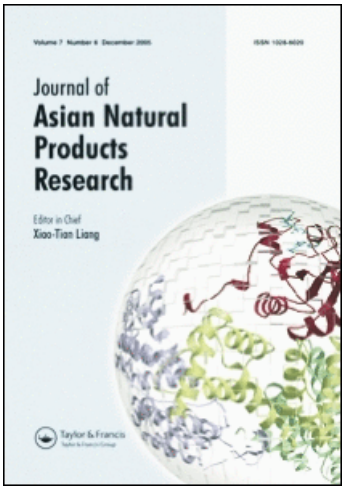

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Sesquiterpene lactones from *Ixeris sonchifolia* (Bge.) Hance II

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Four new sesquiterpene lactones, sonchifoliasolides D (**1**), E (**2**), F (**3**) and G (**4**) were isolated from the aerial parts of *Ixeris sonchifolia* (Bge.) Hance. The structures of compounds **1**–**4** were established on the basis of their spectroscopic data.

Keywords: *Ixeris sonchifolia*; Compositae; sesquiterpene lactones; sonchifoliasolides

1. Introduction

Ixeris sonchifolia (Bge.) Hance, (Compositae), known as Baojingkumaicai, is a perennial plant that grows in various places of the North area and Mongolia in China. This plant is used as a folk medicine for the treatment of many kinds of diseases such as enteritis, dysentery, fester inflammation, hematemesis, headache, toothache, impetigo, and haemorrhoid [1]. The known constituents of this plant include several flavonoids [2] and sesquiterpene lactones [3–7]. Because of our interest in biological activity of sesquiterpene lactones related to the medicinal effects of *I. sonchifolia,* we studied on sesquiterpene lactones from this plant. In this paper, we report the isolation and structural elucidation of four new guaianolide-type sesquiterpene lactones sonchifoliasolides D–G from the EtOAc extracts of the aerial parts of *I. sonchifolia*.

2. Results and discussion

The ethanolic extract of air-dried aerial parts of *I. sonchifolia* was defatted by extraction with hexane. The EtOH layer was concentrated, diluted with H_2O, and extracted with ethyl acetate. Four new compounds (**1**–**4**) were purified by chromatography on silica gel and HPLC from the ethyl acetate extract and subjected to detailed spectroscopic analysis in order to establish their chemical structures.

Sonchifoliasolide D (**1**) had the molecular formula $C_{15}H_{18}O_4$, based on HREIMS at *m/z* 262.1208 $[M]^+$. The IR spectrum of **1** showed the presence of hydroxyl (3479 cm^{-1}), α,β-unsaturated five-membered ring carbonyl (1735 and 1671 cm^{-1}) and α,β-unsaturated γ-lactone (1761 and 1671 cm^{-1}) groups. The ^{13}C NMR spectrum (Table 1) displayed 15 carbon resonances, including lactone and ketone carbonyl signals at δ 169.8 and 210.3, respectively, and two olefine carbons at δ 138.6 and 120.5. Two signals for carbon bearing oxygen were observed at δ? 70.8 and 81.9. Based on the DEPT and HMQC spectra, the remaining carbon resonances were due to two methyls, two methylenes including one exo-olefine carbon, seven methines, and two quaternary carbons. The ^1H NMR (Table 1) spectrum showed one methyl singlet at δ 2.32 (3H, s) connected to an olefin carbon, one methyl doublet at δ 0.77 (3H, d, $J = 7.2$ Hz), three olefinic protons including one singlet at

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Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1**–**4**.

	1		**2**		**3**		**4**	
	δ_C	δ_H *J* (Hz)	δ_C	δ_H *J* (Hz)	δ_C	δ_H *J* (Hz)	δ_C	δ_H *J* (Hz)
1	46.4	3.20 m	46.6	3.22 m	55.6	2.02 m	53.4	2.77 dd (7.9, 4.0)
2	210.3		210.7		205.7		208.3	
3	132.7	6.10 s	132.4	6.08 s	129.2	6.25 d (1.6)	129.9	6.37 d (2.0)
4	179.4		179.8		174.9		180.4	
5	53.1	3.18 m	53.2	3.10 t (8.0)	49.9	3.08 m	51.1	3.22 m
6	81.9	4.35 t (9.6)	81.7	4.67 t (10.0)	86.3	3.79 t (10.0)	82.1	4.51 t (10.0)
7	41.5	2.24 m	41.1	1.89 m	53.4	2.62 m	46.2	2.27 m
8	32.1	2.24 m	32.8	2.69 m	21.8	1.98 m	22.0	1.66 m
		1.75 m		1.70 m		1.46 m		1.56 m
9	70.8	4.14 m	70.9	4.09 m	35.2	2.22 m	34.2	1.73 m
						1.84 m		1.61 m
10	40.4	2.64 m	41.3	2.56 m	30.2	1.81 m	33.7	2.00 m
11	138.6		43.9	2.78 m	138.6		39.5	2.69 m
12	169.8		178.2		169.6		178.9	
13	120.5	6.28 d (3.2)	12.8	1.23 d (7.6)	118.6	6.19 d (3.0)	11.2	1.24 d (6.4)
		5.59 d (3.2)				5.51 d (3.0)		
14	14.0	0.77 d (7.2)	14.0	0.70 d (7.4)	19.5	1.29 d (6.7)	15.0	0.76 d (7.2)
15	19.3	2.32 s	17.0	2.28 s	62.4	4.78 d (18.0)	62.4	4.61 d (18.0)
						4.54 d (18.0)		4.68 d (18.0)

δ 6.10 (1H, s), two exo-olefine methylenes at δ 6.28 (1H, d, $J = 3.2$ Hz) and 5.59 (1H, d, $J = 3.2$ Hz), two oxymethines at δ 4.35 (1H, t, $J = 9.6$ Hz) and 4.14 (1H, m), respectively. The HMBC correlations of H-3, H-5, and H-10 with C-2 at δ 210.3, and H-1 and H-15 with C-3 at δ 132.7 indicated that the ketone carbonyl group was located at C-2, and a carbon–carbon double bond was located at C-3 and C-4 positions. The HMBC correlations between H-1, H-10, and H-14 with C-9 at δ 70.8 indicated that the hydroxyl group was located at C-9. The HMBC correlations (Figure 2) of four carbon atoms of the γ-lactone ring including C-12 (δ 169.8)/H-13; C-11/H-7 and H-13; C-7/H-5 and H-13; and C-6/H-1, H-5, and H-8 indicated that they belonged to the guaianolide-type sesquiterpene lactone. Therefore, **1** possesses the guaianolide structure of 2-oxoguaia-3,11(13)-dieno-12,6-lactone. The coupling constants between H-5, H-6, and H-7 ($J_{5,6} = J_{6,7} = 9.6$ Hz) indicated a *trans* relationship of H-5/H-6 and H-6/H-7 and the existence of a *trans*-fused γ-lactone. The orientations of H-6 and C-10 Me were determined to be β, and the orientations of H-1, H-5, H-7, and H-9 were determined to be α due to the NOESY correlations (Figure 2) of H-1/H-5, H-5/H-7, H-6/H-14, and H-7/H-9. Thus, **1** was determined to be 9β-hydroxy-2-oxoguaia-3,11(13)-dieno-12,6-lactone (Figure 1).

Sonchifoliasolide E (**2**) had the molecular formula $C_{15}H_{20}O_4$, based on HREIMS at *m*/*z* 264.1357 [M^+]. The IR spectrum of **2** showed

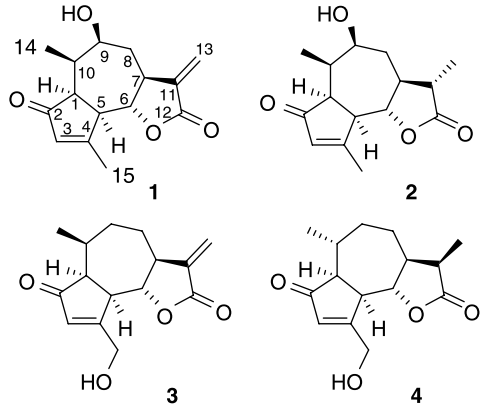

Figure 1. Structures of compounds **1**–**4**.

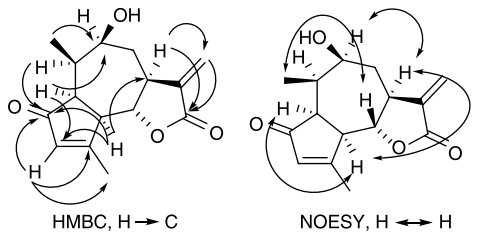

Figure 2. Key HMBC and NOE correlations of compound **1**.

the presence of hydroxyl (3421 cm^{-1}), α,β-unsaturated five-membered ring carbonyl (1698 and 1621 cm^{-1}), and γ-lactone (1775 cm^{-1}) groups. The ^{13}C and ^{1}H NMR spectra of **2** (Table 1) were similar to those of **1**, except that the C═C double bond between C-11 and C-13 in **1** was hydrogenated in **2**, which was confirmed by the presence of ^{1}H and ^{13}C signals at δ_H 2.78 (m), 1.23 (d, $J = 7.6$ Hz) and δ_C 43.9, 12.8. Meanwhile, the HMBC correlations between H-11 and H-7 with C-13 (δ 12.8) and between H-13 and H-6 with C-12 (δ 178.2) further supported the above result. Hence, **2** possesses the guaianolide structure of 9-hydroxy-2-oxoguaia-3-eno-12,6-lactone. The NOESY correlations of H-11 with H-6 and H-13 with H-5 indicated that C-11 Me was determined to be α. Thus, **2** was determined to be 11βH-9β-hydroxy-2-oxoguaia-3-eno-12,6-lactone (Figure 1).

Sonchifoliasolide F (**3**) had the molecular formula $C_{15}H_{18}O_4$, based on HREIMS at *m/z* 262.1211 [M^+]. The IR spectrum of **3** showed the existence of hydroxyl (3456 cm^{-1}), α,β-unsaturated five-membered ring carbonyl (1699 and 1620 cm^{-1}), and α,β-unsaturated γ-lactone (1758 and 1620 cm^{-1}) groups. The ^{13}C and ^{1}H NMR spectra of **3** (Table 1) were similar to those of **1**, except for the obvious difference at positions of C-9 and C-15. Comparing with compound **1**, C-9 in **3** shifted upfield from 70.8 to 35.2, while C-15 in **3** shifted downfield from 19.3 to 62.4, suggesting that the hydroxyl group was located at C-15 position in **3**, instead of C-9 position in **1**. The HMBC correlations between H-3 and H-5 with C-15 (δ 62.4) further supported the above result. Thus, **3** was determined to be 15-hydroxy-2-oxoguaia-3,11(13)-dieno-12,6-lactone (Figure 1).

Sonchifoliasolide G (**4**) had the molecular formula $C_{15}H_{20}O_4$, based on HREIMS at *m/z* 264.1365 [M^+]. The IR spectrum of **4** showed the existence of hydroxyl (3410 cm^{-1}), α,β-unsaturated five-membered ring carbonyl (1673 and 1609 cm^{-1}), and γ-lactone (1770 cm^{-1}) groups. The ^{13}C and ^{1}H NMR spectra of **4** (Table 1) were similar to those of **3**, except that the C═C double bond between C-11 and C-13 in **3** was hydrogenated in **4**, which was confirmed by the presence of ^{1}H and ^{13}C signals at δ_H 2.69 (m), 1.24 (d, $J = 6.4$ Hz), and δ_C 39.5, 11.2. Meanwhile, the HMBC correlations between H-11 and H-7 with C-13 (δ 11.2) and between H-13 and H-6 with C-12 (δ 178.9) further supported the above result. Hence, **4** possesses the guaianolide structure of 15-hydroxy-2-oxoguaia-3-eno-12,6-lactone. The NOESY correlations of H-11 with H-14, H-13 with H-6, and H-14 with H-7 indicated that C-11 Me was determined to be β, and C-10 Me to be α. Thus, **4** was determined to be 10βH-11αH-15-hydroxy-2-oxoguaia-3-eno-12,6-lactone (Figure 1).

3. Experimental

3.1 General experimental procedures

Melting points were determined on an X-6 micromelting-point apparatus and are uncorrected. Optical rotations were measured using an AUTOPOL δ digital polarimeter. IR spectra were measured in KBr disks using a Magna FTIR-750 infrared spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured with a Bruker-DRX 400 spectrometer in $CDCl_3$, using TMS as internal standard. MS were recorded on a MAT-95 mass spectrometer. Silica gel (200–300 mesh and GF_{254} Type 60, Qingdao Marine Chemical Co. Qingdao City of China) was used for column chromatography and TLC. The columns of HPLC were PREP-SIL

10 × 250 mm and 5μ particle size (GL Sciences Inc., Tokyo City, Japan).

3.2 Plant material

The aerial parts of *I. sonchifolia* were collected in Linyun city of Liaoning Province, China, in July 2005. The plant was identified by Prof. Wei Sha, Department of Life Science and Engineering, Qiqihar University. A voucher specimen (WI-02-2005) is deposited at the Natural Organic Laboratory, Faculty of Chemistry, Qiqihar University.

3.3 Extraction and isolation

Air-dried aerial parts of *I. sonchifolia* (3.4 kg) were extracted with 95% EtOH (22.0 l) for 3 days. The EtOH extracts were concentrated to 500 ml and extracted in turns with petroleum ether (4 × 300 ml), EtOAc (4 × 300 ml), and *n*-BuOH (4 × 300 ml). The EtOAc extracts were concentrated to give an oil material (64.0 g), there 20.0 g was separated into 11 fractions (F_1–F_{11}) by silica gel column chromatography (silica gel 356 g), eluting with petroleum ether–EtOAc (6:4 3.3 l, EtOAc 2.5 l), and EtOAc–MeOH (7:3 3.0 l). Fraction F_5 (897.9 mg) was purified by column chromatography on silica gel into three fractions (F_{5-1}–F_{5-3}), using a gradient of petroleum ether and EtOAc. Fraction F_{5-2} was further purified by HPLC (*n*-hexane–EtOAc 2:3, 4 ml/min^{-1}) to give **1** (t_R = 19.90 min, 7.4 mg) and **2** (t_R = 34.81 min, 33.9 mg). Fraction F_{5-3} was further purified by HPLC (*n*-hexane–EtOAc 1:3, 4 ml/min^{-1}) to give **4** (t_R = 23.33 min, 14.0 mg). Fraction F_4 (481.4 mg) was purified by column chromatography on silica gel into three fractions (F_{4-1}–F_{4-3}), using a gradient of petroleum ether and EtOAc. Fraction F_{4-2} was further purified by HPLC (*n*-hexane–EtOAc 2:3, 4 ml/min^{-1}) to give **3** (t_R = 23.62 min, 18.3 mg).

*3.3.1 Sonchifoliasolide D (**1**)*

White needles (EtOAc), mp 177.3–179.5°C, $[\alpha]_D^{20}$ + 198.7 (*c* 0.00223, MeOH); IR ν_{max}^{KBr} cm^{-1}: 3479 (OH), 1735, 1761 (C=O), 1671 (C=C); UV λmaxMeOH nm (log ε): 290 (2.27); ^{1}H NMR ($CDCl_3$, 400 MHz); and ^{13}C NMR ($CDCl_3$, 100 MHz) spectral data (Table 1). HREIMS *m/z* 262.1208 $[M]^+$ (calculated for $C_{15}H_{18}O_4$, 262.1205).

*3.3.2 Sonchifoliasolide E (**2**)*

White needles (EtOAc), mp 140.9–142.0°C; $[\alpha]_D^{20}$ + 130.9 (*c* 0.00307, MeOH); IR ν_{max}^{KBr} cm^{-1}: 3421 (OH), 1775, 1698 (C=O), 1621 (C=C); UV λ_{max}^{MeOH} nm (log ε): 286 (2.77); ^{1}H NMR ($CDCl_3$, 400 MHz); and ^{13}C NMR ($CDCl_3$, 100 MHz) spectral data (Table 1). HREIMS *m/z* 264.1357 $[M]^+$ (calculated for $C_{15}H_{20}O_4$, 264.1362).

*3.3.3 Sonchifoliasolide F (**3**)*

White needles (EtOAc), mp 86.8–89.3°C; $[\alpha]_D^{20}$ + 85.9 (*c* 0.0017, MeOH); IR ν_{max}^{KBr} cm^{-1}: 3456 (OH), 1758, 1699 (C=O), 1620 (C=C); UV λ_{max}^{MeOH} nm (log ε): 290 (2.89); ^{1}H NMR ($CDCl_3$, 400 MHz); and ^{13}C NMR ($CDCl_3$, 100 MHz) spectral data (Table 1). HREIMS *m/z* 262.1201 $[M]^+$ (calculated for $C_{15}H_{18}O_4$, 262.1205).

*3.3.4 Sonchifoliasolide G (**4**)*

White needles (MeOH), mp 122.3–124.5 °C, $[\alpha]_D^{20}$ + 53.0 (*c* 0.00213, MeOH); IR ν_{max}^{KBr} cm^{-1}: 3410 (OH), 1770, 1673 (C=O), 1609 (C=C); UV λ_{max}^{MeOH} nm (log ε): 284 (2.86); ^{1}H NMR ($CDCl_3$, 400 MHz); and ^{13}C NMR ($CDCl_3$, 100 MHz) spectral data (table 1). HREIMS *m/z* 264.1365 $[M]^+$ (calculated for $C_{15}H_{20}O_4$, 264.1362).

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