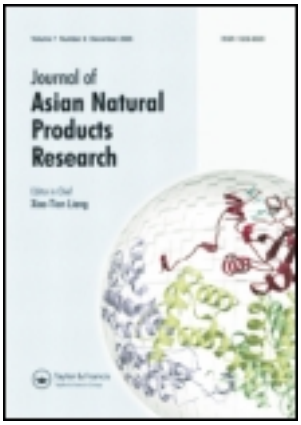

Journal of Asian Natural Products Research

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/ganp20

Sesquiterpenoids from *Inula racemosa*

Li-Wei Xu [a b] & Yan-Ping Shi [a]

[a] Key Laboratory of Chemistry of Northwestern Plant Resource and Key Laboratory for Natural Medicines of Gansu Province, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou, 730000, China

[b] Graduate University of Chinese Academy of Sciences, Beijing, 100039, China

Available online: 25 May 2011

To cite this article: Li-Wei Xu & Yan-Ping Shi (2011): Sesquiterpenoids from *Inula racemosa* , Journal of Asian Natural Products Research, 13:06, 570-574

To link to this article: http://dx.doi.org/10.1080/10286020.2011.575066

Journal of Asian Natural Products Research
Vol. 13, No. 6, June 2011, 570–574

Sesquiterpenoids from *Inula racemosa*

Li-Wei Xu[ab] and Yan-Ping Shi[a]*

[a]*Key Laboratory of Chemistry of Northwestern Plant Resource and Key Laboratory for Natural Medicines of Gansu Province, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China;* [b]*Graduate University of Chinese Academy of Sciences, Beijing 100039, China*

(*Received 30 December 2010; final version received 21 March 2011*)

Phytochemical research on the roots of *Inula racemosa* yielded nine sesquiterpenoids including a new nor-eudesmane-type sesquiterpenoid, 11,12,13-trinoreudesm-5-en-7β,8α-diol (**1**). The structures of isolated compounds were elucidated by extensive spectroscopic methods including 1D and 2D NMR. The structure of compound **2** was confirmed by single-crystal X-ray diffraction analysis.

Keywords: Compositae; *Inula racemosa*; sesquiterpenoids; eudesmanolide

1. Introduction

The genus *Inula* comprises *ca*. 100 species and is distributed mainly over Asia and Europe. *Inula racemosa* Hook. f. Poshkar, known as 'manu', has long been used in Chinese folk medicine to regulate the function of the stomach, alleviate pain, and be used as antimicrobial agents [1,2]. Previous studies have demonstrated that the constituents of *I. racemosa* growing outside China were sesquiterpene lactones [3–5], aplotaxene, and phenylacetonitrile [6]. *I. racemosa* has also been investigated in China. Tan et al. [7] isolated some lignans and sesquiterpene lactones from *Artemisia sieversiana* and *I. racemosa*, which are collected from Gansu Province. Zhang et al. [8] reported two new eudesmane-type sesquiterpene lactones from *I. racemosa* collected in Tibet region in 2008. We also carried out the phytochemical research on a sample collected in Qinghai Province, and the examination led to the isolation of a new nor-eudesmane, 11,12,13-trinoreudesm-5-en-7β,8α-diol (**1**) together with eight known sesquiterpenolides (**2**–**9**) (Figure 1). This paper deals with the isolation and structural elucidation of these compounds.

2. Results and discussion

Compound **1** was isolated as a pale gum. Its HR-ESI-MS experiment could not give quasi-molecular ion peak. Therefore, the acylation of **1** was done and compound **1a** was obtained. The molecular formula of **1a** was deduced as $C_{16}H_{24}O_4$ from the HR-ESI-MS spectrum, then the molecular formula of **1** was also assigned as $C_{12}H_{20}O_2$ inferring the presence of three degrees of unsaturation. The ^{1}H NMR spectrum of **1** indicated the presence of two methyl groups [δ_H 1.14 (s, 3H), 1.13 (d, 3H, $J = 7.6$ Hz)], two oxygenated methine [δ_H 3.95 (1H, dd, $J = 1.6$, 7.6 Hz) and 3.51 (1H, ddd, $J = 4.4$, 7.6, 12.0 Hz)], and one olefinic proton at δ 5.24. The ^{13}C NMR and DEPT spectra of **1**

*Corresponding author. Email: shiyp@licp.cas.cn

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020.2011.575066
http://www.informaworld.com

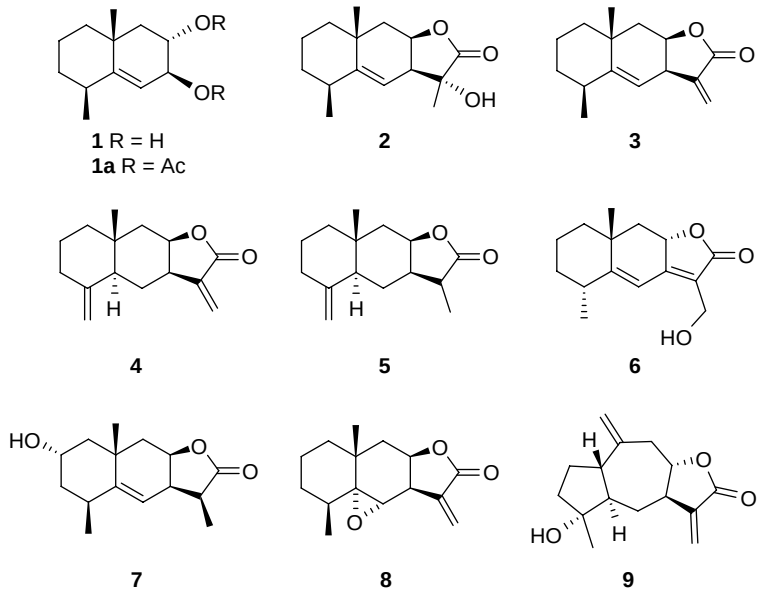

Figure 1. Structures of compounds **1**–**9**.

showed 12 carbon signals including two CH_3, four CH_2, four CH (two oxygenated carbons at δ 71.7 and 73.6, and one olefinic carbon at δ 122.1), and two quaternary carbons (one olefinic carbon at δ 149.9). All of the protons were assigned to the corresponding C-atoms by an HMQC experiment. The NMR spectral data suggested that compound **1** was a nor-eudesmane sesquiterpene. The structure of **1** could be confirmed by its HMBC experiment (Figure 2), in which the correlations of CH_3-14 (δ_H 1.14, s) with C-1 (δ_C 40.6), C-5 (δ_C 149.9), and C-9 (δ_C 45.3), as well as CH_3-15 (δ_H 1.13, d) with

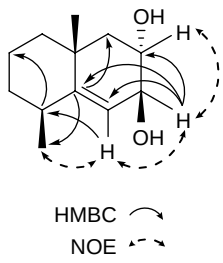

Figure 2. Selected HMBC and NOE correlations of compound **1**.

C-3 (δ_C 33.3) and C-5 (δ_C 149.9) indicated the two methyl groups located at C-10 and C-4; the correlations of H-7 (δ_H 3.95, dd) with C-5 (δ_C 149.9), C-6 (δ_C 122.1), C-8 (δ_C 71.7), and C-9 (δ_C 45.3), together with H-8 (δ_H 3.51, ddd) with C-7 (δ_C 73.6), indicated that the two OH groups were attached to C-7 and C-8, respectively.

The relative configuration of **1**, i.e. CH_3-15, CH_3-14, and H-8 with β-orientation, H-7 with α-orientation, could be assigned by coupling constants and the NOESY experiment and by comparing with compounds **2** and **3**. First, in its ^1H NMR spectrum, the typical coupling constants, $J_{8,9\alpha} = 12.0$ Hz, $J_{8,9\beta} = 4.4$ Hz indicated that H-8 was β-orientation; $J_{7,8\beta} = 7.6$ Hz indicated that H-7 was α-orientation, in correspondence with NOE correlations between H-6 with H-4 and H-7 in the NOESY experiment (Figure 2). Then, the β-orientation of CH_3-14 and CH_3-15 should be identical with that of known compounds, 11α-hydroxy-eudesm-5-en-8β,12-olide (**2**) and alantolactone (**3**) on the biogenetic reasoning, because there

was large amount of compound **3** in species *I. racemosa* [9]. Consequently, compound **1** was determined as 11,12,13-trinoreudesm-5-en-7β,8α-diol.

On the basis of NMR spectral data and comparison with those reported in the literature, the known sesquiterpenolides isolated from this plant material were identified as 11α-hydroxy-eudesm-5-en-8β,12-olide [8], alantolactone [10], isoalantolactone [10], 11,13-dihydroisoalantolactone [10], macrophyllilactone E [10], 11,13-dihydro-2α-hydroxyalantolactone [11], 5α,6α-epoxyalantolactone [12], and inuviscolide [13]. Among them, 11α-hydroxy-eudesm-5-en-8β,12-olide (**2**) has been recently reported, but its structure was further confirmed by X-ray crystallographic analysis in this paper (Figure 3).

3. Experimental

3.1 General experimental procedures

Optical rotations were measured on a PerkinElmer model 341 polarimeter with a 1 dm cell. IR spectra were obtained on a Nicolet NEXUS 670 FT-IR spectrometer. The NMR spectra of compounds in $CDCl_3$ were measured on a Varian INOVA 400 MHz NMR spectrometer with TMS as an internal standard. HR-ESI-MS was carried out on a Bruker APEX II mass spectrometer and ESI-MS was on a HP-5988 mass spectrometer.

Silica gel (200–300 mesh) used for column chromatography (CC) and silica GF_{254} (10–40 μm) for TLC were both supplied by the Qingdao Marine Chemical Factory (Qingdao, China). TLC was detected at 254 nm, and spots were visualized by spraying with 98% H_2SO_4 in EtOH (v/v, 95:5) followed by heating.

3.2 Plant material

The roots of *I. racemosa* were collected in Datong County of Qinghai Province, China, in September 2009. It was identified by Dr Huan-Yang Qi, and the voucher specimen (ZY2010I01) has been deposited in the Key Laboratory for Natural Medicine of Gansu Province, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, China.

3.3 Extraction and isolation

The air-dried and powdered roots of *I. racemosa* (9.0 kg) were extracted with EtOH (3 × 3 h) at 60°C. The crude extract was mixed with H_2O (2 liters) to form a suspension and then partitioned successively with petroleum ether (60–90°C), EtOAc, and *n*-BuOH. The petroleum ether

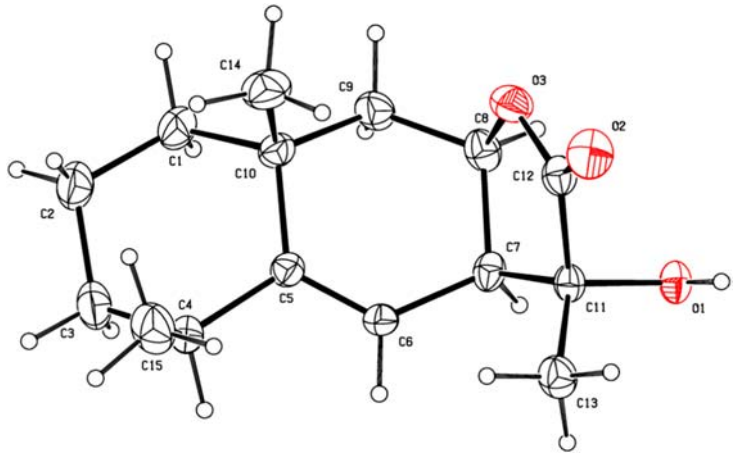

Figure 3. X-ray crystal structure of compound **2**.

and EtOAc soluble part (300 g) were subjected to silica gel CC eluted with petroleum ether–acetone (v/v) (100:1, 50:1, 30:1, 20:1, 10:1, 8:1, 5:1, 3:1, 2:1, 1:1, 0:100, and MeOH) to give eight fractions (Fr. 1–8). Fractions 2 and 3 (150 g) were separated by silica gel CC, using a petroleum ether–EtOAc gradient system, to give several sub-fractions. Further purification of each sub-fraction through repeated chromatography with petroleum ether–EtOAc (v/v, 10:1) gave compounds **3** (30 g), **4** (20 g), and **5** (10 g). Fractions 4 and 5 (10 g) were separated by silica gel CC, using a petroleum ether–acetone gradient system, to give seven sub-fractions (Fr. 4.1–4.7). Fraction 4.1 (1 g) through repeated chromatography with petroleum ether–acetone (v/v, 10:1) gave compound **8** (10 mg). Fraction 4.5 (1 g) was subjected to the CC eluting with petroleum ether–acetone (v/v, 5:1) to give compound **2** (30 mg). Fraction 4.6 (3 g) was purified through repeated chromatography with petroleum ether–acetone (v/v, 4:1) to give compounds **6** (13 mg) and **7** (20 mg), and with petroleum ether–acetone (v/v, 3:1) to give compounds **1** (5 mg) and **9** (9 mg).

*3.3.1 11,12,13-Trinoreudesm-5-en-7β,8α-diol (**1**)*

Pale gum; $[\alpha]_D^{20}$ −10 ($c = 0.2$, acetone); IR (KBr) ν_{max}: 3377, 2925, 2860, 1453, 1061, 1022, 683 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; ESI-MS *m/z* 219.2 $[M + Na]^+$; HR-ESI-MS for **1a** *m/z* 303.1560 $[C_{16}H_{24}O_4 + Na]^+$ (calcd for $C_{16}H_{24}O_4Na$, 303.1567); the ^1H NMR spectral data of compound **1a**, see Table 1.

*3.3.2 Crystallographic data of **2***

$C_{15}H_{22}O_3$, Mr = 250.33, trigonal, space group P3(2), $a = 23.821(8)$, $b = 23.821(8)$, $c = 6.545(3)$ Å, $V = 3216(2)$ Å^3, $Z = 9$, $D_{calc} = 1.163$ g/cm^3. The final *R*-value was 0.0482 ($R_w = 0.0926$ for 4858 reflections [$I > 2\sigma(I)$]. The detailed crystallographic data of **2** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers

Table 1. ^1H and ^{13}C NMR spectral data of compounds **1** and **1a** (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR, $CDCl_3$, *J* in Hz, δ in ppm).

	1		**1a**
Position	δ_H	δ_C	δ_H
1	1.42 (2H, m)	40.6	–
2	1.24 (2H, m)	17.9	–
3	1.50 (2H, m)	33.3	–
4	2.55 (1H, m)	38.7	2.52 (1H, m)
5	–	149.9	–
6	5.24 (1H, d, $J = 1.6$)	122.1	5.26 (1H, d, $J = 2.8$)
7	3.95 (1H, dd, $J = 1.6, 7.6$)	73.6	5.17(1H, dd, $J = 2.8, 5.2$)
8	3.51 (1H, ddd, $J = 4.4, 7.6, 12.0$)	71.7	4.94 (1H, ddd, $J = 4.4, 7.2, 11.8$)
9	1.60 (1H, dd, $J = 4.4, 13.2$)	45.3	–
	1.46 (1H, m)		
10	–	37.6	–
11	–	–	–
12	–	–	–
13	–	–	–
14	1.14 (3H, s)	29.0	1.16 (3H, s)
15	1.13 (3H, d, $J = 7.6$)	21.1	1.15 (3H, d, $J = 7.2$)
$COCH_3$	–		2.02 (3H, s, $COCH_3$)
	–		2.04 (3H, s, $COCH_3$)

CCDC 802257. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(0)1223 336033 or Email: deposit@ccdc.cam.ac.uk).

References

[1] Jiangsu College of New Medicine, *Jiangsu College of New Medicine, a Comprehensive Dictionary of the Traditional Chinese Medicines* (Suzhou Jiangsu, China, 1977), p. 627.
[2] T.J. Tsarong, *Tibetan Medicinal Plants* (Tibetan Medical Publications, Kalimpong, India, 1994).
[3] F. Bohlmann and W. Ang, *Phytochemistry* **24**, 1009 (1985).
[4] R. Goyal, B.R. Chhabra, and P.S. Kalsi, *Phytochemistry* **29**, 2341 (1990).
[5] P.S. Kalsi, R. Goyal, K.K. Talwar, and B.R. Chhabra, *Phytochemistry* **28**, 2093 (1989).
[6] M.M. Bokadia, A.J. Macleod, S.C. Mehta, B.K. Mehta, and H. Patel, *Phytochemistry* **25**, 2887 (1986).
[7] R.X. Tan, H.Q. Tang, J. Hu, and B. Shuai, *Phytochemistry* **49**, 157 (1998).
[8] T. Zhang, W. Xiao, T. Gong, Y. Yang, R.Y. Chen, and D.Q. Yu, *J. Asian Nat. Prod. Res.* **12**, 788 (2010).
[9] Y.Q. Yang, Master degree thesis, Henan University of Science and Technology at Luoyang, China, 2009.
[10] Y.M. Zhao, Master degree thesis, Hebei Medical University at Shijiazhuang, China, 2007.
[11] M.A. Al-Yahya, S. Khafagy, A. Shihata, J.F. Kozlowski, M.D. Antoun, and J.M. Cassady, *J. Nat. Prod.* **47**, 1013 (1984).
[12] A.T. Kulyyasov, T.S. Seitembetov, K.M. Turdybekov, and S.M. Adekenov, *Chem. Nat. Compd* **32**, 869 (1996).
[13] J.S. Mossa, F.S. El-Feraly, I. Muhammad, K. Zaw, Z.H. Mbwambo, J.M. Pezzuto, and H.H.S. Fong, *J. Nat. Prod.* **60**, 550 (1997).