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A NOVEL SESQUITERPENOID FROM THE LEAVES OF *Cinnamomum subavenium*

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*A novel sesquiterpenoid, subamol ((3-methoxy-5*H*-9,10-dihydroxybenzo[3,4]cyclohepta[1,2-*f*])inden-7-yl)-methanol)) (**1**), along with six compounds, including one ionone: (+)-abscisic acid (**2**); and five benzenoids: syringaldehyde (**3**),* trans*-coumaric acid (**4**),* cis*-coumaric acid (**5**), vanillic acid (**6**), and* p*-hydroxybenzoic acid (7), were isolated from the leaves of* Cinnamomum subavenium *Miq (Lauraceae). These compounds were identified and characterized by physical and spectral evidence.*

Keywords: *Cinnamomum subavenium* Miq, Lauraceae, subamol, sesquiterpenoid.

Cinnamomum subavenium Miq (Lauraceae) is a medium-sized evergreen tree, found in Central to Southern Mainland China, Burma, Cambodia, Taiwan, Malaysia, and Indonesia [1]. In the course of screening for biologically and chemically novel agents from Formosan Lauraceous plants [2–10], *C. subavenium* was chosen for further phytochemical investigation. The MeOH extract of its leaves was subjected to solvent partitioning and chromatographic separation to afford six pure substances. The chemical constituents in the leaves of *C. subavenium* were separated by column chromatography.

Investigation of the MeOH extract of the leaves has led to the isolation of seven compounds, one novel sesquiterpenoid: subamol ((3-methoxy-5*H*-9,10-dihydroxybenzo[3,4]cyclohepta[1,2-*f*])inden-7-yl)-methanol) (**1**); one ionone: (+)-abscisic acid (**2**) [11]; and five benzenoids: syringaldehyde (**3**) [12], *trans*-coumaric acid (**4**), *cis*-coumaric acid (**5**) [13], vanillic acid (**6**) [14], and *p*-hydroxybenzoic acid (**7**) [15]. These compounds were obtained and characterized by comparison of their physical and spectral data (UV, IR, NMR, and MS) with values in the literature. Among them, **1** was found for the first time from the leaves of this species. We report the isolation and structural elucidation of subamol (**1**).

Subamol (**1**) was isolated as a white, amorphous powder with a molecular formula of $C_{17}H_{16}O_4$, as determined by HR-EI-MS (obsd. $[M]^+$ at *m/z*: 284.1044; calcd $[M]^+$ 284.1045). This formula agrees with deductions from the ^1H and ^{13}C NMR data. The UV spectrum contained absorption bands typical of 5*H*-dibenzo[*a,c*]cycloheptene derivatives [3]. The IR spectrum of **1** showed characteristic absorption indicating the presence of hydroxy functionality peaks at 3400 cm^{-1}. The ^1H NMR resonances of **1** were well dispersed in $CDCl_3$ and displayed an ABX pattern (H-4 at δ 6.70, H-2 at 6.76, and H-1 at 7.36) and singlets at δ 7.17, 7.18 for H-11 and H-8 in the aromatic region, accounting for five protons. A singlet at δ 3.97 indicated the presence of the 3-OMe group. The C-6 olefinic proton (δ 6.16, t, J = 7.5 Hz) is coupled to the neighboring C-5 and C-12 methylene protons, which showed coupling constant at δ 2.78 (1H, dd, J = 13.0, 6.5 Hz, H-5a), 3.05 (1H, dd, J = 12.5, 8.0 Hz, H-5b), 4.36 (1H, d, J = 12.5 Hz, H-12a), and 4.53 (1H, d, J = 12.5 Hz, H-12b), respectively. The ^{13}C NMR and DEPT spectra of **1** showed 17 resonances comprising one methyl, two methylene, six methines, and eight quaternary carbons. The structure **1** was also confirmed by 2D NMR experiments. A COSY correlation was observed between H-1 and H-2, and between H-5 and H-6. The HECTOR experiment showed that the carbon signals at δ 32.8 for C-5, 127.2 for C-6, and 66.2 for C-12 were correlated to the proton signals at δ 2.78 and 3.05 for H-5, δ 6.16 for H-6, and δ 4.36 and 4.53 for H-12, respectively. Thus, the structure of **1** was elucidated as (3-methoxy-5*H*-9,10-dihydroxybenzo[3,4]cyclohepta-[1,2-f])inden-7-yl)-methanol, which was further confirmed by NOESY and HMBC experiments (Fig. 1).

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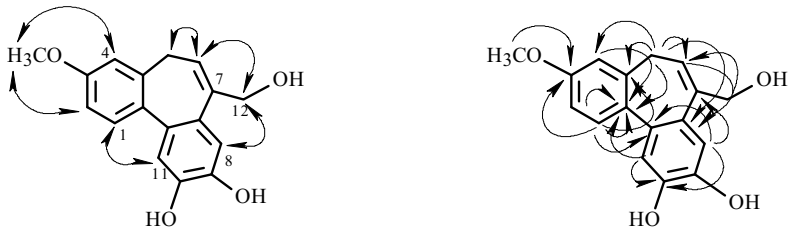

a *b*

Fig. 1. Key correlations observed for analysis of NOESY (*a*) and HMBC (*b*) spectra of compound **1**.

EXPERIMENTAL

UV spectra were obtained in MeCN, and IR spectra were measured on a Hitachi 260–30 spectrophotometer. ^{1}H NMR (500 MHz), HECTOR, HMBC, COSY, NOESY, and DEPT spectra were obtained on a Varian (Unity Plus) NMR spectrometer. Low-resolution FAB-MS and low-resolution EI-MS spectra were collected on a Jeol JMS-SX/SX 102A mass spectrometer or Quattro GC/MS spectrometer having a direct inlet system. High-resolution EI-MS spectra were measured on a Jeol JMS-HX 110 mass spectrometer. Silica gel 60 (Merck, 70–230 mesh, 230–400 mesh) was used for column chromatography. Precoated silica gel plates (Merck, Kieselgel 60F-254), 0.20 mm and 0.50 mm, were used for analytical TLC and preparative TLC, respectively, and visualized with 50% H_2SO_4.

The leaves of *C. subavenium* were collected from Wulai Hsiang, Taipei County, Taiwan in May, 2005. A voucher specimen (Cinnamo. 5) was characterized by one of the authors (Y.-R. H.) and deposited in the Basic Medical Science Education Center, Fooyin University, Kaohsiung County, Taiwan. The air-dried leaves of *C. subavenium* (11.0 kg) were extracted with MeOH (50 L × 6) at room temperature, and a MeOH extract (326.5 g) was obtained upon concentration under reduced pressure. The MeOH extract, suspended in H_2O (1 L), was partitioned with $CHCl_3$ (2 L × 5) to give fractions soluble in $CHCl_3$ (198.5 g) and H_2O (101.2 g). Then, the H_2O extract was partitioned with BuOH (2 L × 5) to give fractions soluble in BuOH (77.5 g). The BuOH-soluble fraction (77.5 g) was chromatographed over silica gel (800 g, 70–230 mesh) using CH_2Cl_2–MeOH mixtures as eluents to produce seven fractions. A part of fraction 1 (6.33 g) was subjected to silica gel chromatography, eluting with CH_2Cl_2–MeOH (80:1), and enriched gradually with MeOH to furnish four fractions (1-1–1-4). Fraction 1-1 (1.65 g) was further purified on a silica gel column using CH_2Cl_2–MeOH mixtures to obtain syringaldehyde (**3**) (16 mg, 0.0206%). Part of fraction 2 (3.88 g) was subjected to Si gel chromatography by eluting with CH_2Cl_2–MeOH (60:1) to obtain mixtures of *trans*-coumaric acid (**4**) and *cis*-coumaric acid (**5**) (11 mg, 0.0142%). Part of fraction 3 (4.39 g) was subjected to Si gel chromatography by eluting with CH_2Cl_2–MeOH (50:1), then enriched with acetone to furnish 5 fractions (3-1–3-5). Fraction 3-2 (1.16 g) was further purified on a silica gel column using CH_2Cl_2–MeOH mixtures to obtain vanillic acid (**5**) (6 mg, 0.0077%). Then, fraction 3-4 (1.57 g) was further purified on a silica gel column using CH_2Cl_2–MeOH mixtures to obtain (+)-abscisic acid (**2**) (20 mg, 0.0258%). Part of fraction 4 (5.22 g) was subjected to Si gel chromatography by eluting with CH_2Cl_2–MeOH (40:1), then enriched with acetone to furnish 5 fractions (4-1–4-5). Fraction 4-3 (2.05 g) was further purified on a silica gel column using CH_2Cl_2–MeOH mixtures to obtain subamol (**1**) (24 mg, 0.0310%). Then, fraction 4-5 (1.95 g) was further purified on a silica gel column using CH_2Cl_2–MeOH mixtures to obtain *p*-hydroxybenzoic acid (**6**) (14 mg, 0.0181%).

Subamol [(3-methoxy-5*H*-9,10-dihydroxybenzo[3,4]-cyclohepta[1,2-*f*])inden-7-yl)-methanol] (1): white amorphous powder. UV (MeCN, λ_{max}, nm, log ε): 235 (3.21), 255 (3.66), 290 (2.15). IR (neat, ν_{max}, cm^{-1}): 3400 (br, OH), 3000, 1700, 1250. MS-EI (70eV, *m/z*, %): 284 $[M]^+$ (20), 265 (15), 255 (5), 239 (25), 192 (39), 154 (13), 149 (17), 137 (22), 134 (42), 129 (13), 116 (25), 109 (42), 97 (100), 83 (70), 69 (90). HR-MS-EI: *m/z* $[M]^+$ calcd for $C_{17}H_{16}O_4$: 284.1045; found: 284.1044. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.78 (1H, dd, J = 13.0, 6.5, H-5a), 3.05 (1H, dd, J = 12.5, 8.0, H-5b), 3.97 (3H, s, 3-OMe), 4.36 (1H, d, J = 12.5, H-12a), 4.53 (1H, d, J = 12.5, H-12b), 6.16 (1H, t, J = 7.5, H-6), 6.70 (1H, d, J = 3.0, H-4), 6.76 (1H, dd, J = 8.4, 3.0, H-2), 7.17 (1H, s, H-11), 7.18 (1H, s, H-8), 7.36 (1H, d, J = 8.4, H-1). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 32.8 (C-5), 55.6 (3-OMe), 66.2 (C-12), 107.3 (C-8), 107.5 (C-11), 111.5 (C-4), 111.8 (C-2), 127.2 (C-6), 129.7 (C-7a), 131.0 (C-1), 131.1 (C-11b), 134.5 (C-11a), 137.7 (C-7), 143.3 (C-4a), 146.1 (C-9), 146.7 (C-10), 159.9 (C-3).

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