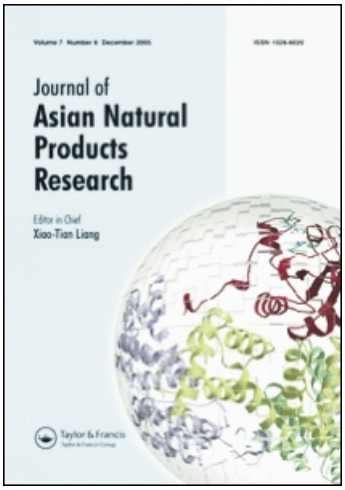

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A NEW CYCLOARTANE SAPONIN FROM *CIMICIFUGA ACERINA*

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A new cycloartane saponin along with two known compounds, cimigenol and cimigenol 3-*O*-β-D-xyloside, was isolated from the rhizomes of *Cimicifuga acerina* (Sieb. et Zucc.) Tanaka (Ranunculaceae). The structure of the new compound was elucidated as 3′-*O*-acetyl cimigenol 3-*O*-β-D-xyloside on the basis of chemical and spectral evidence.

Keywords: *Cimicifuga acerina*; Ranunculaceae; Cycloartane saponin; 3′-*O*-acetyl cimigenol 3-*O*-β-D-xyloside

INTRODUCTION

The rhizomes of the genus *Cimicifuga* (Ranunculaceae) are used to promote eruption, detoxicate and cure ptosis in traditional Chinese medicine [1]. The extract of *C. racemosa* (black cohosh) has been used successfully to treat menopausal symptoms in Europe and America [2]. A large number of cycloartane glycosides have been isolated from some *Cimicifuga* species [3,4]. As part of a continuing project on the investigation of triterpene glycosides of the Ranunculaceae plant [5–8], we now report the isolation and structure elucidation (Fig. 1) of a new cycloartane saponin (**1**), together with two known compounds cimigenol (**2**) and cimigenol 3-*O*-β-D-xylopyranoside (**3**) from *C. acerina* (Sieb. et Zucc.) Tanaka.

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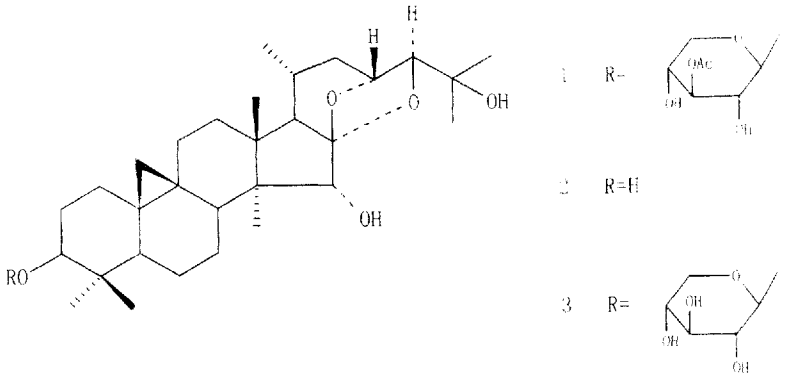

FIGURE 1 Structures of compounds **1**, **2** and **3**.

RESULTS AND DISCUSSION

Air-dried rhizomes of *C. acerina* were extracted with hot ethanol. The ethanol extract was subjected to silica gel column chromatography and afforded compounds **1**, **2** and **3**.

Compound **1** was isolated as white powder. The FAB-MS m/z: 685 $[M+Na]^+$ in combination with ^{13}CNMR data (Table I) gave its molecular formula as $C_{37}H_{58}O_{10}$. The ^{1}HNMR spectrum of **1** exhibited the presence of cyclopropane methylene at δ 0.28 and 0.50 (each 1H, d, $J=3.9$ Hz, 19-H), a secondary methyl group at δ 0.83 (3H, d, $J=6.4$ Hz, 21-H), six tertiary methyl groups at δ 1.00, 1.13, 1.17, 1.24, 1.46, 1.49, an acetyl group at δ 1.98, two methylene protons bearing oxygen at δ 4.73 (1H, d, $J=9.3$ Hz, 23-H) and 3.77 (1H, s, 24-H), and an anomeric proton at δ 4.83 (1H, d, $J=7.3$ Hz, 1′-H). The ^{13}CNMR spectrum of **1** showed the corresponding signals due to cyclopropane methylene at δ 30.8, methine carbons bearing oxygen at δ 71.8 (C-23), 88.7 (C-3) and 90.1 (C-24), an anomeric carbon at δ 107.1 (C-1′) and an acetyl group at δ 170.7 and 21.1, a quaternary carbons bearing oxygen at δ 70.9 (C-25) and a ketal carbon at δ 110.9 (C-16).

Upon hydrolysis with 0.5 N HCl or 5 N NH_4OH, **1** afforded cimigenol (**2**) and cimigenol 3-*O*-β-D-xylopyranoside (**3**), respectively, identified by direct comparison of the high performance thin layer chromatography (HPTLC) and NMR data with authentic samples.

It was obvious that **1** has an acetyl group by analysis of the NMR data. Further comparison of the ^{13}CNMR chemical shifts (Table I) of the sugar portion revealed that the signal due to C-3′ of xylose showed a downfield shift from δ 78.5 in **3** to δ 79.3 in **1**, and C-2′ and C-4′ signals exhibited

TABLE I ^{13}CNMR chemical shifts of compounds **1**, **2** and **3** (δ, in pyridine-d_5)*

C	1	2	3	C	1	2	3
1	32.3	32.5	32.4	20	24.0	23.9	24.0
2	30.0	30.9	30.1	21	19.4	19.4	19.4
3	88.7	77.8	88.5	22	38.1	38.0	38.1
4	41.2	40.9	41.8	23	71.8	71.7	71.8
5	47.5	47.3	47.5	24	90.1	90.0	90.1
6	20.9	21.2	21.0	25	70.9	70.8	70.9
7	27.1	27.0	27.1	26	25.6	26.2	25.6
8	48.5	48.6	48.6	27	25.3	25.2	25.3
9	20.0	19.8	19.9	28	11.7	11.7	11.7
10	26.4	26.7	26.4	29	26.3	26.0	26.3
11	26.6	26.4	26.6	30	15.3	14.7	15.4
12	34.0	33.9	34.0				
13	41.8	41.7	41.8	Xyl 1′	107.1		107.5
14	47.2	47.1	47.2	2′	73.0		75.5
15	80.1	80.1	80.1	3′	79.3		78.5
16	111.9	111.8	111.9	4′	69.2		71.2
17	59.5	59.4	59.5	5′	66.7		67.1
18	19.5	19.4	19.5	$OCOCH_3$	170.7		
19	30.8	31.2	30.8	$OCOCH_3$	21.1		

*Signals were assigned with the aid of DEPT, ^{1}H–^{1}H and ^{1}H–^{13}C COSY experiments. Xyl: β-D-Xylopyranosyl residue.

significant highfield shifts from δ 75.5 and 71.2 in **3** to δ 73.0 and 69.2 in **1**, respectively. Thus, the acetyl group in **1** must be linked to 3′-hydroxyl of xylose. The above results were also confirmed by HMBC experiment. In the HMBC spectrum of **1**, correlations were observed not only between 1′-H (δ 4.83) of xylose and C-3 (δ 88.7) of aglycone but also between 3′-H (δ 5.72) of xylose and an acetyl carbon (δ 170.7). All available evidence suggested that compound **1** is a new triterpene glycoside whose structure is 3′-*O*-acetyl cimigenol 3-*O*-β-D-xylopyranoside.

Compounds **2** and **3** have been reported in the previous literatures [9–11]. Their ^{13}CNMR data were measured and showed in Table I.

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were uncorrected. IR spectra were recorded as KBr discs. The NMR spectra were run at 400 MHz spectrometer with TMS as an internal standard. The FAB-MS spectra were recorded in NBA matrix in the positive ion mode on a Finnigan MAT TSQ 7000 spectrometer. TLC was carried out using GF_{254}. Vanillin–H_2SO_4 (saponin, sapogenin) and thymol–H_2SO_4 (sugar) were used as staining reagents.

Plant Materials

The rhizomes of *C. acerina* were collected in Shi-Tai, Anhui province of China in September 1996, and authenticated by Mr. Lin Tianxin. A voucher specimen has been deposited in the herbarium of China Pharmaceutical University.

Extraction and Isolation

The air-dried rhizomes (4.0 kg) of *C. acerina* were successively extracted three times with 95% EtOH for 3 h each under reflux. The EtOH extract was evaporated to dryness and the residue was dissolved in water and fractionated by successive extraction with petroleum ether (1000 ml × 3), EtOAc (1000 ml × 3) and n-BuOH (1000 ml × 3) to give a petroleum ether-soluble fraction (*ca.* 8 g), an EtOAc-soluble fraction (*ca.* 340 g) and a n-BuOH-soluble fraction (*ca.* 30 g). The EtOAc-soluble fraction (*ca.* 200 g) was subjected to column chromatography on silica gel using petroleum ether–EtOAc (100 : 0–1 : 1) and gave compound **1** (15 mg), **2** (1200 mg), and **3** (1500 mg).

Compound **1** White powder, m.p. 260–262°C. FAB-MS *m/z*: 685 $[M+Na]^+$. IR ν_{max}^{KBr} cm^{-1} : 3450, 2940, 1734, 1630, 1060, 992. ^{1}HNMR (pyridine-d_5) δ: 0.28 and 0.50 (each 1H, d, $J = 3.9$ Hz, 19-H), 0.83 (3H, d, $J = 6.4$ Hz, 21-H), 1.00 (3H, s, 30-H), 1.13 (3H, s, 18-H), 1.17 (3H, s, 28-H), 1.24 (3H, s, 29-H), 1.46 (3H, s, 27-H), 1.49 (3H, s, 26-H), 1.98 (3H, s, acetyl group), 3.46 (1H, dd, $J = 11.5, 4.2$ Hz, 3-H), 3.77 (1H, s, 24-H), 4.23 (1H, m, 15-H), 4.73 (1H, d, $J = 9.3$ Hz, 23-H), 4.83 (1H, d, $J = 7.3$ Hz, 1′-H), 4.03 (1H, m, 2′-H), 5.72 (1H, t, $J = 9.2$ Hz, 3′-H), 3.74 and 4.30 (each 1H, m, 5′-H). ^{13}CNMR data see Table I.

Acid Hydrolysis of 1

A solution of **1** (8 mg) in 50% MeOH containing 0.5 N HCl was heated under reflux for 2 h and neutralized with Na_2CO_3. The neutralized solution was extracted with EtOAc. The EtOAc solution was subjected to chromatographic separation over silica gel using $CHCl_3$–CH_3OH (99 : 1–9 : 1) as eluent to yield colorless needles, which was identified as cimigenol by comparison of IR and NMR with that of compound **2**. The water layer was examined by HPTLC to show the presence of xylose.

Alkaline Hydrolysis of 1

A solution of **1** (2 mg) in 50% MeOH containing 5 N NH_4OH was heated under reflux for 5 h. The reaction mixture was neutralized with 1% HCl and

extracted with EtOAc. The EtOAc layer showed the presence of cimigenol 3-*O*-β-D-xylopyranoside by comparison of HPTLC with compound **3**.

Compound **2** Colorless needles, m.p. 232–234°C. IR ν_{max}^{KBr} cm^{-1}: 3446, 3030, 2959, 1630, 1452, 1376. ^{1}HNMR (pyridine-d_5) δ: 0.35 and 0.60 (each 1H, d, $J=3.9$ Hz, 19-H), 0.88 (3H, d, $J=7.5$ Hz, 21-H), 1.11 (3H, s, 30-H), 1.19 (3H, s, 18-H), 1.21 (3H, s, 28-H), 1.23 (3H, s, 29-H), 1.48 (3H, s, 27-H), 1.50 (3H, s, 26-H), 3.55 (1H, dd, $J=11.5$, 4.4 Hz, 3-H), 3.79 (1H, d, $J=0.5$ Hz, 24-H), 4.30 (1H, brs, 15-H), 4.78 (1H, brd, $J=8.7$ Hz, 23-H). ^{13}CNMR data see Table I.

Compound **3** White powder, m.p. 262–265°C. FAB-MS *m/z*: 621 $[M+H]^+$, 643 $[M+Na]^+$. IR ν_{max}^{KBr} cm^{-1}: 3450, 2928, 2850, 1625, 1381, 1060. ^{1}HNMR (pyridine-d_5) δ: 0.26 and 0.50 (each 1H, d, $J=3.9$ Hz, 19-H), 0.83 (3H, d, $J=7.3$ Hz, 21-H), 1.04 (3H, s, 30-H), 1.12 (3H, s, 18-H), 1.17 (3H, s, 28-H), 1.29 (3H, s, 29-H), 1.45 (3H, s, 27-H), 1.48 (3H, s, 26-H), 3.50 (1H, dd, $J=11.7, 4.4$ Hz, 3-H), 4.73 (1H, d, $J=9.3$ Hz, 23-H), 3.75 (1H, s, 24-H), 4.85 (1H, d, $J=7.3$ Hz, 1′-H), 4.15 (1H, t, $J=9.0$ Hz, 3′-H). ^{13}CNMR data see Table I.

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