

## A NEW DIPHENYL ETHER FROM THE LICHEN

### *Parmotrema praesorediosum*

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*A new diphenyl ether, named praesorether P (1), was isolated from the lichen Parmotrema praesorediosum (Nyl.) Hale. Its chemical structure was elucidated on the basis of extensive spectroscopic analysis including HR-ESI-MS and NMR as well as comparison with previously published data.*

**Keywords:** *Parmotrema praesorediosum*, diphenyl ether, praesorether.

Lichens are well known for containing a diversity of secondary metabolites including monocyclic phenols, depsides, depsidones, xanthenes, and terpenoids that possess unique chemical structures with unknown functions. Therefore, lichens are attractive for pharmacological and chemical studies [1]. In our previous studies on chemical constituents of the lichen *Parmotrema praesorediosum* (Nyl.) Hale (Parmeliaceae), we have reported seven novel diphenyl ethers [2–5]. Herein, we continue our research on the isolation and structure elucidation of a new diphenyl ether from this lichen. Its chemical structure was unambiguously determined by analysis of 1D and 2D NMR and high-resolution ESI mass spectroscopic data, as well as by comparison of the NMR data with those in the literature.

Compound **1** was isolated as a yellow solid. Its molecular formula was established as C<sub>29</sub>H<sub>26</sub>O<sub>14</sub> through the protonated molecular ion peak at *m/z* 599.1397 [M + H]<sup>+</sup> in the HR-ESI-MS spectrum. Its IR absorptions implied the presence of hydroxyl (3250 cm<sup>-1</sup>), ester carbonyl (1731 cm<sup>-1</sup>), and aromatic (1648, 1455 cm<sup>-1</sup>) functionalities.

The <sup>1</sup>H NMR spectrum of **1** displayed signals for two methyl groups at δ 2.43 and 2.27 (each 3H, s), three methoxy groups at δ 3.95, 3.25, and 3.18 (each 3H, s), a methylene group at δ 3.96 (s), an acetal proton at δ 5.46 (s), two aromatic protons at δ 6.65 and 6.38 (each 1H, s), and one aldehyde proton at δ 10.19 (s).

The combination of <sup>13</sup>C NMR and HSQC spectra of **1** revealed 29 carbons including one formyl group (δ 194.1), three carbonyl carbons (δ 166.2, 169.4, and 173.0), 18 aromatic carbons in the range of 164–103 ppm, six of which were oxygenated and two of which were aromatic methine carbons (δ 115.2 and 113.5), one acetal carbon (δ 101.9), three oxymethyl carbons (δ 56.7, 52.4, and 51.9), one methylene carbon (δ 17.3), and two methyl groups at δ 24.0 and 20.9.

The comparison of spectral features of **1** with praesorether C [3], a compound isolated from the same subfraction but slightly more polar, showed that they had the same basic framework possessing three aromatic rings in which rings A and B are connected through an ether linkage, rings B and C are joined together via a methylene bridge, and ring B is fused to a five-membered lactol ring at C-1' and C-6' [6–8].

A comparison of their 1D NMR data showed that they were similar, the only difference being the chemical shift values of two carbons in the C ring with the methylene group C-8' (Δδ<sub>H</sub> = -0.10, Δδ<sub>C</sub> = -2.7) and the methyl group C-8'' (Δδ<sub>H</sub> = -0.18, Δδ<sub>C</sub> = +4.7) although they were measured in the same deuterated solvent CDCl<sub>3</sub>. The variation in the NMR chemical shift values of these carbons could be due to the different positions of the substituents in the methyl orsellinate-moiety C ring. A possible candidate could be the B ring via the methylene bridge linked to the C ring at an aromatic carbon adjacent to two hydroxyl groups instead of to an aromatic carbon adjacent to one hydroxyl group and one methyl group as in praesorether C [9, 10].

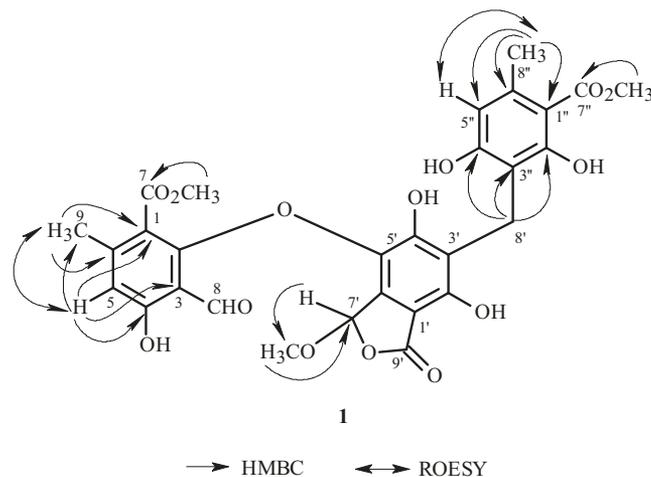


Fig. 1. Key HMBC and ROESY correlations of **1**.

Indeed, the HMBC experiments (Fig. 1) proved this proposition. The methylene protons ( $H_2-8'$ ) of **1** correlated with three aromatic carbons of the C ring at  $\delta$  160.5 (C-2''), 110.0 (C-3''), and 160.3 (C-4''). Two of these three were oxygenated carbons. From these findings, the methylene carbon of the B ring was linked to the C ring at C-3''. The HMBC cross peaks proved that the three remaining substituents were of a methyl orsellinate moiety. Consequently, compound **1** was established as a new diphenyl ether derivative and named praesorether P.

## EXPERIMENTAL

**General.** The NMR spectra were measured on a Varian NMR System-500 or INOVA-500 spectrometer at 500 MHz for  $^1H$  NMR and 125 MHz for  $^{13}C$  NMR with TMS as internal standard. The HR-ESI-MS were recorded on an Exactive mass spectrometer (Thermo Fisher Scientific). The optical rotations were measured on a Jasco DIP-370 digital polarimeter. The IR spectra were measured on a Shimadzu FTIR-8200 infrared spectrophotometer. TLC was carried out on silica gel 60 F254 or silica gel 60 RP-18 F254S (Merck), and spots were visualized by spraying with a solution of 5% vanillin in ethanol followed by heating at 100°C. Gravity column chromatography was performed with silica gel 60 (0.040–0.063 mm, Merck). All NMR experiments were performed at ambient temperature.

**Plant Material.** The lichen thalli of *P. praesorediosum* were collected on the bark of Dipterocarpus sp. at Tan Phu forest, Dong Nai Province, Vietnam in June 2009. The botanical species of *Parmotrema praesorediosum* (Nyl.) Hale was identified by MSc. Vo Thi Phi Giao, Faculty of Biology, University of Science, National University, Ho Chi Minh City. A voucher specimen (No. US-B020) was deposited in the Herbarium of the Department of Organic Chemistry, Faculty of Chemistry, University of Science, National University, Ho Chi Minh City, Vietnam.

**Extraction and Isolation.** The thallus material (5.0 kg) was washed under flow of tap water and then air-dried at ambient temperature to obviate thermally induced decomposition prior to being ground into a fine powder. The ground powder sample (3.0 kg) was macerated with methanol at room temperature to afford a crude methanol extract (450 g). The crude extract (450 g) was subjected to silica gel solid-phase extraction and successively eluted with the solvents petroleum ether (60–90°C) (PE),  $CHCl_3$ , EtOAc, acetone, and MeOH to afford the corresponding extracts: PE extract (40 g),  $CHCl_3$  extract (105 g), EtOAc extract (50 g), acetone extract (45 g), and MeOH extract (37 g).

The  $CHCl_3$  extract (105 g) was subjected to silica gel column chromatography and eluted with the solvent system PE–EtOAc with increasing ethyl acetate to give 23 fractions C1–C23. Fraction C19 (6.1 g) was applied to a silica gel column and eluted with a gradient solvent system of  $CHCl_3$ –acetone (95:5) to give three subfractions (C19a–C19c). Subfraction C19b (3.2 g) was rechromatographed with silica gel and eluted with  $CHCl_3$ –acetone (98:2) to give six subfractions (C19ba–C19bf). Subfraction C19ba (169.6 mg) was subjected to preparatory TLC ( $CHCl_3$ –MeOH, 98:2 and 95:5) to afford **1** (6.9 mg).

**Praesorether P (1).** Yellow solid,  $[\alpha]_D^{21} +3.7^\circ$  ( $c$  0.49,  $CHCl_3$ ). IR (KBr,  $\nu_{max}$ ,  $cm^{-1}$ ): 3250, 1731, 1648, 1455, 1271. HR-ESI-MS  $m/z$ : 599.1397  $[M + H]^+$  (calcd for  $C_{29}H_{27}O_{14}$ , 599.1402); 621.1213  $[M + Na]^+$  (calcd for  $C_{29}H_{26}O_{14}Na$ , 621.1220).  $^1H$  NMR (500 MHz,  $CDCl_3$ ,  $\delta$ , ppm, J/Hz): 2.27 (3H, s, H-9), 2.43 (3H, s, H-8''), 3.18 (3H, s, 7'-OCH<sub>3</sub>), 3.25 (3H, s, 7-OCH<sub>3</sub>),

3.95 (3H, s, 7''-OCH<sub>3</sub>), 3.96 (2H, s, H-8'), 5.46 (1H, s, H-7'), 6.38 (1H, s, H-5''), 6.65 (1H, s, H-5), 10.19 (1H, s, H-8), 11.96 (1H, s, 4-OH). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, δ, ppm): 17.3 (C-8', CH<sub>2</sub>), 20.9 (C-9, CH<sub>3</sub>), 24.0 (C-8'', CH<sub>3</sub>), 51.9 (7-OCH<sub>3</sub>), 52.4 (7''-OCH<sub>3</sub>), 56.7 (7'-OCH<sub>3</sub>), 101.9 (C-7', CH), 103.9 (C-1', C), 104.6 (C-1'', C), 110.0 (C-3'', C), 111.5 (C-3, C), 113.5 (C-5'', CH), 115.2 (C-5, CH), 116.2 (C-1, C), 118.1 (C-3', C), 131.6 (C-6', C), 134.9 (C-5', C), 142.4 (C-6'', C), 147.6 (C-6, C), 150.8 (C-2', C), 156.9 (C-2, C), 160.3 (C-4'', C), 160.5 (C-2'', C), 163.5 (C-4, C), 166.2 (C-7, C=O), 169.4 (C-9', C=O), 173.0 (C-7'', C=O), 194.1 (C-8, C=O).

## ACKNOWLEDGMENT

We are grateful to MSc. Vo Thi Phi Giao for the identification of the *Parmotrema* specimens. Thanks are also due to Kobe Pharmaceutical University for help in the experiments.

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