

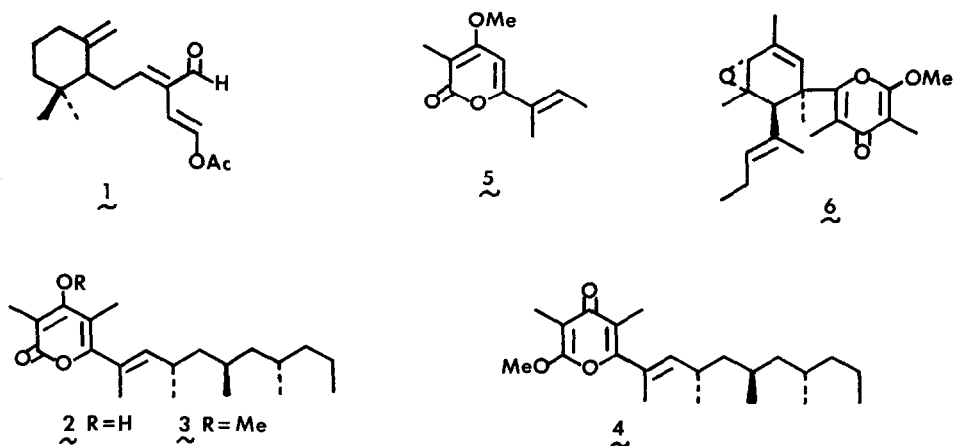
PECTINATONE, A NEW ANTIBIOTIC FROM THE MOLLUSC SIPHONARIA PECTINATA

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Summary: A new polypropionate antibiotic with a γ -hydroxy- α -pyrone ring was isolated from the marine mollusc Siphonaria pectinata

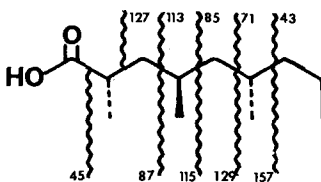
Marine molluscs of the families Onchidiacea and Siphonariacea are trail following species¹ that possess "repugnatorial glands" that secrete defensive chemical substances.² Previously, Ireland and Faulkner isolated potent antibiotic onchidal (1) as the active constituent produced by repugnatorial glands on the dorsum of Onchidella binneyi.³ We now wish to report the isolation of a new antibiotic pectinatone (2) (active against gram (+) bacteria; Staphylococcus aureus, Bacillus subtilis, yeast Candida albicans, Saccharomyces cerevisiae) from skin extracts of Siphonaria pectinata.



Siphonaria pectinata collected on the sea wall at the entrance of Key Biscayne, Florida were soaked in MeOH for five days. The MeOH extract was evaporated and the residue partitioned between H₂O and CHCl₃ to give 530 mg of organic oil. Silica gel column chromatography of 244 mg of oil eluting with EtOAc/iso-octane (4:6) gave 181 mg of 2 that crystallized on standing in

CH_2Cl_2 (HRMS: obs. 334.2503; calc. 334.2508).⁴ A γ -hydroxy- α -pyrone further conjugated to a trisubstituted olefin was indicated by infrared absorptions at 3163, 1685-1649 br, 1624 cm^{-1} ; uv_{max} 301 nm (ϵ 5063); ^{13}C NMR δ 166.5 s, 166.2 s, 159.2 s, 142.9 d, 126.2 s, 107.0 s, 98.8 s, 14.3 q, 11.6 q, 8.7 q; ^1H NMR δ 2.0 (s, 6H), 1.89 (d, 3H, $J=1\text{Hz}$), 5.38 (dq, 1H, $J=10, 1\text{Hz}$), 8.8 (br s). Treatment of 2 with CH_2N_2 gave methyl ethers 3 and 4⁵ in equal quantities, indicative of hydroxy pyrones. The spectral data for 3 were similar to the data reported for nectriapyrone (5),⁶ taking into account a substituent effect for a methyl on the delta carbon. Furthermore, the spectral properties of 4 were virtually identical to tridachione (6),⁷ further solidifying the pyrone assignment in 2. An SFORD experiment with 3 allowed assignment of the ^{13}C resonance at 11.8 ppm to the vinyl methyl group and thus an E configuration to the trisubstituted olefin.

In addition to resonances for the trisubstituted olefin, the ^1H NMR spectrum of 2 contained signals for three secondary and one primary methyl group suggestive of a polypropionate chain. Irradiation of the allylic proton at δ 2.61 collapsed the vinyl proton at 5.38, the methyl at 0.98 and diastereotopic methylene protons at 1.31 and 1.06 defining the first two propionate units. Irradiation of a methylene multiplet centered at 1.23 collapsed the triplet methyl signal at 0.86 and geminally coupled protons at 1.31 and 1.06 fixing the end unit. The two remaining methine protons coalesced at 1.47 ppm. Irradiation of this signal collapsed the doublet methyls at 0.85 and 0.80 as well as methylene protons at 1.17 and 0.93. Ozonolysis, by dropwise addition of a ozone saturated CH_2Cl_2 solution to a CH_2Cl_2 solution of 2 at -78°C gave (workup with Jones' reagent) 2,4,6-trimethylnonanoic acid. The electron impact mass spectrum of the acid showed a weak parent ion which peak matched for $\text{C}_{12}\text{H}_{24}\text{O}_2$ (obs. 200.1764; calc. 200.1776). The spectrum showed additional peaks for the fragmentation pattern shown below.



The methyl ester exhibited a rotation $[\alpha]_D +34.2^0$ (c 0.038, Et_2O) and was assigned 2S, 4R, 6S

absolute configuration (lit. + 35.2°).⁸

Recently, Faulkner isolated a related compound from a siphonaria species from Australia.⁹ This represented the first polypropionate metabolite from this genus.

Acknowledgements

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4. 2: mp 127-9°; [α]_D +62° (c 0.184, CHCl₃); IR 3136 br, 2951, 1685-1649 br, 1624, 1543, 1218 cm⁻¹; ν_{\max} 301 nm (ϵ 5060); ¹³C NMR δ 166.5 s, 166.2 s, 159.2 s, 142.9 d, 126.2 s, 107.0 s, 98.9 s, 45.8 t, 44.7 t, 39.3 t, 30.5 d, 29.7 d, 28.3 d, 21.1 q, 20.2 q, 20.1 q, 19.9 t, 14.7 q, 14.3 q, 11.6 q, 8.7 q; ¹H NMR δ 8.8 (s,1H), 5.38 (dq,1H,J=10,1Hz), 2.64 (m,1H), 2.0 (s,6H), 1.89(d,3H,J=1Hz), 1.47 (m,2H) 1.31 (m,2H), 1.23 (m,2H), 1.17 (m,1H), 1.06 (m,2H), 0.98 (d,3H,J=6Hz), 0.93 (m,1H), 0.86 (t,3H,J=7Hz), 0.85 (d,3H,J=6Hz), 0.80 (d,3H,J=6Hz); HRMS C₂₁H₃₄O₃, req. 334.2509; obs. 334.2503.
5. 3: [α]_D +69.6° (c 1.13, CH₂Cl₂); IR 2965, 1698, 1570 cm⁻¹; ν_{\max} 313 nm (ϵ 6.99 x 10³); ¹³C NMR δ 168.6 s, 165.5 s, 159.3 s, 142.8 d, 126.4 s, 109.8 s, 108.6 s, 60.1 q, 45.8 t, 44.7 t, 39.2 t, 30.5 d, 29.6 d, 28.3 d, 21.1 q, 20.2 q, 20.1 q, 19.9 t, 14.8 q, 14.3 q, 11.8 q, 10.1 q; ¹H NMR δ 5.38 (dq,1H,J=10,1Hz), 3.82 (m,3H), 2.65(m,1H), 2.06 (s,3H), 1.96 (s,3H), 1.90 (d,3H,J=1Hz), 1.48 (m,2H), 1.33 (m,2H), 1.26 (m,2H), 1.16 (m,1H), 1.07 (m,2H), 0.99

(d,3H,J=7Hz), 0.95 (m,1H), 0.88 (t,3H,J=7Hz), 0.86 (d,3H,J=7Hz), 0.82 (d,3H,J=7Hz); HRMS $C_{22}H_{36}O_3$ req.348.266, obs. 348.267.

4: $[\alpha]_D^{25} +51.1^0$ (c 1.10, CH_2Cl_2); IR 2970, 1660, 1595 cm^{-1} ; uv_{max} 261 nm (ϵ 7.66 x 10^3); ^{13}C NMR δ 181.6 s, 161.9 s, 158.6 s, 143.5 d, 129.8 s, 117.6 s, 99.3 s, 55.1 q, 45.8 t, 44.7 t, 39.2 t, 30.5 d, 29.6 d, 28.3 d, 21.1 q, 20.3 q, 20.1 q, 19.9 t, 14.6 q, 14.3 q, 11.7 q, 6.8 q; 1H NMR δ 5.46 (bd,1H,J=1,10Hz), 3.95 (s,3H), 2.68 (m,1H), 2.0 (s,3H), 1.94 (d,3H,J=1Hz), 1.89 (s,3H), 1.50 (m,2H), 1.37 (m,2H), 1.26 (m,2H), 1.18 (m,1H), 1.10 (m,2H), 1.03 (d,3H,J=7Hz), 0.98 (m,1H), 0.88 (d,3H,J=7Hz), 0.87 (t,3H,J=7Hz), 0.82 (d,3H,J=7Hz); HRMS $C_{22}H_{36}O_3$ req. 348.266, obs. 348.266.

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