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SESQUITERPENE LACTONES FROM *IXERIS SONCHIFOLIA*

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Key Word Index—*Ixeris sonchifolia*; Compositae; sesquiterpene lactones; guaianolide; 8-desoxyartelin; ixerin Z; 9α-hydroxyzaluzalin C.

Abstract—The whole plant of *Ixeris sonchifolia* afforded two new guaianolide sesquiterpene lactones named 8-desoxyartelin [3-hydroxy-1(10),3-guaiadiene-12,6-olide-2-one] and ixerin Z [1(10),3,11(13)-guaiatriene-12,6-olide-2-one-3-*O*-glucopyranoside], along with the known compound 9α-hydroxyzaluzalin C, whose structure and stereochemistry wee determined by spectroscopic methods. © 1998 Published by Elsevier Science Ltd. All rights reserved

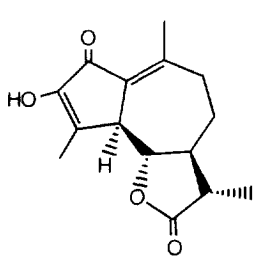
INTRODUCTION

The whole herb of *Ixeris sonchifolia* Hance is used as an anti-inflammatory and haemostatic folk remedy in China. Studies on other species of this genus revealed the presence of sesquiterpene lactones [1–7] which showed wide biological activities e.g. cytotoxicity [8], anti-repellant and antifeedant to some insects [9–11]. This paper reports on the isolation of sesquiterpene lactones from *I. sonchifolia*.

RESULTS AND DISCUSSION

Two new sesquiterpene lactones 8-desoxyartelin (**1**) and ixerin Z (**2**), and the known 9α-hydroxyzaluzalin C (**3**) were isolated from the whole herb. 8-Desoxyartelin (**1**), *M*, 262, was assigned the molecular formula $C_{15}H_{18}O_4$. IR absorptions showed the presence of a hydroxyl (3471 cm^{-1}) and a γ-lactone carbonyl (1766, 1672 cm^{-1}) group. The ^1H NMR spectrum (Table 1) established the presence of three methyl groups, of which, two were assigned to 14,15 vinyl methyls [δ 2.16 (3H, *s*, H-15), δ 2.46 (3H, *s*, H-14)], and one to the α-methyl in a δ-lactone ring [δ 1.25 (3H, *d*, $J = 7.0$ Hz)]. The signal at δ 3.54 (1H, *t*, $J = 10.0$ Hz) was assigned to H-6 which was coupled both with H-5 [δ 3.27 (1H, *brd*, $J = 10.0$ Hz)] and H-7 [δ 1.95 (1H, *dd*, $J = 10.0, 2.0$ Hz)] and thus established the *trans*-diaxial relationship of these three protons. Since the naturally occurring guaianolides have an α-oriented H-7 [12], this meant that the orientation of H-5 and H-6 were α and β, respectively.

Fifteen carbon signals were observed in ^{13}C NMR spectrum (Table 2) of **1**, the two most downfield signals were assigned to a lactone carbonyl (δ 177.7) and an α,β-unsaturated ketone carbonyl (δ 189.3). The other signals were those for four tertiary olefinic carbons, two methylenes, four methines including one oxygen-bearing carbon, and three methyls.



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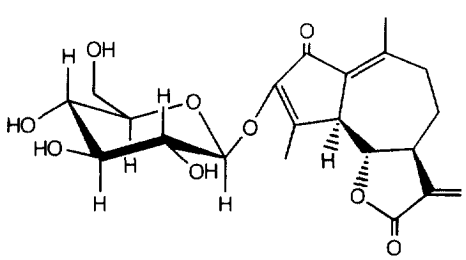

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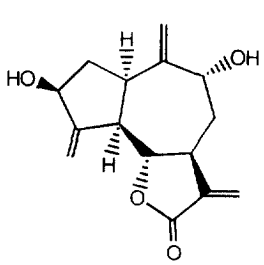

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Table 1. ^{1}H NMR data of compounds **1** and **2** (400 MHz)

H	1*	2†
5	3.27 (1H, *brd*, J = 10.0)	3.22 (1H, *d*, J = 10.0)
6	3.54 (1H, *t*, J = 10.0)	3.17 (1H, *t*, J = 10.0, 12.2)
7	1.95 (1H, *dd*, J = 10.0, 2.0)	2.74 (1H, *brt*, J = 12.2)
8	1.97 (1H, *m*)	1.06 (1H, *dd*, J = 12.2, 8.0)
	1.35 (1H, *dt*, J = 13.0, 2.0)	2.29 (1H, overlapped)
9	2.45 (1H, overlapped)	1.89 (1H, *brd*, J = 11.0)
	2.36 (1H, *m*)	2.08 (1H, *m*)
11	2.25 (1H, *q*, J = 7.0)	
13	1.25 (1H, *d*, J = 7.0)	6.19 (1H, *brs*), 5.19 (1H, *brs*)
14	2.46 (3H, *s*)	2.42 (3H, *brs*)
15	2.16 (3H, *s*)	2.31 (3H, *brs*)
1′		6.25 (1H, *d*, J = 7.0)

* Measured in $CDCl_3$.
† Measured in pyridine-d_5.

Table 2. ^{13}C NMR data of compounds **1** and **2**

C	1*	2†
1	154.2	153.0
2	189.3	188.9
3	152.5	153.7
4	136.8	146.1
5	47.4	52.4
6	85.6	85.1
7	55.8	47.9
8	25.2	24.1
9	37.3	36.9
10	128.7	124.6
11	41.4	139.5
12	177.7	169.1
13	12.2	117.9
14	22.0	21.7
15	14.0	14.9
1′		101.6
2′		75.3
3′		78.3
4′		71.1
5′		78.3
6′		62.3

* Measured in $CDCl_3$.
† Measured in pyridine-d_5.

Careful examination of the H-^{1}H COSY, HMQC and HMBC data allowed the unambiguous assignment of all signals. The stereochemistry of H-11 was determined by NOE experiments. Signal enhancement was observed for H-11 on irradiating H-6, and vice versa. **1** was thus shown to be 8-desoxyartelin.

Ixerin Z (**2**) was assigned the molecular formula $C_{21}H_{26}O_9$ (FAB-MS and EI-MS). IR absorption bands were observed at 3406 (hydroxyl), 1768 and 1678 cm^{-1} (carbonyl). The ^{1}H NMR spectrum (Table 1) contained the characteristic signals [δ 6.19 (1H, *brs*, H-13a, and δ 5.19 (1H, *brs*, H-13b)] of an α-methylene-γ-lactone moiety. Signals for two vinyl methyls at [δ 2.31 (3H, *brs*, H-15) and 2.42 (3H, *brs*, H-14)] and a sugar moiety were also observed. A double doublet at δ 3.17 (1H, J = 10.0, 12.2 Hz) was assigned to H-6, which was coupled with H-5 [δ 3.22 (1H, *d*, J = 10.0 Hz)] and H-7 [δ 2.74 (1H, *brt*, J = 12.2 Hz)]. This established the *trans*-diaxial relationship of the vicinal protons. The stereochemistry of these protons was considered to be H-5α, H-6β, since H-7 in naturally occurring guaianolides have α-orientation [12]. The ^{13}C NMR data (Table 2) of **2** showed the presence of 21 carbons. Of the eight unsaturated carbons, two were attributed to a lactone carbonyl [δ 169.1 (C-12)] and an α,β-unsaturated ketone carbonyl [δ 188.9 (C-2)] and six were olefinic carbons; of the 13 alkyl carbons, seven were oxygen-bearing carbons of which six were derived from the glucose moiety. The remaining signals were those of two methines, two methylenes and two methyls. The absolute configuration of the glucose moiety could not be deduced from the NMR data. The anomeric configuration was determined to be β from the $J_{H1'-H2'}$ value (7.0 Hz) [13]. Based on the above evidence, **2** was identified as 1(10),3,11(13)-guaiatriene-12,6-olide-2-one-3-*O*-glucopyranoside.

9α-Hydroxyzaluzalin C (**3**) was identified by direct comparison with published data [12].

EXPERIMENTAL

General

Mps: uncorr; ^{1}H NMR and ^{13}C NMR: 400 MHz and 100 MHz, respectively; 2D-NMR data (^{1}H-^{1}H COSY, HMQC, HMBC, NOESY): 400 MHz using standard pulse sequences. $CDCl_3$ and pyridine-d_5 were used as solvents, with TMS as int. standard; FT-IR: KBr; CC: silica gel (coarse silica gel, 100–200 mesh); TLC: precoated silica gel plates (Merck, silica gel 60 F_{254}).

Plant material

I. sonchifolia Hance was purchase from the Nanjing Company of Traditional Chinese Medicine, in February 1991. The voucher specimen (No. WZT910100) is deposited in the Herbarium of the Department of Pharmacognosy, China Pharmaceutical University.

Extraction and isolation

I. sonchifolia (5 kg) was extracted with hot 95% EtOH. The extract was evaporated to dryness and extracted successively with petrol, $CHCl_3$ and MeOH. The $CHCl_3$ extract was applied to a silica gel column which was eluted with *n*-hexane–$CHCl_3$–MeOH (1:1:0–0:1:1). Repeated chromatography and purification gave compound **3** (20 mg), **2** (25 mg) and **3** (8 mg).

8-*Desoxyartelin* (**1**)

Fine needles ($CHCl_3$), mp 208–211°. UV λ_{max}^{MeCN} nm: 234, 215; $[\alpha]_D^{28}$ +40.2° ($CHCl_3$, *c* 0.1); IR ν_{max}^{KBr} cm^{-1}: 3471 (—OH), 1766, 1672 (=C=O), 1623, 1404, 1215, 989; EI-MS (probe) 70 eV, *m/z* (rel. int): 262 $[M]^+$ (98), 247 $[M-CH_3]^+$ (30), 189 (100), 161 (38), 151 (47), 112 (19), 19 (29); ^1H NMR ($CDCl_3$, 400 MHz): Table 1; ^{13}C-NMR ($CDCl_3$, 100 MHz): Table 2.

Ixerin Z (**2**)

Amorphous powder. UV λ_{max}^{MeCN} nm: 267, 198; $[\alpha]_D^{28}$ +35.1° (MeOH, *c* 0.1); IR ν_{max}^{KBr} cm^{-1}: 3406 (—OH), 1768, 1678 (=C=O), 1620, 1387, 1211, 1074; positive ion FAB-MS *m/z*: 445 $[M+Na]^+$, 422 $[M]^+$. EI-MS (probe) 70 eV, *m/z* (rel. int): 260 $[M+1-C_6H_{11}O_5]^+$ (100), 245 (13), 214 (15), 189 (53), 161 (29), 151 (28), 134 (25), 107 (22); ^1H-NMR (pyridine-d_5, 400 MHz): Table 1; ^{13}C NMR (pyridine-d_5, 100 MHz): Table 2.

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