Studies on the Constituents of *Cimicifuga* Species. XIX.[1] Eight New Glycosides from *Cimicifuga simplex* WORMSK.

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Eight new glycosides were isolated from *Cimicifuga simplex* (Ranunculaceae), and their structures were determined to be 23-*O*-acetyl-7,8-didehydroshengmanol-3-*O*-α-L-arabinopyranoside (1), 24-*epi*-24-*O*-acetyl-7,8-didehydrohydroshengmanol-3-*O*-β-D-galactopyranoside (2), 7,8-didehydrocimigenol-3-*O*-β-D-galactopyranoside (3), 24-*epi*-24-*O*-acetylhydroshengmanol-3-*O*-β-D-galactopyranoside (4), cimigenol-3-*O*-β-D-galactopyranoside (5), 25-*O*-methylcimigenol-3-*O*-β-D-galactopyranoside (6), 25-*O*-acetylcimigenol-3-*O*-β-D-galactopyranoside (7) and 25-*O*-acetylcimigenol-3-*O*-β-D-glucopyranoside (8). Genuine aglycones were obtained by the hydrolysis of 1—7 with lactase F[Amano] and of 8 with cellulase T[Amano]4. Acerinol was prepared from 7,8-didehydrocimigenol and showed antilipemic effects.

Key words *Cimicifuga simplex*; cycloartane glycoside; 7,8-didehydrocycloartane glycoside; lactase; cellulase; antilipemic effect

We recently reported on the isolation of four new triterpenic xylosides from the aerial parts of *Cimicifuga simplex*.[1] In our continuing work, we isolated eight new glycosides (**1**—**8**) from the same herb. This paper deals with the isolation and structural elucidation of these glycosides (**1**—**8**), along with conversion to 7,8-didehydrocimigenol (**1b**), acerinol (**1c**), 24-*epi*-didehydrocimigenol (**2b**), 24-*epi*-acerinol (**2c**) and cimigol (**4b**) from the aglycones (**1a**, **2a**, **4a**) and the antilipemic effects as biological properties of acerinol (**1c**).

Glycosides **1**—**8** were obtained as described in the experimental section by repeated chromatographies on silica gel (SiO_2), octadecylsilanized silicic acid (ODS) columns, HPLC and preparative TLC (pTLC) of the methanol extract of the underground parts and the aerial parts of the title plant.

Glycoside **1** was obtained from the underground parts as colorless needles, mp 239—240 °C, $[\alpha]_D$ −55.5°, and the molecular formula was determined to be $C_{37}H_{56}O_{10}$ on the basis of positive high resolution secondary ion mass spectroscopy (pos. HR-SI-MS) and the data of the ^{13}C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ^1H- and ^{13}C-NMR signals were assigned using ^1H–^1H shift correlation spectroscopy (^1H–^1H COSY) and ^{13}C–^1H COSY, and heteronuclear multiple bond correlation (HMBC) spectra as shown in Tables 1 and 2. The spectra of **1** showed the presence of 23-acetoxy and 24,25-epoxy groups on a side chain of a cycloartane derivative[2-4] (23-H, 24-H, CH_3CO, C-23, C-24, C-25, C-26, C-27), and also a 7(8)-double bond on a cycloartane nucleus[5] (7-H, 19-H_2, C-7, C-8, C-19).

Treatment of **1** with lactase F[Amano] provided a genuine aglycone, **1a**, mp 89—90 °C, $C_{32}H_{48}O_6$, $[\alpha]_D$ −75.2°, which was formulated as (23*R*,24*S*)-23-acetoxy-24,25-epoxy-9,19-cyclolanost-7-en-16-one-3β,15α-diol named 23-*O*-acetyl-7,8-didehydroshengmanol, as shown in Fig. 1. This formulation was certificated as follows: The molecular formula was clarified by pos. HR-SI-MS. The circular dichroism (CD) of **1** showed a strong negative Cotton effect ($[\theta]_{317}$ -9.77×10^3), clarifying the presence of a 16-keto group on a cycloartane skeleton.[2] **1a** was converted to 7,8-didehydro cimigenol (**1b**), which was identified by comparison of the spectral data with the reported data,[6] on 1% Na_2CO_3 treatment followed by 5% AcOH treatment as shown in Fig. 2. This conversion suggested the presence of a 16-keto group and the stereochemistry of the 23*R* and 24*S* configurations in **1** and **1a**.

Reflux of **1b** in 50% AcOH provided acerinol (**1c**), certifying that **1**, **1a** and **1b** have a 9,19-cyclolanost-7-en-3β-ol system.[5] The stereochemistry of 15-hydroxy and a secondary methyl group (C-21) has not been reported in acerinol (**1c**),[7] but by the nuclear Overhauser effect (NOE) between 18-H_3 and 15β-H, and 21-H_3 and 17α-H in the rotating frame nuclear Overhauser effect spectroscopy (ROESY) spectrum of **1c**, 15α-hydroxy (15*R*) and 20*R* configurations were established at this time, as shown in Fig. 2.

The ^1H-NMR spectrum of **1** showed the presence of an α-L-arabinopyranosyl group. Acidic hydrolysis of **1** provided L-arabinose, $[\alpha]_D$ +73.5°, as identified by TLC and HPLC. The ^{13}C-NMR spectrum of **1** showed that C-3 appeared at δ 88.19 by a glycosylation shift of 10.46 ppm from that of **1a**. Thus, **1** should be formulated as 23-*O*-acetyl-7,8-didehydroshengmanol-3-*O*-α-L-arabinopyranoside, as shown in Fig. 1.

Glycosides **2**—**5** were obtained from the *n*-BuOH fraction and glycosides **6**—**8** from the aqueous fraction of MeOH extracts of the aerial parts by treatments similar to **1**.

Glycoside **2** was obtained as colorless needles, mp 243—244 °C, $[\alpha]_D$ −11.4°, and the molecular formula was determined to be $C_{38}H_{60}O_{12}$ by both pos. HR-SI-MS and the data of the ^{13}C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ^1H- and ^{13}C-NMR signals were assigned as with **1** and are summarized in Tables 1 and 2.

Treatment of **2** with lactase F[Amano] provided a genuine aglycone **2a**, mp 229—230 °C, $[\alpha]_D$ −18.5°, $C_{32}H_{50}O_7$, which was formulated as 24-*O*-acetyl-7,8-

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Table 1. ^{1}H-NMR Data of New Glycosides and New Aglycones

	1[a]	1a[a]	2[a]	2a[a]	3[a]	4[a]
1	1.38, 1.78	1.23, 1.69	1.23, 1.75	1.26, 1.37	1.29, 1.67	1.24, 1.70
2	1.95, 2.37	1.98, 2.32	1.94, 2.43	1.94, 2.00	1.28, 1.95	1.92, 2.43
3	3.50 dd (4.0, 11.5)	3.56 dd (5.0, 10.0)	3.52 dd (4.0, 11.8)	3.54 dd (4.0, 11.8)	3.51 dd (4.2, 11.3)	3.54 dd (4.3, 11.3)
5	1.35	1.37	1.35	1.32	1.35	1.31
6	1.62, 1.98	1.73, 1.99	1.84, 1.98	1.70, 1.95	1.60, 1.82	0.82 ddd (12.5, 12.5, 12.5) 1.70
7	6.10 dd (2.5, 8.0)	6.15 dd (2.0, 7.5)	5.99 d (8.8)	6.03 d (8.8)	6.05 dd (7.0, 7.5)	1.22, 2.10
8						1.92
11	1.24, 2.15	1.76, 2.25	1.27, 2.17	1.32, 2.22	1.15, 2.17	1.25, 2.15
12	1.92, 2.00	1.95, 2.01	1.59, 1.64	1.67, 1.74	1.63, 1.87	1.55, 1.70
15	4.56 s	4.58 s	4.45 s	4.47 s	4.54 s	4.14 s
17	2.30	2.31 d (7.5)	1.82 d (10.0)	1.83 d (10.0)	1.51 d (11.3)	1.85
18	1.32 s	1.34 s	1.33 s	1.29 s	1.16 s	1.32 s
19	0.55 d (3.8) 1.08 d (3.8)	0.61 d (4.0) 1.12 d (4.0)	0.49 d (3.8) 1.08 d (3.8)	0.58 d (4.0) 1.15 d (4.0)	0.47 d (4.0) 1.05 d (4.0)	0.26 d (4.1) 0.56 d (4.1)
20	2.17	2.17	1.79	1.77	1.50	1.80
21	1.23 d (6.3)	1.25 d (6.5)	1.01 d (6.3)	1.03 d (5.0)	0.90 d (6.3)	0.98 d (6.3)
22	1.78, 2.87	1.77, 2.88	1.84, 2.10	1.87, 2.11	1.10, 2.30	1.85, 2.15
23	5.41 ddd (2.5, 8.8, 8.8)	5.42 ddd (2.5, 8.8, 8.8)	4.45 m	4.45 m	4.75 d (9.0)	4.45 m
24	3.05 d (8.8)	3.06 d (8.8)	5.73 d (8.8)	5.74 d (8.8)	3.80 s	5.74 d (8.5)
26	1.42 s	1.44 s	1.49 s	1.50 s	1.49 s	1.46 s
27	1.30 s	1.28 s	1.45 s	1.46 s	1.46 s	1.45 s
28	1.43 s	1.42 s	1.44 s	1.45 s	1.42 s	1.24 s
29	1.28 s	1.24 s	1.25 s	1.22 s	1.30 s	1.22 s
30	1.05 s	1.13 s	1.03 s	1.11 s	1.03 s	1.02
$COCH_3$	2.01 s	2.04 s	2.12	2.10		2.12
OCH_3						
1′	4.80 d (8.0)		4.83 d (8.8)		4.86 d (8.8)	4.88 d (8.8)
2′	4.45 dd (8.0, 8.0)		4.43 dd (8.8, 8.8)		4.45 dd (8.8, 8.8)	4.45 dd (8.8, 8.8)
3′	4.17 dd (3.5, 8.0)		4.16 dd (2.5, 8.8)		4.15 dd (3.1, 8.8)	4.16 dd (3.1, 8.8)
4′	4.33 dd (2.5, 3.5)		4.59 d (2.5)		4.57 d (3.1)	4.59 d (3.1)
5′	3.82 dd (2.5, 13.5) 4.32 dd (2.5, 13.5)		4.09 dd (6.3, 6.3)		4.07 dd (6.3, 6.3)	4.09 dd (6.3, 6.3)
6′			4.43 dd (6.3, 11.3) 4.48 dd (6.3, 11.3)		4.43 dd (6.3, 11.3) 4.48 dd (6.3, 11.3)	4.43 dd (6.3, 11.3) 4.48 dd (6.3, 11.3)

	4a[a]	5[a]	6[b]	7[b]	8[b]
1	1.25, 1.64	1.17, 1.54	1.15, 1.52	1.15, 1.53	1.15, 1.52
2	1.90, 2.08	1.93, 2.44	1.90, 2.43	1.92, 2.45	1.89, 2.43
3	3.55 dd (4.3, 11.3)	3.54 dd (4.1, 11.3)	3.53 dd (3.8, 11.0)	3.55 dd (3.8, 11.3)	3.54 dd (3.8, 11.3)
5	1.37	1.31	1.30	1.30	1.30
6	0.87 ddd (12.5, 12.5, 12.5) 1.66	0.74 ddd (12.5, 12.5, 12.5) 1.54	0.68 ddd (12.5, 12.5, 12.5) 1.53	0.70 ddd (12.5, 12.5, 12.5) 1.53	0.71 ddd (12.5, 12.5, 12.5) 1.53
7	1.31, 2.12	1.20, 2.08	1.20, 2.08	1.20, 2.10	1.20, 2.10
8	1.90	1.70	1.62	1.70	1.70
11	1.15, 1.99	1.06, 2.08	1.05, 2.20	1.03, 2.10	1.05, 2.08
12	1.59, 1.75	1.54, 1.70	1.50, 1.67	1.53, 1.70	1.53, 1.60
15	4.16 s	4.25 s	4.23 s	4.28 s	4.26 s
17	1.82 d (8.2)	1.51 d (11.3)	1.46 d (11.0)	1.47 d (11.0)	1.47 d (11.0)
18	1.27 s	1.16 s	1.13 s	1.15 s	1.15 s
19	0.35 d (4.0) 0.64 d (4.0)	0.26 d (4.0) 0.54 d (4.0)	0.25 d (4.2) 0.50 d (4.2)	0.25 d (3.9) 0.50 d (3.9)	0.24 d (4.0) 0.51 d (4.0)
20	1.81	1.65	1.67	1.65	1.65
21	0.99 d (6.0)	0.87 d (6.3)	0.87 d (6.5)	0.87 d (6.5)	0.87 d (6.5)
22	1.90, 2.14	1.02, 2.28	1.00, 2.25	1.01, 2.30	1.02, 2.29
23	4.44 m	4.74 d (8.8)	4.60 d (11.0)	4.64 d (11.0)	4.61 d (9.0)
24	5.74 d (8.5)	3.76 s	3.69 s	4.13 s	4.13 s
26	1.50 s	1.48 s	1.39 s	1.70 s	1.70 s
27	1.46 s	1.46 s	1.29 s	1.67 s	1.67 s
28	1.24 s	1.20 s	1.20 s	1.21 s	1.21 s
29	1.21 s	1.32 s	1.27	1.30 s	1.33 s
30	1.09	1.04 s	1.03 s	1.04 s	1.07 s
$COCH_3$	2.10			2.02	2.00
OCH_3			3.24		
1′		4.88 d (8.8)	4.88 d (8.5)	4.90 d (8.5)	4.96 d (8.5)
2′		4.45 dd (8.8, 8.8)	4.45 dd (8.0, 8.5)	4.47 dd (8.5, 8.5)	4.05 dd (8.5, 8.5)
3′		4.15 dd (3.5, 8.8)	4.17 dd (3.5, 8.0)	4.19 dd (3.5, 8.5)	4.27 dd (8.5, 8.5)
4′		4.58 d (3.5)	4.57 d (3.5)	4.59 d (3.5)	4.21 dd (8.5, 8.5)
5′		4.08 dd (6.3, 6.3)	4.09 dd (6.0, 6.0)	4.10 dd (6.0, 6.0)	3.98 m
6′		4.42 dd (6.2, 11.3) 4.48 dd (6.2, 11.3)	4.42 dd (6.0, 11.3) 4.48 dd (6.0, 11.3)	4.42 dd (6.0, 11.3) 4.48 dd (6.0, 11.3)	4.38 dd (5.3, 11.8) 4.56 dd (2.4, 11.8)

a) Obtained on a JEOL α-400; *b*) on a Varian XL-300 in pyridine-d_5 containing D_2O.

Table 2. ^{13}C-NMR Data of New Glycosides and New Aglycones

	1[a]	1a[a]	2[a]	2a[a]	3[a]	4[a]	4a[a]	5[a]	6[b]	7[b]	8[b]
1	30.29	30.57	30.37	30.66	30.37	32.31	31.34	32.43	32.03	32.06	32.14
2	29.45	30.74	29.51	30.78	29.51	30.03	32.06	30.86	29.60	29.68	29.69
3	88.19	77.73	88.33	77.75	88.44	88.56	77.95	90.18	88.36	88.36	88.61
4	40.42	40.25	40.38	40.24	40.37	41.29	41.12	41.32	40.89	40.92	41.01
5	42.68	42.45	42.76	42.52	42.73	47.52	42.42	47.64	47.18	47.21	47.32
6	21.52	21.56	21.86	22.15	21.78	21.21	21.35	21.07	20.66	20.71	20.81
7	115.11	115.30	113.48	113.66	114.32	26.48	26.55	26.42	26.01	26.06	26.22
8	147.26	147.25	149.46	149.08	148.04	48.94	49.13	48.61	48.25	48.28	48.40
9	19.40	20.98	21.21	21.07	21.28	19.99	20.04	19.99	19.52	19.21	19.68
10	28.57	28.52	28.47	28.65	28.44	27.37	27.38	27.16	26.30	26.33	26.42
11	25.23	25.31	25.44	25.53	25.57	26.58	26.72	26.48	26.09	26.13	26.12
12	33.57	33.59	33.87	33.89	34.11	34.00	34.03	34.13	33.69	33.69	33.79
13	40.87	40.90	41.60	41.63	41.32	42.20	42.23	41.94	41.48	41.48	41.59
14	49.52	49.55	50.05	50.06	50.68	46.76	46.78	47.35	46.82	46.85	46.95
15	80.87	80.92	80.09	80.13	78.15	82.10	82.17	80.20	79.61	79.69	79.81
16	220.32	220.34	103.20	103.21	112.32	102.98	102.99	112.01	111.61	112.10	112.20
17	60.14	60.16	60.77	60.78	59.45	60.90	60.94	59.61	59.03	59.07	59.17
18	21.85	21.88	22.55	22.59	21.65	20.39	20.40	19.61	19.19	19.21	19.29
19	28.51	28.92	28.43	28.78	28.24	30.69	30.96	30.07	30.56	30.68	30.69
20	27.97	28.14	27.14	27.82	24.02	27.10	27.12	24.11	23.66	23.62	23.72
21	19.87	19.87	21.64	21.64	19.76	21.47	21.47	19.49	19.19	19.21	19.29
22	37.35	37.38	32.80	32.82	38.29	32.96	32.98	38.19	37.77	37.59	37.69
23	72.03	72.04	74.26	74.27	72.12	74.11	74.12	71.88	71.31	71.38	71.38
24	65.26	65.26	81.37	81.39	90.28	81.18	81.20	88.72	87.76	86.46	86.55
25	58.53	58.53	72.18	72.17	70.98	72.77	72.26	70.96	78.74	83.01	83.04
26	19.40	19.40	27.07	27.09	25.47	26.77	27.12	25.81	19.19	21.25	21.33
27	24.75	24.76	27.37	27.37	27.07	27.07	27.07	26.74	21.60	23.00	23.11
28	18.80	18.85	18.14	18.20	18.44	11.77	11.82	11.79	11.47	11.52	11.59
29	25.81	26.20	25.88	26.20	25.85	25.79	26.17	25.48	25.40	25.44	25.55
30	14.30	13.66	14.33	13.68	14.32	15.43	14.86	15.44	15.06	15.11	15.25
CO	170.32	170.61	170.35	170.31		170.34	170.35			170.20	170.18
CH_3	20.98	22.14	21.10	21.08		21.05	21.06			22.07	22.13
OCH_3									48.95		
1′	107.34		107.41		107.41	107.43		107.43	106.89	107.21	106.46
2′	72.98		73.26		73.23	73.28		73.26	72.58	73.08	75.37
3′	74.65		75.50		75.48	75.52		75.51	74.85	75.47	78.22
4′	69.51		70.33		70.32	70.34		70.33	69.60	70.04	71.47
5′	66.76		76.81		76.78	76.78		76.76	76.14	76.67	77.85
6′			62.50		62.50	62.50		62.49	61.75	62.25	62.57

a) Measured at 100 MHz; *b*) at 75.4 MHz.

didehydrohydroshengmanol as follows. The molecular formula was certificated by pos. HR-SI-MS. The IR spectrum showed broad hydroxyl bands and an acetyl band. ^{1}H- and ^{13}C-NMR signals of **2a** showed the presence of 24-*O*-acetoxy-16,23-epoxy-15,16-diol and 7(8)-ene groups on a cycloartane skelton (7-H, 19-H_2, 15-H, 23-H, 24-H, CH_3CO, C-7, C-8, C-19, C-15, C-16, C-23, C-24). **2a** was treated with 1% Na_2CO_3, followed by acidification with 50% acetic acid to afford a desacetyl dehydrate (**2b**), mp 236—237 °C, $[\alpha]_D$ +6.0°, $C_{30}H_{46}O_5$, which was identified as 24-*epi*-7,8-didehydrocimigenol.[6] Heating **2b** in dioxane–AcOH (1 : 1) provided 24-*epi*-acerinol (**2c**).[6,8] The conversion from **2a** to **2b**, and then to **2c**, suggested the presence of 3β-hydroxy-7,8-didehydro-9,19-cyclolanostane and (23*R*,24*R*)-24-acetoxy-16-hydroxy-16,23-epoxy moieties.

The CD spectrum of a **2a**–shift reagent adduct (CCl_4) showed a strong positive Cotton effect ($[\theta]_{313}$ $+8.9\times10^4$) and a negative Cotton effect ($[\theta]_{285}$ -7.3×10^4), certificating the presence of 15α,16α-dihydroxy groups on a cycloartane nucleus.[9] Thus, **2a** should be formulated as (23*R*,24*R*)-24-acetoxy-16,23-epoxy-9,19-cyclolanost-7-en-3β,15α,16α-triol, named 24-*epi*-24-*O*-acetyl-7,8-didehydrohydroshengmanol.

The ^{1}H-NMR spectrum of **2** showed the presence of a β-D-galactopyranosyl group. Acidic hydrolysis of **2** gave D-galactose, $[\alpha]_D$ +44.6°, as identified by TLC and HPLC. The ^{13}C-NMR spectrum of **2** showed that C-3 appeared at δ 88.33 by a glycosylation shift of 10.58 ppm from that of **2a**. Thus, **2** should be formulated as 24-*epi*-24-*O*-acetyl-7,8-didehydrohydroshengmanol-3-*O*-β-D-galactopyranoside, as shown in Fig. 1. Galactosides **3**—**7** were also formulated as 3-*O*-β-D-galactopyranosides, as in **2**.

Glycoside **3** was obtained as colorless needles, mp >300 °C, $[\alpha]_D$ −9.2°, and the molecular formula was determined to be $C_{36}H_{56}O_{10}$ by pos. HR-SI-MS and the data of the ^{13}C-NMR spectrum. The IR spectrum showed strong hydroxyl bands. The ^{1}H- and ^{13}C-NMR signals were assigned as in **1** and are summarized in Tables 1 and 2.

Enzymatic hydrolysis of **3** provided a genuine aglycone **1b**, mp 227—228 °C, $[\alpha]_D$ 0°, $[\alpha]_{450}$ −8.7°, $[\alpha]_{400}$ −21.7°, $[\alpha]_{300}$ −160.8°, $C_{30}H_{46}O_5$, which was identified to 7,8-didehydrocimigenol by comparison of the spectral data

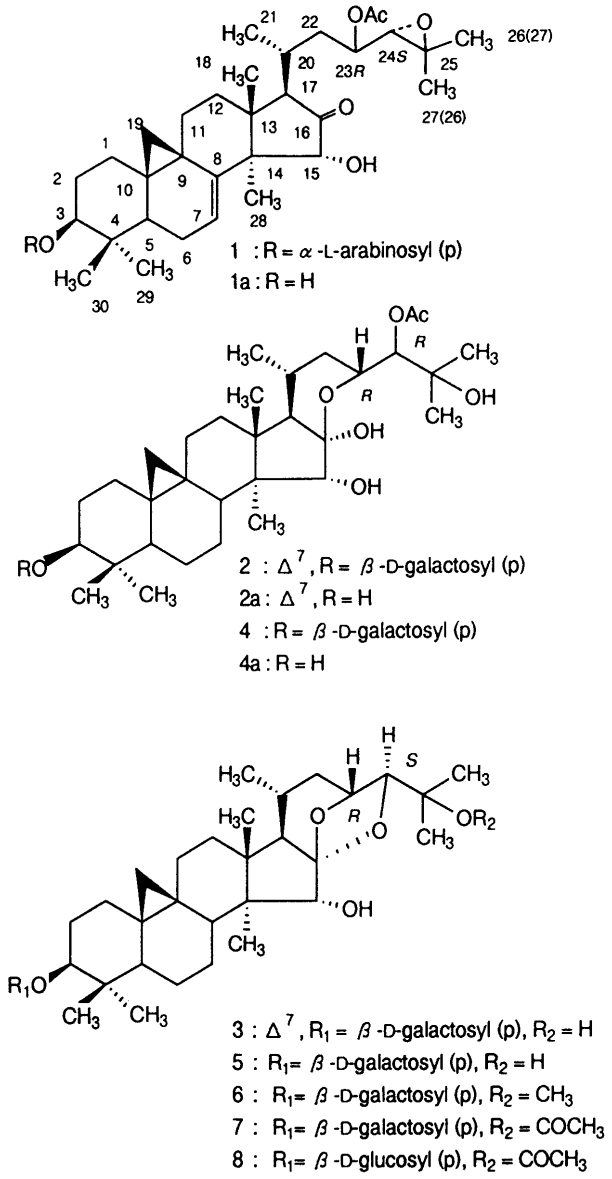

Fig. 1. Structures of New Glycosides and New Aglycones

with those of reported data.[6] D-Galactose was identified by acidic hydrolysis of **3**. Thus, **3** should be formulated as 7,8-didehydrocimigenol-3-*O*-*β*-D-galactopyranoside, as shown in Fig. 1.

Glycoside **4** was obtained as an inseparable mixture with **2** (2 : 4 = 1 : 5), and the molecular formula was determined to be $C_{38}H_{62}O_{12}$ by pos. HR-SI-MS and the data of the ^{13}C-NMR spectrum. The ^{1}H- and ^{13}C-NMR signals were assigned as in **1** and are summarized in Tables 1 and 2.

Enzymatic hydrolysis of **4** provided a genuine aglycone **4a**, mp 194—195 °C, $[\alpha]_D$ +16.2°, $C_{32}H_{52}O_7$, which was supposed to be a 7,8-dihydro derivative of **2a**, named 24-*epi*-24-*O*-acetylhydroshengmanol, as follows. The molecular formula was certificated by the pos. HR-SI-MS. The IR spectrum showed broad hydroxyl bands and an acetyl band. The CD of a **4a**–shift reagent adduct (CCl_4) showed a strong positive Cotton effect ($[\theta]_{313}$ +7.4 × 10^4) and a negative Cotton effect ($[\theta]_{287}$ −6.6 × 10^4), certificating the presence of 15α,16α-dihydroxy groups on a cycloartane nucleus.[9] **4a** was transferred to cimigol (**4b**),[10] by deacetylation with 1% Na_2CO_3, followed by reflux in dioxane–AcOH (1 : 1), suggesting the presence of a (23*R*,24*R*)-24-*O*-acety-16-hydroxy-16,23-epoxy moiety in **4a**. The stereochemistry of a 15*β*-hydroxy group has been reported in cimigol,[10] but by observation of a NOE between 18-H_3 and 15*β*-H in a ROESY spectrum of **4b**, the 15-hydroxy group was revised to an α orientation at this time, as shown in **4b**.

The high resolution ^{1}H-NMR spectra of the samples of cimigol, its diacetate and its diketone used before for the structural elucidation showed a contamination of the 7-ene congeners (*ca.* 20%) at this time. It seems that the preparation of the diacetates and diketo derivatives from a mixture of cimigol and its 7-ene congener and the purification of their 24,25-dehydrates by chromatographies should have led to a wrong conclusion of a 15*β*-hydroxy group in cimigol at that time.

D-Galactose was identified by the acidic hydrolysis of **4**, as in **2**. Thus, **4** should be formulated as 24-*epi*-24-*O*-acetylhydroshengmanol-3-*O*-*β*-D-galactopyranoside, as shown in Fig. 1.

Glycoside **5** was obtained as colorless needles, mp 229—230 °C, $[\alpha]_D$ +22.9°, and the molecular formula was determined to be $C_{36}H_{58}O_{10}$ by pos. HR-SI-MS and the data of the ^{13}C-NMR spectrum. The IR spectrum showed strong hydroxyl bands at 3600—3200 cm^{-1}. The ^{1}H- and ^{13}C-NMR signals are summarized in Tables 1 and 2.

An aglycone **5a**, mp 233—234 °C, $[\alpha]_D$ +38.2°, $C_{30}H_{48}O_5$ was obtained by hydrolysis of **5** with lactase F[Amano] and was identified as cimigenol[11] by direct comparison of TLC, IR and ^{1}H-NMR spectra with those of an authentic specimen. D-Galactose was identified by the acidic hydrolysis of **5**, as in **2**. Thus, **5** should be formulated as cimigenol-3-*O*-*β*-D-galactopyranoside, as shown in Fig. 1.

Glycoside **6** was obtained as colorless needles, mp 209—210 °C, $[\alpha]_D$ +20.4°, and the molecular formula was determined to be $C_{37}H_{60}O_{10}$ by pos. HR-SI-MS and the data of the ^{13}C-NMR spectrum. The IR spectrum showed strong hydroxyl bands. The ^{1}H- and ^{13}C-NMR signals are summarized in Tables 1 and 2. The spectra of **6** were partially similar to those of **5** except for an additional signal due to a methoxy group. An aglycone **6a**, mp 241—242 °C, $[\alpha]_D$ +38.2°, $C_{31}H_{50}O_5$ was obtained by the hydrolysis of **6** with lactase F[Amano] as in **2**, and it was identified to 25-*O*-methylcimigenol by direct comparison of the TLC, IR and ^{1}H-NMR spectra with those of an authentic specimen.[3,12] D-Galactose was identified by the acidic hydrolysis of **6**. Thus, **6** should be formulated as 25-*O*-methylcimigenol-3-*O*-*β*-D-galactopyranoside, as shown in Fig. 1.

Glycoside **7** was obtained as colorless needles, mp 213—214 °C, $[\alpha]_D$ +18.7°, and the molecular formula was determined to be $C_{38}H_{60}O_{11}$ by pos. HR-SI-MS and the data of the ^{13}C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ^{1}H- and ^{13}C-NMR signals are summarized in Tables 1 and 2. The spectra of **7** were similar to those of **6**, except for a signal due to an acetoxy group in spite of a methoxy group.

An aglycone **7a**, mp 191—192 °C, $[\alpha]_D$ +34.1°, $C_{32}H_{50}O_6$, was obtained by the hydrolysis of **7** with lactase F[Amano], and was identified as 25-*O*-acetyl cimigenol

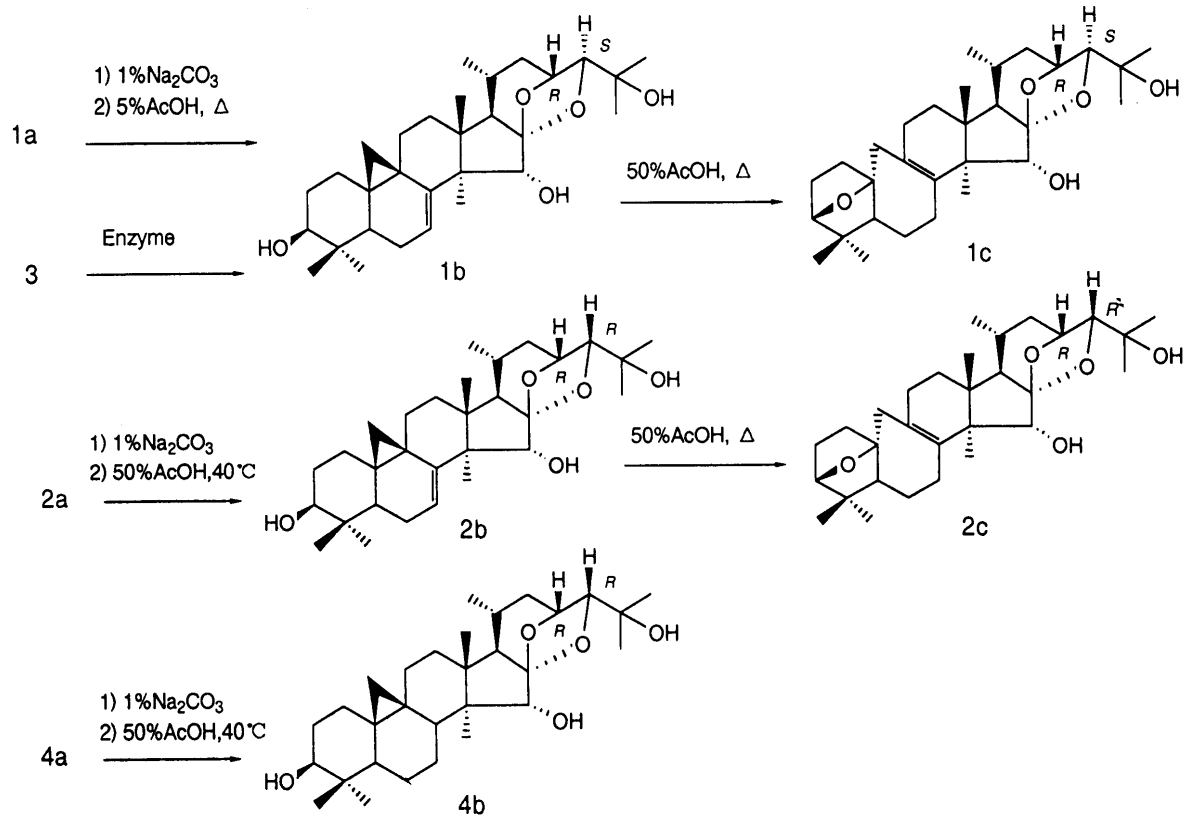

Fig. 2. Chemical Conversion of New Genuine Aglycones

by direct comparison of TLC, IR and ^{1}H-NMR spectra with those of an authentic specimen.[13,14] D-Galactose was identified by acidic hydrolysis of **7**, as with **2**. Thus, **7** should be formulated as 25-*O*-acetylcimigenol-3-*O*-*β*-D-galactopyranoside, as shown in Fig. 1.

Glycoside **8** was obtained as colorless needles, mp 216—217 °C, $[\alpha]_D$ +20.6°, and the molecular formula was determined to be $C_{38}H_{60}O_{11}$ by both pos. HR-SI-MS and the data of the ^{13}C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ^{1}H- and ^{13}C-NMR signals are summarized in Tables 1 and 2. The spectra of **8** were similar to those of **7**, except for the signals due to the 3-*O*-*β*-D-glucopyranosyl group, in spite of those of the 3-*O*-*β*-D-galactopyranosyl group.[14] 25-*O*-Acetylcimigenol (**7a**) was obtained by hydrolysis of **8** with cellulase T[Amano]4 and was identified by the direct comparison of TLC, IR and ^{1}H-NMR spectra with those of an authentic specimen.[13,14] D-Glucose was identified by the acidic hydrolysis of **8** as with the previous report.[15] Thus, **8** should be formulated as 25-*O*-acetylcimigenol-3-*O*-*β*-D-glucopyranoside, as shown in Fig. 1.

All of the ^{1}H- and ^{13}C-NMR signals of acerinol (**1c**) and 24-*epi*-acerinol (**2c**) were assigned using the data of ^{1}H–^{1}H COSY, ^{13}C–^{1}H COSY, HMBC and ROESY spectra and are summarized in Table 3. Drastic changes in the structures in the conversion of 7,8-didehydrocimigenol (**1b**) and 24-*epi*-7,8-didehydrocimigenol (**2b**) to acerinol (**1c**) and 24-*epi*-acerinol (**2c**) partially produced a large migration of signals, and several signals of **2c** have been assigned differently from the reported data.[6]

Acerinol (**1c**) was subjected to 61 items of biological assay by Pan. Lab. (Tai-wan), because of the interesting structure of a modified polyoxygenated triterpene, and only antilipemic effects were positive in hyperlipemic mice induced by injection (i.v.) of a surfactant, Triton WR-1339.

Table 3. ^{1}H- and ^{13}C-NMR Data of **1c** and **2c**

	1c	2c		1c	2c
C-1	36.74	36.74	1-H	1.50, 1.68	1.43, 1.63
C-2	25.43	25.88	2-H	1.67, 1.87	1.66, 1.86
C-3	84.89	84.87	3-H	3.73 d (5.0)	3.72 d (5.0)
C-4	45.29	45.29	5-H	1.26	1.26 d (11.3)
C-5	55.15	55.15	6-H	1.46, 1.90	1.45, 1.86
C-6	32.56	32.20	7-H	2.08, 2.58	2.07, 2.59
C-7	31.26	31.30			
C-8	137.37	137.69			
C-9	123.98	123.48			
C-10	90.14	89.84			
C-11	31.08	31.19	11-H	2.04, 2.88	2.04, 2.89
C-12	23.27	23.22	12-H	1.63, 1.75	1.42, 1.49
C-13	41.44	41.29	15-H	4.44 s	4.41 s
C-14	49.72	49.89	17-H	1.45	1.71
C-15	75.48	75.96	18-H	0.97	1.00
C-16	112.32	112.53	19-H	1.83 d (13.8)	1.81 d (13.8)
C-17	57.73	58.98		3.27 d (13.8)	3.27 d (13.8)
C-18	17.44	17.37	20-H	1.70	1.72
C-19	36.28	36.27			
C-20	24.30	23.53			
C-21	20.26	20.12	21-H	0.89 d (8.0)	0.99 d (6.3)
C-22	38.10	29.69	22-H	1.04, 2.28	1.96, 2.64
C-23	72.14	73.94	23-H	4.76 d (8.8)	4.60
C-24	89.81	84.06	24-H	3.77 s	3.70 d (4.5)
C-25	70.88	68.57	26-H	1.47	1.39
C-26	27.18	30.67	27-H	1.45	1.26
C-27	25.88	25.97	28-H	1.22	1.14
C-28	17.51	17.52	29-H	0.91	0.91
C-29	24.94	24.96	30-H	0.96	0.96
C-30	23.52	23.76			

Therefore, a similar experiment was carried out and the results are shown in the experimental section. Clofibrate (300 mg/ml) showed 37% plasma triglycerides and 77% plasma cholesterol level to the control, while **1c** (100 mg/ml) and (200 mg/ml) showed 1.4% and 1.5% triglycerides, and a 31% and 37% cholesterol level, respectively. It is interesting that **1c** has stronger antilipemic effects than clofibrate. These antilipemic effects were found neither in normal mice nor in spontanously diabetic mice.[16] A study for clarifying the mechanisms of the antilipemic effects with acerinol (**1c**) against hyperlipemic mice induced by Triton will be continued.

Experimental

General The instruments used in this work were as follows: a Yanagimoto micromelting apparatus (for melting points, uncorrected); a JASCO digital polarimeter (for specific rotation, measured at 20 °C), a JASCO ORD/UV-5 and a JASCO J-20A spectrometer (for ORD and CD, measured at 20 °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 Varian XL-300 and a JEOL α-400 (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. HPLC was conducted on a Gilson 305 pump equipped with a JASCO 830-RI as a detector and a JASCO Model 800. Silica gel 60 F_{254} (Merck) precoated TLC plates were used, and detection was carried out by 40% H_2SO_4 followed by heating.

Isolation of 1 The dried underground parts (100 g) of *Cimicifuga simplex* grown in the experimental station for medical plant studies, Faculty of Pharmaceutical Sciences, Tohoku University, were extracted with methanol (200 ml × 3) under reflux for 2 h each. After evaporation *in vacuo*, the extract (11.0 g) was partitioned between *n*-BuOH–EtOAc (50 : 50) and water three times. The soluble fraction to the organic solvents (4.4 g) was chromatographed on silica gel (120 g, 3 cm × 33 cm). After elution with $CHCl_3$ (80 ml × 8) and $CHCl_3$–MeOH (20 : 1) (80 ml × 6), fractions (450 mg) eluted with $CHCl_3$–MeOH (20 : 1) (80 ml × 3) were rechromatographed on ODS (80 g, 3.0 × 20 cm) and eluted with MeOH–H_2O (2 : 1), then MeOH–H_2O (4 : 1). The latter fraction was subjected to pTLC [solvent: $CHCl_3$–MeOH (5 : 1)] and HPLC [column: Cosmosil 10ph (10 μm, i.d. 4.6 × 250 mm); solvent: MeOH–H_2O–CH_3CN (10 : 10 : 3); column temperature: 40 °C; effluent speed: 1 ml/min]. Recrystallization of the fraction at t_R 10 min from MeOH provided glycoside **1** (45 mg) as colorless needles, mp 239—240 °C, $[\alpha]_D$ −55.5, $C_{37}H_{56}O_{10}$. Pos. HR-SI-MS: *m/z* 661.3948 [(M+H)$^+$], error ±0, pos. SI-MS: *m/z* 661 [(M+H)$^+$], *m/z* 683 [(M+Na)$^+$]. IR (KBr) cm^{-1}: 3600—3300 (OH), 1738 (acetyl group). CD: $[\theta]_{317}$ -9.77×10^3 ($c = 1 \times 10^{-4}$, MeOH) ^{1}H- and ^{13}C-NMR: Tables 1, 2.

Isolation of 2—6 After the elution of 7β-hydroxy-23-*O*-acetylshengmanol xyloside in the chromatography of the *n*-BuOH fraction from MeOH extracts of the aerial parts of *Cimicifuga simplex* (6.1 kg), the adsorbed materials were eluted with $CHCl_3$–MeOH (5 : 1) as in the previous report.[3] The eluates were rechromatographed on ODS (100 g, i.d. 3.2 × 24 cm). Fractions eluted with MeOH–H_2O (3 : 1) were subjected to HPLC [column: CrestPak C18T-5 (5 μm, i.d. 4.6 × 250 mm); solvent: MeOH–H_2O–CH_3CN (10 : 11 : 3); effluent speed: 1 ml/min; column temperature, 40 °C] to afford mixtures of **2**—**4** and **3**—**5**. The former mixture was separated into each by HPLC using YMC C8 (5 μm, i.d. 20 × 250 mm) as a column and MeOH–H_2O (70 : 30) as a solvent. Recrystallization from MeOH provided **2** as colorless needles (35 mg), while **4** was a mixture with **2** [4 : 2 (5 : 1)] (15 mg). The latter mixture was subjected to HPLC using Develosil PhA-T-5 (5 μm, 20 × 250 mm) as a column, and CH_3CN–H_2O (35 : 65) as a solvent to afford **3** and **5**. Recrystallization from MeOH provided **3** (10 mg) as colorless needles and **5** (7 mg) as colorless needles.

Glycoside **2**: Colorless needles, mp 243—244 °C, $[\alpha]_D$ −11.4° (*c* = 1.1, MeOH), $C_{38}H_{60}O_{12}$. Pos. HR-SI-MS: *m/z* 691.4037 [(M−OH)$^+$], error: −1.7 (m mass). Pos. SI-MS: *m/z* 691 [(M−OH)$^+$]. IR (KBr) cm^{-1}: 3650—3200 (OH), 1718 (CH_3CO). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

Glycoside **3**: Colorless needles, mp >300 °C, $[\alpha]_D$ −9.2° (*c* = 0.9, MeOH). $C_{36}H_{56}O_{10}$. Pos. HR-SI-MS: *m/z* 649.3944 [(M+H)$^+$], error: −0.4 (m mass), pos. SI-MS: *m/z* 649 [(M+H)$^+$]. IR (KBr) cm^{-1}: 3600—3200 (OH). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

Glycoside **4**: $C_{38}H_{62}O_{12}$. Pos. HR-SI-MS: *m/z* 733.4126 [(M+Na)$^+$], error: −1.0 (m mass). Pos. SI-MS: *m/z* 733 [(M+Na)$^+$]. ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

Glycoside **5**: Colorless powder, mp 229—230 °C, $[\alpha]_D$ +22.9° (*c* = 0.6, MeOH), $C_{36}H_{58}O_{10}$. Pos. HR-SI-MS: *m/z* 651.4112 [(M+H)$^+$], error: +0.7 (m mass). Pos. SI-MS: *m/z* 651 [(M+H)$^+$]. IR (KBr) cm^{-1}: 3600—3200 (OH). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

Isolation of 6—8 The crystalline precipitates (3 g) from the aqueous fraction after removal of the *n*-BuOH fraction from MeOH extracts of the aerial parts of *Cimicifuga simplex* (6.1 kg) were chromatographed on SiO_2 [150 g, i.d. 4.0 × 30.0 cm, and two diglycosides eluted with $CHCl_3$–MeOH (10 : 1—0 : 1)], as in the previous report.[14] Fractions eluted with $CHCl_3$–MeOH (5 : 1) (228 mg) were rechromatographed on ODS (100 g, i.d. 3.2 × 24 cm). Fractions eluted with MeOH were subjected to HPLC [column: Cosmosil 10ph (10 μm, i.d. 4.6 mm × 250 mm); solvent: MeOH–H_2O–CH_3CN (10 : 9 : 3); effluent speed: 1 ml/min; column temperature, 40 °C] to afford **6** (5.6 mg), **7** (7.7 mg) and **8** (15.8 mg) after recrystalization from MeOH.

Glycoside **6**: Colorless powder, mp 209—210 °C, $[\alpha]_D$ +20.4° (*c* = 0.5, MeOH), $C_{37}H_{60}O_{10}$. Pos. HR-SI-MS: *m/z* 665.4293 [(M+H)$^+$], error: +3.2 (m mass). Pos. SI-MS: *m/z* 665 [(M+H)$^+$]. IR (KBr) cm^{-1}: 3600—3200 (OH). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

Glycoside **7**: Colorless powder, mp 213—214 °C, $[\alpha]_D$ +18.7° (*c* = 0.6, MeOH), $C_{38}H_{60}O_{11}$. Pos. HR-SI-MS: *m/z* 693.4201 [(M+H)$^+$], error: −0.9 (m mass). Pos. SI-MS: *m/z* 693 [(M+H)$^+$]. IR (KBr) cm^{-1}: 3600—3200 (OH), 1739 (acetyl). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

Glycoside **8**: Colorless needles, mp 216—217 °C, $[\alpha]_D$ +20.6° (*c* = 0.7, MeOH), $C_{38}H_{60}O_{11}$. Pos. HR-SI-MS: *m/z* 693.4199 [(M+H)$^+$], error: −1.1 (m mass). Pos. SI-MS: *m/z* 693 [(M+H)$^+$]. IR (KBr) cm^{-1}: 3600—3300 (OH), 1737 (acetyl). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

Hydrolysis of 1—7 with Lactase F[Amano] **1** (13.2 mg) was dissolved in 1% ethanolic AcOH (20 ml), then water (40 ml) was added with stirring and the solution was adjusted to pH 4.5 by the dropwise addition of AcOH. Lactase F[Amano] (from *Aspergillus oizae*, 200 mg) was added. The solution was stirred for 2 d at 25 °C. Then, the reaction solution was shaken with EtOAc (30 ml × 3), and after washing the joined 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 *n*-hexane–EtOAc (1 : 1) to afford **1a** as colorless needles (4.0 mg) after purification with HPLC and recrystallization from MeOH. Similar treatments of **2** (26.5 mg), a mixture (27.5 mg) of **3** and **5** (3 : 2), a mixture (13.0 mg) of **2** and **4** (1 : 5) and a mixture (18.0 mg) of **6** and **7** (2 : 1) provided **2a** (13.5 mg), **1b** (5.4 mg), **4a** (5.0 mg), **5a** (6.1 mg), **6a** (3.8 mg) and **7a** (2.0 mg) as aglycones.

1a: mp 89—90 °C, $[\alpha]_D$ −75.2° (*c* = 0.29, MeOH), $C_{32}H_{48}O_6$. Pos. HR-SI-MS: *m/z* 529.3514 [(M+H)$^+$], error: −0.3 (m mass). Pos. SI-MS: *m/z* 529 [(M+H)$^+$]. IR ($CHCl_3$) cm^{-1}: 3600—3300 (OH), 1737 (acetyl). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2.

2a: mp 229—230 °C, $[\alpha]_D$ −18.5° (*c* = 0.4, MeOH). $C_{32}H_{50}O_7$. Pos. HR-SI-MS: *m/z* 546.3552 [(M)$^+$], error: −0.2 (m mass). Pos. SI-MS: *m/z* 546 [(M)$^+$], 529 [(M−OH)$^+$]. IR ($CHCl_3$) cm^{-1}: 3600—3250 (OH), 1744 (acetyl). ^{1}H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2. CD of **2a**–Eu(fod)$_3$: $[\theta]_{313} = +8.9 \times 10^4$, $[\theta]_{285} = -7.3 \times 10^4$ ($c = 1.1 \times 10^{-7}$ M of **2a**, 1.1×10^{-7} M of Eu(fod)$_3$, CCl_4).

1b: mp 227—228 °C, $[\alpha]_D$ ±0° (*c* = 0.5, MeOH). ORD: $[\alpha]_{450}$ −8.7°, $[\alpha]_{400}$ −21.7°, $[\alpha]_{300}$ −160.8° (*c* = 0.46, MeOH). $C_{30}H_{46}O_5$. Pos. HR-SI-MS: *m/z* 487.3423 [(M+H)$^+$, error: 0.2 (m mass). Pos. SI-MS: *m/z* 487 [(M+H)$^+$], 509 [(M+Na)$^+$]. IR ($CHCl_3$) cm^{-1}: 3500—3200 (OH). ^{1}H-NMR (pyridine-d_5) δ: 3.52 (dd, *J* = 4.8, 11.0 Hz, 3-H), 6.10 (dd, *J* = 1.9, 7.5 Hz, 7-H), 4.57 (s, 15-H), 1.20 (s, 18-H), 0.55 (d, *J* = 4.0 Hz, 19-H), 1.11 (d, *J* = 4.0 Hz, 19-H), 0.91 (d, *J* = 6.3 Hz, 21-H), 4.76 (br d, *J* = 8.8 Hz, 23-H), 3.80 (s, 24-H), 1.50 (s, 26-H), 1.47 (s, 27-H), 1.43 (s, 28-H), 1.18 (s, 29-H), 1.10 (s, 30-H). ^{13}C-NMR (pyridine-d_5) δ: 77.81 (C-3), 114.47 (C-7), 148.01 (C-8), 78.20 (C-15), 112.32 (C-16), 72.11 (C-23), 90.28 (C-24), 70.97 (C-25). ^{1}H-NMR ($CDCl_3$ containing D_2O) δ: 3.32 (dd, *J* = 4.0, 11.6 Hz, 3-H), 5.63 (dd, *J* = 2.3, 6.9 Hz, 7-H), 4.12 (s, 15-H), 1.03 (s, 18-H$_3$), 0.89 (d, *J* = 6.9 Hz, 21-H$_3$), 4.48 (br d, *J* = 9.5 Hz, 23-H), 3.46 (s, 24-H), 1.20 (s, 26-H$_3$), 1.20 (s, 27-H$_3$), 1.04 (s, 28-H$_3$), 1.00 (s, 29-H$_3$), 0.85 (s, 30-H$_3$). ^{1}H-NMR ($CDCl_3$) data were identical

to the reported ones of 7,8-didehydrocimigenol.[6]

4a: mp 194—195 °C, $[\alpha]_D$ +16.2° (c=0.5, MeOH). $C_{32}H_{52}O_7$. Pos. HR-SI-MS: m/z 531.3693 [$(M-OH)^+$, error: 1.0 (m mass). Pos. SI-MS: m/z 531 [$(M-OH)^+$], 571 [$(M+Na)^+$]. IR ($CHCl_3$) cm^{-1}: 3500—3200 (OH), 1744 (acetyl). ^1H- and ^{13}C-NMR (pyridine-d_5) δ: Tables 1, 2. CD of **4a**–Eu(fod)$_3$: $[\theta]_{313}=+7.4\times10^4$, $[\theta]_{287}=-6.6\times10^4$ ($c=3.0\times10^{-7}$ M of **4a**, 3.0×10^{-7} M of Eu(fod)$_3$, CCl_4).

5a: mp 233—234 °C, $C_{30}H_{48}O_5$. Pos. HR-SI-MS: m/z 489.3589 [$(M+H)^+$, error: +1.2 (m mass). Pos. SI-MS: m/z 489 [$(M+H)^+$]. IR ($CHCl_3$) cm^{-1}: 3450—3200 (OH). The ^1H-NMR spectrum and Rf value in TLC were identical to those of cimigenol.[9]

6a: mp 241—242 °C, $[\alpha]_D$ +38.2° (c=0.25, $CHCl_3$). IR ($CHCl_3$) cm^{-1}: 3550—3300 (OH). The ^1H-NMR spectrum and Rf value in TLC were identical to those of 25-*O*-metylcimigenol.

7a: mp 191—192 °C. IR ($CHCl_3$) cm^{-1}: 3550—3300 (OH), 1725 (acetyl). The ^1H-NMR spectrum and Rf value in TLC were identical to those of 25-*O*-acetylcimigenol.

Hydrolysis of 8 with Cellulase T[Amano]4 **8** (7.2 mg) was treated similarly to **1**—**7** with cellulase T[Amano]4 (from *Trichoderma viride*, 200 mg), in spite of lactase F[Amano]. 25-*O*-Acetylcimigenol (**8a**) was obtained as colorless needles (4.0 mg) by recrystallization from MeOH and was identified by direct comparison of the ^1H-NMR spectra with an authentic specimen.

Identification of L-Arabinose **1** (13 mg) was dissolved in 50% AcOH solution (1 ml) and refluxed for 3 h. The reaction solution was shaken with EtOAc (30 ml × 3), and the water layer was concentrated *in vacuo*. L-Arabinose, $[\alpha]_D$ +73.5° [c=0.2, MeOH–H_2O (1 : 1)], was obtained by HPLC [column: LiChrosolb NH_2 (5 μm, i.d. 4.6 × 250 mm); solvent: CH_3CN–H_2O (4 : 1); column temperature: 40 °C; effluent speed: 1 ml/min; t_R 6.4 min], and it showed the same Rf value (0.51) on TLC [*n*-PrOH–H_2O (85 : 15)].

Identification of D-Galactose and D-Glucose **2** (10.0 mg) was dissolved in MeOH (0.7 ml), and 1 N HCl (2 ml) was added, then the reaction solution was refluxed for 1 h. After being shaken with EtOAc (30 ml × 3) to remove the aglycone, the water layer was refluxed again for 1 h in order to hydrolyze methyl galactosides, and was then subjected to an Amberlite IR-35 column. Elution with water afforded D-galactose $[\alpha]_D$ +44.6° [c=0.26, MeOH–H_2O (1 : 1)], which was purified by HPLC [the same conditions as above: t_R 10.2 min] and TLC [Rf: 0.39, *n*-PrOH–H_2O (85 : 15)]. D-Galactose was also obtained from a mixture (3.0 mg) of **2** and **4**, one (4.3 mg) of **3** and **5**, one (3.4 mg) of **6** and **7** by the same treatment as above and identified by HPLC [column: Shodex RS-Pak DC-613, solvent: CH_3CN–H_2O (4 : 1), effluent speed: 1 ml/min, column temperature: 70 °C] equipped with a chiral detector OR-1: t_R 23 min, α_D + 10—15°.[17] D-Glucose was obtained from **8** (3 mg) by the same treatment as above and was identified by HPLC (the same conditions) equipped with a chiral detector OR-1: t_R 20 min, α_D + 10°.

Conversion of 1a to 1b **1** (1.3 mg) was dissolved to MeOH (1 ml), and 2% Na_2CO_3 (1 ml) was added and the solution was stirred at room temperature overnight. The solution neutralized by 5% AcOH, was shaken with EtOAc (10 ml × 3). The residue after removal of the solvent was dissolved to dioxane (0.5 ml) and 5% AcOH (0.5 ml) and heated on a boiling water bath for 2 h. After evaporation of the solvents *in vacuo*, the products were chromatographed on SiO_2 (12 g). The fractions eluted with *n*-hexane–EtOAc (1 : 1), which was provided **1b** (1.0 mg) as colorless needles by recrystallization from EtOAc, which was identified by comparison of the TLC and ^1H-NMR spectrum with those of a genuine aglycone of **3**.

Conversion of 1b to 1c **1b** (2.0 mg) was dissolved to MeOH (1 ml) and AcOH (1 ml) and heated on a boiling water bath for 1 h. The product obtained after the same treatment as above was identified as acerinol (**1c**) by direct comparison of the ^1H-NMR spectrum and TLC with those of an authentic specimen. ^1H- and ^{13}C-NMR (pyridine-d_5) δ: Table 3.

Conversion of 2a to 2b **2a** (7.8 mg) was stirred in 1% Na_2CO_3 [MeOH (2 ml) and 2% Na_2CO_3 (2 ml)] for 24 h at room temperature. After neutralization with 5% AcOH, the mixture was shaken with EtOAc (20 ml × 3) and washed with water. The residue after evaporation of the solvent was dissolved in dioxane (1 ml) and AcOH (1 ml), then warmed at 40 °C for 1 h. The product was chromatographed on SiO_2 (10 g), eluated with *n*-hexane–EtOAc (2 : 1), and purified by HPLC to give **2b**, mp 236—237 °C, $[\alpha]_D$ +6.0° (c=0.6, MeOH). $C_{30}H_{46}O_5$, pos. HR-SI-MS: m/z 487.3415 [$(M+H)^+$], error: −0.6 m mass; pos. SI-MS: m/z 487 [$(M+H)^+$]. IR ($CHCl_3$) cm^{-1}: 3550—3200 (OH). ^1H-NMR (pyridine-d_5) δ: 3.45 (dd, J=3.1, 10.6 Hz, 3-H), 6.12 (dd, J=1.5, 8.5 Hz, 7-H), 4.53 (s, 15-H), 1.22 (s, 18-H_3), 1.00 (d, J=6.0 Hz, 21-H_3), 4.62 (ddd, J=1.9, 4.0, 9.8 Hz, 23-H), 3.74 (d, J=4.0 Hz, 24-H), 1.43 (s, 26-H_3), 1.29 (s, 27-H_3), 1.31 (s, 28-H_3), 1.21 (s, 29-H_3), 1.12 (s, 30-H_3). ^{13}C-NMR (pyridine-d_5) δ: 78.68 (C-3), 114.50 (C-7), 148.13 (C-8), 78.20 (C-15), 112.32 (C-16), 73.90 (C-23), 84.13 (C-24), 68.64 (C-25). ^1H-NMR ($CDCl_3$ containing D_2O) δ: 3.33 (dd, J=4.0, 11.6 Hz, 3-H), 5.62 (dd, J=2.3, 7.4 Hz, 7-H), 4.04 (s, 15-H), 1.02 (s, 18-H_3), 0.91 (d, J=6.9 Hz, 21-H_3), 4.44 (ddd, J=2.3, 4.5, 10.2 Hz, 23-H), 3.58 (d, J=4.0 Hz, 24-H), 1.24 (s, 26-H_3), 1.33 (s, 27-H_3), 1.07 (s, 28-H_3), 1.00 (s, 29-H_3), 0.87 (s, 30-H_3). ROESY (pyridine-d_5): NOE between 18-H_3 (δ 1.22) and 15β-H (δ 4.53) (15α-OH). The above physical data and ^1H-NMR ($CDCl_3$) data were identical with the reported ones of 24-*epi*-7,8-didehydrocimigenol.

Conversion of 2b to 2c **2b** (3.0 mg) was treated as in the conversion of **1b** to **1c** to provide **2c** as colorless needles (2.5 mg), mp 212—213 °C, $[\alpha]_D$ +59.3° (c=1.0, MeOH). $C_{30}H_{46}O_5$. EI-MS: m/z 486 [$(M)^+$]. CI-MS: 487 [$(M+H)^+$]. ^1H- and ^{13}C-NMR (pyridine-d_5) δ: Table 3. These data were identical with the reported ones of 24-*epi*-acerinol,[3] except the assignment of some ^1H- and ^{13}C-NMR signals ($CDCl_3$). ROESY: NOEs between 18-H_3 and 15β-H, 21-H_3 and 17α-H, and 28-H_3 and 17α-H.

Conversion of 4a to 4b **4a** (1.5 mg) was treated as in the conversion of **1a** to **1b** to provide **4b** as colorless needles (1.0 mg), mp 277—278 °C. TLC (Rf: 0.5, *n*-hexane–EtOAc (1 : 1) and ^1H-NMR (pyridine-d_5) spectrum were identical with those of an authentic specimen of cimigol. ROESY: NOEs between 18-H_3 (δ 1.22) and 15β-H (δ 4.25), 18-H_3 and 20-H (δ 1.75), 29-H_3 (δ 1.21) and 3-H (δ 3.54), and 28-H_3 (δ 1.10) and 17α-H (δ 1.75).

Screening of the Antilipemic Effects of Acerinol (1c) ICR mice (10 per group), male, 6 weeks old, were used. Triton WR-1339 solution (62.5 mg/ml of 0.15 M-NaCl) was prepared, and 450 mg/kg was given i.v., then 0.25% CMC suspension (10 ml/kg) was given p.o. and the same volume of the suspension was given after 20 h. Blood (0.5 ml) was taken 23 h later, and after the usual treatment, the cholesterol and triglycerides content was measured by the members of the Research Center of Takeda Pharmaceutical Company. The results: control—body weight gain (BW-gain), −7.4 ± 0.5 g; plasma triglycerides, 1980 ± 1007 mg/ml (TG, 100%); plasma cholesterol, 560 ± 180 mg/ml (CH, 100%); clofibrate (300 mg/kg)—BW-gain, −7.3 ± 0.6 g; TG, 57%; CH, 77%; **1c** (100 mg/kg)—BW-gain, −7.8 ± 1.1 g; TG, 1.4%; CH, 31%; **1c** (300 mg/kg)—BW-gain, 7.4 ± 1.0 g; TG, 1.5%; CH, 37%.

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