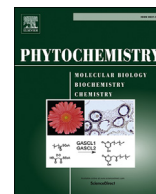




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Phytochemistry

journal homepage: www.elsevier.com/locate/phytochemNew erythritol derivatives from the fertile form of *Roccella montagnei*

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ABSTRACT

Chemical investigation of the methanol extract of the fertile form of *Roccella montagnei* collected in Vietnam afforded twelve secondary metabolites, including five new montagnetol derivatives, orsellinylmontagnetols A–D and a furanyl derivative together with seven known compounds. Their chemical structures were elucidated by analysis of 1D and 2D NMR and high resolution mass spectroscopic data. The relative stereochemistry of two chiral centers (C-2 and C-3) of orsellinylmontagnetols A and B was elucidated by comparison of their coupling constants and the specific rotation with those reported in the literature while the absolute stereochemistry was determined by the application of a modified Mosher method for the hydroxy group at C-3. The absolute configuration (2R,3S) of the butanetetraol moiety of these compounds is in accordance with that of erythrin, a recognized chemotaxonomic marker of the genus *Roccella*. Five of these compounds were evaluated for their cytotoxic activities against four cancer cell lines. Only orsellinylmontagnetol A exerted a moderate activity against MCF-7 cell line with an IC₅₀ value of 68.39 ± 3.46 μM.

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1. Introduction

Lichens are symbiotic systems consisting of a mycobiont (the dominating fungal partner), one or more photobionts (algal partner) and a complex microbial consortium comprising a wide array of heterotrophic bacteria and fungi (Grube and Berg, 2009; Spribille et al., 2016) with more than 1000 specialized metabolites described so far from lichen sources. The majority of secondary metabolites

are produced by the fungal partner (Nash, 2008), and display specific chemical skeletons (Stocker-Wörgötter, 2008; Elix, 2014). In a given species, quantities and in some cases the nature of these extrolites can be modified according to ecological and physiological conditions (Białońska and Dayan, 2005; Stocker-Wörgötter, 2008). Nowadays, innovative analytical techniques help pinpointing new metabolites and streamlining their isolation with high probability to obtain bioactive compounds (Boustie and Grube, 2005).

Lichens from coastal habitats in Vietnam have seldom been studied chemically. In the course of a systematic research on lichen substances from the Vietnamese biota, the fertile form of the lichen *Roccella montagnei* (syn. *R. bellangeriana*) was examined. It occurs in the southern part of Vietnam and has not yet been studied with chemical and biological methods apart from scarce data obtained

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by thin layer chromatography (Aptroot and Schumm, 2011).

Phytochemical studies of *Roccella* spp. lichens have been conducted over more than one hundred years (Hesse, 1906) showing that they produce a diverse range of metabolites such as meso-erythritol (Huneck and Follmann, 1967), dibenzofurans (Culberson, 1969; Huneck et al., 1991, 1993; Huneck and Yoshimura, 1996; Huneck, 2001), chromones (Aberhart and Overton, 1969; Huneck, 1972; Huneck et al., 1992), N-containing compounds (Bohman-Lindgren and Ragnarsson, 1972; Ramakrishnan and Subramanian, 1964), carbohydrates (Carbonero et al., 2005), and terpenoids (Murty and Subramanian, 1958, 1959). Among them, erythrin and lecanoric acid were found in most *Roccella* species (Tehler et al., 2010) with the former being reported as a principal secondary product reaching up to 7.3% in *R. montagnei* (Feige et al., 1986; Huneck and Follmann, 1967; Thadhani et al., 2010; Parrot et al., 2015). The genus *Roccella* has been recently revised, describing 24 main species which are restricted to coastal habitats (Tehler et al., 2010).

Herein reported are the isolation and structure elucidation of five new compounds, using the Mosher's method to assess their stereochemistry. The cytotoxic activities at the concentration of 100 µg/mL against liver hepatocellular carcinoma (HepG2), human lung cancer (NCI-H460), cervical cancer (Hela) and human breast cancer (MCF-7) cell lines were also evaluated for five compounds **1**, **3**, **5**, **6**, and **8**.

2. Results and discussion

The fertile form of *Roccella montagnei* thalli was collected on tree barks in Tuy Phong district, Binh Thuan province, Vietnam. A detailed chromatographic fractionation of its methanol extract led to the isolation of five new compounds (**1**–**5**), along with seven metabolites (**6**–**12**) already described (Fig. 1).

D-(+)-Montagnetol (**6**), D-(+)-erythrin (**8**) and lecanoric acid (**9**)

are the main markers of *R. montagnei* (Huneck and Follman, 1967; Basset et al., 2010; Thadhani et al., 2010) and were isolated as major compounds of this lichen. Besides orsellinic acid (**11**) and methyl orsellinate (**12**) (Lopes et al., 2008) which correspond to monoaromatic moieties found in many lichens, five new montagnetol derivatives (**1**–**5**) were isolated from *R. montagnei*. The relative stereochemistry of the two chiral centers, C-2 and C-3 of orsellinylmontagnetols A–D was elucidated by comparison of their coupling constants and their specific rotation with those reported in the literature (Basset et al., 2010; Hawkes and Lewis, 1984) while the absolute stereochemistry was determined by the application of a modified Mosher method (Hoye et al., 2007) for a hydroxy group at C-3 in **1** and **2**. Among the new isolated products, the structure of **5**, a ring-closure derivative of **6**, indicated an unusual structural feature.

Compound **1** was isolated as an optically active white amorphous powder, whose molecular formula was established to be C₂₀H₂₂O₁₀ based on its negative-ion mode HRESIMS data (*m/z* 421.1128 [M–H][–], calcd for C₂₀H₂₂O₁₀ – H, 421.1140). The ¹H NMR spectrum, in accordance with ¹³C and HSQC spectra (Table 1), showed two aromatic methyls (δ_H 2.50 and 2.41, δ_C 24.4 and 24.5), two pairs of *meta*-coupled methines (δ_H 6.21, 6.23, each *d*, 2.0 Hz, δ_C 101.7, 101.8 and δ_H 6.25, 6.27, each *d*, 2.0 Hz, δ_C 112.5, 112.6), four pairs of substituted aromatic carbons (δ_C 105.1, 105.2, 144.6, 144.7, 163.6, 163.7, 166.2, 166.5), one pair of carboxyl carbons (δ_C 171.9, 172.4) attributable to two orsellinyl units (2 × C₈H₇O₃) and signals of one butanetetraol unit, including two *sp*³ oxygenated methylenes, CH₂-1 (δ_H 4.91, *dd*, 12.3, 2.7 Hz, H-1a; δ_H 4.74, *dd*, 12.3, 6.9 Hz, H-1b; δ_C 64.6) and CH₂-4 (δ_H 3.79, *m*, H-4a; δ_H 3.72, *m*, H-4b; δ_C 64.0) and two *sp*³ oxygenated methines, CH-2 (δ_H 5.68, *ddd*, 7.2, 6.3, 2.4 Hz; δ_C 74.1) and CH-3 (δ_H 4.13, *m*; δ_C 71.8).

These chemical features were reminiscent of those of (+)-D-montagnetol (**6**), except for the presence of one more orsellinyl unit. This supplementary core was confirmed by the HRESIMS

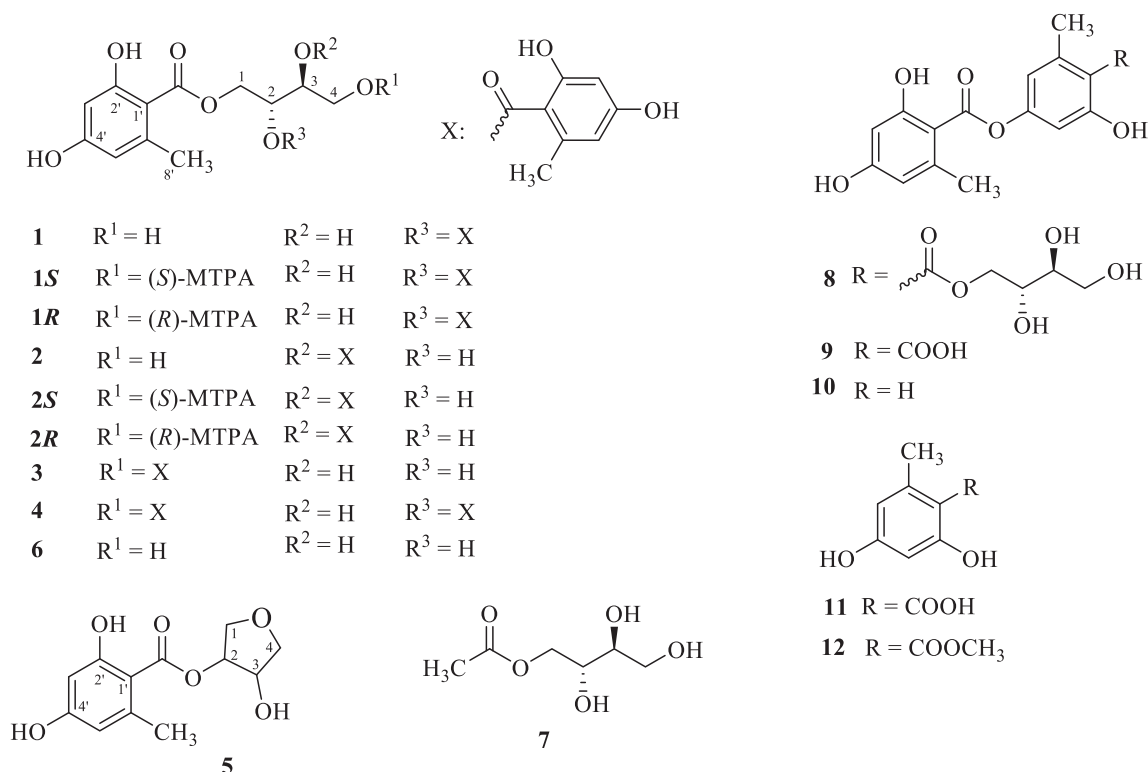


Fig. 1. Chemical structures of **1**–**12**.

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