

Short Note

# (S\*)-2,7,8-Trihydroxychroman-4-one

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**Abstract:** Reticumanone (1), a new chromanone, isolated from the leaves of *Cinnamomum reticulatum* Hay (Lauraceae), has been characterized as  $(S^*)$ -2,7,8-trihydroxychroman-4-one, by means of spectroscopic methods.

Keywords: Cinnamomum reticulatum Hay; Lauraceae; reticumanone; chromanone

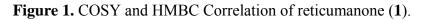
# 1. Introduction

The *Cinnamoum* species (Lauraceae) have been used in folk medicine for sweating, antipyretic, and analgesic effect [1]. There is only one paper describing the constituents of *Cinnamomum reticulatum* Hay [1]. In the course of screening for biologically and chemically novel agents from Formosan Lauraceous plants [2–17], *C. reticulatum* Hay was chosen for further phytochemical investigation. In this paper, we report the isolation and structural elucidation of this new chromanone compound (1).

# 2. Results and Discussion

Reticumanone (1), obtained as a white amorphous powder (CHCl<sub>3</sub>), was assigned the molecular formula C<sub>9</sub>H<sub>8</sub>O<sub>5</sub> by HR-EIMS at m/z [M]<sup>+</sup> 196.0374 (calcd for C<sub>9</sub>H<sub>8</sub>O<sub>5</sub>, 196.0372). UV  $\lambda_{max}$  at 273, 310 (sh), 322 nm, IR bands at 1660 cm<sup>-1</sup> and a signal appearing at  $\delta$  182.4 in the <sup>13</sup>C-NMR spectrum indicate the chromanone skeleton of this compound [18]. The IR spectrum revealed the presence of a

hydroxyl group absorption at v 3400 cm<sup>-1</sup>. The <sup>1</sup>H-NMR spectrum of **1** showed one set of AB doublet signals at  $\delta$  6.81 (1H, d, J = 8.8), and 7.31 (1H, d, J = 8.8), one methine proton at  $\delta$  5.32 (1H, dd, J = 9.0, 3.4), and two methylene protons at  $\delta$  2.67 (1H, dd, J = 16.8, 9.0)/3.08 (1H, dd, J = 16.8, 3.4), indicating that **1** was probably a 2,7,8-trihydroxychroman-4-one. The <sup>13</sup>C-NMR spectrum indicated that compound **1** had a total of 9 carbons, with the skeleton consisting of a chroman-4-one. The carbons of the chroman-4-one were assigned, from <sup>13</sup>C-NMR and DEPT experiments, one methylene at  $\delta$  45.9 (C-3); three methines at  $\delta$  92.4 (C-2), 126.8 (C-6) and 131.4 (C-5); and five quaternary carbons at  $\delta$  111.8 (C-4a), 135.7 (C-8), 150.6 (C-8a), 152.1 (C-7) and 182.9 (C-4). The structure of **1** was also confirmed by 2D NMR experiments. A COSY correlation was observed between H-2 and H-3, and between H-5 and H-6 (Figure 1). The HETCOR experiment showed that the carbon signals at  $\delta$  9.2.4 for C-2, 45.9 for C-3, 131.4 for C-5 and 126.8 for C-6 were correlated to the proton signals at  $\delta$  5.32 for H-2, 2.67/3.08 for H-3, 7.31 for H-5 and 6.81 for H-6, respectively. The relative configuration of **1** was determined by 2D NOESY analysis. The observation of the NOESY correlation from H-3eq. to H-2 suggested that H-2 was in the  $\beta$ -configuration (Figure 2). Thus, the structure of **1** was determined to be (*S\**)-2,7,8-trihydroxychroman-4-one and has been named reticumanone.



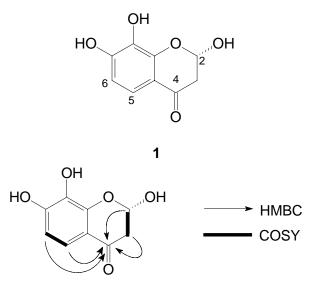
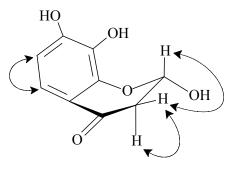


Figure 2. NOESY Correlations of reticumanone (1).



# 3. Experimental

#### 3.1. General

UV spectra were obtained on a Jasco UV-240 spectrophotometer in CH<sub>3</sub>CN, IR spectra were measured on a Hitachi 260-30 spectrophotometer. <sup>1</sup>H NMR (400 MHz), HETCOR, HMBC, COSY, NOESY, and DEPT spectra were obtained on a Varian (Unity Plus) NMR spectrometer. Low-resolution EIMS spectra were collected on a Jeol JMS-SX/SX 102A mass spectrometer or Quattro GC/MS spectrometer having a direct inlet system. High-resolution EIMS spectrum was 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 60 F-254), 0.20 mm and 0.50 mm, were used for analytical TLC and preparative TLC, respectively, visualized with 50% H<sub>2</sub>SO<sub>4</sub>.

#### 3.2. Plant Material

The leaves of *C. reticulatum* Hay were collected from Pingtung County, Taiwan, May 2005. Plant material was identified by Professor 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.

#### 3.3. Extraction and Isolation

The air-dried leaves of *C. reticulatum* Hay (3.4 kg) were extracted with *n*-hexane (30 L × 5) and CHCl<sub>3</sub> (30 L × 5) at room temperature and a *n*-hexane extract (43.5 g) and CHCl<sub>3</sub> 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 4 (10.62 g) was subjected to silica gel chromatography by eluting with CHCl<sub>3</sub>-MeOH (60:1), enriched with MeOH to furnish five further fractions (4-1–4-5). Fraction 4-2 (2.56 g) was further purified on a silica gel column using CHCl<sub>3</sub>-MeOH mixtures to obtain reticumanone (4 mg).

**Reticumanone** ((*S*\*)-2,7,8-trihydroxychroman-4-one) (1): White amorphous powder (CHCl<sub>3</sub>);  $[\alpha]^{25}_{D}$ -12.6° (c 0.005, CHCl<sub>3</sub>); UV/Vis (CH<sub>3</sub>CN):  $\lambda_{max}$  (log  $\varepsilon$ ): 273 (3.62), 310 (sh), 322 (3.00) nm; IR (neat)  $\nu_{max}$ : 3400 (br, OH), 2920, 2850, 1660 (C=O), 1250 cm<sup>-1</sup>; MS (EI, 70 eV): *m/z* (%): 196 [M]<sup>+</sup> (45), 179 (57), 163 (64), 147 (100), 90 (32); HR-MSEI: *m/z* [M]<sup>+</sup> calcd for C<sub>9</sub>H<sub>8</sub>O<sub>5</sub>: 196.0372; found: 196.0374; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.67 (1H, dd, *J* = 16.8, 9.0 Hz, H-3ax.), 3.08 (1H, dd, *J* = 16.8, 3.4 Hz, H-3eq.), 5.32 (1H, dd, *J* = 9.0, 3.4 Hz, H-2), 6.81 (1H, d, *J* = 8.8 Hz, H-6), 7.31 (1H, d, *J* = 8.8 Hz, H-5); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 45.9 (C-3, CH<sub>2</sub>), 92.4 (C-2, CH), 111.8 (C-4a, C), 126.8 (C-6, CH), 131.4 (C-5, CH), 135.7 (C-8, C), 150.6 (C-8a, C), 152.1 (C-7, C), 182.9 (C-4, C).

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# References

- 1. Kuo, Y.H.; Shue, M.J. New esters, 2-(4-hydroxy-3-methoxyphenyl)ethyl hexa- and octacosanoates from the leaves of *Cinnamomum reticulatum* Hay. *J. Chin. Chem. Soc.* **1991**, *38*, 65–69.
- 2. Lin, R.J.; Cheng, M.J.; Huang, J.C.; Lo, W.L.; Yeh, Y.T.; Yen, C.M.; Lu, C.M.; Chen, C.Y. Cytotoxic compounds from the stems of *Cinnamomum tenuifolium*. J. Nat. Prod. 2009, 72, in press.
- Chen, C.Y.; Chen, C.H.; Lo, Y.C.; Wu, B.N.; Wang, H.M.; Lo, W.L.; Yen, CM; Lin, R.J. Anticancer activity of Isoobtusilactone A from *Cinnamomum kotoense*: Involvement of apoptosis, cell-cycle dysregulation, mitochondria regulation, and reactive oxygen species. *J. Nat. Prod.* 2008, 71, 933–940.
- 4. Chen, C.Y.; Hsu, Y.L.; Tsai, Y.C.; Kuo, P.L. Kotomolide A arrests cell cycle progression and induces apoptosis through the induction of ATM/p53 and the initiation of mitochondrial system in human non-small cell lung cancer A549 cells. *Food Chem. Toxicol.* **2008**, *46*, 2476–2484.
- 5. Kuo, P.L.; Chen, C.Y.; Tzeng, T.F.; Lin, C.C.; Hsu, Y.L. Involvement of reactive oxygen species/c-Jun NH<sub>2</sub>-terminal kinase pathway in kotomolide A induces apoptosis in human breast cancer cells. *Toxicol. Appl. Pharmacol.* **2008**, *229*, 215–226.
- 6. Kuo, S.Y.; Hsieh, T.J.; Wang, Y.D.; Lo, W.L.; Hsui, Y.R.; Chen, C.Y. Cytotoxic constituents from the leaves of *Cinnamomum subavenium*. *Chem. Pharm. Bull.* **2008**, *56*, 97–101.
- Liu, T.Z.; Cheng, J.T.; Yiin, S.J.; Chen, C.Y.; Chen, C.H.; Chen, C.H. Isoobtusilactone A induces both caspase–dependent and –independent apoptosis in Hep G2 cells. *Food Chem. Toxicol.* 2008, 46, 321–327.
- 8. Lin, R.J.; Lo, W.L.; Wang, Y.D.; Chen, C.Y. A novel cytotoxic monoterpenoid from the leaves of *Cinnamomum subavenium. Nat. Prod. Res.* **2008**, *22*, 1055–1059.
- 9. Chen, C.Y.; Chen, C.H.; Wong, C.H.; Liu, Y.W.; Lin, Y.S.; Wang, Y.D.; Hsui, Y.R. Cytotoxic constituents of the stems of *Cinnamomum subavenium*. J. Nat. Prod. **2007**, 70, 103–106.
- Chen, C.Y.; Hsu, Y.L.; Chen, Y.Y.; Hung, J.Y.; Huang, M.S.; Kuo, P.L. Isokotomolide A, a new butanolide extracted from the leaves of *Cinnamomum kotoense*, arrests cell cycle progression and induces apoptosis through the induction of p53/p21 and the initiation of mitochondrial system in human non-small cell lung cancer A549 cells. *Eur. J. Pharmacol.* 2007, *574*, 94–102.
- Chen, C.Y.; Liu, T.Z.; Chen, C.H.; Wu, C.C.; Cheng, J.T.; Yiin, S.J.; Shih, M.K.; Wu, M.J.; Chern, C.L. Isoobtusilactone A-induced apoptosis in human hepatoma Hep G2 cells is mediated via increased NADPH oxidase-derived reactive oxygen species (ROS) production and the mitochondria-associated apoptotic mechanisms. *Food Chem. Toxicol.* 2007, 45, 1268–1276.

- 12. Kuo, P.L.; Chen, C.Y.; Hsu, Y.L. Isoobtusilactone A induced cell cycle arrest and apoptosis through reactive oxygen species/apoptosis signal-regulating kinase 1 signaling pathway in human breast cancer cells. *Cancer Res.* **2007**, *67*, 7406–7420.
- 13. Chen, C.H.; Lo, W.L.; Liu, Y.C.; Chen, C.Y. Chemical and cytotoxic constituents from the leaves of *Cinnamomum kotoense*. J. Nat. Prod. **2006**, *69*, 927–933.
- 14. Chen, C.Y. Butanolides from the stem of *Cinnamomum kotoense*. *Nat. Prod. Commun.* **2006**, *1*, 453–455.
- 15. Hsieh, T.J.; Chen, C.H.; Lo, W.L.; Chen, C.Y. Lignans from the stem of *Cinnamomum camphora*. *Nat. Prod. Commun.* **2006**, *1*, 21–25.
- 16. Hsieh, T.J.; Su, C.C.; Chen, C.Y.; Liou, C.H.; Lu, L.H. Using experimental studies and theoretical calculations to analyze the molecular mechanism of coumarin, *p*-hydroxybenzoic acid, and cinnamic acid. *J. Mol. Struct.* **2005**, *741*, 21–25.
- 17. Chen, C.Y.; Hsieh, S.L.; Hsieh, M.M.; Hsieh, S.F.; Hsieh, T.J. Substituent chemical shift of rhamnosides from the stems of *Cinnamomum osmophleum*. *Chin. Pharm. J.* **2004**, *56*, 141–146.
- 18. Ngo, L.V.; Thi, C.P. An unusual *m*-hydroxyacetophenone and three new chromanone derivatives from *Chrysothamnus viscidiflorus*. *Phytochemistry* **1981**, *20*, 485–487.

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