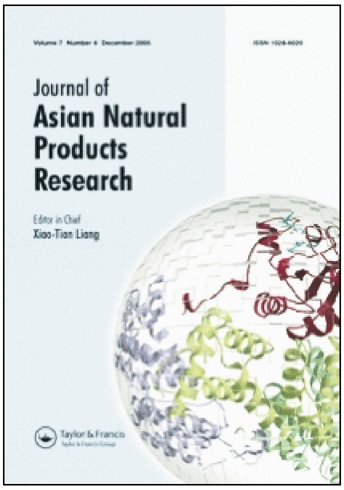

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

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

Wen-Zhi Zhang[ab]; Xin-Li Li[b]; Min-Jie Wang[b]; Ling-Gang Shi[b]; De-Feng Zhao[a]; Shu-Jun Zhang[b]
[a] State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian, China [b] Department of Chemistry and Engineering, Qiqihar University, Qiqihar, China

To cite this Article Zhang, Wen-Zhi , Li, Xin-Li , Wang, Min-Jie , Shi, Ling-Gang , Zhao, De-Feng and Zhang, Shu-Jun(2008) 'Sesquiterpene lactones from *Ixeris sonchifolia* (Bge.) Hance', Journal of Asian Natural Products Research, 10: 8, 753 — 758

To link to this Article: DOI: 10.1080/10286020802031015

URL: http://dx.doi.org/10.1080/10286020802031015

Journal of Asian Natural Products Research
Vol. 10, No. 8, August 2008, 753–758

Taylor & Francis
Taylor & Francis Group

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

Wen-Zhi Zhang[ab], Xin-Li Li[b], Min-Jie Wang[b], Ling-Gang Shi[b], De-Feng Zhao[a]
and Shu-Jun Zhang[b]*

[a]*State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116012, China;*
[b]*Department of Chemistry and Engineering, Qiqihar University, Qiqihar 161006, China*

(*Received 11 October 2007; final version received 26 January 2008*)

Four new sesquiterpene lactones, 11-*epi*-8-desoxyartelin (**1**), sonchifoliasolide A (**2**), sonchifoliasolide B (**3**), and sonchifoliasolide C (**4**) were isolated from the roots 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

Kudiezi, known as Baojingkumaicai (*Ixeris sonchifolia* (Bge.) Hance, Compositae), is a perennial plant that is found in various places of the northern area of China and Mongolia. 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 heamorrhoid [1]. Studies of this genus revealed the presence of sesquiterpene lactones [2–4]. In this paper, we report four new guaiane-type sesquiterpene lactones from the EtOAc extracts of the roots of the plant.

2. Results and discussion

11-*Epi*-8-desoxyartelin (**1**) had the molecular formula $C_{15}H_{18}O_4$, based on HR-EI-MS at *m/z* 262.1201 $[M]^+$. The IR spectrum of **1** showed the presence of hydroxyl ($3327\,cm^{-1}$), α,β-unsaturated five-membered ring carbonyl (1691 and $1621\,cm^{-1}$), and γ-lactone ($1747\,cm^{-1}$) groups. The ^{13}C NMR spectrum (Table 1) displayed 15 carbon resonances, including lactone and ketone carbonyl signals at δ 178.8 and 189.2, respectively. One signal for carbon bearing oxygen was observed at δ 85.0. The ^1H NMR (Table 1) spectrum showed two broad methyl singlets, connected to the olefinic carbon at δ 2.18 and 2.48, one methyl doublet at δ 1.13 (3H, d, $J = 7.7\,Hz$), and one oxymethine at δ 3.76 (1H, dd, $J = 10.2$, $10.2\,Hz$). Based on the DEPT and HMQC spectra, the remaining carbon resonances were due to three methyls, two methylenes, three methines, and four quaternary carbons. The connections between the protonated carbons (C-5 to C-6, C-6 to C-7, C-7 to C-8, C-7 to C-11, C-8 to C-9, and C-11 to C-13) were determined by the analysis of a ^1H–^1H COSY spectrum. The HMBC correlations of H-5 with C-1 (δ 128.7) and the carbonyl carbon (C-2, δ 189.2); H-5 and H-15 with C-3 at δ 152.3, and H-5, H-14 with C-1, indicated that the ketone carbonyl group was located at C-2, and two carbon–carbon double bonds were located at C-3 and C-4, and C-1 and C-10 positions, respectively. The HMBC correlations of four carbon atoms of the γ-lactone ring (C-12, δ 178.8/H-7, H-11,

---

*Corresponding author. Email: shjzhang2005@126.com

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020802031015
http://www.informaworld.com

Table 1. ^1H 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	128.7		46.6	3.17 m	46.9	2.86 dd (9.6, 4.0)	46.8	3.17 m
2	189.2		210.2		209.1		209.5	
3	152.3		131.4	6.08 br s	132.6	6.09 s	131.8	6.08 s
4	136.4		179.8		179.3		179.5	
5	48.3	3.29 d (10.2)	51.9	3.26 m	53.0	3.09 br t (9.6)	52.2	3.24 m
6	85.0	3.76 dd (10.2, 10.2)	81.2	4.61 dd (10.5, 9.5)	81.6	4.31 dd (9.6, 9.6)	81.6	4.61 dd (10.5, 9.5)
7	51.5	2.19 m	40.0	3.13 m	41.1	2.71 m	40.0	3.12 m
8	23.5	1.40 br dd (1.4, 12.2)	28.3	2.37 d (14.4)	29.4	1.72 ddd (2.4, 12.0, 14.8)	28.1	2.36 d (14.4)
		2.44 m		1.61 ddd (2.1, 14.4, 12.0)		2.22 m		1.58 ddd (14.4, 12.0, 2.1)
9	37.4	2.35 ddd (1.4, 6.1, 14.4)	77.6	3.94 m	72.8	5.16 m	76.5	3.87 br s
		1.87 m						
10	154.3		39.0	2.60 m	38.0	2.68 m	39.0	2.50 m
11	39.4	2.70 ddd (7.7, 7.7, 15.2)	139.4		137.8		139.7	
12	178.8		169.4		170.0		169.8	
13	10.2	1.13 d (7.7)	119.3	α = 6.07 d (3.2)	121.0	α = 6.25 d (3.2)	119.7	α = 6.07 d (3.2)
				β = 5.67 d (3.2)		β = 5.46 d (3.2)		β = 5.69 d (3.2)
14	22.1	2.48 s	13.1	0.63 d (7.3)	13.7	0.75 d (7.6)	13.5	0.62 d (7.5)
15	14.2	2.18 s	18.6	2.21 s	19.3	2.29 s	18.9	2.21 s
1′			101.8	4.35 d (7.8)			100.8	4.37 d (7.6)
2′			73.5	2.99 m			73.5	3.16 m
3′			76.4	3.19 m			76.4	3.15 m
4′			70.2	3.04 m			70.2	3.22 m
5′			77.1	3.15 m			73.9	3.39 m
6′			61.4	3.69 dd (11.7, 2.0)			64.1	4.09 dd (12.0, 6.8)
				3.44 dd (11.7, 5.1)				4.30 dd (12.0, 1.6)
1″					170.7		171.7	
2″					41.0	3.58 s	39.4	3.54 s
3″					125.2		124.7	
4″					130.2	7.11 d (8.4)	130.4	7.04 d (8.4)
5″					115.7	6.78 d (8.4)	115.2	6.67 d (8.4)
6″					155.5		156.3	
7″					115.7	6.78 d (8.4)	115.2	6.67 d (8.4)
8″					130.2	7.11 d (8.4)	130.4	7.04 d (8.4)

and H-13; C-11/H-7, H-13; C-7/H-5, H-6, and H-13; C-6/H-5, H-7, and H-11) indicated that **1** belongs to the guaianolide-type sesquiterpene lactone. The coupling constant of H-6 ($J_{5,6} = 10.2$ Hz and $J_{6,7} = 10.2$ Hz) indicated a trans-relationship between H-5 and H-6, and the existence of a trans-fused γ-lactone. The stereochemistry of H-6 and C-11 Me was determined to be β-oriented due to the NOESY correlations (H-6/H-13, H-5/H-7). Thus, **1** was determined to be 11αH-3-hydroxy-2-oxoguaia-3,1(10)-dieno-12,6-lactone (Figure 1).

Sonchifoliasolide A (**2**) had the molecular formula $C_{21}H_{28}O_9$ based on HR-EI-MS at *m/z* 424.1730 [M^+]. The IR spectrum of **2** showed the presence of a hydroxyl (3396 cm^{-1}), α,β-unsaturated five-membered ring carbonyl (1685 and 1616 cm^{-1}), and α,β-unsaturated γ-lactone (1762 and 1616 cm^{-1}) groups. The ^{13}C NMR spectrum (Table 1) displayed 21 carbon resonances, including lactone and ketone carbonyl signals at δ 169.4 and 210.2, respectively. Two signals for carbons bearing oxygen were observed at δ 81.2 and 77.6, in addition to six oxygenated carbon signals of a hexose. Based on the DEPT and HMQC spectra, it can be concluded that the remaining carbon resonances were due to two methyls, two methylenes including one *exo*-olefine carbon, five methines, and two quaternary carbons. The ^1H NMR (Table 1) spectrum showed one methyl singlet connected to an olefin carbon at δ 2.21 (3H, s), one methyl doublet at δ 0.63 (3H, d, $J = 7.3$ Hz), three olefinic protons including two *exo*-olefine methylenes at δ 6.07 (1H, d, $J = 3.2$ Hz) and 5.67 (1H, d, $J = 3.2$ Hz), two oxymethines at δ 4.61 (1H, dd, $J = 10.5$, 10.5 Hz) and 3.94 (1H, m), respectively. One anomeric proton of a sugar showed δ 4.35 (1H, d, $J = 7.8$ Hz), while four oxymethine and one oxymethylene protons showed δ 3.0–3.5. The HMBC correlations of H-1, H-3, and H-10 with the carbonyl carbon (C-2, δ 210.2), and H-1, H-5, and H-15 with the olefinic carbon (C-3, δ 131.4) 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 of the four carbon atoms of the γ-lactone ring (C-12, δ 169.4/H-13; C-11/H-7 and H-13; C-7/H-5, H-9, and H-13; C-6/H-1, H-5, H-7, and H-8), and the correlation of H-9 with the anomeric carbon of sugar, indicated that the sugar was attached at C-9. Hence, **2** possesses a guaianolide structure of 2-oxoguaia-3,11(13)-dieno-12,6-lactone-9-*O*-glucoside. The coupling constant of H-6 ($J_{5,6} = 9.5$ Hz

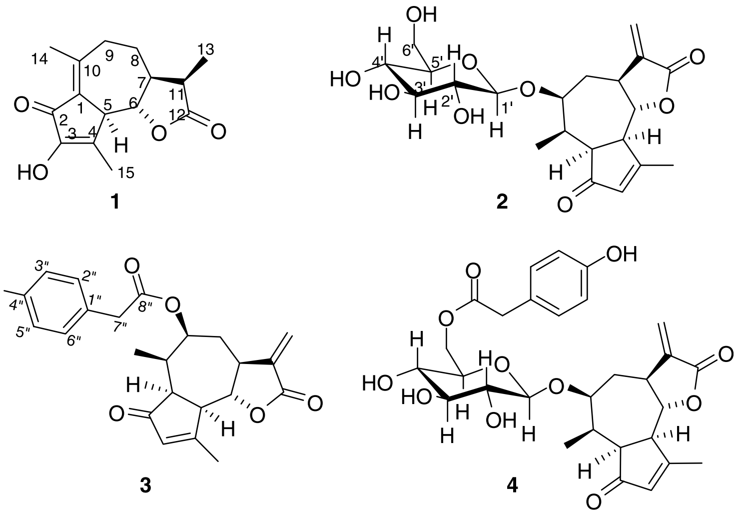

Figure 1. Structures of compounds **1**–**4**.

and $J_{6,7} = 10.5$ Hz) indicated a trans-relationship between H-5 and H-6 and the existence of a trans-fused γ-lactone. The orientations of H-6 and C-10 Me were determined to be β and those of H-1, H-5, H-7, and H-9 were determined to be α from the NOESY correlations of H-1/H-5, H-1/H-14, H-6/H-14, and H-7/H-9 (Figure 2) [5]. Thus, **2** was determined to be 2-oxoguaia-3,11(13)-dieno-12,6-lactone-9β-*O*-β-D-glucopyranoside (Figure 1).

Sonchifoliasolide B (**3**) had the molecular formula $C_{23}H_{24}O_6$ based on HR-EI-MS at *m/z* 396.1577 [M^+]. The IR spectrum of **3** showed the existence of hydroxyl (3435 cm^{-1}), α,β-unsaturated five-membered ring carbonyl (1735 and 1697 cm^{-1}), and α,β-unsaturated γ-lactone (1770 and 1697 cm^{-1}) groups. Compound **3** showed very similar ^{13}C and ^{1}H NMR spectra to those of **2** except for the vicinity of the substituting group at C-9 (Table 1). On comparison of the NMR spectra with those of **2**, the ^{1}H NMR spectrum of **3** showed additional resonance peaks of the aromatic AA′BB′ signals at δ 6.78 (2H, d, $J = 8.4$ Hz) and 7.11 (2H, d, $J = 8.4$ Hz), and the methylene singlet at δ 3.58 (2H, s), and the signals of glucose were absent. The ^{13}C NMR spectrum showed additional eight carbon signals, and the signals of glucose were absent. The substituting group was determined to be *p*-hydroxylphenylacetyl from the HMBC experiment. Hence, **3** possesses the guaianolide structure of 9-*p*-hydroxylphenyl-acetyloxy-2-oxoguaia-3,11(13)-dieno-12,6-lactone. Compound **3** showed NOESY correlations similar to those of **2** expect for the substituting group at C-9. Thus, the structure of **3** was determined to be 9β-(*p*-hydroxyphenylacetyloxy)-2-oxo-guaia-3,11(13)-dieno-12,6-lactone (Figure 1).

Sonchifoliasolide C (**4**) had the molecular formula $C_{29}H_{34}O_{11}$ based on HR-EI-MS at *m/z* 558.2105 [M^+]. The IR spectrum of **4** showed the existence of hydroxyl (3425 cm^{-1}), α,β-unsaturated five-membered ring carbonyl (1683 and 1616 cm^{-1}), and α,β-unsaturated γ-lactone (1743 and 1616 cm^{-1}) groups. Compound **4** showed ^{13}C and ^{1}H NMR spectra very similar to those of **2** except for the additional signals of the *p*-phenyl group at δ 6.67 (2H, d, $J = 8.4$ Hz) and 7.04 (2H, d, $J = 8.4$ Hz), and the methylene group at δ 3.54 (2H, s). The HMBC correlations of the ester carbonyl at δ 171.7 with H-6′ at δ 4.09 (1H, m) and 4.30 (1H, m) were shown, respectively. Hence, **4**

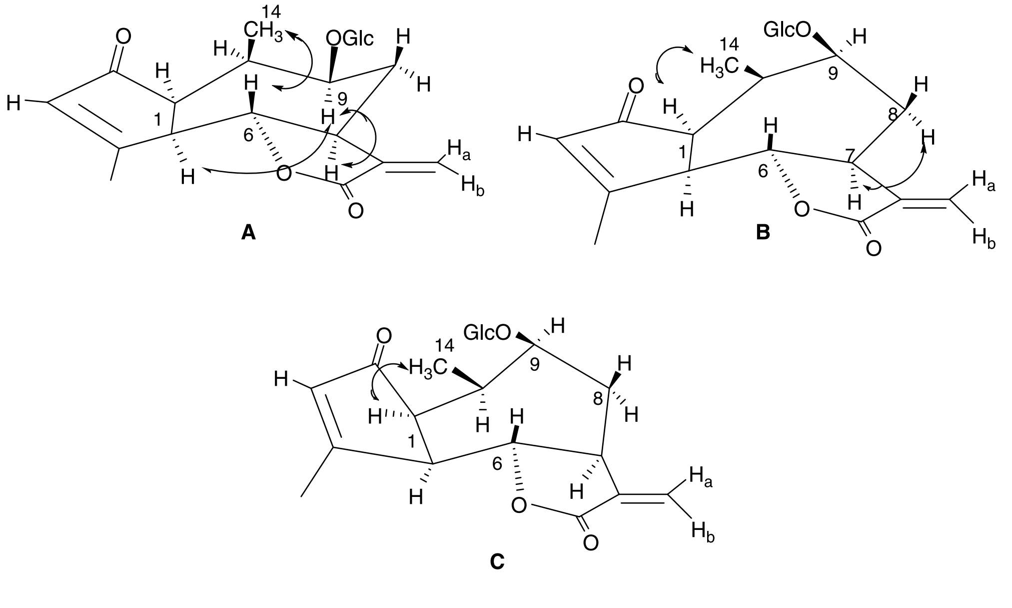

Figure 2. Kew NOESY correlations of the conformations **A**, **B**, and **C**.

possesses the guaianolide structure of 9-(6′-*p*-hydroxylphenylacetyloxy)-β-D-glucopyranosyloxy-2-oxoguaia-3,11(13)-dieno-12,6-lactone. Compound **4** showed NOESY correlations similar to those of **2** expect for the substituting group at C-6′. Thus, the structure of **4** was determined as 9β-(6′-*p*-hydroxyl- phenylacetyloxy)-β-D-glucopyranosyloxy-2-oxoguania-3,11(13)-dieno-12,6-lactone (Figure 1).

3. Experimental

3.1 General experimental procedures

Melting points were using an X-6 micromelting apparatus and are uncorrected. Optical rotations were measured using an AUTOPOL V digital polarimeter. IR spectra were measured in KBr disks using the Magna FTIR-750 infrared spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Bruker-DRX 400 spectrometer in DMSO-d_6 or $CDCl_3$, using TMS as the 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, China) was employed for column chromatography and TLC. The columns of HPLC were PREP-ODS (column A) and PREP-SIL (column B), both 10 × 250 mm with a particle size of 5 μ (GL Sciences Inc., Tokyo, Japan).

3.2 Plant material

The roots of *I. sonchifolia* (Bge.) Hance were collected from Linyun, Liaoning Province, China in July 2005. The plant was identified by Professor Wei Sha, Department of Life Science and Engineering, Qiqihar University. A voucher specimen (WI-02-2005) has been deposited at the Natural Organics Laboratory, Faculty of Chemistry, Qiqihar University.

3.3 Extraction and isolation

Air-dried roots of *I. sonchifolia* (1.5 kg) were extracted with 95% EtOH (5.5 l) for 4 days. The EtOH extracts were concentrated to 300 ml and extracted by turns with petroleum ether (4 × 500 ml), EtOAc (5 × 400 ml), and *n*-BuOH (4 × 300 ml). The EtOAc extracts were concentrated to give an oil (20.9 g), which was separated into nine fractions (F_1–F_9) by silica gel column chromatography (silica gel, 326 g), eluting with petroleum ether–EtOAc (5:5 2 l, 1:9 3 l), and EtOAc–MeOH (7:3 2 l, 1:9 3 l). Fraction F_1 (550 mg) was separated by column chromatography on silica gel into four fractions (F_{1-1}–F_{1-4}), using a gradient of petroleum ether and EtOAc. Fraction F_{1-3} was further separated by HPLC (column A, MeOH–H_2O 6:4, 4 ml/min^{-1}) to give **1** ($t_R = 11.02$ min, 17 mg). Fraction F_{1-4} was separated by HPLC (column A, MeOH–H_2O 5:5, 4 ml/min^{-1}) to give **3** ($t_R = 19.06$ min, 11 mg). Fractions F_7 (4.1 g) and F_8 (7.8 g) were recrystallized from MeOH to give **4** (256 mg) and **2** (2.4 g), respectively.

3.3.1 11-Epi-*8-desoxyartelin (**1**)*

White needles (EtOAc), mp 190.7–190.9°C, $[\alpha]_D^{20} + 112.7$ (*c* 0.0011, MeOH); IR $v_{r\max}^{\mathrm{KB}}$ (cm^{-1}): 3327 (OH), 1742, 1670 (C=O), 1621 (C=C); UV $\lambda_{\max}^{\mathrm{MeOH}}$ (nm) (log ε): 208 (4.08), 267 (4.19); ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1. HR-EI-MS *m/z* 262.1201 $[M]^+$ (calcd for $C_{15}H_{18}O_4$, 262.1205).

*3.3.2 Sonchifoliasolide A (**2**)*

White needles (MeOH), mp 147.8–149.9°C; $[\alpha]_D^{20} + 144$ (*c* 0.0780, MeOH); IR $v_{r\max}^{\mathrm{KB}}$ (cm^{-1}): 3396 (OH), 1762, 1686 (C=O), 1616 (C=C); UV $\lambda_{\max}^{\mathrm{MeOH}}$ (nm) (log ε): 290 (2.86); ^{1}H NMR (DMSO-d_6, 400 MHz), and ^{13}C NMR (DMSO-d_6, 100 MHz), see Table 1. HR-EI-MS *m/z* 424.1730 $[M]^+$ (calcd for $C_{21}H_{28}O_9$, 424.1733).

*3.3.3 Sonchifoliasolide B (**3**)*

White needles (MeOH), mp 81.2–82.4°C; $[\alpha]_D^{20} + 112.8$ (*c* 0.0032, MeOH); IR $v_{r\max}^{\mathrm{KB}}$ (cm^{-1}): 3435 (OH), 1771, 1735, 1697

(C=O), 1616, 1516 (C=C); UV $\lambda_{\max}^{\mathrm{MeOH}}$ (nm) (log ε): 278 (3.66); ^{1}H NMR ($CDCl_3$, 400 MHz), and ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1. HR-EI-MS *m*/*z* 396.1577 $[M]^+$ (calcd for $C_{23}H_{24}O_6$, 396.1573).

*3.3.4 Sonchifoliasolide C (**4**)*

White needles (MeOH), mp 227.0–229.4°C, $[\alpha]_D^{20} + 78.0$ (*c* 0.2090, MeOH); IR $\nu_{r\max}^{\mathrm{KB}}$ (cm^{-1}): 3425 (OH), 1743, 1684 (C=O), 1616 (C=C); UV $\lambda_{\max}^{\mathrm{MeOH}}$ (nm) (log ε): 284 (3.86); ^{1}H NMR (DMSO-d_6, 400 MHz), and ^{13}C NMR (DMSO-d_6, 100 MHz), see Table 1. HR-EI-MS *m*/*z* 558.2105 $[M]^+$ (calcd for $C_{29}H_{34}O_{11}$, 558.2101).

Acknowledgements

This work was supported by the Ministry of Education, China (No. 2042045). We thank Mr Jun Li for the measurement of NMR spectra.

References

[1] *Zhong Yao Da Ci Dian*, Jangsu New Medical College, Jangsu China, pp. 1300 (1985).
[2] X.Z. Feng, S.X. Xu, and S.G. Ma, *CJMC* **9**, 309 (1999).
[3] Ha Sook Chung, *Food Sci. Biotechnol.* **10**, 433 (2001).
[4] J.Y. Ma, Z.T. Wang, L.S. Xu, G.J. Xu, S. Kadota, and T. Namba, *Phytochemistry* **48**, 201 (1998).
[5] S.J. Zhang, J.L. Wang, H.Y. Xue, Q.G. Deng, F.L. Xing, and M. Ando, *J. Nat. Prod.* **65**, 1927 (2002).