Journal of Natural Products
Vol. 53, No. 3, pp. 732-734, May-Jun 1990

DIYNE ENOL ETHERS OF GLYCEROL FROM A NEW ZEALAND SPONGE, *PETROSIA HEBES*

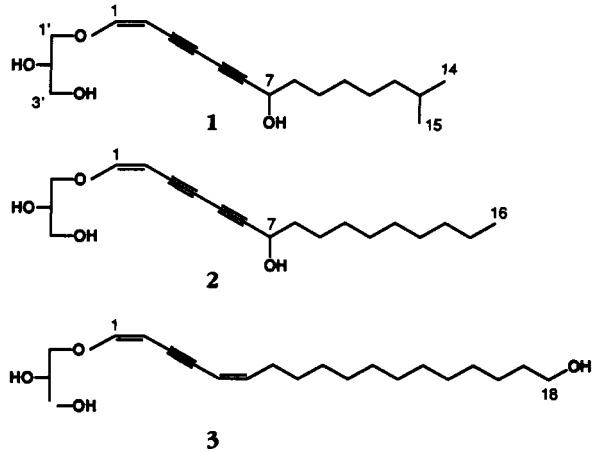
NIGEL B. PERRY,* ELEANOR G. BECKER, JOHN W. BLUNT, ROBIN J. LAKE, and MURRAY H.G. MUNRO

Department of Chemistry, University of Canterbury, Christchurch, New Zealand

ABSTRACT.—An extract of the sponge *Petrosia hebes* contained diyne enol ethers **1** and **2**, a new class of glyceryl ether.

Esterified glyceryl ethers are commonly encountered in a wide variety of organisms (1). However, with the exception of the mutagenic fecapentaenes [isolated from human feces but of bacterial origin (2)], unesterified monoalkyl and monoalkenyl ethers of glycerol are typically marine natural products (3,4). We now report that an extract of the New Zealand sponge *Petrosia hebes* Lendenfeld (family Nepheliospongidae, order Nepheliospongida) contained the two diyne enol ethers **1** and **2**, examples of a new class of glyceryl ether. Previous reports on *P. hebes* have described other lipid components, which were similar to those of the Mediterranean sponge *Petrosia ficiformis* Poiret. The phospholipids contained mainly two long-chain, branched fatty acids, together with mono-brominated analogues (5). The major sterol of both *P. hebes* and *P. ficiformis* was petrosterol (6).

P. hebes was investigated because an extract was toxic toward P388 leukemia cells. The P-388-active components were a complex series of long-chain polyalkyne triols and tetraols, as found in *P. ficiformis* (7) but not previously reported in *P. hebes*. During this bioactivity-directed study, it was noticed that the ^{1}H-nmr spectra of two fractions showed the presence of another class of compound, with coupled (6.4 Hz) doublets at 6.5 and 4.5 ppm. Reversed-phase liquid chromatography (rplc) on these fractions gave two related compounds **1** and **2**, which were not significantly cytotoxic (P-388 ID_{50}'s >6 and >11 μg/ml, respectively). The doublets in the ^{1}H-nmr spectra were assigned to an oxygenated double bond with *Z* stereochemistry, as found in the raspailynes, e.g., **3** (4). Both **1** and **2** also showed ^{1}H- and ^{13}C-nmr signals corresponding to a 1′-glyceryl ether. The ^{1}H-nmr spectra of the two compounds differed in that the minor component (less



retained on rplc) contained an alkyl chain terminated by an isopropyl group and the major component had an unbranched alkyl chain. Ms yielded molecular formulae of $C_{18}H_{28}O_4$ and $C_{19}H_{30}O_4$, respectively, i.e., five degrees of unsaturation. Comparison of the uv spectra with that of a model compound showed the presence of a diyne enol ether chromophore (8). The remaining feature in the ^{1}H-nmr spectra of the two compounds was a one-proton triplet at 4.37 ppm that showed a long range (0.8 Hz) coupling to the β proton on the double bond. This was interpreted as $^7J_{HH}$ through a diyne (9) and the chemical shift was appropriate for a -C≡C-CH.OH-CH_2- signal (10). The structures of these two compounds were therefore **1** and **2**, fully in accord with the ^{13}C-nmr spectra, apart from the difficulty in observing the alkyne carbon signals (despite the two chiral centers, neither showed any circular dichroism over the range 250–350 nm).

This is the first report of diyne enol ethers of glycerol. The most closely related natural products are the raspailynes, e.g., **3**, enyne enol ethers of glycerol from two *Raspailia* sponges (4). Despite the similarities between **1** and **2** and the raspailynes, some of which are also terminally branched (4), the genus *Raspailia* (family Raspailiidae, order Axinellida) is not related to *Petrosia*. The glyceryl ethers **1** and **2** and the long-chain polyalkynes (which make up ca. 7% of the lipids) are probably cell membrane components, along with the unusual fatty acids and sterols previously described (5,6).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mass spectra were recorded on Finnegan 4500 (dci) or VG7070F (high resolution) instruments. Uv (MeOH) and ir (film) spectra were recorded on Varian DMS 100 and Pye Unicam SP3-300 spectrometers, respectively. Nmr spectra, of CD_3OD solutions at 23° were recorded at 300 MHz for ^{1}H and 75 MHz for ^{13}C on a Varian XL300 spectrometer. Chemical shifts are given in ppm on the δ scale (followed by assignment, couplings in Hz and multiplicity), referenced to the solvent peaks: CHD_2OD at 3.30 and CD_3OD at 49.3.

SPONGE COLLECTION.—*P. hebes*, University of Canterbury voucher specimen 87PK02-07, was collected in February 1987, from the Poor Knights Islands (174° 44.2′ E, 35° 28.3′ S) off the northeast coast of New Zealand, at a depth of 33 m inside a sea arch.

EXTRACTION AND ISOLATION OF **1** AND **2**.—The sponge (178 g) was blended with $MeOH/CH_2Cl_2$ and filtered to give an extract (9.8 g) that was partitioned between EtOAc and H_2O. The EtOAc fraction (1.32 g) was subjected to two stages of reversed-phase flash chromatography (11). The fractions eluted with MeOH-H_2O (90:10 and 95:5) (0.35 g) were then subjected to Si gel (Davisil, 35–70 μm, 150 Å) cc. The fractions eluted with $CHCl_3$-MeOH (95:5 and 90:10) (16 mg and 10 mg) were then subjected to rplc [Lobar Lichroprep column, 310 × 25 mm, packed with RP-18, 40–63 μm, eluted with MeOH-H_2O (8:2)] to give compounds **1** and **2** (3 and 4 mg).

3-{[(1Z)-7-hydroxy-13-methyltetradeca-1-ene-3,5-diynyl]oxy}-1,2-propanediol [**1**].—A brown oil: hreims $[M]^+$ 308.1984 ($C_{18}H_{28}O_4$ requires 308.1987); dcims (NH_3) $[M+NH_4]^+$ 326; λ max (log ε) 292 nm (3.83), 276 (3.91), 262 (3.78), 223 (4.15); ν max 3350, 2925, 2860, 2225, 1620, 1460, 1100, 1060, 725 cm^{-1}; ^{1}H nmr 6.65 (d, 6.4, H-1), 4.53 (dd, 6.4, 0.9, H-2), 4.37 (td, 6.8, 0.8, H-7), 4.03 (dd, 11.0, 4.3, H-1′), 3.94 (dd, 11.0, 5.9, H-1′), 3.8 (m, H-2′), 3.45–3.65 (m, H-3′), 1.25–1.7 (m), 0.88 (d, 6.6, H-14 and H-15); ^{13}C nmr 161.60 (C-1), 84.35 (C-2), 76.29 (C-1′), 72.35 (C-2′), 64.03 (C-3′), 63.60 (C-7), 40.40 (C-12), 39.12 (C-8), 31.05, 30.91 (C-10 and C-11), 29.41 (C-13), 26.62 (C-9), 23.32 (C-14 and C-15).

3-{[(1Z)-7-hydroxyhexadeca-1-ene-3,5-diynyl]oxy}-1,2-propanediol [**2**].—A brown oil: hreims $[M]^+$ 322.2132 ($C_{19}H_{30}O_4$ requires 322.2144); dcims (NH_3) $[M+NH_4]^+$ 340; λ max (log ε) 292 nm (3.97), 276 (4.05), 262 (3.90), 223 (4.29); ν max 3375, 2925, 2870, 2225, 1620, 1100, 1060, 725 cm^{-1}; ^{1}H nmr 6.52 (d, 6.4, H-1), 4.53 (dd, 6.4, 0.8, H-2), 4.37 (td, 6.7, 0.8 Hz, H-7), 4.04 (dd, 11.0, 4.3, H-1′), 3.94 (dd, 11.0, 5.9, H-1′), 3.81 (m, H-2′), 3.45–3.65 (m, H-3′), 1.6–1.7 (m, H-8), 1.2–1.45 (m), 0.89 (t, 6.8 Hz, H-16); ^{13}C nmr 161.6 (C-1), 84.36 (C-2), 76.29 (C-1′), 72.35 (C-2′), 64.05 (C-3′), 64.60 (C-7), 39.14 (C-8), 33.35 (C-14), 30.94, 30.71, 30.67 (C-10, -11, -12, and -13), 26.61 (C-9), 24.02 (C-15), 14.72 (C-16).

ACKNOWLEDGMENTS

Research support from the Harbor Branch

Oceanographic Institution, Fort Pierce, Florida, is gratefully acknowledged. We thank C.N. Battershill, Australian Institute of Marine Sciences, for the sponge collection and identification; G. Barns for bioassays; L.K. Pannell, National Institute of Diabetes, Digestive and Kidney Diseases, NIH, Bethesda, for ms measurements; and the Canterbury Medical Research Foundation and the New Zealand University Grants Committee for equipment.

LITERATURE CITED

1. F. Snyder, Ed., "Ether Lipids: Chemistry and Biology," Academic Press, New York, 1972.
2. N. Hirai, D.G.I. Kingston, R.L. Van Tassell, and T.D. Wilkins, *J. Nat. Prod.*, **48**, 622 (1985).
3. G.M. Smith and C. Djerassi, *Lipids*, **22**, 236 (1987).
4. G. Guella, I. Mancini, and F. Pietra, *Helv. Chim. Acta*, **70**, 1050 (1987).
5. W.M.D. Wijekoon, E. Ayanoglu, and C. Djerassi, *Tetrahedron Lett.*, **25**, 3285 (1984).
6. J.-H. Cho and C. Djerassi, *J. Chem. Soc., Perkin Trans. 1*, 1307 (1987).
7. G. Cimino, A. De Giulio, S. De Rosa, and V. Di Marzo, *Tetrahedron Lett.*, **30**, 3563 (1989).
8. F. Bohlmann, W. Sucrow, and I. Queck, *Chem. Ber.*, **97**, 2586 (1964).
9. D.G. Morris, in: "The Chemistry of Triple-bonded Functional Groups. Part 2." Ed. by S. Patai and Z. Rappoport, Wiley, Chichester, 1983, p. 1035.
10. G. Guella, I. Mancini, and F. Pietra, *Helv. Chim. Acta*, **70**, 1400 (1987).
11. J.W. Blunt, V.L. Calder, G.D. Fenwick, R.J. Lake, J.D. McCombs, M.H.G. Munro, and N.B. Perry, *J. Nat. Prod.*, **50**, 290 (1987).

Received 9 November 1989