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Branched Chain Mono-Glycerol Ethers from a Taiwanese Marine Sponge of the Genus *Aaptos*

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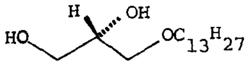
Abstract: 3-(13-Methylhexadecyloxy)-1,2-(*S*)-propanediol (6) and 3-(15-methyloctadecyloxy)-1,2-(*S*)-propanediol (7) were isolated from an *Aaptos* species of marine sponge from Taiwanese waters and characterized by spectroscopic methods. Homolog 6 was independently synthesized.

Marine sponges are a source of many unusual compounds including a variety of simple fatty acid derivatives that have not been reported from terrestrial sources.[1] Recently Myers and Crews[2] isolated (*S*)-3-tridecyloxy-1,2-propanediol (1) from an unidentified red marine sponge. This was the first report of a glycerol ether from a sponge and the first isolation of such from a marine invertebrate without a prior hydrolysis step. The glycerol ethers chimyl alcohol (2), batyl alcohol (3), and selachyl alcohol (4) have long been recognized as components of marine animal liver oils, occurring as the corresponding fatty acid esters.[3] Similarly, glycerol ethers such as 5 are found in seven different species of *Sargassum* algae, again in ester form.[4] We report herein the direct isolation of 3-(13-methylhexadecyloxy)-1,2-(*S*)-propanediol (6) and its homolog 3-(15-methyloctadecyloxy)-1,2-(*S*)-propanediol (7) from the alcoholic extracts of a yellow sponge of the *Aaptos* genus[5,6] collected off Penhu Island, Taiwan.



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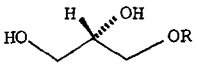
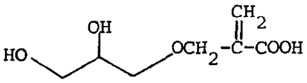


2 R = $-(CH_2)_{17}CH_3$
3 R = $-(CH_2)_{15}CH_2$
4 R = $-(CH_2)_8CH{=}CH(CH_2)_7CH_3$



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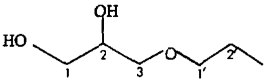
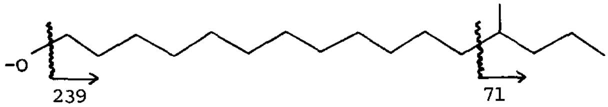
The methanol extracts of the homogenized sponge were partitioned between ethyl acetate and water, and the ethyl acetate soluble material was then chromatographed on silica gel (methylene chloride/ethyl acetate, 9:1) to give 6 and 7 as an inseparable mixture.[7] Molecular formulas of $C_{20}H_{42}O_3$ (major component) and $C_{22}H_{46}O_3$ were established by high resolution mass spectroscopy for the two homologs. Infrared analysis revealed strong OH absorption (ν = 3510 cm^{-1}). The 250 MHz ^1H NMR spectrum showed four sets of signals corresponding to protons on oxygen-bearing carbons and accommodated by partial structure:

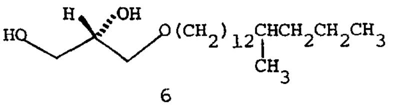


Thus, a multiplet at δ 3.87 is assigned to H-2 and signals at δ 3.64 (dd, *J*=6, 12 Hz) and δ 3.75 (dd, *J*=4, 12 Hz) to the two non-equivalent methylene protons at C-1. The C-3 protons are equivalent, appearing as a doublet (*J*=4 Hz) at δ 3.55, and the C-1' protons give rise to a triplet at δ 3.50. These assignments were confirmed by conversion of the diol to the diacetate whereupon the H-2 multiplet shifted downfield to δ 5.2 and the C-1 protons to δ 4.17 (dd, *J*=6, 12 Hz) and δ 4.35 (dd, *J*=4, 12 Hz). Irradiation of the multiplet at δ 5.2 collapsed the doublet at δ 3.56 (H-3) and converted the signals at δ 4.35 and δ 4.17 (H-1) to a pair of doublets (*J*=12 Hz). Similarly, the geminal coupling constant of 12 Hz between the two non-equivalent protons at C-1 was lost upon irradiation of either the signal at δ 4.35 or δ 4.17.

The identity of the alkyl side chain was established by mass spectral and NMR analysis. The presence of a methyl branch is indicated by a 3-proton doublet at δ 0.84 in the ^{1}H NMR spectrum. A terminal methyl appears as a triplet at δ 0.87. ^{13}C NMR likewise shows two methyl groups (δ 19.5, q and 14.0, q). In the mass spectrum, a sesquential loss of twelve methylene units is observed for the major homolog. A peak at *m/z* 71 corresponds to C_5H_{11} allowing the assignment of the alkyl moiety as 13-methylhexadecyl (15-methyloctadecyl for the minor homolog):



This establishes the gross structure of the ethers as **6** and **7**.



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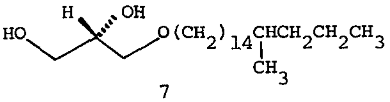

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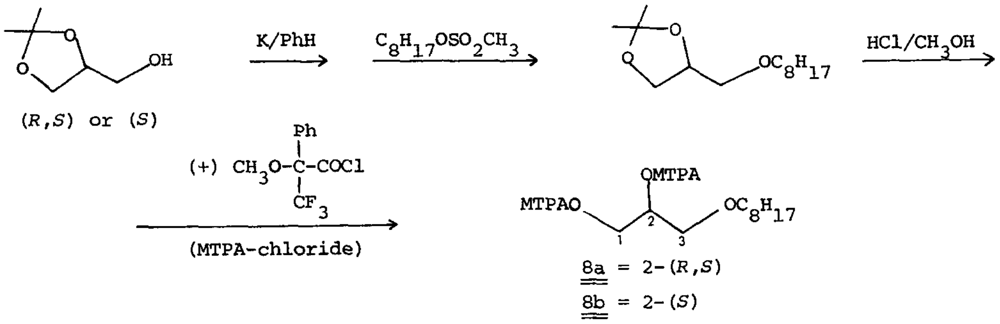
The configuration of C-2 in the glyceryl moiety was determined by derivatization with (+)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride (MTPA-chloride).[8] (*R*,*S*)-*bis*-(+)-MTPA octyl ether **8a** and (*S*)-*bis*-(+)-MTPA octyl ether **8b** were prepared from the corresponding protected glycerols (commercially available) as shown in Scheme I. HPLC[9] resolved the epimeric mixture **8a**, with the (*S*)-isomer eluting first. The C-1 protons of pure **8b** appeared as two doublets of doublets one centered at δ 4.60 and the other at δ4.34 in the ^{1}H NMR. The (*R*,*S*)-mixture, **8a**, displayed these same signals plus a second set, centered at δ 4.70 and 4.39 (Figure I). The latter set is



SCHEME I

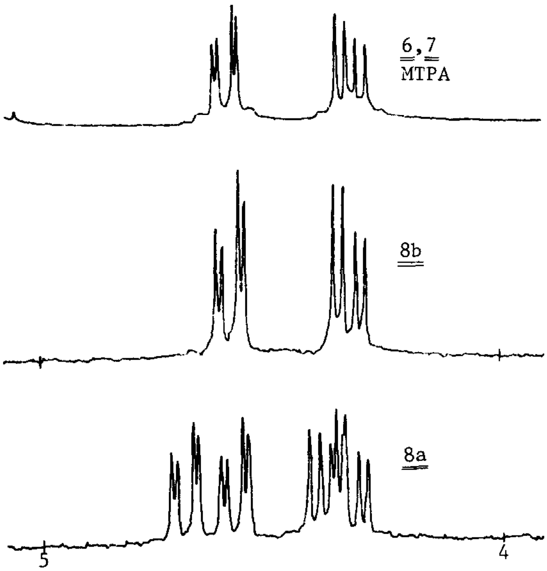
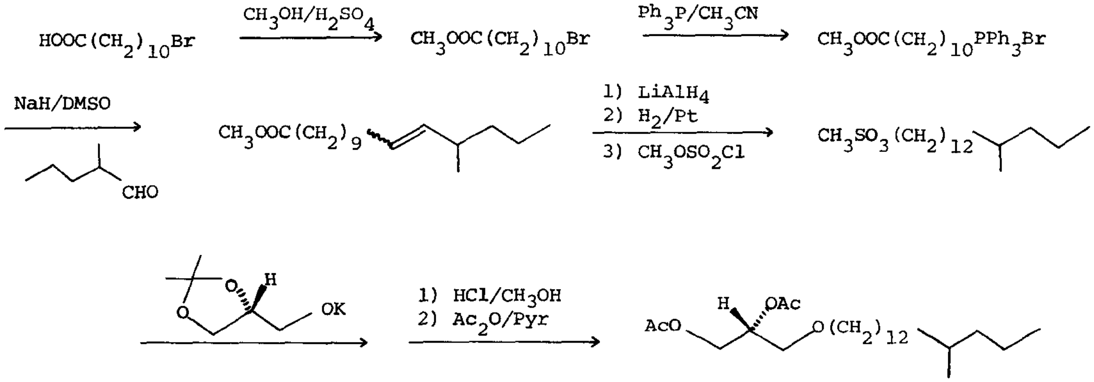


FIGURE I: 250 MHz ^1H NMR Spectra of 8a, 8b, and 6,7 (+)-MTPA Esters

thus ascribed to the (*R*)-isomer. A comparison of the ^1H NMR spectrum of the (+)-MTPA ester of natural products 6 and 7 with the synthetic octyl ethers 8a and 8b clearly established the natural products as the (*S*)-isomers as they displayed doublets of doublets at δ 4.56 and δ 4.31 but lacked those characteristic of the (*R*)-isomer (Figure I).

A total synthesis of 6 was carried out to verify structure (Scheme II). Attempts to construct the alkyl side chain directly via copper coupling reactions were unsuccessful. It was obtained instead by a Wittig coupling between the phosphonium salt derived from methyl 11-bromoundecanoate and 2-methylpentanal followed by reduction. The mesylate of the derived alcohol was converted to the glyceryl ether in the same fashion as that used for construction of the octyl ethers 8a and 8b. Acetylation of the synthetic material afforded the diacetate which was identical (TLC, IR, and NMR) to the diacetate derived from the natural product.



SCHEME II

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1. See, for example, R. J. Wells, *Tetrahedron Lett.*, 2637 (1976); G. Cimino and S. De Stefano, *ibid.*, 1325 (1977); M. B. Yunker and P. J. Scheuer, *ibid.*, 4651 (1978); R. D. Walkup, G. C. Jamieson, M. R. Ratcliff, and C. Djerassi, *Lipids*, **16**, 631 (1981); E. Ayanoglu, R. D. Walkup, D. Sica, and C. Djerassi, *ibid.*, **17**, 617 (1982); E. Ayanoglu, J. M. Kornprobst, A. Aboud-Bichara, and C. Djerassi, *Tetrahedron Lett.*, **24**, 1111 (1983).
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4. T. Kusmi, M. Ishitsuka, T. Iwashita, H. Naoki, T. Konno, and H. Kakisawa, *Chemistry Lett.*, 1393 (1981).
5. A voucher specimen has been deposited at the Smithsonian Institute, Washington, D.C., U.S. National Museum Catalog Number 32396.
6. To our knowledge only one other report on the chemistry of a member of this genus has appeared. From *Aaptos aaptos* a heterocyclic amine, aaptamine, was isolated: H. Nakamura, J. Kobayashi, and Y. Ohizumi, *Tetrahedron Lett.*, **23**, 5555 (1982).
7. IR (CCl_4): ν 3610, 3400, 2890, 2790, 1440, 1410, 1350, 1090, 1060 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.87 (1H, m), 3.75 (1H, dd, J=4, 12 Hz), 3.64 (1H, dd, J=6, 12 Hz), 3.55 (2H, d, J=4 Hz), 3.50 (2H, t), 1.27-1.57 (m), 0.87 (3H, t), 0.84 (3H, d, J=7 Hz); ^{13}C NMR ($CDCl_3$) δ 72.2 (t), 71.7 (t), 70.4 (d), 64.1 (t), 36.9 (t), 32.6 (d), 31.8 (t), 29.9, 29.5, 29.4, 29.3, 26.9 (t), 25.9 (t), 22.5 (t), 19.5 (q), 14.0 (q).
8. J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, **34**, 2543 (1969); J. A. Dale and H. S. Mosher, *J. Am. Chem. Soc.*, **95**, 512 (1973).
9. 10 μ Ultrasil column (Beckman), 50:50 CH_2Cl/C_6H_{14}

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