

Article

## A New Cadinane Sesquiterpene from the Marine Brown Alga *Dictyopteris divaricata*

Wei Wen<sup>1,2</sup>, Fang Li<sup>2</sup>, Nai-Yun Ji<sup>1,\*</sup>, Xiao-Ming Li<sup>3</sup>, Chuan-Ming Cui<sup>3</sup>, Xiao-Dong Li<sup>1,2</sup>, Li-Na Zhang<sup>1,2</sup>, Qin-Zhao Xue<sup>1</sup> and Bin-Gui Wang<sup>3</sup>

<sup>1</sup> Yantai Institute of Coastal Zone Research for Sustainable Development, Chinese Academy of Sciences, Yantai 264003, China; E-mails: wenwei\_500@sina.com (W.W.), Imnli@163.com (X.-D.L.), Zhang.ln@163.com (L.-N.Z.), qzxue@yic.ac.cn (Q.-Z.X.)

<sup>2</sup> Qingdao University of Science & Technology, Qingdao 266042, China; E-mail: iceli\_2003@126.com (F.L.)

<sup>3</sup> Institute of Oceanology, Chinese Academy of Sciences, Qingdao 266071, China; E-mails: lixmqd@yahoo.com.cn (X.-M.L.), chuanming-cui@163.com (C.-M.C.), wangbg@ms.qdio.ac.cn (B.-G.W.)

\* Author to whom correspondence should be addressed; E-mail: nyji@yic.ac.cn

Received: 25 May 2009, in revised form: 11 June 2009 / Accepted: 23 June 2009 /

Published: 24 June 2009

---

**Abstract:** A sample of the marine brown alga *D. divaricata* collected off the coast of Yantai (P.R. China) was dried, powdered, and extracted with the mixture of CHCl<sub>3</sub> and MeOH (1:1, v/v). By a combination of silica gel and Sephadex LH-20 column chromatography and preparative TLC, a new cadinane sesquiterpene 1,4-epoxymuurolan-5 $\beta$ -ol (**1**) was isolated from this species. Its structure was established by detailed MS and NMR spectroscopic analysis, as well as comparison with literature data.

**Keywords:** *Dictyopteris divaricata*; sesquiterpene; cadinane

---

### Introduction

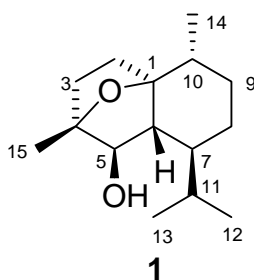
Marine brown algae of the genus *Dictyopteris* are prolific sources of sesquiterpenes, and cadinane is a main carbon skeleton type [1-8]. In our investigations on the structurally interesting and biologically active terpenes from Chinese marine algae, we examined the chemical constituents of *D.*

*divaricata* collected off the coast of Yantai and as a result, a new cadinane sesquiterpene, 1,4-epoxymurolan-5 $\beta$ -ol (**1**) has been isolated and characterized for the first time. This paper reports the isolation and structural elucidation of compound **1** (Figure 1).

## Results and Discussion

The dried and powdered alga *D. divaricata* was extracted with a mixture of CHCl<sub>3</sub> and MeOH (1:1, v/v). The concentrated extracts were partitioned between H<sub>2</sub>O and EtOAc. The EtOAc-soluble fraction was further purified by a combination of silica gel and Sephadex LH-20 column chromatography, as well as preparative TLC, to yield compound **1**. Compound **1** was obtained as a colorless oil. The broad IR absorption at  $\nu_{\max}$  3,452 cm<sup>-1</sup> indicated the presence of a hydroxyl group in the molecule. The positive electrospray ionization mass spectrometry (ESIMS) exhibited a characteristic quasimolecular ion peak at  $m/z$  261 [M+Na]<sup>+</sup>. The molecular formula was determined as C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> on the basis of HRESIMS ( $m/z$  261.1829 [M+Na]<sup>+</sup>, calcd. for C<sub>15</sub>H<sub>26</sub>O<sub>2</sub>Na, 261.1830), suggesting three degrees of unsaturation. The <sup>1</sup>H-NMR spectrum of **1** (Table 1) displayed one methyl singlet, three methyl doublets, and one broad singlet, attributed to an oxygenated methine. The <sup>13</sup>C-NMR spectrum (Table 1), along with the DEPT and HSQC experiments revealed the presence of four methyl, four methylene, five methine, and two quaternary carbon atoms. A detailed comparison of the above spectra data with those reported for 1,4-epoxymurolan-5 $\alpha$ -ol revealed that **1** differed from this last compound mainly at C-5 ( $\delta_C$  85.5 d) [9], suggesting that compound **1** may be a C-5 isomer of 1,4-epoxymurolan-5 $\alpha$ -ol. The <sup>1</sup>H-<sup>1</sup>H COSY correlations as shown in Table 1 and the observed HMBC correlations from H-12 to C-7, C-11, and C-13, from H-13 to C-7, C-11, and C-12, from H-14 to C-1, C-9, and C-10, from H-15 to C-3, C-4, and C-5, and from H-5 to C-3, C-4, C-6, C-7, and C-15 confirmed the planar structure of **1**. The relative configuration of **1** was determined by analysis of NOESY spectrum and coupling constants. The NOESY correlations between H-5 and H-7, H-2a indicated H-5, H-7 and C-2 to be located on the same face of the molecule. The same orientation of C-14 and C-2 was suggested on the basis of the NOESY correlation between H-14 and H-2b. H-6 and C-15 were assigned on the same face according to the observed NOESY correlation between H-6 and H-15. H-6 was located on the opposite face of H-7 based on the large coupling constant (11.6 Hz) between them. The above evidence established the structure of **1** to be 1,4-epoxymurolan-5 $\beta$ -ol (Figure 1), the C-5 epimer of 1,4-epoxymurolan-5 $\alpha$ -ol [9]. Compound **1** was tested for the toxicity against brine shrimp (*Artemia salina*) [10]. However, it exhibited no toxicity against brine shrimp at 100  $\mu$ g/mL.

**Figure 1.** Structure of compound **1**.



**Table 1.**  $^1\text{H}$  and  $^{13}\text{C}$ -NMR data and  $^1\text{H}$ - $^1\text{H}$  COSY correlations of compound **1** (in  $\text{CDCl}_3$ ,  $\delta$  in ppm,  $J$  in Hz).

No.	$\delta_{\text{C}}$	$\delta_{\text{H}}$	$^1\text{H}$ - $^1\text{H}$ COSY
1	87.1 s		
2a	34.6 t	1.42 (ddd, 12.5, 9.6, 5.8)	H-2b, H-3a, H-3b
2b		1.94 (ddd, 12.5, 12.1, 4.0)	H-2a, H-3a, H-3b
3a	29.4 t	1.30 (ddd, 12.1, 11.9, 5.8)	H-3b, H-2a, H-2b
3b		2.21 (ddd, 11.9, 9.6, 4.0)	H-3a, H-2a, H-2b
4	85.7 s		
5	85.5 d	3.46 (br s)	H-6
6	56.0 d	1.26 (d, 11.6)	H-5, H-7
7	47.3 d	1.14 (dddd, 12.1, 11.6, 2.1, 1.6)	H-6, H-8a, H-8b
8a	23.7 t	0.89 (dddd, 12.9, 12.6, 12.1, 2.1)	H-7, H-8b, H-9a, H-9b
8b		1.54 (br dd, 12.9, 3.1)	H-7, H-8a, H-9a, H-9b
9a	31.7 t	1.23 (m)	H-8a, H-8b, H-9b, H-10
9b		1.62 (m)	H-8a, H-8b, H-9a, H-10
10	34.9 d	1.59 (m)	H-9a, H-9b, H-14
11	27.3 d	1.80 (hept d, 6.9, 1.6)	H-7, H-12, H-13
12	16.0 q	0.80 (d, 6.9)	H-11
13	21.8 q	0.94 (d, 6.9)	H-11
14	15.3 q	1.01 (d, 6.5)	H-10
15	19.6 q	1.41 (s)	

## Experimental

### General

NMR spectra were recorded in  $\text{CDCl}_3$  with TMS as internal standard on a Bruker Avance 500 MHz NMR spectrometer operating at 500 and 125 MHz for  $^1\text{H}$  and  $^{13}\text{C}$ , respectively. Low and high resolution mass spectra were determined on a VG Autospec 3000 mass spectrometer. The IR spectrum was obtained on a JASCO FT/IR-4100 Fourier Transform infrared spectrometer. Optical rotation was measured on a JASCO P-1020 polarimeter. Column chromatography was performed with silica gel (200-300 mesh, Qingdao Haiyang Chemical Co., Qingdao, P.R. China), RP-18 reversed-phase silica gel (YMC), and Sephadex LH-20 (Pharmacia). TLC was carried out with precoated silica gel plates (GF-254, Qingdao Haiyang Chemical Co., Qingdao, P.R. China). All solvents were of analytical grade.

### Algal Material

The brown alga *Dictyopteris divaricata* was collected off the coast of Yantai (lat.  $37^\circ 31' 15''\text{N}$ , long.  $121^\circ 26' 59''\text{E}$ ), Shandong Province, P. R. China, in July 2008, and a voucher specimen (MBA0807) has been deposited at the Bio-Resource Laboratory of Yantai Institute of Coastal Zone Research for Sustainable Development, Chinese Academy of Sciences.

### Extraction and Isolation

Dried and powdered alga *D. divaricata* (2 kg) was extracted with the mixture of CHCl<sub>3</sub> and MeOH (1:1, v/v). The concentrated extract was partitioned between H<sub>2</sub>O and EtOAc. The EtOAc-soluble fraction (90 g) was fractionated by silica gel column chromatography [petroleum ether (PE)/EtOAc gradient] to give ten fractions, I-X. Fraction VII, eluted with PE/EtOAc 2:1, was further purified by Sephadex LH-20 (CHCl<sub>3</sub>/CH<sub>3</sub>OH) and RP-18 (CH<sub>3</sub>OH/H<sub>2</sub>O 3:1) column chromatography and preparative TLC (PE/EtOAc 3:1) to afford *1,4-epoxymurolan-5β-ol* (**1**, 9.1 mg) as a colorless oil;  $[\alpha]_D^{25} -29.2^\circ$  (c=0.33, CHCl<sub>3</sub>); IR (KBr) cm<sup>-1</sup>: 3,452, 2,962, 2,954, 2,870, 1,458, 1,377, 1,065; <sup>1</sup>H-NMR and <sup>13</sup>C-NMR: see Table 1; ESIMS *m/z*: 261 [M+Na]<sup>+</sup>; HRESIMS *m/z*: 261.1829 [M+Na]<sup>+</sup>, calcd. for C<sub>15</sub>H<sub>26</sub>O<sub>2</sub>Na, 261.1830.

### Brine Shrimp Assays

Brine shrimp assays were performed as previously described [10].

### Acknowledgements

This work was financially supported by the Foundation of the Chinese Academy of Sciences for President's Scholarship (awarded to N.-Y. J.), Open Foundation of Shandong Oriental Ocean Sci-Tech Co., Ltd, Chinese Academy of Sciences for Key Topics in Innovation Engineering (kcx2-yw-225), and Key Technology Research and Development Program of Shandong Province (2007GG2QT06020).

### References and Notes

1. Song, F.; Xu, X.; Li, S.; Wang, S.; Zhao, J.; Yang, Y.; Fan, X.; Shi, J.; He, L. Minor sesquiterpenes with new carbon skeleton from the brown alga *Dictyopteris divaricata*. *J. Nat. Prod.* **2006**, *69*, 1261-1266.
2. Song, F.; Xu, X.; Li, S.; Wang, S.; Zhao, J.; Cao, P.; Yang, Y.; Fan, X.; Shi, J.; He, L.; Lü, Y. Norsesquiterpenes from the brown alga *Dictyopteris divaricata*. *J. Nat. Prod.* **2005**, *68*, 1309-1313.
3. Song, F.; Fan, X.; Xu, X.; Zhao, J.; Yang, Y.; Shi, J. Cadinane sesquiterpenes from the brown alga *Dictyopteris divaricata*. *J. Nat. Prod.* **2004**, *67*, 1644-1649.
4. König, G.M.; Wright, A.D. Concerted application of a shift reagent and 2D NOESY to the structure determination of new natural products from the tropical brown alga *Dictyopteris delicatula*. *Magn. Reson. Chem.* **1995**, *33*, 178-183.
5. Segawa, M.; Yamano, K.; Shrahama, H. A germacrane-type sesquiterpene from the brown alga *Dictyopteris divaricata*. *Phytochemistry* **1990**, *29*, 973-974.
6. Suzuki, M.; Kowata, N.; Kurosawa, E.; Kobayashi, H.; Tanaka, I. The structure of a germacrane-type sesquiterpene alcohol, a possible precursor of guaiane-type sesquiterpenes from the brown alga *Dictyopteris divaricata*. *Chem. Lett.* **1990**, *19*, 2187-2190.
7. Kajiwara, T.; Hatanaka, A.; Tanaka, Y.; Kawai, T.; Ishihara, M.; Tsuneya, T.; Fujimura, T. Volatile constituents from marine brown algae of Japanese *Dictyopteris*. *Phytochemistry* **1989**, *28*, 636-639.

8. Suzuki, M.; Kowata, N.; Kurosawa, E. Epicubebol and related sesquiterpenoids from the brown alga *Dictyopteris divaricata*. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2366-2368.
9. Chyu, C.F.; Ke, M.R.; Chang, Y.S.; Chien, S.C.; Kuo, Y.H. New cadinane-type sesquiterpenes from the roots of *Taiwania cryptomerioides* HAYATA. *Helv. Chim. Acta* **2007**, *90*, 1514-1521.
10. Solis, P.N.; Wright, C.W.; Anderson, M.M.; Gupta, M.P.; Phillipson, J.D. A microwell cytotoxicity assay using *Artemia salina* (Brine shrimp). *Planta Med.* **1993**, *59*, 250-252.

*Sample Availability:* Samples of compound **1** are available from the authors.

© 2009 by the authors; licensee Molecular Diversity Preservation International, Basel, Switzerland. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/3.0/>).