NEOLIGNAN, PHENYLPROPANOID AND IRIDOID GLYCOSIDES FROM PIEDICULARIS VERTICILLATA

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Key Word Index—Pedicularis verticillata; Scrophulariaceae; neolignan glycosides; phenylpropanoid glycosides; iridoid glycosides; verticillatosides A and B.

Abstract—Two new neolignan glycosides, named verticillatosides A and B were isolated from an ethanolic extract of whole plants of Pedicularis verticillata, along with the 11 known compounds, verbascoside, cis-tanosides C and D, 7-deoxy-8-epi-loganic acid, 8-epi-loganic acid, plantarenaloside, geniposidic acid, euphroside, aucubin, boschnaloside and caryoptoside. On the basis of spectral and chemical evidence, verticillatosides A and B were determined to be rel-(7S,8R)-A7'-9,9'-dihydroxy-3,5'-dimethoxy-7-O-3',8-O-4'-neolignan-4-O-β-D-glycoside and rel-(7R,8S)-A7'-9,9'-dihydroxy-3,5'-dimethoxy-7-O-3',8-O-4'-neolignan-4-O-β-D-glycoside, respectively. © 1997 Elsevier Science Ltd. All rights reserved

INTRODUCTION

The genus Pedicularis comprises ca 329 species in China [1]. Of these, many have been used in the traditional Chinese system of medicine to treat diuresis, exhaustion, collapse and senility [2]. Recent pharmacological studies on phenylpropanoid glycosides from P. striata [3] and P. lasiophrys [4] showed that they had strong scavenging effects on superoxide and antioxidation effects [5]. In continuation of our studies on Pedicularis species, we now report the isolation and structural elucidation of two new neolignan glycosides, verticillatosides A (1) and B (2) from whole plants of P. verticillata, along with the 11 known compounds, verbascoside (3) [6], cistanosides C (4) [8], and D (5) [8], 7-deoxy-8-epi-loganic acid (6) [9], 8-epi-loganic acid (7) [10], plantarenaloside (8) [11], geniposidic acid (9) [12], euphroside (10) [13, 14], aucubin (11) [7], boschnaloside (12) [11] and caryoptoside (13) [15]. Among them, compounds 6, 7 and 13 were isolated for the first time from the genus Pedicularis.

RESULTS AND DISCUSSION

The IR spectrum (KBr) of compound 1 showed absorption bands at 3323 (hydroxyl), 1512 and 1601 cm⁻¹ (phenyl). The FAB mass spectrum showed quasi-molecular ion peaks at m/z 543 [M+Li]+ and 559 [M+Na]+, suggesting the molecular formula to be C₅₃H₇₀O₁₂, which was also supported by ¹³C NMR and DEPT data. The ¹H NMR spectrum showed the presence of two methoxyl groups at δ 3.77 (3H, s) and δ 3.71 (3H, s), five aromatic protons at δ 6.83 (1H, d, J = 1.6 Hz, H-6'), 7.02 (1H, d, J = 1.6 Hz, H-2'), 7.03 (1H, d, J = 1.5 Hz, H-2), 6.65 (1H, dd, J = 8.0, 1.5 Hz, H-6), 6.98 (1H, d, J = 8.0 Hz, H-5), (E)-coniferyl alcohol signals at δ 4.07 (1H, br d, J = 5.7 Hz, H-9'), 6 6.23 (IH, dt, J = 15.7, 5.7 Hz, H-8') and 6 6.44 (IH, d, J = 15.7 Hz, H-7') [16], two methylene protons at δ 4.75 (1H, d, J = 7.2 Hz, H-7), δ 4.29 (1H, m, H-8) and an anomeric proton of a sugar at δ 4.85 (1H, d, J = 7.8 Hz, H-1' of Glu). Comparison between the ¹H and ¹³C NMR data of 1 with those of eusiderin E [17] indicated that 1 is a benzodioxane-type neolignan glycoside. In an HMBC experiment, the correlations of δ 145.3 (C-4) with δ 6.44 (H-7') of Glu and 6.98 (H-5); δ 148.4 (C-3) with δ 3.71 (-OMe) and 7.03 (H-2); δ 130.2 (C-1') with δ 6.44 (H-7') and 7.02 (H-2'); and δ 149.7 (C-5') with δ 3.77 (-OMe) and 6.83 (H-6'), suggested the site of glycosidation at C-4, a methoxyl at C-3, the other methoxyl and (E)-coniferyl alcohol side-chain at C-5' and C-1' of the aglycone, respectively. The glucose had the β-configuration according to the coupling constant (J = 7.8 Hz) of H-1' (δ 4.85) of glucose. The configuration of H-7 and H-8 could be confirmed as trans [18] from their large coupling constant (J = 7.2 Hz) in the ¹H NMR spectrum. Thus,

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verticillatoside A was elucidated as \textit{rel-}(7\textit{S},8\textit{S})-\Delta^7-9,9'-dihydroxy-3,5'-dimethoxy-7-O-3',8-O-4'-neolignan-4-O-\beta-D-glycoside.

The UV, IR, $^1$H and $^{13}$C NMR spectra of compound 2 were similar to those of 1. However, the coupling constant between H-7 and H-8 in compound 2 showed a small value for ($J_{7,8} = 2.4$ Hz), which is clearly less than that in 1 ($J_{7,8} = 7.2$ Hz), indicating that 2 is a cis-isomer of 1 \cite{18}. This was confirmed by the $^{13}$C NMR spectrum (191 \textit{ppm}; compound 1: C-7, $\delta$ 84.1; C-8, $\delta$ 71.4; compound 2: C-7, $\delta$ 83.5; C-8, $\delta$ 70.7). Thus, verticillatoside B was established to be \textit{rel-}(7\textit{R},8\textit{S})-\Delta^7-9,9'-dihydroxy-3,5'-dimethoxy-7-O-3',8-O-4'-neolignan-4-O-\beta-D-glycoside.

**EXPERIMENTAL.**

\textbf{Plant material.} Whole plants of \textit{P. verticillata} Maxim. were collected in Zhang county, Gansu province of China in August 1989. It was identified by Professor Zhang Guo-Liang of Lanzhou University. A voucher specimen (PV-001) is preserved at the Herbarium of our institute.

\textbf{Extraction and isolation.} Dried whole plants (2.9 kg) were extracted with 95\% EtOH (10 l x 3) at room temp. for a week each time. After concn of the combined extracts under red. pres. the residue was diluted with hot H$_2$O and the H$_2$O-insoluble material removed by filtration through Celite. The filtrate was then extracted with petrol (60-90\%).

The EtOAc portion (165 g) was chromatographed over silica gel and eluted with CHCl$_3$-MeOH (30:1 to 2:1); 3 frs were obtained. Fr. 1 (CHCl$_3$-MeOH, 30:1 to 2:1) on repeated silica gel cc eluting with CHCl$_3$-MeOH (8:1), yielded pure compounds 4 (50 mg) and 5 (20 mg). Fr. 2 (CHCl$_3$-MeOH, 10:1) was purified by silica gel cc eluting with CHCl$_3$-MeOH (8:1) to give compounds 6 (40 mg) and 12 (20 mg). Fr. 3 (CHCl$_3$-MeOH, 4:1) was subjected to polyamide cc eluting with H$_2$O, then with MeOH-H$_2$O (4:1), to obtain pure compound 3 (100 mg).

The $n$-BuOH portion (75 g) was chromatographed over silica gel and eluted with CHCl$_3$-MeOH (20:1 to 2:1); 4 frs were obtained. Fr. 1 (CHCl$_3$-MeOH, 14:1) on repeated chromatographic purification by silica gel CC eluting with EtOAc-EtOH (8:1), gave pure compounds 10 (25 mg) and 13 (20 mg). Fr. 2 (CHCl$_3$-MeOH, 10:1) was chromatographed over silica gel and eluted with CHCl$_3$-MeOH (8:1) providing a mixt. which was then purified by HPLC (Partisil 10 ODS-C$_8$, MeOH-H$_2$O, 1:4); compounds 1 (15 mg) and 2 (10 mg) were obtained. Fr. 3 (CHCl$_3$-MeOH, 6:1) on repeated silica gel CC eluting with CHCl$_3$-MeOH (6:1) and EtOAc-EtOH (6:1) gave pure compounds 8 (30 mg) and 9 (50 mg). Fr. 4 was chromatographed on a polyamide column. A mixt. was obtained when eluted with H$_2$O but eluting with MeOH-H$_2$O (1:4) gave compound 3 (150 mg). The mixt. was chromatographed over silica gel and eluted with CHCl$_3$-MeOH (6:1) to obtain compounds 7 (50 mg) and 11 (20 mg).

All of the known compounds were identified by comparison with either their spectral data with those reported in the lit. or using authentic samples (TLC).

\textbf{Compound 1.} White amorphous powder. [\alpha]$_{D}^{25}$ -8.0$^\circ$ (MeOH; c, 0.50). UV \textit{\lambda}_{max}: 201, 266 nm. IR (KBr): 3323 cm$^{-1}$ (OH), 1512, 1601 cm$^{-1}$ (phenyl). FAB-MS: 543 [M+Li]$^+$ and 559 [M+Na]$^+$. $^{13}$C NMR (400 MHz, DMSO-$d_6$, TMS): $\delta$ 7.03 (1H, d, $J = 1.5$ Hz, H-2), 6.98 (1H, d, $J = 8.0$ Hz, H-5), 6.65 (1H, d, $J = 1.5$, 8.0 Hz, H-6), 4.75 (1H, d, $J = 7.2$ Hz, H-7), 4.29 (1H, m, H-8), 3.89 (2H, br d, $J = 1.5$ Hz, H-9), 7.02 (1H, d, $J = 1.6$ Hz, H-2'), 6.83 (1H, d, $J = 1.6$ Hz, H-6'), 7.44 (1H, d, $J = 15.7$ Hz, H-7'), 6.23 (1H, d, $J = 15.7$, 5.7 Hz, H-8'), 4.07 (2H, br d, $J = 5.7$ Hz, H-9'), 4.85 (1H, d, $J = 7.8$ Hz, glu-1), 3.77 (OCH$_3$), 3.71 (OCH$_3$).

\textbf{Compound 2.} White amorphous powder. [\alpha]$_{D}^{25}$ -32$^\circ$ (MeOH; c 0.50). UV \textit{\lambda}_{max}: 201, 266 nm. IR (KBr): 3324 cm$^{-1}$ (OH), 1512, 1601 cm$^{-1}$ (phenyl). FAB-MS: 543 [M+Li]$^+$ and 559 [M+Na]$^+$. $^{13}$C NMR (400 MHz, DMSO-$d_6$, TMS): $\delta$ 136.0 (C-1, C), 109.8 (C-2, CH), 148.4 (C-3, C), 145.5 (C-4, C), 118.7 (C-5, CH), 119.2 (C-6, CH), 84.1 (C-7, CH), 71.4 (C-8, CH), 60.6 (C-9, CH$_2$), 130.2 (C-1', C), 111.3 (C-2', CH$_2$), 147.5 (C-3', C), 135.7 (C-4', C), 149.7 (C-5', C), 115.4 (C-6', CH), 128.5 (C-7', CH), 128.6 (C-8', CH), 61.6 (C-9', CH$_2$), 100.2 (C-1', CH), 73.3 (C-2', CH), 76.9 (C-3', CH), 69.7 (C-4', CH), 77.0 (C-5', CH), 60.5 (C-6', CH$_2$), 55.5 (OCH$_3$), 55.6 (OCH$_3$).

\textbf{Compound 2.} White amorphous powder. [\alpha]$_{D}^{25}$ -32$^\circ$ (MeOH; c 0.50). UV \textit{\lambda}_{max}: 201, 266 nm. IR (KBr): 3324 cm$^{-1}$ (OH), 1512, 1604 cm$^{-1}$ (phenyl). FAB-MS: 543 [M+Li]$^+$ and 559 [M+Na]$^+$. $^{13}$C NMR (400 MHz, DMSO-$d_6$, TMS): $\delta$ 136.0 (C-1, C), 109.8 (C-2, CH), 148.4 (C-3, C), 145.5 (C-4, C), 118.7 (C-5, CH), 119.2 (C-6, CH), 84.1 (C-7, CH), 71.4 (C-8, CH), 60.6 (C-9, CH$_2$), 130.2 (C-1', C), 111.3 (C-2', CH$_2$), 147.5 (C-3', C), 135.7 (C-4', C), 149.7 (C-5', C), 115.4 (C-6', CH), 128.5 (C-7', CH), 128.6 (C-8', CH), 61.6 (C-9', CH$_2$), 100.2 (C-1', CH), 73.3 (C-2', CH), 76.9 (C-3', CH), 69.7 (C-4', CH), 77.0 (C-5', CH), 60.5 (C-6', CH$_2$), 55.5 (OCH$_3$), 55.6 (OCH$_3$).
8.0 Hz, H-6), 4.80 (1H, d, J = 2.4 Hz, H-7), 4.30 (1H, m, H-8), 3.78 (2H, br, d, J = 12.0 Hz, H-9), 7.02 (1H, d, J = 1.6 Hz, H-2'), 6.82 (1H, d, J = 1.6 Hz, H-6'), 6.44 (1H, d, J = 15.7 Hz, H-7'), 6.23 (1H, dt, J = 15.7, 5.7 Hz, H-8'), 4.09 (2H, br, d, J = 5.7 Hz, H-9'), 4.85 (1H, br, d, J = 7.8 Hz, glu-1), 3.77 (OCH3), 3.71 (OCH3). 13C NMR (100 MHz, DMSO-d6, TMS): δ 136.0 (C-1, C), 109.8 (C-2, CH), 148.4 (C-3, C), 145.5 (C-4, C), 118.7 (C-5, CH), 119.1 (C-6, CH), 83.5 (C-7, CH), 70.7 (C-8, CH), 60.6 (C-9, CH2), 130.1 (C-1', C), 111.3 (C-2', CH), 147.5 (C-3', C), 135.7 (C-4', C), 149.7 (C-5', C), 115.4 (C-6', CH), 128.5 (C-7', CH), 128.6 (C-8', CH), 61.6 (C-9', CH2), 100.1 (C-1', CH), 73.3 (C-2', CH), 76.9 (C-3', CH), 69.7 (C-4', CH), 77.0 (C-5', CH), 60.5 (C-6', CH2), 55.5 (OCH3), 55.6 (OCH3).

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