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# A NOVEL SESQUITERPENE LACTONE FROM *Ixeris sonchifolia*

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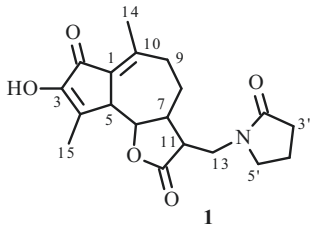
*One novel sesquiterpene lactone, sonchifoliactone A1 (**1**), along with one known compound, sonchifoliactone A (**2**), were isolated from the water extract of the whole plant of* Ixeris sonchifolia *Hance. The structures of these compounds were elucidated through spectroscopic techniques including HR-MS and 2D NMR.*

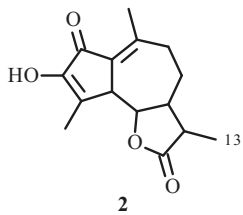
**Keywords**: *Ixeris sonchifolia*, sesquiterpene lactones, sonchifoliactone A1.

*Ixeris sonchifolia* Hance is a bitter, perennial herb known as kudiezi or mantianxing that belongs to the genus *Ixeris* of the *Cichorieae* tribe of the Asteraceae. It is widely distributed and cultivated in northeastern areas of China, Japan, and Korea [1]. In Chinese folklore, it has been used to treat cardiovascular diseases. Previous phytochemical investigations on plants of the genus *Ixeris* showed that the active principles were mainly flavonoids, sesquiterpene lactones, triterpenoid saponins [2–6].

Isolation studies on the water extract of the whole plant of *Ixeris sonchifolia* Hance resulted in the isolation of one novel sesquiterpene lactone, named sonchifoliactone A1 (**1**), along with one known sesquiterpene lactone, named sonchifoliactone A (**2**) [7].




**1**




**2**

Compound **1** was obtained as a white amorphous powder. Its molecular formula was determined as $C_{19}H_{23}NO_5$ at *m/z* 344.1500 (calcd 344.1492) $[M - H]^-$ by HR-ESI-MS. All proton and carbon signals of compound **1** were completely assigned with the aid of two-dimensional NMR experiments such as COSY, DEPT, HMQC, and HMBC (Fig. 1). All proton and carbon signals of compound **1** were quite similar to those of compound **2** (Table 1). However, the proton and carbon signals assignable to 13-exomethyl of compound **2** were changed in the $^1$H NMR and $^{13}$C NMR spectra of compound **2**. Instead, several new proton and carbon signals were found assignable to an *N*-methyl-2-pyrrolidinone (Table 1). These results implied that an *N*-methyl-2-pyrrolidinone was added to 13-exomethyl of **2** to yield compound **1**. This was supported by the HMBC correlations of H-13$\alpha$ ($\delta$ 3.56) with C-12 carbonyl carbon ($\delta$ 176.5) and also by the correlation between H-13$\alpha$ with C-2′ ($\delta$ 175.2) and C-5′ ($\delta$ 48.0) of *N*-methyl-2-pyrrolidinone. Their stereochemistry was considered to be H-5$\alpha$, H-6$\beta$, since the naturally occurring guaianolides have $\alpha$-orientation at H-7 [8]. The configuration of *N*-methyl-2-pyrrolidinone is $\alpha$, as judged from the coupling constant (J = 15.9 Hz) between H-7 and H-11 [9]. From these spectroscopic data, compound **1** was tentatively named sonchifoliactone A1.

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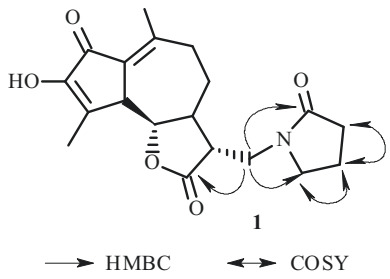
TABLE 1. $^{1}H$ (500 MHz) and $^{13}C$ NMR (125 MHz) Data of Compound **1** (DMSO-$d_6$, δ, ppm, J/Hz) and Compound **2** ($CDCl_3$, δ, ppm, J/Hz)

| C atom | **1** | | **2** | |
|---|---|---|---|---|
| | $\delta_H$ | $\delta_C$ | $\delta_H$ | $\delta_C$ |
| 1 | – | 128.8 | – | 128.8 |
| 2 | – | 189.1 | – | 189.1 |
| 3 | 9.20 (1H, s) | 154.0 | – | 154.0 |
| 4 | – | 135.9 | – | 135.9 |
| 5 | 3.43 (1H, m) | 47.9 | 3.27 (1H, d, J =10.0) | 47.9 |
| 6 | 3.61 (1H, t, J = 12.5) | 85.7 | 3.54 (1H, t, J = 10.0) | 85.7 |
| 7 | 2.13 (1H, m) | 55.9 | 1.94 (1H, dt, J = 14.0, 11.8) | 55.9 |
| 8 | 1.96 (1H, m), 1.25 (1H, m) | 25.9 | 1.99 (1H, m), 1.33 (1H, m) | 25.9 |
| 9 | 2.39 (1H, m), 2.18 (1H, m) | 37.3 | 2.44 (1H, m), 2.35 (1H, m) | 37.3 |
| 10 | – | 152.3 | – | 152.3 |
| 11 | 2.71 (1H, td, J = 15.9, 6.4) | 44.5 | 2.23 (1H, dq, J = 13.8, 7.0) | 41.1 |
| 12 | – | 176.5 | – | 177.7 |
| 13 | 3.56 (1H, m), 3.45 (1H, m) | 40.2 | 1.26 (1H, d, J = 6.9) | 12.4 |
| 14 | 2.39 (3H, s) | 21.6 | 2.47 (3H, s) | 22.2 |
| 15 | 2.00 (3H, s) | 14.5 | 2.17 (3H, s) | 14.1 |
| 2′ | – | 175.2 | | |
| 3′ | 2.23 (2H, m) | 30.6 | | |
| 4′ | 1.93 (2H, m) | 18.2 | | |
| 5′ | 3.37 (1H, m), 3.30 (1H, m) | 48.0 | | |




**1**

HMBC COSY

**Fig. 1.** Structure and key HMBC and $^{1}H$–$^{1}H$ COSY correlations of compound **1**.

## EXPERIMENTAL

**General Experimental Procedures.** IR spectra were determined on an IFS 55 infrared spectrophotometer with KBr disks. The $^{1}H$ and $^{13}C$ NMR data were recorded on a Bruker Biospin NMR spectrometer with TMS as the internal standard. Mass spectra were obtained on a LTQ-Orbitrap high-resolution mass spectrometer. Column chromatography was performed on silica gel (200–300 mesh; Qingdao Haiyang Chemicals) and Sephadex LH-20 (Merck, Darmstadt, Germany).

**Plant Material.** The whole plants of *I. sonchifolia* were collected from Haicheng City, Liaoning Province of China in September 2013. It was identified by Prof. Jian-Qiu Lu, Center of Scientific Experiment, Beijing University of Chinese Medicine. A voucher specimen (No. 20130901) was deposited in the same department.

**Extraction and Isolation.** The whole plants of *I. sonchifolia* (10 kg) were ground and extracted with water (3 × 60 L) for 1 h each time, and then the filtrate extracts were combined and loaded on a glass column (10 × 1500 cm) containing 3000 g D101 macroporous resin. First, water was used to remove the unabsorbed substances until the eluted solution became nearly colorless, and then different concentrations of aqueous ethanol (10%, 30%, 50%, and 95%) were used to elute the column. All of the fraction were concentrated under reduced pressure to give a black residue. The fraction eluted with 95% aqueous ethanol was subject to silica gel column chromatography using $CH_2Cl_2$–MeOH (100:1–0:1, v/v) as eluent to obtain six fractions (Fr. E1–E6). Fraction E3 was purified by Sephadex LH-20 using $CH_2Cl_2$–MeOH (1:1, v/v) repeatedly to yield compound **2**. Compound **1** was obtained from Fr. E4 using Sephadex LH-20 eluting with $CH_2Cl_2$–MeOH (1:1, v/v).

**Sonchifoliactone A1 (1).** White amorphous powder. UV spectrum (MeOH, $\lambda_{max}$, nm): 274. IR (KBr, ν, $cm^{-1}$): 3446, 2924, 2853, 1669, 1663, 1653, 1635, 1457, 1400. HR-ESI-MS *m/z* 344.1500 $[M - H]^-$ (calcd for $C_{19}H_{22}NO_5$, 344.1492). For $^1H$ and $^{13}C$ NMR data, see Table 1.

**Sonchifoliactone A (2)**. White needle crystals. UV spectrum (MeOH, $\lambda_{max}$, nm): 276. IR (KBr, ν, $cm^{-1}$): 3473, 2975, 2926, 2875, 1766, 1672, 1623, 1216, 1185, 989. HR-ESI-MS *m/z* 261.1133 $[M - H]^-$ (calcd for $C_{15}H_{17}O_4$, 261.1121). For $^1H$ and $^{13}C$ NMR data, see Table 1.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