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J. Nat. Prod., **1994**, 57 (6), 849-851 • DOI:
10.1021/np50108a029 • Publication Date (Web): 01 July 2004

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DC 20036

A NEW SESQUITERPENE/PHENOL FROM THE AUSTRALIAN MARINE BROWN ALGA *PERITHALIA CAUDATA*

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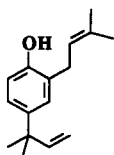
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ABSTRACT.—A chemical re-investigation of the Australian marine brown alga *Perithalia caudata* has resulted in the isolation of the known reverse isoprenylated aromatic [**1**] and the related chroman [**2**], along with the new sesquiterpene/phenol [**3**]. The structure of [**3**] was confirmed by spectroscopic analysis.

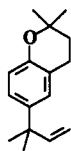
Natural products of mixed sesquiterpene and quinol biosynthesis are common to marine brown algae and sponges (1). Known examples include acyclic, monocyclic, and bicyclic analogues with varying degrees of oxygenation and/or substitution in the aromatic subunit. This report describes the isolation and identification of a new example of this structural class from an Australian marine brown alga.

Extraction of a sample of *Perithalia caudata* Womersley (Sporochnaceae) with EtOH-CH₂Cl₂ (9:1), followed by partitioning of the CH₂Cl₂-solubles and normal-phase (silica) chromatography, resulted in the isolation of three prenylated aromatics. The major component was identified by spectroscopic comparison as the known *Perithalia caudata* metabolite [**1**] (2). Likewise, one of the minor components was identified as the chroman [**2**], which had previously been described (2) via acid- or uv-catalyzed cyclization of **1**. Our attempts to induce this cyclization through exposure of **1** to Si gel at room temperature in the presence of sunlight, O₂ and common extraction solvents over prolonged periods, proved

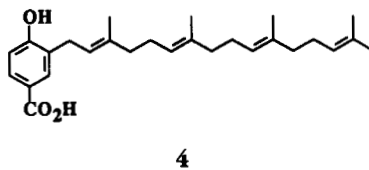
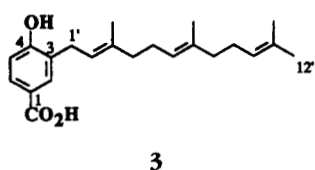
unsuccessful. Despite this, given the potential for such a process to occur during extraction and purification, it is difficult to confirm that **2** is a natural product and not an artifact of the isolation procedure. The remaining metabolite **3** displayed ¹H- and ¹³C-nmr resonances that were consistent with a farnesyl side-chain incorporating an all trans geometry (3), as well as a trisubstituted benzene and a carboxylic acid moiety. These features, together with a molecular formula of C₂₂H₃₀O₃, required that **3** be a farnesyl-substituted hydroxybenzoic acid. The presence of the phenolic functionality was supported by a characteristic ir absorption (3360 cm⁻¹). The hydroxybenzoic acid moiety was also supported by the appearance of a significant ion peak at *m/z* 151 in the mass spectrum, corresponding to benzylic cleavage (C-1'-C-2'). Although the ¹H-nmr spectrum (CDCl₃) of **3** displayed two aromatic protons with coincident resonances, a 1,2,4-aromatic substitution pattern was apparent from the appearance of the isolated aromatic proton as an ortho-coupled doublet (*J*=8.8 Hz). This assignment was further confirmed by analysis of the ¹H-nmr spectrum (C₆D₆) of **3**, which clearly revealed ortho-, ortho-/meta-, and meta-coupled aromatic protons, respectively. Irradiation of the benzylic methylene associated with the farnesyl side-chain revealed an nOe (2.8%) to the meta-coupled aromatic proton, thus placing them on adjacent aromatic carbons. That the meta- and ortho-/meta-coupled aromatic protons were significantly



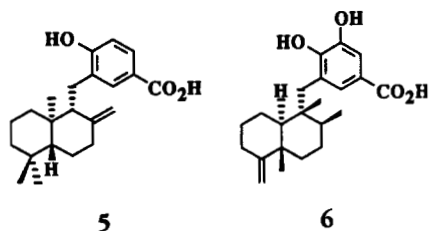
1



2



deshielded with respect to the ortho-coupled aromatic proton permitted the substitution pattern to be established as shown. Compound **3** is structurally related to the corresponding isoprene homologue **4** previously isolated from the sponge *Ircinia* sp. (4). Marine sesquiterpenes incorporating a prenylated *p*-hydroxybenzoic acid functionality, although uncommon, have been described from both brown algae (e.g., *Dictyopteris undulata*, zonic acid [**5**] (5)); and sponges (e.g., *Siphonodictyon coralliphagum*, siphonodictyic acid [**6**] (6)). To date



compound **3** represents the only example of this structure class incorporating an acyclic farnesyl side-chain.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Details of procedures can be found in Butler and Capon (7).

PLANT MATERIAL.—A sample of the alga *Perithalia caudata* (210 g dry wt, Melbourne University Herbarium N° MELU-A035023) collected by hand (scuba) offshore from Flinders, Victoria, was packed in ice and transported to the laboratory, where it was transferred to a polythene sample bottle and steeped in EtOH-CH₂Cl₂ (9:1).

EXTRACTION AND ISOLATION.—The decanted plant extract was then partitioned into CH₂Cl₂-solubles (9.10 g) and CH₂Cl₂-insolubles (8.78 g), with the former extract being subjected to further fractionation by rapid Si gel filtration [10%

stepwise gradient from petroleum ether (40–60°) to EtOAc] to yield **1** (2.252 g, 1.072%) plus a mixed fraction. The latter material was resolved by reversed-phase hplc (2.0 ml/min 5% H₂O/MeOH through a Phenomenex Ultracarb 5 μm ODS-20 250 × 10 mm column) to yield **2** (40 mg, 0.019%) and **3** (45 mg, 0.021%).

4-Hydroxy-3-(1'-((2'E,6'E)-3',7',11'-trimethyl-2',6',10'-dodecatrienyl))-benzoic acid [3**].**—A colorless oil. Ir ν max (film) 3360, 1680, 1600 cm⁻¹; ¹H nmr (400 MHz, CDCl₃) δ 1.59 (6H, s, CH₃-7' and 11'), 1.67 (3H, s, CH₃-3'), 1.78 (3H, s, H₃-12'), 2.12 (8H, m, H₂-4', -5', -8', and -9'), 3.39 (2H, d, J=7.3 Hz, H₂-1'), 5.08 (2H, m, H-6' and -10'), 5.33 (1H, ddd, J=7.1, 7.1, and 1.4 Hz, H-2'), 6.83 (1H, d, J=8.8 Hz, 5-H), 7.88 (2H, m, H-2 and H-6); ¹H nmr (400 MHz, C₆D₆) δ 1.52 (6H, s, CH₃-7' and -11'), 1.57 (3H, s, CH₃-3'), 1.68 (3H, s, H₃-12'), 2.10 (8H, m, H₂-4', -5', -8', and -9'), 3.24 (2H, d, J=7 Hz, H₂-1'), 5.21 (2H, m, H-6' and H-10'), 5.31 (1H, m, H-2'), 6.39 (1H, d, J=8.4 Hz, H-5), 8.02 (1H, dd, J=8.4 and 2.2 Hz, H-6), 8.15 (1H, d, J=2.8 Hz, H-2); ¹³C nmr (100 MHz, CDCl₃) 16.0^a, 16.3^a, 17.7^a (CH₃-3', -7', -11'), 25.7 (q, C-12'), 26.4^b (t, C-9'), 26.7^b (t, C-8'), 29.4^b (t, C-5'), 30.9^b (t, C-4'), 39.7 (t, C-1'), 115.1 (d, C-5), 121.0 (d, C-2'), 121.5^c (s, C-3), 123.6^c (s, C-6'), 124.4 (d, C-10'), 127.0^d (s, C-1), 130.4 (d, C-6), 131.3^d (s, C-7'), 132.5 (d, C-2), 135.5^d (s, C-3'), 139.0 (s, C-11'), 159.4 (s, C-4), 171.6 (s, C-7') ppm, assignments with identical superscripts^{a,b,c} or ^d may be interchanged; eims (70 eV) m/z 342 (2), 189 (10), 161 (9), 151 (34), 135 (18), 109 (19), 93 (21), 81 (42), 69 (100), 54 (27); hreims m/z 342.2193 (C₂₂H₃₀O₃ requires 342.2195), 151.0396 (C₈H₇O₃ requires 151.0395).

ACKNOWLEDGMENTS

We acknowledge G. Kraft for identifying the algal specimen. This research was funded by the Australian Research Council.

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Received 14 December 1993