

PHYCOPSISENONE, A NEW PHENOLIC SECONDARY METABOLITE FROM THE SPONGE *PHYCOPSIS* SP.¹

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ABSTRACT.—Crotonic acid, phenylacetic acid, 4-hydroxyphenylacetic acid, methyl 4-hydroxyphenylacetate, 4-hydroxybenzaldehyde, 4-isobutyl- α -methylbenzyl alcohol [**1**], and a new phenolic derivative, phycopsisenone [**2**], have been isolated from the sponge *Phycopsis* sp., and characterized by interpretation of spectral data.

Numerous prenylated aromatic compounds have been isolated from marine flora and fauna (1). Particularly large numbers of these compounds have been reported from brown algae (2). For example, a bis-prenylated phenol, 2,4-bis-(3-methylbutenyl)-phenol, isolated from the brown algae *Encyothalia cliftonii* (3) and *Penithalia caudata* (4), showed significant feeding deterrence towards the herbivorous sea urchin *Tripneustes esculentus*. Two aromatic sesquiterpenes, curcuphenol and dehydrocurcuphenol, isolated from the sponge *Epipolasis* sp. (5), exhibited strong inhibitory activity against H⁺ and K⁺ ATPase. In search of biologically active secondary metabolites from marine invertebrates, we investigated a sponge, *Phycopsis* sp., collected from the Tuticorin coast, Tamilnadu, India, during April 1993. A 1:1 CH₂Cl₂-MeOH extract of this organism exhibited antibacterial activity against *E. coli* and *B. subtilis*.

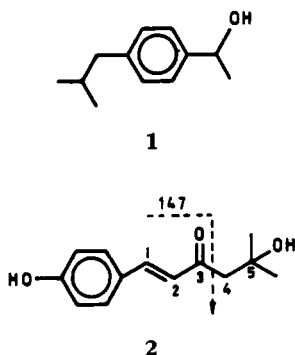
The CH₂Cl₂-MeOH (1:1) extract of the sponge was subjected to gel filtration chromatography followed by Si gel cc, resulting in the isolation of crotonic acid (50 mg), phenylacetic acid (150 mg), 4-hydroxyphenylacetic acid (150 mg), methyl 4-hydroxyphenylacetate (25 mg), 4-hydroxybenzaldehyde (50 mg), 4-

isobutyl- α -methylbenzyl alcohol [**1**] (40 mg), and phycopsisenone [**2**] (50 mg).

Compound **1** was obtained as an oil, $[\alpha]_D -0.9^\circ$ ($c=1$, CHCl₃), and identified as 4-isobutyl- α -methylbenzyl alcohol by the study of its ¹H-nmr and mass spectral data. Compound **1** is a key intermediate in the synthesis of ibuprofen (6), an antiinflammatory drug. To establish the stereochemistry of the secondary alcohol in **1**, its (*R*)-MTPA ester was prepared (7). The ¹H-nmr spectrum of the (*R*)-MTPA-ester of **1** was consistent with the presence of a diastereomeric mixture, composed of the (*S*)- and (*R*)- isomers in a 3:2 ratio. The small negative optical rotation observed for compound **1** compared with that of the synthetic *R*(+)- isomer (8) was attributed to the predominance of the (*S*)- isomer in the isolated sample.

Phycopsisenone [**2**] was obtained as a crystalline solid, which analyzed for C₁₃H₁₆O₃ by combustion analysis. A methanolic solution of **2** showed a coloration with FeCl₃, implying the phenolic nature of the compound. The ir bands at 3450, 1680, 1640, 1560 cm⁻¹ indicated the presence of hydroxyl and α,β -unsaturated carbonyl groups. The ¹H-nmr spectrum of compound **2** contained signals for two Me groups attached to an oxygen-bearing carbon at δ 1.3 (6H, s), an uncoupled methylene group at δ 2.8 (2H, s), and a para-disubstituted benzene ring with resonances at δ 6.9 (2H, d, $J=7$ Hz) and 7.5 (2H, d, $J=7$ Hz). Furthermore,

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the ^1H -nmr spectrum revealed the presence of a trans-disubstituted double bond, in conjugation with a carbonyl group, at δ 6.6 (1H, d, $J=13.7$ Hz) and 7.6 (1H, d, $J=13.7$ Hz). From an analysis of the foregoing spectral data, the structure of phycopsisene was established as **2**, 5-hydroxy-1-(4-hydroxyphenyl)-5-methyl-1-hexen-3-one, which was supported by its ^{13}C -nmr and mass [m/z 147 (100)] spectral data. A literature survey revealed only a lone report on the genus, i.e., for *Phycopsis terpinis*, which afforded the isolation of sesquiterpene thiocyanates (9).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were measured with a Jasco Dip-370 polarimeter. ^1H -Nmr (200 MHz) and ^{13}C -nmr (50 MHz) spectra were recorded on a Varian Gemini-200 MHz spectrometer, using TMS as an internal standard. Chemical shifts are reported in δ (ppm) values and coupling constants (J) are in Hz. Uv and ir spectra were recorded on a Shimadzu spectrometer. Mass spectra were recorded on a Finnigan-MAT 1020 instrument.

ANIMAL MATERIAL.—The sponge *Phycopsis* sp. was collected using scuba at 40 ft depth from the Tuticorin coast, Tamilnadu, India, during April 1993. A voucher specimen is on deposit at the NIO Museum Goa, India.

EXTRACTION AND ISOLATION.—The freshly collected specimen (400 g wet wt) was extracted with CH_2Cl_2 -MeOH (1:1) (3 \times 2 liters) at room temperature. The combined extract was filtered and solvent was removed under reduced pressure. The crude extract (2 g) was subjected to gel filtration cc (Sephadex LH-20) using CH_2Cl_2 -MeOH (1:1) as eluent. The fractions thus obtained were subjected to cc on Si gel using hexane/EtOAc

gradients and yielded 4-isobutyl- α -methylbenzyl alcohol [**1**] (40 mg), phycopsisene [**2**] (50 mg), 4-hydroxybenzaldehyde (50 mg), methyl 4-hydroxyphenylacetate (25 mg), phenylacetic acid (150 mg), crotonic acid (50 mg), and 4-hydroxyphenylacetic acid (150 mg). Phycopsisene [**2**] was obtained as a colorless crystalline solid, mp 135°; *anal.*, found C, 70.72%, H, 7.21%, required for $\text{C}_{13}\text{H}_{16}\text{O}_3$, C, 70.88%, H, 7.32%; uv (MeOH) λ max (log ϵ) 225 (7949) nm; ir (KBr) ν max 3450 (OH), 1680 (CO), 1640, 1560 cm^{-1} ; ^1H nmr (CDCl_3 , 200 MHz) δ 7.6 (1H, d, $J=13.7$ Hz), 7.5 (2H, d, $J=7$ Hz), 6.9 (2H, d, $J=7$ Hz), 6.6 (1H, d, $J=13.7$ Hz), 2.8 (2H, s), 1.3 (6H, s); ^{13}C nmr (CDCl_3 , 50 MHz) δ 201.7 s, 158.4 s, 143.7 d, 130.5 d (2 \times C), 126.7 s, 124.5 d, 116.1 d (2 \times C), 70.6 s, 50.5 t, 29.4 q, 29.2 q; eims (70 eV) m/z [$\text{M}]^+$ 220 (10), 202 (4), 162 (20), 147 (100), 107 (65).

PREPARATION OF (R)-MTPA ESTER OF COMPOUND 1.—A solution of **1** (5 mg, 0.02 mmol) in CH_2Cl_2 (1 ml) was treated at room temperature with *R*-MTPA (7 mg), DCC (5 mg), and DMAP (5 mg) for 5 min. The reaction mixture was diluted with Et_2O , worked up as usual, then charged onto a Si gel column. Elution with 5% EtOAc in hexane gave the *R*-MTPA ester of **1**.

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LITERATURE CITED

1. D.J. Faulkner, *Nat. Prod. Rep.*, **1**, 251 (1984).
2. R.E. Moore, in: "Marine Natural Products: Chemical and Biological Perspectives." Ed. by P.J. Scheuer, Academic Press, New York, Vol. 1, 1978, p. 43.
3. V. Roussis, R.L. King, and W. Fenical, *Phytochemistry*, **34**, 107 (1993).
4. A.J. Blackman, G.I. Rogers, and J.K. Volkman, *Phytochemistry*, **27**, 3686 (1986).
5. N. Fusetani, M. Sugano, S. Matsunaga, and K. Hashimoto, *Experientia*, **43**, 1234 (1987).
6. "American Drug Index." Ed. by N.F. Billips, J.B. Lippincott, Philadelphia, 29th Ed., 1985.
7. J.A. Dale, D.L. Dull, and H.S. Mosher, *J. Org. Chem.*, **34**, 2543 (1969).
8. S.-H. Hsu, S.-S. Wu, and Y. Fong, *Tetrahedron Lett.*, **31**, 6403 (1990).
9. T.A. Pham, T. Ichiba, W.Y. Yoshida, P.J. Scheuer, T. Uchida, T. Junichi, and T. Higa, *Tetrahedron Lett.*, **32**, 4843 (1991).

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