Photosensitized Oxygenation Reactions of Phytol and Its Derivatives

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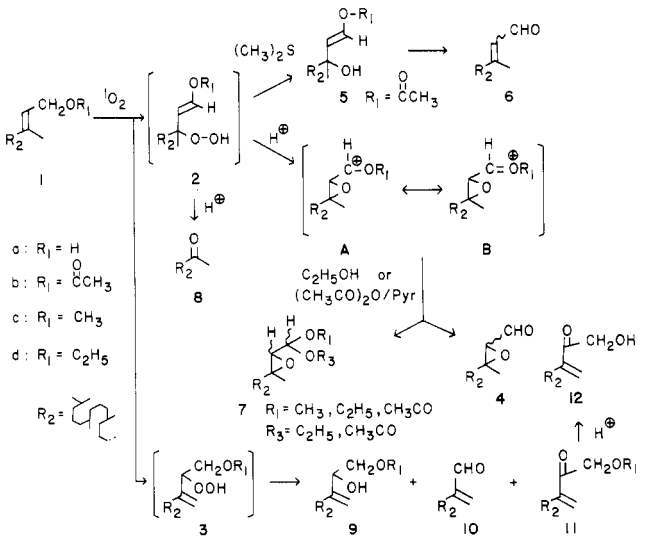
It has been reported that α,β-epoxy aldehydes and β-hydroperoxyhomoallyl alcohols are practically the sole oxygenation products of the 3-methyl-3-alkyl-substituted allyl alcohols.[1] On the other hand, the esters and ethers of allyl alcohols have been found to be essentially inert toward singlet oxygen.[2,3] We have now established that phytol (**1a**), which is a typical 3-methyl-3-alkyl-substituted allyl alcohol, and its derivatives such as phytyl acetate (**1b**), methyl phytyl ether (**1c**), and ethyl phytyl ether (**1d**) constitute excellent reaction partners for the addition of $^1O_2$.

The photosensitized oxygenation of phytols (**1a–d**) was carried out in ethanol containing either rose bengal (RB) or methylene blue (MB) as a sensitizer. The reaction mixture was treated with either a reducing agent, dimethyl sulfide (DMS) or trimethyl phosphite ($(CH_3O)_3P$), or with acetic anhydride/pyridine (Ac_2O/Pyr) to aid in cleavage of the O–O bond. In order to clarify the different reactivity of the allyl alcohols with singlet oxygen, the β value was measured in the rose bengal sensitized photooxygenation system at room temperature.[4] The reaction conditions, yields of the products, and β values are shown in Table I. Table I shows that the reactivity of phytols toward $^1O_2$ follows the order **1a** > **1d** ≥ **1c** > **1b**. 6,10,14-Trimethyl-2-pentadecanone (**8**) has been well-known as a constituent of essential oil of jasmin.[5] The total selectivities could not be altered markedly by varying the sensitizing dye for the reactions of **1a** and **1b**. However, the change was observed for the reactions of **1c** and **1d**: with MB, epoxy acetals **7c** and **7d** and β-hydroxyhomoallyl alcohol monoalkyl ethers **9c** and **9d** were the major products, but with RB, the formation of **7c** and **7d** was suppressed and the yield of **8** was increased.

When $(CH_3O)_3P$, which was the better reducing agent as compared to DMS, was used in the place of DMS, the yield of the reduction product, **9b** of the hydroperoxide **3b**, was slightly increased. The treatment of the reaction mixture for **1b** with reducing agent yielded an γ-acetoxy allyl alcohol (**5b**), which was further converted to a (*Z*/*E*)-vinylaldehyde (**6**). However, the epoxy derivatives **4** or **7** and/or ketone **8** were identical with **1a**, **1c**, and **1d** with the same treatment. The O–O bonds of hydroperoxides **2b** and **3b** were cleaved by the action of Ac_2O/Pyr to produce mainly **4**, **7b**, and **11b**. Up to now, no allyl alcohol (**5b**), acylal (**7b**), and epoxy acetal (**7c** and **7d**) formation reactions have been observed for instance in the photooxygenation reactions of allyl alcohols such as the 3,3-dialkyl-substituted allyl alcohols,[1] Δ^4- and Δ^5-steroidal olefins with an allylic hydroxy group at C-3 and C-7,[2] thujopsenol,[6] (–)-*cis*-pulegol,[7] and β-damascols.[8] The mechanisms of formation of epoxy derivatives **4** and **7** including a carbonium ion (A) or an oxonium ion intermediate (B) are proposed as shown in Scheme I.

Scheme I



Aldehyde **10** is probably yielded by an acid-catalyzed reaction during the isolating procedure. This mechanism is supported by the formation of a ketone from α-hydroxy hydroperoxide fragmentation in the photooxygenation of β-damascol.[8] The reaction pathway leading to α-ketol derivatives **11** is very similar to those proposed in the photooxygenations of calarene[9] and the cyclohexadiene derivative.[10]

Experimental Section

Infrared (IR) spectra were recorded on liquid films; absorptions are given in reciprocal centimeters. Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained on a Hitachi R-20A spectrometer; chemical shifts (δ) are expressed in parts per million down field from internal tetramethylsilane. Gas–liquid chromatography (GLC) was performed with a flame ionization detector having a Carbowax 20M fused silica capillary column (30 m × 0.23 mm) (column, 200 °C; injector and detector, 250 °C; nitrogen flow 0.7 mL/min). Preparative gas chromatography was performed with a TCD and 2 m × 4 mm Carbowax 20M on Chromosorb WAW DMCS (60–80 mesh). The oven temperature was set at 200 °C, and helium was used as the carrier gas. Silica gel 60 (70–230 mesh) (Merck) was used for column chromatography, and preparative TLC was carried out on 20 × 20 cm glass plates coated with Macherey-Nagel silica gel SIL G-200 UV_{254} precoated sheets (2.0 mm) containing a fluorescent indicator. The preparative HPLC was performed on an instrument equipped with a refractive index detector and a GPC column using chloroform as eluant.

Methyl phytyl ether (**1c**) and ethyl phytyl ether (**1d**) were prepared from sodium phytoxide with methyl iodide and ethyl iodide, respectively.[11] The other starting materials were commercially available. All of the starting materials were purified by column chromatography and preparative TLC [**1a**, R_f 0.27 (1:9 ethyl acetate–hexane); **1b**, R_f 0.82 (3:7 ethyl acetate–hexane); **1c**, R_f 0.85 (1:4 ethyl acetate–hexane); **1d**, R_f 0.88 (1:4 ethyl acetate–hexane)].

General Photooxygenation Procedure. The ethanol solutions (300 mL) containing phytols **1a–d** (1.0 g) and methylene blue (MB; 0.04 g) or rose bengal (RB; 0.10 g) were irradiated for

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Table I. Photooxygenation of Phytols

compd	sensitizer	irradn time, h	subsequent transformation	conversion, %	total yield of 4–12, %	relative area % as determined by GLC									β,[a] M
						4	5	6	7	8	9	10	11	12	
1a	MB	3	DMS	97	90	55[b]					41	4			
1a	RB	1	DMS	90	82	62[c]					30	8			1.3
1b	MB	10	DMS	95	88		40			1	42	4	11	3	
1b	MB	10	$(CH_3O)_3P$	95	89		43			1	52	1	4		
1b	MB	10	Ac_2O/Pyr	95	82	10[d]			33[e]	2		1	54		
1b	RB	8	DMS	83	76		33	4[f]			56	4	3		7.8
1c	MB	3.5	DMS	88	81				47[g]	2	48		3		
1c	RB	1.8	DMS	87	72				8[h]	17	74		1		3.7
1d	MB	2.5	DMS	81	75				56[i]	4	40				
1d	RB	1.5	DMS	84	74				29[j]	14	53	4			3.0

[a] Calculated, based on an average value for photosensitized oxygenation for 1-methylcyclohexene of 1.5×10^{-3} M. [b] Cis/trans, 8:19. [c] Cis/trans, 27:35. [d] Cis/trans, 4:6. [e] Cis/trans, 11:22. [f] *E*/*Z*, 1:1. [g] Two isomers, 16:31. [h] Two isomers, 7:1. [i] Cis/trans, 20:36. [j] Cis/trans, 8:21.

various periods in an oxygen stream by a water-cooled 400-W high-pressure mercury lamp (Riko UVL-400HA) in a Pyrex container. To avoid overoxidation, after 81–97% conversion (GLC) the oxygenation was stopped. The solvent was removed, and the photolysate was subjected to silica gel column chromatography (Wakogel C-200) with ether eluant to remove the MB or RB. After evaporation of ethyl ether, the hydroperoxides obtained were reduced by adding 2 mL of 50% dimethyl sulfide–benzene solution at 0 °C and stirring for 12 h. The resulting mixtures (0.2–0.4 g) were analyzed directly by GLC and separated by preparative TLC (eluting with various ratios of ethyl acetate–hexane mixtures). After evaporation of the solvent and excess dimethyl sulfide, the products were identified by MS, IR, and ^{1}H NMR (see Table I).

MB-Sensitized Photooxygenation of 1a. Phytol (**1a**) was photooxygenated as above, and subsequent preparative TLC (eluting with 1:9 ethyl acetate–hexane) of the product (0.3 g) gave aldehyde **10** (R_f 0.60, 10 mg), α,β-epoxy aldehyde **4** (R_f 0.41, 145 mg), and β-hydroxyhomoallyl alcohol **9a** (R_f 0.12, 109 mg).

2-Methylidene-6,10,14-trimethylpentadecanal (10): IR (neat) 2945, 1705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.1–1.7 (19 H, m), 2.23 (2 H, m), 5.98 (1 H, m), 6.24 (1 H, m), 9.54 (1 H, s); MS, *m*/*z* 280 (M$^+$, 0.5), 249 (4), 125 (54), 111 (54), 97 (81), 84 (88), 81 (65), 71 (96), 70 (84), 57 (100), 56 (72), 55 (68). Anal. Calcd for $C_{19}H_{36}O$: 280.2766. Found: 280.2768.

3,7,11,15-Tetramethyl-2,3-epoxyhexadecanal (4): cis/trans mixture ca. 4:9; IR (neat) 2935, 1732, 1468, 1388 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.23 (21 H, m), 1.42 (s, $CH_3C(3)$, typical of *cis*-**4**), 1.45 (s, $CH_3C(3)$, typical of *trans*-**4**), 3.15 (d, J = 5 Hz, HC(2), typical of *cis*-**4**), 3.17 (d, J = 5 Hz, HC(2), typical of *trans*-**4**), 9.50 (d, J = 5 Hz, HC(1), typical of *trans*-**4**), 9.52 (d, J = 5 Hz, HC(1), typical of *cis*-**4**) [the cis and trans dispositions of the aldehyde groups were further confirmed by using a shift reagent]; MS, *m*/*z* (relative intensity) [*cis*-**4**] 310 (M$^+$, 0.1), 295 (1), 137 (5), 101 (23), 108 (17), 97 (18), 95 (17), 85 (100), [*trans*-**4**] 310 (M$^+$, 0.1), 295 (1), 137 (1), 125 (2), 85 (100). Anal. Calcd for *cis*-$C_{19}H_{35}O_2$: 295.2637. Found: 295.2639. Calcd for *trans*-$C_{19}H_{35}O_2$: 295.2637. Found: 295.2644.

3-Methylidene-7,11,15-trimethylhexadecane-1,2-diol (9a): IR (neat) 3380, 2925, 1450 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.22 (19 H, m), 1.97 (2 H, m), 2.74 (2 H, m), 3.65 (2 H, m), 4.17 (1 H, m), 4.98 (1 H, m), 5.13 (1 H, m); MS, *m*/*z* (relative intensity) 312 (M$^+$, 9), 281 (30), 263 (18), 139 (29), 69 (100). Anal. Calcd for $C_{20}H_{40}O_2$: 312.3028. Found: 312.3035.

MB-Sensitized Photooxygenation of 1b. Phytyl acetate (**1b**) was photooxygenated as above. The reaction mixture was then analyzed directly by GLC and subsequent preparative TLC (eluting with 3:7 ethyl acetate–hexane) of the product (0.3 g) gave aldehyde **10** (R_f 0.79, 8 mg), α-ketol acetate **11b** (R_f 0.64, 28 mg), γ-acetoxyallyl alcohol **5b** (R_f 0.57, 101 mg), α-ketol **12** (R_f 0.55, 7 mg), and β-hydroxyhomoallyl alcohol monoacetate **9b** (R_f 0.43, 107 mg). Ketone **8** and aldehyde **10** were identified by comparison with known samples using GC and GC/MS.

3-Methylidene-2-oxo-7,11,15-trimethylhexadecanyl acetate (11b): IR (neat) 2930, 1760, 1705, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.22 (19 H, m), 2.18 (3 H, s), 2.20 (2 H, m), 5.07 (2 H, s), 5.82 (1 H, m), 5.95 (1 H, m); MS, *m*/*z* (relative intensity) 311 (13), 310 (M$^+$ – 42, 67), 292 (33), 143 (40), 109 (100), 99 (63), 57 (60). Anal. (determined for M$^+$ – 42 peak) Calcd for $C_{20}H_{38}O_2$: 310.2871. Found: 310.2868.

(*E*)-3-Hydroxy-3,7,11,15-tetramethyl-1-hexadecenyl acetate (5b): IR (neat) 3480, 2930, 1760, 1225, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.23 (21 H, m), 1.33 (3 H, s), 1.98 (1 H, br s), 2.12 (3 H, s), 5.53 (1 H, d, J = 12 Hz), 7.30 (1 H, d, J = 12 Hz); MS, *m*/*z* (relative intensity) 337 (M$^+$ – 17, 42), 297 (33), 295 (19), 149 (8), 130 (100), 129 (96), 87 (95), 43 (100). Anal. (determined for M$^+$ – 17 peak) Calcd for $C_{22}H_{41}O_2$: 337.3106. Found: 337.3106.

3-Methylidene-2-oxo-7,11,15-trimethylhexadecanol (12): IR (neat) 3480, 2940, 1685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.22 (19 H, m), 2.30 (2 H, m), 3.35 (1 H, br s), 4.58 (2 H, s), 5.84 (1 H, m), 5.97 (1 H, m); MS, *m*/*z* (relative intensity) 310 (M$^+$, 3), 279 (19), 261 (21), 71 (90), 57 (100). Anal. Calcd for $C_{20}H_{38}O_2$: 310.2871. Found: 310.2878.

2-Hydroxy-3-methylidene-7,11,15-trimethylhexadecanyl acetate (9b): IR (neat) 3450, 2925, 1745, 1235 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.23 (19 H, m), 2.0 (2 H, m), 2.09 (3 H, s), 2.76 (1 H, br s), 4.14 (2 H, m), 4.20 (1 H, m), 4.97 (1 H, m), 5.14 (1 H, m); MS, *m*/*z* 354 (M$^+$, 0.1), 312 (3), 140 (13), 43 (100). Anal. Calcd for $C_{22}H_{42}O_3$: 354.3134. Found: 354.3133.

Conversion of 5b to 6. A $CHCl_3$ solution (0.3 mL) of **5b** (60 mg) was kept at room temperature for 7 days, and the resulting reaction mixture was analyzed by GLC. Two peaks were observed with retention times of 6.6 and 7.5 min. The two were identified as (*Z*)-**6** (14 mg) and (*E*)-**6** (28 mg), respectively, on the basis of their spectral data.

(*Z*)-3,7,11,15-Tetramethyl-2-hexadecenal ((*Z*)-6): IR (neat) 2925, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.22 (19 H, m), 1.97 (3 H, d, J = 2 Hz), 2.57 (2 H, t(m), J = 7 Hz), 5.88 (1 H, d(m), J = 8 Hz), 9.99 (1 H, d, J = 8 Hz); MS, *m*/*z* (relative intensity) 294 (M$^+$, 0.5), 163 (5), 149 (29), 111 (57), 98 (22), 95 (55), 84 (100). Anal. Calcd for $C_{20}H_{38}O$: 294.2922. Found: 294.2919.

(*E*)-3,7,11,15-Tetramethyl-2-hexadecenal ((*E*)-6): IR (neat) 2925, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.22 (19 H, m), 2.15 (3 H, d, J = 2 Hz), 2.57 (2 H, m), 5.88 (1 H, d(m), J = 8 Hz), 10.04 (1 H, d, J = 8 Hz); MS, *m*/*z* (relative intensity) 294 (M$^+$, 0.5), 163 (10), 149 (21), 111 (39), 98 (28), 97 (36), 95 (39), 84 (100). Anal. Calcd for $C_{20}H_{38}O$: 294.2922. Found: 294.2922.

MB-Sensitized Photooxygenation of 1c. Methyl phytyl ether (**1c**) was photooxygenated as above, and subsequent preparative TLC (eluting with 1:4 ethyl acetate–hexane) of the product (0.3 g) gave ketone **8** (R_f 0.70, 3 mg), epoxy acetal **7c** (R_f 0.66, 111 mg), α-keto methyl ether **11c** (R_f 0.47, 6 mg), and β-hydroxyhomoallyl alcohol monomethyl ether **9c** (R_f 0.37, 100 mg).

3,7,11,15-Tetramethyl-2,3-epoxyhexadecanal ethyl methyl acetal (7c): two isomers ca. 1:2; IR (neat) 2920, 1460, 1055 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.0–2.0 (27 H, m), 2.85 (1 H, d, J = 7 Hz), 3.41 (3 H, s), 3.71 (2 H, q, J = 7 Hz), 4.25 (1 H, d, J = 7 Hz); MS, *m*/*z* (relative intensity) 339 (M$^+$ – 31, 0.6), 325 (1), 89 (100). Anal. (determined for M$^+$ – 31 peak) Calcd for $C_{22}H_{43}O_2$: 339.3262. Found: 339.3263.

Methyl 3-methylidene-2-oxo-7,11,15-trimethylhexadecanyl ether (11c): IR (neat) 2920, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–0.9

(12 H, m), 1.22 (19 H, m), 2.25 (2 H, m), 3.46 (3 H, s), 4.44 (2 H, s), 5.77 (1 H, m), 5.95 (1 H, m); MS, m/z (relative intensity) 324 (M^+, 3), 279 (6), 138 (20), 112 (100). Anal. Calcd for $C_{21}H_{40}O_2$: 324.3028. Found: 324.3030.

2-Hydroxy-3-methylidene-7,11,15-trimethylhexadecanyl methyl ether (9c): IR (neat) 3450, 2920, 2860, 1460, 1115 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.22 (19 H, m), 2.0 (2 H, m), 2.55 (1 H, br s), 3.40 (3 H, s), 3.4 (2 H, m), 4.25 (1 H, m), 4.95 (1 H, m), 5.22 (1 H, m); MS, m/z (relative intensity) 326 (M^+, 10), 294 (7), 115 (71), 111 (50), 83 (100). Anal. Calcd for $C_{21}H_{42}O_2$: 326.3184. Found: 326.3177.

MB-Sensitized Photooxygenation of 1d. Ethyl phytyl ether (**1d**) was photooxygenated and analyzed by GLC as above, and subsequent preparative TLC (eluting with 1:4 ethyl acetate–hexane) of the product (0.3 g) gave trans-epoxy acetal *trans*-**7d** (R_f 0.73, 73 mg), ketone **8** (R_f 0.70, 6 mg), cis-epoxy acetal *cis*-**7d** (R_f 0.63, 40 mg), and β-hydroxyhomoallyl alcohol monoethyl ether **9d** (R_f 0.43, 71 mg).

***trans*-3,7,11,15-Tetramethyl-2,3-epoxyhexadecanal diethyl acetal (*trans*-7d)**: IR (neat) 2925, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.1–1.6 (28 H, m), 2.87 (1 H, d, J = 6.8 Hz), 3.71 (4 H, m), 4.34 (1 H, d, J = 6.8 Hz) [the cis and trans dispositions of the acetal groups were further confirmed by using a shift reagent]; MS, m/z (relative intensity) 339 (M^+ - 45, 0.1), 311 (7), 310 (38), 103 (100). Anal. (determined for M^+ - 45 peak) Calcd for $C_{22}H_{43}O_2$: 339.3262. Found: 339.3267.

***cis*-3,7,11,15-Tetramethyl-2,3-epoxyhexadecanal diethyl acetal (*cis*-7d)**: IR (neat) 2925, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.1–1.6 (28 H, m), 2.86 (1 H, d, J = 6.7 Hz), 3.70 (4 H, m), 4.32 (1 H, d, J = 6.7 Hz); MS, m/z (relative intensity) 339 (M^+ - 45, 0.1), 311 (7), 310 (26), 103 (100). Anal. (determined for M^+ - 45 peak) Calcd for $C_{22}H_{43}O_2$: 339.3262. Found: 339.3269.

Ethyl 2-hydroxy-3-methylidene-7,11,15-trimethylhexadecanyl ether (9d): IR (neat) 3450, 2925, 1465, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.22 (22 H, m), 1.98 (2 H, m), 2.68 (1 H, br s), 3.46 (2 H, m), 3.55 (2 H, q, J = 7 Hz), 4.25 (1 H, m), 4.94 (1 H, m), 5.15 (1 H, m); MS, m/z (relative intensity) 340 (M^+, 6), 294 (13), 129 (47), 111 (43), 83 (100). Anal. Calcd for $C_{22}H_{44}O_2$: 340.3341. Found: 340.3336.

Reduction of Hydroperoxides 2b and 3b by Trimethyl Phosphite ($(CH_3O)_3P$). Phytyl acetate (**1b**) was photooxygenated as previously described. The obtained hydroperoxides (**2b** and **3b**) were reduced by adding 1 mL of $(CH_3O)_3P$ at 0 °C with stirring for 12 h. The resulting mixtures were analyzed directly by GLC (see Table I).

Reactions of Hydroperoxides 2b and 3b with Ac_2O/Pyr. Phytyl acetate (**1b**) was photooxygenated as previously described. The obtained hydroperoxides (**2b** and **3b**) were treated with 1 mL of acetic anhydride in 0.8 mL of pyridine (Ac_2O/Pyr) at room temperature and allowed to stand for 2 h. The resulting mixture were analyzed directly by GLC. Subsequent preparative TLC (eluting with 3:7 ethyl acetate–hexane; R_f 0.58~0.70) and preparative HPLC of product (0.23 g) gave two acylals, *trans*-**7b** (54 mg) and *cis*-**7b** (27 mg), in addition to 11 (130 mg).

***trans*-3,7,11,15-Tetramethyl-2,3-epoxyhexadecylidene diacetate (*trans*-7b)**: IR (neat) 2925, 1765, 1240, 1205 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.39 (24 H, m), 2.11 (6 H, s), 2.99 (1 H, d, J = 8 Hz), 6.64 (1 H, d, J = 8 Hz) [the cis and trans dispositions of the acylal group were further confirmed by using a shift reagent]; MS, m/z (relative intensity) 353 (M^+ - 59, 1), 293 (1), 269 (2), 144 (38), 102 (52), 43 (100). Anal. (determined for M^+ - 59 peak) Calcd for $C_{22}H_{41}O_3$: 353.3055. Found: 353.3046.

***cis*-3,7,11,15-Tetramethyl-2,3-epoxyhexadecylidene diacetate (*cis*-7b)**: IR (neat) 2925, 1765, 1240, 1200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–0.9 (12 H, m), 1.33 (24 H, m), 2.11 (6 H, s), 3.01 (1 H, d, J = 8 Hz), 6.68 (1 H, d, J = 8 Hz); MS, m/z (relative intensity) 353 (M^+ - 59, 0.5), 293 (0.5), 269 (2), 144 (19), 102 (28), 43 (100). Anal. (determined for M^+ - 59 peak) Calcd for $C_{22}H_{41}O_3$: 353.3055. Found: 353.3064.

Registry No. **1a**, 150-86-7; **1b**, 10236-16-5; **1c**, 66432-64-2; **1d**, 66432-65-3; **2a**, 100605-80-9; **2b**, 100605-82-1; **2c**, 100605-84-3; **2d**, 100605-86-5; **3a**, 100605-81-0; **3b**, 100605-83-2; **3c**, 100605-85-4; **3d**, 100605-87-6; **4**, 100759-12-4; **5**, 100605-88-7; (*E*)-**6**, 100605-89-8; (*Z*)-**6**, 100605-90-1; **7b** (R_3 = CH_3CO), 100605-91-2; **7c** (R_3 = C_2H_5), 100605-92-3; **7d** (R_3 = C_2H_5), 100605-93-4; **8**, 16825-16-4; **9a**, 100605-94-5; **9b**, 100605-95-6; **9c**, 100605-96-7; **9d**, 100605-97-8; **10**, 100605-98-9; **11b**, 100655-22-9; **11c**, 100605-99-0; **12**, 100606-00-6.

6α,7α,17β-Trihydroxy-15β,17-oxidospongian-16-one 7-Butyrate: A New Diterpene Lactone from an Australian *Aplysilla* Species

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A growing number of diterpenes of the spongian-type have been isolated[1,2] from sponges of the orders Dendroceratida and Dictyoceratida. In addition, the isolation of norrisolide[3] and other rearranged spongian metabolites[4] from spongivorous nudibranchs of the genus *Chromodoris* implies additional but as yet undiscovered sponge sources of these diterpenes. The recent X-ray structural elucidation[2] of lactone **1** from the Caribbean sponge *Igernella notabilis* prompts us to report the isolation of the corresponding 6α-hydroxy derivative **2** (see Chart I) from an Australian *Aplysilla sp.*

A pink, thinly encrusting sponge of the genus *Aplysilla* was collected in Port Phillip Bay, Australia. Flash chromatography of the dichloromethane-soluble portion of the methanol extract with hexanes gave a small amount of ambliofuran (**3**), identified by comparison of the spectral data with the literature values.[5] Further elution with ether/hexane mixtures afforded the crystalline lactone **2**, mp 212–213 °C. More polar fractions yielded, after high-performance LC, the minor methyl ester **8**.

The lactone **2** had a molecular formula of $C_{24}H_{36}O_7$ that was inferred from ^{13}C NMR and mass spectral data. The ^1H NMR spectrum indicated that lactone **2** was a butyrate ester of a diterpene, and hydrolysis of **2** with potassium carbonate in methanol gave the expected triol **4**. The differences observed between the ^{13}C NMR spectra of **1** and **2** (Table I) could be rationalized by proposing that lactone **2** was the 6α-hydroxy derivative of lactone **1**. This proposal was supported by the following ^1H NMR data. Irradiation of the equatorial H-7 proton signal at δ 4.93 collapsed the axial H-6 proton signal at δ 4.18 to a doublet of doublets (J = 11.5, 6.0 Hz). Irradiation of the H-6 signal in turn sharpened the H-7 signal to a singlet and collapsed the axial H-5 signal at δ 1.47 (d, 1 H, J = 11.5 Hz) to a singlet (observed by difference decoupling).

Selected nuclear Overhauser effect difference spectroscopy (NOEDS) experiments (Table II) confirmed the regio- and stereochemical relationships of all functional groups. Irradiation of the H-17α signal enhanced the signals of

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