Chemistry of Natural Compounds, Vol. 45, No. 3, 2009

SESQUITERPENE AND IRIDOIDS FROM *Valeriana pseudofficinalis* ROOTS

Bao-Kang Huang,[1*] Lu-Ping Qin,[1*] Yu-Ming Liu,[2]
Qiao-Yan Zhang,[1] and Han-Chen Zheng[1]

UDC 547.972

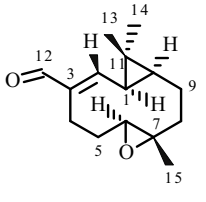
*A new sesquiterpene, named valeriene (**1**), along with three iridoids, namely valepotriate (**2**), dihydrovaltrate (**3**) and acevaltrate (**4**) were isolated from the ethyl acetate extract of* Valeriana pseudofficinalis *roots. The structures of these compounds were determined by 1D and 2D NMR, MS techniques, and X-ray single crystal diffractometry. This is the first report of the chemical components isolated from this plant.*

Key words: *Valeriana pseudofficinalis*, iridoids, valeriene, valepotriates.

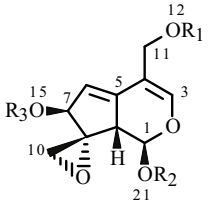
Valeriana officinalis L. (Valeriana) has a distribution nearly throughout Euroasia. The roots and rhizomes of it have been used in traditional medicine as a sedative for centuries. There are about 31 species of the Valeriana genus in China. Many iridoids associated with the sedative activity have been isolated from the roots and rhizomes of species in this genus [1, 2]. A new species, *Valeriana pseudofficinalis* C. Y. Chen, which is distinguished from *V. officinalis* both by its morphological and chemical characteristics, has been widely used for muscle aches and pains in China [3, 4]. In this work, our investigation on the EtOAc extract from *V. pseudofficinalis* roots resulted in the isolation of a new sesquiterpene, named valeriene (**1**), along with three known iridoids, namely valepotriate (**2**), dihydrovaltrate (**3**), and acevaltrate (**4**). All of components were isolated from *V. pseudofficinalis* for the first time. This present paper describes the structure elucidation of these compounds.

Valeriene (**1**) was isolated as a white crystal, mp 157–159°C; UV (MeOH, λ_{max}): 264 nm; ES-MS (*m/z*): 257 $[M+Na]^+$, 491 $[2M+Na]^+$; EI-MS (*m/z*): 234(M^+), 219 $(M-CH_3)^+$. The HREIMS spectrum of **1** showed the molecular ion at *m/z* 234.1623, which establishes the molecular formula as $C_{15}H_{22}O_2$ (calcd 234.1620) with five degrees of unsaturation. Its ^{13}C NMR (Table1) and DEPT spectrum indicated the presence of 15 carbons: three methyl carbons, four methylene carbons, three methine carbons, and three quaternary carbons.

The IR spectrum (KBr, 1672, 1629 cm^{-1}) and its ^{13}C NMR (δ 193.8, 155.2, 142.8) and DEPT indicated the presence of an α,β-unsaturated aldehyde. The HMBC spectrum shows the relations of δ 9.38 with 155.2, 142.8 ppm, δ 193.8 with δ 6.71, which indicated the presence of an α,β-unsaturated aldehyde.



1



2 - 4

2: $R_1 = COCH_3$, $R_2 = R_3 = COCH_2CH(CH_3)_2$
3: $R_1 = R_2 = COCH_2CH(CH_3)_2$, $R_3 = COCH_3$, 5,6-dihydro
4: $R_1 = COCH_3$, $R_2 = COCH_2\text{-}C(CH_3)_2\text{-}OCOCH_3$
$R_3 = COCH_2CH(CH_3)_2$

1) School of Pharmacy, Second Military Medical University, Shanghai 200433, P. R. China, fax: +086 21 81871301, e-mail: hbkcn@163.com; lpqin@smmu.edu.cn; 2) Research Center of New Drug, Naval Medical Research Institute, Shanghai 200433, P. R. China, fax: +086 21 81883187, e-mail: xiaoliu888627@sohu.com. Published in Khimiya Prirodnykh Soedinenii, No. 3, pp. 308–310, May–June, 2009. Original article submitted October 31, 2007.

0009-3130/09/4503-0363

TABLE 1. ^{13}C NMR (DEPT, 125 MHz) and ^{1}H NMR (500 MHz) Data of Compound **1** (δ, ppm, J/Hz)

C atom	δ_C	δ_H	DEPT	HMBC (C/H)
1	28.3	1.81 (1H)	CH	
2	155.2	6.71 (1H, d, J = 9.0)	CH	4, 11
3	142.8		C	
4	19.5	2.52 (1H); 2.41 (1H)	CH_2	
5	27.4	2.09 (1H, dd, J = 3.0, 13.0); 1.03 (1H)	CH_2	
6	61.3	2.95 (1H, dd, J = 3.0, 11.0)	CH	7
7	59.1		C	7, 9
8	21.2	1.77 (1H); 1.03 (1H)	CH_2	
9	39.4	2.03 (1H, dd, J = 5.0, 13.0); 1.04 (1H)	CH_2	7
10	37.9	1.09 (1H)	CH	13, 14
11	23.4		C	13, 14
12	193.8	9.38 (1H, s)	CH	2, 3, 4
13	27.6	1.14 (3H, s)	CH_3	11
14	15.1	1.21 (3H, s)	CH_3	11
15	16.8	0.84 (3H, s)	CH_3	7

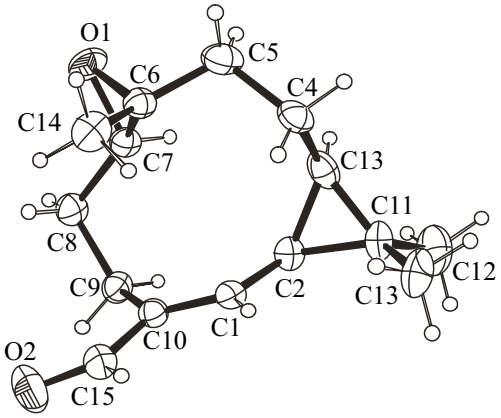


Fig. 1. The X-ray structure of compound **1**.

Its ^{1}H–^{1}H COSY spectrum shows the correlations of δ 6.71 (155.2, 2-CH) with δ 1.81 (28.3, 1-CH), δ 1.81 (28.3, 1-CH) with δ 1.09 (37.9, 10-CH), δ 1.09 (37.9, 10-CH) with δ 2.03 (39.4), δ 1.04 (39.4), δ 2.03 (39.4) with 1.77 (21.2), indicating the presence of the partial connectivities =CH-CH-CH-CH_2-CH_2, correlations δ 2.95 with δ 2.09, δ 1.03, δ 2.09 (27.4) with δ 2.52, δ 2.41, indicating the presence of the partial connectivities -O-CH-CH_2-CH_2.

In the HMBC spectrum, δ 6.71 correlated with 23.4; δ 1.14 and δ 1.21 correlated with δ 23.4 and δ 37.9, indicating the C1, C10, and C11 connecting the cyclic ring δ 2.03, 1.04 correlated with 59.1, δ 0.84 correlated with 59.1 and δ 61.3, indicating the connectivity of C6 (δ 61.3, CH) and C7 (δ 59.1, C). The ^{13}C chemical shifts of C6 and C7 shifted downfield indicated the connectivity of C6 and C7 with an oxygen bridge.

The NOESY spectrum shows the relations of δ 6.71 with 9.38, indicating the *trans* diene. Finally, the structure was confirmed by X-ray single crystal diffractometry (Fig. 1). Thus compound **1** was identified as 6,7-epoxy-3-methenyl- 11,11,7-trimethyl-[8.1.0]-2-hendecene, named valeriene.

EXPERIMENTAL

General Experimental Procedures. Melting points (mp) were determined by a Boetius-PHMK05 apparatus (Boetius, Germany) and were uncorrected. UV spectra were measured on a Shimadzu UV-2452 spectrometer (Kyoto, Japan). IR spectra were obtained on KBr pellets using a Hitachi IR 270-50 spectrophotometer (Hitachi, Japan). The ^{1}H and ^{13}C NMR spectra were obtained on INOVA-500 and 125 MHz devices (Varian, San Francisco, USA) with TMS as an internal standard. ESI-MS

measurements were undertaken on an HP5989A spectrometer (Palo Alto, USA). X-ray structure studies were undertaken on a Bruker-AXS SMART1000 CCD X-ray single crystal diffractometer (Bruker, Germany). TLC and column chromatography were performed on plates precoated with silica gel F254 and silica gel (200–300 mesh; Qingdao Marine Chemical Ltd., Qingdao, China), respectively. Solvents were analytical reagent grade.

Plant Materials. *V. pseudofficinalis* L. was collected from Jinfo Mountain, Nanchuan District of Chongqin in China (N:28°52.345′, E: 107°27.109′, Alt 1480 m), and authenticated by Prof. Hanchen Zheng, Second Military Medical University. The voucher specimens were deposited at the Herbarium of Department of Pharmacognosy, Second Military Medical University, Shanghai, P. R. China (No. 2005028).

Extraction and Isolation. Air-dried and course powders of *Valeriana pseudofficinalis* roots (8 kg) were extracted three times with 95% ethanol under reflux. After removal of the solvent by evaporation, the extracts were partitioned between EtOAc and H_2O to afford an EtOAc-soluble portion (65.8 g). A part (42.5g) of the EtOAc-soluble portion was chromatographed on a silica gel (300–400 mesh; 1500 g) column, eluting with a petroleum ether–EtOAc mixture to afford 30 fractions. Fraction 5 was separated by column chromatography over silica gel (300–400 mesh; 800 g) eluted with an ethyl ether– EtOAc gradient (6:1) to obtain compound **1** (80 mg). Fractions 15–18 (1.8 g) were further separated by CC (3×80 cm) over silica gel eluted with ethyl ether–EtOAc (30:1~1:1) to yield compounds **2** (26 mg) and **3** (35 mg). Fraction 24 (1.7 g) was subjected to repeated chromatographic separation and purification to give compound **4** (18 mg). The monocrystal was obtained by cooling the saturated solution of methanol, and its structure was confirmed by X-ray analysis on a single crystal.

Compound 1: colorless crystal ($CHCl_3$), mp 157–159°C; UV (MeOH, λ_{max}, nm): 264; IR (KBr, cm^{-1}): 2924, 1672, 1628, 1444, 1206, 1129, 1034, 877, 759; ESI-MS (*m/z*): 257 $[M+Na]^+$, 491 $[2M+Na]^+$; EI-MS (*m/z*): 234 (M^+), 219 $(M-CH_3)^+$; HR-EI-MS *m/z*, 234.1623 [calcd for $C_{15}H_{22}O_2$, 234.1620]; ^1H NMR, ^{13}C NMR spectral data are given in Table 1. The results of the X-ray crystallographic analysis are shown in Fig. 1.

Compound 2: yellow oil; UV (MeOH, λ_{max}, nm): 202, 256; IR (KBr, cm^{-1}): 2959, 2927, 1735, 1639, 1609, 1289, 1226, 1144, 1089; MS (*m/z*): 422 (M^+), 321, 261, 219, 191; ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.98 (3H, s, H-19), 1.00 (3H, s, H-20), 1.10 (3H, s, H-25), 1.15 (3H, s, H-26), 2.08 (3H, s, H-14), 2.10–2.25 (6H, m, H-17, 18, 23, 24), 2.90, 3.02 (2H, d, [AB], J = 4.9, H-10), 3.44 (1H, dd, J_1 = 10.1, J_2 = 2.6, H-9), 4.66, 4.75 (2H, d, [AB], J = 12.2, H-11), 5.36 (1H, d, J = 2.9, H-6), 5.85 (1H, t, $J_1 = J_2$ = 2.8, H-7), 5.98 (1H, d, J = 10.1, H-1), 6.70 (1H, s, H-3); ^{13}C NMR ($CDCl_3$, δ, ppm): 20.9 (C-14), 22.2 (C-25, C-26), 22.3 (C-19, C-20), 25.5 (C-24), 25.8 (C-18), 43.0 (C-9, C-23), 43.3 (C-17), 47.9 (C-10), 60.8 (C-11), 64.1 (C-8), 83.0 (C-7), 92.5 (C-1), 108.4 (C-4), 118.6 (C-6), 140.9 (C-5), 148.4 (C-3), 170.2 (C-16), 170.9 (C-22), 172.4 (C-13) [5, 6].

Compound 3: white needle crystal (ether–hexane 1:9), mp 62–63°C; UV (MeOH, λ_{max}, nm): 202; IR (KBr, cm^{-1}): 2960, 2872, 1764, 1730, 1670, 1434, 1376, 1250, 1090, 1023; MS (*m/z*): 425 (M^+), 323, 221, 179, 161, 133; ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.98, 0.95 (6H, s, H-16, 17, 25, 26), 2.00 (3H, s, H-20), 2.19, 2.21 (2H, m, H-15, H-24), 2.23 (4H, d, J = 6.56, H-14, 23), 2.24 (2H, m, H-6), 2.72 (1H, dd, J_1 = 5.33, J_2 = 5.35, H-9), 2.83, 3.07 (2H, [AB], J = 4.91, H-10), 2.97 (1H, m, H-5), 4.46, 4.69 (2H, [AB], J = 12.29, H-11), 4.95 (1H, t, J = 5.72, H-7), 5.83 (1H, d, J = 5.36, H-1), 6.5 (1H, s, H-3); ^{13}C NMR ($CDCl_3$, δ, ppm): 21.0 (C-20), 22.3 (C-16, 17, 25, 26), 25.5 (C-24), 25.7 (C-15), 32.5 (C-5), 35.1 (C-6), 39.5 (C-9), 43.2 (C-23), 43.3 (C-14), 48.7 (C-10), 63.3 (C-11), 64.1 (C-8), 76.7 (C-7), 88.4 (C-1), 110.8 (C-4), 142.2 (C-3), 169.8 (C-19), 171.1 (C-22), 173.0 (C-13) [5–7].

Compound 4: white needle crystal (ether–hexane 1:9), mp 80–81; UV (λ_{max}, nm): 202, 256; IR (KBr): 2962, 1759, 1725, 1374, 1320, 1250, 1227, 1030, 970; MS (*m/z*): 480 (M^+), 421, 361, 321, 258, 247, 236,176, 148, 83; ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.98 (6H, d, J = 6.5, H-19, 20), 1.51 (6H, s, H-25, 26), 1.98 (3H, s, H-29), 2.06 (3H, s, H-14), 2.18 (3H, m, H-17,18), 2.87, 3.03 (1H, d, [AB], J = 4.8, H-10), 2.89 (2H, s, H-23), 3.41 (1H, dd, J_1 = 10, J_2 = 2.5, H-9), 4.65, 4.75 (2H, d, [AB], J = 12.3, H-11), 5.38 (1H, d, J = 2.63, H-6), 5.86 (1H, t, $J_1 = J_2$ = 2.70, H-7), 5.97 (1H, d, J = 10.1, H-1), 6.71 (1H, s, H-3); ^{13}C NMR ($CDCl_3$, δ, ppm): 20.9 (C-14), 22.2 (C-29), 22.3 (C-19, 20), 25.5 (C-18), 26.6 (C-25), 26.7 (C-26), 42.9 (C-9, C-17), 44.0 (C-23), 47.9 (C-10), 60.7 (C-11), 64.0 (C-8), 79.2 (C-24), 83.3 (C-7), 92.5 (C-1), 108.2 (C-4), 118.3 (C-6), 141.2 (C-5), 148.6 (C-3), 169.5 (C-28), 170.3 (C-16, C-22), 170.8 (C-13) [6, 8].

ACKNOWLEDGMENT

This research was funded by the National Natural Science Foundation of China (No. 30270152) and Shanghai-Unilever Research & Development Fund (No. 06SU07005).

REFERENCES

1. *Dictionary of Chinese Crude Drugs*, in: Chinese, Chiang Su New Medicinal College, Ed. Shanghai Scientific Technologic Publisher, Shanghai, 2003, p. 2631.
2. Huang Baokang, Zheng Hanchen, Qin Luping, Zheng Qinming, and Xin Hailiang, *J. Chin. Med. Mater*., **27**, No. 9, 632 (2004).
3. Chen Hubiao, Zhu Jianmin, Zhao Yuying, and Yan Benhou, *Chin. Trad. Pat. Med.*, **21**, No. 12, 652 (1999).
4. Chen Hubiao and Cheng Jingron, *Bull. Bot. Res*., **11**, No.3, 29 (1991).
5. P. W. Thies, *Tetrahedron*, **24**, No.1, 313 (1968).
6. P. W. Thies, E. Finner, and S. David, *Planta Med*., **41**, No.1, 15 (1981).
7. Nedyalka V. Handjieva, Nevena N. Mollova, and Simeon S. Popov, *Planta Med*., 198 (1987).
8. Zhang Renwei,Wu Huaxin, and Li Qinhua, *Acta Bot Yunnan*, **8**, No.1, 107 (1986).