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3-HYDROXY-7-PHENYL-4*E*,6*E*-HEPTADIENOIC ACID FROM AN ASCIDIAN *DIDEMNUM GRANULATUM*

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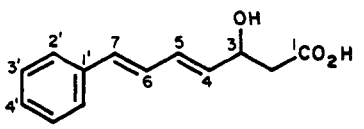
ABSTRACT.—A new hydroxy phenylheptadienoic acid [**1**] has been isolated from the ascidian *Didemnum granulatum* collected from the Gulf of Eilat in the Red Sea.

Phenylpolyenes (polyketides) were earlier reported from brown algae (1–5) and from opisthobranchs (6–7). We report here the isolation and structure elucidation of a new hydroxy phenyldienoic acid [**1**] from an encrusting pale pink ascidian, *Didemnum granulatum* (family Didemnidae, class Ascidiacea) collected from the Red Sea.

From the EtOAc extract of *D. granulatum* we have isolated, after chromatography over a Sephadex LH-20 column, a carboxylic acid [**1**]. The carboxylic group of **1** (ν max 3300–2500 br, 1710 cm^{-1}) was confirmed by micromethylation with CH_2N_2 (δ_H 3.76s, $COOCH_3$).

Compound **1** has a molecular formula of $C_{13}H_{14}O_3$ which was established by hreims ($[M]^+$, *m/z* 218.0923, 100%, Δ mmu 2) and was supported by ^{13}C-nmr data including the DEPT experiment, and ^1H-nmr data. The ^{13}C-nmr spectrum showed, besides a carboxylic carbon [δ 177.5 (s)], one methinoxy [δ 72.9 (d)] one single methylene [δ 47.9 (t)], and seven sp^2 carbons (one singlet and six overlapping doublets). The latter functionalities were in full agreement with the ^1H-nmr data (See Experimental). The proton chemical shifts, coupling constants, double resonance irradiations and the COSY nmr experiment established the structure of **1** as 3-hydroxy-7-phenyl-4*E*,6*E*-heptadienoic acid whose stereochemistry remains to be deduced. The compound was too unstable for performing bioassays.



1

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Given in Isaacs *et al.* (8).

ISOLATION OF ACID **1**.—The sample of the *D. granulatum* (190 g, dry wt, YK 8983, August 1989; a voucher specimen is deposited at the Department of Zoology at Tel Aviv University collected from the Gulf of Eilat in the Red Sea at a depth of 15–20 m) was freeze-dried and extracted with EtOAc to give a brownish oil (0.2 g). This EtOAc extract was chromatographed on Sephadex LH-20, with hexane-EtOAc-MeOH (2:1:1) to give the acid **1** (20 mg, 10% w/w of the crude extract) as an unstable yellow-brown solid; $[\alpha]_D$ +5° (*c*=0.5, MeOH); uv, λ max (EtOH) 233, 280, 306 nm; eims *m/z* 218 ($[M]^+$, 100), 200 ($[M]^+-H_2O$, 32), 156 ($[M]^+-H_2O-CO_2$, 74); ir (KBr) ν max 3300–2500, 1710 cm^{-1}; ^1H nmr (200 MHz, DMSO-d_6) δ 6.78 (2H, d, *J*=7.5 Hz, H-2', -6'), 6.65 (2H, t, *J*=7.5 Hz, H-3', -5'), 6.55 (1H, t, *J*=7.5 Hz, H-4'), 6.22 (1H, dd, *J*=10.5 and 15.7 Hz, H-6), 5.90 (1H, d, *J*=15.7 Hz, H-7), 5.70 (1H, dd, *J*=10.5 and 15.1 Hz, H-5), 5.21 (1H, dd, *J*=15.1 and 6.0 Hz, H-4), 3.79 (1H, dd, *J*=6.0 Hz, H-3), 1.69 (2H, d, *J*=6.0 Hz, H_2-2); ^{13}C nmr (50.7 MHz DMSO-d_6) δ 177.5 (s, C-1), 142.7 (d, C-4), 142.3 (s, C-1'), 136.9 (d, C-7), 134.5 (d, C-5), 133.9 (d, C-3', -4', -5'), 132.7 (d, C-6), 131.5 (d, C-2', -6'), 72.9 (d, C-3), 47.9 (t, C-2). A ^1H-^1H COSY experiment showed correlations between: H_2-2/H-3; H-3/H-4, -5; H-4/H-5; H-5/H-6; H-6/H-7; H-7/H-2', H-2'/H-3',-4', and between H-3'/H-4'.

Methylation of **1** (2 mg) with CH_2N_2 in $(C_2H_5)_2$ O-MeOH (1:1, 1 ml) afforded methyl 3-

hydroxy-7-phenyl-4,6-heptadienoate. ^{1}H nmr ($CDCl_3$, 200 MHz) δ 7.42 (2H, d, J=7 Hz, H-2′, -6′), 7.30 (2H, t, J=7 Hz, H-3′, -5′), 7.29 (1H, t, J=7 Hz, H-4′), 6.68 (1H, dd, J=10 and 15 Hz, H-6), 6.60 (1H, d, J=15 Hz, H-7), 6.50 (1H, dd, J=10 and 15 Hz, H-5), 5.86 (1H, dd, J=5 and 15 Hz, H-4), 4.69 (1H, m, H-3), 3.76 (3H, s, OMe) δ 2.63 (2H, br s, H_2-2); ir (neat) ν max 1720, 1210 cm^{-1}.

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