Chemical Constituents of *Senecio procumbens*

Amira Arciniegas,a Ana L. Pérez-Castorena,*a José Luis Villaseñor,b Alfonso Romo de Vivar a

a Instituto de Química, bInstituto de Biología, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán 04510, D.F., México
Tel: +52-55-5622-4412, Fax: +52-55-5622-2217, E-mail: alperezc@servidor.unam.mx

Recibido el 20 de abril del 2005; aceptado el 15 de junio del 2005.

**Abstract.** A chemical study of *Senecio procumbens* afforded the 12-membered macrocyclic diester pyrrolizidine alkaloids senecionine (1), senecivernine (2), retrorsine (3) and their N-oxides, together with 132-hydroxyphaeophytin a (4), caffeic acid methyl ester (5), and cacticin (6). The identification of these compounds was accomplished by comparison of their spectral features with those reported in literature. The structures of compounds 1, and those of the N-oxides of 1 and 3 were confirmed by comparison with authentic samples. In addition, the 1H and 13C NMR spectroscopies of 2 N-oxide are reported since they were not available in the literature.

**Keywords:** *Senecio procumbens*, Asteraceae, Senecioneae, Pyrrolizidine alkaloids.

**Introduction**

The genus *Senecio* is known as an important source of pyrrolizidine alkaloids (PAs) [1, 2], many of them being toxic to livestock and humans [3]. Sesquiterpenes, mainly those with an eremophilane skeleton, and flavonoids are also among their characteristic metabolites [4]. As a continuation of our research on this genus [5], we studied the chemical composition of *Senecio procumbens* Kunth which, to our knowledge, has no previous chemical studies. In this paper we report the isolation of three 12-membered macrocyclic diester (PAs) (1-3), one phaeophytin (4), one phenylpropanoid (5) and one flavonoid glycoside (6).

**Results and Discussion**

The methanolic extract of roots of *S. procumbens*, which gave positive Dragendorff test, was submitted to a reductive process (Zn/aq. H2SO4) [6]. The reduced extract produced senecionine (1) [7a, 8], a (4:3) mixture of senecionine (1) and senecivernine (2) [7, 8], retrorsine (3) N-oxide [7a, 8], and a (4:3) mixture of the N-oxides of 1 and 2. The reduction of the mixture of N-oxides of 1 and 2 by Zn/aq. H2SO4 produced a mixture of free bases. The presence of N-oxides, in spite of the reductive treatment, could be due to a partial reduction, to a transformation of the free alkaloids into their N-oxides on standing with CHCl3 at room conditions [9], or both. The methanolic extract of the aerial parts of *S. procumbens* gave positive Dragendorff test and produced senecionine (1) and its N-oxide. The acetonic extract afforded 132-hydroxyphaeophytin a (4) [10], caffeic acid methyl ester (5) [11], cacticin (6) [12, 13], and β-sitosteryl glucopyranoside. From the hexanic extract only waxes and a mixture of β-sitosterol-stigmasterol were isolated. Compounds 1-6 were identified by comparison of their spectral features with those reported in literature. The structures of senecionine (1), its N-oxide, retrorsine (3) N-oxide, β-sitosterol, stigmasterol, and β-sitosterol β-D-glucopyranoside were confirmed by comparison with authentic samples. We report the 1H and 13C NMR data of the N-oxide of senecivernine (2), since they were not available in literature. Assignments were achieved by means of 1D and 2D NMR experiments, in which the characteristic deshielding effect of...
Chemical Constituents of Senecio procumbens

N-oxides on the 3, 5 and 8 positions, was evident [14]. Assignation of the Me-18, Me-19 and Me-20 signals were confirmed by an HMBC experiment. This showed the interaction of H-18 with C-11; the three bond correlation of H-19 with C-12 and C-14 and that of H-20 with the vinylic singlet of C-15.

The 1-dehydro twelve membered macrocyclic pyrrolizidine alkaloids found in S. procumbens are commonly isolated from species of this genus and are known to be potentially toxic [3]. Flavonoids and phenylpropanoids are also frequent in Senecio species; nevertheless, phaeophytins have not been previously reported for this genus.

Experimental

General Experimental Procedures

Melting points were determined on a Fisher Jones melting point apparatus and are uncorrected. Optical rotations were determined on a Nicolet Magna-IR 750 spectrometer. EIMS data were determined on a JEOL JMS-AX505HA mass spectrometer at 70 eV. 1H NMR and 13C NMR data were determined on a JASCO DIP-360 digital polarimeter. IR spectra were recorded on a Nicolet Magna-IR 750 spectrometer. Melting points were determined on a Fisher Jones melting point apparatus and are uncorrected. Optical rotations were determined on a Varian Unity 300 instrument. Chemical shifts were referred to TMS (δ 0). Standard Varian programs were used for COSY spectra at 300 MHz. HETCOR experiments were obtained for 1JCH = 140 Hz at 75 MHz. COLOC experiments were obtained for 1JCH = 9 Hz at 75 MHz. Vacuum column chromatographies (VCCs) were performed using Silica gel 60 G Merck.

Plant Material

Senecio procumbens Kunth (Asteraceae, Senecioneae) is an herbaceous, perennial, alpine species, 5-18 cm tall [15]. It was collected in November 2002 near to the first lake of the crater of the Nevado de Toluca, State of Mexico, Mexico, at an altitude of ca. 4000 m. A voucher specimen was deposited at the Herbarium of the Instituto de Biología, UNAM, Mexico (MEXU 1045507).

Extraction and Isolation

Dried and ground roots (130 g) of S. procumbens were extracted with MeOH until the extract gave a negative test with Dragendorff reagent. The extract was concentrated and treated with Zn/aq. H2SO4 [6] to give 2.2 g of alkaloidal residue. This was purified by vacuum column chromatography (VCC) and eluted with hexane-CHCl3-MeOH mixtures of increasing polarity. From fractions obtained with CHCl3-MeOH 19:1, senecionine (1, 58 mg), mp 235-7°C and a (4:3) mixture of senecionine and senecivernine (2, 120 mg) [7, 8], were isolated. Fractions eluted with CHCl3-MeOH 9:1 afforded senecionine and senecivernine N-oxides as a (4:3) mixture (245 mg). Reduction of this mixture by Zn/aq. H2SO4 produced the free bases. Fractions collected with CHCl3-MeOH 7:3 were further purified by VCC, eluted with CHCl3-MeOH 4:1, to afford retrorsine N-oxide (3-N-oxide), mp 145-7°C [7, 8].

Dried and ground aerial parts (700 g) of S. procumbens were extracted successively with hexane, acetone and MeOH. Only the methanolic extract gave positive test with Dragendorff reagent. After purification by VCC the hexane extract (12 g) produced waxes and a β-sitosterol-stigmasterol mixture (150 mg). The acetonic extract (13 g) was worked up by VCC eluted with hexane-EtOAc mixtures of increasing polarity. Fractions collected with hexane-EtOAc 4:1 (2.5 g), after two successive VCCs eluted with hexane-EtOAc 17:3 and hexane-Me2CO 9:1, afforded 125 mg of 132-hydroxypheophytin a (4), mp 110-112°C, [α]20D −51.6 (c 0.2, pyridin) [12, 13], and β-sitosteryl β-D-glucopyranoside (450 mg). The methanolic extract was submitted to a reductive process to obtain the alkaloidal portion (1.9 g). Purification of this portion by VCC eluted with CHCl3-MeOH mixtures of increasing polarity produced senecionine (1, 13 mg) and senecionine N-oxide (40 mg) from fractions collected with CHCl3-MeOH 19:1 and 9:1, respectively.

Senecivernine N-oxide (2 N-oxide): 1H NMR (500 MHz, CD3OD) δ 6.26 (1H, br d, J = 2.0 Hz, H-2), 4.70 (1H, br d, J = 12.5 Hz, H-3a), 4.29 (1H, dd, J = 12.5, 1.0 Hz, H-3b), 3.76 (1H, m, H-5a), 3.76 (1H, m, H-5b), 2.86 (1H, ddd, J = 12.0, 7.0, 4.5 Hz, H-6a), 2.39 (1H, dddd, J = 12.0, 6.0, 2.5, 2.5 Hz, H-6b), 5.53 (1H, ddd, J = 6.0, 4.5, 2.5 Hz, H-7), 4.84 (1H, br s, H-8), 5.36 (1H, dd, J = 12.0, 1.5 Hz, H-9a), 4.31 (1H, br d, J = 12.0 Hz, H-9b), 1.71 (3H, qd, J = 7.0, 1.5 Hz, H-13), 2.62 (1H, q, J = 7.5, 1.5 Hz, H-14), 1.34 (3H, s, H-18), 0.82 (3H, d, J = 7.0 Hz, H-19), 1.09 (3H, d, J = 7.5 Hz, H-20), 5.91 (1H, br s, H-21a), 5.36 (1H, br s, H-21b); 13C NMR (125 MHz, CDCl3) δ 131.1 (C-1), 131.5 (C-2), 78.7 (C-3), 69.4 (C-5), 33.3 (C-6), 75.1 (C-7), 96.6 (C-8), 60.5 (C-9), 178.3 (C-11), 78.7 (C-12), 42.3 (C-13), 37.4 (C-14), 148.1 (C-15), 169.3 (C-16), 26.6 (C-18), 5.9 (C-19), 12.5 (C-20), 123.1 (C-21).

Acknowledgements

We are indebted to Ma. de los Angeles Peña, Elizabeth Huerta, Isabel Chávez, Héctor Ríos, Nieves Zavala, Rocío Patiño, Javier Pérez, Luis Velasco, Eréndida Ríos and Gabriela Salcedo for their technical assistance.

References