Notes

Two New Cyclolanostanol Xylosides from the Aerial Parts of *Cimicifuga dahurica*

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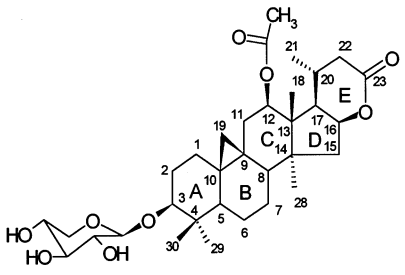
From the aerial parts of *Cimicifuga dahurica*, two new cyclolanostanol xylosides, cimilactone A (**1**) and cimilactone B (**2**), and three known compounds were isolated. On the basis of spectral and chemical evidence, the structures of **1** and **2** were determined to be 12*β*-acetoxy-3*β*-*O*-D-xylopyranosyloxy-24,25,-26,27-tetranor-9,19-cyclolanost-16,23-lactone (**1**) and 12*β*-acetoxy-3*β*-*O*-D-xylopyranosyloxy-24,25,26,27-tetranor-9,19-cyclolanost-7-ene-16,23-lactone (**2**). The known compounds were identified as cimigenol 3-*O*-*β*-D-xylopyranoside, 23-*O*-acetylshengmanol-3-*O*-*β*-D-xylopyranoside, and 25-*O*-acetylcimigenol-3-*O*-*β*-D-xylopyranoside, respectively.

The dried rhizomes of *Cimicifuga dahurica* (Turcz.) Maxim. (Ranunculaceae) are used as the traditional medicine "Sheng Ma" and are included in the *Chinese Pharmacopeia* (2000 edition).[1] This drug is used as a cooling and detoxifying agent and for the treatment of some types of headache.[1] Its chemical constituents have been investigated, and several phenolic glycosides[2] and triterpenoid saponins[3] were isolated and identified. We wish to report from the aerial parts of *C. dahurica* two new cyclolanostanol xylosides, cimilactones A (**1**) and B (**2**), together with the known xylosides cimigenol 3-*O*-*β*-D-xylopyranoside, 23-*O*-acetylshengmanol-3-*O*-*β*-D-xylopyranoside, and 25-*O*-acetylcimigenol-3-*O*-*β*-D-xylopyranoside. This paper deals with the isolation and structural elucidation of the compounds **1** and **2**.



	R
1	—
2	$\Delta^{7,8}$

Cimilactone A (**1**) was obtained as colorless needles, mp 255−256 °C (MeOH), $[\alpha]_D^{20}$ −36.7 °(*c* 0.75, $CHCl_3$−MeOH, 1:1). Its molecular formula was determined to be $C_{33}H_{50}O_9$ (*m*/*z* 613.3345 $[M + Na]^+$, calcd 613.3347) by positive high-resolution secondary-ion mass spectrometry (HRSIMS). The IR spectrum of **1** showed a broad hydroxyl band (3650−3200 cm^{-1}, 1090, 1045 cm^{-1}) and absorptions at 1740, 1720, 1290, 1255 cm^{-1} due to two carbonyl groups. In the ^1H NMR spectrum (Table 1), two characteristic cyclopropane protons at *δ* 0.19 and 0.55 (each 1H, d, *J* = 4.0 Hz), an acetyl methyl group at *δ* 2.11, four singlet methyl signals at *δ* 0.83, 1.00, 1.23, and 1.31, a secondary methyl signal at *δ* 0.95, and three oxygen-bearing methine groups at *δ* 3.45, 4.78, and 5.05, as well as the signals of a sugar unit at *δ* 3.73, 4.05, 4.15, 4.21, and 4.35 and an anomeric proton at 4.84 (1H, d, *J* = 7.5 Hz), were observed. On acid hydrolysis, D-xylose was detected from the aqueous fraction by TLC analysis (*n*-BuOH−AcOH−H_2O, 4:1:1) and by comparing with an authentic sample. Analysis of the data obtained led to the conclusion that **1** is a cyclolanostanol-type xyloside. Comparison of ^{13}C NMR data of **1** with 27-deoxyactein,[4] which was clarified very recently as 23-*epi*-26-deoxyactein,[5] showed similar chemical shifts except for the signals assignable to C-16, C-17, and the side chain from C-23 through C-27. This suggested that the A−D rings, the cyclopropane ring, and the substituents at C-3 and C-12 were the same for these two compounds. The ^{13}C NMR spectrum of **1** showed 33 signals, which were assigned with the aid of 2D NMR ($^1H-^1H$ COSY, HMQC, HMBC spectra) including a methylene carbon ascribable to a cyclopropane ring at *δ* 29.2 (C-19), methine carbons at *δ* 87.7 (C-3), 80.0 (C-16), and 76.2 (C-12), five carbons for the sugar unit, and two carbonyl groups at *δ* 173.3 (C-23) and 170.2 (−*C*$OOCH_3$). These data suggested that **1** is a tetranor-9,19-cyclolanostanol-3-*O*-*β*-D-xylopyranoside with an acetyl group at C-12 and an ester carbonyl at C-23, resulting from a loss of four carbons, C-24 to C-27 of 23-*epi*-26-deoxyactein.

Considering the degree of unsaturation of **1** and the absorption band at 1740 cm^{-1} observed in its IR spectrum, this suggested that the oxygenated carbon signal appearing

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Table 1. NMR Spectral Data of Compounds **1** and **2** (500 MHz for ^{1}H and 125 MHz for ^{13}C in C_5D_5N, δ ppm, J in Hz)

	1[a]		**2**[a]	
position	^{13}C	^{1}H	^{13}C	^{1}H
1	31.5	1.09 (m), 1.51 (m)	30.2	1.11 (m), 1.56 (m)
2	29.5	1.87 (m), 2.27 (m)	29.5	1.86 (m), 2.24 (m)
3	87.7	3.45 (dd, J = 11, 4)	87.8	3.43 (dd, J = 11, 4)
4	40.8		40.4	
5	46.5	1.23 (m)	42.3	1.17 (m)
6	20.0	0.69 (m), 1.46 (m)	21.3	1.51 (m), 1.82 (m)
7	25.2	0.90 (m), 1.23 (m)	114.5	5.10 (d, J = 6)
8	45.5	1.59 (dd, J = 11.5, 5)	147.2	
9	19.7		21.4	
10	26.4		28.9	
11	36.0	1.15 (dd, J = 16, 3)	36.3	1.22 (m)
		2.69 (dd, J = 16, 9)		2.90 (dd, J = 16, 9)
12	76.2	5.05 (dd, J = 9, 3)	76.2	5.18 (d, J = 9)
13	48.2		47.8	
14	47.9		50.8	
15	43.4	1.80 (m), 1.96 (m)	42.7	2.15 (m), 2.21 (m)
16	80.0	4.78 (dd, J = 14, 7.5)	80.4	4.89 (dd, J = 13.5, 8)
17	53.2	2.13 (d, J = 7.5)	54.0	2.10 (d, J = 8)
18	12.9	1.23	14.7	1.26
19	29.2	0.19 (d, J = 4)	28.4	0.49 (d, J = 4)
		0.55(d, J = 4)		1.01[b]
20	26.4	1.99 (m)	26.8	2.01 (m)
21	21.6	0.95 (d, J = 6)	21.9	0.96 (d, J = 6)
22	38.2	2.25 (m), 2.45 (m)	38.5	2.27 (m), 2.45 (m)
23	173.3		173.5	
28	19.1	0.83	26.7	1.03
29	25.3	1.31	25.6	1.31
30	14.9	1.00	14.2	1.01[b]
CH_3CO	170.2		170.7	
CH_3CO	21.0	2.11	21.8	2.16
1′	107.2	4.84 (d, J = 7.5)	107.5	4.83 (d, J = 7.5)
2′	75.2	4.05 (t, J = 8.0)	75.6	4.03 (t, J = 8.0)
3′	78.3	4.15 (t, J = 8.5)	78.6	4.15 (t, J = 8.5)
4′	71.9	4.21 (m)	71.2	4.22 (m)
5′	66.8	3.73 (t, J = 11)	67.1	3.72 (t, J = 11)

[a] Signals were assigned by ^{1}H−^{1}H COSY, HMQC, NOESY, and HMBC spectra. [b] Signals overlapped.

at δ 80.0 (C-16) formed new lactone ring E with the carbonyl group at δ 173.3 (C-23). The ^{13}C NMR signal at δ 173.3 was assigned to C-23 by the long-range correlation between resonances of the carbonyl group at δ 173.3 and the protons at δ 2.25 and 2.45 (H-22) in the HMBC spectrum. The substituents at C-3 and C-12 in **1** must have the same configuration (β) as 23-*epi*-26-deoxyactein owing to the identical coupling constants of the geminal protons, and the coupling constants ($J_{16,17}$ = 7.5 Hz) suggested H-16 and H-17α to be *cis*-related.[6] The signal at δ 4.78 (H-16) gave cross-peaks with the signals at δ 0.83 (H-28) and 2.13 (H-17α) in the NOESY spectrum and served to finalize the assignment of the relative stereochemistry of **1**. From all of the above evidence, **1** was determined as 12β-acetoxy-3β-*O*-D-xylopyranosyloxy-24,25,26,27-tetranor-9,19-cyclolanost-16,23-lactone and has been named cimilactone A.

Cimilactone B (**2**) was obtained as colorless needles, mp >300 °C (MeOH), $[\alpha]_D^{20}$ −80.0° (*c* 0.50, $CHCl_3$−MeOH, 1:1), and the molecular formula was determined to be $C_{33}H_{48}O_9$ (*m*/*z* 611.3193 $[M + Na]^+$, calcd 611.3190) by positive HRSIMS. The IR spectrum of **2** showed a broad hydroxyl band (3650−3200 cm^{-1}, 1050 cm^{-1}) and absorptions at 1740, 1720, 1295, 1250 cm^{-1} due to one or more carbonyl groups. The ^{13}C NMR signals in **2** were assigned with the help of 2D NMR spectroscopy and were similar to those of **1** (Table 1), except for the signals of a C-7, C-8 double bond and their α-, β-, and γ-carbons (C-5 through C-10, and C-14 and C-28). By comparison of ^{13}C NMR data of **2** with **1** and the consideration of the substituent effects, the double bond could be assigned at C-7, C-8. On hydrolysis with 5% HCl, D-xylose was detected from the aqueous fraction by TLC analysis (*n*-BuOH−AcOH−H_2O, 4:1:1). On the basis of the interpretation of all of the 1D and 2D NMR assignments made, compound **2** was assigned as 12β-acetoxy-3β-*O*-D-xylopyranosyloxy-24,25,26,27-tetranor-9,19-cyclolanost-7-ene-16,23-lactone and has been named cimilactone B.

The known compounds cimigenol 3-*O*-β-D-xylopyranoside, 23-*O*-acetylshengmanol-3-*O*-β-D-xylopyranoside, and 25-*O*-acetylcimigenol-3-*O*-β-D-xylopyranoside were confirmed by comparison of their physical and spectral data with those published in the literature.[7,8]

Experimental Section

General Experimental Procedures. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Optical rotations were obtained on a Perkin-Elmer 341 polarimeter. IR spectra were recorded on a Perkin-Elmer 983G spectrometer. NMR spectra were recorded on a Bruker AM-500 (500 MHz) instrument, and chemical shifts were referenced to TMS. HRSIMS were measured on a Bruker APEX II mass spectrometer.

Plant Material. The aerial parts of *C. dahurica* were collected in Maojingba, Kalaqin Qi, Inner Mongolia Autonomous Region, People's Republic of China, in September 1999 and were identified by Associate Professor Ruile Pan of the Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College. A voucher specimen (XA-99-09) has been deposited at this same institute.

Extraction and Isolation. The powdered air-dried aerial parts of *C. dahurica* (14.5 kg) were extrated exhaustively with boiling 80% EtOH. The alcoholic solution was concentrated in vacuo to yield a syrup-like extractive (2 kg), which was mixed with siliceous earth (80−100 mesh, 2.2 kg) and eluted with hexane, EtOAc, and 95% EtOH to give three fractions, f_1 (160 g), f_2 (210 g), and f_3 (400 g).

Fraction f_2 was subjected to column chromatography over silica gel (100−200 mesh, 2500 g) and eluted with solvent mixtures of $CHCl_3$−MeOH [(100:0) to (50:50)], yielding eight fractions (1−8). Fraction 3 (12 g) was chromatographed on silica gel (100−200 mesh, 300 g), eluted with hexane−Me_2CO (7:3) as solvent, to afford three subfractions, 3a, 3b, and 3c. Subfraction 3a (1.1 g) was chromatographed on octadecylsilanized silicic acid (ODS) with MeOH−H_2O (5:1) to afford 23-*O*-acetylshengmanol-3-*O*-β-D-xylopyranoside (200 mg). Subfraction 3c (2 g) was chromatographed on ODS with MeOH−H_2O (5:1) to afford compound **1** (16 mg), compound **2** (22 mg), and 25-*O*-acetylcimigenol-3-*O*-β-D-xylopyranoside (120 mg). Fraction 4 (20 g) was chromatographed on silica gel (100−200 mesh, 300 g), eluted with $CHCl_3$−MeOH (95:5), to afford 30 subfractions. Cimigenol 3-*O*-β-D-xylopyranoside (30 mg) was obtained from fractions 16−18.

Cimilactone A (1): colorless needles, mp 255−256 °C (MeOH), $[\alpha]_D^{20}$ −36.7° (*c* 0.75, $CHCl_3$−MeOH, 1:1); IR (KBr) ν_{max} 3650−3200, 1740, 1720, 1290, 1255, 1090, 1045 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Table 1; positive HRSIMS *m*/*z* 613.3345 $[M + Na]^+$, calcd for $C_{33}H_{50}O_9Na$.

Cimilactone B (2): colorless needles, mp >300 °C (MeOH), $[\alpha]_D^{20}$ −80.0° (*c* 0.50, $CHCl_3$−MeOH, 1:1); IR (KBr) ν_{max} 3650−3200, 1740, 1720, 1295, 1250, 1050 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Table 1; positive HRSIMS *m*/*z* 611.3193 $[M + Na]^+$, calcd for $C_{33}H_{48}O_9Na$ 611.3190.

Cimigenol 3-*O*-β-D-xylopyranoside: white amorphous powder, mp 264−265 °C (MeOH); IR, ^{1}H NMR, and ^{13}C NMR data consistent with literature values;[7] FABMS *m*/*z* 621.4 $[M + H]^+$.

23-*O*-Acetylshengmanol-3-*O*-β-D-xylopyranoside: colorless needles, mp 283−285 °C (MeOH); IR, ^{1}H NMR, and ^{13}C NMR data consistent with literature values;[7] FABMS *m*/*z* 663.6 $[M + H]^+$.

25-*O*-Acetylcimigenol-3-*O*-β-D-xylopyranoside: colorless needles, mp 227−228 °C (MeOH); IR, ^{1}H NMR, and ^{13}C

NMR data consistent with literature values;[8] FABMS *m*/*z* 663.6 $[M + H]^+$.

Acid Hydrolysis of Compounds 1 and 2. Compounds **1** and **2** (each 5 mg) were refluxed with 5% HCl in MeOH (5 mL) for 8 h. Each mixture was diluted with H_2O and neutralized with Na_2CO_3. The neutral hydrolysate revealed the presence of D-xylose by TLC [*n*-BuOH−AcOH−H_2O (4:1:1)] when compared with an authentic sample. The authentic sample was purchased from the Pfanstienl Chemical Corporation, Waukengan, IL (lot no. 1279).

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References and Notes

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