Ten New Rearranged Spongian Diterpenes from Two *Dysidea* Species

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Ten new rearranged spongian-type diterpenes have been isolated from two Red Sea *Dysidea* sponges. All new compounds embody either a perhydroazulene or a $\Delta^{5(10)}$-octalin system as the carbobicyclic portion and contain one of four heterocycles, that is, a disubstituted dihydrofuran, a trisubstituted γ-lactol, a trisubstituted δ-lactone, or a 2,7-dioxabicyclo[3.2.1]octane. Structures of all compounds were elucidated from spectral data, mainly by 1D and 2D NMR techniques, by mass spectra, and by comparison with other related known diterpenes. Four of the new compounds, shahamines B–E (**4–7**), were chemically correlated with the known aplyviolacene (macfarlandin E). CH_4 versus NH_3 CI mass spectra, performed on several of the new compounds, are discussed.

Several rearranged spongian diterpenoids have been reported from dorid nudibranchs of the genus *Chromodoris*.[1-3] These shell-less marine molluscs are believed to have acquired the spongian-related compounds from sponges on which they feed, and, indeed, such diterpenoids have also been isolated from sponges.[4-5] Macfarlandin E (aplyviolacene)[6] (**1**) is a representative of such a diterpene, which is found both in nudibranchs and sponges.[3,6] We report herein isolation of 10 new rearranged spongianes from two different sponges of the genus *Dysidea*; *Dysidea* sp. (1) and *Dysidea* sp. (2).

The extracts of *Dysidea* sp. (1) collected near Shaab Mahamud in the Red Sea at a depth of 15m contained a mixture of six rearranged spongian metabolites: macfarlandin E (**1**, 0.4% dry wt), shahamin[7] A (**3**, 0.12%), shahamin B (**4**, 0.007%), shahamin C (**5**, 0.015%), shahamin D (**6**, 0.007%), and shahamin E (**7**, 0.035). A second specimen of the sponge contained compounds **1** (0.4%), **3** (0.07%), **5** (0.15%), shahamin F (**9**, 0.1%), and shahamin G (**10**, 0.05%).

Dysidea sp. (2) collected in the same habitat as sp. (1) afforded a mixture of four compounds: shahamin F (**9**, 0.15%), shahamin H (**11**, 0.02%), shahamin I (**12**, 0.12%) and shahamin J (**13**, 0.01%).

Compound **1**, the major constituent of both samples of *Dysidea* sp. (1), $C_{24}H_{34}O_7$, was identified on the basis of its spectral data (IR, $[\alpha]_D$, ^1H NMR) as macfarlandin E,[3] which is identical with aplyviolacene.[6] The structure of the latter compound was determined as the result of an X-ray analysis of its 12-desacetoxy counterpart, aplyviolene (**2**).[6] On the basis of COSY 45 and ^1J H–C correlation experiments, several of the ^{13}C NMR lines (carbons no. 1–3, 8, 13) of **1** were reassigned (Table III).[3]

The ^{13}C NMR data for the nonfunctionalized carbons of shahamin A (**3**), $C_{23}H_{34}O_5$, were nearly identical with those of **1**, and hence a perhydroazulene system was also inferred for **3**. This was also in full agreement with the *m/e* 191, 177, 165, 150, 135, 121 series of peaks in the EI mass spectrum. The same series of peaks were also observed for compounds **4–7**. The functionalized moiety of **3**, however, differed considerably; the oxygenated bicyclic system of **1** and **2** was replaced by a disubstituted dihydrofuran.

The IR, mass, and NMR spectra of **3** revealed the presence of a methyl ester, an acetate, and a cyclic enol ether (C-13 to C-16, Tables I and III).[8] The suggested dihydrofuran moiety was unequivocally confirmed by a COSY 45 and a H–C correlation experiments. The former experiment correlated H-12 with H-13, H-16α and H-16β, and H-15 with H-13 and H-16α (H-16α was distinguished from H-16β by a nuclear Overhauser enhancement observed between H-16α and H-13α, see Table IV). A 3.6-Hz coupling constant between H-12 and H-13 and an NOE enhancement between these two protons (Table IV) point to restricted rotation around the C-12, C-13 bond. As shown below, shahamins B–E (**4–7**) were chemically correlated with macfarlandin E (aplyviolacene), **1**. On the basis of the hypothesis that all five compounds, **3–7**, are formed from a common biosynthetic precursor (Scheme I, m), we suggest for shahamin A the stereochemistry shown in Figure 1. This tentative stereochemistry is also in agreement with the measured NOE's (Table IV). Nuclear Overhauser enhancements confirm, on the one hand, the configurations of the perhydroazulene portion (the stereochemistry of C-4, 5, 8, and 9; the cis junction also being confirmed by the 7.9-Hz coupling constant[6] between H-5 and H-9) and, on the other hand, also the relationship between the two portions of the molecule (correlations between H-13 and -15, H-9 and -17, and H-7 and -9 respectively, Table IV). The NOE's assisted also with the proton signal assignments, e.g. H-2α,3α,7α, etc.

The structure of **3** is in full agreement with the cleavage of the C-13 side chain in the mass spectrum (EI, *m/e* 259, $M^+ - C_5H_7O_4$) as well as the easy abstraction of, most likely, H-12 (CH_4 CI, *m/z* 390, $MH^+ - 1$, 100%) due to the stable derived cation.

Cleavage of the O-11 to C-15 bond (in **1**) readily illustrates the relationship between compounds **3** and **1** (see Scheme I). Absence of MeOH during the extractions with nonpolar solvents (petroleum ether and chloroform, see the Experimental Section) of the sponge excludes the possibility of **3** being an artifact.

Comparison of the ^1H NMR data for the C-1 to C-10 portion of shahamin B (**4**), $C_{21}H_{34}O_5$, with those of **1** and **3** (Table I) and the *m/e* 191 fragment in the EI and CI mass spectrum indicated the presence of the same perhydroazulene system. The functionalities for **4** were found to be a carbomethoxyl, a hydroxyl and a γ-lactol; the two OH groups were lost readily in the mass spectrum (CI CH_4, *m/z* 331, $MH^+ - 2H_2O$, 35%) and could be acetylated to

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(1) Hochlowski, J. E.; Faulkner, D. J.; Matsumoto, G. K.; Clardy, J. *J. Org. Chem.* **1983**, *48*, 1141.
(2) Molinski, T. F.; Faulkner, D. J. *J. Org. Chem.* **1986**, *51*, 2601.
(3) Molinski, T. F.; Faulkner, D. J.; Cun-Leng, H.; Van Duyne, G. D.; Clardy, J. *J. Org. Chem.* **1986**, *51*, 4564.
(4) Karuso, P.; Skelton, B. W.; Taylor, W. C.; White, A. H. *Aust. J. Chem.* **1984**, *37*, 1081.
(5) Sullivan, B.; Faulkner, D. J. *J. Org. Chem.* **1984**, *49*, 3204.
(6) Hambley, T. W.; Poiner, A.; Taylor, W. C. *Tetrahedron Lett.* **1986**, *27*, 3281.
(7) Shaham in Hebrew means black-brown, the color of the sponges.
(8) The numbering system employed for **3** and all the other new compounds throughout this report (Figures 1 and 2), as with **1**, implies that compounds **3–7** and **9–13** are rearranged spongian diterpenes.

0022-3263/88/1953-4801$01.50/0

Table I. Proton NMR Data of Compounds 1 and 3–7[a]

H	δ (mult, J in Hz)					
	1	3	4	5	6	7
1α	2.42 (br dd)	2.35 (br dd)	2.36 (br dd)	2.39 (br dd)	2.39 (br dd)	2.37 (br dd)
1β	1.87 (ddt)	1.77 (ddt)	1.85 (ddt)	1.82 (ddt)	1.85 (ddt)	1.80 (br t, 12.7)
2α	1.42 (ddq)	1.39 (ddq)	1.35 (ddq)	1.41 (ddq)	1.45 (ddq)	1.38 (ddq)
2β	1.76 (dm)	1.78 (dm)	1.78 (m)	1.78 (dm)	1.77 (m)	1.77 (m)
3α	1.31 (m)	1.25 (dm)	1.26 (m)	1.24 (dm)	1.30 (dm)	1.28 (m)
3β	1.62 (m)	1.69 (dt)	1.66 (dt)	1.61 (dt)	1.63 (dt)	1.65 (dt)
5α	1.92 (dt, 10.0, 9.0)	2.13 (dt, 10.0, 7.9)	1.90 (dt, 10.0, 8.8)	1.93 (dt, 10.0, 8.8)	1.90 (dt, 10.0, 8.0)	1.93 (dt, 10.0, 8.8)
6α	1.77 (m)	1.79 (m)	1.78 (m)	1.74 (m)	1.73 (m)	1.74 (m)
6β	1.77 (m)	1.79 (m)	1.78 (m)	1.78 (m)	1.77 (m)	1.75 (m)
7α	1.95 (m)	1.93 (ddd)	1.90 (m)	1.75 (m)	1.77 (m)	1.75 (m)
7β	1.62 (m)	1.62 (ddd)	1.60 (m)	1.53 (br dd)	1.50 (m)	1.50 (m)
9α	2.75 (d, 9.0)	2.64 (d, 7.9)	1.58 (d, 8.8)	2.78 (d, 8.8)	2.75 (d, 8.8)	2.77 (d, 8.8)
12β	5.80 (d, 5.0)	5.11 (d, 3.6)	4.69 (d, 7.0)	5.44 (d, 7.2)	4.39 (d, 7.2)	4.52 (d, 7.4)
13	2.87 (ddd, 5.0, 3.8, 0.8)	3.20 (dddd, 9.0, 3.6, 2.0, 1.0)	2.55 (ddt, 7.0, 4.9, 3.3)	2.68 (dddd, 7.2. 4,1, 3.9, 2.9)	2.68 (dddd, 7.2, 6.7, 3.5, 2.5)	2.64 (dddd, 7.4, 6.9, 4.0, 2.7)
14	2.67 (dd, 3.8, 2.5)		2.08 (d, 3.3)	2.30 (ddd, 12.3, 6.9, 3.9)	2.28 (ddd, 12.4, 6.7, 3.9)	2.01 (ddd, 12.3, 6.6, 4.0)
15α	5.73 (d, 2.5, 0.8)	6.27 (d, 1.0)		4.39 (dd, 12.1, 6.9)	4.37 (dd, 12.1, 3.9)	4.36 (dd, 11.8, 6.6)
15β			5.41 (br s)	4.27 (dd, 12.3, 12.1)	4.19 (dd, 12.4, 12.1)	4.19 (dd, 12.3, 11.8)
16α		4.18 (dd, 9.5, 9.0)	3.82 (dd, 10.4, 4.9)	4.16 (dd, 11.3, 2.9)	4.05 (dd, 11.1, 2.5)	3.81 (dd, 11.3, 2.7)
16β	6.49 (br s)	4.63 (dd, 9.5, 2.0)	3.95 (dd, 10.4, 3.3)	4.32 (dd, 11.3, 4.1)	4.48 (dd, 11.1, 3.5)	3.61 (dd, 11.3, 6.9)
17-Me	1.09 (s)	1.09 (s)	0.96 (s)	1.01 (s)	1.06 (s)	0.97 (s)
18-Me	0.96 (s)	0.90 (s)	0.87 (s)	0.96 (s)	0.96 (s)	0.95 (s)
19-Me	0.99 (s)	0.97 (s)	0.93 (s)	0.88 (s)	0.98 (s)	0.99 (s)
20Z	4.68 (d, 1.8)	4.62 (d, 2.3)	4.62 (d, 2.4)	4.62 (d, 1.9)	4.60 (d, 0.9)	4.67 (d, 0.9)
20E	4.88 (d, 2.0)	4.84 (d, 2.5)	4.82 (d, 2.0)	4.88 (d, 1.9)	4.88 (d, 1.9)	4.88 (d, 1.9)
12-OAc	2.22 (s)	2.15 (s)		2.22 (s)		
16-OAc	2.11 (s)			2.07 (s)	2.01 (s)	
11-OMe		3.73 (s)	3.80 (s)			

[a] 360 MHz, $CDCl_3$, assignment from COSY 45 experiments and J values from 1D spectra.

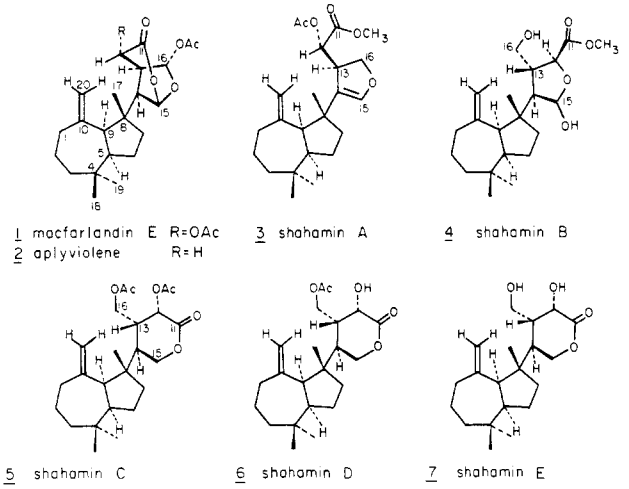


Figure 1. Structures of compounds 1–7.

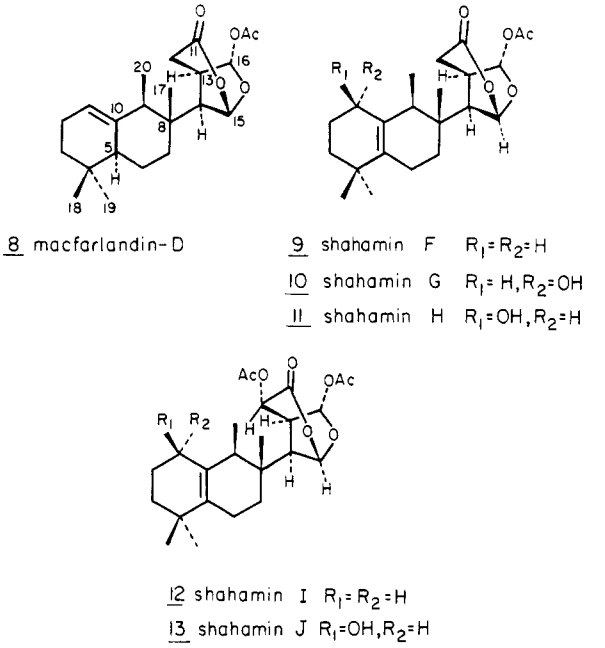


Figure 2. Structures of compounds 8–13.

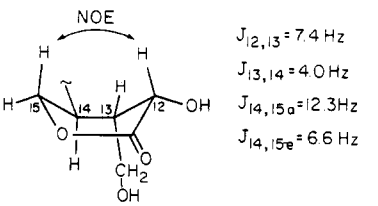


Figure 3. Conformation of the δ-lactone of shahamin E (7).

give **4a** (see the Experimental Section). A COSY 45 experiment and the mass spectrum fragmentations (see the Experimental Section) confirmed the existence of a trisubstituted γ-lactol (C-11 to C-16). Coupling constants of 7.0 Hz between H-12 and H-13, 3.3 Hz between H-13 and H-14, and 1.0 Hz between H-14 and H-15 agree with dihedral angles of ca. 160°, 120°, and 80°, respectively, between the corresponding protons. A 60° angle in the alternative 20°, 60°, and 100° set is geometrically impossible. The skeleton of **4** is the same as that of **1** and **3**: As in **3** the 11-carboxylic acid is also esterified; however, in **4** the 15-aldehyde moiety closes a γ-lactol to C-12. (Scheme I). The configurations of all the chiral centers, except that at C-15, were unequivocally established by sodium bis(2-methoxyethoxy)aluminium hydride (Red-Al, Aldrich) in toluene reduction of compound **4** to furnish after acetylation the same tetraacetate **14**, obtained from compound **1** under the same reduction conditions (Figure 4). The stereochemistry of C-15 remains ambiguous.

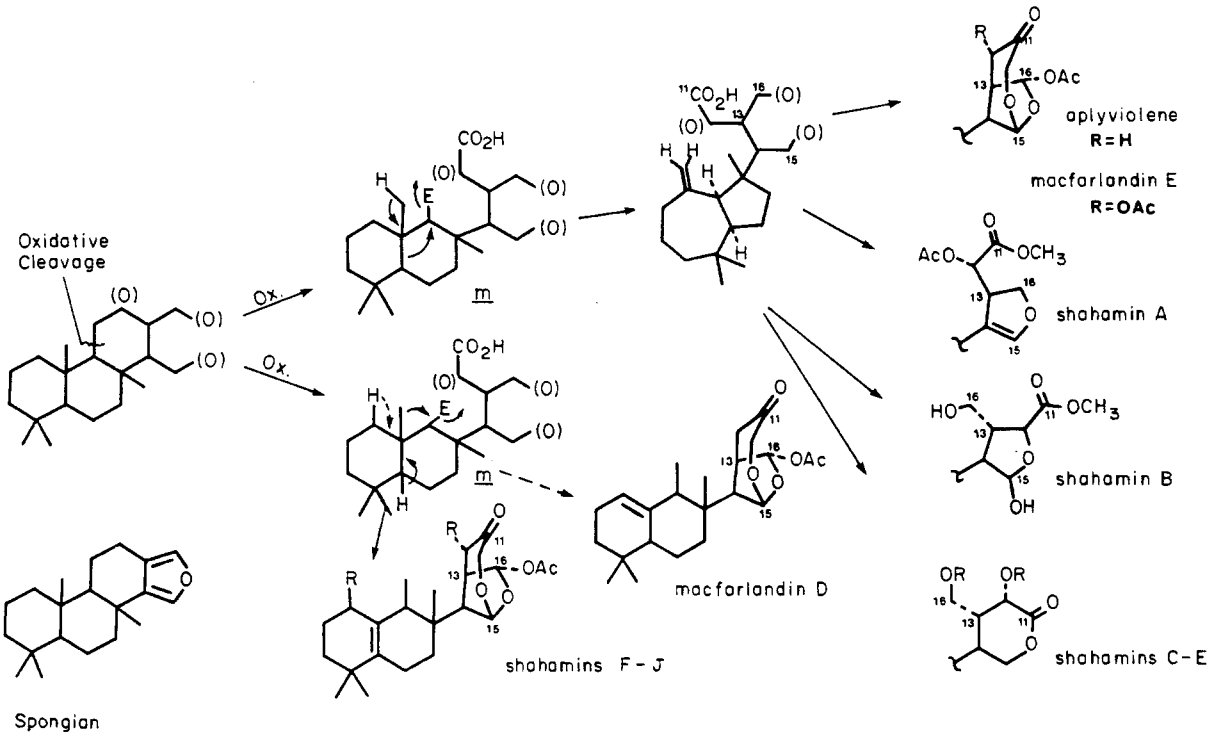
Shahamins C–E (compounds **5**, $C_{24}H_{36}O_6$; **6**, $C_{22}H_{34}O_5$; and **7**, $C_{20}H_{32}O_4$), are closely related. All three contain

Table II. Proton NMR Data of Compounds 9–13[a]

H	δ (mult, J in Hz)				
	9	10	11	12	13
1α	1.98 (m)		4.21 (br s)	2.01 (m)	4.22 (br s)
1β	2.02 (m)	3.25 (t, 9.0)	7.97 (br s)[b]	2.08 (m)	8.09 (br s)[b]
2α	1.57 (m)	1.79 (dddd, 9.0, 6.4, 15.1, 3.9)	1.66 (tt, 14.0, 3.0)	1.63 (m)	1.54 (tt, 14.0, 3.0)
2β	1.62 (m)	2.15 (ddd, 15.1, 9.0, 5.9)	2.20 (dq, 14.0, 3.0)	1.58 (m)	2.18 (dq, 14.0, 3.0)
3α	1.38 (ddd, 3.7, 7.8, 11.9)	1.50 (dd, 18.3, 6.4)	1.37 (dq, 12.8, 3.1)	1.38 (ddd, 3.5, 8.0, 12.0)	1.33 (dq, 12.8, 3.1)
3β	1.46 (ddd, 3.9, 7.5, 11.9)	1.78 (ddd, 18.3, 6.4, 5.9)	1.80 (ddd, 2.5, 12.8, 14.0)	1.42 (ddd, 4.3, 7.2, 12.0)	1.80 (ddd, 2.5, 12.8, 14.0)
6α	1.67 (m)	1.84 (m)	2.06 (m)	1.69 (m)	2.06 (m)
6β	2.16 (m)	2.03 (m)	2.22 (m)	2.16 (m)	2.19 (m)
7α	1.57 (m)	1.71 (m)	1.68 (m)	1.55 (m)	1.65 (m)
7β	1.62 (m)	1.77 (m)	1.74 (m)	1.65 (m)	1.76 (m)
9α	1.77 (br q, 6.9)	2.74 (q, 7.2)	2.08 (dq, 1.0, 7.0)	1.85 (br q, 6.8)	2.24 (dq, 1.0, 6.9)
12α	2.66 (br d, 19.7)	3.73 (br d, 19.7)	2.69 (br d, 19.7)		
12β	2.97 (dd, 19.7, 5.9)	3.01 (dd, 19.7, 5.9)	3.01 (dd, 19.7, 5.7)	5.86 (d, 5.2)	5.87 (d, 5.3)
13	2.47 (ddd, 5.9, 3.7, 1.0)	2.55 (ddd, 5.9, 3.9, 1.3)	2.48 (ddd, 5.7, 3.0, 1.0)	2.67 (ddd, 5.2, 4.0, 1.1)	2.68 (ddd, 5.3, 3.0, 1.0)
14	2.68 (dd, 3.7, 2.8)	2.79 (dd, 3.9, 2.5)	2.56 (dd, 3.0, 2.7)	2.89 (dd, 4.0, 2.5)	2.72 (dd, 3.0, 2.6)
15α	5.62 (dd, 2.8, 1.0)	5.74 (dd, 2.5, 1.3)	5.68 (dd, 2.7, 1.0)	5.66 (dd, 2.5, 1.1)	5.67 (dd, 2.6, 1.0)
16β	6.04 (s)	6.17 (s)	6.14 (s)	6.45 (s)	6.47 (s)
17-Me	0.98 (s)	0.99 (s)	1.03 (s)	1.03 (s)	1.07 (s)
18-Me	0.96 (s)	0.96 (s)	1.02 (s)	0.98 (s)	1.02 (s)
19-Me	0.97 (s)	1.06 (s)	1.03 (s)	0.99 (s)	1.03 (s)
20-Me	0.94 (d, 6.9)	1.24 (d, 7.2)	1.10 (d, 7.0)	0.98 (d, 6.8)	1.09 (d, 6.9)
12-Ac				2.20 (s)	2.23 (s)
16-OAc	2.04 (s)	2.07 (s)	2.07 (s)	2.04 (s)	2.07 (s)

[a] 360 MHz, $CDCl_3$, assignment from COSY 45 experiments and J values from 1D spectra. [b] OH.

Scheme I. Suggested Biogenesis of Shahamins A–J



δ-lactones attached to the perhydroazulene portion indicated by the *m/e* 191 fragment (Experimental Section) and by the NMR data (Tables I and III).

Shahamin C (**5**) showed no hydroxyl absorption in its IR spectrum but did exhibit IR and ^1H and ^{13}C NMR signals (see Tables I and III), which suggested the presence of the δ-lactone (1746 cm^{-1}) (CH_4 CI, *m/z* 405, $MC_2H_5^+ - CO_2$, 4%) and two acetate groups (*m/z* 301, $MH^+ - 2HOAc$, 100%). A COSY 45 experiment and the mass spectrum confirmed the substitution pattern of the δ-lactone of **5** as shown in Figure 1.

Shahamins D and E (**6** and **7**, respectively) were suggested on the basis of the mass spectra (Experimental

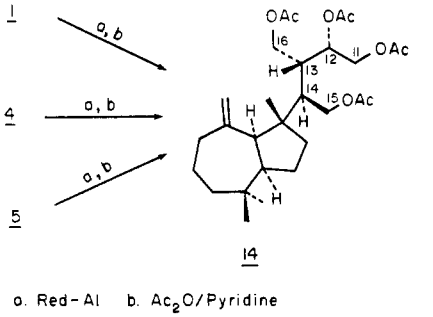


Figure 4. Correlation of compounds **4** and **5** with **1** by reduction and acetylation.

Table III. ^{13}C NMR Chemical Shifts of Compounds 1, 3, 5, 7, 9, and 12[a]

C no.	1[b]	3[b]	5[c]	7[c]	9[b]	12[b]
1	37.5 (t)	36.6 (t)	37.2 (t)[d]	37.2 (t)[d]	20.9 (t)	20.9 (t)
2	28.3 (t)	28.9 (t)	28.8 (t)	28.9 (t)	19.5 (t)	19.5 (t)
3	38.0 (t)	37.7 (t)	37.7 (t)[d]	37.7 (t)[d]	40.0 (t)	40.0 (t)
4	45.4 (s)	46.4 (s)	48.2 (s)	48.4 (s)	33.5 (s)	33.5 (s)
5	54.2 (d)	51.9 (d)	54.8 (d)[e]	54.8 (d)[e]	133.3 (s)	133.2 (s)
6	26.9 (t)	25.3 (t)	26.1 (t)	26.1 (t)	30.9 (t)	30.9 (t)
7	38.4 (t)	38.7 (t)	37.8 (t)[d]	37.9 (t)[d]	30.3 (t)	30.3 (t)
8	36.1 (s)	36.1 (s)	36.2 (s)	36.3 (s)	33.9 (s)	33.7 (s)
9	57.7 (d)	57.7 (d)	54.7 (d)[e]	54.7 (d)[e]	42.8 (d)	42.7 (d)
10	152.5 (s)	152.9 (s)	153.8 (s)	153.7 (s)	130.7 (s)	130.8 (s)
11	165.8 (s)	168.9 (s)	169.1 (s)	165.8 (s)	170.7 (s)	165.9 (s)
12	66.3 (d)	72.3 (d)	66.8 (d)	68.4 (d)	33.3 (t)	66.4 (d)
13	44.4 (d)	45.6 (d)	45.4 (d)	45.0 (d)	37.5 (d)	43.8 (d)
14	51.8 (d)	122.7 (s)	36.3 (d)	39.8 (d)	43.1 (d)	46.1 (d)
15	101.2 (d)	143.8 (d)	66.0 (t)[f]	66.4 (t)[f]	100.7 (d)	101.2 (d)
16	96.2 (d)	72.5 (t)	64.3 (t)[f]	65.3 (t)[f]	101.2 (d)	96.1 (d)
17	24.5 (q)	26.8 (q)	20.8 (q)	21.3 (q)	14.9 (q)	15.0 (q)
18	34.2 (q)	33.9 (q)	34.5 (q)	34.5 (q)	27.9 (q)	27.9 (q)
19	25.9 (q)	26.1 (q)	25.6 (q)	25.6 (q)	28.2 (q)	28.1 (q)
20	115.2 (t)	114.7 (t)	115.3 (t)	115.5 (t)	22.1 (q)	22.8 (q)
CO-Ac	169.3 (s)	169.3 (s)	169.6 (s)		169.4 (s)	169.4 (s)
CO-Ac	169.3 (s)		170.8 (s)			169.4 (s)
CH_3-Ac	21.0 (q)	20.7 (q)	20.7 (q)		20.9 (q)	20.8 (q)
CH_3-Ac	20.5 (q)		20.6 (q)			20.4 (q)
OCH_3		52.0 (q)				

[a] 90.53 MHz, $CDCl_3$. [b] Assignment from H–C correlation experiment. [c] Broad-band decoupling and DEPT experiments, tentative assignment. [d–f] These signals may be interchanged.

Table IV. Nuclear Overhauser Enhancement Data

irradiated signal	enhanced signals				
	1	3	7	9	12
H-1α		H-2α, H-20E			
H-3α					Me-18 (5)
H-3β					Me-18 (5)
H-5α		H-9	H-9, Me-19		
H-9α	H-5, H-12, H-15, H-20Z	H-5, H-12, H-13, H-15, H-20Z, Me-19	H-5, H-20Z, Me-19	H-12β, H-14, Me-20	H-12β (4), H-13 (5), H-14 (1), H-15 (1)
H-12α				H-12β, H-16	
H-12β		H-13, Me-17	H-13, H-15, Me-17	H-12α, H-13, H-14	H-9 (1), H-13 (2), Me-20 (1)
H-13		H-9, H-12, H-16, Me-17	H-12, H-20Z, Me-17	H-9, H-14, H-16	H-9 (5), H-12 (5), H-14 (7), H-16 (5)
H-14				H-9, H-12β, H-13, H-15, Me-20	H-9 (1), H-12β (1), H-13 (5), H-15 (6)
H-15α		H-7α, H-9, Me-17	H-7α, H-9, H-14, H-15β, Me-17	H-14	H-14 (3)
H-15β			H-12, H-15α		
H-16α		H-16β	H-14, H-16β		
H-16β	H-13	H-13, H-16α	H-9, H-13	H-12α, H-13	H-13 (1)
Me-17	H-12, H-13, H-14	H-7β, H-12, H-13, H-15, H-20Z	H-7β, H-13, H-15, H-20Z	H-9, H-14	H-9 (12), H-14 (5)
Me-18		H-3β, H-5	H-3β, H-5	H-2α, H-2β	H-2α (10), H-2β (10)
Me-19	H-9	H-2α, H-5, H-9	H-2α, H-5, H-9	H-2α, H-2β	H-2α (10), H-2β (10)
Me-20				H-12	H-12 (11)
H-20E	H-1α, H-20Z	H-1α, H-20Z	H-1α, H-20Z		
H-20Z	H-9, H-12, H-20E	H-9, H-20E, Me-17, Me-19	H-9, H-20E, Me-19		

Section) and their NMR data (Tables I and III), including a COSY experiment to be the corresponding 16-monoacetate and the corresponding diol of **5** (Figure 1). Indeed, overnight acetylation (Ac_2O/pyridine, room temperature) of both furnished compound **5**. All three compounds (**5–7**) possess the same skeleton as compounds (**1–4**). This was confirmed by Red-Al reduction of **5**, followed by acetylation to afford the same tetraacetate **14** furnished also by compounds **1** and **4**, (vide supra, Figure 4). The coupling constants of the lactone moiety in compounds **5–7** ($J_{12,13\beta}$ = 7.0 Hz, $J_{13\beta,14}$ = 4 Hz, $J_{14,15\alpha}$ = 6.6 Hz, and $J_{14,15\beta}$ = 12.3 Hz, Table I) and NOE enhancements (Table IV and Figure 3) point to a twisted-boat conformation of the δ-lactone in such a way that C-12 and C-15 are the flag pole atoms as indicated by the strong NOE enhancement between H-12 and H-15 (Table IV). Examination of a Dreiding model of compounds **5–7** indicated that the measured NOE's (Table IV) are in full agreement with the proposed structure and could not be simultaneously observed if **5** (or **6** and **7**) had the epimeric C-14 configuration. Moreover, the NOE's clearly indicate that the major C-8 to C-14 rotamer is the conformer drawn in Figure 1 (C-13 close to C-9 and C-15 to C-7).

Shahamin F (**9**) gave the molecular formula $C_{22}H_{32}O_5$ from ^{13}C NMR and mass measurements. Comparisons of the ^1H and ^{13}C NMR data for the C-11 to C-16 site, of **9**, with those of aplyviolene (**2**)[6] and macfarlandin D (**8**)[3] indicated the presence of the same dioxabicyclo[3.2.1]octane ring system. However, the rest of the molecule was different from that of **2**, **8**, and the other previously described compounds (**3–7**). Three singlet methyls, one doublet methyl, and 10 other C atoms, out of which two

are singlet vinyls (see Tables II and III), led us to propose a $\Delta^{5(10)}$-octalin (rather than a $\Delta^{1(10)}$ as in **8**). Eventually, the suggested $\Delta^{5(10)}$-octalin structure was unequivocally confirmed by homo and hetero (short and long range) correlations and also was found to be in full agreement with the mass spectrum (CH_4 CI, m/z 191, $C_{14}H_{23}^+$, 12%, and 189, $C_{14}H_{21}^+$, 17%, see the Experimental Section).[9]

Long-range couplings between CH_3-17 and C-10 and between CH_3-18 and CH_3-19 and C-5 established the location of the double bond, while long-range couplings between CH_3-20 and carbons 7, 8, 9, and 14 established the connection between both ring systems.

As before with shahamin C (**5**), most significant for the structure elucidation was the NOE experiment (Table IV). This experiment was not only in full agreement with the octalin and the oxygenated bicyclo system but it also confirmed their relative stereochemistry. Examination of a Dreiding model revealed that the observed NOE's (especially the enhancements of H-12–15 with H-7–9, see Table IV) could not be simultaneously observed if **9**, as in the case of **5** above, had the epimeric C-14 configuration (an epimeric C-14 stereochemistry means that the configuration of one of the two bicyclic portions of the molecule has to be changed).

Compounds **10–13** (Figure 2), which are described now, had in common the $\Delta^{5(10)}$-octalin portion and the same oxabicyclo[3.2.1]octane system as in **9** but differed in containing additional hydroxyl and/or acetates.

Shahamin G (**10**), $C_{22}H_{32}O_6$, was identified as the 1α-hydroxy (IR 3480 cm^{-1}) derivative of **9** by comparison of spectral data and a COSY experiment. The latter experiment enabled the complete proton line assignment (Table II). This assignment determined inter alia unequivocally the location of the OH group at C-1 according to the ^2J to ^4J H–H correlations of the C-1 to C-4-Me_2 segment. Furthermore, the almost equal vicinal coupling constant of H-1 with the C-2 protons (J = 9 Hz) suggests according to a Dreiding model a twisted boat conformation of the corresponding ring ($\Phi_{1\beta,2\beta} \approx 10°$ and $\Phi_{1\beta,2\alpha} \approx 170°$).

A *W*-arrangement between H-3β and Me-18 and the relative low field resonances (in comparison with **9**) of both H-9 and Me-20 due to the neighbor 1α-hydroxyl agree well with the proposed twist-boat stereochemistry of ring A.

Shahamin H (**11**), $C_{22}H_{32}O_6$, is the C-1-OH isomer of **10**. Both compounds gave identical mass spectral data (Experimental Section) and very similar NMR spectra except for the vicinity of the alcohol function (Table II). The location of the OH group on C-1 was determined independently in the same way as described for **10** above. As in **10** because of the coupling constants of H-1α to H-3α, the conformation of ring-A is assumed to be a twisted chair, a conformation (Dreiding model) in which the latter two protons are in a "*W*"-arrangement.

Both shahamins I (**12**) and J (**13**), $C_{24}H_{34}O_7$ and $C_{24}H_{34}O_8$, respectively, possess the $\Delta^{5(10)}$-octalin portion of **9**, and compound **13** carries in addition the same 1β-hydroxyl as **11**. Both **12** and **13** also share the acetoxy dioxabicyclo[3.2.1]octane system of **1** (Figure 2). 1D and 2D NMR (COSY 45) experiments established unambiguously the C-12 position for the acetate (Table II) with the same relative stereochemistry as in macfarlandin E (**1**).[3,6]

Worth mentioning is the comparison of the CH_4 CI and NH_3 CI mass spectra performed on compounds **1**, **4a**, and **9–13**. Ammonia chemical ionization mass spectrometry (NH_3 CI) has recently emerged as a useful technique for qualitative analysis of acid labile compounds. Ammonia, because of its lower proton affinity, produces less energetic ions than methane. Thus whereas with CH_4 compounds **1**, **4a**, and **9–13** fail to show a molecular ion, adduct ions of the type $[MH(NH_3)_n]^+$ are seen with NH_3.

In general, $H^+(NH_3)_n$ will protonate organic compounds with PA (proton affinity) > 205 kcal/mol to give $[MH]^+$ ions; when the PA is in the range of ~188 to <205 kcal/mol the ammonia CI mass spectra shows $[MNH_4]^+$ adduct ions. On the other hand, $[MNH_4]^+$ is not formed to a significant extent if the proton affinity of M is less than ~188 kcal/mol, it also appears that a lone pair of electrons at the basic site is a necessary prerequisite for formation of $[MNH_4]^+$.[10,11] For the present purpose it is sufficient to note that oxygen-containing compounds have proton affinities in the range of 180–205 kcal/mol. Furthermore, the formation of stable $[MNH_4]^+$ ions show that the PA(M) are greater than 188 kcal/mol.

In the case of compounds **1**, **4a**, and **9–13** the difference in proton affinity between the compound and the ammonia is no more than 17 kcal/mol, therefore the $[MNH_4]^+$ ion is formed with little excess energy and is relatively stable. The NH_3 CI spectrum of the monoacetate **9**, however, shows the $[MNH_4]^+$ and also the MH^+ peaks. The proton affinity of the monoacetate **9** is less than that of the diacetates **1**, **4a**, and **12**—thus the PA is greater, and we are in the range where the $[MH]^+$ ion is observed.

Possible biogenesis relationships between the spongians and macfarlandins D and E as suggested by Faulkner[5] and the new shahamins are illustrated in Scheme I.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 177 spectrophotometer. Optical rotations were measured on a Perkin-Elmer Model 243B polarimeter with a 2.5-cm microcell. Low-resolution mass spectra were recorded on a Finnigan-4021 mass spectrometer; source temperature 220–230 °C; pressure of reagent gases for CI spectra: CH_4, 0.28 Torr, and NH_3, 0.15–0.20 Torr; the electron energies in EI mode were 25–35 eV. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-360 spectrometer, equipped with an Aspect 3000 computer and operating at 360.1 and 90.5 MHz for ^1H and ^{13}C, respectively. All chemical shifts are reported with respect to Me_4Si (δ 0).

The 2D NMR experiments were measured on samples in $CDCl_3$ at 298 K. The H–H shift correlation experiments were performed with a COSY 45 sequence.[12] The two-dimensional maps were composed of 512 × 2K data point spectra. A 1-s recycle delay was allowed between each pulse sequence. Quadrature detection was applied in both dimensions by using the 16-step phase cycling for N-type peak selection. Data were multiplied with sine bell shaping function, zero filled to 1K × 2K and then Fourier transformed and symmetrized.

The ^1H–^{13}C shift correlation experiments were performed with the regular heteronuclear shift correlation pulse sequence.[13] The two dimensional maps were composed of 256–300 × 2K data point spectra. A 1-s recycle delay was allowed between each pulse sequence. The time for the development of the polarization transfer, $\tau_1 = 2\ J^{-1}$, and the refocusing time for antiphase multiplet components, $\tau_2 = 4\ J^{-1}$, were adjusted to give maximum enhancement for $^1J_{H-C}$ = 135 Hz, or J_{H-C} = 10 Hz in "long-range" experiments.

Quadrature detection was applied in both directions by using eight-step phase cycling for N-type peak selection. Data were multiplied with sine bell shaping function, zero filled to 1K × 2K and then Fourier transformed.

(9) The mass spectra of compounds **9–13** point clearly to the two halves of the molecule as with compounds **1** and **3–7**. In case of compounds **9** and **12** a peak at m/e 189 prevails over the peak at 191 (observed for compounds **3–7**) and in case of the alcohols **10**, **11**, and **13**, the m/e 205 peak overrides the peak at 207.

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The sponge specimens were collected at the southern part of the Gulf of Suez, in July 1986 and July 1987. The samples were deep-frozen immediately after collection, freeze-dried, and then extracted with petroleum ether, chloroform, and 10% methanol in chloroform.

The petroleum ether and the chloroform crude extracts of each of the three specimens were separated by flash chromatography on silica H by using solvent of gradually increasing polarity from petroleum ether through ethyl acetate and on RP-18 with solvent of gradually decreasing polarity from 50% methanol in water through methanol.

The first sample of *Dysidea* sp. (1), which has been collected near Shaab Mahamud in the Red Sea in July 1986, afforded 13 g of dry material. The second sample of *Dysidea* sp. (1), which has been collected near Shaab Mahamud in July 1987, furnished 10 g of dry material. The sample of *Dysidea* sp. (2), which has been collected near Beacon Rock, Red Sea, in July 1986, yielded 27 g of dry material.

From the petroleum ether extract of the first sample of *Dysidea* sp. (1), we obtained, in order of elution, macfarlandin E (1), shahamin A (3), and shahamin C (5). From the chloroform extract of the same sample we obtained, in order of elution, shahamin D (6), shahamin B (4), and shahamin E (7).

From the petroleum ether extract of the second sample of *Dysidea* sp. (1), we obtained, in order of elution, macfarlandin E (1), shahamin F (9), shahamin A (3), and shahamin C (5). And from the chloroform extract of the same sample we obtained shahamin G (10).

From the petroleum ether extract of the sample of *Dysidea* sp. (2), we obtained, in order of elution, shahamin I (12), shahamin F (9), shahamin J (13), and shahamin H (11). Shahamin J (13) and shahamin H (11) were also obtained from the chloroform extract of this sample.

Macfarlandin E (1): oil; $[\alpha]_D$ −34° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) 2870, 2860, 1770, 1755, 1425, 1360, 1260, 1030, and 940 cm^{-1}; mass spectra (EI), *m/e* (relative intensity) 375 (M − $C_2H_3O_2$, 9), 315 (375 − AcOH, 13), 297 (315 − H_2O, 3), 287 (315 − CO, 2), 191 ($C_{14}H_{23}^+$, 17), and 137 ($C_{10}H_{17}^+$, 100); (CI, methane), *m/z* (relative intensity) 449 (MCH_3^+, <1), 421 (MCH_3 − CO, 2), 405 (MCH_3 − CO_2, 2), 391 (MH −CO_2, <1), 375 (10), 315 (100), 297 (27), 287 (12), 191 (28), and 137 (6); (CI, ammonia), *m/z* (relative intensity) 452 (MNH_4^+, 31), 424 (MNH_4 − CO, 1), 408 (MNH_4 − CO_2, 1), 393 (MNH_4 − $C_2H_3O_2$, 12), 391 (2), 375 (10), 315 (100), 297 (3), 287 (2), 191 (6), and 137 (2).[14]

Shahamin A (3): oil; $[\alpha]_D$ +25° (*c* 0.006, $CHCl_3$); IR ($CHCl_3$) 3005, 2965, 1775, 1755, 1420, 1375, 1260, 1235, 1200, and 1030 cm^{-1}; mass spectra (EI), *m/e* (relative intensity) 390 (M^+, 15), 389 (14), 330 (M − AcOH, 10) 329 (10), 259 (M − $C_5H_7O_4$, 60), 258 (51), 252 (M − $C_{10}H_{18}$, 44), 191 ($C_{14}H_{23}^+$, 45), 190 (18), and 69 (100); (CI, methane), *m/z* (relative intensity) 391 (MH^+, 71), 390 (M^+, 100), 331 (MH − AcOH, 18), 330 (21), 313 (MH − AcOH − H_2O, 24), 312 (28), 259 (10), 258 (13), 257 (20), 256 (31), 252 (20), 191 (37), and 190 (85).

Shahamin B (4): oil; IR ($CHCl_3$) 3450, 2975, 1765, 1365, 1260, 1195, 1020 cm^{-1}; mass spectra (CI, methane), *m/z* (relative intensity) 367 (MH^+, <1), 349 (MH − H_2O, 41), 331 (MH − $2H_2O$, 35), 317 (349 − MeOH, 3), 313 (331 − H_2O, 5), 289 (349 − $C_2H_4O_2$, 29), 271 (289 − H_2O, 10), 215 (30) and 191 ($C_{14}H_{23}^+$, 100); (EI), *m/e* (relative intensity) 191 (10), 177 (3), 149 (48), 135 (42), 121 (42), 109 (54), 95 (100), 81 (88), and 69 (74).

Shahamin C (5): oil; $[\alpha]_D$ +81° (*c* 0.01, $CHCl_3$); IR ($CHCl_3$) 2955, 2932, 2865, 1774 (sh), 1746, 1385, 1362, 1240, and 1030 cm^{-1}; mass spectra (CI, methane), *m/z* (relative intensity) 421 (MH^+, 52), 379 (MH − C_2H_2O, 18), 361 (MH − AcOH, 44), 319 (379 − AcOH, 29), 303 (20), 301 (MH − 2AcOH, 100), 287 (361 − CH_3OAc, 4), 273 (301 − CO, 16), 191 ($C_{14}H_{23}^+$, 44), 177 ($C_{13}H_{21}^+$, 21), 163 ($C_{12}H_{19}^+$, 87), 149 ($C_{11}H_{17}^+$, 21), and 109 ($C_8H_{13}^+$, 25).

Shahamin D (6): oil; IR ($CHCl_3$) 3453, 2955, 2936, 2862, 1763, 1743, 1360, 1260, and 1030 cm^{-1}; mass spectra (CI, methane), *m/z* (relative intensity) 379 (MH^+, 24) 361 (MH − H_2O, 9), 337 (MH − C_2H_2O, 3), 319 (361 − C_2H_2O, 40), 303 (24), 301 (361 − AcOH, 33), 287 (MH − AcOH − CH_3OH, 8), 273 (301 − CO, 13), 191 ($C_{14}H_{23}^+$, 29), 177 ($C_{13}H_{21}^+$, 100), 163 (45), 149 (17), and 109 (16).

Shahamin E (7): oil; $[\alpha]_D$ +72° (*c* 0.02, $CHCl_3$); IR ($CHCl_3$) 3450, 2955, 2929, 2859, 1747, 1360, 1255, and 1025 cm^{-1}; mass spectra (CI, methane), *m/z* (relative intensity) 337 (MH^+, 80), 319 (MH − H_2O, 57) 303 (4), 301 (MH − $2H_2O$, 42), 273 (301 − CO, 17), 191 ($C_{14}H_{23}^+$, 52), 177 ($C_{13}H_{21}^+$, 22), 163 ($C_{12}H_{19}^+$, 100), 149 (12), and 109 (37).

Shahamin F (9): oil; $[\alpha]_D$ −49.6° (*c* 0.001, $CHCl_3$); IR ($CHCl_3$) 3000, 2980, 2960, 1748, 1380, 1235, 1190, 1005, and 940 cm^{-1}; mass spectra (CI, methane), *m/z* (relative intensity) 377 (MH^+, <1) 317 (MH − AcOH, 100), 299 (317 − H_2O, 21), 289 (317 − CO, 2), 271 (2), 257 (2), 239 (2), 191 ($C_{14}H_{23}^+$, 12), and 189 ($C_{14}H_{21}^+$, 17); mass spectra (CI, ammonia), *m/z* (relative intensity) 394 (MNH_4^+, 26), 377 (MH^+, 1), 334 (394 − AcOH, 8), 317 (MH^+ − AcOH, 100), and 191 ($C_{14}H_{23}^+$, 4).

Shahamin G (10): oil; IR ($CHCl_3$) 3500, 2980, 1750, 1735, 1380, 1235, 1190, 1007, and 940 cm^{-1}; mass spectra (CI, methane), *m/z* (relative intensity) 349 (MH^+ − CO_2, 11), 331 (349 − H_2O, 100), 313 (22), 303 (7), 285 (8), 275 (20), 247 (9), 223 (20), 207 (3), 205 ($C_{14}H_{21}O^+$, 23), 189 (2), and 187 (3); mass spectra (CI, ammonia), *m/z* (relative intensity) 427 ($MN_2H_7^+$, 100), 409 (MN_2H_7 − H_2O, 37), 391 (409 − H_2O, 8), 366 (MNH_4^+ − AcOH, 27), 349 (409 − AcOH, 14), 348 (366 − H_2O, 28), 331 (MH^+ − H_2O − CO_2, 93), 223 (20), and 205 ($C_{14}H_{21}O^+$, 11).

Shahamin H (11): oil; IR ($CHCl_3$) 3400, 2960, 1765, 1750, 1735, 1380, 1360, 1240, 1190, 1005, and 940 cm^{-1}; mass spectrum (CI, ammonia), *m/e* (relative intensity) 427 ($MN_2H_7^+$, 2), 408 (100), 392 (M^+, 2), 366 (8), 348 (11), 331 (57), 315 (57), 315 (32), 205 (3), and 187 (3).

Shahamin I (12): oil; $[\alpha]_D$ −48.3° (*c* 0.005, $CHCl_3$); IR ($CHCl_3$) 3005, 1750, 1735, 1380, 1240, 1195, 1035, 980, and 935 cm^{-1}; mass spectra (CI, methane), *m/z* (relative intensity) 389 (MH − H_2CO_2, 4), 375 (MH − AcOH, 68), 357 (375 − H_2O, 2), 347 (375 − CO, 9), 329 (375 − H_2CO_2, 21), 315 (MH − 2AcOH, 100), 297 (315 − H_2O, 18), 287 (315 − CO, 9), 191 ($C_{14}H_{23}^+$, 13), and 189 ($C_{14}H_{21}^+$, 33); mass spectra (CI, ammonia), *m/e* (relative intensity) 452 (MNH_4^+, 12), 392 (MNH_4 − AcOH, 6), 375 (MH − AcOH, 100), 332 (MNH_4 − 2AcOH, 4), 315 (MH − 2AcOH, 60), and 191 (3).

Shahamin J (13): oil; IR ($CHCl_3$) 3500, 2960, 1770, 1755, 1735, 1470, 1235, 1200, and 985 cm^{-1}; mass spectrum (CI, methane), *m/z* (relative intensity) 391 (MH^+ − AcOH, 7) 389 (MH^+ − H_2O − CO_2, 16), 373 (391 − H_2O, 13), 347 (391 − CO_2, 24), 331 (MH^+ − 2AcOH, 60), 329 (391 − H_2O − AcOH, 100), 313 (331 − H_2O, 84), 205 ($C_{14}H_{21}O^+$, 42), 189 ($C_{14}H_{21}^+$, 39), and 187 (205 − H_2O, 35); mass spectra (CI, ammonia), *m/z* (relative intensity) 485 ($MN_2H_7^+$, 23), 468 (MNH_4^+, 17), 467 (485 − H_2O, 100), 451 (MH^+, 3), 450 (M^+, 10), 408 (468 − AcOH, 9), 407 (5), 406 (M − CO_2, 12), 391 (11), 390 (M − AcOH, 16), 373 (38), 331 (21), 392 (51), 313 (69), 205 (23), 189 (16), 187 (14).

Acetylation of Shahamin B (4) To Give 4a. Compound 4 (1 mg) was treated with one drop of 1:1 mixture of Ac_2O/pyridine. The reaction mixture was allowed to stand overnight at room temperature and then evaporated under vacuum. The residue (1 mg) was found to be a single product by TLC and ^1H NMR analyses; compound **4a**: oil; IR ($CHCl_3$) 2980, 2960, 1770, 1755, 1360, 1255, 1090, and 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.37 (s, 1 H), 4.82 (d, 2.7, 1 H), 4.69 (d, 2.7, 1 H), 4.51 (d, 7.1, 1 H), 4.31 (dd, 10.8, 7.1, 1 H) 4.25 (dd, 10.8, 2.7, 1 H) 4.25 (dd, 10.8, 2.7, 1 H), 3.78 (s, 3 H), 2.74 (m, 1 H), 2.66 (d, 8.8, 1 H), 2.11 (s, 3 H), 2.07 (s, 3 H), 0.99 (s, 3 H), 0.94 (s, 3 H), 0.85 (s, 3 H); mass spectra (CI, methane), *m/z* (relative intensity) 419 (MH − CH_3OH, <1), 391 (MH − AcOH, 25), 331 (MH − 2AcOH, 100), 313 (331 − H_2O, 19), 271 (331 − $C_2H_4O_2$, 47), 215 (12), and 191 ($C_{14}H_{23}^+$, 64); mass spectra (CI, ammonia) *m/z* (relative intensity) 468 (MNH_4^+, 2), 438 (MNH_4 − H_2CO, 6), 419 (MH − MeOH, 10), 408 (MNH_4 − AcOH, 47), 391 (MH − AcOH, 96), 331 (MH − 2AcOH, 100), 315 (69), 271 (46), and 191 (64).

Acetylation of Shahamin D (6) and E (7) To Give Shahamin C (5). Compounds 6 (1 mg) and 7 (2 mg) were treated with Ac_2O/pyridine in the same manner as described above (for compound 4) to give a single product, which was found to be identical in all respects (TLC, IR, and NMR) with the authentic sample of shahamin C (5).

Reduction of Macfarlandin E (1) To Give Compound 14. A solution of 13.6 mg of 1 in 10 mL of toluene was treated with 6 mL of sodium aluminum bis(methoxyethoxy)hydride (70% in

(14) For ^1H NMR data, see Tables I and II; for ^{13}C NMR data, see Table III.

benzene). The mixture was refluxed for 5 h, left to stand overnight, and then treated with an ice-cooled solution of 10% aqueous NaOH (3 mL) in order to decompose the excess of reagent. The mixture was poured into a separatory funnel containing 50 mL of EtOAc and 15 mL of 10% aqueous NaOH, and after rapid equilibration the aqueous phase was separated and reextracted twice with 50 mL of EtOAc. After drying over $MgSO_4$ and evaporation in vacuo at room temperature, the residual gum (about 80% pure) was acetylated (Ac_2O/pyridine) in the usual manner and then chromatographed on silica H, with 15% ethyl acetate in petroleum ether solution as eluant. Pure **14** (10 mg) was eluted in the fourth fraction. Compound **14**: oil; $[\alpha]_D$ +8° (*c* 0.002, $CHCl_3$); IR ($CHCl_3$) 2930, 2870, 1725, 1370, 1240, 1200, and 1030 cm^{-1}; ^1H NMR ($CDCl_3$) assigned by COSY 45 experiment: 5.37 (ddd, 6.9, 6.3, 2.1, H-12), 4.83 (d, 2.2, H-20*E*), 4.66 (d, 1.8, H-20*Z*), 4.56 (dd, 12.4, 2.1, H-11), 4.48 (dd, 11.8, 3.3, H-15), 4.21 (d, 6.9, H-16 and 16′), 4.02 (dd, 11.8, 8.5, H-15′), 3.99 (dd, 12.4, 6.9, H-11′), 2.79 (d, 8.8, H-9α), 2.72 (br, dt, 6.3, 6.9, H-13), 2.32 (br dd, 12.7, 3.5, H-1α), 2.09 (s, 3 H), 2.07 (s, 3 H), 2.04 (s, 3 H), 2.03 (s, 3 H, 11, 12, 15, and 16-OAc's), 1.87 (br d, 8.5, H-14), 1.86 (m, H-1β), 1.85 (m, H-5α), 1.73 (m, H-2β), 1.68 and 1.65 (m, H-6α,6β), 1.65 and 1.60 (m, H-7α,7β), 1.59 (m, H-3β), 1.36 (m, H-2α), 1.26 (m, H-3α), 0.98 (s, 19-CH_3), 0.94 (s, 18-CH_3), 0.88 (s, 17-CH_3); mass spectrum (CI, ammonia), *m/z* (relative intensity) 526 (MNH_4^+, 100), 449 (MH^+ – AcOH, 5), 389 (MH^+ – 2AcOH, 6), 329 (MH^+ – 3AcOH, 4), and 269 (MH^+ – 4AcOH, 2).

Reduction of Shahamin B (3) To Give Compound 14. Compound **4** (1 mg) in toluene (2 mL) was treated with Red-Al solution (1 mL) in the same manner described for **1**. The residue obtained after the usual workup was acetylated to give compound **14** (0.5 mg), identical in all respects with the compound obtained from **1**.

Reduction of Shahamin C (5) To Give Compound 14. Compound **5** (3.6 mg) in toluene (5 mL) was treated with Red-Al (2.6 mL) in the same manner described for **1**. The usual workup followed by acetylation furnished compound **14** (2.5 mg), identical in all respects with the compound obtained from **1**.

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Cycloaddition Reactions of 1,1-Dimethylallene with Substituted Alkynes

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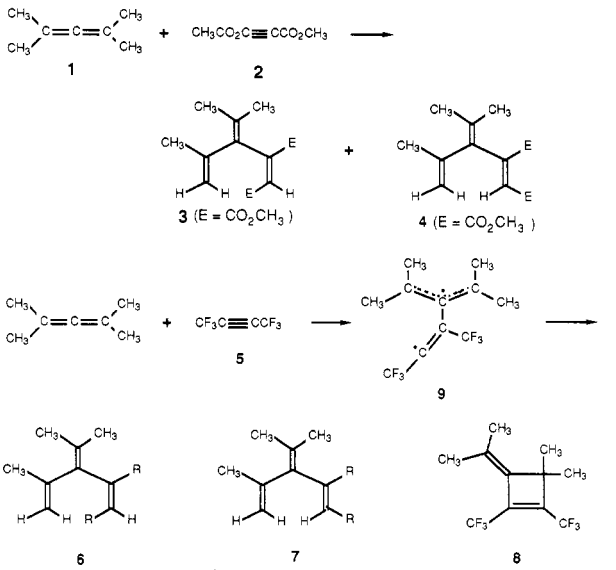
The cycloaddition reactions of 1,1-dimethylallene with ethyl propiolate, ethyl phenylpropiolate, dimethyl acetylenedicarboxylate, and phenylacetylene have been studied. All reactions produce excellent yields of substituted 3-isopropylidenecyclobutenes. Ene products were formed in less than 2% yield. The substituted 3-isopropylidenencyclobutenes are extremely reactive substances, undergoing extensive decomposition or polymerization on exposure to air or attempted purification by chromatographic techniques.

Introduction

One of the major research efforts in our laboratories has focused on the mechanisms of the (2 + 2) cycloaddition reactions of substituted allenes with electronegatively substituted alkenes.[1] These reactions have been shown to proceed via two-step, diradical-intermediate mechanisms. Although ene reactions often compete with cycloaddition reactions, the cycloaddition reactions of the substituted allenes studied in our laboratories have shown that ene reactions, if they occur, result in only very minor product formation.[1] In contrast, a review of the literature of the cycloaddition reactions of substituted allenes with electron-deficient alkynes suggests that ene reactions, when possible, might be the dominant mode of reaction. The reaction of 2,4-dimethyl-2,3-pentadiene (tetramethylallene, **1**) with dimethyl acetylenedicarboxylate (**2**) results in the formation of only the *E* and *Z* ene products **3** and **4**.[2] No (2 + 2) cycloaddition product was apparently formed.[2] The reaction of **1** with hexafluoro-2-butyne (**5**) produced predominantly the *E* and *Z* ene products **6** and **7**, with the (2 + 2) cycloaddition product **8** being formed in only approximately 11% yield.[2] The product distribution of **6**, **7**, and **8** as a function of temperature has been studied; the relative amount of **8** remaining constant leads to the conclusion that **6**, **7**, and **8** are derived from a common intermediate, the diradical **9**.[3]



The reactions of dimethylallene (DMA, **10**) with dimethyl acetylenedicarboxylate and hexafluoro-2-butyne

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