Pergamon

PII: S0031-9422(97)00115-5

Phytochemistry, Vol. 45, No. 6, pp. 1271–1273, 1997

0031-9422/97 $17.00 + 0.00

NEOLIGNAN, PHENYLPROPANOID AND IRIDOID GLYCOSIDES FROM *PEDICULARIS VERTICILLATA*

SU BAO-NING, YANG LI and JIA ZHONG-JIAN*

Department of Chemistry and State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou, 730000, People's Republic of China

(*Received in revised form* 3 *January* 1997)

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, cistanosides 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-(7*S*,8*S*)-Δ^{7}-9,9′-dihydroxy-3,5′-dimethoxy-7-*O*-3′,8-*O*-4′-neolignan-4-*O*-β-D-glycoside and rel-(7*R*,8*S*)-Δ^{7}-9,9′-dihydroxy-3,5′-dimethoxy-7-*O*-3′,8-*O*-4′-neolignan-4-*O*-β-D-glycoside, respectively.

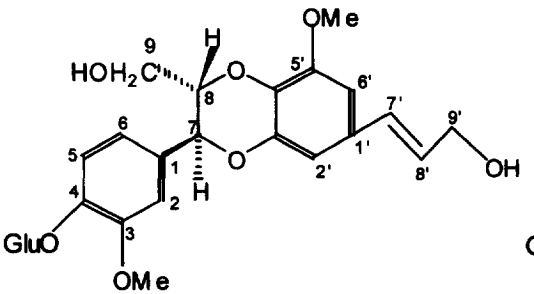
INTRODUCTION

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*.

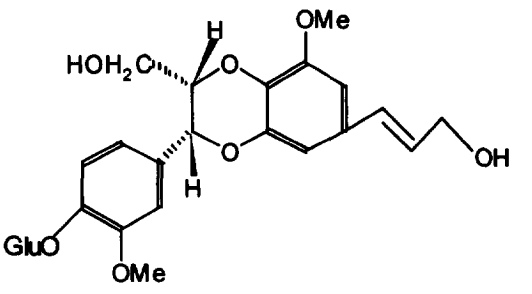
RESULTS AND DISCUSSION

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 formula ion peaks at *m/z* 543 $[M+Li]^+$ and 559 $[M+Na]^+$, suggesting the molecular formula to be $C_{26}H_{32}O_{12}$, which was also supported by ^{13}C 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 (2H, *br d*, J = 5.7 Hz, H-9′), δ 6.23 (1H, *dt*, J = 15.7, 5.7 Hz, H-8′) and δ 6.44 (1H, *d*, J = 15.7 Hz, H-7′) [16], two methenyl 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 ^{13}C 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_c 145.5 (C-4) with δ_H 4.85 (H-1″ of Glu) and 6.98 (H-5); δ_c 148.4 (C-3) with δ_H 3.71 (-OMe) and 7.03 (H-2); δ_c 130.2 (C-1′) with δ_H 6.44 (H-7′) and 7.02 (H-2′); and δ_c 149.7 (C-5′) with δ_H 3.77 (-OMe) and 6.83 (H-6′), suggested the site of glycosidation at C-4, a methoxyl δ 3.71 at C-3, the other methoxyl and (*E*)-coniferyl alcohol sidechain 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,

* Author to whom correspondence should be addressed.



1. 7S, 8S



2. 7R, 8S

verticillatoside A was elucidated as rel-(7*S*,8*S*)-$\Delta^{7'}$-9,9′-dihydroxy-3,5′-dimethoxy-7-*O*-3′,8-*O*-4′-neolignan-4-*O*-β-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** [18]. This was confirmed by the ^{13}C NMR spectrum [19] (compound **1**: C-7, δ 84.1; C-8, δ 71.4; compound **2**: C-7, δ 83.5; C-8, δ 70.7). Thus, verticillatoside B was established to be rel-(7*R*,8*S*)-$\Delta^{7'}$-9,9′-dihydroxy-3,5′-dimethoxy-7-*O*-3′,8-*O*-4′-neolignan-4-*O*-β-D-glycoside.

EXPERIMENTAL

Plant material. Whole plants of *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.

Extraction and isolation. Dried whole plants (2.9 kg) were extracted with 95% EtOH (10 l × 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_2O and the H_2O-insoluble material removed by filtration through Celite. The filtrate was then extracted with petrol (60–90°), EtOAc and *n*-BuOH.

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, 12:1) 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_2O, then with MeOH–H_2O (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_{18}, MeOH–H_2O, 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_2O but eluting with MeOH–H_2O (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).

Compound **1**. White amorphous powder. $[\alpha]_D^{20}$ −8.0° (MeOH; *c*, 0.50). UV λ_{max}^{MeOH}: 201, 266 nm. IR (KBr): 3323 cm^{-1} (OH), 1512, 1601 cm^{-1} (phenyl). FAB-MS: 543 $[M+Li]^+$ and 559 $[M+Na]^+$. ^{1}H NMR (400 MHz, DMSO-d_6 TMS): δ 7.03 (1H, *d*, *J* = 1.5 Hz, H-2), 6.98 (1H, *d*, *J* = 8.0 Hz, H-5), 6.65 (1H, *dd*, *J* = 1.5, 8.0 Hz, H-6), 4.75 (1H, *d*, *J* = 7.2 Hz, H-7), 4.29 (1H, *m*, H-8), 3.80 (2H, *br d*, *J* = 12.0 Hz, H-9), 7.02 (1H, *d*, *J* = 1.6 Hz, H-2′), 6.83 (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′), 4.07 (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). ^{13}C NMR (100 MHz, DMSO-d_6, 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), 119.2 (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), 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).

Compound **2**. White amorphous powder. $[\alpha]_D^{20}$ −32° (MeOH; *c* 0.50). UV λ_{max}^{MeOH}: 200, 266 nm. IR (KBr): 3324 cm^{-1} (OH), 1513, 1604 cm^{-1} (phenyl). FAB-MS: 543 $[M+Li]^+$ and 559 $[M+Na]^+$. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.03 (1H, *d*, *J* = 1.5 Hz, H-2), 6.99 (1H, *d*, *J* = 8.0 Hz, H-5), 6.65 (1H, *dd*, *J* = 1.5,

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, *d*, J = 7.8 Hz, glu-1), 3.77 (OCH_3), 3.71 (OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6, 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, CH_2), 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′, CH_2), 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″, CH_2), 55.5 (OCH_3), 55.6 (OCH_3).

REFERENCES

1. *Flora Republicae Popularis Sinicae*, Vol. 67. Institutum Academiae Science Press, Beijing, 1979, p. 348.
2. Jiangsu New Medical College, *Chinese Medicine Dictionary*, Shanghai People's Publishing House, China, 1977, p. 286.
3. Liu, Z.-M. and Jia, Z.-J., *Phytochemistry*, 1991, **30**, 1341.
4. Jia, Z.-J., Liu, Z.-M. and Wang, C.-Z., *Phytochemistry*, 1992, **31**, 263.
5. Li, J., Zheng, R.-L., Liu, Z.-M. and Jia, Z.-J., *Acta Pharmacologica Sinica*, 1992, **13**, 427.
6. Jia, Z.-J. and Gao, J.-J., *Phytochemistry*, 1993, **34**, 1188.
7. Wang, C.-Z., Jia, Z.-J. and Liao, J.-C., *Indian Journal of Chemistry*, 1995, **34B**, 914.
8. Kobayashi, H., Karasawa, H., Miyase, T. and Fukushinca, S., *Chemical and Pharmaceutical Bulletin*, 1984, **32**, 3880.
9. Bianco, A., Passacantilli, P., Righi, G., Garbarino, J. A., Gambaro, V., Serafini, M. and Nicoletti, M., *Planta Medica*, 1986, **52**, 55.
10. Nishimura, H., Sasaki, H., Morota, T., Chin, M. and Mitsuhashi, H., *Phytochemistry*, 1989, **28**, 2705.
11. Ozaki, Y., Johne, S. and Hesse, M., *Helvetica Chimica Acta*, 1979, **62**, 708.
12. Chaudhuri, R. K., Afifi-Yazar, F. U. and Sticher, O., *Tetrahedron*, 1980, **36**, 2317.
13. Sticher, O. and Salama, O., *Helvetica Chimica Acta*, 1981, **64**, 78.
14. Damtoft, S., Jensen, S. R. and Nielsen, B. J., *Phytochemistry*, 1981, **20**, 2717.
15. Damtoft, S., *Phytochemistry*, 1992, **31**, 175.
16. Hattoti, M., Yang, X.-W., Shu, Y.-Z., Kakiuchi, N., Tezuka, Y., Kikuchi, T. and Namba, T., *Chemical and Pharmaceutical Bulletin*, 1988, **36**, 648.
17. Cavalcante, S. H., Yoshida, M. and Gottlieb, O. R., *Phytochemistry*, 1985, **24**, 1051.
18. Fang, J.-M., Lee, C.-K. and Cheng, Y.-S., *Phytochemistry*, 1992, **31**, 3659.
19. Silva, M. S., Barbosa-Filho, J. M., Yoshida, M. and Gottlieb, O. R., *Phytochemistry*, 1989, **28**, 3477.