A New Cadinane Sesquiterpene from the Marine Brown Alga

Dictyopteris divaricata

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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 CHCl₃ 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-5β-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-5β-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 CHCl₃ and MeOH (1:1, v/v). The concentrated extracts were partitioned between H₂O 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 νmax 3,452 cm⁻¹ indicated the presence of a hydroxyl group in the molecule. The positive electrospray ionization mass spectrometry (ESIMS) exhibited a characteristic quasi-molecular ion peak at m/z 261 [M+Na]⁺. The molecular formula was determined as C₁₅H₂₆O₂ on the basis of HRESIMS (m/z 261.1829 [M+Na]⁺, calc. for C₁₅H₂₆O₂Na, 261.1830), suggesting three degrees of unsaturation. The ¹H-NMR spectrum of 1 (Table 1) displayed one methyl singlet, three methyl doublets, and one broad singlet, attributed to an oxygenated methine. The ¹³C-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-5α-ol revealed that 1 differed from this last compound mainly at C-5 (δC 85.5 d) [9], suggesting that compound 1 may be a C-5 isomer of 1,4-epoxymurolan-5α-ol. The ¹H-¹H 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-5β-ol (Figure 1), the C-5 epimer of 1,4-epoxymurolan-5α-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 μg/mL.

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

| No. | $\delta_C$ | $\delta_H$ | $^1$H-$^1$H COSY |
|-----|------------|------------|------------------|
| 1   | 87.1 s     | 1.42 (ddd, 12.5, 9.6, 5.8) | H-2b, H-3a, H-3b |
| 2a  | 34.6 t     | 1.94 (ddd, 12.5, 12.1, 4.0) | H-2a, 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 CDCl$_3$ with TMS as internal standard on a Bruker Avance 500 MHz NMR spectrometer operating at 500 and 125 MHz for $^1$H and $^{13}$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°31’15”N, long. 121°26’59”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$_3$ and MeOH (1:1, v/v). The concentrated extract was partitioned between H$_2$O and EtOAc. The EtOAc-soluble fraction (90 g) was fractioned 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$_3$/CH$_3$OH) and RP-18 (CH$_3$OH/H$_2$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° (c=0.33, CHCl$_3$); IR (KBr) cm$^{-1}$: 3,452, 2,962, 2,954, 2,870, 1,458, 1,377, 1,065; $^1$H-NMR and $^{13}$C-NMR: see Table 1; ESIMS $m/z$: 261 [M+Na]$^+$; HRESIMS $m/z$: 261.1829 [M+Na]$^+$, calcd. for C$_{15}$H$_{26}$O$_2$Na, 261.1830.

Brine Shrimp Assays

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

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

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