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Novel isolation of resveratrol dimer *O*-glucosides with enantiomeric aglycones from the leaves of *Shorea cordifolia*

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ABSTRACT

Two *O*-glucosides of resveratrol dimers, ampelopsin F-11b-*O*-β-glucopyranosides with enantiomeric aglycones [cordifoloside A (**1**) and cordifoloside B (**2**)] and an enantiomer of the aglycone [(−)-ampelopsin F] were isolated from the leaves of *Shorea cordifolia* (Dipterocarpaceae). These structures were identified on the basis of spectroscopic evidence and their absolute configurations were elucidated using circular dichroism data. This is the first report on oligostilbenoids that demonstrates the co-occurrence of diastereomeric *O*-glucosides with enantiomeric aglycones in this family.

1. Introduction

Plants belonging to the family Dipterocarpaceae are representative sources of oligostilbenoids that are composed of resveratrol. The chemical aspects of oligostilbenoids from this family have increasingly accumulated over the last decade, which has resulted in the elucidation of a variety of structures depending on various fused skeletons of bicyclic as well as heterocyclic systems and stereoisomerism (Ito, 2011). Oligostilbenoids from plants are biogenetically classified into two groups depending on whether they possess dihydrobenzofuran rings (group A) or not (group B) (Sotheeswaran and Pasupathy, 1993). In group B compounds, dibenzobicyclo[3.2.1]octadiene has been attributed mainly to ampelopsin F, which has been isolated from the families Vitaceae (Oshima et al., 1993), Dipterocarpaceae (Ito et al., 2003), and Leguminosae (Luo et al., 2001). Each family possesses a stereospecific biosynthetic pathway for the oxidative condensation of two resveratrols that definitely produces one enantiomer, as represented by (+)-ampelopsin F in Vitaceae and (−)-ampelopsin F in Dipterocarpaceae and Leguminosae. In the present study, we focused on the oligostilbenoids of *Shorea cordifolia* (Syn *Doona nervosa*) and achieved the isolation and determination of the absolute configurations of two new isomeric stilbene dimers, ampelopsin F-11b-*O*-β-glucopyranosides with the enantiomeric aglycones [cordifoloside A (**1**) and cordifoloside B (**2**)]. The absolute configurations were determined on the basis of the circular dichroism (CD) spectra of **1** and **2**.

2. Results and discussion

An acetone extract of *S. cordifolia* leaves was subjected to open column chromatography (CC) based on DMS. Further purification with silica gel CC, gel filtration using Sephadex LH-20 CC, reverse-phase CC using a Sep-Pak cartridge (ODS), and preparative HPLC using two stationary phases (ODS and chorester) facilitated the isolation of oligostilbenoids. Cordifolosides A (**1**) and B (**2**) were obtained as pale brown optically active solids (**1**: $[\alpha]_D^{25}$ −31.8, **2**: $[\alpha]_D^{25}$ −15.2) with positive reactions to Gibbs and $FeCl_3$ reagents and had the same planar structure composed of two resveratrol units and a glucopyranosyl group. Their ^1H and ^{13}C NMR spectra were very similar, as shown in Figs. S1 and S2 (Supporting

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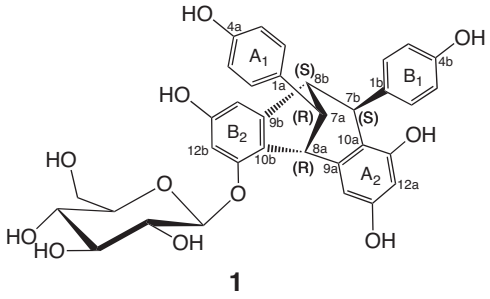

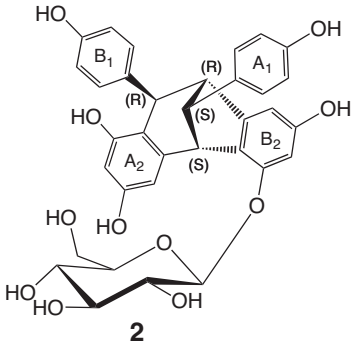

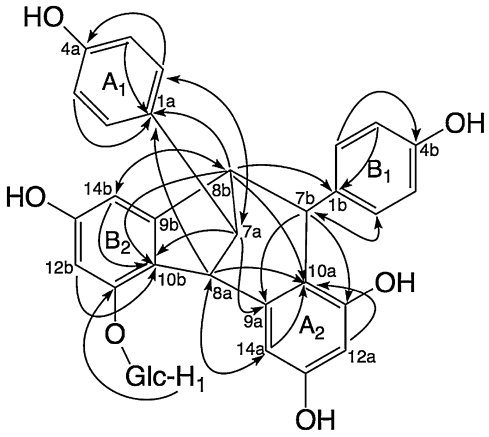

Fig. 1. CH long-range correlations in the HMBC spectrum of **1**.

information). Structural analyses of the new compounds (**1** and **2**) were similar. Thus, the protocol followed for compound **1** is described in detail below and comparative results based on isomerism are discussed. The known compound [(−)-ampelopsin F ($[\alpha]_D^{25}$ −29.0)] was characterized by complete analysis of its spectral data (MS, NMR, and optical rotation) and comparisons with previously reported spectral data (Luo et al., 2001; Oshima et al., 1993).

Cordifoloside A (**1**) showed an $[M+Na]^+$ ion at *m*/*z* 639.1852 in ESI–MS, which is attributable to the molecular formula $C_{34}H_{32}O_{11}$. The assignments of the ^{1}H- and ^{13}C NMR spectra of **1** in acetone-d_6 are shown in Table 1. These assignments were primarily made on the basis of DQF COSY and HMQC as well as HMBC experiments. The ^{13}C NMR spectra of **1** exhibited 30 signals for 34 carbons, including four sp_3 methine carbons, five oxygenated sp_3 methine carbons, an sp_3 methylene carbon, 12 sp_2 methine carbons, six sp_2 quaternary carbons, and six oxygenated sp_2 quaternary carbons. Based on these data and 19° of unsaturation, compound **1** was considered to have three condensed rings in addition to four aromatic rings. The ^{1}H NMR spectrum (measured at room temperature) contained two *ortho*-coupled aromatic signals from two *p*-hydroxyphenyl groups (ring A_1 and B_1) at δ_H 6.80 [H-2a(6a)]/6.58 [H-3a(5a)] and δ_H 7.08 [H-2b(6b)]/6.75 [H-3b(5b)]. These were correlated with the ^{13}C NMR signals at δ_C 129.3 [C-2a(6a)]/115.6 [C-3a(5a)] and δ_C 129.9 [C-2b(6b)]/115.6 [C-3b(5b)] in the HMQC spectrum of **1**. Four signals of *meta*-coupled aromatic protons were apparent at δ_H 6.14 (H-12a), δ_H 6.58 (H-14a), δ_H 6.35 (H-12b), 6.70 (H-14b), and there were cross peaks with the ^{13}C NMR signals at δ_C 101.0 (C-12a), δ_C 106.0 (C-14a), δ_C 102.7 (C-12b), and δ_C 106.7 (C-14b), respectively, in the HMQC spectrum of **1**. These signals were assigned to two resorcinol-type aromatic rings (rings A_2 and B_2). Four benzylic protons were present in an aliphatic methine sequence at δ_H 4.19 (H-7b), δ_H 3.42 (H-8b), δ_H 3.66 (H-7a), and δ_H 4.19 (H-8a), which correlated with the ^{13}C NMR resonances at δ_C 47.1 (C-7b), δ_C 58.0 (C-8b), δ_C 50.4 (C-7a), and δ_C 50.1 (C-8a), respectively. The presence of a β-glucopyranose moiety [δ_C 102.4 (C-glc-1), 74.9 (C-glc-2), 77.8 (C-glc-3), 71.2 (C-glc-4), 77.7 (C-glc-5), and 62.6 (C-glc-6); anomeric proton at δ_H 4.74 (H-glc-1)] was supported by NMR data, which yielded the composition $C_{28}H_{22}O_6$ for the aglycone of **1**. These partial structures were connected by HMBC correlations (Fig. 1). In the spectrum, significant ^3J correlations were observed among H-7a/C-2a(6a), H-8a/C-14a, H-7b/C-2b(6b), and H-8b/C-14b, indicating that the rings A_1, A_2, B_1, and B_2 were attached at C-7a, C-8a, C-7b, and C-8b, respectively, thus facilitating the deduction of the two resveratrol units in **1** (resveratrols A and B). Additional cross-peaks were observed among H-7a/C-10b, H-7b/C-11a, and H-glc-1/C-11b, which supported the C–C bonds and *O*-glucosidic linkages, i.e., C-8a/C-10b, C-7b/C-10a, and C-7a/O/C-11b, respectively. The relative stereostructure of **1** was elucidated as follows. The configurations of C-8a and C-8b in the framework of the bicyclo ring system were *R* and *S*, respectively, and four configurations attributable to the other two asymmetric centers (C-7a and C-7b) are proposed for **1**. In the NOESY experiment of **1** (Fig. S3), an NOE was observed between H-7a/H-2b(6b), which can be explained only by a co-facial orientation of H-7a and ring B_1. Fig. 2 represents the configuration after energy minimization using PCMODEL with the Merck molecular force field (MMFF94), where the calculated dihedral angle of H-7a/C-7a–H-8a/C-8a (78.9°), H-8b/C-8b–H-7a/C-7a (84.4°), and H-7b/C-7b–H-8b/C-8b (77.6°) agreed with singlet peaks for H-7a, H-8a, H-7b, and H-8b, due to the small coupling constant of H-7a/H-8a, H-8b/H-7a, and H-7b/H-8b. The ^{1}H and ^{13}C

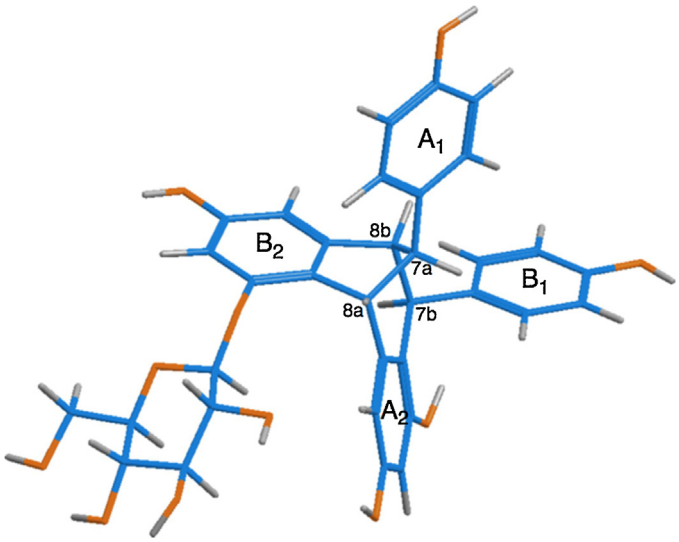

Fig. 2. Calculated three-dimensional structure of **1**. 3D structures generated by employing PCMODEL 9.3 (Serena Software, Box 3076, Bloomington, IN 47402-3076) molecular-modeling program software using MMFF94 force field (MM2 type) for energy minimization.