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-didehydroshengmanol-3-*O*- β -D-galactopyranoside (**2**), 7,8-didehydrocimigenol-3-*O*- β -D-galactopyranoside (**3**), 24-*epi*-24-*O*-acetylshengmanol-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]. 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 (SiO₂), 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, $[\alpha]_D -55.5^\circ$, and the molecular formula was determined to be C₃₇H₅₆O₁₀ on the basis of positive high resolution secondary ion mass spectroscopy (pos. HR-SI-MS) and the data of the ¹³C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ¹H- and ¹³C-NMR signals were assigned using ¹H—¹H shift correlation spectroscopy (¹H—¹H COSY) and ¹³C—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 derivative²⁻⁴⁾ (23-H, 24-H, CH₃CO, C-23, C-24, C-25, C-26, C-27), and also a 7(8)-double bond on a cycloartane nucleus⁵⁾ (7-H, 19-H₂, C-7, C-8, C-19).

Treatment of **1** with lactase F[Amano] provided a genuine aglycone, **1a**, mp 89—90°C, C₃₂H₄₈O₆, $[\alpha]_D -75.2^\circ$, which was formulated as (23*R*,24*S*)-23-acetoxy-24,25-epoxy-9,19-cyclolanost-7-en-16-one-3 β ,15 α -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 ($[\theta]_{317} -9.77 \times 10^3$), 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% Na₂CO₃ 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-3 β -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-H₃ and 15 β -H, and 21-H₃ and 17 α -H in the rotating frame nuclear Overhauser effect spectroscopy (ROESY) spectrum of **1c**, 15 α -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, $[\alpha]_D +73.5^\circ$, as identified by TLC and HPLC. The ¹³C-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, $[\alpha]_D -11.4^\circ$, and the molecular formula was determined to be C₃₈H₆₀O₁₂ by both pos. HR-SI-MS and the data of the ¹³C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ¹H- and ¹³C-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, $[\alpha]_D -18.5^\circ$, C₃₂H₅₀O₇, which was formulated as 24-*O*-acetyl-7,8-

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Table 1. ¹H-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)	0.61 d (4.0)	0.49 d (3.8)	0.58 d (4.0)	0.47 d (4.0)	0.26 d (4.1)
	1.08 d (3.8)	1.12 d (4.0)	1.08 d (3.8)	1.15 d (4.0)	1.05 d (4.0)	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)		4.09 dd (6.3, 6.3)		4.07 dd (6.3, 6.3)	4.09 dd (6.3, 6.3)
6'	4.32 dd (2.5, 13.5)		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)	0.74 ddd (12.5, 12.5, 12.5)	0.68 ddd (12.5, 12.5, 12.5)	0.70 ddd (12.5, 12.5, 12.5)	0.71 ddd (12.5, 12.5, 12.5)
	1.66	1.54	1.53	1.53	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)	0.26 d (4.0)	0.25 d (4.2)	0.25 d (3.9)	0.24 d (4.0)
	0.64 d (4.0)	0.54 d (4.0)	0.50 d (4.2)	0.50 d (3.9)	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-d₅ containing D₂O.

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. ^1H - 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-H₂, 15-H, 23-H, 24-H, CH₃CO, C-7, C-8, C-19, C-15, C-16, C-23, C-24). **2a** was treated with 1% Na₂CO₃, followed by acidification with 50% acetic acid to afford a desacetyl dehydrate (**2b**), mp 236–237 °C, $[\alpha]_{\text{D}} + 6.0^\circ$, C₃₀H₄₆O₅, 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 3 β -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 (CCl₄) showed a strong positive Cotton effect ($[\theta]_{313} + 8.9 \times 10^4$) and a negative Cotton effect ($[\theta]_{285} - 7.3 \times 10^4$), certifying the presence of 15 α ,16 α -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-

3 β ,15 α ,16 α -triol, named 24-*epi*-24-*O*-acetyl-7,8-didehydrohydroshengmanol.

The ^1H -NMR spectrum of **2** showed the presence of a β -D-galactopyranosyl group. Acidic hydrolysis of **2** gave D-galactose, $[\alpha]_{\text{D}} + 44.6^\circ$, 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, $[\alpha]_{\text{D}} - 9.2^\circ$, and the molecular formula was determined to be C₃₆H₅₆O₁₀ by pos. HR-SI-MS and the data of the ^{13}C -NMR spectrum. The IR spectrum showed strong hydroxyl bands. The ^1H - 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, $[\alpha]_{\text{D}} 0^\circ$, $[\alpha]_{450} - 8.7^\circ$, $[\alpha]_{400} - 21.7^\circ$, $[\alpha]_{300} - 160.8^\circ$, C₃₀H₄₆O₅, 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 C₃₈H₆₂O₁₂ by pos. HR-SI-MS and the data of the ¹³C-NMR spectrum. The ¹H- and ¹³C-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, [α]_D +16.2°, C₃₂H₅₂O₇, 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 (CCl₄) showed a strong positive Cotton effect ([θ]₃₁₃ +7.4 × 10⁴) and a negative Cotton effect ([θ]₂₈₇ –6.6 × 10⁴), certifying the presence of 15 α ,16 α -dihydroxy groups on a cycloartane nucleus.⁹⁾ 4a was transferred to cimigol (4b),¹⁰⁾ by deacetylation with 1% Na₂CO₃, followed by

reflux in dioxane–AcOH (1:1), suggesting the presence of a (23*R*,24*R*)-24-*O*-acetyl-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-H₃ 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 ¹H-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, [α]_D +22.9°, and the molecular formula was determined to be C₃₆H₅₈O₁₀ by pos. HR-SI-MS and the data of the ¹³C-NMR spectrum. The IR spectrum showed strong hydroxyl bands at 3600–3200 cm^{–1}. The ¹H- and ¹³C-NMR signals are summarized in Tables 1 and 2.

An aglycone 5a, mp 233–234 °C, [α]_D +38.2°, C₃₀H₄₈O₅ was obtained by hydrolysis of 5 with lactase F[Amano] and was identified as cimigenol¹¹⁾ by direct comparison of TLC, IR and ¹H-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, [α]_D +20.4°, and the molecular formula was determined to be C₃₇H₆₀O₁₀ by pos. HR-SI-MS and the data of the ¹³C-NMR spectrum. The IR spectrum showed strong hydroxyl bands. The ¹H- and ¹³C-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, [α]_D +38.2°, C₃₁H₅₀O₅ 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 ¹H-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, [α]_D +18.7°, and the molecular formula was determined to be C₃₈H₆₀O₁₁ by pos. HR-SI-MS and the data of the ¹³C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ¹H- and ¹³C-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, [α]_D +34.1°, C₃₂H₅₀O₆, 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 ¹H-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, [α]_D +20.6°, and the molecular formula was determined to be C₃₈H₆₀O₁₁ by both pos. HR-SI-MS and the data of the ¹³C-NMR spectrum. The IR spectrum showed strong hydroxyl bands and an acetyl band. The ¹H- and ¹³C-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 ¹H-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 ¹H- and ¹³C-NMR signals of acerinol (**1c**) and 24-*epi*-acerinol (**2c**) were assigned using the data of ¹H-¹H COSY, ¹³C-¹H 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

Table 3. ¹H- and ¹³C-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			

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.

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 spontaneously 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 D₂O, 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 F₂₅₄ (Merck) precoated TLC plates were used, and detection was carried out by 40% H₂SO₄ 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 $\times$ 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 $\times$ 33 cm). After elution with CHCl₃ (80 ml $\times$ 8) and CHCl₃-MeOH (20 : 1) (80 ml $\times$ 6), fractions (450 mg) eluted with CHCl₃-MeOH (20 : 1) (80 ml $\times$ 3) were rechromatographed on ODS (80 g, 3.0 $\times$ 20 cm) and eluted with MeOH-H₂O (2 : 1), then MeOH-H₂O (4 : 1). The latter fraction was subjected to pTLC [solvent: CHCl₃-MeOH (5 : 1)] and HPLC [column: Cosmosil 10 ph (10 μ m, i.d. 4.6 $\times$ 250 mm); solvent: MeOH-H₂O-CH₃CN (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, C₃₇H₅₆O₁₀. Pos. HR-SI-MS: *m/z* 661.3948 [(M+H)⁺], error $\pm$ 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 $\times$ 10³ (*c* = 1 $\times$ 10^{–4}, MeOH) ¹H- and ¹³C-NMR: Tables 1, 2.

Isolation of 2–6 After the elution of 7 β -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 CHCl₃-MeOH (5 : 1) as in the previous report.³⁾ The eluates were rechromatographed on ODS (100 g, i.d. 3.2 $\times$ 24 cm). Fractions eluted with MeOH-H₂O (3 : 1) were subjected to HPLC [column: CrestPak C18T-5 (5 μ m, i.d. 4.6 $\times$ 250 mm); solvent: MeOH-H₂O-CH₃CN (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 μ m, i.d. 20 $\times$ 250 mm) as a column and MeOH-H₂O (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 μ m, 20 $\times$ 250 mm) as a column, and CH₃CN-H₂O (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), C₃₈H₆₀O₁₂. 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 (CH₃CO). ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2.

Glycoside 3: Colorless needles, mp >300°C, $[\alpha]_D$ –9.2° (*c* = 0.9,

MeOH), C₃₆H₅₆O₁₀. 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). ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2.

Glycoside 4: C₃₈H₆₂O₁₂. Pos. HR-SI-MS: *m/z* 733.4126 [(M+Na)⁺], error: –1.0 (m mass). Pos. SI-MS: *m/z* 733 [(M+Na)⁺]. ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2.

Glycoside 5: Colorless powder, mp 229–230°C, $[\alpha]_D$ +22.9° (*c* = 0.6, MeOH), C₃₆H₅₈O₁₀. 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). ¹H- and ¹³C-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 SiO₂ [150 g, i.d. 4.0 $\times$ 30.0 cm, and two diglycosides eluted with CHCl₃-MeOH (10 : 1–0 : 1)], as in the previous report.¹⁴⁾ Fractions eluted with CHCl₃-MeOH (5 : 1) (228 mg) were rechromatographed on ODS (100 g, i.d. 3.2 $\times$ 24 cm). Fractions eluted with MeOH were subjected to HPLC [column: Cosmosil 10 ph (10 μ m, i.d. 4.6 mm $\times$ 250 mm); solvent: MeOH-H₂O-CH₃CN (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 recrystallization from MeOH.

Glycoside 6: Colorless powder, mp 209–210°C, $[\alpha]_D$ +20.4° (*c* = 0.5, MeOH), C₃₇H₆₀O₁₀. 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). ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2.

Glycoside 7: Colorless powder, mp 213–214°C, $[\alpha]_D$ +18.7° (*c* = 0.6, MeOH), C₃₈H₆₀O₁₁. 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). ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2.

Glycoside 8: Colorless needles, mp 216–217°C, $[\alpha]_D$ +20.6° (*c* = 0.7, MeOH), C₃₈H₆₀O₁₁. 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). ¹H- and ¹³C-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 oryzae*, 200 mg) was added. The solution was stirred for 2 d at 25°C. Then, the reaction solution was shaken with EtOAc (30 ml $\times$ 3), and after washing the joined EtOAc layer with water and drying it over Na₂SO₄, the solvent was evaporated *in vacuo*. The residue was chromatographed on SiO₂ (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), C₃₂H₄₈O₆. Pos. HR-SI-MS: *m/z* 529.3514 [(M+H)⁺], error: –0.3 (m mass). Pos. SI-MS: *m/z* 529 [(M+H)⁺]. IR (CHCl₃) cm^{–1}: 3600–3300 (OH), 1737 (acetyl). ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2.

2a: mp 229–230°C, $[\alpha]_D$ –18.5° (*c* = 0.4, MeOH), C₃₂H₅₀O₇. 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 (CHCl₃) cm^{–1}: 3600–3250 (OH), 1744 (acetyl). ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2. CD of **2a**–Eu(fod)₃: $[\theta]_{313}$ = +8.9 $\times$ 10⁴, $[\theta]_{285}$ = –7.3 $\times$ 10⁴ (*c* = 1.1 $\times$ 10^{–7} M of **2a**, 1.1 $\times$ 10^{–7} M of Eu(fod)₃, CCl₄).

1b: mp 227–228°C, $[\alpha]_D$ $\pm$ 0° (*c* = 0.5, MeOH). ORD: $[\alpha]_{450}$ –8.7°, $[\alpha]_{400}$ –21.7°, $[\alpha]_{300}$ –160.8° (*c* = 0.46, MeOH). C₃₀H₄₆O₅. 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 (CHCl₃) cm^{–1}: 3500–3200 (OH). ¹H-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). ¹³C-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). ¹H-NMR (CDCl₃ containing D₂O) 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-H₃), 0.89 (d, *J* = 6.9 Hz, 21-H₃), 4.48 (br d, *J* = 9.5 Hz, 23-H), 3.46 (s, 24-H), 1.20 (s, 26-H₃), 1.20 (s, 27-H₃), 1.04 (s, 28-H₃), 1.00 (s, 29-H₃), 0.85 (s, 30-H₃). ¹H-NMR (CDCl₃) data were identical

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

4a: mp 194–195 °C, $[\alpha]_D + 16.2^\circ$ ($c=0.5$, 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 (CHCl₃) cm^{-1} : 3500–3200 (OH), 1744 (acetyl). ¹H- and ¹³C-NMR (pyridine-*d*₅) δ : Tables 1, 2. CD of **4a**–Eu(fod)₃: $[\theta]_{313} = +7.4 \times 10^4$, $[\theta]_{287} = -6.6 \times 10^4$ ($c=3.0 \times 10^{-7}$ M of **4a**, 3.0×10^{-7} M of Eu(fod)₃, CCl₄).

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 (CHCl₃) cm^{-1} : 3450–3200 (OH). The ¹H-NMR spectrum and *R*_f value in TLC were identical to those of cimigenol.⁹⁾

6a: mp 241–242 °C, $[\alpha]_D + 38.2^\circ$ ($c=0.25$, CHCl₃). IR (CHCl₃) cm^{-1} : 3550–3300 (OH). The ¹H-NMR spectrum and *R*_f value in TLC were identical to those of 25-O-methylcimigenol.

7a: mp 191–192 °C. IR (CHCl₃) cm^{-1} : 3550–3300 (OH), 1725 (acetyl). The ¹H-NMR spectrum and *R*_f 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 $\times$ 3), and the water layer was concentrated *in vacuo*. L-Arabinose, $[\alpha]_D + 73.5^\circ$ ($c=0.2$, MeOH–H₂O (1:1)), was obtained by HPLC [column: LiChrosorb NH₂ (5 μ m, i.d. 4.6 $\times$ 250 mm); solvent: CH₃CN–H₂O (4:1); column temperature: 40 °C; effluent speed: 1 ml/min; *t*_R 6.4 min], and it showed the same *R*_f value (0.51) on TLC [*n*-PrOH–H₂O (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 $\times$ 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 $[\alpha]_D + 44.6^\circ$ ($c=0.26$, MeOH–H₂O (1:1)), which was purified by HPLC [the same conditions as above: *t*_R 10.2 min] and TLC [*R*_f: 0.39, *n*-PrOH–H₂O (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: CH₃CN–H₂O (4:1), effluent speed: 1 ml/min, column temperature: 70 °C] equipped with a chiral detector OR-1: *t*_R 23 min, $\alpha_D + 10$ –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, $\alpha_D + 10^\circ$.

Conversion of 1a to 1b **1** (1.3 mg) was dissolved to MeOH (1 ml), and 2% Na₂CO₃ (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 $\times$ 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 SiO₂ (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 ¹³C-NMR (pyridine-*d*₅) δ : Table 3.

Conversion of 2a to 2b **2a** (7.8 mg) was stirred in 1% Na₂CO₃ [MeOH (2 ml) and 2% Na₂CO₃ (2 ml)] for 24 h at room temperature. After neutralization with 5% AcOH, the mixture was shaken with EtOAc (20 ml $\times$ 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 SiO₂ (10 g), eluted with *n*-hexane–EtOAc (2:1), and purified by HPLC to give **2b**, mp 236–237 °C, $[\alpha]_D + 6.0^\circ$ ($c=0.6$, 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 (CHCl₃) 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-H₃), 1.00 (d, *J*=6.0 Hz, 21-H₃), 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-H₃), 1.29 (s, 27-H₃), 1.31 (s, 28-H₃), 1.21 (s, 29-H₃), 1.12 (s, 30-H₃). ¹³C-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 (CDCl₃ containing D₂O) 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-H₃), 0.91 (d, *J*=6.9 Hz, 21-H₃), 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-H₃), 1.33 (s, 27-H₃), 1.07 (s, 28-H₃), 1.00 (s, 29-H₃), 0.87 (s, 30-H₃). ROESY (pyridine-*d*₅): NOE between 18-H₃ (δ 1.22) and 15 β -H (δ 4.53) (15 α -OH). The above physical data and ¹H-NMR (CDCl₃) 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, $[\alpha]_D + 59.3^\circ$ ($c=1.0$, MeOH). $C_{30}H_{46}O_5$, EI-MS: m/z 486 $[(M)^+]$. CI-MS: 487 $[(M+H)^+]$. ¹H- and ¹³C-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 ¹³C-NMR signals (CDCl₃). ROESY: NOEs between 18-H₃ and 15 β -H, 21-H₃ and 17 α -H, and 28-H₃ and 17 α -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 (*R*_f: 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-H₃ (δ 1.22) and 15 β -H (δ 4.25), 18-H₃ and 20-H (δ 1.75), 29-H₃ (δ 1.21) and 3-H (δ 3.54), and 28-H₃ (δ 1.10) and 17 α -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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References and Notes

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