J = 7.4 Hz); CD (aqueous HCl, pH 2.5), $[\theta]_{209}$ +2950. 2(R)-Hydroxy-3(S)-methylpentanoic acid (D-alloisoleucic acid) was eluted second: ^{1}H NMR ($CDCl_3$) δ 4.222 (1 H, d, J = 6.4 Hz), 2.099 (1 H, m), 1.63 (1 H, dqd), 1.35 (1 H, dqd), 1.051 (3 H, d, J = 6.8 Hz), 0.926 (3 H, t, J = 7.5 Hz); negative CD curve at 209 nm in aqueous HCl.

The hydroxy acid from the acid hydrolyzate of majusculamide C had a ^{1}H NMR spectrum that was identical with that of isoleucic acid and a positive CD curve, $[\theta]_{209}$ +2990 (aqueous HCl, pH 2.5).

L-*N*-Methylisoleucine. Sublimed synthetic amino acid[10] showed a positive CD curve, $[\theta]_{211}$ +6880 (0.5N HCl). The literature[12] reports $[\theta]_{212}$ +5146. The crude amino acid from the acid hydrolyzate of majusculamide C showed a positive Cotton effect, $[\theta]_{211}$ +4140 (0.5 N HCl).

Acknowledgment. This research was supported by Grant CHE79-25416 from the Natonal Science Foundation. High-frequency NMR studies at the University of Hawaii were made possible by NSF Grant CHE81-00240. We thank Dr. Kenneth Straub at the University of California Bio-organic, Biomedical Mass Spectrometry Facility (A. L. Burlingame, Director), supported by NIH Grant RR00719, for determining the SIMS and field-desorption mass spectra.

Registry No. 1, 83712-17-8; 4, 79851-67-5; ethyl 4-acetamido-2,2-dimethyl-3-oxopentanoate, 87883-44-1; 2(S)-hydroxy-3(S)-methylpentanoic acid, 51576-04-6.

Arenarol and Arenarone: Sesquiterpenoids with Rearranged Drimane Skeletons from the Marine Sponge *Dysidea arenaria*

Francis J. Schmitz,* Vijai Lakshmi, Douglas R. Powell, and Dick van der Helm*

Department of Chemistry, University of Oklahoma, Norman, Oklahoma 73019

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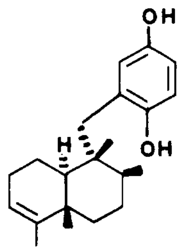
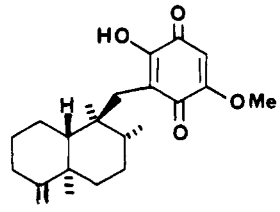
Two new sesquiterpenoids, arenarol (**3a**) and arenarone (**4**), having identical rearranged drimane skeletons bearing hydroquinol and hydroquinone moieties, respectively, are reported from the Pacific sponge *Dysidea arenaria*. The structure of arenarol was determined by X-ray analysis of its diacetate which crystallizes in the space group $P2_12_12_1$ with unit-cell dimensions (138 K) a = 9.964 (5), b = 6.81 (2), and c = 33.33 (5) Å. The crystal structure was determined from 2268 data. The final R value is 0.065. Arenarol was chemically correlated with arenarone by silver oxide oxidation. Detailed 400-MHz ^{1}H NMR analysis of arenarol assisted by 2-D J-resolved and 2-D homocorrelation spectroscopy is tabulated.

Marine algae and sponges have yielded a variety of compounds having a hydroquinone moiety attached to a terpenoid skeleton, the latter varying from sesqui-, di-, or sesterterpene units and also from acylic propyprenyl chains.[1] Included among these are two sesquiterpenes which have enantiomeric rearranged drimane skeletons, avarol[2] (**1**) from the Mediterranean sponge *Dysidea avara* and illimaquinone[3] (**2**) from the Pacific sponge *Hippiospongia metachromia* (Chart I). In our continuing search[4] for cytotoxic compounds from marine organisms, we have isolated from the Pacific sponge *Dysidea arenaria* a mildly cytotoxic hydroquinone–quinone pair of compounds, arenarol (**3a**) and arenarone (**4**), having the same rearranged sesquiterpene skeleton as avarol and illimaquinone, but with *cis*- rather than *trans*-decalin stereochemistry. In this paper we describe the structures of the new compounds as established by X-ray analysis and chemical interconversion.

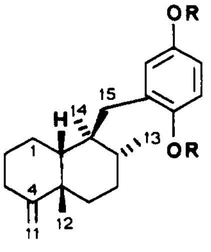
Chart I



1



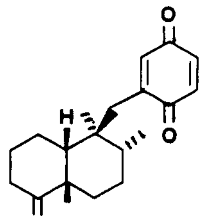
2



3a R = H

3b R = Ac

3c R = CH_3



4

Specimens were frozen shortly after collection at -9 M at Truk Island lagoon and kept frozen until the workup. Chloroform–methanol (1:1) extracts of freeze–dried specimens were partitioned between chloroform and water, and the chloroform solubles were chromatographed in chloroform–methanol over Sephadex LH-20. Selected fractions were purified further by column chromatography over silica gel and finally by high-pressure liquid chromatography (HPLC) over a C_{18} bonded-phase column with 15%

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[1] Higa, T. In "Marine Natural Products: Chemical and Biological Perspectives"; Scheuer, P. J., Ed.; Academic Press: New York, 1981; Vol. IV, Chapter 3.

[2] Minale, L.; Riccio, R.; Sodano, G. *Tetrahedron Lett.* **1974**, 3401. de Rosa, S.; Minale, L.; Riccio, R.; Sodano, G. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1408.

[3] Luibrand, R. T.; Erdman, T. R.; Vollmer, J. J.; Scheuer, P. J.; Finer, J.; Clardy, J. *Tetrahedron* **1979**, *35*, 609.

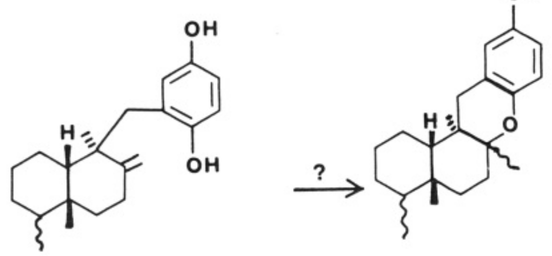
[4] Cf.: Schmitz, F. J.; Michaud, D. P.; Schmidt, P. G. *J. Am. Chem. Soc.* **1982**, *104*, 6415. Schmitz, F. J.; Prasad, R. S.; Gopichand, Y.; Hossain, M. B.; van der Helm, D. *J. Am. Chem. Soc.* **1981**, *103*, 2467.

0022-3263/84/1949-0241$01.50/0

aqueous methanol to give pure arenarol [**3a**: mp 128–130 °C; $[\alpha]_D$ +19° (*c* 0.1, $CHCl_3$)] and **4**: yellow oil; $[\alpha]_D$ +8.3° (*c* 0.18, $CHCl_3$). Molecular formulas for **3a** and **4** of $C_{21}H_{30}O_2$ and $C_{21}H_{28}O_2$, respectively, were established by combustion and mass spectral data.

The predominant isomer **3a** showed hydroxyl absorption in the infrared (3380 cm^{-1}) and UV absorption (MeOH) at 220 nm (ϵ 4085) and 293 (2723), compatible with a hydroquinone structure,[2] and readily formed a diacetate, **3b**. In its ^1H NMR spectrum **3a** showed two quaternary methyl signals (δ 0.93 and 1.06), a methyl doublet (δ 0.96), an AB quartet (14 Hz, d's at δ 2.52 and 2.72), an exocyclic methylene absorption (δ 4.71, 4.72, ea 1 H), and a complex 3-proton aromatic absorption (δ 6.55–6.70). The molecular formula and these spectral features indicated that arenarol (**3a**) contained a monosubstituted hydroquinone unit linked to a sesquiterpene unit similar to that of avarol (**1**),[2] but with an exocyclic methylene group as found in illimaquinone (**2**)[3] or zonarol.[5] This conclusion was also supported by the mass spectrum of **3a** which showed very dominant fragmentation with loss of $C_7H_7O_2$ corresponding to a hydroquinone unit plus a benzylic methylene group as is present in **1**. In order to establish whether **3a** and **1** might be merely double bond isomers, we methylated arenerol (**3a**) (CH_3I/K_2CO_3), and the product, **3c**, was subjected to catalytic hydrogenation (Pt). Of the several reduction products isolated, none had ^1H NMR spectral properties identical with those of dihydroavarol dimethyl ether.[2] A more detailed ^1H NMR analysis of **3a** revealed that the quaternary methyl signal at δ 0.92 was geminal to the benzylic methylene group [nuclear Overhauser enhancement (NOE) of the methylene signals by irradiation at δ 0.92] and that as in **1** and **2** this quaternary methyl group was trans to the C-10 proton (δ 1.38, br d, J = 6.6 Hz; irradiation at δ 1.38 sharpens the δ 0.92 signal). However, the C-10 proton experienced an NOE from irradiation of the second quaternary methyl (δ 1.06), indicating that arenarol had a cis-fused ring system in contrast to the trans-fused arrangements in **1** and **2**. Thus the tentative structures i and **3a** (undefined stereochemistry at C-8) emerged as candidates for arenarol.

Detailed ^1H NMR decoupling studies at 300 MHz indicated that a signal (δ 1.84) assignable to a proton β to the exocyclic methylene group was more compatible with a proton at C-2 in **3a** than at C-6 in i, thus leading to a preference for structure **3a**. However, acid treatment (C_6H_6, *p*-TSOH, room temperature overnight; reflux $^1/_2$ h) of arenarol yielded a single new product (60% yield) isomeric with **3a**. The ^1H NMR spectrum of this isomeric compound was compatible with a structure such as ii which would result from the expected acid catalyzed cyclization of i.[6,7] To resolve these conflicting data and clarify the stereochemistry of the secondary methyl group in arenarol, we carried out X-ray analysis of the derived diacetate **3b**.



i ii

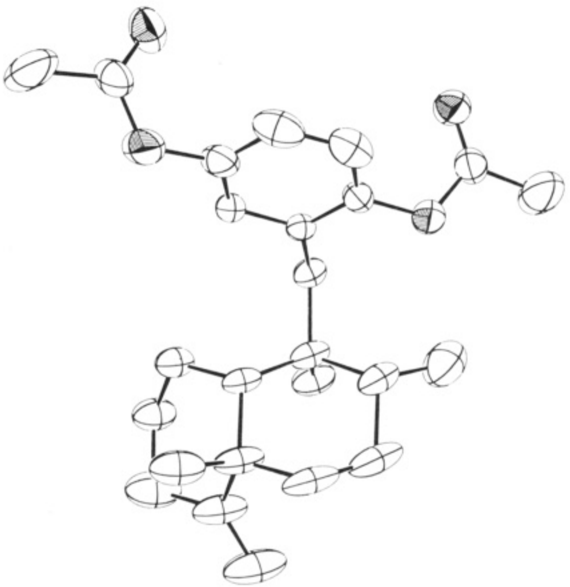


Figure 1. Perspective view of **3b**. The oxygen atoms are marked with crosshatching.

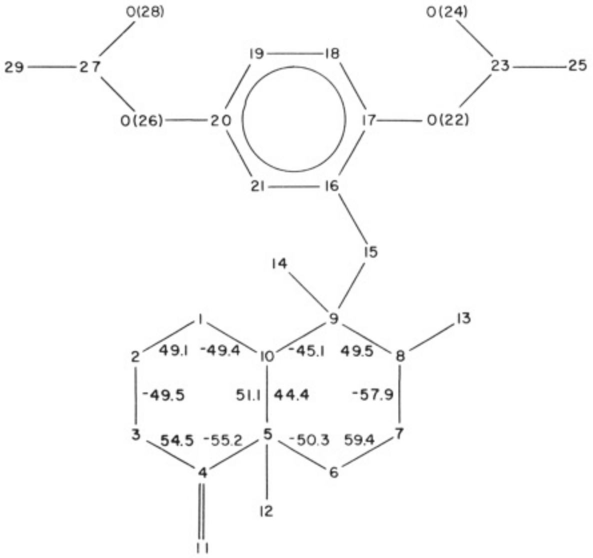


Figure 2. Selected conformational angles for **3b**.

The structure determined for **3b** is shown in Figure 1.[8] The cis-fused rings are both in chair conformations with the exocyclic methylene group attached at C(4). Both the benzyl carbon C(15) and the methyl group bonded to C(8) are attached equatorially. The ring containing the exo-

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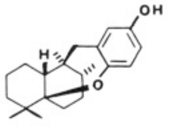
(5) Fenical, W.; McConnell, O. *Experientia* **1975**, *31*, 1004.

(6) Fenical, W.; Sims, J. J.; Squatrito, D.; Wing, R. M.; Radlick, P. C. *J. Org. Chem.* **1973**, *38*, 2383.

(7) In light of the confirmed structure for **3a**, a possible structure for this rearranged product is iii. This could arise by protonation of the exocyclic methylene group, methyl migration, and ring closure involving the quinol. This structure is compatible with ^1H NMR data but is not rigorously established: ^1H NMR (300 MHz, $CDCl_3$) δ 0.77 (3 H, d, J = 7.5 Hz), 0.92, 0.93, 1.13 (each 3 H, s), 2.54 (2 H, br s with small side peaks at ±17 Hz), 4.30 (1 H, br s, OH), 6.48 (1 H, d, J = 2.75 Hz), 6.60 (1 H, dd, J = 2.75, 8 Hz), 6.69 (d, J = 8 Hz).



iii

(8) Johnson, C. K. "ORTEP"; Report ORNL-3794, revised; Oak Ridge National Laboratory: Oak Ridge, TN, 1971.

Table I. ^{1}H NMR Chemical Shifts and Multiplicities for 3a at 400 MHz[a]

proton at C	shift, δ	mult	J, Hz
1 (H_a)	1.98	t of t	14, 6
1 (H_e)	~2.15	overlap with H_{3e} not resolved	
2 (H_a)	1.85	q of t	~13.6, 13.6, 13.6, 5.4, 5.4
2 (H_e)	1.72	br dt	13.6, 5.4, 5.4
3 (H_a)	2.49	sextet of t	13, 13 (gem, aa), 6.6 (ae), 2.2 (allylic)
3 (H_e)	2.15	overlap with H_{13} not resolved	
6 (H_a)	1.02	overlap with H-13 and H-14 not resolved	
6 (H_e)	2.05	br d	14, small
7 (H_a)	1.58	q of d	~13, 2.7
7 (H_e)	1.24	dq	~13, 3.4
8 (H_a)	1.45	d of dq	~13, 2.7, 7
10	1.38	br d	6.6
11	4.71, 4.72	m	
12	0.92	s	
13	0.96	d	7
14	1.06	s	
15	2.52	d	14
	2.72	d	14
Ar	6.60	dd	7, 2.5
Ar	6.61	d	2.5
Ar	6.58	d	7

[a] For $CDCl_3$ solutions.

cyclic methylene group is flattened around C(1) and C(2) as indicated by the conformational angles shown in Figure 2. This flattening is due to steric interactions between atoms C(2) and C(14) (distance = 3.242 (7) Å). The absolute configuration was not determined.

While the X-ray analysis of **3b** was underway, a 400-MHz ^{1}H NMR study of **3a** was carried out, including acquisition of 2-dimensional J-resolved[9a,b] and 2-dimensional homocorrelation spectra.[9a,c] With the X-ray structure in hand, it was possible with these data to make a complete assignment of the high-field proton spectrum of **3a** (see Table I).

Arenarone (**4**) lacked hydroxyl absorption in the infrared but exhibited carbonyl absorption at 1660 cm^{-1}. Since all of the distinctive features in the ^{1}H NMR spectrum of **4** were very similar to those of **3a**, it was suspected that **4** was the quinone oxidation product of **3a**. This relationship was confirmed when silver oxide oxidation of **3a** gave in 80% yield a product identical by spectral analysis with **4**.

Both arenarol and arenarone are cytotoxic, the ED_{50}'s against P388 lymphocytic leukemia being 17.5 and 1.7 μg/mL, respectively.[10]

Arenarol (**3a**)[16] and arenarone (**4**)[16] have the same rearranged drimane skeleton as do **1** and **2**; however, **3a** and **4** have cis-fused ring systems rather than the trans fusion found in **1** and **2**. The ^{1}H NMR data indicate that arenarol has the same conformation in solution as in the crystalline state; i.e., H-8 is axial (one 13-Hz J), and H-10 and H-13 are trans diaxial (small W coupling).

Experimental Section[11]

Isolation of Arenarol (3a) and Arenarone (4). Specimens were collected at −9 m in Truk Island lagoon and frozen shortly after collection. After freeze–drying the specimens (57 g) were cut into small pieces and extracted five times at room temperature with 1-L portions of methanol–chloroform (1:1). The combined extracts were concentrated on a rotary evaporator, and the residue (14.5 g) was partitioned between chloroform and water. The chloroform solubles were chromatographed over Sephadex LH-20 (450 g, 2 in. × 3$^1/_4$ ft column) with chloroform–methanol (1:1). A fraction (1 g) shown by TLC analysis to contain predominantly **3a** with small amounts of **4** was recrystallized (chloroform–hexane) to give 800 mg of crystals and 200 mg of residue in the mother liquors. The 800 mg of crystals were chromatographed over silica gel with chloroform as the eluent. Fractions containing **3a** were pooled and chromatographed over silica gel again with chloroform to give 400 mg of nearly pure **3a**. An analytical sample was purified by HPLC by using a 5-μm C_{18} reversed-phase column with 15% aqueous methanol as the eluent. For **3a**: mp 128–130 °C (chloroform–hexane); $[\alpha]_D$ +19° (c 0.1, $CHCl_3$); IR 3380 (br, OH); UV (CH_3OH) λ_{max} 220 nm (ϵ 4085), 293 (2723), 312 (510); ^{1}H NMR, see Table I; ^{13}C NMR ($CHCl_3$, 62.9 MHz) δ 18.1 (q), 19.1 (q), 22.6 (t), 25.0 (t), 27.6 (t), 32.0 (t), 32.97 (q), 37.58 (d), 37.60 (t), 37.7 (t), 39.41 (s), 43.6 (s), 46.5 (d), 105.8 (t), 114.0 (d), 116.4 (d), 119.5 (d), 126.4 (s), 148.9 (s), 149.4 (s), 153.5 (s); HRMS, m/e 314.22305 (M^+; calcd for $C_{21}H_{30}O_2$ 314.22458); MS (low resolution, 70 eV), m/e (relative intensity) 314 (M^+, 22), 280 (9), 192 (12), 191 (58), 167 (13), 149 (20), 135 (27), 125 (17), 124 (100), 121 (19), 109 (25), 95 (31). Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.25; H, 9.55. Found: C, 80.11; H, 9.55.

The fraction (50 mg) immediately preceeding the 1-g fraction of **3a** + **4** from the Sephadex LH-20 chromatography cited above and the 200-mg mother liquor residue from recrystallization of crude **3a** were combined and chromatographed over silica gel (250 g) with chloroform to give 100 mg of pure **4**: yellow oil; $[\alpha]_D$ +8.3° (c 0.18, $CDCl_3$); IR 1660, 1590 cm^{-1}; UV (CH_3OH) λ_{max} 245 nm (ϵ 4753), 330 (245); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.90 (3 H, d, J = 7 Hz), 0.93, 1.06 (each 3 H, s), 2.41 (1 H, d, J = 14 Hz), 2.68 (1 H, d, J = 14 Hz), 2.45 (1 H, m), 4.73 (2 H, br s), 6.50–6.80 (3 H, m); ^{13}C NMR (25 MHz, $CDCl_3$) δ 17.4, 19.1, 22.2, 24.7, 27.8, 31.9, 33.1, 36.1, 38.1, 39.0, 39.7, 44.9, 48.2, 106.2, 135.8, 135.9, 137.1, 147.7, 153.0, 187.0 (2 C=O); MS (low resolution, 70 eV), m/e (relative intensity) 312 (M^+, 4.3), 297 (1.1), 279 (1.5), 192 (16), 191 (39), 190 (17), 189 (58), 175 (18), 161 (35), 149 (27), 135 (31), 121 (39), 95 (100), 93 (39), 91 (39).

Oxidation of 3a to 4. To a solution of 5 mg of **3a** in 50 mL of dry ether was added 50 mg of silver oxide, and the heterogeneous mixture was stirred overnight at room temperature. The reaction mixture was filtered and the solvent evaporated to give 4 mg of a yellow oil which was pure by TLC criteria. The IR, MS, and ^{1}H NMR of this product were identical with those of naturally occurring **4**.

Acetylation of 3a. A solution of 10 mg of **3a** in 0.5 mL of dry pyridine and 0.5 mL of acetic anhydride was allowed to stand overnight at room temperature, and then the mixture was diluted with water and extracted with chloroform. The chloroform solution was washed with water and dried over Na_2SO_4, and the solvent was evaporated to give 8 mg of a solid which was recrystallized (hexane–chloroform) to give pure **3b**: mp 105 °C; IR 1765, 1210, 1170 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 0.92, 1.06 (each 3 H, s), 0.96 (3 H, d, J = 7 Hz), 2.30, 2.34 (each 3 H, s), 2.55, 2.68 (each 1 H, d, J = 14 Hz), 4.74 (2 H, br s), 7.0 (3 H, m); MS (low resolution, 70 eV), m/e (relative intensity) 398 (M^+, 3.5), 383

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(9) See, for example: (a) Bax, A. "Two-Dimensional Nuclear Magnetic Resonance in Liquids"; Delft University Press, D. Reidel Publishing Co.: Boston, 1982. (b) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703 and references cited therein. (c) Bax, A.; Freeman, R.; Morris, G. *J. Magn. Reson.* **1981**, *42*, 164 and references cited therein.

(10) Gueran, R. I.; Greenberg, N. H.; Macdonald, M. M.; Schumacher, A. M.; Abbott, B. J. *Cancer Chermother. Rep.* **1972**, *3*, No. 2, 1. Effective doses (ED_{50}) in the tissue culture tests are expressed as concentrations in micrograms/milliliter of test material in the growth medium that causes 50% inhibition of cell growth. "Active" materials display an ED_{50} ≤ 20 μg/mL. PS(P388) refers to in vitro lymphocytic leukemia.

(11) Melting points are uncorrected. IR spectra were taken on a Perkin-Elmer 298 instrument, UV spectra on Perkin-Elmer Lambda 3 and Cary 118 spectrophotometers, and optical rotations on a Perkin-Elmer 141 polarimeter. ^{1}H NMR spectra were taken on Varian XL-100 (100 MHz) and Nicolet (300 MHz) instruments and ^{13}C spectra on Varian XL-100 (25 MHz) or IBM (20 MHz) instruments; signals are reported in parts per million (δ) downfield from internal tetramethylsilane. Mass spectra were taken on a Hewlett-Packard 5985 (low resolution) and a CEC 110 (Du Pont, Monrovia, CA; high resolution) spectrometers. LiChrosorb Si60 5-μm silica gel and 5-μm C_{18} preparative (10 mm × 25 cm) columns were used for HPLC separations with a differential refractometer detector. Merck silica gel 60 (230–240 mesh) was used for column chromatography.

(4), 328 (3), 191 (40), 177 (21), 166 (8), 165 (11), 149 (12), 135 (23), 123 (32), 121 (32), 109 (30), 107 (22), 105 (13), 95 (100), 93 (22), 91 (20), 81 (18), 79 (20), 77 (13).

Methylation of 3a To Give 3c. A mixture of 50 mg of **3a**, 5 mL of methyl iodide, and 20 mg of potassium carbonate in 4 mL of dry acetone was heated under reflux for 72 h. The reaction mixture was filtered, the solvent evaporated, and the residue partitioned between chloroform and water. The chloroform solution was dried (Na_2SO_4), the solvent evaporated, and the residue chromatographed over silica gel (hexane eluant) to give 10 mg of pure **3c**: mp 72–73 °C [from hexane–chloroform (1:1)]; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90, 1.03 (each 3 H, s), 0.97 (3 H, d, $J = 7$ Hz), 2.45 (1 H, m), 2.55, 2.78 (each 1 H, d, $J \approx 13$ Hz), 3.72, 3.76 (each 3 H, s), 4.69, 4.71 (each 1 H, br s, $=CH_2$), 6.70–6.78 (3 H, m); MS (low resolution 70 eV), m/e (relative intensity) 342 (M^+, 2.7), 328 (5), 192 (3), 191 (15), 177 (5), 175 (3), 152 (44), 149 (6), 138 (68), 137 (20), 135 (17), 121 (28), 109 (26), 107 (15), 105 (7), 95 (100), 93 (12), 91 (10), 81 (15), 79 (13), 77 (9).

X-ray Analysis. Colorless crystals of the acetate **3b** were grown by evaporation from a chloroform–hexane solution. Data were collected by using a single crystal (0.08 × 0.15 × 0.35 mm) mounted on an Enraf-Nonius CAD-4 diffractometer with Ni-filtered Cu Kα radiation and a nitrogen-stream cooling device (temperature = 138 ± 2 K). Systematic absences established the space group $P2_12_12_1$. Lattice constants were determined from a least-squares fit to the $\pm 2\theta$ values of 48 intensity maxima (low temperature, $a = 9.964$ (5) Å, $b = 6.81$ (2) Å, $c = 33.33$ (5) Å, $V = 2262.6$ Å^3; room temperature, $a = 10.133$ (1) Å, $b = 6.998$ (2) Å, $c = 32.971$ (3) Å, $V = 2337.9$ Å^3, $\rho_{calcd} = 1.132$ for $Z = 4$). Data were collected by using the θ–2θ technique to a maximum $2\theta = 150°$. From 2720 unique data 2268 data were considered observed ($F > 4\sigma(F)$).

The structure was solved by the direct-methods program MULTAN.[12] The structure was refined by full-matrix least-squares techniques[13] using weights of $w = 1/\sigma^2(F)$. After initial anisotropic refinement, positions for all hydrogen atoms were determined from a difference electron density map. Hydrogen atoms were included in the structure factor calculations, but their position and temperature parameters were not refined. Refinement converged to $R = 0.065$, $R_w = 0.066$, and $S = 2.51$. The final difference map had a maximum density of 0.45 e/Å^3 near a methyl hydrogen. The next largest peak had a density of 0.25 e/Å^3. Neutral atom scattering factors for O and C were taken from Cromer and Mann.[14] Scattering factors for H were from Stewart, Davidson, and Simpson.[15]

Acknowledgment. This research was supported by grants from the Office of Sea Grant, NOAA, U.S. Department of Commerce (NA80AA-D00089) and the National Cancer Institute (CA 17562). We thank R. Clayshulte for specimen collection and Dr. K. Reutzler, Smithsonian Institution, Washington, DC for sponge identification. We thank Dr. Paul Schmidt, Oklahoma Medical Research Foundation, Oklahoma City, for the use of a 300-MHz NMR spectrometer and Dr. S. L. Wirthlin, Bruker Instrument Co., NJ, for all 400-MHz NMR spectra. High-resolution mass spectra were kindly provided by Dr. C. Costello at the Massachusetts Institute of Technology mass spectral laboratory supported by a grant (principal investigator Professor K. Biemann) from the Biotechnology Research Branch, Division of Research Resources. We thank the University of Oklahoma computing center for providing computing facilities and service.

Registry No. 3a, 87764-13-4; **3b**, 87764-14-5; **3c**, 87764-15-6; 4, 87764-16-7.

Supplementary Material Available: Tables of atomic positions, thermal parameters, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

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(12) Main, P.; Fiske, S. J.; Hull, S. E.; Lessigner, L.; Germain, G.; Declercq, J.-P.; Woolfson, M. M. "MULTAN 80, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data"; Universities of York, England and Louvain-la-Neuve, Belgium, 1980.

(13) Sheldrick, G. M. "SHELX-76. Program for Crystal Structure Determination"; University Chemical Laboratory: Cambridge, England, 1976.

(14) Cromer, D. T.; Mann, J. B. *Acta Crystallogr., Sect. A* **1968**, *A24*, 321.

(15) Stewart, R. F.; Davidson, E. R.; Simpson, W. T. *J. Chem. Phys.* **1965**, *42*, 3175.

(16) Arenerol and arenerone have also been isolated from an unidentified *Dysidea* sp. from Ponape: private communication from Dr. D. J. Faulkner, Scripps Institution of Oceanography, La Jolla, CA.

Synthesis and Photochemical Studies of a Diazomalonyl-Containing Galactocerebroside Analogue. A Glycolipid Photolabeling Reagent[1]

John Wydila and Edward R. Thornton*

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104

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The synthesis of a galactocerebroside-based photolabeling reagent is described. The reagent is a structural analogue of the native lipid, containing a diazomalonamide group incorporated in the acyl chain. Photolysis studies in THF–H_2O resulted in the isolation and characterization of the water insertion product, demonstrating the molecule's capacity for intermolecular OH insertion. Photolysis of the reagent while incorporated into phospholipid vesicles gave the water insertion product, demonstrating that the bilayer membrane organization still permits access of water to the photogenerated carbene intermediate.

Galactocerebroside is a simple glycosphingolipid found in high concentrations in the myelin sheath, where it constitutes 20% by weight of the dry lipid.[2] In contrast to more complex glycosphingolipids, some of which have been proven to be cell receptors,[3] galactocerebroside seems to play a structural role in the neural membrane. Studies

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(2) (a) Johnson, A. C.; McNabb, A. R.; Rossiter, R. J. *Biochem. J.* **1948**, *43*, 578. (b) Lapetina, E. G.; Soto, E. F.; De Robertis, E. *J. Neurochem.* **1968**, *15*, 437.

(3) Hakomori, S. *Annu. Rev. Biochem.* **1981**, *50*, 733.

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