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PYRROLE ALKALOIDS FROM *Alhagi sparsifolia*[a]

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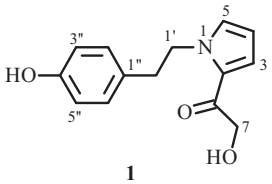
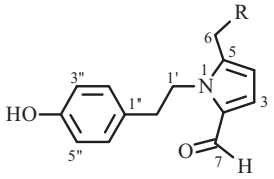
*The novel pyrrole alkaloid alhagifoline A (**1**) together with the two known analogs pyrrolezanthine (**2**) and pyrrolezanthine-6-methyl ether (**3**) were isolated from the aerial part of* Alhagi sparsifolia. *Their structures were established based on spectral (HR-ESI-MS, ^{1}H and ^{13}C NMR, ^{1}H–^{1}H COSY, HSQC, HMBC) data. Compounds **2** and **3** were isolated from the genus* Alhagi *for the first time.*

Keywords: *Alhagi sparsifolia*, Leguminosae, pyrrole alkaloids, alhagifoline A.

Alhagi sparsifolia Shap. (camelthorn) is a perennial undershrub of the family Leguminosae that is broadly distributed in Kazakhstan, Uzbekistan, Turkmenistan, Kyrgyzstan, and Tajikistan. Large thickets are found in desert zones of Inner Mongolia, Gansu and Qinghai Provinces, and Xinjiang Autonomous Region, China [1]. It is usually used in traditional Uyghur medicine to relieve physical fatigue and for colds, rheumatic pain, diarrhea, stomach pain, headache, toothache, and cancer. Catechins, proanthocyanidins, coumarins, flavonoids, and sterols were reported previously in this plant [2, 3]. In continuation of research on the discovery of new bioactive compounds from traditional Uyghur medicinal plants [3], we report the isolation and identification of the new pyrrole alkaloid **1** together with the two known analogs pyrrolezanthine (**2**) and pyrrolezanthine-6-methyl ether (**3**) from the aerial part of *A. sparsifolia*.



1



2, 3

2: R = OH

3: R = OCH_3

Compound **1** was obtained as yellow needles with empirical formula $C_{14}H_{15}NO_3$ as determined by (+)-HR-ESI-MS analysis (*m*/*z* 246.1124 $[M + H]^+$; calcd for $C_{14}H_{16}NO_3$, 246.1130). The IR spectrum of **1** showed characteristic absorption bands for hydroxyls at 3228 cm^{-1}; carbonyl, 1661; and 1,4-disubstituted benzene ring, 1612, 1450, and 817. The UV absorption at 199 and 286 nm indicated the presence of a phenol and ketone. The PMR and HSQC spectra of **1** (Table 1) showed seven olefinic protons at δ 6.93 (2H, d, J = 8.4 Hz, H-2″,6″) and 6.66 (2H, d, J = 8.4 Hz, H-3″,5″) that belonged to a 1,4-disubstituted benzene ring and at 7.06 (1H, dd, J = 4.2, 1.8 Hz, H-3), 6.07 (1H, dd, J = 4.2, 2.4 Hz, H-4), and 6.85 (1H, dd, J = 2.4, 1.8 Hz, H-5), to a mono-substituted pyrrole ring. There were also one hydroxymethylene at 4.63 (2H, s, H-7) and one ethylene at 4.50 (2H, t, J = 7.2 Hz, H-1′) and 2.89 (2H, t, J = 7.2 Hz, H-2′). The ^{13}C NMR and HSQC spectra showed the presence of three secondary (one oxidized), seven tertiary, and four quaternary C atoms, including one C-atom carboxyl group. These data were observed in all ^{1}H and ^{13}C NMR resonances except those of the two exchangeable protons. An analysis of ^{1}H–^{1}H COSY NMR data allowed three isolated proton of spin systems belonging to C-2″(6″)–C-3″(5″), C-3–C-5, and C-1′–C -2′ to be identified (Fig. 1).

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TABLE 1. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) Spectra of **1** (CD_3OD, δ, ppm, J/Hz)

C atom	δ_H	δ_C	HMBC (H→C)
2	–	128.1	–
3	7.06 (1H, dd, J = 4.2, 1.8)	120.6	C-2, C-4, C-5
4	6.07 (1H, dd, J = 4.2, 2.4)	109.5	C-2, C-3, C-5
5	6.85 (1H, dd, J = 2.4, 1.8)	132.7	C-2, C-3, C-4
6	–	190.0	–
7	4.63 (2H, s)	65.2	C-2, C-6
1′	4.50 (2H, t, J = 7.2)	52.6	C-1″, C-2′, C-2, C-5
2′	2.89 (2H, t, J = 7.2)	38.3	C-2″, 6″, C-1′
1″	–	130.7	–
2″, 6″	6.93 (2H, d, J = 8.4)	131.1	C-3″, 5″, C-2″, 6″, C-4″, C-1″, C-2′
3″, 5″	6.66 (2H, d, J = 8.4)	116.3	C-2″, 6″, C-3″, 5″, C-4″, C-1″
4″	–	157.2	–

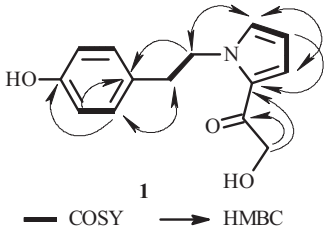

Fig. 1. Key to ^{1}H—^{1}H COSY and HMBC correlations of alhagifoline A (**1**).

The remaining fragments of **1** were confirmed fully by HMBC correlations (Fig. 1). The pyrrolezanthine (**2**) [4] and pyrrolezanthine-6-methyl ether skeletons (**3**) [5] were established. HMBC correlations from H-3″,5″ to C-1″ and from H-2″,6″ to C-4″ related to the benzene ring. Correlations from H-4 and H-5 to C-2 and H-3(5) to C-5(3) indicated that a pyrrole ring was present; cross peaks of H-1′ with C-1″, C-2, and C-5, an ethylene group on the benzene ring and the pyrrole N atom. Thus, the structure of **1** was established as 2-hydroxy-1-[1-(4-hydroxyphenethyl)-1*H*-pyrrol-2-yl]ethanone, which we called alhagifoline (**1**).

The compounds **2** and **3**, which were isolated for the first time from the genus *Alhagi*, were identified as pyrrolezanthine (**2**) [4] and pyrrolezanthine-6-methyl ether (**3**) [5] based on NMR data.

EXPERIMENTAL

Melting points were determined on a Yanaco MP-S3 apparatus. UV spectra were recorded on a Shimadzu UV-2550 spectrophotometer. IR spectra were taken using a Bio-Rad FTS 165 spectrophotometer. NMR spectra were recorded in CD_3OD (δ_H 3.31/δ_C 49.2) on a Varian VNMRS 600 MHz spectrometer. 2D NMR experiments (^{1}H–^{1}H COSY, HSQC, HMBC) were carried out using standard Varian microprogram. HR-ESI-MS spectra were measured using a QSTAR Elite mass spectrometer (Applied Biosystems). Chromatography used HPD-600 macroporous resin (Cangzhou Baoen Chemical Co., Ltd., China), silica gel (Qingdao Haiyang Chemical Co., Ltd., China), and Sephadex LH-20 (Amersham Pharmacia Biotech, Sweden).

Plant Material. The aerial part of *A. sparsifolia* was collected from Toksan, Xinjiang, Uyghur Autonomous Region, China, in August 2007 and was identified by Prof. G. M. Shen (Xinjiang Institute of Ecology and Geography, CAS). A representative specimen (XJBI702C) was deposited in the XIEG herbarium.

Extraction and Isolation of 1–3. Dried aerial part of *A. sparsifolia* (10 kg) was extracted with EtOH (50%, 3×). The extracts were evaporated *in vacuo* to a crude extract (1300 g) that was suspended in H_2O and worked up successively with petroleum ether, CH_2Cl_2, and *n*-BuOH. The *n*-BuOH extract (210 g) was dissolved in H_2O and chromatographed over column of macroporous resin HPD-600 with elution by H_2O and EtOH (10, 30, 60, and 95%) to afford five fractions. The EtOH (95%) eluate (18 g) was chromatographed over silica gel (column chromatography) (100-200 size, 600 g) with elution by

$CHCl_3$:MeOH (from 1:0 to 0:1) to afford 12 fractions. Fast column chromatography of the fractions over silica gel using $CHCl_3$:MeOH (50:1 to 1:1) and petroleum ether:Me_2CO (9:1 to 1:1) as eluents and Sephadex LH-20 ($CHCl_3$:MeOH, 1:1) afforded **1** (2 mg), **2** (7 mg), and **3** (2 mg).

Alhagifoline A (1), $C_{14}H_{15}NO_3$, yellow needles (MeOH), mp 130–132°C. UV spectrum (MeOH, λ_{max}, nm, log ε): 199 (4.37), 286 (3.91). IR spectrum (KBr, ν, cm^{-1}): 3228, 2921, 1661, 1612, 1517, 1468, 1450, 1417, 1381, 1323, 1232, 1037, 950, 817, 737, 699. HR-ESI-MS (+-ion mode, *m*/*z*): 246.1124 $[M + H]^+$ (calcd for $C_{14}H_{16}NO_3$, 246.1130). Table 1 presents the ^1H and ^{13}C NMR spectra.

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