

SPONGIALACTONE A, A NEW SPONGIAN DITERPENE FROM *SPONGIA ARABICA*

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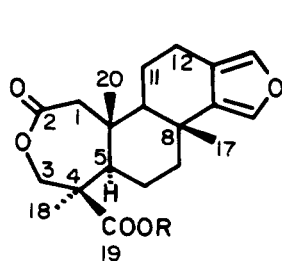
In the course of our investigation on the constituents of Red Sea organisms, we have isolated from the sponge *Spongia arabica* (*Spongia officinalis* var. *arabica*, Vacelet) (Spongiidae) a structurally novel metabolite, spongialactone A, for which we propose structure **1**. Compound **1**, which is a minor constituent of the lipophilic extract of this invertebrate, represents the first spongian (1) with a ring-A lactone, although other spongians with oxygenated C,D rings are known (2,3).

From the same sponge we have isolated as the two major compounds the known $3\alpha, 17, 19$ -trihydroxyspongia-13(16), 14-dien-2-one [**4**] (1) and the $3\beta, 17, 19$ -trihydroxy spongian derivative **5** and as a minor constituent the new 19-acetoxy- 3α -hydroxyspongia-13(16), 14-dien-2-one [**6**] (0.1% dry wt). Compound **6** is the acetate of the known diol $3\alpha, 19$ -dihydroxy-spongia-13(16), 14-dien-2-one (1).

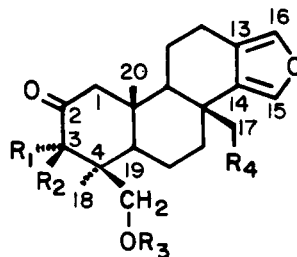
The structures of compounds **4-6** were readily established by comparison of their spectral data with those reported (1). Hydrolysis of acetate **6** gave the known parent diol (1).

Compound **1**, an amorphous powder, $C_{20}H_{26}O_5$ (cims m/z $[MH]^+$ 347), eight

unsaturations, ν max 3600–3000 br, 1730, 1165 cm^{-1} , contains two carbonyls and two double bonds according to its ^{13}C -nmr spectrum and must, therefore, be tetracyclic. Comparison of the nmr data of **1** with those of **6** (Table 1) indicated that both compounds had the same B, C, and D rings. However, ring A was found to differ completely; the ^{13}C -nmr signal for the ketone carbonyl group in compound **6** was replaced with signals for two new carbonyl groups (δ_c 173.9 and 179.5 ppm). Of these, one belongs to a carboxylic acid, as could be shown by methylation with CH_2N_2 to form the ester **2** and acetylation to the mixed anhydride **3** (ν max 1830 and 1760 cm^{-1}). The other carbonyl (δ_c 173.9 ppm) was assigned to a lactone ring. Two isolated methylenes (Table 1) were assigned to C-1 α to the CO group and to C-3 vicinal to the ring oxygen. The ir data suggest a δ lactone (1730 cm^{-1}) rather than a possible γ lactone. Unequivocal proof for the structure of **1** was obtained from a series of 2D nmr experiments, that is, a COSY (4), a RELAY (5) (Table 2), and a C-H correlation (6) (Table 1) as well as from a NOEDS experiment, which showed the enhancements illustrated in Table 3.



- 1** R = H
2 R = Me
3 R = Ac



- | | R ₁ | R ₂ | R ₃ | R ₄ |
|----------|----------------|----------------|----------------|----------------|
| 4 | OH | H | H | OH |
| 5 | H | OH | H | OH |
| 6 | OH | H | Ac | H |

TABLE 1. ^1H - and ^{13}C -nmr Data for Compounds **1** and **6**.^{a,b}

Carbon	Compound			
	1		6	
	δ_{C} (mult)	δ_{H} (mult, J in Hz)	δ_{C} (mult)	δ_{H} (mult, J in Hz)
1	45.8 t	2.61 (brd, 11.7, α) 2.91 (brd, 11.7, β)	53.8 t	2.16 (d, 18.5, α) 2.64 (d, 18.5, β)
2	173.9 s		203.5 s	
3	72.9 t	3.93 (brd, 10.4, α) 4.45 (brd, 10.4, β)	74.9 d	4.64 (d, 4.1)
4	52.6 s		44.8 s	
5	56.4 d	2.12 (dt, 10.2, 2.8)	54.4 d	2.10 (m) ^c
6	19.6 t	1.69 (m, $J_{\text{gem}} = 10.3$, α, β)	19.3 t	1.67 (m, α, β) ^c
7	39.9 t	1.78 (brt, 10.3, α) 2.03 (brd, 10.3, β)	40.1 t	1.67 (m, α, β) ^c
8	34.8 s		34.0 s	
9	53.3 d	1.24 (m) ^c	56.5 d	1.35 (m) ^c
10	39.3 s		38.5 s	
11	22.3 t	1.72 (m, α) ^{c,d} 1.24 (m, β) ^{c,d}	20.7 t	1.67 (m, α, β) ^{c,d}
12	20.7 t	2.76 (dd, 16.2, 5.5, α) 2.44 (ddd, 16.2, 6.8, 3.0, β)	20.1 t	2.78 (dd, 16.0, 5.5, α) 2.39 (ddd, 16.0, 7.3, 3.3, β)
13	119.2 s		119.1 s	
14	136.9 s		136.2 s	
15	134.8 d	7.00 (s)	133.3 d	7.09 (brd, 1.4)
16	137.1 d	7.00 (s)	137.0 d	7.05 (brt, 1.4)
17	26.2 q	1.19 (s)	25.4 q	1.29 (s)
18	16.3 brq	1.24 (s)	21.1 q	1.22 (s)
19	179.5 s		66.8 t	4.19 (d, 11.5) 4.04 (d, 11.5)
20	14.1 q	1.01 (s)	20.2 q	0.84 (s)

^a360 and 90 MHz, respectively, in CDCl_3 .^bThe relationships between the protons and carbons were established by a C-H correlation experiment ($J = 140$ Hz), and between the protons by a COSY experiment.^cOverlapping with other protons; location determined by the COSY experiment.^dThese protons are part of a complex ABMNP system.TABLE 2. Correlations Between Protons of Compound **1**.

Proton	COSY-45 correlations	Long range correlations (RELAY experiment) ^a
1 α	1 β	5 α
3 β	3 α , Me-18	Me-18
5	6 α , 6 β	7 α , 7 β , Me-18
7 β	7 α	Me-17
9	11 α , 11 β	11 α , 12 α , 12 β
11 α	11 β , 12 α , 12 β	
12 α	12 β	16
15		Me-17

^aThe mixing time (τ_{m}) is of utmost importance in the RELAY experiment, and no single optimum value exists. By performing a number of RELAY experiments with different τ_{m} values one may be able to identify certain types of spin systems directly. Under non-optimal conditions long-range cross peaks as in COSYLR also occur.

TABLE 3. NOEDS Correlations of Compound 1.

Protons irradiated	Observed nOe (%)
3 β	3 α (23), Me-18 (4)
1 β	11 α (7)
1 α	3 α (10), 5 (3)

The above spectra together with the NOEDS experiment is the basis of the proposed stereochemistry at C-4 (Me-18 and COOH-19) and C-5 (Figure 1). The relative configurations of the rest of the chiral centers were established by the comparison of the nmr data with that of the reference compounds.

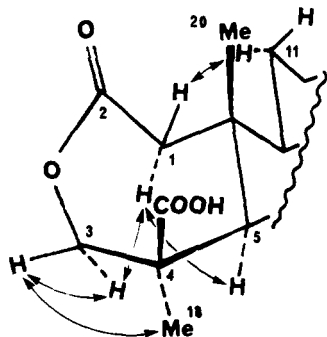


FIGURE 1. The stereochemistry of ring A of **1** as established by nOe experiments.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All nmr spectra (in CDCl_3) with TMS as internal standard) were obtained with a Bruker AM-360 spectrometer equipped with an ASPECT 3000 computer. Ir spectra were recorded on a Perkin-Elmer Model 177 spectrophotometer. Mass spectra were recorded with a Finnigan 4020 quadrupole spectrometer equipped with a data system. Ionizing conditions for ei were 23–26 eV and for ci (NH_3) 70 eV.

The sponge was collected in the straits of the Gulf of Eilat near the Gordon reef in July 1985. A voucher specimen has been kept in our collection in Tel Aviv (YK1796).

Freeze-dried material (55 g) was ground and extracted with cold petroleum ether and then with CH_2Cl_2 to give 2.5 g of viscous, dark oil. Repeated Sephadex LH-20 columns eluted with CHCl_3 -heptane-MeOH (1:2:1) and flash chromatography on a Si gel-H column eluted with petroleum ether/EtOAc afforded compounds **1**–**6**.

Compound 1 (0.5% of the crude extract).—Amorphous powder; cims m/z $[\text{MH}]^+$ 347 (100%), 301 (45%), 275 (21%), 231 (4%); $[\alpha]^{25}_{\text{D}} + 15^\circ$ ($c = 0.025$, CHCl_3); ^1H nmr, and ^{13}C nmr see Table 1. Found: C 69.29, H 7.04; $\text{C}_{20}\text{H}_{26}\text{O}_5$ requires C 69.34, H 7.56.

Methylation of 1.—Compound **1** (10 mg) in Et_2O (2 ml) was treated with a solution of CH_2N_2 in Et_2O (5 ml) at room temperature overnight to afford, after evaporation, compound **2** (9 mg): an oil; eims m/z $[\text{M}]^+$ 360 (78%), 345 (100%), 303 (42%), 285 (24%), 187 (5%); ir ν max 2900, 1750, 1725, 1220 cm^{-1} ; ^1H nmr (CDCl_3) 3.65 s (OMe); all other resonance lines are the same as in **1**.

Acetylation of 1.—Compound **1** (5 mg) was treated with Ac_2O -pyridine (1:1) (0.3 ml) at room temperature overnight to afford, after evaporation, compound **3** (4 mg): an oil; ir ν max 2900, 1830, 1760 cm^{-1} ; ^1H nmr (CDCl_3) 2.20 s (Ac); all other peaks identical with those of **1**.

Compounds 4 and 5 (2% of the crude extract).—These were found to be identical with compounds reported (as compounds **5** and **9**) by Kazlauskas *et al.* (1).

Compound 6 (0.1% of the crude extract).—Oil; cims m/z $[\text{MH}]^+$ 373 (100%), 313 (14%), 300 (2%); $[\alpha]^{25}_{\text{D}} + 10^\circ$ ($c = 0.005$, CHCl_3); ^1H nmr and ^{13}C nmr see Table 1. Found: C 70.53, H 8.04; $\text{C}_{22}\text{H}_{30}\text{O}_5$ requires C 70.60, H 8.07.

Hydrolysis of 6.—Compound **6** (10 mg) was treated with a solution of K_2CO_3 -MeOH (4:96) (2 ml) for 30 min at room temperature to afford, after neutralization and evaporation of the organic layer, a compound reported (as compound **3**) by Kazlauskas *et al.* (1).

ACKNOWLEDGMENTS

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