Triacetate 6: oil; ^{1}H NMR (360 MHz, DMSO-d_6) δ 2.00 (s, 3 H), 2.25 (s, 3 H), 2.27 (s, 3 H), 3.13 (m, 2 H), 3.26 (s, 3 H), 3.38 (s, 3 H), 3.77 (s, 3 H), 3.84 (s, 3 H), 4.67 (m, 1 H), 4.78 (m, 1 H), 6.71 (s, 1 H), 6.83 (s, 1 H), 7.08 (dd, 1 H, J = 7.8, 1.9 Hz), 7.14 (s, 1 H), 7.15 (d, 1 H, J = 1.9 Hz), 7.23 (d, 1 H, J = 7.8 Hz).

Diacetate 7: oil; ^{1}H NMR (360 MHz, DMSO-d_6) δ 2.25 (s, 3 H), 2.38 (s, 3 H), 2.96 (m, 2 H), 3.31 (s, 3 H), 3.34 (s, 3 H), 3.70 (s, 3 H), 3.78 (s, 3 H), 3.86 (s, 3 H), 4.62 (m, 1 H), 4.70 (m, 1 H), 6.67 (s, 1 H), 6.77 (s, 1 H), 7.08 (dd, 1 H, J = 7.8, 1.9 Hz), 7.16 (d, 1 H, J = 1.9 Hz), 7.23 (d, 1 H, J = 7.8 Hz), 7.30 (s, 1 H).

Triacetate 8: oil; ^{1}H NMR (360 MHz, DMSO-d_6) δ 2.20 (s, 3 H), 2.24 (s, 3 H), 2.27 (s, 3 H), 3.10 (m, 2 H), 3.29 (s, 3 H), 3.83 (s, 3 H), 3.88 (s, 3 H), 4.56 (m, 1 H), 4.84 (m, 1 H), 6.59 (s, 1 H), 6.83 (s, 1 H), 7.14 (s, 1 H), 7.25 (s, 1 H), 7.26 (d, 1 H, J = 1.8 Hz), 7.32 (dd, 1 H, J = 8.0, 1.8 Hz), 7.38 (d, 1 H, J = 8.0 Hz).

Hexaacetate 9: amorphous solid; ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.25 (s, 3 H), 2.26 (s, 3 H), 2.30 (s, 3 H), 2.31 (s, 3 H), 2.32 (s, 3 H), 2.37 (s, 3 H), 7.08 (s, 1 H), 7.13 (d, 1 H, J = 7.4 Hz), 7.30 (s, 1 H), 7.39 (d, 1 H, J = 1.9 Hz), 7.41 (d, 1 H, J = 1.9 Hz), 7.42 (s, 1 H), 7.45 (s, 1 H), 7.58 (s, 1 H), 9.32 (d, 1 H, J = 7.4 Hz); HRDEIMS, obsd (M^+) m/z 709.1416, $C_{37}H_{27}NO_{14}$ requires 709.1432.

Single-Crystal X-ray Analysis of Lamellarin E (2). Crystals of lamellarin E were grown from a methanol solution by slow evaporation. Crystals formed in the triclinic class with a = 8.165 (3), b = 13.228 (4), and c = 17.9892 (4) Å, α = 59.143 (14)°, β = 89.732 (16)°, γ = 110.495(15)°. The crystal density (1.3 g/cm^3) indicated that two units of composition $C_{29}H_{25}O_9N\cdot CH_3OH$ formed the unit cell. The space group had to be either P_1 (Z = 2) or $P\bar{1}$ (Z = 1).

All unique diffraction maxima with $2\theta < 114°$ were collected by using graphite-monochromated Cu Kα radiation (1.54178 Å) and variable speed, 1° ω scans. After correction for Lorentz, polarization, and background effects, 3040 reflections (83%) were judged observed ($F_o > 3\sigma(F_o)$). A phasing model was found in space group $P\bar{1}$ using the MULTAN series of programs.[17] All non-hydrogen atoms were found by recycling plausible molecular fragments. Hydrogen atoms were located on a ΔF synthesis following partial refinement. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and fixed isotropic hydrogens have converged to a current residual of 0.073 for the observed data. Additional crystallographic information is available as described in the paragraph entitled Supplementary Material Available at the end of this paper.

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Supplementary Material Available: Tables of fractional coordinates, thermal parameters, interatomic distances, and interatomic and torsional angles for lamellarin E (7 pages). Ordering information is given on any current masthead page.

(17) All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were FOBS, a data reduction program by G. D. Van Duyne, Cornell University, 1987; MULTAN80 and RANTAN80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1980; BLS78A, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a locally modified crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1987; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu and G. Van Duyne, Cornell University, 1985.

Sesterterpene Sulfates from a Sponge of the Family Halichondriidae

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A marine sponge of the family Halichondriidae from California contained a sulfated sesterterpene hydroquinone and five sulfated sesterterpenes. The structures of halisulfates 1–5 (**1–5**) were elucidated by interpretation of spectral data and a structure is proposed for halisulfate 6 (**6**).

Among the wide variety of secondary metabolites that have been isolated from marine sponges,[1] relatively few sulfate esters have been described. The most frequently encountered sulfate esters are the steroidal sulfates[2] and phenolic sulfates.[3] During a search for biologically active sponge metabolites, we have found five sulfated sesterterpene furans and a sulfated sesterterpene hydroquinone in a Californian sponge of the family Halichondriidae. In this paper we report the structural elucidation of a sulfated sesterterpene hydroquinone, halisulfate 1 (**1**), and five sulfated sesterterpene furans, halisulfates 2–6 (**2–6**) (Chart I).

The dark brown sponge was collected at −30 m in Scripps Canyon, La Jolla, CA. The dichloromethane-soluble material from a methanol extract was chromatographed on Sephadex LH-20 with 1:1 dichloromethane–methanol as eluant to obtain two fractions that inhibited *Staphylococcus aureus* and *Candida albicans*. Halisulfate 1 (**1**), mp >300 °C (darkens at ~200 °C), crystallized from the more polar fraction. The less polar fraction was separated on reversed-phase HPLC using 30% aqueous am-

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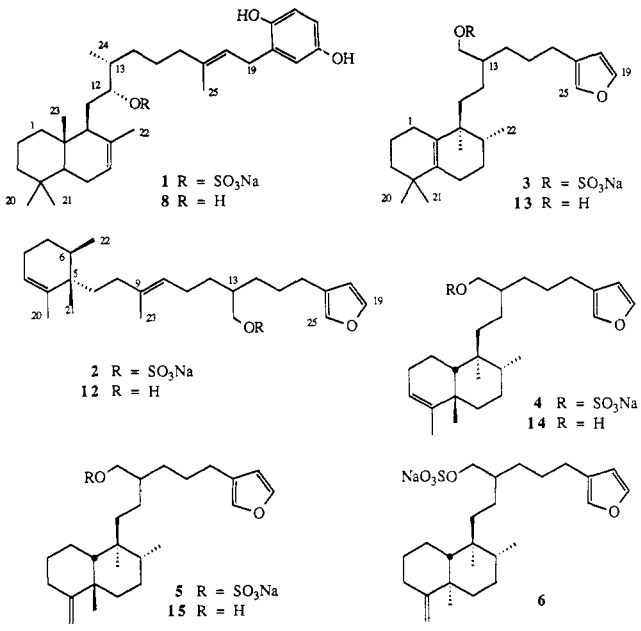
0022-3263/88/1953-4574$01.50/0

Chart I

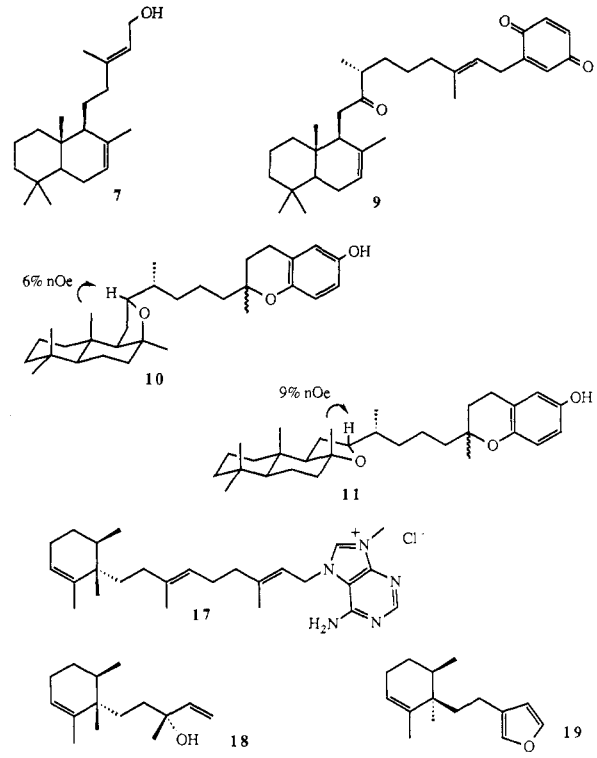


monium acetate solution (0.5 M) in methanol as eluant to obtain the halisulfate 2 (**2**), a 1:1 mixture of halisulfates 3 (**3**) and 4 (**4**), and a 3:1 mixture of halisulfates 5 (**5**) and 6 (**6**).

The high-resolution FAB mass spectrum of the halisulfate 1 (**1**) indicated a molecular formula of $C_{31}H_{47}O_6S$-Na. The infrared spectrum contained a broad hydroxyl band at 3200–3600 cm^{-1} and a strong sulfate band at 1250 cm^{-1}. Signals in the ^1H NMR spectrum at δ 6.42 (dd, 1 H, J = 8, 3 Hz), 6.56 (d, 1 H, J = 8 Hz), and 6.60 (d, 1 H, J = 3 Hz) suggested the presence of an alkyl-substituted hydroquinone. The ^{13}C NMR spectrum contained 10 signals in the sp^2 region that were assigned to the aromatic ring and two trisubstituted olefinic bonds. The ^1H NMR signals at δ 5.29 (br s, 1 H), 5.29 (t, 1 H, J = 7 Hz), and 1.67 (s, 6 H) confirmed the presence of two methyl-substituted trisubstituted olefins and a signal at 4.48 (d, 1 H, J = 5.4 Hz) suggested the presence of a secondary *O*-sulfate group. The olefinic triplet at δ 5.29 was coupled to a benzylic signal at 3.19 (d, 2 H, J = 7 Hz), suggesting a $C(CH_3)$=$CHCH_2Ar$ moiety. Four additional methyl signals at δ 0.70 (s, 3 H), 0.78 (s, 3 H), 0.86 (s, 3 H), and 0.91 (d, 3 H, J = 7 Hz) were observed. These data require that the hydroquinone must have a bicyclic ring system that contains a trisubstituted olefinic bond: comparison of the ^{13}C NMR spectrum with that of labda-7,13-dien-15-ol (**7**)[4] indicated that both molecules have the same bicyclic ring system. The 2D C–H correlation experiment together with a COLOC experiment allowed assignment of both the ^1H and ^{13}C NMR spectra and enabled us to propose two possible structures with a trans-trisubstituted olefin at C-17 and the *O*-sulfate at either C-12 or C-14.

Hydrolysis of the sulfate ester followed by oxidation of the resulting alcohol **8** with pyridinium chlorochromate gave ketone **9** (Chart II). The ^1H NMR spectrum of ketone **9** contained two overlapping signals at δ 2.60 (m, 2 H) due to the protons at C-9 and C-13: irradiation at δ 2.60 collapsed the methylene signals at δ 2.37 (dd, 1 H, J = 18, 4 Hz) and 2.45 (dd, 1 H, J = 18, 1 Hz) to an AB quartet, sharpened the olefinic methyl signal at δ 1.55, and collapsed the methyl signal at δ 1.07 (d, 3 H, J = 7 Hz) to

Chart II



a singlet. These data are consistent with the structure proposed for halisulfate 1 (**1**) in which the *O*-sulfate group is at C-12.

Treatment of the alcohol (**8**) with 3% *p*-toluenesulfonic acid on silica gel[5] in benzene at room temperature gave a 1:1 mixture of ethers **10** and **11**, each of which was a mixture of isomers at C-17, which resulted in doubling of the ^1H NMR signal due to the methyl group at C-17. However, the signals assigned to hydrogens about the tetrahydrofuran ring were unaffected by the stereochemistry at C-17 and the stereochemistry at C-12 could be determined by NOEDS measurements. In the ether **10**, the C-8 methyl group is equatorial and a 6% enhancement of the C-12 proton signal at δ 3.50 was observed on irradiation of the C-10 methyl signal at δ 0.91. In the ether **11**, irradiation of the axial C-8 methyl signal at δ 1.12 resulted in a 9% enhancement of the C-12 proton signal at δ 3.90. Since the C-9 proton is axial (W-coupling to C-10 methyl), the stereochemistry at C-12 must be as shown. The stereochemistry at C-13 has not been firmly established but we prefer 12*R**,13*R** based on the small coupling constant ($J_{12,13}$ < 1 Hz) which is appropriate for a cis relationship of the protons in a preferred conformation about the 12–13 bond that places the two largest groups in a trans arrangement.[6]

The high resolution FAB mass spectra of halisulfate 2 (**2**) and the mixtures of halisulfates 3 (**3**) and 4 (**4**) and halisulfates 5 (**5**) and 6 (**6**) indicated that all of these compounds were isomeric, each having the molecular formula $C_{25}H_{39}O_5SNa$. The infrared, ^1H NMR, and ^{13}C NMR spectra indicated the presence of a sulfate ester of primary alcohol and a 3-substituted furan in each compound. The ^1H NMR spectra also contained an unusual signal at δ 6.70–6.85 (br s, 2 H, D_2O exchangeable) that was eventually assigned to a molecule of water associated with the sulfate groups.

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(6) No absolute configuration should be implied from these data.

Table I. ^{13}C and ^{1}H NMR Spectral Data for Halisulfate 1 (1) Compared with the Relevant ^{13}C NMR Spectral Data for Labda-7,13-dien-15-ol (7)

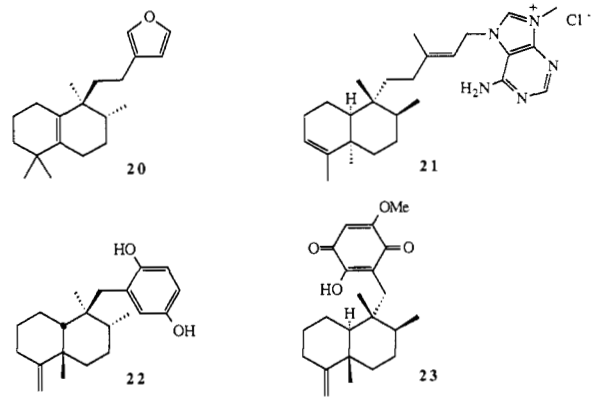
	1		7, $\delta(^{13}C)$,
C no.	$\delta(^{13}C)$, ppm	$\delta(^{1}H)$, ppm (mult, H, J)	ppm
1	39.8	1.70 (m, 1 H), 1.23 (m, 1 H)	39.2
2	19.9	1.43 (m, 1 H)	19.9
3	43.3	1.47 (m, 1 H), 1.08 (m, 1 H)	43.3
4	33.6		33.0
5	52.0	1.24 (m, 1 H)	54.6
6	24.9	1.93 (m, 2 H)	25.7
7	123.9	5.29 (br s, 1 H)	122.4
8	136.8		135.3
9	49.3	2.23 (m, 1 H)	50.2
10	37.4		36.9
11	27.7	1.60 (m, 2 H)	
12	85.7	4.48 (dd, 1 H, J = 5.4, 1 Hz)	
13	38.2	2.30 (m, 1 H)	
14	34.3	1.33 (m, 1 H), 1.12 (m, 1 H)	
15	27.4	1.38 (m, 1 H)	
16	41.0	2.00 (t, 2 H, J = 8 Hz)	
17	136.7		
18	124.8	5.29 (br t, 1 H, J = 7 Hz)	
19	29.2	3.16 (d, 2 H, J = 7 Hz)	
20	33.7	0.78 (s, 3 H)	33.2
21	22.5	0.86 (s, 3 H)	21.9
22	23.0	1.67 (br s, 3 H)	22.3
23	14.2	0.70 (s, 3 H)	13.6
24	13.7	0.91 (d, 3 H, J = 7 Hz)	
25	16.3	1.67 (br s, 3 H)	
1′	130.1		
2′	148.6		
3′	117.5	6.56 (d, 1 H, J = 8.Hz)	
4′	114.8	6.42 (dd, 1 H, J = 8, 3 Hz)	
5′	150.8		
6′	118.0	6.60 (d, 1 H, J = 3 Hz)	

Acid-catalyzed hydrolysis of a mixture of halisulfates allowed four of the corresponding primary alcohols **12–15** to be isolated. Examination of the ^{13}C NMR data (Table II) suggested that the primary alcohols **12–15** all possessed the same ten-carbon unit, starting at C-12, that contained both the furan and primary alcohol moieties. The remaining $C_{15}H_{25}$ portions of the sesterterpenes **12–15** were all familiar from prior studies of marine metabolites.

The ^{1}H NMR spectrum of the alcohol **12** contained methyl signals at δ 1.57 (br s, 6 H), 0.87 (d, 3 H, J = 7 Hz), and 0.86 (s, 3 H). The allylic methyl signal was coupled to two signals at 5.10 (t, 1 H, J = 7 Hz) and 5.42 (br s, 1 H) that were due to olefinic protons in a linear isoprenoid chain and a cyclohexene ring, respectively. These data suggested a $C_{15}H_{25}$ portion identical with that found in ageline A (**17**)[7] and comparison of the ^{13}C NMR spectra for the two compounds (Table II) showed an excellent correlation that confirmed the presence of the 1-alkyl-1,2,6-trimethyl-2-cyclohexene ring system. The ^{1}H NMR chemical shifts of the methyl signals at C-5 and C-6 require the cis stereochemistry found in ageline A (**17**, δ 0.85, 0.85) and striatol (**18**, δ 0.87, 0.88)[8] rather than the trans stereochemistry of micricionin (**19**, δ 1.08, 0.99).[9] The relative stereochemistry at the remaining methine carbon (C-13) could not be determined in any of the primary alcohols **12–15**.[6]

The $C_{15}H_{25}$ portion of alcohol **13** was bicyclic and contained a tetrasubstituted olefin [^{13}C NMR δ 132.6 (s), 136.8 (s)], four methyl groups [^{1}H NMR δ 0.80 (s, 3 H), 0.82 (d, 3 H, J = 7 Hz), 0.95 (s, 3 H), 0.97 (s, 3 H)], two quaternary carbons [^{13}C NMR δ 34.5 (s), 40.6 (s)], and one methine carbon [33.6 (d)]. These data, particularly the ^{13}C NMR spectrum (Table II), were compatible with the bicyclic ring system found in 5,10-dehydroambliol B (**20**) (Chart III), the stereochemistry of which was known from the X-ray study of ambliol B.[10] The stereochemistry at C-8 and C-9 was confirmed by a difference decoupling experiment that showed H-8 to be axial (J = 10, 7, 7, 7, 2 Hz) and a NOEDS experiment in which irradiation of the C-9 methyl group (δ 0.80) caused enhancements of the H-1α (δ 2.00, 18%) and H-7α (δ 1.65, 20%).[6]

Chart III



The alcohol **14** contained the *cis*-clerodane ring system. The ^{1}H and ^{13}C NMR data indicated the presence of a trisubstituted olefin [δ 5.27 (br s, 1 H); δ 123.1 (d), 139.9 (s)], four methyl groups [δ 0.74 (d, 3 H, J = 7 Hz), 0.79 (s, 3 H), 1.02 (s, 3 H), 1.68 (br s, 3 H); δ 33.0 (q), 19.7 (q), 17.4 (q), 16.0 (q)], as well as two methine [δ 37.3 (d), 44.6 (d)] and two quaternary [δ 36.9 (s), 40.1 (s)] carbons. The ^{13}C NMR data are compared with those of agelasine A (**21**)[11] in Table II. In a NOEDS experiment, irradiation of the C-5 methyl signal at δ 1.02 resulted in the enhancement of signals at 1.98 (br dt, 1 H, J = 12, 6 Hz, 16%) and 1.32 (br d, 1 H, J = 6 Hz, 10%) assigned to H-1β and H-10β, respectively. A difference decoupling experiment again indicated H-8 [δ 1.43 (m, 1 H, J = 11, 7, 7, 7, 3 Hz)] to be axial.[6]

The ^{1}H and ^{13}C NMR spectra of alcohol **15** were similar to those of alcohol **14** except that the signals for the 3,4-trisubstituted olefin were replaced by those assigned to a 4,20-methylene group [δ 4.72 (br s, 1 H), 4.71 (br s, 1 H); δ 151.0 (s), 105.7 (t)]. Comparison of the ^{13}C NMR spectra of alcohol **15** and arenerol (**22**)[12] (Table II) indicated that alcohol **15** was also a *cis*-clerodane. The cis geometry was confirmed by a NOEDS experiment in which irradiation of the C-5 methyl signal at δ 1.08 (s, 3 H) caused enhancements of the C-10 proton signal at 1.38 (br d, 1 H, J = 5 Hz, 8%), the H-1β signal at 1.98 (tt, 1 H, J = 13, 5 Hz, 34%), and the H-3β signal at 2.15 (m, 1 H, 17%).[6]

Comparison of the NMR spectra of halisulfate 2 (**2**) and alcohol **12** revealed that the only differences were those expected as a result of hydrolysis of a sulfate ester and that the carbon skeleton and stereochemistry were identical. The NMR spectra of the mixture of halisulfates 3 (**3**) and 4 (**4**) were entirely consistent with a 1:1 mixture of the sulfate esters of alcohols **13** and **14**. The NMR spectra of the mixture of halisulfates 5 (**5**) and 6 (**6**) indicated a 3:1

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Table II. Comparison of ^{13}C NMR Spectral Data for Alcohols 12–15 with Those of Model Compounds 17 and 20–22

C no.	12	17	13	20	14	21	15	22
1	25.5	25.5	27.3	27.9	17.8	17.6	21.2	22.6
2	27.1	27.0	20.0	19.9	28.8	28.8	27.5	27.6
3	123.8	122.4	40.0	40.3	123.1	123.1	31.8	32.0
4	139.6	139.5	34.5	4.7	139.9	139.7	151.0	153.5
5	40.4	40.3	132.6	132.9	40.1	40.2	43.6	43.6
6	33.2	33.1	5.8	26.2	37.8	36.1	38.3	37.6
7	34.2	34.1	25.1	25.6	24.1	24.0	23.2	25.0
8	35.3	35.1	33.5	33.6	37.3	37.4	38.3	37.6
9	136.3	136.9	40.6	41.0	36.9	37.7	39.5	39.5
10	124.0	124.0	136.8	137.5	44.6	45.7	46.8	46.5
11	30.6		30.5		25.0		23.5	
12	31.0		33.6		35.0		35.4	
13	40.0		41.4		41.2		41.3	
14	25.1		25.1		25.1		25.1	
15	27.3		27.4		27.5		27.5	
16	30.6		30.5		30.6		30.7	
17	125.1		125.1		125.1		125.1	
18	110.9		111.0		111.0		111.0	
19	138.8		138.8		138.8		138.9	
20	15.8	15.8	29.2	29.4	19.7	19.7	105.7	105.8
21	19.2	19.2	21.3	21.3	33.0	33.0	33.0	33.0
22	21.1	21.0	27.7	27.6	16.0	16.0	16.0	18.1
23	16.3	16.2	16.1	16.3	17.4	17.3	19.9	19.1
24	65.5		65.9		65.7		65.8	
25	142.7		142.7		142.7		142.7	

mixture of compounds, in which the major component was the sulfate ester of alcohol **15**. The ^1H NMR signals of the minor constituent at δ 4.49 (br s, 0.5 H), 1.02 (s, 0.75 H), 0.78 (s, 0.75 H), and 0.72 (d, 0.75 H, J = 7 Hz) were very similar to those that might be expected of the *trans*-clerodane ring system [cf. ilimaquinone (**23**)].[13] Unfortunately, neither halisulfate 6 (**6**) nor the corresponding alcohol were obtained in pure form so that the structural assignment of halisulfate 6 (**6**) must be regarded as tentative.

Halisulfate 1 (**1**) inhibited the growth of *Staphylococcus aureus* and *Candida albicans* at 5 μg/disk and of *Bacillus subtilis* at 50 μg/disk in standard in vitro antimicrobial assays, inhibited cell division in fertilized sea urchin eggs (*Lytechinus pictus*, 70% inhibition) at a concentration of 8 μg/mL,[14] and caused 100% inhibition of the enzyme phospholipase A_2 at a concentration of 16 μg/mL.[14] Halisulfates 2–5 (**2–5**), assayed as mixtures, all showed similar antimicrobial activity against *S. aureus*, *C. albicans*, and *B. subtilis* at 20 μg/disk but were inactive in the sea urchin assay. A mixture of halisulfates 2–4 (**2–4**) inhibited PMA-induced inflammation in the mouse ear edema assay and inhibited PLA_2 in an in vitro assay.[14] In contrast with alcohol **13**, alcohol **14** inhibited the growth of *S. aureus*, *E. coli*, and two marine bacteria, *Vibrio anguillarum* and *Benechea harveyi* 392, at 50 μg/disk.

Experimental Section

Extraction and Chromatography. The dark brown sponge was collected at −30 m in Scripps Canyon, La Jolla, CA, and was immediately frozen. The freeze-dried sponge (8.6 g) was sliced and soaked in methanol for 3 days. The solvent was filtered and removed in vacuo. The residue was partitioned between dichloromethane and water. The organic extracts were dried over sodium sulfate and evaporated to obtain a dark brown oil (1.64 g). The oil was chromatographed on Sephadex LH-20 with 1:1 methanol–dichloromethane as eluant to obtain two antimicrobial fractions. Fraction B gave crystals of halisulfate 1 (**1**, 219.9 mg, 2.6% dry weight) from dichloromethane. Fraction A was rechromatographed on Sephadex LH-20 with 2:1:1 hexane–methanol–dichloromethane as eluant to obtain two antimicrobial fractions. These were purified by HPLC on ODS Partisil (70% methanol–30% 0.5 M NH_4OAc) yielding halisulfate 2 (**2**), a 1:1 mixture of halisulfates 3 (**3**) and 4 (**4**), and a 3:1 mixture of halisulfates 5 (**5**) and 6 (**6**).

Halisulfate 1 (1): white needles, $[\alpha]_D$ −27.3° (*c* 0.01, MeOH); IR (KBr) 3600–3100, 1250 cm^{-1}; ^{13}C NMR (CD_3OD) see Table I; ^1H NMR (CD_3OD) see Table I; FABMS, obsd m/z 593.2910, $C_{31}H_{47}SO_6Na$ + Na requires 593.2889.

Halisulfate 2 (2): white solid; IR (KBr) 3600–3100, 1670, 1640, 1250, 985 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 1 H), 7.24 (br s, 1 H), 6.85 (br s, 2 H, D_2O exchangeable), 6.27 (br s, 1 H), 5.42 (br s, 1 H), 5.08 (br t, 1 H, J = 6 Hz), 3.95 (br d, 2 H, J = 5.4 Hz), 2.41 (t, 2 H, J = 7.6 Hz), 1.60 (s, 6 H), 0.87 (d, 3 H, J = 7.2 Hz), 0.86 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 142.6 (d), 138.8 (d), 137.0 (s), 132.6 (s), 125.1 (s), 111.1 (d), 71.2 (t), 40.5 (s), 40.4 (t), 37.3 (d), 34.5 (s), 33.5 (d), 30.5 (t), 29.2 (q), 27.8 (q), 27.2 (t), 27.0 (t), 25.8 (t), 25.0 (t), 24.9 (t), 21.3 (q), 20.0 (q), 16.2 (q).

Mixture of halisulfates 3 (3) and 4 (4): white solid; IR ($CHCl_3$) 3600–3100, 1670, 1640, 1250, 985 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 1 H), 7.22 (br s, 1 H), 6.78 (br s, 2 H, D_2O exchangeable, 6.24 (br s, 1 H), 5.42 (br s, 0.5 H), 3.92 (m, 2 H), 2.40 (t, 2 H, J = 6 Hz), 1.57 (br s, 1.5 H), 0.96 (s, 1.5 H), 0.94 (s, 1.5 H), 0.86 (s, 1.5 H), 0.85 (s, 1.5 H), 0.81 (d, 1.5 H, J = 7 Hz), 0.80 (d, 1.5 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 142.6 (d), 138.8 (d), 137.0 (s), 132.6 (s), 125.1 (s), 111.1 (d), 71.2 (t), 40.5 (s), 40.4 (t), 37.3 (d), 34.5 (s), 33.5 (d), 30.5 (t), 29.2 (q), 27.8 (q), 27.2 (q), 27.0 (t), 25.8 (t), 25.0 (t), 24.9 (t), 21.3 (q), 20.0 (q), 16.2 (q).

Mixture of halisulfates 5 (5) and 6 (6): white solid; IR ($CHCl_3$) 3600–3100, 1670, 1640, 1350, 985 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33 (br s, 1 H), 7.21 (br s, 1 H), 6.80 (br s, 2 H, D_2O exchangeable), 6.26 (br s, 1 H), 4.72 (s, 0.75 H), 4.70 (s, 0.75 H), 4.49 (br s, 0.5 H), 3.90 (m, 2 H), 2.47 (m, 0.75 H), 2.39 (t, 2 H, J = 6 Hz), 1.12 (s, 2.25 H), 1.02 (s, 0.75 H), 0.80 (s, 2.25 H), 0.78 (s, 0.75 H), 0.75 (d, 2.25 H, J = 7 Hz), 0.72 (d, 0.75 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 142.6 (d), 138.8 (d), 137.0 (s), 132.6 (s), 125.1 (s), 111.1 (d), 71.2 (t), 40.5 (s), 40.4 (t), 37.3 (d), 34.5 (s), 33.5 (d), 30.5 (t), 29.2 (q), 27.8 (q), 27.2 (t), 27.0 (t), 25.8 (t), 25.0 (t), 24.9 (t), 21.3 (q), 20.0 (q), 16.2 (q).

Hydrolysis of Halisulfate 1 (1). Hydrochloric acid (1 N, 0.5 mL) was added to solution of the hydroquinone **1** (20 mg) in methanol (5 mL) and the mixture was refluxed for 2.5 h. The reaction mixture was cooled to room temperature and ethyl acetate (15 mL) was added. This solution was washed with water (2 × 15 mL) and dried over anhydrous sodium sulfate, and the solvent was removed. The residue was purified by HPLC on Partisil (5% methanol in dichloromethane) to obtain the alcohol **8** (14.1 mg,

(13) Luibrand, R. T.; Erdman, T. R.; Vollmer, J. J.; Scheuer, P. J.; Finer, J.; Clardy, J. *Tetrahedron* **1979**, *35*, 609. Capon, R. J.; MacLeod, J. K. *J. Org. Chem.* **1987**, *52*, 5059.

(14) Data from the laboratory of Robert S. Jacobs.

99% yield) as a colorless oil: IR ($CHCl_3$) 3600–3200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.68 (d, 1 H, J = 3.2 Hz), 6.65 (d, 1 H, J = 8.6 Hz), 6.57 (dd, 1 H, J = 8.6, 3.2 Hz), 5.40 (br s, 1 H), 5.33 (br t, 1 H, J = 8.3 Hz), 4.73 (br s, 1 H, D_2O exchangeable), 3.49 (m, 1 H), 3.33 (dd, 1 H, J = 18, 4.3 Hz), 3.26 (dd, 1 H, J = 18, 4.0 Hz), 2.12 (br t, 2 H, J = 6.5 Hz), 2.00 (m, 1 H), 1.98 (m, 1 H), 1.67 (br s, 3 H), 1.63 (br s, 3 H), 0.92 (d, 3 H, J = 6.8 Hz), 0.87 (s, 3 H), 0.86 (s, 3 H), 0.74 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 150.0 (s), 147.5 (s), 137.9 (s), 135.0 (s), 128.2 (s), 122.7 (d), 122.0 (d), 116.3 (d), 116.0 (d), 113.5 (d), 77.4 (d), 50.3 (d), 50.0 (d), 42.2 (t), 40.1 (d), 39.6 (t), 36.3 (s), 33.1 (q), 32.3 (t), 31.3 (t), 28.4 (t), 24.6 (t), 23.8 (t), 22.5 (q), 21.9 (q), 18.8 (t), 15.6 (q), 15.5 (q), 13.6 (q).

Oxidation of Alcohol 8 to Ketone 9. The alcohol **8** (14 mg) was dissolved in dichloromethane (2 mL) and pyridinium chlorochromate (20 mg) was added. This mixture was stirred at room temperature for 2 h, taken up in diethyl ether (25 mL), and filtered through Celite. The solvent was removed and the residue was purified by HPLC on Partisil (diethyl ether) to obtain the ketone **9** (9.2 g, 64% yield) as a colorless oil: IR ($CHCl_3$) 1710, 1660, 1600 cm^{-1}; UV (hexane) 310 nm (ϵ 4700), 245 (9170), 213 (5080); ^1H NMR ($CDCl_3$) δ 6.80 (d, 1 H, J = 10 Hz), 6.75 (br d, 1 H, J = 10 Hz), 6.55 (br s, 1 H), 5.42 (br s, 1 H), 5.15 (t, 1 H, J = 6.8 Hz), 3.12 (d, 2 H, J = 6.8 Hz), 2.60 (m, 2 H), 2.45 (dd, 1 H, J = 18, 12 Hz), 2.37 (dd, 1 H, J = 18, 4 Hz), 2.03 (m, 2 H), 2.00 (m, 1 H), 1.88 (m, 1 H), 1.61 (br s, 3 H), 1.59 (br s, 3 H), 1.09 (d, 3 H, J = 7.2 Hz), 0.88 (s, 3 H), 0.87 (s, 3 H), 0.75 (s, 3 H); HRMS, m/z 464.3290, $C_{31}H_{44}O_3$ requires 464.3290.

Cyclization of Alcohol 8 To Obtain Ethers 10 and 11. The alcohol **8** (7.0 mg) was dissolved in dry benzene (3 mL) containing silica gel coated with 3% *p*-toluenesulfonic acid and the suspension was stirred at room temperature under nitrogen for 12 h. The mixture was then filtered through cotton and purified by HPLC on Partisil (1:1 diethyl ether–hexane) to obtain the ether **10** (2.4 mg, 34% yield) and the ether **11** (1.8 mg, 25% yield).

Ether 10: ^1H NMR ($CDCl_3$) δ 6.64 (d, 1 H, J = 8.3 Hz), 6.53 (dd, 1 H, J = 8.3, 2.9 Hz), 6.53 (d, 1 H, J = 2.9 Hz), 3.50 (ddd, 1 H, J = 12, 7.2, 1.8 Hz), 2.69 (t, 2 H, J = 6.5 Hz), 2.02 (dd, 1 H, J = 9, 5 Hz), 1.87 (dd, 1 H, J = 13, 6 Hz), 1.80 (dd, 1 H, J = 13, 8 Hz), 1.24 (s, 3 H), 1.12 (s, 1.5 H), 1.11 (s, 1.5 H), 0.91 (s, 3 H), 0.86 (s, 6 H), 0.78 (d, 1.5 H, J = 7 Hz), 0.78 (d, 1.5 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 130.8, 128.8, 117.8, 115.4, 114.5, 111.1, 83.0, 81.5, 68.2, 59.3, 51.3, 42.2 (2 C), 40.8, 40.7, 39.9, 39.8, 38.8, 36.2, 35.3, 34.7, 33.4, 33.1, 32.2, 32.0, 31.0, 30.5, 24.0, 23.8, 23.5, 23.4, 22.0, 21.1, 21.0, 18.5 (2 C), 15.7, 15.4 (several carbon atoms give 2 signals); HRMS, m/z 468.3597, $C_{31}H_{46}O_3$ requires 468.3603.

Ether 11: ^1H NMR ($CDCl_3$) δ 6.65 (d, 1 H, J = 8.6 Hz), 6.57 (dd, 1 H, J = 8.6, 2.9 Hz), 6.53 (d, 1 H, J = 2.9 Hz), 3.90 (m, 1 H), 2.69 (t, 2 H, J = 6.5 Hz), 1.91 (dt, 1 H, J = 11.5, 2.9, 2.9 Hz), 1.25 (s, 3 H), 1.12 (s, 3 H), 0.87 (s, 3 H), 0.84 (d, 1.5 H, J = 7 Hz), 0.83 (d, 1.5 H, J = 7 Hz), 0.82 (s, 3 H), 0.81 (s, 3 H); HRMS, m/z 468.3600, $C_{31}H_{46}O_3$ requires 468.3603.

Hydrolysis of Halisulfates 2–6. HCl (1 N, 1 mL) was added to a solution of a mixture of furans **2–6** (61.3 mg) in methanol (10 mL) and the mixture was refluxed for 2 h. After cooling to room temperature, the solution was taken up in dichloromethane (30 mL) and washed with water (2 × 30 mL). The organic solubles were dried over anhydrous sodium sulfate, the solvent removed, and the residue purified by HPLC on Partisil (10% ethyl acetate in hexane), giving the alcohols **12** (4.0 mg), **13** (1.0 mg), **14** (2.0 mg), and **15** (2.8 mg).

Alcohol 12: colorless oil; IR ($CHCl_3$) 3600–3100, 1500, 1460, 1380, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 1 H), 7.21 (br s, 1 H), 6.27 (br s, 1 H), 5.42 (br s, 1 H), 5.10 (br t, 1 H, J = 7 Hz), 3.56 (d, 2 H, J = 4 Hz), 2.41 (t, 2 H, J = 8 Hz), 2.00 (br q, 2 H, J = 7 H), 1.57 (s, 6 H), 0.87 (d, 3 H, J = 7.2 Hz), 0.86 (s, 3 H); ^{13}C NMR ($CDCl_3$) see Table II; HRMS, m/z 372.3028, $C_{25}H_{40}O_2$ requires 372.3028.

Alcohol 13: colorless oil; IR ($CHCl_3$) 3600–3200, 1500, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 1 H), 7.21 (br s, 1 H), 6.27 (br s, 1 H), 3.57 (d, 2 H, J = 4 Hz), 2.42 (t, 2 H, J = 8 Hz), 2.00 (m, 1 H), 1.95 (m, 3 H), 1.65 (m, 1 H), 1.34 (dqd, 1 H, J = 10, 7, 2 Hz), 0.97 (s, 3 H), 0.95 (s, 3 H), 0.82 (d, 3 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) see Table II; HRMS, m/z 372.3028, $C_{25}H_{40}O_2$ requires 372.3028.

Alcohol 14: colorless oil; IR ($CHCl_3$) 3600–3200, 1500, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 1 H), 7.21 (br s, 1 H), 6.27 (br s, 1 H), 5.27 (br s, 1 H), 3.57 (d, 2 H, J = 4 Hz), 2.42 (t, 2 H, J = 8 Hz), 2.10 (m, 1 H), 2.00 (m, 2 H), 1.68 (s, 3 H), 1.43 (dqd, 1 H, J = 11, 7, 3 Hz), 1.35 (m, 1 H), 1.02 (s, 3 H), 0.79 (s, 3 H), 0.74 (d, 3 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) see Table II; HRMS, m/z 372.3030, $C_{25}H_{40}O_2$ requires 372.3028.

Alcohol 15: colorless oil; IR ($CHCl_3$) 3600–3200, 1500, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 1 H), 7.22 (br s, 1 H), 6.27 (br s, 1 H), 4.72 (d, 1 H, J = 2.5 Hz), 4.71 (d, 1 H, J = 2.5 Hz), 3.55 (d, 2 H, J = 4 Hz), 2.50 (m, 1 H), 2.42 (t, 2 H, J = 8 Hz), 2.17 (m, 1 H), 2.09 (m, 1 H), 1.42 (dqd, 1 H, J = 10, 7, 2 Hz), 1.13 (s, 3 H), 0.81 (s, 3 H), 0.74 (d, 3 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) see Table II; HRMS, m/z 372.3028, $C_{25}H_{40}O_2$ requires 372.3028.

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