Studies on the Constituents of *Cimicifuga* Species. XXI.[1] Two New Cyclolanostanol Xylosides, Bugbanosides A and B from *Cimicifuga simplex* WORMSK.

Akiko KUSANO,[a] Masayuki TAKAHIRA,[a] Makio SHIBANO,[a] Toshio MIYASE[b] and Genjiro KUSANO*,[a]

Osaka University of Pharmaceutical Sciences,[a] 4–20–1 Nasahara, Takatsuki, Osaka 569–1094, Japan, School of Pharmaceutical Sciences, University of Shizuoka,[b] 52–1 Yada, Shizuoka 422–8526, Japan.
Received December 26, 1997; accepted February 12, 1998

Two new cyclolanostanol xylosides, bugbanosides A and B, were isolated from the underground parts of *Cimicifuga simplex* WORMSK. (Ranunculaceae). Bugbanosides A and B were formulated as 20(*R*), 23(*R*), 24(*R*), 25(*S*), 26(*S* and *R*)-16β,23:23,26:24,25-triepoxy-1α,3β,26-trihydroxy-9,19-cyclolanost-7-ene 3-*O*-β-D-xylopyranoside and 20(*R*), 23(*R*), 24(*R*), 25(*S*), 26(*S* and *R*)-16β,23:23,26:24,25-triepoxy-1α,3β,26-trihydroxy-9,19-cyclolanostane 3-*O*-β-D-xylopyranoside respectively, by spectroscopic and chemical methods.

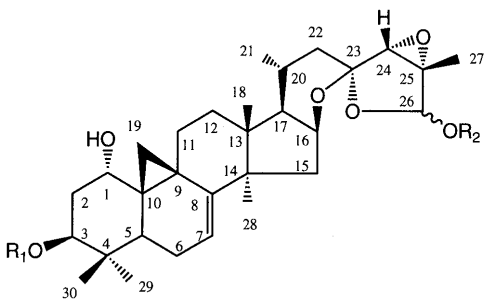
Key words *Cimicifuga simplex*; Ranunculaceae; 9,19-cyclolanostane; epoxyhemiacetal; xyloside; bugbanoside A—B

Cimicifuga (*C.*) *simplex* WORMSK. (Ranunculaceae) is one of the parental plants of *Cimicifuga* Rhizoma, which has been used as an anti-inflammatory, analgesic, and antipyretic in Japanese and Chinese folk medicine and traditional Chinese medicine. During a series of chemical investigations of *Cimicifuga* species, we have reported many triterpenic glycosides from the aerial and underground parts of *C. simplex*.[1,2] In continuing this work, we isolated two new cyclolanostanol xylosides, bugbanosides A and B, from the underground parts of *C. simplex*, which are characteristic constituents of *C. simplex* along with cimicifugoside.[1] This paper deals with the isolation and structural elucidation of these xylosides.

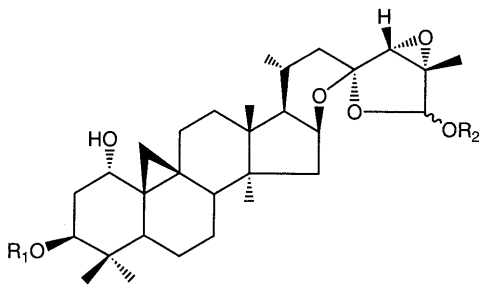
Bugbanosides A (**1**) and B (**2**) were obtained as described in the experimental section by repeated chromatography on octadecylsilanized silicic acid (ODS) and silica-gel (SiO_2) columns, and HPLC of the methanol extract of the underground parts of *C. simplex*.

Bugbanoside A (**1**) was obtained as colorless needles, mp 205—206 °C, $[\alpha]_D$ −42.7°, and the molecular formula was determined to be $C_{35}H_{52}O_{10}$ on the basis of positive secondary ion mass spectroscopy (pos. SI-MS) *m/z*: 655 $(M+Na)^+$, 615 $(M-OH)^+$, high resolution (HR) SI-MS *m/z*: 615.3545 $(M-OH)^+$ and ^{13}C-NMR spectral data. The IR spectrum showed strong hydroxyl bands at 3250—3600 cm^{-1}. The ^{1}H- and ^{13}C-NMR signals were attributed by using ^{1}H–^{1}H correlated spectroscopy (COSY), ^{13}C–^{1}H COSY, heteronuclear multiple bond connectivity (HMBC), and rotating frame nuclear Overhauser effect (ROE) difference spectroscopy spectra.

Bugbanoside A (**1**) behaved as two epimeric compounds (**1***S* and **1***R*) in solution as is the case with cimicifugoside and actein.[1] The separation of **1***S* and **1***R* was achieved by HPLC [column, Cosmosil 10Ph (i.d. 8.0 × 250 mm); solvent, MeCN–H_2O (3:7); effluent rate, 2 ml/min; column temperature, 40 °C; t_R, 16′ and 22′], but evaporation of the solvent *in vacuo* regenerated the same mixture of **1***S* and **1***R* (ratio = *ca.* 3:1). Then, spectroscopic analysis was carried out on the mixture. The ^{1}H-NMR spectra of **1** showed distinct signals and satellites (3:1) due to H-7, H-15, H-18, H-19, H-21, H-24, H-26, H-27, H-28, H-29 and H-30 as indicated with underlines in Table 1, while the other protons were found as homogeneous signals. The major signals were assigned to **1***S* and the satellite signals to **1***R* by ROEs and in the light of the solvent (pyridine-d_5) effect[3]: the major signals at δ_H 3.86 and 1.75 were assigned to H-24 and H-27 of **1***S* by paramagnetic effects of the 26β-hydroxy group, while the



1*S* : R_1 = β-D-xyl(p), R_2=H (26β-OH)
1*R* : R_1 = β-D-xyl(p), R_2=H (26α-OH)
1a*S* : R_1=H, R_2=H (26β-OH)
1a*R* : R_1=H, R_2=H (26α-OH)
1b*S* : R_1 = β-D-xyl(p), R_2=Me (26β-OMe)
1b*R* : R_1 = β-D-xyl(p), R_2=Me (26α-OMe)



2*S* : R_1 = β-D-xyl(p), R_2=H (26β-OH)
2*R* : R_1 = β-D-xyl(p), R_2=H (26α-OH)
2a*S* : R_1=H, R_2=H (26β-OH)
2a*R* : R_1=H, R_2=H (26α-OH)
2b*S* : R_1 = β-D-xyl(p), R_2=Me (26β-OMe)
2b*R* : R_1 = β-D-xyl(p), R_2=Me(26α-OMe)

Fig. 1. Structures of Bugbanosides A (**1**), B (**2**) and Their Derivatives

* To whom correspondence should be addressed.

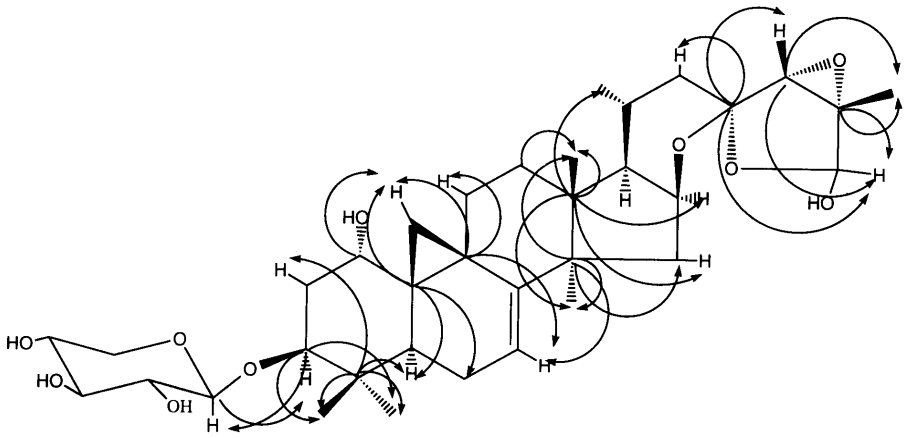


Fig. 2. Selected Correlations Observed in HMBC Spectra of Bugbanoside A (**1**)

Table 1. ^{1}H-NMR Data of **1**, **2** and Their Derivatives

	1*S*	**1***R*	**1a***S*	**1a***R*	**1b***S*	**1b***R*	**2***S*	**2***R*	**2a***S*	**2a***R*	**2b***S*	**2b***R*
1	3.93 s	3.93 s	3.95 s	3.95 s	3.94 s	3.95 s	3.81 s	3.81 s	3.82 s	3.83 brs	3.81 s	3.81 brs
2	2.25, 2.74	2.25, 2.74	2.23, 2.40	2.23, 2.40	2.26, 2.74	2.26, 2.75	2.23, 2.69	2.23, 2.69	2.19, 2.38	2.19, 2.38	2.22, 2.70	2.23, 2.70
3	4.39	4.39	4.42	4.42	4.39 dd (12.0, 4.0)	4.40 dd (12.0, 4.2)	4.33	4.33	4.37	4.37	4.33 dd (12.0, 4.1)	4.33 dd (11.8, 4.2)
5	2.28	2.28	2.23	2.23	2.28	2.30	2.39	2.39	2.38	2.38	2.40 dd (12.0, 4.1)	2.41 dd (12.0, 4.5)
6	1.69, 1.93	1.69, 1.95	1.76, 2.00	1.76, 2.00	1.70, 1.98	1.70, 1.98	0.80, 1.60	0.80, 1.60	0.87, 1.66	0.87, 1.66	0.81, 1.62	0.83, 1.65
7	5.10 dd (7.9, 1.9)	5.18 dd (7.9, 1.9)	5.13 dd (7.9, 1.9)	5.21 dd (7.9, 1.9)	5.18 dd (8.0, 2.0)	5.19 dd (8.0, 2.0)	1.18, 1.24	1.18, 1.24	1.18, 1.23	1.18, 1.23	1.25, 1.32	1.25, 1.34
8	—	—	—	—	—	—	1.63	1.63	1.68	1.68	1.64	1.66
11	1.44, 2.92	1.44, 2.92	1.53, 2.96	1.53, 2.96	1.52, 2.93	1.50, 2.93	1.42, 2.66	1.42, 2.66	1.46, 2.70	1.46, 2.70	1.42, 2.66	1.45, 2.68
12	1.78 (2H)	1.78 (2H)	1.74, 1.78	1.74, 1.78	1.75 (2H)	1.73 (2H)	1.58, 1.64	1.58, 1.64	1.62, 1.74	1.62, 1.74	1.58, 1.71	1.60, 1.71
15	1.79, 1.96	1.96, 2.14	1.78, 1.97	1.92, 2.18	1.88 dd (12.2, 8.0) 2.15	1.90 dd (12.0,7.8) 2.14	1.48, 1.78	1.58, 1.96	1.50 dd (12.5, 7.5) 1.80 dd (12.5, 7.5)	1.67 1.98 dd (12.5, 7.5)	1.55 1.94 dd (12.5, 8.0)	1.58 1.95 dd (12.5, 8.0)
16	4.67	4.67	4.69	4.69	4.63 ddd (7.8, 7.8, 7.8)	4.65 ddd (7.8, 7.8, 7.8)	4.59	4.59	4.60	4.60	4.53 ddd (8.0, 8.0, 8.0)	4.56 ddd (8.0, 8.0, 8.0)
17	1.58	1.58	1.59	1.59	1.59	1.58	1.58	1.58	1.60	1.60	1.62	1.59
18	1.23 s	1.24 s	1.27 s	1.28 s	1.22 s	1.23 s	1.25 s	1.25 s	1.27 s	1.27 s	1.23 s	1.24 s
19	0.68 d (4.0) 1.17 d (4.0)	0.69 d (4.0) 1.19 d (4.0)	0.73 d (4.0) 1.23 d (4.0)	0.75 d (4.0) 1.25 d (4.0)	0.68 d (4.0) 1.17 d (4.0)	0.69 d (4.0) 1.19 d (4.0)	0.38 d (4.0) 0.69 d (4.0)	0.39 d (4.0) 0.71 d (4.0)	0.44 d (4.0) 0.75 d (4.0)	0.45 d (4.0) 0.77 d (4.0)	0.38 d (4.0) 0.70 d (4.0)	0.39 d (4.2) 0.72 d (4.2)
20	1.84	1.84	1.86	1.86	1.84	1.80	1.84	1.84	1.86	1.86	1.80	1.76
21	0.95 d (6.3)	0.92 d (6.3)	0.96 d (6.5)	0.94 d (6.5)	0.94 d (6.5)	0.92 d (6.5)	0.92 d (6.0)	0.90 d (6.0)	0.92 d (6.5)	0.91 d (6.5)	0.91 d (6.5)	0.89 d (6.3)
22	1.64, 2.23	1.64, 2.23	1.70, 2.22	1.70, 2.22	1.60, 2.21	1.58, 2.24	1.63, 2.21	1.63, 2.21	1.64, 2.24	1.64, 2.24	1.59, 2.17	1.59, 2.20
24	3.86 s	3.72 s	3.87 s	3.73 s	3.78 s	3.65 s	3.87 s	3.73 s	3.88 s	3.74 s	3.76 s	3.66 s
26	5.71 s	5.72 s	5.72 s	5.74 s	5.03 s	5.23 s	5.70 s	5.71 s	5.17 s	5.63 s	5.04 s	5.20 s
27	1.75 s	1.60 s	1.76 s	1.60 s	1.59 s	1.52 s	1.75 s	1.59 s	1.75 s	1.60 s	1.59 s	1.51 s
28	1.05 s	1.10 s	1.08 s	1.13 s	1.12 s	1.12 s	0.91 s	0.96 s	0.93 s	0.98 s	0.98 s	0.98 s
29	1.41 s	1.42 s	1.29 s	1.30 s	1.40 s	1.42 s	1.39 s	1.41 s	1.29 s	1.30 s	1.40 s	1.41 s
30	1.11 s	1.12 s	1.15 s	1.16 s	1.10 s	1.12 s	1.08 s	1.10 s	1.12 s	1.13 s	1.08 s	1.10 s
OCH_3					3.47	3.57					3.47 s	3.55 s
1′	4.86 d (7.9)	4.86 d (7.9)			4.85 d (8.0)	4.86 d (8.0)	4.87 d (7.8)	4.87 d (7.8)			4.86 d (8.0)	4.87 d (8.0)
2′	4.02 dd (7.9, 8.1)	4.02 dd (7.9, 8.1)			4.01 dd (8.1, 8.0)	4.02 dd (8.0, 8.0)	4.01 dd (8.1, 7.8)	4.01 dd (8.1, 7.8)			4.01 dd (8.3, 8.0)	4.02 dd (8.2, 8.0)
3′	4.08 dd (8.1, 8.8)	4.08 dd (8.1, 8.8)			4.08 dd (8.5, 8.1)	4.09 dd (8.5, 8.0)	4.09 dd (8.1, 8.5)	4.09 dd (8.1, 8.5)			4.09 dd (8.5, 8.3)	4.10 dd (8.5, 8.2)
4′	4.18 ddd (10.0, 8.8, 5.0)	4.18 ddd (10.0, 8.8, 5.0)			4.18 ddd (10.8, 8.5, 5.0)	4.18 ddd (11.0, 8.5, 5.0)	4.18 ddd (10.0, 8.5, 5.0)	4.18 ddd (10.0, 8.5, 5.0)			4.17 ddd (10.5, 8.5, 5.3)	4.20 ddd (10.5, 8.5, 5.3)
5′	3.54 dd (11.1, 10.0) 4.21 dd (11.1, 5.0)	3.54 dd (11.1, 10.0) 4.21 dd (11.1, 5.0)			3.54 dd (11.0, 10.8) 4.20 dd (11.0, 5.0)	3.54 dd (11.0, 11.0) 4.21 dd (11.0, 5.0)	3.58 dd (11.3, 10.0) 4.22 dd (11.3, 5.0)	3.58 dd (11.3, 10.0) 4.22 dd (11.3, 5.0)			3.57 dd (10.8, 10.5) 4.22 dd (10.8, 5.3)	3.57 dd (11.0, 10.5) 4.23 dd (11.0, 5.3)

Obtained on a JEOL α-400 in pyridine-d_5. Underlines indicate distinct signals due to the isomers 26*S* and 26*R* in the solution.

Table 2. ^{13}C-NMR Data of **1**, **2** and Their Derivatives

	1*S*	**1***R*	**1a***S*	**1a***R*	**1b***S*	**1b***R*	**2***S*	**2***R*	**2a***S*	**2a***R*	**2b***S*	**2b***R*
1	72.15	72.15	72.36	72.36	72.17	72.18	72.39	72.39	72.56	72.56	72.43	72.41
2	37.88	37.88	38.98	38.98	37.89	37.90	37.90	37.90	39.02	39.02	37.91	37.91
3	83.99	83.99	72.73	72.73	84.01	84.01	84.36	84.36	73.13	73.13	84.39	84.38
4	40.74	40.74	40.52	40.52	40.76	40.76	41.48	41.48	41.24	41.24	41.51	41.50
5	36.39	36.39	36.23	36.23	36.35	36.39	40.14	40.14	40.05	40.05	40.15	40.13
6	21.54	21.54	21.84	21.84	21.57	21.57	20.69	20.69	20.98	20.98	20.73	20.73
7	113.22	113.22	113.40	113.51	113.34	113.37	26.33	26.33	26.34	26.34	26.23	26.22
8	150.18	150.18	149.78	149.78	149.76	150.17	47.55	47.60	47.60	47.68	47.58	47.58
9	21.95	21.95	21.99	21.99	21.97	21.97	20.59	20.59	20.65	20.65	20.67	20.68
10	33.12	33.12	33.45	33.45	33.14	33.16	31.06	31.06	31.36	31.36	31.06	31.08
11	25.09	25.09	25.19	25.19	25.10	25.07	25.90	25.90	25.96	25.96	25.91	25.81
12	33.14	33.14	33.17	33.17	33.14	33.10	33.36	33.36	33.38	33.38	33.37	33.31
13	44.01	44.01	44.03	44.06	44.01	44.06	46.53	46.70	44.55	46.65	46.68	46.66
14	50.00	50.08	50.04	50.11	50.13	50.10	44.70	44.70	44.70	44.70	44.69	44.73
15	42.61	42.71	42.63	42.72	42.72	42.67	44.06	44.20	44.08	44.19	44.14	44.10
16	73.43	73.43	73.45	73.50	73.60	73.66	73.26	73.26	73.26	73.35	73.42	73.49
17	57.20	57.15	57.23	57.18	57.15	57.07	56.88	56.88	56.90	56.88	56.84	56.76
18	22.95	22.95	22.99	22.99	22.95	22.96	20.64	20.64	20.64	20.60	20.59	20.57
19	28.16	28.16	28.28	28.30	28.20	28.21	29.94	29.94	30.10	30.15	29.95	29.94
20	26.26	26.26	26.28	26.40	26.40	25.88	26.18	26.18	26.08	26.08	26.31	25.86
21	20.48	20.45	20.49	20.45	20.43	20.42	20.48	20.40	20.43	20.43	20.41	20.40
22	37.43	37.43	37.46	37.00	37.23	36.72	37.50	37.50	37.60	37.20	37.39	36.86
23	106.15	103.70	106.17	103.71	106.51	104.33	106.12	103.60	106.13	103.67	106.48	104.29
24	63.56	63.00	63.57	62.99	62.48	61.97	63.57	63.80	63.58	63.02	62.50	62.00
25	65.52	63.90	65.53	63.90	64.59	62.48	65.50	63.90	65.51	63.91	64.58	62.47
26	98.62	98.20	98.52	98.23	103.98	103.38	98.50	98.21	98.49	98.21	103.95	103.36
27	13.05	13.10	13.06	13.13	12.67	13.06	13.06	13.10	13.06	13.13	12.68	13.05
28	26.79	26.85	26.81	26.88	26.90	26.88	19.54	19.60	19.56	19.61	19.62	19.61
29	25.87	25.87	26.23	26.23	25.87	25.93	25.81	25.85	26.20	26.20	25.83	25.99
30	13.54	13.54	12.82	12.82	13.54	13.56	14.66	14.66	14.02	14.02	14.67	14.68
OCH_3					54.96	56.36					54.92	56.33
1′	107.53	107.53			107.53	107.55	107.60	107.60			107.60	107.60
2′	75.64	75.64			75.65	75.65	75.63	75.63			75.63	75.63
3′	78.57	78.57			78.57	78.59	78.57	78.57			78.58	78.58
4′	71.20	71.20			71.20	71.22	71.22	71.22			71.23	71.23
5′	66.99	66.99			66.99	67.01	67.00	67.00			67.00	67.00

Measured at 100.4 MHz. Underlines indicate distinct signals due to the isomers 26*S* and 26*R* in the solution.

satellite signals at δ_H 3.72 and 1.60 were assigned to those of **1***R* by the weaker effect of the reversed 26α-hydroxy group. Thus, the other major signals were assigned to protons due to **1***S* and the satellite signals were assigned to those of **1***R* as in the case of cimicifugoside and actein.[1] The ^{13}C-NMR spectra (in pyridine-d_5) also showed some distinct signals and satellites attributed to C-14, C-15, C-17, C-21 and C-23—C-28 as indicated with underlines in Table 2.

^{1}H- and ^{13}C-NMR spectra of **1***S* indicated the presence of the following partial structures: a 1,3-dihydroxypropanyl moiety (H-1: δ 3.93, br s; C-: δ 72.15; H-2: δ 2.25, 2.74; C-2: δ 37.88, H-3: δ 4.39, C-3: δ 83.99), a trisubstituted double bond (H-7: δ 5.10, dd, J=7.9, 1.9 Hz; C-7: δ 113.22, C-8: δ 150.18), a cyclopropane (H-19: δ 0.68, 1.17, each, d, J=4.0 Hz; C-19: δ 28.16), an isolated ethylene (H-11: δ 1.44, 2.92; C-11: δ 25.09; H-12: δ 1.78 (2H); C-12: δ 33.14), five tertiary methyl groups (H-18: δ 1.23, s; C-18: δ 22.95; H-27: δ 1.75, s; C-27: δ 13.05, H-28: δ 1.05, s; C-28: δ 26.79; H-29: δ 1.41, s; C-29: δ 25.87; H-30: δ 1.11, s; C-30: δ 13.54), a secondary methyl group (H-21: δ 0.95, d, J=6.3 Hz; C-21: δ 20.48), 16,23 : 23,26 : 24,25-triepoxyl moiety (H-16: δ 4.67; C-16: δ 73.43; C-23: δ 106.15; H-26: δ 5.71; C-26: δ 98.62; H-24: δ 3.86; C-24: δ 63.56, C-25: δ 65.52), a hemiacetal moiety (H-26, C-26, C-23), and β-xylopyranosyl moiety[1] (H-1′: δ 4.86, d, J=7.9 Hz; C-1: δ 107.53, other protons: δ 3.54—4.21; carbons: δ 66.99—78.59).

The connectivities of these partial structures were determined on the basis of the HMBC spectrum to establish the structure (**1***S*). As shown in Fig. 2, C-23 showed long-range correlations with H-24, H-26 and H-22 (δ_H 1.64); C-24 with H-27 and H-26; C-25 with H-26 and H-27; C-14 (δ_C 50.00) with H-28, H-18, H-15 (δ_H 1.79) and H-7; C-13 (δ_C 44.01) with H-21, H-18, H-28, H-15 and H-16; C-10 (δ_C 33.12) with H-19, H-6 (δ_H 1.93) and H-5 δ_HH 2.28); C-9 (δ_C 21.95) with H-19, H-11 (δ_H 1.44) and H-7; C-4 (δ_C 40.74) with H-29, H-30, H-2 and H-5; C-3 with H-30, H-29 and H-1′; C-1 with H-19; C-1′ with H-3. Similar signals and HMBC correlations were also observed in **1***R*. Markedly deshielded shifts of characteristic cyclopropane methylene groups were rationalized by the presence of a 1α-hydroxy group and 7,8-double bond.

The relative stereochemistry of **1***S* was determined on the basis of ROE difference spectra. Irradiation at H-18 and H-28 increased the signal intensities of H-15β (δ_H 1.79), H-20 (δ_H 1.84) and H-24, and H-17α (δ_H 1.54) and H-16α, respectively, and irradiation at H-27 increased those of H-24 and H-26. Similarly, irradiation at H-29 and H-30 increased those of H-3α, H-5α (δ_H 2.28), H-30

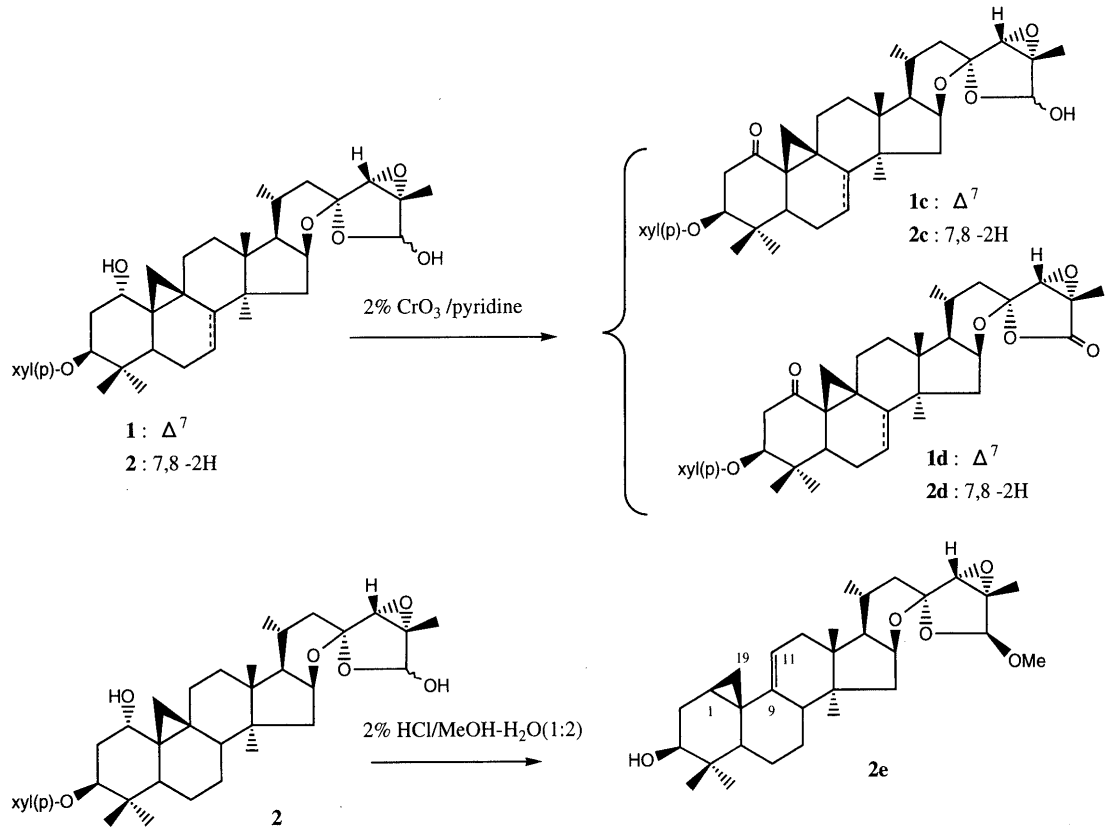


Fig. 3. Convertion of Bugbanosides A (**1**) and B (**2**)

and H-1′, and H-2β (δ_H 2.25) and H-29, respectively.

Based on a comparison of ^{1}H- and ^{13}C-NMR spectral data with those of cimicifugoside, it is proposed that **1** corresponds to a 1α-hydroxy-12-deacetoxy derivative of cimicifugoside.

Treatment of **1** with methanol containing *p*-toluenesulfonic acid gave two methyl ethers (**1b***S*, mp 191—192 °C, $C_{36}H_{54}O_{10}$, $[\alpha]_D$ −16.1° and **1b***R*, mp 179—180 °C, $C_{36}H_{54}O_{10}$, $[\alpha]_D$ −58.1°). The ^{1}H- and ^{13}C-NMR signals of both methyl ethers were assigned to **1b***S* and **1b***R* as shown in Tables 1 and 2 in the light of the data of 26(*S*)- and 26(*R*)-*O*-methylcimicifugoside, 26(*S*)- and 26(*R*)-*O*-methylactein.[1] ROEs were observed between H-24 and H-27, H-26 and H-27, H-17 and H-21, and H-16α and H-21 in the ROE difference spectra of **1b***S* and **1b***R*, suggesting that the relative stereochemistry of the side-chain moieties is present.

Treatment of **1** with Collin's reagent provided a keto compound (**1c**), mp 275—276 °C, $C_{35}H_{50}O_{10}$ and a ketolactone (**1d**), mp 220—221 °C, $C_{35}H_{48}O_{10}$. The mass spectrum of **1c** *m/z*: 631 $(M+H)^+$ indicated a didehydro derivative of **1**. The IR spectrum showed an absorption band at 1682 cm^{-1} due to a carbonyl group. The ^{1}H-NMR spectrum showed the absence of a carbinyl proton (H-1) and deshielded signals of H-19. The ^{13}C-NMR spectrum showed a signal at δ_C 208.70 due to a carbon of a newly introduced carbonyl group. These data suggested that **1c** should be a 1-keto derivative of **1** (Fig. 3). The circular dichroism (CD) spectrum of **1c** showed a negative Cotton effect ($\Delta\varepsilon_{285}$: −5.55) due to a 1-keto-cycloartane derivative.[4] The IR spectrum of **1d** showed a hydroxyl band at 3200—3600 cm^{-1}, an epoxy-γ-lactone band at 1786 cm^{-1},[5] and a carbonyl band at 1677 cm^{-1}. The ^{1}H-NMR spectrum showed the absence of carbinyl protons (H-1 and H-26). These data suggested that **1d** shoud be a 1-ketolactone of **1**. The CD spectrum of **1d** showed 2 negative Cotton effects ($\Delta\varepsilon_{285}$: −5.03 and $\Delta\varepsilon_{235}$: −10.90). The former Cotton effect was similar with that of **1c**, while the latter effect was similar to that of cimicifugenin A lactone,[5] namely $\Delta\varepsilon_{232}$: −5.84 at this time. Because the absolute stereostructure of cimicifugoside has been established,[1] the above data allowed us to conclude that **1** is a 9,19-cyclolanostane and the absolute steric configulation of the basic skeleton and side-chain moiety is 1(*S*), 3(*S*), 16(*S*), 20(*R*), 23(*R*), 24(*R*), 25(*S*), 26(*S* and *R*).

Treatment of **1** with Cellulase T [Amano] 4 provided a genuine aglycone **1a**, mp 159—160 °C, $C_{30}H_{44}O_6$, pos. HR-SI-MS *m/z*: 501.3214 $(M+H)^+$, $[\alpha]_D$ −41.1°. IR ($CHCl_3$) cm^{-1}: 3200—3600, which was formulated as 20(*R*), 23(*R*), 24(*R*), 25(*S*), 26(*S* and *R*)-16β,23 : 23,26 : 24,25-triepoxy-1α,3β,26-trihydroxy-9,19-cyclolanost-7-ene as shown in Fig. 1. All the ^{1}H- and ^{13}C-NMR signals could be assigned to this structure (Tables 1 and 2).

The sugar was identified as D-xylose by TLC, HPLC and an $[\alpha]_D$ +20.1° after hydrolysis of **1** with 2% HCl. The sugar connecting position (C-3) was identified by HMBC and the glycosylation shift of C-3 ($\Delta\delta$: 11.26 ppm) between **1** and **1a**. Thus, the stereostructure of **1** was formulated as 20(*R*), 23(*R*), 24(*R*), 25(*S*), 26(*S* and *R*)-16β,23 : 23,26 : 24,25-triepoxy-1α,3β,26-trihydroxy-9,19-cyclolanost-7-ene 3-*O*-β-D-xylopyranoside.

Bugbanoside B (**2**) was obtained by preparative HPLC along with **1** as colorless needles, mp 244—245 °C, $[\alpha]_D$

$-21.3°$, and the molecular formula was determined to be $C_{35}H_{54}O_{10}$ by pos. SI-MS *m/z*: 657 $(M+Na)^+$, 617 $(M-OH)^+$, pos. HR-SI-MS *m/z*: 617.3683 $(M-OH)^+$ and ^{13}C-NMR spectral data. The IR spectrum showed strong hydroxyl bands at 3250—3600 cm^{-1}. The ^1H- and ^{13}C-NMR signals were similar to those of **1** except for the absence of a 7(8)-double bond (Tables 1 and 2). Some signals were found with a third high satellite due to the C26 is omerism, and then the higher signals were attributed to **2***S* and the lower ones to **2***R* as in **1**.

Two methyl ethers (**2b***S* and **2b***R*) were prepared as in **1** and their NMR signals are summarized in Tables 1 and 2. Collin's oxidation of **2** provided a 1-keto derivative (**2c**) (Fig. 3), mp 217—218 °C, $C_{35}H_{52}O_{10}$, and 1-ketolactone (**2d**), mp 207—208 °C, $C_{35}H_{50}O_{10}$. The IR and ^1H-NMR spectra of **2c** and **2d** indicated the 1-keto and 1-ketolactone of **2**, as in **1c** and **1d**. The CD spectrum of **2c** showed a negative Cotton effect ($\Delta\varepsilon_{290}$: -1.45), and that of **2d** showed 2 negative Cotton effects ($\Delta\varepsilon_{288}$: -1.11 and $\Delta\varepsilon_{225}$: -7.19), establishing the absolute stereostructure.

Treatment of **2** with cellulase provided a genuine aglycone (**2a**), mp 152—153 °C, $[\alpha]_D$ $-2.5°$, $C_{30}H_{46}O_6$, pos. HR-SI-MS *m/z*: 502.3285 $(M)^+$ as in **1**. Treatment of **2** with 2% HCl provided D-xylose ($[\alpha]_D$ $+21.6°$) and a rearranged aglycone (**2e**). A concerted elimination–rearrangement mechanism from 1α-hydroxy-9,19-cyclolanostane glycosides to 1,19-cyclolanost-9(11)-ene derivatives has been reported.[6] The characteristic ^1H- and ^{13}C-NMR signals due to a 1,19-cyclopropane methylene group and 9(11)-double bond were found in the spectra of **2e** and suggested the presence of a 1α-hydroxy group in **2** (Fig. 3). The sugar connecting position was identified by HMBC and there was a glycosylation shift of C-3 ($\Delta\delta$: 11.26 ppm). Thus, the absolute stereostructure of **2** was formulated as 20(*R*), 23(*R*), 24(*R*), 25(*S*), 26(*S* and *R*)-16β,23 : 23,26 : 24,25-triepoxy-1α,3β,26-trihydroxy-9,19-cyclolanostane 3-*O*-β-D-xylopyranoside (a 7,8β-dihydro derivative of bugbanoside A (**1**)).

It is interesting that *C. simplex* contains a second group of xylosides with a 16β,23 : 23,26 : 24,25-triepoxy group as a side-chain, following a first group of actein from *C. racemosa*,[7] cimicifugoside and actein from *C. simplex*,[1,2] and acetylacteol-3-*O*-arabinoside from *C. foetida*.[8] Bugbanosides A and B along with cimicifugoside seem to be characteristic compounds of *C. simplex*, because they have not yet been detected in *C. acerina*, and *C. japonica* and some other *Cimicifuga* species. Studies on the biological activities such as nucleoside tranport inhibition of the second group of the xylosides are in progress.[9]

Experimental

General The instruments used in this investigation were as follows: a Yanagimoto micromelting apparatus (for melting points, uncorrected); a JASCO DIP-1000 digital polarimeter (for specific rotation, measured at 23 °C); a JASCO J-500 spectrometer (for CD, measured at 23 °C); a Perkin–Elmer 1720X-FT IR spectrometer (for IR spectra); a Hitachi M-80 spectrometer (for MS spectra); and a Varian Gemini-200, a JEOL α-400 and a Varian Unity-INOVA-500 instrument (for NMR spectra, measured in pyridine-d_5 solution containing a few drops of D_2O, on the δ scale using tetramethylsilane as an internal standard). Column chromatography was carried out on silica-gel (Wakogel C-200) and ODS-A (YMC) columns. HPLC was carried out using a Gilson 305 pump equipped with a JASCO 830-RI detector. Silica-gel 60 F_{254} (Merck) precoated TLC plates were used and detection was carried out by spraying with 40% H_2SO_4 followed by heating.

Isolation of 1 and 2 *Cimicifuga simplex* was grown at the Experimental Station for Medicinal Plant Studies, Faculty of Pharmaceutical Sciences, Tohoku University for seven years. The underground parts were obtained and dried at 60 °C in a drying room for several days. The powdered materials (100 g) were extracted three times with 300 ml boiling MeOH. After evaporation of the solvent, the extracts were dissolved in water (50 ml) and the mixture was extracted five times with EtOAc–*n*-BuOH (1 : 1), (100 ml). The residue of the upper layer after washing with water and evaporation of the solvent was chromatographed on ODS (100 g). The MeOH–H_2O (3 : 1) eluate was subjected to SiO_2 chromatography (60 g) and the fraction eluted with $CHCl_3$–MeOH (9 : 1) was subjected to preparative HPLC [column, Develosil PhA-5 (i.d. 10.0 × 250 mm); solvent, MeOH–H_2O–MeCN (10 : 10 : 3); effluent rate, 2 ml/min; column temperature, 40 °C]. The fraction at t_R 10 min was again subjected to HPLC [column, Cosmosil 10Ph (i.d. 8.0 × 250 mm); solvent, MeCN–H_2O (3 : 7); effluent rate, 2 ml/min; column temperature, 40 °C] to give **1** (colorless prisms, 145 mg) and **2** (colorless needles, 80 mg) by recrystallization from MeOH. **1**: mp 205—206 °C, $[\alpha]_D$ $-42.7°$ ($c=0.43$, MeOH). Pos. SI-MS *m/z*: 655 $(M+Na)^+$, 615 $(M-OH)^+$. Pos. HR-SI-MS *m/z*: 615.3545 $(C_{35}H_{52}O_{10}-OH)^+$, error: 1.5 m.m.u.. IR (KBr) cm^{-1}: 3600—3200 (OH). ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2. HMBC: Fig. 2. **2**: mp 244—245 °C, $[\alpha]_D$ $-21.3°$ ($c=0.20$, MeOH). Pos. SI-MS *m/z*: 657 $(M+Na)^+$, 617 $(M-OH)^+$. Pos. HR-SI-MS *m/z*: 617.3683 $(C_{35}H_{54}O_{10}-OH)^+$, error: -0.3 m.m.u.. IR (KBr) cm^{-1}: 3200—3600 (OH). ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2.

Hydrolysis of 1 and 2 with Cellulase **1** (19.2 mg) was dissolved in methanol (1 ml), then 0.03% AcOH (60 ml) was added with stirring. Cellulase T [Amano] 4 (from *Trichoderma viride*, 200 mg) was added to the solution with stirring for 1 d at room temperature. Then, the reaction solution was shaken with EtOAc (100 ml × 3) and, after washing the combined EtOAc layer with water and drying it over Na_2SO_4, the solvent was evaporated *in vacuo*. The residue was chromatographed on SiO_2 (12 g) and eluted with EtOAc to afford **1a** (7.5 mg) as colorless needles after purification with HPLC [column, Develosil PhA-5 (i.d. 4.6 × 250 mm); solvent, MeCN–H_2O (32.5 : 67.5); effluent rate, 1 ml/min; column temperature, 40 °C] and recrystallization from MeOH. **1a**: mp 159—160 °C, $[\alpha]_D$ $-41.1°$ ($c=0.22$, MeOH). Pos. HR-SI-MS *m/z*: 501.3214 $(C_{30}H_{44}O_6+H)^+$, error: 0.1 m.m.u.. IR (KBr) cm^{-1}, 3600—3200 (OH), ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2.

Similar treatments of **2** (9.6 mg) provided **2a** (3.7 mg) as a colorless powder by recrystallization from MeOH. **2a**: mp 152—153 °C, $[\alpha]_D$ $-2.5°$ ($c=0.18$, MeOH). Pos. HR-SI-MS *m/z*: 502.3285 $(C_{30}H_{46}O_6)^+$, error: -0.8 m.m.u.. IR (KBr) cm^{-1}: 3200—3600 (OH). ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2.

Methylation of 1 and 2 **1** (38 mg) was dissolved in 0.5% methanolic *p*-toluenesulfonic acid (5 ml) and the solution was stirred at room temperature for 3 h. Water was added and the mixture was extracted three times with EtOAc–*n*-BuOH (10 : 1), (50 ml). The products were chromatographed on a SiO_2 (15 g) column, and the eluate with $CHCl_3$–MeOH (10 : 1) was subjected to HPLC [column, CrestPak C18T-5 (i.d. 7.15 × 250 mm); solvent, MeOH–H_2O–MeCN (10 : 7 : 3); effluent rate, 2 ml/min; column temperature, 40 °C] to provide **1b***S* (12.7 mg) and **1b***R* (8.2 mg). **1b***S*: colorless needles, mp 191—192 °C, $[\alpha]_D$ $-16.1°$ ($c=1.26$, MeOH). Pos. SI-MS *m/z*: 647 $(C_{36}H_{54}O_{11}+H)^+$. ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2. **1b***R*: colorless powder, mp 179—180 °C, $[\alpha]_D$ $-58.1°$ ($c=0.75$, MeOH). Pos. SI-MS *m/z*: 669 $(C_{36}H_{54}O_{10}+Na)^+$, 629 $(M-OH)^+$. ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2.

Similar treatment of **2** (27 mg) provided **2b***S* (10.8 mg) and **2b***R* (6.2 mg). **2b***S*: colorless powder, mp 204—205 °C, $[\alpha]_D$ $+13.5°$ ($c=0.94$, MeOH). Pos. SI-MS *m/z*: 649 $(C_{36}H_{56}O_{10}+H)^+$. ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2. **2b***R*: colorless powder, mp 255—256 °C, $[\alpha]_D$ $-28.2°$ ($c=0.56$, MeOH). Pos. SI-MS *m/z*: 671 $(C_{36}H_{56}O_{10}+Na)^+$, 631 $(M-OH)^+$. ^1H- and ^{13}C-NMR (pyridine-d_5): Tables 1 and 2.

Oxidation of 1 and 2 with Collin's Reagents **1** (23.4 mg) was dissolved in pyridine (1 ml) and 20% CrO_3-pyridine solution (0.1 ml) was added dropwise with stirring. After stirring for 3.5 h at room temperature, the mixture was extracted with EtOAc (20 ml × 3). The EtOAc fraction was concentrated *in vacuo* and chromatographed on SiO_2 (12 g). The elutate with $CHCl_3$–MeOH (9 : 1) was subjected to HPLC [column, CrestPak C18T-5 (i.d. 7.15 × 250 mm); solvent, MeOH–H_2O–MeCN (10 : 7 : 3);

Effluent rate, 2 ml/min; column temperature, 40 °C] and recrystallized from MeOH to provided **1c** (3.0 mg) and **1d** (3.6 mg). **1c**: colorless needles, mp 275—276 °C. Pos. SI-MS *m/z*: 631 $(C_{35}H_{50}O_{10}+H)^+$. IR (KBr) cm^{-1}: 3250—3600 (OH), 1682 (C=O). ^{1}H-NMR (pyridine-d_5) δ: 3.06 (dd, J=6.3, 17.5 Hz, H-2), 3.24 (dd, J=8.1, 17.5 Hz, H-2), 3.94 (dd, J= 6.3, 8.1 Hz, H-3), 1.90 (m, H-5), 1.61, 1.88 (m, H-6), 5.17 (dd, J= 2.0, 7.0 Hz, H-7), 2.34, 2.10 (each m, H-11), 1.66 (2H, m, H-12), 1.74, 1.94 (each m, H-15, **1c***S*), 1.86, 2.10 (each, m, H-15, **1c***R*), 4.69 (ddd, J=7.5, 7.5, 7.5 Hz, H-16), 1.56 (m, H-17), 1.14 (s, H-18), 1.43, 1.60 (each, d, J=4.0 Hz, H-19, **1c***S*), 1.45, 1.73 (each d, J=4.0 Hz, H-19, **1c***R*), 1.80 (m, H-20), 0.92 (d, J=6.4 Hz, H-21, **1c***S*), 0.90 (d, J=6.4 Hz, H-21, **1c***R*), 2.22, 1.66 (each m, H-22), 3.86 (s, H-24, **1c***S*), 3.72 (s, H-24, **1c***R*), 5.72 (s, H-26, **1c***S*), 5.70 (s, H-26, **1c***R*), 1.77 (s, H-27, **1c***S*), 1.62 (s, H-27, **1c***R*), 1.06 (s, H-28, **1c***S*), 1.10 (s, H-28, **1c***R*), 1.30 (s, H-29, **1c***S*), 1.33 (s, H-29, **1c***R*), 0.99 (s, H-30, **1c***S*), 1.00 (s, H-30, **1c***R*), 4.77 (d, J=7.5 Hz, H-1′), 3.98 (dd, J=7.5, 8.1 Hz, H-2′), 4.11 (dd, J=8.1, 8.1 Hz, H-3′), 4.18 (m, H-4′), 3.69 (dd, J=10.3, 11.2 Hz, H-5′), 4.32 (dd, J=5.5, 11.2 Hz, H-5′). ^{13}C-NMR (pyridine-d_5) δ: 208.70 (C-1), 48.01 (C-2), 84.75 (C-3), 40.73 (C-4, **1c***S*), 40.90 (C-4, **1c***R*), 39.52 (C-5), 22.32 (C-6), 115.70 (C-7), 150.06 (C-8), 31.59 (C-9), 39.76 (C-10), 23.76 (C-11), 32.92 (C-12), 43.92 (C-13), 50.39 (C-14), 42.56 (C-15, **1c***S*), 42.91 (C-15, **1c***R*), 73.32 (C-16), 57.17 (C-17, **1c***S*), 57.13 (C-17, **1c***R*), 22.81 (C-18), 32.29 (C-19), 25.53 (C-20), 20.45 (C-21, **1c***S*), 20.39 (C-21, **1c***R*), 37.34 (C-22), 106.18 (C-23, **1c***S*), 103.73 (C-23, **1c***R*), 63.54 (C-24, **1c***S*), 62.96 (C-24, **1c***R*), 65.54 (C-25, **1c***S*), 63.88 (C-25, **1c***R*),98.52 (C-26, **1c***S*), 98.27 (C-26, **1c***R*), 13.08 (C-27, **1c***S*), 13.16 (C-27, **1c***R*), 26.47 (C-28, **1c***S*), 26.53 (C-28, **1c***R*), 26.21 (C-29, **1c***S*), 25.95 (C-29, **1c***R*), 15.18 (C-30, **1c***S*), 15.40 (C-30, **1c***R*), 107.72 (C-1′), 75.34 (C-2′), 78.58 (C-3′), 71.10 (C-4′), 67.23 (C-5′). CD: $\Delta\varepsilon_{285}$: −5.55 ($c=1.15\times10^{-4}$, MeOH). **1d**: colorless needles, mp 220—221 °C. Pos. SI-MS *m/z*: 651 $(C_{35}H_{48}O_{10}+Na)^+$. IR (KBr) cm^{-1}: 3250—3600 (OH), 1786 (epoxy-γ-lactone), 1677 (C=O). ^{1}H-NMR (pyridine-d_5) δ: 3.09 (dd, J=6.5,17.0 Hz, H-2), 3.27 (dd, J=8.0, 17.0 Hz, H-2), 3.96 (dd, J=6.5, 8.0 Hz, H-3), 1.90 (m, H-5), 1.62, 1.92 (m, H-6), 5.25 (dd, J=2.0, 7.0 Hz, H-7), 2.35, 2.09 (each m, H-11), 1.64 (2H, m, H-12), 1.83, 2.10 (each m, H-15), 4.61 (ddd, J=7.5, 7.5, 7.5 Hz, H-16), 1.64 (m, H-17), 1.10 (s, H-18), 1.45, 1.62 (d, J=4.3 Hz, H-19), 1.80 (m, H-20), 0.92 (d, J=6.4 Hz, H-21), 1.65, 2.22 (each m, H-22), 4.41 (s, H-24), 1.66 (s, H-27), 1.11 (s, H-28), 1.35 (s, H-29), 1.02 (s, H-30), 4.81 (d, J=7.3 Hz, H-1′), 4.02 (dd, J=7.3, 8.5 Hz, H-2′), 4.18 (dd, J=8.5, 8.5 Hz, H-3′), 4.23 (ddd, J=5.5, 8.5, 10.3 Hz, H-4′), 3.74 (dd, J=10.3, 11.2 Hz, H-5′), 4.35 (dd, J=5.5, 11.2 Hz, H-5′). ^{13}C-NMR (pyridine-d_5) δ: 209.09 (C-1), 48.08 (C-2), 84.80 (C-3), 40.79 (C-4), 39.54 (C-5), 22.33 (C-6), 116.11 (C-7), 149.41 (C-8), 31.58 (C-9), 39.66 (C-10), 23.63 (C-11), 32.65 (C-12), 43.88 (C-13), 50.47 (C-14), 42.17 (C-15), 75.75 (C-16), 56.30 (C-17), 22.78 (C-18), 32.36 (C-19), 25.54 (C-20), 20.15 (C-21), 35.45 (C-22), 106.51 (C-23), 62.78 (C-24), 58.66 (C-25), 172.64 (C-26), 11.19 (C-27), 26.47 (C-28), 25.58 (C-29), 15.26 (C-30), 107.79 (C-1′), 75.25 (C-2′), 78.41 (C-3′), 71.01 (C-4′), 67.22 (C-5′). CD: $\Delta\varepsilon_{285}$: −5.03; $\Delta\varepsilon_{235}$: −10,90 ($c=3.56\times10^{-4}$, MeOH).

Similar treatment of **2** (23.6 mg) provided **2c** (3.7 mg) and **2d** (3.1 mg). **2c**: colorless needles, mp 217—218 °C. Pos. SI-MS *m/z*: 633 $(C_{35}H_{50}O_{10}+H)^+$. IR (KBr) cm^{-1}: 3250—3580 (OH), 1699 (C=O). ^{1}H-NMR (pyridine-d_5) δ: 3.20 (2H, m, H-2), 3.89 (m, H-3), 1.82 (m, H-5), 0.95, 1.50 (m, H-6), 1.10, 1.40 (m, H-7), 1.93 (m, H-8), 1.70, 2.47 (each m, H-11), 1.40, 1.65 (each m, H-12), 1.42, 1.70 (each m, H-15, **2c***S*), 1.70, 1.90 (each m, H-15, **2c***R*), 4.60 (m, H-16), 1.60 (m, H-17), 1.07 (s, H-18), 0.90, 1.12 (overlapped, H-19), 1.82 (m, H-20), 0.90 (d, J=6.4 Hz, H-21, **2c***S*), 0.88 (d, J=6.4 Hz, H-21, **2c***R*), 1.62, 2.20 (each m, H-22), 3.86 (s, H-24, **2c***S*), 3.72 (s, H-24, **2c***R*), 5.71 (s, H-26, **2c***S*), 5.70 (s, H-26, **2c***R*), 1.76 (s, H-27, **2c***S*), 1.60 (s, H-27, **2c***R*), 0.92 (s, H-28, **2c***S*), 0.96 (s, H-28, **2c***R*), 1.27 (s, H-29, **2c***S*), 1.29 (s, H-29, **2c***R*), 1.13 (s, H-30, **2c***S*), 1.08 (s, H-30, **2c***R*), 4.78 (d, J=8.0 Hz, H-1′), 3.98 (dd, J=8.0, 8.1 Hz, H-2′), 4.10 (dd, J=8.1, 8.1 Hz, H-3′), 4.18 (ddd, J=5.0, 8.1, 10.6 Hz, H-4′), 3.66 (dd, J=10.6, 11.3 Hz, H-5′), 4.29 (dd, J=5.0, 11.3 Hz, H-5′). ^{13}C-NMR (pyridine-d_5) δ: 209.01 (C-1), 48.34 (C-2), 86.01 (C-3), 40.90 (C-4), 42.89 (C-5), 19.62 (C-6), 23.66 (C-7), 42.89 (C-8), 28.13 (C-9), 38.45 (C-10), 27.59 (C-11), 33.29 (C-12), 44.63 (C-13), 47.08 (C-14), 42.89 (C-15), 72.94 (C-16), 56.55 (C-17), 19.34 (C-18), 27.32 (C-19), 25.73 (C-20), 20.60 (C-21, **2c***S*), 20.55 (C-21, **2c***R*), 37.46 (C-22), 106.15 (C-23, **2c***S*), 103.70 (C-23, **2c***R*), 65.50 (C-24, **2c***S*), 64.50 (C-24, **2c***R*), 63.50 (C-25, **2c***S*), 63.88 (C-25, **2c***R*), 98.48 (C-26, **2c***S*), 98.23 (C-26, **2c***R*), 13.07 (C-27, **2c***S*), 13.12 (C-27, **2c***R*), 18.59 (C-28, **2c***S*), 18.65 (C-28, **2c***R*), 26.43 (C-29, **2c***S*), 26.00 (C-29, **2c***R*), 15.45 (C-30), 107.79 (C-1′), 75.36 (C-2′), 78.57 (C-3′), 71.08 (C-4′), 67.19 (C-5′). CD: $\Delta\varepsilon_{290}$: −1.45 ($c=1.85\times10^{-4}$, MeOH). **2d**: colorless needles, mp 207—208 °C. Pos. SI-MS *m/z*: 653 $(C_{35}H_{50}O_{10}+Na)^+$. IR (KBr) cm^{-1}: 3200—3600 (OH), 1789 (epoxy-γ-lactone), 1685 (C=O). ^{1}H-NMR (pyridine-d_5) δ: 3.18 (dd, J=8.5,17.0 Hz, H-2), 3.24 (dd, J=6.5,17.0 Hz, H-2), 3.89 (dd, J=6.5, 8.5 Hz, H-3), 1.82 (m, H-5), 1.00, 1.52 (m, H-6), 1.14, 1.40 (m, H-7), 1.95 (m, H-8), 1.74, 2.46 (each m, H-11), 1.36, 1.64 (m, H-12), 1.52, 1.86 (each m, H-15), 4.52 (ddd, J=7.5, 7.5, 7.5 Hz, H-16), 1.68 (m, H-17), 1.09 (s, H-18), 0.91, 1.13 (d, J=4.3 Hz, H-19), 1.80 (m, H-20), 0.89 (d, J=6.4 Hz, H-21), 1.63, 2.17 (each m, H-22), 4.39 (s, H-24), 1.64 (s, H-27), 0.96 (s, H-28), 1.31 (s, H-29), 1.10 (s, H-30), 4.80 (d, J=7.5 Hz, H-1′), 4.01 (dd, J=7.5, 8.5 Hz, H-2′), 4.15 (dd, J=8.5, 8.5 Hz, H-3′), 4.20 (ddd, J=5.0, 8.5, 10.0 Hz, H-4′), 3.69 (dd, J=10.0, 11.0 Hz, H-5′), 4.30 (dd, J=5.0, 11.0 Hz, H-5′). ^{13}C-NMR (pyridine-d_5) δ: 209.25 (C-1), 48.34 (C-2), 86.03 (C-3), 40.88 (C-4), 42.75 (C-5), 19.53 (C-6), 23.55 (C-7), 42.68 (C-8), 27.92 (C-9), 38.36 (C-10), 27.22 (C-11), 33.00 (C-12), 44.58 (C-13), 47.11 (C-14), 42.41 (C-15), 75.34 (C-16), 55.65 (C-17), 19.28 (C-18), 27.44 (C-19), 25.52 (C-20), 20.27 (C-21), 35.49 (C-22), 106.44 (C-23), 62.68 (C-24), 58.56 (C-25), 172.51 (C-26), 11.10 (C-27), 18.54 (C-28), 25.69 (C-29), 15.42 (C-30), 107.60 (C-1′), 75.15 (C-2′), 78.29 (C-3′), 70.87 (C-4′), 67.08 (C-5′). CD: $\Delta\varepsilon_{288}$: −1.11; $\Delta\varepsilon_{225}$: −7.19 ($c=3.08\times10^{-4}$, MeOH).

Hydrolysis of 1 and 2 with 2% HCl **1** (12.4 mg) was dissolved in 2% HCl in MeOH–H_2O (1 : 2) solution (3 ml) and the solution was refluxed for 3 h. The reaction solution was diluted with water and the mixture was extracted with EtOAc (30 ml × 3). The water layer was refluxed again for 2 h to hydrolyze methyl xylosides after removal of MeOH by evaporation, and then chromatographed on an Amberlite IR-35 column. Elution with water afforded D-xylose (1.7 mg), $[\alpha]_D$ +20.1° [c=0.17, H_2O–MeOH (1 : 1)], which was identified by HPLC [column, Lichrosorb NH_2 (i.d. 4.6 × 250 mm); solvent, MeCN–H_2O (4 : 1); effluent rate, 1 ml/min; column temperature, 40 °C, t_R 5.2 min] and TLC [*n*-PrOH–H_2O (85 : 15), *Rf*: 0.59] with an authentic specimen. Similar treatment of **2** (20.8 mg) also provided D-xylose (3.0 mg): $[\alpha]_D$ +21.6° [c=0.30, H_2O–MeOH (1 : 1)], which was identified by comparison with an authentic specimen as in **1**. The EtOAc layer of **2** was chromatographed on a SiO_2 (13 g) column and the *n*-hexane–EtOAc (5 : 1) eluates were subjected to HPLC [column, Cosmosil 10 Ph (i.d. 4.6 × 250 mm); solvent, MeOH–H_2O–MeCN (10 : 7 : 6); effluent rate, 1 ml/min; column temperature, 40 °C] to provide **2e** (2.5 mg) as a colorless powder, mp 202—203 °C, $[\alpha]_D$ +55.06° (c=0.08, MeOH). Pos. SI-MS *m/z*: 498 $(C_{31}H_{46}O_5+H)^+$. IR ($CHCl_3$) cm^{-1}: 3300 (OH). ^{1}H-NMR (pyridine-d_5): 1.52 (1H, m, H-1), 1.85, 2.50 (each, 1H, m, H-2), 3.50 (1H, dd, J=6.4, 12.4 Hz, H-3), 2.04 (1H, m, H-5), 1.38 (1H, m, H-6), 2.12 (1H, m, H-7), 1.54 (1H, m, H-8), 5.17 (1H, d, J=4.7 Hz, H-11), 1.60, 2.03 (each, 1H, m, H-12), 1.52, 1.97 (each, 1H, m, H-15), 4.57 (1H, ddd, J=8.0, 8.0, 8.0 Hz, H-16), 1.58 (1H, m, H-17), 0.78 (3H, s, H-18), 0.07 (1H, dd, J=4.3, 9.0 Hz, H-19), 0.78 (1H, overlapped, H-19), 0.90 (3H, d, J=6.0 Hz, H-21), 1.70 (1H, m, H-22), 3.76 (1H, s, H-24), 5.04 (1H, s, H-26), 1.58 (3H, s, H-27), 0.81 (3H, s, H-28), 1.21 (3H, s, H-29), 0.91 (3H, s, H-30). ^{13}C-NMR (pyridine-d_5) δ: 13.59 (C-1), 30.97 (C-2), 75.03 (C-3), 37.51 (C-4), 44.68 (C-5), 28.50 (C-6), 26.27 (C-7), 48.33 (C-8), 145.11 (C-9), 29.73 (C-10), 113.37 (C-11), 36.65 (C-12), 44.20 (C-13), 44.59 (C-14), 42.18 (H-15), 73.39 (C-16), 55.21 (C-17), 17.44 (C-18), 19.84 (C-19), 26.27 (C-20), 20.49 (C-21), 37.34 (C-22), 106.45 (C-23), 62.44 (C-24), 64.60 (C-25), 103.95 (C-26), 12.68 (C-27), 19.23 (C-28), 28.96 (C-29), 15.37 (C-30).

Acknowledgements The authors are grateful to Amano Pharmaceutical Company, Nagoya, for the generous gift of Cellulase T [Amano] 4. They are also grateful to Mr. Minoura for NMR spectra and Mrs. Fujitake for mass spectra at Osaka University of Pharmaceutical Sciences, and to Mr. H. Hayasaka and Mr. K. Ohba of the Faculty of Pharmaceutical Sciences, Tohoku University, for culturing *Cimicifuga simplex* (Sendai and Shizuoka).

References and Notes

1) Kusano A., Takahira M., Shibano M., Miyase T., Kusano G., *Chem. Pharm. Bull.*, **46**, 467—472 (1998).
2) Kusano A., Shibano M., Kusano G., Miyase T., *Chem. Pharm. Bull.*, **44**, 2078—2085 (1996), references therein.
3) Demarco P. V., Farkas E., Doddrell D., Mylari B. L., Wenkert E., *J. Am. Chem. Soc.*, **90**, 5480—5486 (1968).
4) Djerassi C., Klyne W., *J. Chem. Soc.*, **1963**, 2390—2402.
5) Kusano G., Hojyo S., Kondo Y.,Takemoto T., *Chem. Pharm. Bull.*, **25**, 3182—3189 (1977).

6) Kusano A., Shimizu K., Idoji M., Shibano M., Minoura K., Kusano G., *Chem. Pharm. Bull.*, **43**, 279—283 (1995).
7) *a*) Linde H., *Arch. Pharm.*, **311**, 120—138 (1968) and references herein. *b*) Radics L., Kajtar-Peredy M., Corsano S., Standoli L., *Tetrahedron Lett.*, **1975**, 4287— 4290.
8) Kadota S., Li J. X., Tanaka K., Namba T., *Tetrahedron*, **51**, 1143—1161 (1995).
9) Henmi H., Kitame F., Ishida N., Kusano G., Kondo Y., Nozoe S., *J. Pharm. Dyn.*, **2**, 339—349 (1979).