Three Biscembranoids and their Monomeric Counterpart Cembranoid, a Biogenetic Diels–Alder Precursor, from the Soft Coral *Sarcophyton elegans*

Ashgan Bishara,[†] Amira Rudi,[†] Yehuda Benayahu,[‡] and Yoel Kashman*[,†]

School of Chemistry and Department of Zoology, Tel-Aviv University, Ramat Aviv 69978, Israel

Received March 26, 2007

Two new cembranoids, methyl tetrahydrosarcoate (**1**) and methyl tetrahydroisosarcoate (**2**), were isolated from the soft coral *Sarcophyton elegans*, collected at Kitangambwe Kenya, together with four biscembranoids, the known nyalolide (**3**) and the unprecedented desacetylnyalolide (**4**), diepoxynyalolide (**5**), and dioxanyalolide (**6**). The structures and relative stereochemistry of the compounds were elucidated by interpretation of MS, 1D NMR, COSY, HSQC, HMBC, and NOESY experiments. Compound **1** is most likely the dienophile affording, by a Diels–Alder reaction, the four biscembranoids. Dioxanyalolide (**6**) possesses antibacterial activity against *Escherichia coli* at a concentration of 1.25 μg/mL. Methyl tetrahydrosarcoate (**1**) and diepoxynyalolide (**5**) exhibited LC_{50} values of 1.5 μM in a brine shrimp bioassay, while desacetylnyalolide (**4**) was only mildly active.

Soft corals of the genus *Sarcophyton* have proven to be a rich source of a variety of diterepenes, of which cembranoids that exhibit a range of biological activities are the most commonly encountered ones.[1,2] *Sarcophyton glaucum* is one of the more studied organisms. *Sarcophyton* is among the most abundant soft coral genera on many coral reefs, and it tends to form large monospecific "carpets" of up to several square meters.[3]

In addition to cembranoids, several *Sarcophyton* specimens also afford biscembranoids such as methyl sarcophytoate isolated from *Sarcophyton tortuosum*,[4] methyl neosartortuate acetate,[5] and nyalolide.[3] The latter compounds are assumed to be obtained by a Diels–Alder cycloaddition between a cembranoid-diene and cembranoid-dienophiles. One of the two isolated cembranoids, methyl tetrahydrosarcoate (**1**), *vide infra*, is the dienophile which is expected to lead, with the proper diene, to the biscembranoids (Figure 1) as reported in this paper.

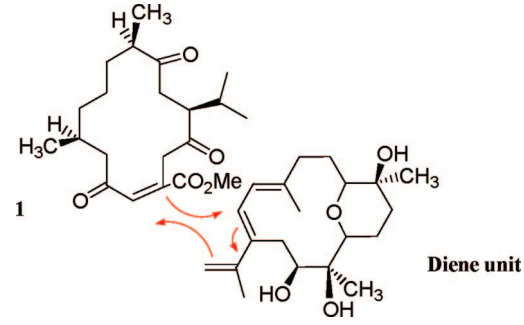


Figure 1. Biogenesis of biscembranoids by Diels–Alder condensation of **1** and an unknown diene.

Results and Discussion

Herewith we report the investigation of *Sarcophyton elegans* (Moser, 1919) collected near Kitangambwe, Kenya. The geographical distribution of *S. elegans* includes various Indo-Pacific reef sites. From this specimen two unprecedented cembranoids were isolated, methyl tetrahydrosarcoate (**1**) and methyl tetrahydroisosarcoate (**2**), together with four biscembranoids, the known nyalolide (**3**)[3] and desacetylnyalolide (**4**), diepoxynyalolide (**5**), and dioxanyalolide (**6**).

Compound **1** was assigned the molecular composition $C_{21}H_{32}O_5$ by HRCIMS $[M + H]^+$ *m/z* 365.2329. Its IR spectrum indicated the presence of an ester carbonyl group (1741 cm^{-1}) and a ketone (1708 cm^{-1}). The NMR data suggested the existence of a conjugated double bond [δ_C 130.8, C-4 and 139.8, C-5; δ_H 7.25 (s, H-5)], three ketones [δ_C 210.2, C-2; 202.6, C-6; 213.8, C-13], and one ester group [δ_C 167.0, C-20; 52.4 q, C-21]. The latter functionalities account for five out of the six degrees of unsaturation of **1**, requiring an additional ring. The MS and 1D and 2D NMR experiments (Table 1) established the methyl tetrahydrosarcoate structure of **1**. The stereochemistry of **1**, based on the structure of **3**, see below, as well as the *E*-configuration of the double bond, was confirmed by NOE correlations (Figure 2).

The spectroscopic data of the second isolated compound (**2**) pointed to an isomeric structure to **1**, namely, a Δ^3 rather than Δ^4 isomer (δ_C 133.4, C-3; 138.8, C-4; δ_H 7.46 s, H-3). As expected, exposing either **1** or **2** to base in a NMR tube ($CDCl_3$ + d_5-pyridine) afforded a mixture of both (Scheme 1). The relative configuration of the chiral centers (C-1, C-8, and C-12) of **2**, as for **1**, is suggested to be the same as in nyalolide, *vide infra*.

The HRMALDIMS of the third isolated compound, **3**, exhibited a pseudomolecular ion $[M + H]^+$ at *m/z* 743.3341. On the basis of the MS and the 43 resonances in the ^{13}C NMR, a $C_{43}H_{66}O_{10}$ formula was suggested. Comparison of the NMR data of **3** to literature data allowed the determination that the compound was nyalolide, a metabolite recently isolated by us from *S. glaucum* collected near Nyali, Mombasa, Kenya. The configuration of **3** was confirmed by X-ray diffraction analysis.[3]

The HRMALDIMS of **4** exhibited a pseudomolecular ion $[M + Na]^+$ at *m/z* 723.4445. The molecular formula $C_{41}H_{64}O_9$ was determined according to the MS and 41 resonances in the ^{13}C NMR spectrum. The latter's carbon and proton chemical shifts were found to be very close to those of nyalolide (**3**).[3] The major difference was the replacement of the secondary OAc group of **3** by a secondary hydroxyl group [δ_C 69.3, C-30, δ_H 3.64 d; δ_C 75.5, C-31; 69.8, C-32, δ_H 3.58 d; δ_C 31.4, C-33, δ_H 2.45 m, (H-33a) and δ_H 2.32 m, (H-33b); δ_C 25.6, C-39; δ_C 18.8, C-40]. Indeed, acetylation of **4** with Ac_2O/pyridine at room temperature, overnight, afforded a monoacetate that was identical in all aspects to nyalolide (**3**). As the structure of nyalolide (**3**) was secured by X-ray diffraction analysis, it became the basis for the suggested stereochemistry of the corresponding chiral centers in cembranoids **1** and **2**, as well as in biscembranoids **5** and **6**. The conformation of **4** in solution was determined from 2D NOESY correlation peaks, as depicted in Figure 3.

* Corresponding author. Tel: +972-3-6408419. Fax: +972-3-6409293. E-mail: kashman@post.tau.ac.il.
[†] School of Chemistry, Tel-Aviv University.
[‡] Department of Zoology, Tel-Aviv University.

10.1021/np070129n CCC: $37.00
Published on Web 11/16/2007

Table 1. NMR Spectral Data of Methyl Tetrahydrosarcoate (**1**) and Methyl Tetrahydroisosarcoate (**2**)

	1[a]			**2**[a]		
position	δ_C, mult.[b]	δ_H (*J* in Hz)	COSY	δ_C, mult.[b]	δ_H (*J* in Hz)	COSY
1	51.4, CH	3.06 dd (11.0, 6.4)	14a, 15	53.5, CH	3.30 ddd (11.0, 5.9, 1.4)	14a, 14b, 15
2	210.2, qC			205.7, qC		
3	42.5, CH_2	4.30 d (18.4)		133.4, CH	7.46 s	
		3.82 d (18.4)				
4	130.8, qC			138.8, qC		
5	139.8, CH	7.25 s	3a	41.9, CH_2	4.50 d (16.5)	
					3.70 d (16.5)	
6	202.6, qC			206.0, qC		
7	50.4, CH_2	2.55 dd (18.9, 9.8)	7b, 8	50.7, CH_2	2.70 dd (17.5, 9.9)	7b, 8
		2.27 m	7a, 8		2.50 br d (17.5)	7a, 8
8	26.7, CH	2.13 m	7a, 7b, 19	28.3, CH	2.24 m	7a, 7b, 19
9	36.9, CH_2	1.28 m	8, 9b, 10b	37.9, CH_2	1.50 m	8, 9b, 10a, 10b
		0.80 m	8, 9a, 10a, 10b		1.12 m	8, 9a, 10a
10	24.9, CH_2	0.90 m	9a, 10b, 11a, 11b	25.7, CH_2	1.04 m	9a, 10b, 11a, 11b
		0.72 m	9a, 9b, 10a, 11b		0.74 m	9a, 9b, 10a, 11b
11	33.5, CH_2	1.40 m (2H)	10a, 10b, 12	34.7, CH_2	1.55 m (2H)	10a, 10b, 12
12	47.8, CH	2.38 m	11	48.2, CH	2.44 m	11
13	213.8, qC			213.3, qC		
14	36.8, CH_2	2.90 dd (17.6, 11.5)	1, 14b	36.3, CH_2	3.20 dd (17.4, 11.5)	1, 14b
		2.17 m	14a		2.30 br d (17.4)	14a
15	29.9, CH	1.88 octet (6.4)	1, 16, 17	29.9, CH	2.08 octet (6.7)	1, 16, 17
16	19.7, CH_3	0.87 d (6.4)	15	19.6, CH_3	1.00 d (6.7)	15
17	20.7, CH_3	0.95 d (6.4)	15	21.0, CH_3	1.09 d (6.7)	15
18	17.2, CH_3	1.08 d (7.0)	12	17.0, CH_3	1.25 d (7.0)	12
19	22.0, CH_3	0.84 d (6.5)	8	22.6, CH_3	1.01 d (7.0)	8
20	167.0, qC			167.4, qC		
21	52.4, CH_3	3.70 s		52.8, CH_3	3.94 s	

[a] Recorded in $CDCl_3$ solution measured at 500 MHz. [b] Recorded in $CDCl_3$ solution measured at 100 MHz, and multiplicities were determined by DEPT and HSQC experiment.

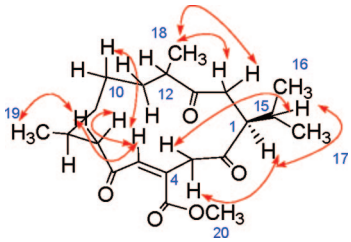


Figure 2. Key NOEs of tetrahydrosarcoate **1**.

The HRMALDIMS of **5** exhibited a pseudomolecular ion $[M + Na]^+$ at *m/z* 705.4292. The molecular formula $C_{41}H_{62}O_8$ was determined on the basis of the MS and the 41 carbon resonances in the ^{13}C NMR spectrum. The 1D and 2D NMR spectra of segments C_1–C_{23} and C_{32}–C_{36} including the attached methyl groups of **5** were essentially identical to those of **4**. However, instead of the tetrahydropyran ring of **3** and **4**, two trisubstituted epoxides were present (δ_C 61.8 CH, 60.0 qC, and 60.1 CH, 63.0 qC; δ_H 2.72 dd and 2.94 d). As with the former compounds, COSY, HSQC, and HMBC experiments established the C_{26}–C_{27} and C_{30}–C_{31} location of the two epoxides. NOEs of the "right" part of **5** (Figure 4) determined the *E*-geometry of both epoxy groups as well as provided further support for the suggested structure. However, the NMR data could not distinguish between α- or *β*-orientations of the oxirane oxygen atom because for both possible configurations the surrounding protons will, approximately, occupy similar positions. Tentatively, on the basis of the configuration of the THP ring of **3**, *vide infra*, a *β*-configuration is also suggested for both epoxides. The latter configuration also agrees with the configuration of **3** and **4**, assuming **5** to be their precursor.

The HRMALDIMS of compound **6** exhibited a pseudomolecular ion at *m/z* 705.4351, which together with the 41 resonance lines in the ^{13}C NMR spectrum established the $C_{41}H_{62}O_8$ formula. The almost identical NMR data of the C_1–C_{23}, C_{32}–C_{36}, and the attached methyl groups in **3**–**6** suggested the same "left" bicyclic part. The ^{13}C NMR of **6** exhibited five oxygen-carrying C atoms (δ_C 85.3 CH, 73.8 qC, 70.8 CH, 76.8 qC, and 71.9 CH). Compound **6** possessed the same formula as **5** with 11 degrees of unsaturation but lacked epoxy groups; therefore, it had to contain two ethereal bridges in addition to the single hydroxyl group. The C-32 location of the latter hydroxyl group was determined according to COSY correlations of protons H-32, H-33a, and H-33b as well as from suitable CH correlations (Figure 5). As expected microacetylation of **6** with Ac_2O/pyridine at room temperature, overnight, afforded the 32-acetoxy monoacetate derivative (δ_C 75.8 CH, C-32; δ_H 4.75 brd, $J = 9.8$; δ_C 170.1 qC, 20.2 CH_3; δ_H 1.94 s). Molecular models excluded the possible dioxabicyclo[2.2.2]octane moiety, due to severe transannular interactions, suggesting a plausible dioxabicyclo[3.2.1]octane system. Distinction between possible [3.2.1] isomers became feasible from the measured NOEs (Figure 6). It is possible that diepoxynyalolide (**5**) is the precursor of both nyalolide (**3**) and dioxanyalolide (**6**) (Scheme 1). A rearrangement of two epoxy groups to a 1,4-dioxane system is known synthetically on a zeolite catalyst.[7]

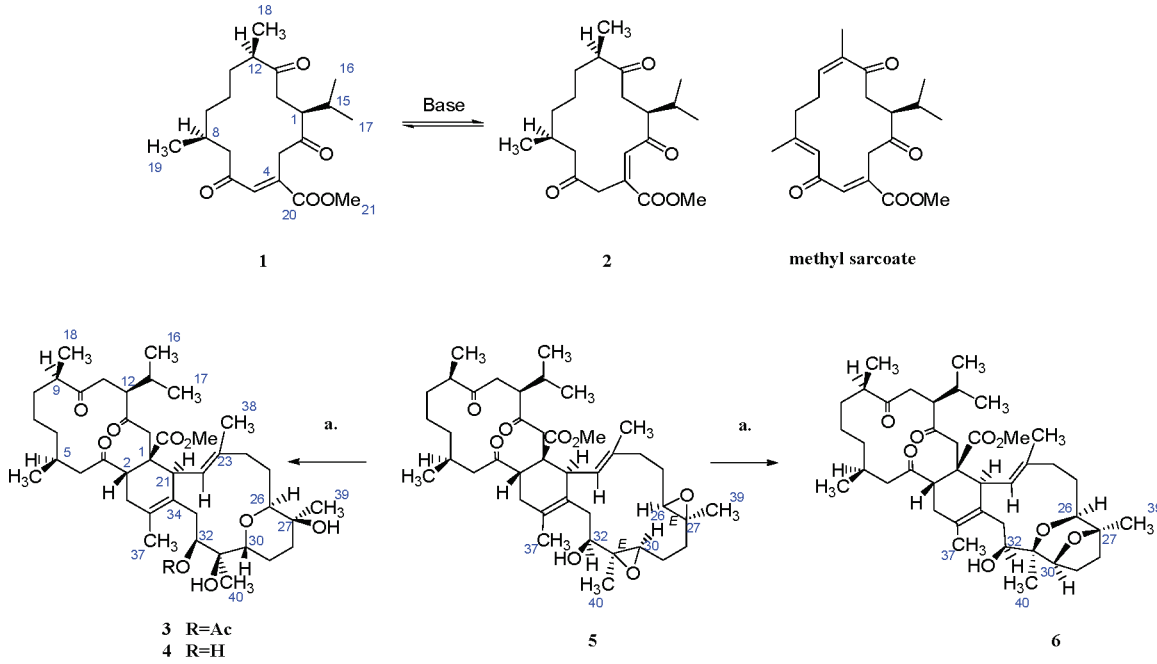
Dioxanyalolide **6** possessed antimicrobial activity against *Escherichia coli* at a concentration of 1.5 *μ*g/mL. In an *Artemia salina* lethality bioassay,[8] compounds **1** and **5** exhibited LC_{50} values of 1.5 *μ*M, whereas desacetylnyalolide (**4**) showed only mild activity.

Experimental Section

General Experimental Procedures. Optical rotations were obtained with a Jasco P-1010 polarimeter. IR spectra were obtained with a Bruker FTIR Vector 22 spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance-500 and Avance-400 spectrometers. All chemical shifts are reported with respect to residual $CHCl_3$ (δ_H 7.25) and (δ_C 77.0). ^1H, ^{13}C, COSY, HMQC, NOESY, and HMBC were recorded using standard Bruker pulse sequences. FABMS and CIMS measurements were recorded on a Fisons, Autospec Q instrument. MALDI HRMS measurements were recorded on an Applied Biosystem Voyager DE-STR MALDI TOF instrument.

Biological Material. The octocoral *Sarcophyton* sp. was collected in Kitangambwe, Kenya, 4°48′49″ S, 39°21′50″ E (December 11, 2004). A voucher specimen is deposited at the Zoological Museum, Tel Aviv University, Israel (ZMTAU CO 32745). This soft coral was collected from a patch reef slope at a depth of 12–15 m, inhabited also by a

Scheme 1. Structures and Transformations of Compounds **1**–**6** and Methyl Sarcoate[6]



large variety of other octocorals, sponges, and tunicates. The geographical distribution of *S. elegans* includes various Indo-Pacific reef sites.

Extraction and Isolation. A freeze-dried sample of *Sarcophyton elegans* (21 g) was homogenized and extracted with EtOAc/MeOH/H_2O (5:5:1) to give, after evaporation, a brown gum (1 g). The gum was partitioned between aqueous MeOH, *n*-hexane, and CH_2Cl_2 under a Kupchan procedure.The CH_2Cl_2 extract (0.5 g) was chromotographed on a Sephadex LH-20 column, eluting with *n*-hexane/MeOH/$CHCl_3$ (2:1:1) to give 15 fractions, which were subsequently subjected to VLC over silica gel, using hexane with increasing proportions of EtOAc as eluent. Fractions 3 and 4 from the VLC (97 mg) afforded with *n*-hexane/EtOAc (8.5:1.5) compound **1** (23 mg 0.11% dry weight) and with *n*-hexane/EtOAc (8:2) compound **2** (19 mg 0.09% dry weight). Fraction 6 eluted with a 1:1 mixture gave nyalolide (**3**) (26 mg 0.12 % dry weight), fraction 7 (53 mg) afforded with *n*-hexane/EtOAc (4:6) compound **4** (24 mg 0.12% dry weight), and fractions 8–10 (98 mg) eluted with 30% EtOAc were further separated by VLC to give compounds **5** and **6** (12 mg, 0.06% and 8.5 mg, 0.04% dry weight, respectively).

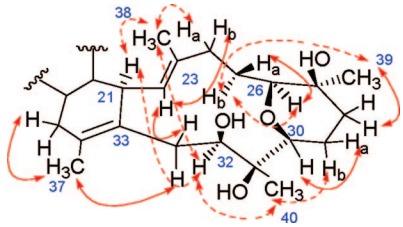


Figure 3. Selected NOEs of desactylnyalolide (**3**).

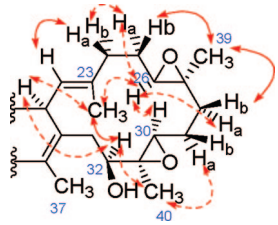


Figure 4. Selected NOEs of diepoxynyalolide (**5**).

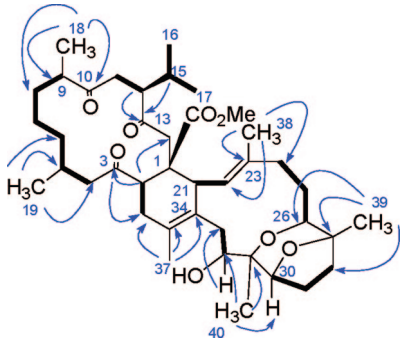


Figure 5. H^1–H^1 COSY and selected HMBC correlations of dioxanyalolide (**6**).

Methyl tetrahydrosarcoate (1): pale yellow oil; $[\alpha]^{25}_D$ +107 (*c* 1.18, CH_2Cl_2); IR (CH_2Cl_2) ν_{max} 3019, 1741, 1708, 1425, 1215, 1031, 928 cm^{-1}; ^{13}C and ^1H NMR see Table 1; CIMS *m/z* 365 (18) [M + H]$^+$, 347 (100) [M + H – H_2O]$^+$; HRCIMS *m/z* 365.2329 (calcd for $C_{21}H_{33}O_5$, 365.2328).

Methyl tetrahydroisosarcoate (2): pale yellow oil; $[\alpha]^{25}_D$ +154 (*c* 0.64, CH_2Cl_3) ; IR (CH_2Cl_2) ν_{max} 3026, 2964, 2874, 1713, 1611, 1464, 1267 cm^{-1}; ^1H and ^{13}C NMR see Table 1; CIMS *m/z* 365 (30) [M + H]$^+$, 347 (100) [M + H – H_2O]$^+$; HRCIMS *m/z* 365.2328 (calcd for $C_{21}H_{33}O_5$, 365.2328).

Nyalolide (3): orthorombic crystals; $[\alpha]^{25}_D$ +92 (*c* 0.87, CH_2Cl_2). Identical spectroscopic data to the published ones.[3]

Desacetylnyalolide (4): colorless oil; $[\alpha]^{25}_D$ +100 (*c* 1.16, CH_2Cl_2); IR (CH_2Cl_2) ν_{max} 3577, 3013, 1746, 1710, 1459, 1382, 1236, 1198, 1068, 923 cm^{-1}; selective partial ^1H NMR data for the THP surrounding ($CDCl_3$ in 500 MHz) δ 3.66 (1H, d, J = 9.2 Hz, H-26), δ 3.64 (1H, d, J = 9.1 Hz, H-30), δ 3.58 (1H, d, J = 10.7 Hz, H-32), δ 2.45 (1H, d, m, H-33a), δ 2.32 (1H, m, H-33b), δ 1.75 (1H, m, H-29a), δ 1.70 (2H,

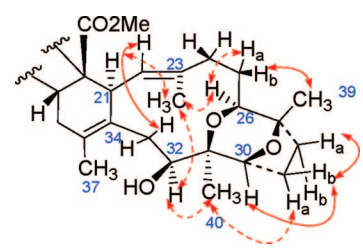


Figure 6. Selected NOEs of dioxanyalolide (**6**).

Table 2. NMR Spectral Data of Diepoxynyalolide (**5**) and Dioxanyalolide (**6**)

	5[a]		**6**[a]	
position	δ_C, mult.	δ_H (*J* in Hz)[b]	δ_C, mult.	δ_H (*J* in Hz)[b]
1	49.0, qC		48.9, qC	
2	46.0, qC	4.00 dd (2.2, 9.1)	47.1, CH	4.01 d (8.2)
3	212.3, qC		214.7, qC	
4	49.6, CH_2	2.47 dd (18.5, 6.3)	49.6, CH_2	2.41 dd (18.3, 6.1)
		2.27 dd (18.5, 6.3)		2.22 dd (18.3, 6.1)
5	26.2, CH	2.05 m	26.5, CH	2.10 m
6	36.3, CH_2	1.23 m	36.9, CH_2	1.21 m
		0.89 m		0.88 m
7	23.9, CH_2	0.95 m (2H)	24.6, CH_2	0.99 m
				0.90
8	32.4, CH_2	1.62 m	32.7, CH_2	1.70 m
		1.40 m		1.40 m
9	47.2, CH	2.35[c]	47.6, CH	2.33[c]
10	212.9, qC		212.8, qC	
11	36.8, CH_2	2.90 m	38.4, CH_2	2.85[c]
		2.17 m		2.25 m
12	51.4, CH	2.91 m	52.1, CH	2.86 m
13	213.9, qC		213.6, qC	
14	48.1, CH_2	3.20 d (19.4)	49.7, CH_2	3.30 d (19.2)
		3.08 d (19.4)		3.00 d (19.2)
15	29.2, CH	1.90 m	29.8, CH	1.90 m
16	18.9, CH_3	0.83 d (6.7)	19.7, CH_3	0.83 d (6.5)
17	20.7, CH_3	0.93 d (6.7)	21.6, CH_3	0.93 d (6.5)
18	16.7, CH_3	1.15 d (7.1)	17.1, CH_3	1.16 d (7.2)
19	21.7, CH_3	0.86 d (6.7)	22.4, CH_3	0.85 d (6.5)
20	173.6, qC		174.1, qC	
21	42.5, CH	3.82 br d (11.3)	41.7, CH	3.72 br d (11.2)
22	126.5, CH	5.18 br d (11.3)	124.5, CH	4.80 d (11.2)
23	137.3, qC		138.7, qC	
24	34.1, CH_2	2.33[c]	39.7, CH_2	2.43[c]
		2.23 m		1.82[c]
25	26.1, CH_2	1.81 m	28.5, CH_2	1.84 m
		1.58 m		1.63 m
26	61.8, CH	2.72 dd (6.0, 3.7)	85.30, CH	4.00 d (8.5)
27	60.0, qC		73.8, qC	
28	35.4, CH_2	2.10 m	35.7, CH_2	2.00 m
		1.52 m		1.71 m
29	23.2, CH_2	1.86 m	21.7, CH_2	2.04 m
		1.47 m		1.57 m
30	60.1, CH	2.94 d (9.1)	70.8, CH	3.63 br d (9.2)
31	63.0, qC		76.8, qC	
32	70.1, CH	3.70[c]	71.9, CH	3.55 d (10.9)
33	34.0, CH_2	2.16[c] (2H)	32.13, CH_2	2.41[c]
				2.31[c]
34	124.7, qC		126.9, qC	
35	128.1, qC		128.1, qC	
36	32.7, CH_2	2.80[c]	33.3, CH_2	2.95[c]
		1.94 m		1.85 m
37	19.9, CH_3	1.67 s	20.8, CH_3	1.67 s
38	16.2, CH_3	1.82 s	20.9, CH_3	1.90 s
39	17.9, CH_3	1.26 s	31.5, CH_3	1.56 s
40	15.9, CH_3	1.33 s	19.7, CH_3	1.34 s
41	51.1, CH_3	3.53 s	51.9, CH_3	3.53 s

[a] Recorded in $CDCl_3$ solution at 500 MHz. [b] a, b for a methylene pair denote the upper (a) and lower field protons (b). [c] Multiplicities were not determined because of overlapping with other signals.

m, H-28a/b), δ 1.60 (1H, m, H-29b); ^{13}C NMR ($CDCl_3$ in 100 MHz) δ 85.0 (CH, C-26), δ 75 (qC, C-31), δ 70.8 (qC, C-27), δ 69.8 (CH, C-32), δ 69.3 (CH, C-30), δ 31.4 (CH_2, C-33), δ 28 (CH_2, C-28), δ 25.6 (CH_3, C-39), δ 20.3 (CH_3, C-38), δ 20.1 (CH_2, C-29), δ 20.0 (CH_3, C-37),), δ 18.8 (CH_3, C-40); HRMS (MALDI) $[M + Na]^+$ *m/z* 723.4445 (calcd for $C_{41}H_{64}O_9Na$, 723.4443).

Diepoxynyalolide (5): pale yellow oil; $[\alpha]^{25}_D$ +68 (*c* 0.52, CH_2Cl_2); IR (CH_2Cl_2) ν_{max} 3011, 2962, 1710, 1461, 1383, 1224, 1054, 926 cm^{-1}; ^{13}C and ^1H NMR see Table 2; HRMS (MALDI) $[M + Na]^+$ *m/z* 705.4292 (calcd for $C_{41}H_{62}O_8Na$, 705.4337).

Dioxanylolide (6): colorless oil; $[\alpha]^{25}_D$ +5005 (*c* 0.23, CH_2Cl_2) ; IR (CH_2Cl_2) ν_{max} 3680, 3019, 1754, 1708, 1426, 1233, 1071, 927 cm^{-1}; ^{13}C and ^1H NMR see Table 2 HRMS (MALDI) $[M + Na]^+$ *m/z* 705.4351 (calcd for $C_{41}H_{62}O_8Na$, 705.4337).

Biological Activity. Brine Shrimp (*Artemia salina*) Toxicity Bioassay.[8] Ten brine shrimp were transferred to each sample vial containing various compounds in concentrations of 10, 100, and 1000 μg/mL that were maintained under illumination. Survivors were counted after 24 h at 26 °C, and the percentage of deaths at each dose was recorded. The latter data enabled the estimation of LC_{50} values. Each test was performed in duplicate.

Acknowledgment. We thank A. Sacher (of the Maiman Institute for Proteome Research, Tel Aviv University) for performing the electrospray mass measurements. Special thanks are due to C. O. Oduol, Assistant Director of Fisheries, Mombasa, Ministry of Agriculture and Rural Development, Fisheries Department, Kenya, for issuing the collection permit for the research expedition. M. Ilan and R. Gottlieb (National Center for High Throughput Screening (HTS) of Novel Bioactive Compounds, Tel Aviv University) are acknowledged for their biological evaluation of the compounds.

Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **1**, **4**, **5**, and **6**, including COSY and HMBC for compound **1**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Faulkner, D. J *Nat. Prod. Rep.* **1991**, *8*, 97, and previous reports in the same series.

(2) Blunt, J. W.; Copp, B. R.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. *Nat. Prod. Rep.* **2004**, *21*, 1–49.

(3) Feller, M.; Rudi, A.; Berer, N.; Goldberg, I.; Stein, Z.; Benayah, Y.; Schleyer, M.; Kashman, Y *J. Nat. Prod* **2004**, *67*, 1303–1308.

(4) Kusumi, T.; Igari, M.; Ishitsuka, M. O.; Ichikawa, A.; Itezono, Y.; Nakayama, N.; Kakisawa, H. *J. Org. Chem.* **1990**, *55*, 6286–6289.

(5) Leone, P. A.; Bowden, B. F.; Carroll, A. R.; Coll, J. C.; Meehan, G. V. *J. Nat. Prod.* **1993**, *56*, 521–526.

(6) Ishitsuka, M. O.; Kusumi, T.; Kakisawa, H. *Tetrahedron Lett.* **1991**, *32* (25), 2917–2918.

(7) Fasi, A.; Panlinko, I.; Kiricdi, I. *J. Catal.* **1999**, *188* (2), 385–392.

(8) Meyer, B. N.; Ferrigni, N. R.; Putnam, J. E.; Nichols, D. E.; McLaughlin, J. L. *Plant Res.* **1982**, *45*, 31–34.

(9) Kupchan, S. M. *J. Org. Chem.* **1977**, *34*, 2349–2357.

NP070129N