b, 9, 19**
6	36.1 CH_2 *35.6*	a 1.3 m b 0.87 m	**a 1.18 m** **b 0.92 m**	*1.04 m* *0.8*[d]	4a, 4b, 19	6b, 5 6a, **7**		**4b, 8b, 9, 18, 19**
7	23.5 CH_2 *22.9*	0.93 m	**1.00 m**	*1.00 m*		**6b**, 8a, 8b	*9*	**6b, 8b, 9, 18, 19**
8	31.6 CH_2 31.0	a 1.47 m b 1.36 m	**a 1.57 m** **b 1.41 m**	1.50 m *1.26*[d]	18	7, **8b, 9** 7, **8a, 9**	9	6b, 9, 18
9	46.2 CH *45.0*	2.34 m	2.36 m	2.31 m	18,**7**	**8a, 8b, 18**	*7, 8a, 11b, 16, 17*	**6b, 18**
10	213.4 qC *213.3*				8b, 9 11a, 11b, 18,			
11	37.3 CH_2 37.4	a 2.9 m b 2.19 d (16.9)	**a 2.91 m** **b 2.17 m**	*2.73 m* *2.38 m*	12, 15, **9**	11b, 12 11a, 12	9	**12, 15**
12	51.5 CH *50.7*	2.83 dd (11.6; 4.2)	**2.88 m**	*2.78 m*	11a,11b, 15,16,17, **14a,b** 11b, 12, **14a, 14b**	**15**	*43*	**11**
13	212.8 qC *212.2*							
14	48.2 CH_2 47.6	3.25 d (19.4) 3.12 d (19.4)	**3.28 d (19.4)** **3.10 d (19.4)**	*3.14 d (19.6)* *2.91 d (19.6)*	2, 36a	14b 14a		
15	29.2 CH *28.8*	1.93 m	**1.98 m**	*1.84 m*	11b, 12, 16, 17	**12,** 16, 17		**12, 16, 17**
16	18.6 CH_3 *18.6*	0.83 d (6.8)	0.84 d (7.0)	0.75 d (6.8)	12, 17	15	*9, 12*	**12, 17**
17	20.6 CH_3 *20.4*	0.93 d (6.8)	**0.94 d (6.7)**	*0.85 d (6.8)*	12,15, 16	15	*9, 12*	**12, 16**
18	16.3 CH_3 *15.9*	1.14 d (6.9)	**1.14 d (6.5)**	*1.09 d (7.2)*		9	*12*	**6b, 8b, 9**
19	21.7 CH_3 *21.3*	0.84 d (7.6)	**0.86 d (7.0)**	*0.79 d (6.7)*		**4a, 5**		**4b, 6b, 9, 18**
20	173.7 qC *173.0*				2, 21, 41, 14a, 14b			
21	40.7 CH *40.3*	3.7 m	**3.88 d (11.5)**	*3.51 bd (11.7)*	2, 14, 33a, **22**	22, 37	22, 32, 38	**37, 38**
22	124.7 CH *124.0*	4.83 d (11.4)	**4.87 d (11.5)**	*4.67 bd (11.7)*	24a, 38	21, 38	21, 33b	**37, 38**
23	140.4 qC *139.7*					24a, 38		
24	38.4 CH_2 *38.4*	a 2.45 dt (12.6; 4.2) b 1.9 m	**a 2.49 bd (11.5)** **b 1.89 m**	*2.35 m* *2.31 m*	22, 26, 38	24b, **25b** 24a, **25b**	**25a, 26**	
25	26.6 CH_2 *27.0*	a 2.12 m b 1.54 m	**a 2.14 m** **b 1.57 m**	*1.82 m* *1.47 m*		25b, **26** 24a, 24b, 25a		**24a, 24b, 26**
26	85.0 CH *84.0*	3.70 m	**3.70 d (10.3)**	*3.58 bd (9.5)*	24a, 28a, 25b, *27*, 39	**25a**	*28a, 39*	**24a, 24b, 25a**
27	69.7 qC 68.3			*(OH) 4.03 (s)*	26, *29* 28a, *27*, 39		*26*	
28	31.6 CH_2 *32.2*	a 1.7 m b 1.6 m	a 1.69 m **b 1.49 m**	1.50 m *1.36 m*	26,*27*, 39	29a,29b, **30** **29a**	26	**29a, 29b, 30**
29	20.0 CH_2 *19.8*	a 1.68 m b 1.57 m	**a 1.60 bd (11.8)** **b 1.72 m**	*1.68 m* *1.36 m*	28a, *31*	28a, 28b, 30 28a, 30	**30**	
30	69.2 CH *69.9*	3.62 dd (11.3; 2.4)	3.64 bd (9.8)	3.40[d]	*31*, 40	29a, 29b, **28a**	*33b*	**29a, 29b**
31	75.6 qC 74.6			(OH) 4.29 (s)	30,*31*, **33a,** 40		*33b*	
32	75.6 CH 73.9	4.94 bd (7.1)	4.97 dd (1.6; 11.8)	4.98 bd (11.8)	30, 31, 33a, 40	33a, **33b**	*21, 33b, 38, 40*	33a
33	28.2 CH_2 28.4	a 2.78 m b 2.17 m	a 2.76 dd (11.8; 14.4) **b 2.19 m**	2.61 dd (13.9; 11.8) *2.00 m*		32, 33b **32,** 33a	*37* *22, 30, 31, 32*	**32, 37**

Table 1. Continued.

	δ_C[a]	δ_H (J, Hz)[a] T = 297 K $CDCl_3$	δ_H (J, Hz)[c] T = 320 K $CDCl_3$	δ_H (J, Hz)[b] T = 297 K DMSO-d_6	HMBC (H to C)	COSY	ROESY DMSO-d_6	HSQC-TOCSY
34	125.0 qC					21, 22, 37		
	125.1					2, **32,** 33a, 36a, 37		
35	126.4 qC							
	125.5							
36	32.6 CH_2	a 2.91 m	**a 2.91 m**	*2.86 m*	2, 37	2, 36b, **37**		**2, 37**
	32.0	b 1.86 bd (18.9)	**b 1.89 m**	*1.81 m*		2, 36a		
37	19.8 CH_3	1.63 s	**1.65 s**			21, **36a**	*33a*	
	19.8							
38	20.0 CH_3	2.00 d (1.1)	**2.03 d (1.0)**	*1.90 bs*	22	22	*21, 32*	**22**
	19.8							
39	25.5 CH_3	1.11 s	**1.12 s**	*0.99 s*	27		26	
	28.0							
40	18.7 CH_3	1.13 s	**1.14 s**	*0.93 s*	30, *31*		*32*	
	18.3							
41	51.0 CH_3	3.52 s	**3.53 s**	*3.41 s*				
	51.0							
42	170.2 qC					32, 43		
	169.4							
43	20.3 CH_3	1.93 s	**1.93 s**	*1.80 s*			*12*	
	20.4							

[a] $^1J_{CH}$ correlations were determined by a HMQC experiment, and C atom resonance multiplicities by DEPT. [b] All data recorded in DMSO-d_6 are given in italics. [c] Data recorded in $CDCl_3$ at 320 K are given in bold. [d] Overlapping with a methyl group.

that was assumed to afford the biscembranoid vide supra, as already found for previously investigated cembrane dimers.[12] Indeed, an NOE between the CO_2CH_3 methyl group and H-2, in $CDCl_3$, confirmed their cis configuration. Additionally, an NOE between H-21 and CH_3-38 and the absence of an NOE between CH_3-38 and H-22 (well known for the *Z* configuration) established the 22*E* geometry of this double bond as well as the orientation of the double bond.

Other coupling constants and NOEs that contributed to the determination of the stereochemistry of C-21,22(23), and C-30−33 of **15** were the following. *J*'s (relationship): $J_{21,23}$ = 11.7 Hz (anti), $J_{29,30}$ = 11.3 Hz (diaxial), $J_{32,33a}$ = 11.8 Hz (anti); NOEs between H-30 and -33b; H-22 and -33b; H-33a and O*H*-31 and CH_3-37; and H-32 and -21 and CH_3-38.

The conformational mobility of ring A (temperature dependent) prevented the stereochemistry determination of C-5, -9, and -12. From biogenetic considerations, it was suggested to be as in methyl sarcophytoate.[19] The configuration of C-27 (of sp^3 hybridization rather than sp^2 in other known dimers) could not be determined.

To solve the above-mentioned questions, an X-ray diffraction analysis of the crystal of nyalolide, from petroleum ether/acetone, was undertaken.[21,22] The latter X-ray analysis established the full structure of **15** including the four problematic chiral centers (C-5, -9, -12, and -27), which were difficult to assign by NMR techniques; see Figure 2.

As mentioned above, the chemical content of *S. glaucum* is known to change remarkably from one specimen to another. Indeed, the second investigated specimen of *S. glaucum*, collected on Kitungamwe Reef, Kenya, did not contain nyalolide (**15**), but rather a monomeric cembranoid identified as 16-oxosarcoglaucol acetate (**16**) and three sesquiterpenes.[20] The three sesquiterpenes were identified as *trans*-calamanene (**14**), (+)-viridiflorol (**13**), and the new guaiacophine (**17**). Calamanene[18,25] and viridiflorol,[17,26] known terrestrial sesquiterpenes, were previously reported from marine sources and their structures determined by comparison of MS and NMR data with literature values.

Compound **16** was assigned the molecular composition $C_{23}H_{30}O_6$ by HREIMS [M^+] at *m/z* 402.2046, Δmmu +1.0, and its ^{13}C NMR spectrum. The existence of four double bonds (δ_C 159.8 qC, 124.8 qC; 121.6 CH, 145.6 qC; 142.5 CH, 129.9 qC; 128.3 CH, 134.4 qC) (PND and DEPT experiments) and three carbonyl groups (δ_C 176.8, 170.1, and 168.0), accounting for seven of the nine degrees of unsaturation, suggested **16** to be bicyclic. 1D NMR data and comparisons with the chemical shifts of known cembranoids suggested the following functional moieties: a butenolide (as in sarcophine), a secondary acetate, two trisubstituted double bonds, and an α,β-unsaturated methyl ester. The MS and 1D and 2D NMR experiments, including COSY, HMQC, and HMBC, were mainly used for the structure elucidation of 16-oxosarcoglaucol acetate, closely related to sarcoglaucol[8] and the more recent 16-oxosarcoglaucol.[23] Replacement of the latter's alcohol group by an acetate was in full agreement with the measured $\Delta\delta_C$ values of C-12, -13, and -14. Sarcoglaucol[8] was previously reported from *S. glaucum* and its derivative from *S. cherbonnieri*.[23]

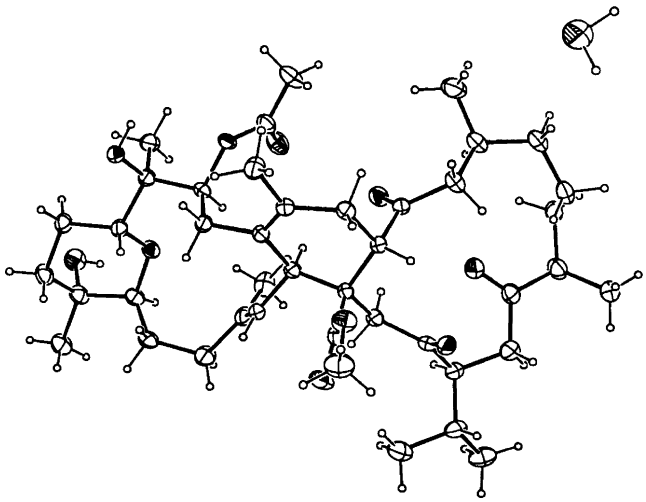

Figure 2. ORTEP presentation of nyalolide (**15**).

Compound **17**, designated guaiacophine, showed an HREIMS [M^+] at *m/z* 218.1674, Δmmu +1.5, for a molecular formula of $C_{15}H_{22}O$ and, therefore, possessed five degrees of unsaturation. The NMR (PND and DEPT experiments) data indicated the presence of two double

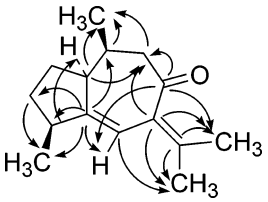

Figure 3. Selective C−H correlations (HMBC) of **17**.

bonds (a trisubstituted one, δ_C 151.7 qC and 117.6 CH, and a tetrasubstituted one, δ_C 138.4 qC and 136.9 qC) and a ketone (δ_C 206.0 qC, ν 1710 cm^{-1}); therefore **17** had to be bicyclic. Two-dimensional NMR experiments, including COSY, HMQC, and especially HMBC (Figure 3), were mainly used for the structure elucidation of guaiacophine, establishing its guaia-5,7(11)-dien-8-one structure. Furthermore, on the basis of NOEs the stereochemistry of **17** with both CH_3-14 and -15 on one side of the molecule, opposite H-1, was established. NOEs were seen between CH_3-14 and H-3β and H-6; between CH_3-15 and H-2β, H-3β, and H-9β on one side of the molecule, and between H-1α and H-10α on the other side.

Compounds **15**−**17** were found to be mildly cytotoxic (GI_{50} ca. 10 μM) against P-338, A-549, HT-29, and MEL-28 tumor cells.[24]

Experimental Section

General Experimental Procedures. IR spectra were recorded on a Nicolet 205 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR were recorded on Bruker Avance 400 and ARX-500 spectrometers. EIMS was recorded on a Fisons Autospec Q instrument. All chemical shifts are reported with respect to TMS (δ_H 0) and $CDCl_3$ or d_6-DMSO (δ_C 77.0 and 39.5), respectively. The diffraction measurements were carried out at ca. 110 K on a Nonius KappaCCD diffractometer, using graphite-monochromated Mo Kα radiation (λ = 0.7107 Å). Intensity data were collected to $2\theta_{max}$ = 55.8°. The crystal structure was solved by direct methods (SIR-97) and refined by full-matrix least-squares on F^2 (SHELXL-97).[21,22] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms attached to carbon were located in calculated positions, while those bound to the O atoms were located in difference Fourier maps. They were refined using a riding model with fixed thermal parameters [$U_{ij} = 1.2U_{ij}$(equiv) for the atom to which they are bonded]. The asymmetric unit of the structure contains one molecule of water, as crystallization solvent.

Animal Material. The soft coral *Sarcophyton glaucum* is widespread in the Indo-Pacific region. It is a highly variable soft coral with respect to shape, coloration, and size of the colonies. The first sample was collected in Nyali, off Mombasa, Kenya, during a field trip conducted in March 2002, and the second sample was collected at Kitungamwe Reef, south of Kisiti National Marine Park, Kenya (almost on the Kenya Tanzania border), at −6−10 m, in February 2003. The colonies are abundant there at a depth of 6−14 m. Voucher specimens are deposited at the Zoological Museum of Tel-Aviv University under the collection numbers ZMTAU Co 31697 and 31695.

Sarcophyton elegans has been recorded in various reef sites across the Indo-Pacific Ocean. The current sample was collected at Shelly Beach, off Likoni, Kenya, at −10−15 m, on February 8, 2003. A voucher specimen is deposited at the Zoological Museum of Tel-Aviv University under the collection number ZMTAU Co 31694.

Extraction and Isolation. A freeze-dried sample of *S. glaucum* (48 g) was extracted with EtOAc to give, after evaporation, a brown gum (810 mg). The gum was partitioned between acqueous methanol, *n*-hexane, and $CHCl_3$. The latter fraction (270 mg) was subjected to Sephadex LH-20 chromatography, eluting with hexane/MeOH/$CHCl_3$ (2:1:1) followed by Si gel vacuum liquid chromatography eluting with hexane/EtOAc (8:2) to produce nyalolide (**15**, 10 mg, 2 × 10^{-2}% dry weight). The same compound was also obtained from *S. elegans* under the same procedure (3 × 10^{-2}% dry weight). The second sample of *S. glaucum*, collected on Kitungamwe Reef, Kenya, gave from the hexane fraction, obtained as above, and following a Si gel vacuum liquid chromatography (eluting with hexane to hexane/EtOAc, 9:1), *trans*-calamanene[19,24] (**14**, 1 mg, 10^{-3}% dry weight), guaiacophine (**17**, 16 mg, 1.6 × 10^{-2}% dry weight), (+)-viridiflorol[18,25] (**13**, 2 mg, 2 × 10^{-3}% dry weight), and 16-oxosarcoglaucol acetate (**16**, 12 mg, 1.2 × 10^{-2}%).

Nyalolide (**15**, 10 mg, 2 × 10^{-2}% dry weight): orthorombic crystals; $[\alpha]_D^{25}$ +98° (*c* 0.08, $CHCl_3$); IR ($CDCl_3$) ν_{max} 3030, 1744, 1461, 900 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m*/*z* 742 [M$^+$] (91), 724 [M − H_2O] (45), 706 [M − 2H_2O] (8), 682 (89), 665 (98), 647 (100), 632 (23), 622 (34), 605 (66); CIMS *m*/*z* 743 [MH$^+$] (100). Crystal data: $C_{43}H_{66}O_{10}\cdot H_2O$, molecular weight 760.97, orthorhombic, space group $P2_12_12_1$, a = 13.5360-(2) Å, b = 14.8460(2) Å, c = 20.7930(4) Å, V = 4178.5(1) Å^3, Z = 4, ρ_{calcd} = 1.210 g cm^{-3}, 32 855 collected reflections, 9875 unique reflections (R_{int} = 0.059), final R1 = 0.052 (wR2 = 0.124) for 7513 reflections with $F_o > 4\sigma(F_o)$, R1 = 0.078, wR2 = 0.138 for all unique data.

16-Oxosarcoglaucol acetate (16): an oil; $[\alpha]_D^{25}$ +81° (*c* 0.07, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1720 cm^{-1}; ^{1}H NMR (d_6-acetone, 400 MHz) δ 5.79 (1H, d, J = 10.3 Hz, H-2), 4.99 (1H, d, J = 10.3 Hz, H-3), 2.30 (2H, m, H_2-5), 2.38 (1H, m, H-6), 3.13 (1H, m, H-6′), 5.68 (1H, dd, J = 3.0, 8.2 Hz, H-7), 1.99 (1H, m, H-9), 2.67 (1H, m, H-9′), 2.05 (1H, m, H-10), 2.31 (1H, m, H-10′), 5.36 (1H, dd, J = 5.1, 10.9 Hz, H-11), 5.27 (1H, d, J = 10.4, H-13), 2.38 (1H, m, H-14), 3.13 (1H, m, H-14′), 1.75 (3H, s, CH_3-17), 1.92 (3H, s, CH_3-18), 1.67 (3H, s, CH_3-20), 1.97 (3H, s, OAc), 3.72 (3H, s, OCH_3); ^{13}C NMR (d_6-acetone, 100 MHz) δ 159.8 (qC, C-1), 77.3 (CH, C-2), 121.6 (CH, C-3), 145.6 (qC, C-4), 38.5 (CH_2, C-5), 26.3 (CH_2, C-6), 142.5 (CH, C-7), 129.9 (qC, C-8), 35.3 (CH_2, C-9), 23.9 (CH_2, C-10), 128.3 (CH, C-11), 134.4 (qC, C-12), 76.2 (CH, C-13), 33.5 (CH_2, C-14), 124.8 (qC, C-15), 176.8 (qC, C-16), 8.6 (CH_3, C-17), 15.7 (CH_3, C-18), 168.0 (qC, C-19), 10.3 (CH_3, C-20), 170.1 and 20.5 (qC, $COCH_3$), 50.8 (CH_3, OCH_3); HREIMS *m*/*z* 402.2046 (calc for $C_{23}H_{30}O_6$ 402.2042).

Guaiacophine (17): an oil; $[\alpha]_D^{25}$ −20° (*c* 0.01, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1710, 1677 cm^{-1}; ^{1}H NMR (d_6-acetone, 400 MHz) δ 2.83 (1H, m, H-1), 1.70 and 1.78 (2H, m, H_2-2), 1.34 and 1.87 (2H, m, H_2-3), 2.65 (1H, sext., J = 7.1 Hz, H-4), 6.30 (1H, s, H-6), 2.45 (1H, dd, J = 7.3 and 11.5 Hz, H-9), 2.50 (1H, dd, J = 6.8 and 11.5 Hz, H-9′), 2.35 (1H, br sep., J = 6.8 Hz, H-10), 1.85 (3H, s, CH_3-12), 1.86 (3H, s, CH_3-13), 1.17 (3H, d, J = 6.8 Hz, CH_3-14), and 0.93 (3H, d, J = 6.8 Hz, CH_3-15); ^{13}C NMR (d_6-acetone, 100 MHz) δ 45.9 (CH, C-1), 29.2 (CH_2, C-2), 34.4 (CH_2, C-3), 40.7 (CH, C-4), 151.7 (qC, C-5), 117.6 (CH, C-6), 138.4 (qC, C-7), 206.0 (qC, C-8), 51.6 (CH_2, C-9), 36.6 (CH, C-10), 136.9 (qC, C-11), 21.1 (CH_3, C-12), 22.3 (CH_3, C-13), 19.7 (CH_3, C-14) and 16.7 (CH_3, C-15); HREIMS *m*/*z* 218.1674 (calc for $C_{15}H_{22}O$ 218.1671).

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