Diterpenoids from *Fokienia hodginsii*

Dang Viet Hau1,2, Nguyen Thanh Tam1,2, Tran Duc Quan1, Dao Duc Thien1, Bui Xuan Tinh3,
Le Thi Hong Nhung4, Tran Van Loc1, Tran Van Sung1, Trinh Thi Thuy1,2*

1Institute of Chemistry, Vietnam Academy of Science and Technology
2Graduate University of Science and Technology, Vietnam Academy of Science and Technology
3Quang Trung University
4Hanoi University of Industry

Received 27 July 2017; Accepted for publication 28 August 2017

Abstract

In continuous research on the chemical constituents of the twigs and leaves of *Fokienia hodginsii* (Dunn) A. Henry et Thomas growing in Highland, Lam Dong province, 4 diterpenoids, including 3-oxo-totarol (totarolone, 1), 3β-hydroxytotarol (2), 15-nor-labda-8(17),12E-diene-14-carboxaldehyde-19-oic acid (3) and 13-oxo-15,16-dinorlabda-8(17),11E-diene-19-oic acid (4) were isolated. Their structures were elucidated by the spectroscopic methods and comparison with reported data. This is the first report on the isolation of compounds 1, 2 and 3 from this plant.

Keywords. *Fokienia hodginsii*; totarane; nor-labdane diterpenoid.

1. INTRODUCTION

*Fokienia hodginsii* (Dunn) A. Henry et Thomas (synonym *Cupressus hodginsii* Dunn)-“local name Po mu”- belongs to family Cupressaceae. It is a big tree, 20-30 m tall, mainly distributed in China and Vietnam [1]. Po mu tree is known for its beauty, fragrance and high-value wood. Previous investigations of this plant have been mainly focused on the chemical composition of the essential oil [2]. Hitherto, there is only one report on the chemical constituents of this species growing in China. Its main components included diterpenoids: isopimarane, labdane, and icetexane [2]. In our previous chemical investigation, from the ethyl acetate extract of twigs and leaves of this plant growing in Highland, Lam Dong province there yielded two megastigmanes, namely drummondol and vomivoliol [3]. In our continued work on the hexane extract of this plant, 4 diterpenoids as 3-oxototarol (totarolone, 1), 3β-hydroxytotarol (2), 15-nor-labda-8(17),11E-diene-14-carboxaldehyde-19-oic acid (3) and 13-oxo-15,16-dinorlabda-8(17),11E-diene-19-oic acid (4) were isolated and structurally determined.

2. EXPERIMENTAL

2.1. General

H-NMR (500 MHz) and 13C-NMR (125 MHz) were taken on a Bruker Avance AM500 spectrometer using TMS as internal standard for 1H and solvent signal for 13C. ESI-MS was taken on an Agilent 1100 LC-MSD Trap spectrometer. TLC aluminum sheets of silica gel Merck 60 F254 (layer thickness 0.2 mm) were used. Column chromatography (CC) was carried out on silica gel Merck 60 (0.040-0.063 mm) and Sephadex LH-20.

2.2. Plant Material

*F. hodginsii* was collected in Highland, Lam Dong province, Vietnam in August, 2012 and identified by Dr. Nguyen Tien Hiep. A voucher specimen (No. VNMMN. B00005002) is deposited in the Vietnam National Museum of Nature, Vietnam Academy of Science and Technology (VAST), Hanoi, Vietnam.

2.3. Extraction and Isolation

The dried and powdered mixture of twigs and leaves of *F. hodginsii* (900 g) was extracted ultrasonically with methanol - water (90:10, v/v) at 40 °C, three times, each 4 h. After concentration under reduced pressure, the crude extract was suspended in water and sequentially partitioned in *n*-hexane, ethyl acetate and *n*-butanol. The organic solvents were evaporated to yield the corresponding extracts (14.0,
18.3 and 13.2 g, respectively). The hexane extract (14.0 g) was subjected to silica gel column chromatography with gradient elution of n-hexane - EtOAc mixtures (from 100:1 to 70:30) to give twenty fractions (F1-F20). Fraction F10 was separated by a Sephadex LH-20 column with MeOH as eluent to give toratolone (1, 20 mg). Fraction F16 was further purified on a silica gel column eluted with hexane-EtOAc (95:5) to yield 3β-hydroxytoralone (2, 10 mg). Fractions F16 and F12 were repurified on a Sephadex LH-20 column using methanol as eluent to give 13-oxo-15,16-dinorlabda-8(17),11E-diene-19-oxiacid (3, 10 mg) and 15-nor-labda-8(17),12E-diene-14-carboxaldehyde-19-oxiacid (4, 10 mg), respectively.

Taratolone (3-oxototarol, 1): 1H-NMR (500 MHz, CD3OD) δH: 6.95 (1H, d, J = 8.5 Hz, H-11), 6.58 (1H, d, J = 8.5 Hz, H-12), 3.27 (1H, br s, H-15), 3.02 (1H, dd, J = 17.0, 5.5 Hz, H-7a), 2.72 (1H, m, H-7b), 2.68 (1H, m, H-2a), 2.58 (1H, m, H-2b), 1.34, 1.33 (each 3H, d, J = 6.5 Hz, H-15&H-16), 1.29 (3H, s, H-20), 1.17 (3H, s, H-19), 1.14 (3H, s, H-18); 13C-NMR (500 MHz, CD3OD) δC: 220.56 (C-3), 155.12 (C-13), 140.11 (C-9), 134.93 (C-8), 132.05 (C-14), 124.81 (C-11), 115.58 (C-12), 51.52 (C-5), 48.32 (C-4), 39.62 (C-1), 38.39 (C-10), 35.79 (C-2), 30.14 (C-7), 28.85 (C-15), 27.30 (C-18), 25.07 (C-20), 21.68 (C-6), 21.47 (C-19), 20.58, 20.31 (C-16 & C-17).

3β-Hydroxytoralone (2): ESI-MS m/z: 285.1 [M-H2O+H]+. 1H-NMR (500 MHz, CD3OD) δH: 6.92 (1H, d, J = 8.5 Hz, H-11), 6.53 (1H, d, J = 8.5 Hz, H-12), 3.24 (1H, dd, J = 11.5, 5.0 Hz, H-3), 2.96 (1H, dd, J = 16.5, 6.0 Hz, H-7a), 2.71 (1H, m, H-7b), 1.33, 1.32 (each 3H, d, J = 6.5 Hz, H-15 & H-16), 1.17 (3H, s, H-20), 1.07 (3H, s, H-19), 0.89 (3H, s, H-18); 13C-NMR (125 MHz, CD3OD) δC: 155.32 (C-13), 142.29 (C-9), 134.89 (C-8), 132.07 (C-14), 123.78 (C-11), 115.26 (C-12), 79.58 (C-3), 50.93 (C-5), 39.87 (C-4), 39.27 (C-1), 38.56 (C-10), 30.29 (C-7), 28.96 (C-2), 28.76 (C-19), 25.61 (C-20), 20.56 (C-16&17-C-17), 20.43 (C-16). ESI-MS (m/z): 285.1 [M+H2O]+. The spectral data and the molecular formula suggested that 2 had the same carbon skeleton as 1. The NMR spectra of compounds 2 were similar with those of 1 except some changes at C-3. The replacement of ketone group by a hydroxyl in the structure of 2 is indicated by the absence of the ketone group and the presence of a hydroxyl signal [δH 3.24 (dd, J = 11.5, 5.0 Hz, H-3)/δC 79.58 (C-3)], in its NMR spectra. Thus, compound 2 was elucidated as 3β-hydroxytoralone (toraladiol) by comparison with data in the literature.

The molecular formula of 3 was determined to be C19H23O5 based on ion molecular peak at m/z 289.1 [M+H]+ in the negative ESI-MS spectrum. In the 1H and 13C-NMR spectra, characteristic signals for one
ketone group (δC 200.88), one carboxylic acid (δC 180.12), a trans-disubstituted double bond [δH 6.98 (1H, dd, J = 16.0, 10.5 Hz, H-11)/δC 148.67; δH 6.12 (1H, d, J = 16.0 Hz, H-12)/δC 134.58], an exocyclic methylene group [δH 4.83 (s), 4.45 (s), δC 108.87 (t), 149.89 (s)], three tertiary methyl groups, six methine groups, two methine groups were found. These data suggested that compound 3 is a norlabdane diterpenoid. The long-range correlations in the HMBC spectrum between H-18 and C-4, C-19; H-17 and C-7, C-9; H-11, H-12, H-14 and C-13 were suggestive of that a carboxylic acid, an exocyclic methylene and a keton proton group must be located at C-4, C-8 and C-13, respectively. The NOEs correlations between H-9 and the methyl protons H-18 and H-5 implied that these protons were α-oriented. Combined its 1H-, 13C-NMR and 2D-NMR spectral data, compound 3 was determined as 13-oxo-15,16-dinorlabda-8(17),11E-diene-19-oic acid [6].

The molecular formula of 4 was determined to be C30H52O3 based on a molecular ion peak at m/z 303.1 [M-H] in the negative ESI-MS and combination with NMR data. The spectral data and the molecular formula suggested that 4 had the same carbon skeleton as 3 with a difference of a moiety side-chain at C-9. The 1H- and 13C-NMR spectra of 4 showed the characteristic signals for the presence of a 3-methyl-4-oxo-2E-butenyl side chain, which were observed at δH 9.31 (1H, s, H-14), 6.57 (1H, td, J = 6.0, 1.5 Hz, H-12), 1.77 (3H, br s, H-16); δC 197.07 (d, C-14), 158.69 (d, C-12), 140.01 (s, C-13), 9.29 (q, C-16). By comparison of its 1H- and 13C-NMR spectral data with those of 15-norlabda-8(17),12E-diene-14-carboxaldehyde-19-oic acid methyl ester [7], compound 4 was determined as 15-norlabda-8(17),12E-dien-14-carboxaldehyde-19-oic acid. Recently, this compound was also isolated from the twigs and leaves of Fokienia hodginsii growing in China [2].

Except 4, the remaining compounds 1-3 were isolated from this plant for the first time.

Acknowledgment. We would like to thank the National Foundation for Science & Technology Development (NAFOSTED) of Vietnam for financial support for this research (code: 104.01-2013.62).

REFERENCES


2. Xing-De Wu, Juan He, Xing-Yao Li, Liao-Bin Dong, Xun Gong, Liu-Dong Song, Yan Li, Li-Yan Peng, and Qin-Shi Zhao. Diterpenoids from the twigs and leaves of Fokienia hodginsii, J. Nat. Prod., 76(6), 1032-1038 (2013).


Corresponding author: Trinh Thi Thuy
Institute of Chemistry
Vietnam Academy of Science and Technology
No. 18, Hoang Quoc Viet, Cau Giay District, Hanoi
E-mail: thuy@ich.vast.vn.