Chemistry of Natural Compounds, Vol. 47, No. 2, May, 2011 [Russian original No. 2, March–April, 2011]

CHEMICAL CONSTITUENTS FROM THE LEAVES OF *Cinnamomum reticulatum*

Yi-Chen Chia,[1] Hung-Chun Yeh,[2] Yu-Ting Yeh,[2] and Chung-Yi Chen[2]*

UDC 547.597

Reticuol, a novel Cinnamomum *sesquiterpenoid, has been isolated from* Cinnamomum reticulatum *Hay (Lauraceae), together with eight known compounds,* p*-hydroxybenzoic acid, isoanwulignan, 2,6-dimethyl-1,7-octadiene-3,6-diol,* α*-tocopheryl quinone, kaempferol-3-*O*-(2″,4″-di-*E*-*p*-coumaroyl)-*α*-L-rhamnopyranoside, kaempferol-3-*O*-(3″,4″-di-*E*-*p*-coumaroyl)-*α*-L-rhamnopyranoside, pheophorbide a, and aristophyll C. The structure of reticuol was determined on the basis of spectroscopic analysis.*

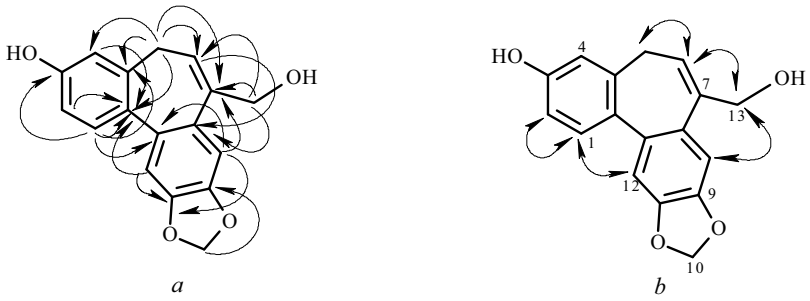
Keywords: *Cinnamomum reticulatum*, Lauraceae, reticuol, sesquiterpenoid.

The *Cinnamomum* species (Lauraceae) have been used in folk medicine for their sweating, antipyretic, and analgesic effects [1]. Previously, we isolated 17 compounds, including two new compounds, cinnaretamine [2] and reticuone [3], and a mixture of 4-hydroxy-3-methoxyphenetyl derivatives [4], one chromanone (reticumanone) [5], two butanolides, two amides, three benzenoids, one lignan, and one steroid from this plant [2–5]. A novel *Cinnamomum* sesquiterpenoid, reticuol (**1**), along with eight known compounds including one benzenoid, *p*-hydroxybenzoic acid [6], one lignan, isoanwulignan [7], one monoterpene diol, 2,6-dimethyl-1,7-octadiene-3,6-diol [8], one quinine, *α*-tocopheryl quinone [9], two acylated flavonol glycosides, kaempferol-3-*O*-(2″,4″-di-*E*-*p*-coumaroyl)-*α*-L-rhamnopyranoside [10], and kaempferol-3-*O*-(3″,4″-di-*E*-*p*-coumaroyl)-*α*-L-rhamnopyranoside [10] and two chlorophylls, pheophorbide a [11] and aristophyll C [12], were isolated and identified from this plant. In this paper, we report the isolation and structural elucidation of this novel skeleton compound, reticuol.

Reticuol (**1**) was obtained as a white amorphous powder from $CHCl_3$. Its molecular formula was deduced as $C_{17}H_{14}O_4$ by HR-ESI-MS (*m/z* 305.0790 ($[M + Na]^+$; calcd 305.0789)). The UV spectrum of reticuol contained absorption bands typical of the 5*H*-dibenzo[*a,c*]cycloheptene derivatives [13]. The IR spectrum of **1** showed characteristic absorption bands due to the presence of hydroxyl (3400 cm^{-1}) and methylenedioxy (1070 and 920 cm^{-1}) groups. The ^1H NMR spectrum of reticuol showed an ABX pattern at δ 6.64 (1H, d, J = 2.8 Hz), 6.69 (1H, dd, J = 8.4, 2.8 Hz), and 7.26 (1H, d, J = 8.4 Hz) for H-4, H-2, and H-1, a singlet at δ 7.04 for H-12, and a singlet at δ 7.12 for H-8 in the aromatic region, in addition to methylenedioxy protons at δ 6.00 (each 1H, d, J = 1.2 Hz), accounting for seven protons. This was assigned as the C-6 methine proton (δ 6.14 (1H, td, J = 8.0, 1.2 Hz)) due to coupling with the neighboring C-5 and C-13 methylene protons, which showed coupling constant at δ 2.66 (1H, dd, J = 12.8, 6.2 Hz, H-5a), 3.03 (1H, dd, J = 12.8, 8.0 Hz, H-5b), 4.27 (1H, d, J = 13.2 Hz, H-13a), and 4.38 (1H, d, J = 13.2 Hz, H-13b). The ^{13}C NMR and DEPT experiments of reticuol showed 17 resonance lines consisting of three methylenes, six methines, and eight quaternary carbons. The structure of reticuol 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 HETCOR experiment showed that the carbon signals at δ 33.9 for C-5, 128.4 for C-6, and 66.1 for C-13 were correlated to the proton signals at δ 2.66 and 3.03 for H-5, δ 6.14 for H-6, and δ 4.27 and 4.38 for H-13, respectively. Thus, the structure of reticuol was elucidated as (3-hydroxy-5*H*-9,11-dioxabenzo[3,4]cyclohepta[1,2-f])inden-7-yl)-methanol, which was further confirmed by NOESY and HMBC experiments (Fig. 1).

1) Department of Food Science & Technology, Tajen University, Pingtung County, Taiwan; 2) School of Medical and Health Sciences, Fooyin University, Kaohsiung County, Taiwan, fax: 886 7 7834548, e-mail: xx377@mail.fy.edu.tw. Published in Khimiya Prirodnykh Soedinenii, No. 2, pp. 203–204, March–April, 2011. Original article submitted February 23, 2010.

 0009-3130/11/4702-0220



a *b*

Fig. 1. HMBC (*a*) and NOESY (*b*) correlations of reticuol (**1**).

EXPERIMENTAL

General. UV spectra were obtained in MeCN, and IR spectra were measured on a Hitachi 260–30 spectrophotometer. ^{1}H NMR (400 MHz), HETCOR, HMBC, COSY, NOESY, and DEPT spectra were obtained on a Varian (Unity Plus) NMR spectrometer. Low-resolution ESI-MS spectra were obtained on an API 3000 (Applied Biosystems) spectrometer, and high-resolution ESI-MS spectra on a Bruker Daltonics APEX II 30e spectrometer. 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. Silica gel 60 (Merck, 70–230 mesh, 230–400 mesh) was used for column chromatography. Precoated silica gel plates (Merck, Kieselgel 60 F-254), 0.20 mm and 0.50 mm, were used for analytical TLC and preparative TLC, respectively, visualized with 50% H_2SO_4.

Plant Material. The leaves of *C. reticulatum* Hay were collected from Pingtung County, Taiwan, May, 2005. Plant material was identified by Prof. Fu-Yuan Lu (Department of Forestry and Natural Resources College of Agriculture, National Chiayi University). A voucher specimen (Cinnamo. 6) was deposited in the School of Medical and Health Sciences, Fooyin University, Kaohsiung County, Taiwan.

Extraction and Isolation. The air-dried leaves of *C. reticulatum* (3.4 kg) were extracted with *n*-hexane (30 L × 5) and $CHCl_3$ (30 L × 5) at room temperature, and an *n*-hexane extract (43.5 g) and $CHCl_3$ extract (151.5 g) were obtained upon concentration under reduced pressure. The *n*-hexane extract (43.5 g) was chromatographed over silica gel (980 g, 70–230 mesh) using *n*-hexane–EtOAc–acetone mixtures as eluents to produce five fractions. Part of fraction 2 (8.92 g) was subjected to silica gel chromatography by eluting with *n*-hexane–EtOAc (100:1), enriched gradually with EtOAc, to furnish three fractions (2-1–2-3). Fraction 2-1 (2.88 g) was further purified on a silica gel column using *n*-hexane–EtOAc mixtures to obtain pheophorbide a (47 mg) and aristophyll C (12 mg). Fraction 2-2 (2.51 g) was further purified on a silica gel column using *n*-hexane–EtOAc mixtures to obtain α-tocopheryl quinone (15 mg). Part of fraction 3 (1.52 g) was subjected to silica gel chromatography by eluting with *n*-hexane–EtOAc (40:1), enriched with EtOAc, to furnish eight further fractions (3-1–3-8). Fraction 3-5 (0.54 g) was further purified on a silica gel column using *n*-hexane–EtOAc mixtures to obtain isoanwulignan (12 mg). The $CHCl_3$ extract (151.5 g) was chromatographed over silica gel (800 g, 70–230 mesh) using *n*-hexane $CHCl_3$–MeOH mixtures as eluents to produce five fractions. Part of fraction 1 (4.82 g) was subjected to silica gel chromatography, by eluting with $CHCl_3$–MeOH (100:1), enriched gradually with MeOH, to furnish five fractions (1-1–1-5). Fraction 1-1 (1.12 g) was further purified on a silica gel column using $CHCl_3$–MeOH mixtures to obtain 2,6-dimethyl-1,7-octadiene-3,6-diol (34 mg). Fraction 1-2 (0.87 g) was further purified on a silica gel column using $CHCl_3$–MeOH mixtures to obtain *p*-hydroxybenzoic acid (17 mg). Part of fraction 4 (10.62 g) was subjected to silica gel chromatography by eluting with $CHCl_3$–MeOH (60:1), enriched with MeOH, to furnish five further fractions (4-1–4-5). Fraction 4-3 (1.89 g) was further purified on a silica gel column using $CHCl_3$–MeOH mixtures to obtain reticuol (6 mg), kaempferol-3-*O*-(2″,4″-di-*E*-*p*-coumaroyl)-α-L-rhamnopyranoside (21 mg), and kaempferol-3-*O*-(3″,4″-di-*E*-*p*-coumaroyl)-α-L-rhamnopyranoside (15 mg).

Reticuol [(3-hydroxy-5*H*-9,11-dioxabenzo[3,4]cyclohepta[1,2-*f*])inden-7-yl)-methanol] (1). White amorphous powder; $[\alpha]_D^{25}$ 0.0° (*c* 0.01, $CHCl_3$). UV (MeCN, λ_{max}, nm, log ε): 235 (3.23), 255 (2.65), 290 (2.11). IR (neat, ν_{max}, cm^{-1}): 3400 (br, OH), 3000, 1700, 1250, 1070, 920 (methylenedioxy). ESI-MS *m/z* 305 $[M + Na]^+$. HR-ESI-MS *m/z* 305.0790 $[M + Na]^+$ (calcd for $C_{17}H_{14}O_4Na$, 305.0789). ^{1}H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 2.66 (1H, dd, J = 12.8, 6.2, H-5a), 3.03 (1H, dd, J = 12.8, 8.0, H-5b), 4.27 (1H, d, J = 13.2, H-13a), 4.38 (1H, d, J = 13.2, H-13b), 6.00 (each 1H, d, J = 1.2, H-10), 6.14 (1H, td, J = 8.0, 1.2, H-6), 6.64 (1H, d, J = 2.8, H-4), 6.69 (1H, dd, J = 8.4, 2.8, H-2), 7.04 (1H, s, H-12), 7.12 (1H, s, H-8), 7.26 (1H, d, J = 8.4, H-1). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 33.9 (C-5), 66.1 (C-13), 102.5 (C-10), 107.0 (C-8), 110.1 (C-12), 113.8 (C-4), 114.1 (C-2), 128.4 (C-6), 130.1 (C-7a), 131.5 (C-1), 131.7 (C-12b), 136.3 (C-12a), 138.7 (C-7), 145.1 (C-4a), 147.6 (C-8a), 147.7 (C-11a), 158.3 (C-3).

ACKNOWLEDGMENT

This investigation was supported by a grant from the National Science Council of the Republic of China (NSC-97-2320-B-242-002-MY3).

REFERENCES

1. Y. H. Kuo and M. J. Shue, *J. Chin. Chem. Soc.*, **38**, 65 (1991).
2. C. Y. Chen and H. C. Yeh, *Nat. Prod. Res.*, **25**, 26 (2011).
3. M. J. Cheng, W. L. Lo, W. S. Tseng, H. C. Yeh, and C. Y. Chen, *Nat. Prod. Res.*, **24**, 732 (2010).
4. I. J. Lin, W. L. Lo, Y. C. Chia, L. Y. Huang, T. M. Cham, W. S. Tseng, Y. T. Yeh, H. C. Yeh, Y. D. Wang, and C. Y. Chen, *Nat. Prod. Res.*, **24**, 775 (2010).
5. M. J. Cheng, W. L. Lo, H. C. Yeh, and C. Y. Chen, *Molbank*, **2009**, M626 (2009).
6. C. Y. Chen, F. R. Chang, C. M. Teng, and Y. C. Wu, *J. Chin. Chem. Soc.*, **46**, 77 (1999).
7. Y. G. Chen, Z. C. Wu, S. H. Gui, Y. P. Lv, X. R. Liao, and F. Halaweish, *Fitoterapia*, **76**, 370 (2005).
8. H. Knapp, M. Straubinger, S. Fornari, N. Oka, N. Watanabe, and P. Winterhalter, *J. Agr. Food Chem.*, **46**, 1966 (1998).
9. I. L. Tsai, Y. F. Jeng, C. Y. Duh, and I. S. Chen, *Chin. Pharm. J.*, **53**, 291 (2001).
10. G. J. Wang, T. H. Tsai, and L. C. Lin, *Phytochemistry*, **68**, 2455 (2007).
11. Y. Nakatani, G. Ourisson, and J. P. Beck, *Chem. Pharm. Bull.*, **29**, 2261 (1981).
12. Y. Y. Chan, Y. L. Leu, and T. S. Wu, *Chem. Pharm. Bull.*, **47**, 887 (1999).
13. D. Budac and P. Wan, *Can. J. Chem.*, **74**, 1447 (1996).