New Triterpenoids from the Red Sea Sponge *Siphonochalina siphonella*

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Clear differences were found when comparing the chemical content of the northern, Gulf of Eilat, to the southern-central, Dahlak archipelago, Red Sea sponge *Siphonochalina siphonella*. The Dahlak sponge was found to be richer in the more polar triterpenes. Nine new compounds (**1**−**4**, **7**, **8**, **15**−**17**) were isolated and identified, among them two sipholane glycosides, sipholenoside A and B (**7** and **8**), and one compound, dahabinone A (**17**), possessing a new skeleton.

The Red Sea sponge *Siphonochalina siphonella* was found to be a rich source of triterpenoids.[1−4] So far, 10 compounds belonging to three different skeleta, namely, the sipholanes,[1,2] siphonellane,[3] and neviotane,[4] have been reported. Examples of the various skeleta, shown below, are sipholenol A (**5**), siphonellinol B (**15**), and neviotine B (**16**) (Scheme 1 and Chart 1).

In the frame of a comparison of northern to southern-central Red Sea organisms, namely, Gulf of Eilat vs Dahlak archipelago, Eritrea, an investigation of the pipe sponge *Siphonochalina siphonella* (family Haliconidea, Levi 1965) was undertaken. As a result, eight new triterpenoids were isolated from the northern sponge, and an additional new compound was isolated from the Dahlak specimen. The comparison showed clear differences in the sponge-triterpenoid compositions from the two regions. Samples collected from the Dahlak region exhibited higher concentrations of the more polar sipholanes; still sipholenol A (**5**) was the major sipholane as in the north (2.5−2.8%, dry wt). The corresponding 4-keto analogue, sipholenone A (**6**),[2] however, was only found in the north sponge (1%, dry wt). Changes were also observed for sipholenol F (**3**) (0.28% in the southern-central against 0.05% in the north), sipholenone D (**2**), and sipholenol H (**4**), which appeared in ca. 10-fold amounts in the southern-central region. It is possible that the chemical changes are connected with the warmer seawater in Dahlak (31 versus 27 °C in Eilat, the highest temperatures in summer).

Results and Discussion

Herewith are reported the structures of the nine new triterpenoids from *S. siphonella* (Chart 1). Four compounds (**1**−**4**) are closely related to sipholenol A (**5**) and its 4-keto analogue, sipholenone A (**6**) (Scheme 1).[2] Two additional compounds, siphonellinol B (**15**) and neviotine B (**16**), are closely related to the earlier reported siphonellinol A[3] and neviotine A.[4] From the northern sponge were also isolated sipholenoside A (**7**), the first glycoside of these triterpenoids, namely, a 19-glycoside of sipholenone D (**2**), and dahabinone A (**17**), a triterpene with a new skeleton, and from the Dahlak sponge another glycoside (**8**) of sipholenol A (**5**). The structure determination of the nine new compounds, including chemical transformation, is described below.

The first four isolated sipholanes (**1** − **4**), like all other known sipholanes, are assembled from two bicyclic systems, a perhydrobenzoxepine and a [5,3,0]bicyclodecane system (the "left" and "right" halves of the molecules, as they will hereafter be addressed), linked together through an ethylene bridge. Because of the latter bridge, the two halves of the sipholanes can freely rotate against each other; therefore, an X-ray diffraction analysis was required for determination of the entire relative configuration.[1] The absolute configuration was later also determined by the modified Mosher method.[5] The proton and especially carbon NMR spectrum are most valuable for identification and comparison of the various parts of these molecules.[6]

Sipholenols G, F, and H (**1**, **3**, and **4**) possess the same left half as sipholenol A (**5**), and sipholenone D (**2**) the same left half as sipholenone A (**6**).[2] All four differ, however, from the known compounds in the right part. All four were chemically related to known sipholanes (see Schemes 1 and 2), thus unambiguously establishing their structures.

Sipholenol G (**1**) analyzed for $C_{30}H_{52}O_5$, possessing one additional oxygen atom over sipholenol A (**5**). Comparison of the ^{13}C NMR spectra of **1** and **5** (Table 1) exhibited identity of the left part of the molecules and replacement of the 15(16)-double bond of the right half of **5** with an epoxy group in **1** (δ_C 60.8 s (C-15) and 61.9 d (C-16); δ_H 2.94 (t, J = 7.5 Hz, H-16)), as in sipholenol B.[2] Clear proof of the structure was obtained by *m*-chloroperbenzoic acid epoxidation of sipholenol A (**5**) to afford sipholenol G (**1**) (32%) and its 15,16-epoxy epimer **9** (22%) (δ_H 2.77 dd (J = 8.2, 4.8 Hz, H-16) against the triplet in **5**) (Scheme 1). The α-epoxy stereochemistry of **1** was determined according to the signal of H-16, which is identical to this proton in sipholenone B, for which the stereochemistry was independently established by chemical transformations.[2]

The second compound, sipholenone D (**2**), analyzed for $C_{30}H_{50}O_4$ and, according to the NMR data (Table 1), was determined to possess the left half of sipholenone A (**6**)[2] and the right part of sipholenol C.[2] Indeed, Jones oxidation (chromic acid in acetone) of the latter compound afforded sipholenone D (**2**) (Scheme 1), confirming the suggested structure.

The third compound, sipholenol F (**3**), which analyzed for $C_{30}H_{52}O_4$ as compound **5**, possesses, according to the ^{13}C NMR data (Table 1), the left half of sipholenol A (**5**) and an isomeric (to **5**) substituted right half.[7] Acid treatment of **3** (p-TsOH in $CHCl_3$) (Scheme 2) afforded two major compounds, the 15,19-diene **12** (10%) (δ 5.50 br dd and 5.29 br s 1H each, 1.67 br s and 1.76 br s 3H each), identical to the compound obtained from **5** under the same acid conditions,[2] and a 15,19-oxido derivative (**11**, 50%) (δ 1.19 and 1.26 s, Me's 15 and 19, respectively) (Scheme 2). Obtaining the 15,19-ethereal bridge in **11** established simultaneously the cis ring junction of the 5,7-bicyclic

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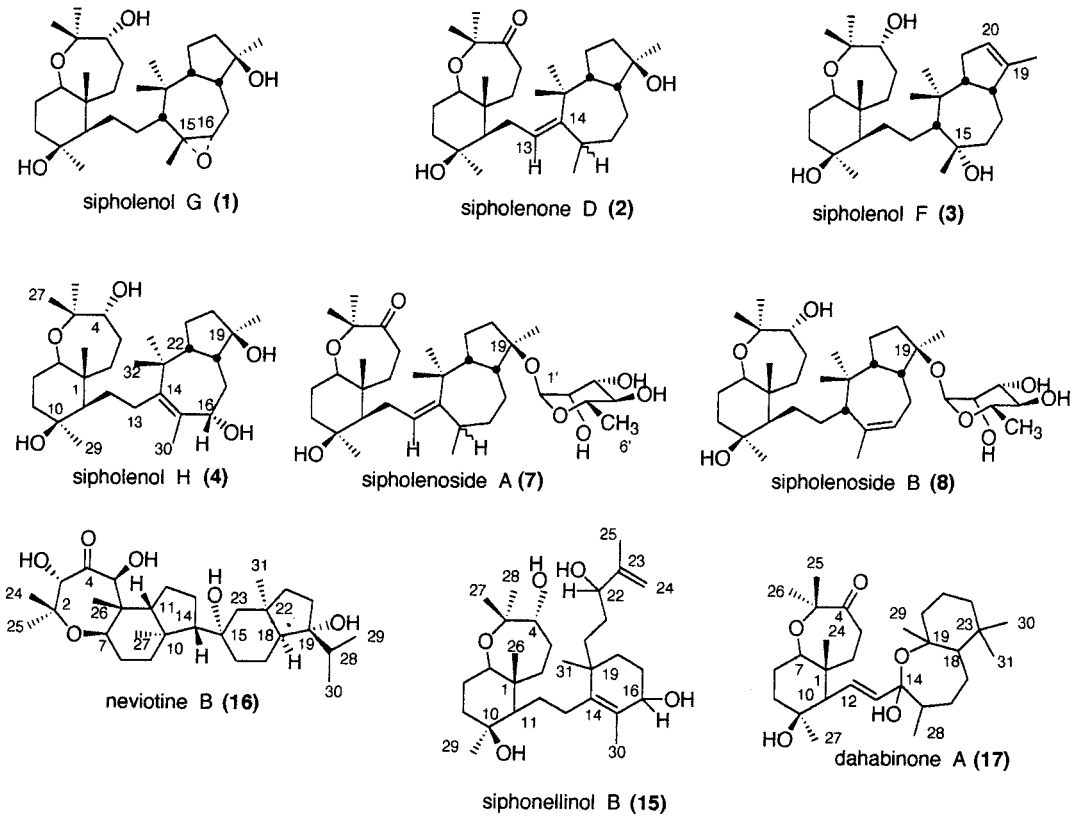
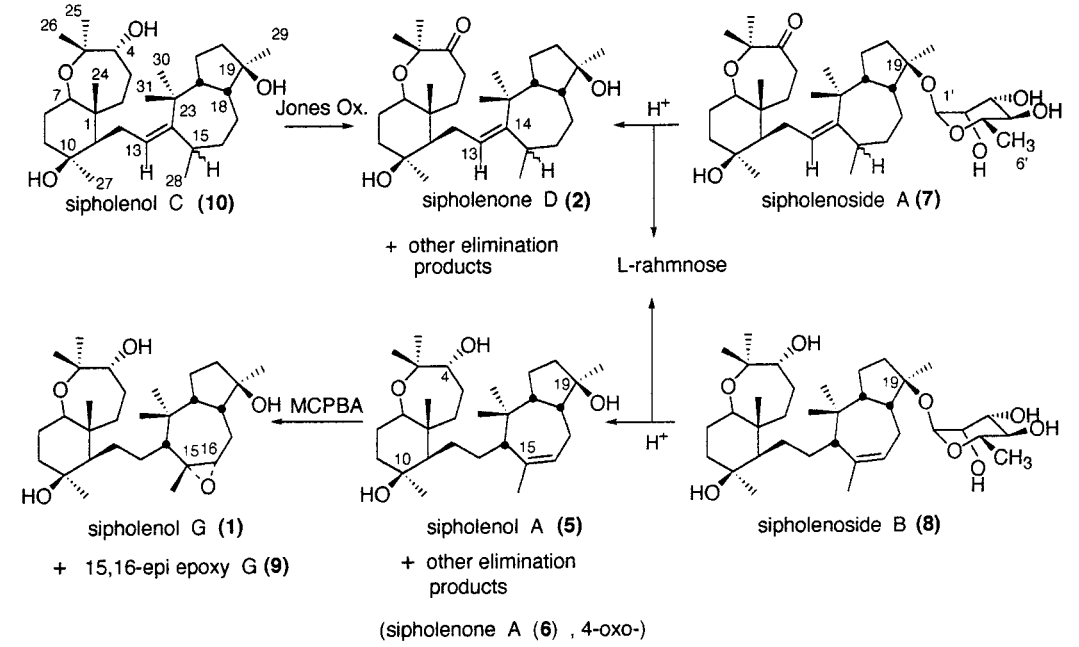
Chart 1



Scheme 1



system and the α-hydroxy stereochemistry of the 15-OH group, both essential for obtaining the ethereal linkage between C-15 and C-19, which are separated by four bonds.

Sipholenol H (**4**), $C_{30}H_{52}O_5$ (*m*/*z* 493, [MH$^+$]), the fourth isolated sipholane of the first group, possesses, according to the ^{13}C NMR data (Table 1), the perhydrobenzoxepine left part of sipholenol A (**5**) and, as the right half, an isomeric structure to sipholenol E's right half.[2] From the ^{13}C NMR data, it was clear that **4** contains, in its right half, one secondary and one tertiary hydroxyl group as well as a tetrasubstituted double bond (δ_C 83.0 d, 72.0 s, 125.8 s, and 143.0 s). As Jones oxidation of sipholenol H (**4**) afforded the same 4,16-dioxo derivative (**14**) as that obtained from oxidation of sipholenol E (**13**)[2] (Scheme 2), compound **4** has to be the 16α-epimer of sipholenol E (**13**). The latter conclusion agrees with the NMR H-16 pattern in **4** and **13**.[2]

In addition to the above four compounds, two considerably more polar ones, designated sipholenoside A (**7**) and B (**8**), were obtained, one (**7**) from the northern sponge and the other (**8**) from the southern-central one. Sipholenoside A analyzed for $C_{36}H_{60}O_8$ from the MS (*m*/*z* 602, [M$^+$ −

Scheme 2

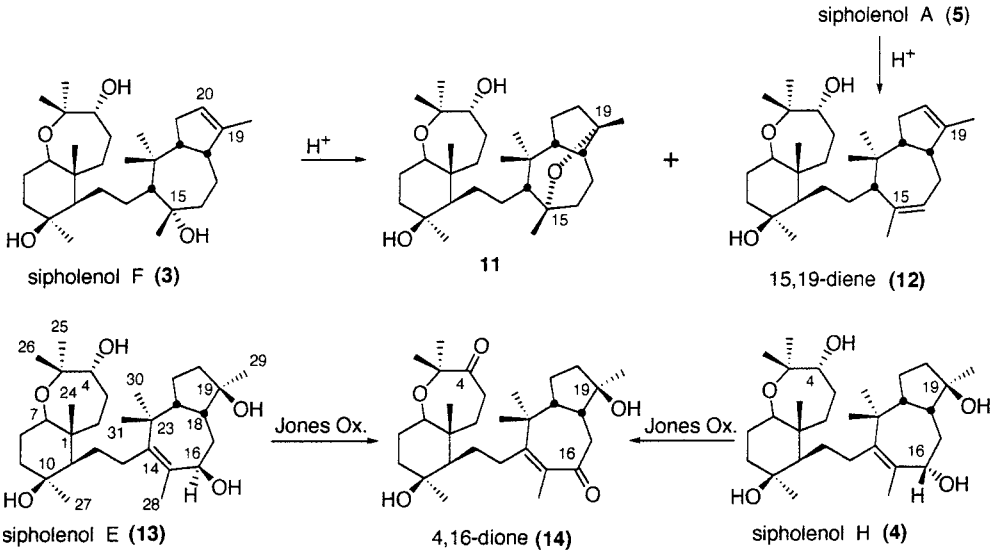


Table 1. ^{13}C NMR Data of Sipholanes **1**−**8**[a,b]

position	1	2	3	4	5	7[d]	8[e]
1	42.6	42.1	42.8	42.4	42.2	42.3	42.6
2	34.0	40.6	34.4	34.2	33.6	40.8	33.6
3	25.2	35.3	25.3	25.0	24.6	35.2	25.1
4	76.6	217.4	77.0	76.4	75.9	216.3	76.5
5	77.9	82.6	77.8	78.2	78.0	82.4	77.2
7	76.6	81.3	76.4	76.4	76.2	81.3	74.1
8	26.6	26.6	26.7	26.3	26.2	26.4	26.6
9	39.0	40.8	39.2	38.8	38.6	41.4	39.0
10	71.8	72.4	72.4	72.0	71.9	72.8	72.6
11	55.8	58.0	56.6	55.2	55.7	58.1	55.7
12	27.6	33.5	27.5	24.8	26.4	32.8	26.7
13	33.1	132.7	29.6	37.9	33.4	134.1	33.6
14	56.0	140.7	42.0	125.8	57.3	139.7	57.5
15	60.8	33.8	72.9	143.0	142.7	33.8	143.3
16	61.9	32.1	39.7	83.0	120.9	31.7	121.1
17	30.4	21.3	30.5	27.4	24.3	20.8	24.2
18	46.9	50.1	47.1	42.1	48.0	46.2	45.1
19	81.3	73.1	135.6	72.0	81.4	78.9	89.3
20	37.0	37.2	121.7	30.3	36.5	37.0	33.8
21	24.0	24.0	36.2	36.1	24.7	23.8	21.4
22	52.9	50.9	47.6	44.7	52.2	51.3	52.9
23	37.1	33.3	34.7	34.4	35.0	32.7	35.4
24	12.8	12.5	13.3	12.5	12.6	12.7	12.9
25	21.2	20.6	21.3	21.1	21.0	20.4	21.3
26	28.9	26.3	28.9	28.7	28.5	24.9	29.1
27	30.0	28.8	30.3	29.9	29.2	28.6	29.5
28	30.4	26.6	28.4	16.7	29.6	25.9	30.1
29	25.3	23.6	21.8	28.3	24.9	22.6	24.9
30	28.1	22.3	24.6	23.2	29.0	23.3	31.8
31	33.4	30.0	35.5	35.3	31.2	28.8	29.8

[a] $CDCl_3$, Brucker AMX-360 or ARX-500 instruments, chemical shifts refer to $CDCl_3$ (δ_C = 77 ppm). [b] Multiplicities were determined by DEPT and HMQC experiments and are as required from the formulas. [c] Interchangeable signals. [d] $\delta_{C-1'\text{ to }6'}$ 93.7 d, 72.5 d, 72.2 d, 74.1 d, 67.8 d, 17.6 q ppm. [e] $\delta_{C-1'\text{ to }6'}$ 94.2 d, 71.9 d, 70.5 d, 72.3 d, 67.6 d, 17.4 q ppm.

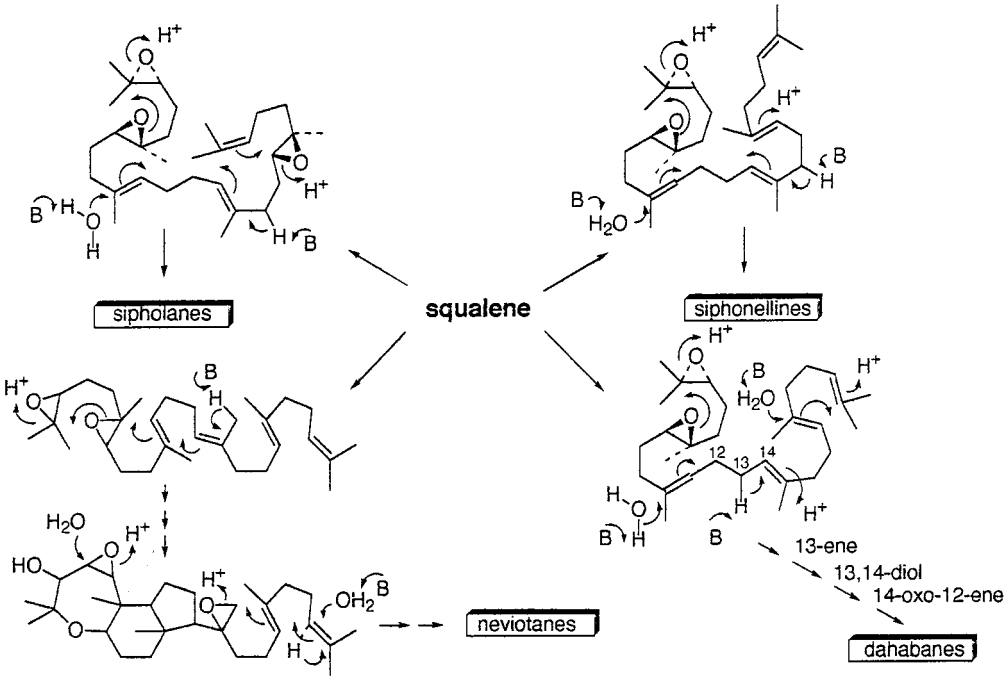
H_2O]) and ^{13}C NMR data (Experimental Section). Characteristic chemical shifts for sugar protons and especially for the anomeric group (δ_H 5.53 br d, J = 1.3 Hz and δ_C 95.1 d, in C_5D_5N) as well as the *m/z* 456 [$M^+ - C_6H_{12}O_5$] fragment, in the MS suggested a glycoside. Comparison of the NMR data of **7** with the NMR data of the known sipholanes established the aglycone as sipholenone D (**2**). An excellent agreement was found for 25 out of the 36 carbon atom signals of **7** with the corresponding ones of sipholenone D (**2**) (Table 1). Furthermore, the observed changes in C-19 (+5.7 ppm), C-18 (−4.0 ppm), and C-22 (+0.4 ppm) pointed to C-19 as the location of attachment of the sugar unit. On the basis of the proton and carbon atom NMR data, the sugar unit was determined to be α-rhamnose.[8−12] Mild acidic hydrolysis of **7** afforded sipholenone D (**2**) and other elimination products that were not identified as well as the sugar unit (Scheme 1). The later monosaccharide was determined upon its NMR specta and optical activity to be α-L-rhamnose.[13]

Sipholenoside B (**8**) analyzed for $C_{36}H_{62}O_8$ from the MS *m/z* 622 [M^+] peak. The NMR and MS data of **8** (Experimental Section) pointed clearly to a second glycoside. Using the same rationale described above for compound **7**, the aglycone of **8**, according to the ^{13}C NMR data, was determined to be sipholenol A (**5**), and the sugar, L-rhamnose, was attached to C-19.

Another compound that was isolated from the northern sponge, with a polarity similar to siphalones **1**−**4**, was siphonellinol B (**15**) (Chart 1). This compound analyzed for $C_{30}H_{52}O_5$ from its CIMS *m/z* 493 [M^+H] and NMR data. The left ring system was found, from the NMR data (Experimental Section), to be identical to the left part of sipholenol A (**5**) and to the corresponding left part of siphonellinol A.[3] The right substituted cyclohexane system of **15** was identical to the corresponding part in siphonellinol A;[3] however, the attached six-carbon chain was different. Instead of the isopropylidene end of siphonellinol A,[3] compound **15** carries a $-CH_2CH(OH)C(CH_3)=CH_2$ end group (δ 4.01 (br t, J = 8.2, H-22), 4.85 (br s) and 4.93 (br s) (2H-24), and 1.71 (s, Me-25)). The latter NMR data are in good agreement with the data of a similar chain in the *Xenia* metabolite xeniaphyllenol.[14]

Neviotine B (**16**) was another triterpene isolated from the northern sponge in minute amounts (0.005%, dry weight). Like neviotine A,[4] **16** also contains seven methyl groups (rather than eight in the sipholanes), and it possesses the same formula, $C_{30}H_{50}O_6$ (*m/z* 507 [M^+H]). Comparison of the NMR data of **16** with those of neviotine A[4] established the same tricyclic half of the molecule. Changes, however, were observed in the second half of the molecule. The MS and IR spectra of **16** are essentially identical to those of neviotine A.[4] Furthermore, CH-correlations of **16** suggested the same hydrindane system as in neviotine A. The almost identical carbon chemical shifts of the five-membered ring of neviotine B and A suggested for **16** a cis ring junction. Hence, the difference between the neviotines, A and B, is most likely due to the

Scheme 3. Biogenesis of the Various Triterpenoids



stereochemistry of C-15. Indeed, the largest changes in chemical shifts were observed for Me-27 and C-15−17 and C-23, surrounding C-15. Tentatively, **16** is suggested to be the 15-epimer of neviotine A (Chart 1).

The last compound that was isolated in minute amounts (0.003%, dry weight) from the northern sponge, collected near Dahab, was designated dahabinone A (**17**). Compound **17** analyzed for $C_{30}H_{50}O_5$ from the EIMS *m/z* 472 [$M^+ - H_2O$] and NMR data (Experimental Section). From the ^{13}C NMR data, it was clear that **17** contains the same left part as sipholenone A (**6**)[2] and that the right half is without precedent. Noticeable in the resonances of the left part was the chemical shift of C-11 (δ 62.1 against 55.2 in sipholenone A (**6**)[2]), a shift that could originate from a neighboring 12(13)-unsaturation in the ethylene bridge. The latter functionality was established by a COSY experiment which combined H-11 to H-13 (δ 1.81 (d, J = 10, H-11); 5.84 (dd, J = 10, 15.6, H-12); 5.64 (d, J = 15.6, H-13)). Of the six degrees of unsaturation of dahabinone A, four were accounted for by the perhydrobenzoxepine system and the bridge double bond; compound **17**'s right part therefore has to be bicyclic. According to the NMR data (experimental), the right half of **17** contains four methyls, three singlets, and one doublet and an ethereal bridge between C-14 (δ 92.3 s) and C-19 (δ 73.8 s). Furthermore, the low field of C-14 suggested a hemiketal carbon atom. Compound **17** changes rapidly under mildly acidic conditions (e.g., acidic $CDCl_3$) to afford an $\alpha\beta$-unsaturated ketone, >C(11)HCH=CHCOCH(CH_3)C(16)H_2− (δ 1.92 (d, J = 10.5, H-11), 6.87 (dd, J = 10.5, 15.6, H-12), 6.33 (d, J = 15.6, H-13), 2.74 (ddq, J = 3.5, 9.4, 7.0, H-15), 1.13 (d, J = 7.0, Me-28) and 1.50 and 1.65 (m, 2H-16); δ_C 61.7 d, 142.4 d, 133.6 d, 202.9 s, 45.4 d, 31.6 C-11−16)).[14] The latter transformation established the C-14 position of the hemiketal, adjacent to the double bond. Characteristic for the suggested structure, of **17**, was also the proton signal of H-18 (δ 2.47 d, J = 5.1), which correlated with three methyl groups (29−31). Being a doublet (coupled with H-17 alone) confirmed the bridge head position of H-18 but could not determine the stereochemistry of the ring junction, as in both the cis and trans configurations, a conformation with a ca. 90° dihedral angle between H-18 and H-17 is possible. One of the methyl groups adjacent to C-18, CH_3-29, according to its chemical shift (δ_H 1.23 s), has to be on C-19 (73.8 s) carrying an oxygen. All the above data and taking into consideration the isoprene rule suggested the oxa-6,7-bicyclic structure of the right part of **17**. The small amount of **17** available and its instability prevented assignment of the right half stereochemistry.

All *S. siphonella* triterpenes are obtained, presumably, by two separate cyclizations from di- or triepoxysqualenes. In case of the sipholanes and neviotanes the cyclization seems to be initiated by the biologically well-known acid-catalyzed opening of the epoxy group, while in the case of the siphonellinoles and dahaboine A cyclization of the right part most likely starts from electrophilic protonation of a double bond (Scheme 3). The suggested biogenesis of the neviotanes seems to involve a more complex route including functionalization of one methyl group, which is later incorporated as a methylene in the hydrindane part. Secondary reactions, mainly oxidations, are responsible for the variety of the isolated triterpenoids.

Experimental Section

General Experimental Procedures. IR spectra were recorded on a Nicolet 205 FT-IR spectrophotometer. LRMS and HRMS were recorded on a Fisons, Autospec Q instrument. ^1H and ^{13}C NMR spectra were recorded on Bruker AMX-360 and ARX-500 spectrometers. All chemical shifts are reported with respect to TMS (δ_H = 0) and $CDCl_3$ (δ_C = 77.0). J values are given in Hz. Optical rotations were measured on a Perker-Elmer Model 141 polarimeter using a 1 cm microcell.

Animal Material. *Siphonochalina siphonella* (Levi, 1965) was collected once near Na'ama in the Gulf of Eilat[2] and a second time near Sarad island, Dahlak archipelago, Eritrea, in September 1995.

Isolation. Compounds **1**−**5**, **7**, and **15**−**17** were isolated from the northern sponge as described previously.[2] The various compounds together with the earlier described compounds[2] were first separated on Sephadex LH-20 and then by repeated chromatographies on Si gel, in amounts of 20−50 mg each (up to 0.0001%, dry wt). The order of the different compounds eminating from the Sephadex LH-20 column, eluted with $CHCl_3$−hexane (2:1), was **2**, **5**, **1**, **4**, **3**, **7**, **15**, **16**, and **17**. The

Eritrean sponge (70 g, dry wt) was extracted three times with EtOAc−MeOH (1:1) to afford, after evaporation, a brown gum (4 g). The latter gum was partitioned between aqueous MeOH and hexane, CCl_4, and $CHCl_3$ to give 1.0, 2.0, and 0.5 g, respectively, leaving 0.5 g in the aqueous phase. The hexane fraction yielded mainly sipholenol A (**5**, 300 mg). The CCl_4 fraction afforded, upon Sephadex LH-20 chromatography eluted with hexane−$CHCl_3$−MeOH (2:1:1) and further separations on VLC Si gel eluted with EtOAc−hexane, sipholenol A (**5**, 1 g), sipholenol F (**3**, 20 mg), sipholenol H (**4**, 8 mg), and sipholenone D (**2**, 8 mg). The $CHCl_3$ fraction afforded additional amounts of sipholenol H (80 mg), sipholenone D (**2**, 50 mg), and sipholenoside B (**8**, 55 mg).

Sipholenol G (1): amorphous powder, $[\alpha]_D$ −30° (*c* 0.05, $CHCl_3$); mp 173−175 °C; IR ($CHCl_3$) ν 3590, 3450, 2920, 2860, 1455, 1440, 1372, 1250 cm^{-1}; ^1H NMR δ 3.77 (d, J = 6.6, H-4), 3.52 (dd, J = 11.9, 3.8, H-7), 2.94 (t, J = 7.5, H-16), 1.01 (s, Me-24), 1.24 (s, Me-25), 1.13 (s, Me-26), 1.22 (s, Me-27), 1.38 (s, Me-28), 1.27 (s, Me-29), 1.04 (s, Me-30), 1.26 (s, Me-31); for ^{13}C NMR see Table 1; CIMS *m/z* (relative intensity) 493 [MH^+] (22), 475 [$MH^+ - H_2O$] (75), 457 [$MH^+ - H_2O$] (100).

Sipholenol D (2): glassy oil, $[\alpha]_D$ −35° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) ν 3450, 2990, 2970, 2870, 1725, 1460, 1390 cm^{-1}; ^1H NMR δ 3.17 (ddd, J = 13.0, 11.0, 2.5, H-3), 2.09 (ddd, J = 11.0, 6.4, 1.8, H-3′), 2.98 (dd, J = 11.4, 3.8, H-7), 2.27 (m, 2H-12), 5.28 (t, J = 7.0, H-13), 2.88 (m, H-15), 1.02 (s, Me-24), 1.31 (s, Me-25), 1.25 (s, Me-26), 1.21 (s, Me-27), 1.12 (d, J = 7.6, Me-28), 1.24 (s, Me-29), 0.88 (s, Me-30), 0.96 (s, Me-31); for ^{13}C NMR see Table 1; EIMS *m/z* 456 [$M^+ - H_2O$] (8), 438 [$M^+ - 2H_2O$] (24), 400 (50), 231 (70), 212 (100).

Sipholenol F (3): glassy oil; $[\alpha]_D$ −24° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) ν 3620, 3450, 2950, 1480, 1385, 1170, 1135, 1090, 915 cm^{-1}; ^1H NMR δ 1.47 and 1.56 (m, 2H-2), 1.71 and 1.98 (m, 2H-3), 3.81 (d, J = 6.7, H-4), 3.52 (dd, J = 4.4, 11.7, H-7), 1.39 and 1.79 (m, 2H-8), 1.51 and 1.63 (m, 2H-9), 0.94 (m, H-11), 1.52 and 1.57 (m, 2H-12), 1.35 and 1.88 (m, 2H-13), 2.08 (m, H-14), 1.06 and 1.75 (m, 2H-16), 1.31 and 1.72 (m, 2H-17), 2.46 (m, H-18), 5.25 (brs, H-20), 1.70 and 1.82 (m, 2H-21), 1.90 (m, H-22), 1.00 (s, Me-24), 1.27 (s, Me-25), 1.13 (s, Me-26), 1.16 (s, Me-27), 1.17 (s, Me-28), 1.73 (s, Me-29), 0.90 (s, Me-30), 1.09 (s, Me-31); for ^{13}C NMR see Table 1; EIMS *m/z* 476 [M^+] (1), 459 (1), 458 (5), 440 (6), 256 (12), 234 (52), 216 (20), 205 (6), 180 (15), 165 (15), 157 (33), 149 (19), 129 (26), 25 (100); HREIMS *m/z* 476.3871 (calcd for $C_{30}H_{52}O_4$ 476.3868).

Sipholenol H (4): glassy oil; $[\alpha]_D$ −42° (*c* 0.1, $CHCl_3$); IR ν ($CHCl_3$) 3630, 3425, 2959, 1450, 1378, 1240 cm^{-1}; ^1H NMR δ 3.75 (d, J = 6.7, H-4), 3.57 (dd, J = 4.8, 12.0, H-7), 0.91 (br d, H-11), 2.06 (dt, J = 6, 12.0, H-13), 2.52 (dt, J = 8.4, 12.0, H-13′), 4.23 (br d, J = 5.7, H-16), 1.79 (ddd, J = 5.7, 13.5, 14.3, H-17), 1.71 (ddd, J = 4.2, 4.6, 14.3, H-18), 2.39 (br d, J = 4.6, H-22), 0.94 (s, Me-24), 1.25 (s, Me-25), 1.12 (s, Me-26), 1.20 (s, Me-27), 1.86 (s, Me-28), 1.23 (s, Me-29), 0.74 (s, Me-30), 1.00 (s, Me-31); CIMS *m/z* 493 [MH^+] (100), 475 (43), 457 (96), 439 (53), 249 (11), 235 (17); HREIMS 474.3716 (calcd for $C_{30}H_{52}O_5 - H_2O$ 474.3711).

Sipholenoside A (7): amorphous solid, $[\alpha]_D$ −18° (*c* 0.1, $CHCl_3$); IR ($CHCl_3$) ν 3450, 2990, 2940, 2865, 1735, 1455, 1380 cm^{-1}; ^1H NMR δ 3.17 (ddd, J = 13.3, 11.1, 2.2, H-3), 2.10 (ddd, J = 11.0, 6.3, 1.9, H-3′), 2.95 (dd, J = 11.9, 4.0, H-7), 5.18 (t, J = 6.7, H-13), 2.81 (m, H-15), 1.03 (s, Me-24), 1.29 (s, Me-25), 1.23 (s, Me-26), 1.21 (s, Me-27), 1.11 (d, J = 7.6, Me-28), 1.21 (s, Me-29), 0.84 (s, Me-30), 0.97 (s, Me-31), 4.97 (br d, J = 1.3, H-1′), 3.70 (br s, H-2′), 3.80 (dd, J = 9.4, 3.1, H-3′), 3.47 (t, J = 9.4, H-4′), 3.87 (dq, J = 9.4, 3.6, H-5′), 1.28 (d, J = 6.3, Me-6′); for ^{13}C NMR see Table 1; EIMS *m/z* 602 [$M^+ - H_2O$] (4), 456 [$M^+ - C_6H_{12}O_6$] (3), 438 [$M^+ - C_6H_{12}O_6 - H_2O$] (10).

Sipholenoside B (8): powder, mp 237° ($CHCl_3$−acetone); $[\alpha]_D$ −22° (*c* 0.5, $CHCl_3$); IR (KBr) ν 3450, 2960, 1255, 1050 cm^{-1}; ^1H NMR δ 1.45 and 1.60 (m, 2H-2), 1.75 and 1.85 (m, 2H-3), 3.85 (d, J = 6.7, H-4), 3.55 (dd, J = 11.9, 6.9, H-7), 1.30 and 1.73 (m, 2H-8), 1.50 and 1.62 (m, 2H-9), 0.86 (br s, H-11), 1.22 and 1.50 (m, 2H-12), 1.79 and 1.95 (m, 2H-13), 5.49 (br d, J = 4.8, H-16), 2.01 and 1.75 (m, 2H-17), 1.82 (m, H-18), 1.60 and 1.67 (m, 2H-20), 1.75 and 1.98 (m, 2H-21), 2.20 (m, H-22), 0.98 (s, Me-24), 1.25 (s, Me-25), 1.14 (s, Me-26), 1.07 (s, Me-27), 1.77 (s, Me-28), 1.24 (s, Me-29), 1.04 (s, Me-30), 1.10 (s, Me-31), 4.95 (br s, H-1′), 3.70 (br d, J = 3.4, H-2′), 3.84 (dd, J = 9.4, 3.4, H-3′), 3.40 (t, J = 9.4, H-4′), 3.85 (dq, J = 9.4, 6.3, H-5′), 1.26 (d, J = 6.3, Me-6′); for ^{13}C NMR see Table 1; EIMS *m/z* 622 [M^+] (2), 604 [$M^+ - H_2O$] (10), 458 [$M^+ - C_6H_{12}O_5$] (58), 440 [$M^+ - C_6H_{12}O_5 - H_2O$] (100).

Siphonellinol B (15): glassy oil, IR ($CHCl_3$) ν 3610, 3450, 2940, 1440, 1400, 1370, 1250, 1225, 1170, 1090 cm^{-1}; ^1H NMR δ 3.82 (d, J = 6.7, H-4), 3.53 (dd, J = 4.2, 11.7, H-7), 3.66 (dd, J = 3.7, 9.7, H-16), 4.01 (br t, J = 8.2, H-22), 4.85 and 4.93 (br s, 2H-24), 1.71 (br s, Me-25), 1.00 (s, Me-26), 1.13 (s, Me-27), 1.27 (s, Me-28), 1.24 (s, Me-29), 1.67 (s, Me-30), 1.06 (s, Me-31); ^{13}C NMR δ 41.9 (s, C-1), 33.5 (t, C-2), 24.3 (t, C-3), 75.7 (d, C-4), 77.0 (s, C-5), 75.5 (d, C-7), 25.7 (t, C-8), 38.3 (t, C-9), 71.2 (s, C-10), 54.9 (d, C-11), 25.6 (t, C-12), 29.6 (t, C-13), 134.6 (s, C-14), 127.7 (s, C-15), 70.4 (d, C-16), 25.7 (t, C-17), 31.3 (t, C-18), 42.0 (s, C-19), 31.4 (t, C-20), 27.7 (t, C-21), 74.9 (d, C-22), 146.1 (s, C-23), 110.2 (t, C-24), 16.7 (q, Me-25), 12.1 (q, Me-26), 28.0 (q, Me-27), 20.3 (q, Me-28), 29.8 (q, Me-29), 19.5 (q, Me-30), 20.6 (q, Me-31); CIMS *m/z* 493 [MH^+] (7), 475 (18), 457 (57), 439 (100), 421 (19); HREIMS 474.3715 ($M - H_2O$), (calcd for $C_{30}H_{50}O_4$ ($M - H_2O$) 474.3711).

Neviotine B (16): glassy oil, $[\alpha]_D$ −53° (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) ν 3590, 3390, 2925, 2915, 1750, 1460, 1450, 1378, 1240, 1140, 1085, 1040, 965, 910 cm^{-1}; ^1H NMR δ 4.14 (s, H-3), 5.08 (s, H-25), 4.97 (dd, J = 3.0, 12.5, H-7), 2.26 (dt, J = 5.0, 11.4, H-21), 1.32 (s, Me-24), 1.20 (s, Me-25), 0.68 (s, Me-26), 1.28 (s, Me-27), 0.91 (d, J = 6.5, Me-29), 0.89 (d, J = 6.5, Me-30), 1.25 (s, Me-31); ^{13}C NMR δ 76.3 (s, C-1), 84.1 (d, C-2), 213.4 (s, C-4), 75.4 (d, C-5), 44.3 (s, C-6), 68.9 (d, C-7), 26.6 (t, C-8), 36.6 (t, C-9), 43.5 (s, C-10), 55.0 (d, C-11), 23.4 (t, C-12), 23.6 (t, C-13), 61.1 (d, C-14), 75.4 (s, C-15), 31.4 (t, C-16), 26.6 (t, C-17), 54.1 (d, C-18), 88.1 (s, C-19), 36.3 (t, C-20), 35.9 (t, C-21), 41.8 (s, C-22), 45.0 (t, C-23), 22.2 (q, Me-24), 26.8 (q, Me-25), 14.6 (q, Me-26), 20.0 (q, Me-27), 33.9 (d, C-28), 17.3 (q, Me-29), 16.8 (q, Me-30), 33.0 (q, Me-31); CIMS *m/z* 507 [MH^+] (19), 489 (66), 473 (12), 471 (58), 457 (47), 439 (21), 407 (29), 389 (100), 371 (77), 102 (72); HREIMS 488.3499 [$M^+ - H_2O$] (calcd for $C_{30}H_{48}O_5$, 488.3503).

Dahabinone A (17): amorphous powder, IR ($CHCl_3$) ν 3400, 2870, 1700, 1460, 1440, 1370, 1170, 1125, 1070 cm^{-1}; ^1H NMR δ 1.15 and 1.68 (m, 2H-2), 3.10 (ddd, J = 13.4, 11.2, 2.2, H-3), 2.03 (m, H-3′), 2.98 (dd, J = 8.7, 6.9, H-7), 1.81 (d, J = 10.1, H-11), 5.84 (dd, J = 15.6, 10.1, H-12), 5.64 (d, J = 15.6, H-13), 2.02 (m, H-15), 2.47 (d, J = 5.1, H-18), 1.16 (s, Me-24), 1.32 (s, Me-25), 1.25 (s, Me-26), 1.20 (s, Me-27), 0.79 (d, J = 7.0, Me-28), 1.23 (s, Me-29), 1.09 (s, Me-30), 1.06 (s, Me-31); ^{13}C NMR δ 41.4 (s, C-1), 40.4 (t, C-2), 35.5 (t, C-3), 217.5 (s, C-4), 82.6 (s, C-5), 81.0 (d, C-7), 27.1 (t, C-8), 38.7 (t, C-9), 71.2 (s, C-10), 62.1 (d, C-11), 125.9 (d, C-12), 133.5 (d, C-13), 92.3 (s, C-14), 40.5 (d, C-15), 35.2 (t, C-16), 28.3 (t, C-17), 46.3 (d, C-18), 73.8 (s, C-19), 41.9 (t, C-20), 24.1 (t, C-21), 32.2 (t, C-22), 33.0 (s, C-23), 12.4 (q, Me-24), 20.6 (q, Me-25), 26.7 (q, Me-26), 28.8 (q, Me-27), 19.2 (q, Me-28), 24.6 (q, Me-29), 25.0 (q, Me-30), 34.2 (q, Me-31); EIMS *m/z* 472 [$M^+ - H_2O$] (14), 454 (8), 447 [$M^+ - C_3H_7$] (23), 370 [$M^+ - H_2O - C_4H_6O_2$] (4), 356 (2), 323 (6), 305 (60), 290 (100), 287 (18), 217 (15), 207 (29), 193 (27), 178 (41), 161 (20), 149 (53); HREIMS 472.3551 [$M^+ - H_2O$] (calcd for $C_{30}H_{48}O_4$, 472.3554).

Epoxidation of Sipholenol A (5) to Sipholenol G (2) and 9. *m*-Chloroperbenzoic acid (36 mg) in CH_2Cl_2 (3 mL) was added to a suspension of sipholenol A (**5**, 55 mg) and Na_2HPO_4 (78 mg) in CH_2Cl_2 (3 mL) at room temperature. After 4 h the solution was washed with aqueous Na_2CO_3 (×2) and then water. The organic phase was dried over $MgSO_4$ and evaporated to give a mixture of compounds **2** and **9** (57 mg), which was separated on a Si gel column eluted with CH_2Cl_2−EtOAc (4:1) to give first sipholenol G (15 mg) and then compound **9** (37 mg).

Compound 9: amorphous powder, mp 174−176°; IR ($CHCl_3$) ν 3575, 3455, 2920, 1445, 1435, 1370, 1250 cm^{-1}; ^1H NMR δ 0.91 (s, 3H), 1.02 (s, 3H), 1.03 (s, 3H), 1.13 (s, 3H), 1.19 (s, 3H), 1.26 (s, 3H), 1.38 (s, 3H), 2.77 (dd, J = 8.2, 4.8, 1H), 3.53 (dd, J = 11.8, 4.2, 1H), 3.78 (d, J = 6.6, 1H); ^{13}C NMR δ 82.6 s, 77.8 s, 76.9 d, 76.5 d, 71.9 s, 60.6 d, 60.6 s, 56.3 d, 52.8 d,

51.1 d, 48.6 d, 42.6 s, 38.9 t, 38.8 t, 34.2 t, 32.3 q, 31.4 q, 30.5 t, 30.2 s, 29.1 q, 27.9 t, 26.7 t, 25.7 t, 25.5 q, 25.5 q, 25.3 t, 24.0 t, 21.6 t, 21.3 q, 12.9 q; CIMS *m*/*z* 493 [M^+H] (53), 475 [$M^+H - H_2O$] (100), 457 [$M^+H - 2H_2O$] (84).

Oxidation of Sipholenol C (10) to Sipholenone D (2). Sipholenol C (**10**, 10 mg) was oxidized with Jones reagent (2 drops) to give, after work up, siphoplenone D (**2**, 5 mg).

Acidic Transformation of Sipholenol F (3) to Compounds 11 and 12. Sipholenol F (**3**, 10 mg) dissolved in $CHCl_3$ (3 mL) in the presence of pTsOH acid (1 mg) was kept at room temperature for 2 weeks. The $CHCl_3$ was then removed under vacuum and the residue applied to a Si gel column using an increasing percentage of EtOAc in hexane as eluent. The less polar compound **12** was eluted with 20% EtOAc and the more polar one, **11**, with 30% EtOAc in hexane (4 mg each). Compound **12** was identical in all respects to the compound obtained from sipholenol A.[2]

Compound 11: viscous gum; IR ($CHCl_3$) ν 3450, 2940, 1460, 1380, 1170, 1080 cm^{-1}; ^1H NMR δ 0.80 (s, 3H), 0.97 (s, 6H), 1.12 (s, 3H), 1.16 (s, 3H), 1.19 (s, 3H), 1.26 (s, 6H), 3.52 (dd, J = 11.9, 4.4, 1H), 3.80 (d, J = 6.6, 1H); EIMS *m*/*z* 476 [M^+] (1), 458 (14), 400 (3), 234 (39), 220 (12), 85 (100).

Oxidation of Sipholenol H (4) and Sipholenol E (13) to 4,6-Dione 14. Sipholenol H (**4**, 5 mg) or sipholenol E (**13**, 5 mg) was dissolved in Me_2CO (5 mL), and one drop of Jones reagent was added at 0 °C. After 15 min the excess oxidant was destroyed by a drop of MeOH. The solvent was removed under vacuum and the residue dissolved in $CHCl_3$ (5 mL). This solution was washed with water, aqueous $NaHCO_3$, and more water, and the solvent was removed under reduced pressure to afford **14** (3 mg) as a amorphous material: IR ($CHCl_3$) ν 3600, 3480, 2930, 1710, 1650, 1460, 1378 cm^{-1}; ^1H NMR δ 2.94 (dd, J = 4.1, 12.0, H-7), 2.20 (dt, J = 6.5, 12.0, H-13), 2.70 (dt, J = 6.5, 12.0, H-13′), 2.34 (br dd, J = 5.8, 18.5, H-17), 2.37 (dd, J = 12.0, 18.5, H-17′), 2.64 (br d, J = 4.9, H-22), 1.17 (s, Me-24), 1.32 (s, Me-25), 1.27 (s, Me-26), 1.18 (s, Me-27), 1.88 (s, Me-28), 1.24 (s, Me-29), 0.74 (s, Me-30), 0.97 (s, Me-31); CIMS *m*/*z* 489 [M^+H] (19), 471 [$M^+H - H_2O$] (100), 453 [$M^+H - 2H_2O$] (24).

Hydrolysis of Sipholenol I (6) to Sipholenol H (14). Sipholenol I (**6**, 5 mg), in pyridine−dioxane (5 mL), was refluxed for 18 h. The reaction mixture was then evaporated under vacuum. The residue afforded, after removing the solvent, sipholenol H (3 mg).

Hydrolysis of Sipholenoside A (7) to Sipholenone D (2). Sipholenoside A (**7**, 15 mg) in MeOH (5 mL) was refluxed with 5% HCl (5 mL) for 6 h. The reaction mixture was then neutralized with aqueous $NaHCO_3$ and the solvent evaporated under vacuum. The residue was dissolved in $CHCl_3$ (10 mL) and then washed with H_2O (2 × 5 mL) to afford sipholenol D (**2**) in the organic phase and l-rhamnose (3 mg)[11] in the aqueous phase. The sugar was purified by chromatography on Sephadex LH-20 eluted with MeOH.

α-L-Rhamnose: white solid, $[\alpha]_D$ −8.5 (*c* 0.05, H_2O); ^1H NMR (pyridine-d_5) δ 5.12, 3.92, 3.81, 3.45, 3.86 and 1.28 (3H) (H-1−H-6); ^{13}C NMR (pyridine-d_5) 95.1 (d, C-1), 74.2 (d, C-2), 73.1 (d, C-3), 74.4 (d, C-4), 69.8 (d, C-5), 18.7 (q, CH_3-6).[11]

Hydrolysis of Sipholenoside B (8) to Sipholenol A (5). Sipholenoside B (**8**, 15 mg) was hydrolyzed in the same manner as described for **7** to afford sipholenol A (**5**) and α-L-rhamnose.

References and Notes

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