DOI 10.5012/bkcs.2010.31.9.2715

A New Pyrrolizidine Alkaloid from *Senecio vulgaris*

Wei-Dong Xie,* Xia Li, and Kyung Ho Row†,*

*Marine College, Shandong University at Weihai, Weihai 264209, P. R. China. *E-mail: wdxie@sdu.edu.cn*
*†Department of Chemical Engineering, Inha University, Incheon 402-751, Korea. *E-mail: rowkho@inha.ac.kr*
Received June 22, 2010, Accepted July 29, 2010

Key Words: *Senecio vulgaris*, Alkaloid, Pyrrolizidine, Vulgarine

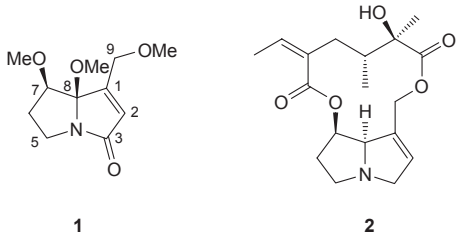
Pyrrolizidine alkaloids (PAs) are hepatotoxins found in a wide variety of plant species, especially *Senecio* (Asteraceae), *Crotalaria* (Leguminaceae), *Heliotroprium*, *Trichodesma* and *Symphytum* (Boraginaceae).[1] They have received extensive chemical and biological investigations because they presumably serve as protective chemicals for the plants and they are the cause of considerable poisoning of liverstock.[2-4] As the most characteristic secondary metabolites of *Senecio* species, large numbers of pyrrrolizidine alkaloids have been isolated from this genus.[5-6] *Senecio vulgaris* Linn., a widespread problematic weed (e.g., in fruit orchard, vegetable garden and lawn), originally grows in Europe and was introduced to most area of the world in nineteenth century. The pyrrrolizidine alkaloids (PAs) of *Senecio vulgaris* have been investigated extensively.[7-11] In the course of our phytochemical investigations of *Senecio* species distributing in northeast China, a new pyrrolizidine alkaloid, named as vulgarine (**1**), and a known one, senecionine (**2**),[12] have been isolated from the less polar extracts of *Senecio vulgaris*. This paper deals with the isolation and structure elucidation of the new pyrrolizidine alkaloid.

Compound **1** was obtained as colorless oil. The IR spectrum showed the absorption bands of carbonyl group at 1711 cm^{-1} and double bond group at 1643 cm^{-1}. The maximum absorption band at 249 nm in UV spectrum indicated that the carbonyl group conjugate with the double bond. Its HRESIMS give the quasi molecular ion peak at *m/z* 228.1226 ($[M+H]^+$, $C_{11}H_{18}NO_4^+$; Calcd 228.1230), implying the molecular formula to be $C_{11}H_{17}NO_4$. Though, compound **1** was negative in the ninhydrin color reaction test, indicating that it is an alkaloid with a tertiary amine group. The ^{1}H NMR signals at δ_H 3.37 (3H, s, MeO-9), 3.16 (3H, s, MeO-7) and 3.07 (3H, s, MeO-8), coupled with the ^{13}C NMR (DEPT) signals at δ_C 59.3 (MeO-9), 56.5 (MeO-7) and 49.8 (MeO-8) (Table 1) indicated distinctly the presence of three methoxy groups. In addition, the ^{1}H, and ^{13}C NMR (DEPT) spectra also showed the signals of a carbonyl group at δ_C 174.2 (C-3), and a trisubstituted double bond group at δ_H 5.97 (1H, dd, J = 1.6, 1.7 Hz, H-2) and δ_C 157.0 (C-1), 125.7 (C-2). The ^{13}C NMR (DEPT) signal at δ_C 103.9 (C-8) suggested the presence of a quaternary carbon atom attached simultaneously with both oxygen and nitrogen atoms. The residual signals were assignd to an oxygenated methine at δ_H 3.60 (1H, dd, J = 3.3, 1.1 Hz, H-7) and δ_C 82.0 (C-7), and three methylenes. The AB system signals of δ_H 4.10 (1H, dd, J = 16.2, 1.6 Hz, H-9a) and δ_H 4.03 (1H, dd, J = 16.2, 1.7 Hz, H-9b) in ^{1}H NMR spectrum, along with the carbon signal of methylene at δ_C 68.3 (C-9) in ^{13}C NMR (DEPT) spectrum indicated that one of the methylenes is oxygenated. These data, coupled with the molecular formula, proposed that **1** has a pyrrolizidine ring system which is a popular structure in *Senecio* species.[13] The structure of **1** was further supported by the HMBC correlaions (Fig. 2). The HMBC correlations of H-9 (δ_H 4.10, 4.03)/C-1 (δ_C 157.0), C-2 (δ_C 125.7) and C-8 (δ_C 103.9), and H-2 (δ_H 5.97)/C-8 (δ_C 103.9) confirmed the locations of the double bond between C-1 and C-2, and the methoxy at C-8. The HMBC corelations of H-5 (δ_H 3.11, 3.48)/C-3 (δ_C 174.2), and H-2 (δ_H 5.97)/C-3 (δ_C 174.2) suggested that a carbonyl group located at C-3. In addition, the ^4J corelations of H-9 (δ_H 4.10, 4.03)/C-3 (δ_C 174.2) were also observed. In the NOESY spectrum, H-7 and MeO-8 did not show NOESY correlation, MeO-7 and MeO-8 showed NOESY correlation mutually, indicating a *cis*-configuration of these two

Table 1. ^{1}H, ^{13}C NMR and DEPT data of **1** ($CDCl_3$, J in Hz, δ ppm, TMS)[a]

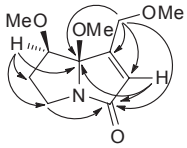
No.	δ (H)	δ (C)
1	-	157.0 s
2	5.97 (1H, dd, J = 1.6, 1.7)	125.7 d
3	-	174.2 s
5	3.11(1H, ddd, J = 11.0, 8.0, 3.0) 3.48 (1H, m)	40.6 t
6	2.25 (2H, m)	30.8 t
7	3.60 (1H, dd, J = 3.3, 1.1)	82.0 d
8	-	103.9 s
9	4.10 (1H, dd, J = 16.2, 1.6) 4.03 (1H, dd, J = 16.2, 1.7)	68.3 t
MeO-7	3.16 (3H, s)	56.5 q
MeO-8	3.07 (3H, s)	49.8 q
MeO-9	3.37 (3H, s)	59.3 q

[a]Measured at 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR.



1 2

Figure 1. The structures of **1** and **2**.



1

Figure 2. The key HMBC correlations for **1**.

methoxy groups. Considering that all the pyrrolizidine alkaloids isolated from *S. vulgaris* possess oxygenated substitutes at C-7 with β configuration,[10,14,15] both MeO-7 and MeO-8 in **1** were presumed to be β orientation. Thus, the structure of **1** was established as figured out and was named as vulgarine (Fig. 1). Owing to the use of MeOH in the course of extraction, it can not be excluded that compound **1** might be an artifact.

Experimental Section

General procedures. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. IR spectrua were recorded with a Bruker Vertex 70 FT-IR spectrometer in KBr. UV spectrum was measured on Varian Cary 100 Scan UV-Visible spectrometer. ^{1}H, ^{13}C NMR (DEPT) and 2D NMR were recorded on Bruker AVANCE 500 spectrometer. HRESIMS spectra were obtained on Bruker APEX II spectrometer with tetramethylsilane as internal reference. Silica gel (200 - 300 and 300 - 400 mesh) used for column chromatography (CC) and low pressure CC were purchased from Qingdao Marine Chemical Factory in China. Silica gel C-18 used for low pressure CC were purchased from Merck.

Plant material. The whole plants of *S. vulgaris* were collected in Changbai Mountains, Jilin Province, P. R. China, in September 2008, and identified by Prof. Jun Lin Yu, Department of Pharmaceutical and Food Science, Tonghua Normal University. A voucher specimen (No. CB200803) is deposited at the herbarium in the Laboratory of Botany, Marine College, Shandong University at Weihai.

Extraction and isolation. The air-dried whole plants of *S. vulgaris* (7.6 kg) were pulverised and extracted with CH_3OH three times (7 days each time) at room temperature. The extract was concentrated under reduced pressure to afford a residue (636 g). This residue was suspended in water (2500 mL) and successiveliy extracted with petroleum ether (bp 60 - 90 ^{o}C) and $CHCl_3$ to give a dry petroleum ether extract (142 g) and $CHCl_3$ extract (126 g), respectively. The $CHCl_3$ extract was separated into four fractions (Fr.1 - Fr.4) by silica gel CC (200 - 300 mesh, 1300 g) with a gradient of hexane-acetone (10:1, 5:1, 3:1 and 1:1) as eluent. Fr.1 (hexane-acetone 10:1; 20.7 g) was further isolated by silica gel CC (200 - 300 mesh, 220 g) with a hexane-EtOAc (20:1 - 0:1) gradient to give four subfractions (Fr.1a - Fr.1b). Fr.1b (hexane-EtOAc 10:1, 2.7 g) was isolated by silica gel CC (300 - 400 mesh) with hexane-acetone CC eluting with H_2O-MeOH (1:1 and 3:1) to yield **1** (6 mg). Fr.4 (hexane-acetone 1:1; 39.0 g) was isolated by silica gel CC (300 - 400 mesh) with $CHCl_3$-acetone (8:1) as eluent to yield white powder. After recrystallization in acetone, **2** (18 mg) was obtained.

Vulgarine (1). Colorless oil; $[\alpha]_D^{20} = -43$ (*c* 0.7, $CHCl_3$); IR (KBr) ν_{max} 2984, 2926, 2908, 2828, 1711, 1650, 1356, 1324, 1124; UV ($CHCl_3$) λ_{max} (log ε) 249 (3.54) nm; HRESIMS *m/z* 228.1226 ($[M+H]^+$, Calcd for $C_{11}H_{18}NO_4^+$: 228.1230); ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (DEPT) (125 MHz, $CDCl_3$): see Table 1.

Senecionine (2). Amorphous powder; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.13 (1H, brs, H-2), 3.87 (1H, ddd, J = 15.6, 3.7, 2.0 Hz, H-3a), 3.33 (1H, ddd, J = 15.6, 6.3, 1.6 Hz, H-3b), 3.20 (1H, brt, J = 8.4 Hz, H-5a), 2.48 (1H, ddd, J = 12.4, 9.2, 5.8 Hz, H-5b), 2.31 (1H, brdd, J = 13.9, 5.6 Hz, H-6a), 2.04 (1H, m, H-6b), 4.95 (1H, m, H-7), 4.20 (1H, m, H-8), 5.43 (1H, J = 11.7 Hz, H-9a), 3.99 (1H, d, J = 11.7 Hz, H-9b), 1.60 (1H, m, H-13), 2.09 (1H, m, H-14a), 1.69 (1H, m, H-14b), 1.25 (3H, s, H-18), 0.85 (1H, d, J = 6.7 Hz, H-19), 5.66 (1H, dq, J = 7.1, 1.2 Hz, H-20), 1.78 (1H, dd, J = 7.1, 1.6 Hz, H-21); ^{13}C NMR (DEPT) (125 MHz, $CDCl_3$) δ 131.5 (C-1, s), 136.9 (C-2, d), 63.1 (C-3, t), 53.2 (C-5, t), 35.0 (C-6, t), 75.1 (C-7, d), 77.8 (C-8, d), 60.8 (C-9, t), 178.4 (C-11, s), 77.4 (C-12, s), 38.5 (C-13, d), 38.4 (C-14, t), 133.2 (C-15, s), 167.8 (C-16, s), 25.1 (C-18, q), 11.3 (C-19, q), 134.3 (C-20, d), 15.2 (C-21, q).

Acknowledgments. This work was financially supported by the Natural Science Foundation of Shandong Province, P. R. China (No. Y2008C98) and the Doctoral Foundation of Shandong Province, P. R. China (No. BS2009YY016).

References

1. Roeder, E. *Pharmazie* **1995**, *50*, 83.
2. Mattocks, A. R. *Nature* **1968**, *217*, 723.
3. Ober, D.; Kaltenegger, E. *Phytochemistry* **2009**, *70*, 1687.
4. Fletcher, M. T.; Mckenzie, R. A.; Blaney, B. J.; Reichmann, K. G. *J. Agric. Food Chem.* **2009**, *57*, 311.
5. Smith, M. W.; Culvenor, C. C. J. *J. Nat. Prod.* **1981**, *44*, 129.
6. Roeder, E. *Pharmazie* **2000**, *55*, 711.
7. Shun, T.; Koluch, J.; Santavy, F. *Coll. Czechoslov. Chem. Commun.* **1960**, *25*, 934.
8. Qualls, C. W.; Segall, H. J. *J. Chromatogr.* **1978**, *150*, 202.
9. Hartmann, T.; Zimmer, M. *J. Plant Physiol.* **1986**, *122*, 67.
10. Hartmann, T.; Toppel, G. *Phytochemistry* **1987**, *26*, 1639.
11. Pieters, L. A.; Vlietinck, H. J. *Planta Med.* **1988**, *54*, 178.
12. Loizzo, M. R.; Tundis, R.; Statti, G. A.; Menichini, F. *Arch. Pharm. Res.* **2007**, *30*, 701.
13. Paiva, J. A.; Barata, L. E. S.; Trigo, J. R. *Biochem. Syst. Ecol.* **2004**, *32*, 1219.
14. Borstel, K. V.; Witte, L.; Hartmann, T. *Phytochemistry* **1989**, *28*, 1635.
15. Tinney, G.; Theuring, C.; Paul, N.; Hartmann, T. *Phytochemistry* **1998**, *49*, 1589.