

A New Sesquiterpene-substituted Benzoic Acid from the Brown Alga *Dictyopteris divaricata*

Fu Hang SONG^{1,3}, Xiao FAN^{1*}, Xiu Li XU^{1,3}, Jie Lu ZHAO², Li Jun HAN¹,
Jian Gong SHI^{2*}

¹Institute of Oceanology, Chinese Academy of Sciences, Qingdao 266071

²Institute of Materia Medica, Chinese Academy of Medical Sciences and
Peking Union Medical College, Beijing 100050

³Graduate School of the Chinese Academy of Sciences, Beijing 100039

Abstract: A new sesquiterpene-substituted benzoic acid has been isolated from the brown Alga *Dictyopteris divaricata* Okam.. Its structure was elucidated as 3-[(2-hydroxy-2,5,5,8a-tetra-methyldecahydro-1-naphthalenyl)methyl]-4-hydroxybenzoic acid, named dictyvaric acid on the basis of spectroscopic methods including IR, HRFABMS, 1D and 2D NMR techniques.

Keywords: Brown alga, *Dictyopteris divaricata*, 3-[(2-hydroxy-2,5,5,8a-tetramethyl-decahydro-1-naphthalenyl)-methyl]-4-hydroxybenzoic acid, dictyvaric acid.

Dictyopteris divaricata is a brown alga belonging to the Dictyotaceae family, and widely distributed along the coast of the Yellow Sea, China. The previous reports indicated that species of this genus contained sesquiterpene-substituted phenols¹⁻², sesquiterpene³⁻⁴ and C₁₁ hydrocarbons⁵⁻⁶. In our investigation of chemical constituents of seaweeds distributed along the coast of Shandong, China, a new sesquiterpene- substituted phenol named dictyvaric acid **1** has been isolated from *D. divarivata*. In this report, we describe the isolation and structure elucidation of **1**.

Figure 1 The key HMBC correlations of **1**

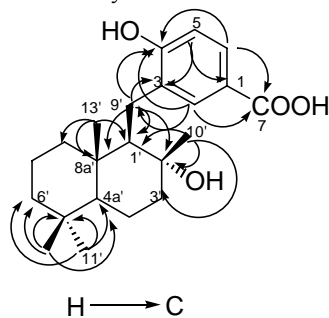
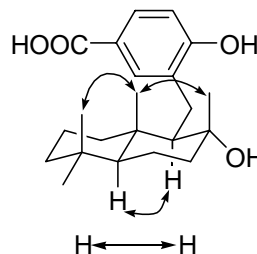


Figure 2 Selective NOESY correlations of **1**



* E-mail: fxiao@ms.qdio.ac.cn; shijg@imm.ac.cn

The air-dried brown alga *Dictyopteris divaricata* was powdered and extracted with 95% EtOH, and the solvent was removed under reduced pressure to give a residue (320.2 g). The ethanolic extract was suspended in water, and then partitioned with EtOAc. The EtOAc extract (120.3 g) was subjected to column chromatography over silica gel eluting with a gradient increasing acetone (0-100%) in petroleum ether to yield 21 fractions based on TLC analysis. The fraction eluted by 20% acetone in petroleum ether was separated over Sephadex LH-20, and then purified by reverse phase HPLC with MeOH as eluent to yield **1**.

Compound **1** was obtained as white needles (MeOH), mp: 256-258°C, $[\alpha]_D^{20} +29$ (c 0.1, CHCl₃). The molecular formula of **1**, C₂₂H₃₂O₄, was determined by negative ion HRFABMS at m/z 359.2248 [M-H]⁻ (calcd. 359.2222). The IR spectrum (KBr) of **1** showed strong broadened absorption bands for carboxyl groups (3429 cm⁻¹) and characteristic bands for conjugated carbonyl (1678 cm⁻¹) and aromatic rings (1614, 1587 and 1502 cm⁻¹). The ¹H NMR spectrum showed a characteristic ABX coupling system attributed to a 1,3,4-trisubstituted benzene moiety at δ_H 7.63 (dd, 1H, $J=10.5, 2.0$), 6.68 (d, 1H, $J=10.5$), and 7.78 (d, 1H, $J=2.0$) in the aromatic region, and signals assignable to four methyl groups attached to quaternary carbons at δ_H 0.77 (s, 3H), 0.80 (s, 3H), 0.94 (s, 3H,) and 1.21 (s, 3H,) in the upfield region. The ¹³C NMR and DEPT spectra of **1** showed twelve carbon signals including one carboxyl, three quaternary carbons (one oxygenated), two methines and six methylenes, beside signals attributed to four methyl groups and the 1,3,4-trisubstituted benzene moiety (see **Table 1**). These data suggested that **1** possessed a sesquiterpene-substituted phenol structure. The ¹H and ¹³C NMR data of sesquiterpene moiety of **1** were very similar to those of the sesquiterpene-substituted phenol yahazunol², except for those data attributed to the phenol moiety of **1**. An extensive comparison of the ¹³C NMR data of **1** with those of yahazunol revealed that the 1,4-dihydroxyphenyl moiety in yahazunol was replaced by the 3-substituted 4-hydroxybenzoic acid moiety in **1**. This was confirmed by 2D NMR experiments of **1**. The proton signals in ¹H NMR spectrum and protonated carbon signals in ¹³C NMR spectrum were unambiguously assigned by ¹H-¹H COSY and HMQC experiments (see **Table 1**). The sesquiterpene moiety was confirmed by the HMBC correlations from both H-11' and H-12' to C-4a', C-5' and C-6'; H-13' to C-1', C-8' and C-8a'; H-9' to C-1', C-2' and C-8a'; as well as from H-10' to C-1', C-2' and C-3'; while the 3-substituted 4-hydroxybenzoic acid moiety was confirmed by the HMBC correlations from both H-2 and H-6 to C-4 and C-7, and from H-5 to C-1 and C-3 (see **Figure 1**). In addition, in the HMBC spectrum the correlations from H-9' to C-2, C-3 and C-4, and from H-2 to C-9' verified the connection between C-9' and C-3 of the two moieties. The relative stereochemistry of **1** was confirmed to be identical to yahazunol by the correlations among H-10', H-12' and H-13', and between H-1' and H-4a' in the NOESY spectrum of **1**. Therefore, the primary structure of **1** was determined as 3-[(2-hydroxy-2,5,5,8a-tetramethyldecahydro-1-naphthalenyl) methyl]-4-hydroxybenzoic acid, named as dictyvaric acid.

Table 1 ^1H and ^{13}C NMR data of compound **1**^a (δ ppm, J Hz)

No.	δ_{H}	δ_{C}	No.	δ_{H}	δ_{C}
1		123.1 s	5'		34.1 s
2	7.78 (d, 1H, 2.0)	134.5 d	6' α	1.01 (td, 1H, 13.0, 3.5)	43.0 t
3		131.1 s	6' β	1.26 (m, 1H)	
4		161.0 s	7' α	1.55 (m, 1H)	19.3 t
5	6.68 (d, 1H, 10.5)	116.7 d	7' β	1.27 (m, 1H)	
6	7.63 (dd, 1H, 10.5, 2.0)	130.2 d	8' α	0.57 (td, 1H, 13.0, 3.5)	41.7 t
7		171.7 s	8' β	1.69 (br.d, 1H, 13.0)	
1'	1.53 (dd, 1H, 11.5, 1.5)	62.9 d	8a'		41.0 s
2'		75.3 s	9' α	2.56 (dd, 1H, 15.0, 11.5)	27.3 t
3' α	1.48 (td, 1H, 13.0, 3.5)	44.7 t	9' β	2.80 (dd, 1H, 15.0, 1.5)	
3' β	1.84 (dt, 1H, 13.0, 3.5)		10'	1.21 (s, 3H)	24.2 q
4' α	1.63 (ddt, 1H, 13.0, 2.0, 3.5)	21.4 t	11'	0.80 (s, 3H)	33.9 q
4' β	1.30 (ddt, 1H, 13.0, 2.0, 3.5)		12'	0.77 (s, 3H)	21.9 q
4a'	0.89 (dd, 1H, 13.0, 2.0)	57.5 d	13'	0.94 (s, 3H)	15.9 q

^a NMR data were measured in CD_3OD at 500 MHz for proton and at 125 MHz for carbon. The assignments were based on DEPT, ^1H - ^1H COSY, HMQC and HMBC experiments.

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References

1. W. Fenical, J.J. Sims, K. Squatrito, R.M. Wing, P. Radlick, *J. Org. Chem.*, **1973**, 38(13), 2383.
2. M. Ochi, H. Kotsuki, K. Muraoka, T. Tokoroyama, *Bull. Chem. Soc. Jpn.*, **1979**, 52(2), 629.
3. M. Suzuki, N. Kowata, E. Kurosawa, H. Kobayashi, I. Tanaka, *Chem. Lett.*, **1990**, 228(12), 2187.
4. G. M. Koenig, A. D. Wright, *Magn. Reson. Chem.*, **1995**, 33(3), 178.
5. K. Yamada, H. Tan, H. Tatsumatsu, M. Ojika, *Tetrahedron*, **1986**, 42(14), 3775.
6. W. Boland, D. G. Müller, *Tetrahedron Lett.*, **1987**, 28 (3), 307.

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