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Acylated Iridoid and Phenylethanoid Glycosides from the Aerial Parts of *Scrophularia nodosa*

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From the aerial parts of *Scrophularia nodosa* L. (Scrophulariaceae), eighteen acylated iridoid glycosides and nine phenylethanoid glycosides were isolated. The structures of eight new iridoid and two new phenylethanoid glycosides were elucidated on the basis of chemical and spectroscopic evidences.

In our previous paper,[1] we reported the isolation and the structural elucidation of triterpene saponins, which were closely related to saikosaponins from *Bupleurum falcatum* L.,[2] from *Scrophularia kakudensis* Franch. Another *Scrophularia* species, *Scrophularia nodosa* L. (Scrophulariaceae) is widely spreaded in Europe and has been used as a folk medicine for cancer.[3] Weinges et al. [4] reported the presence of aucubin, harpagide and 6-rhamnosyl catalpol in the alkaline extract of *S. nodosa*. Grabia et al.[5] also reported the presence of harpagide, harpagoside, harpagide acetate, ferulic acid, vanillic acid, *p*-hydroxybenzoic acid, caffeic acid, protocatechuic acid, glucose, fructose, saccharose, and raffinose in this plant. In this paper, we report on the isolation and structural elucidation of eighteen acylated iridoid glycosides and nine phenylethanoid glycosides from the aerial parts of *S. nodosa*. Among them, eight iridoid glycosides (scrophulosides A_1−A_8) and two phenylethanoid glycosides (scrophulosides B_1−B_2) are new compounds.

Results and Dicussion

The aerial parts of *S. nodosa* were extracted with ether, and the residue was extracted with methanol. The methanolic extract was passed through an Amberlyst A-27 column, and the eluate was concentrated and dissolved in water. The water solution was passed through a Mitsubishi Diaion HP-20 column, and the adsorbed material was eluted successively with water, methanol−water (6:4) and methanol. The methanol−water (6:4) eluate and the methanol eluate were chromatographed on a preparative ODS column, followed by repeated semipreparative HPLC on a reversed phase column [ODS, PhA]. The methanol−water (6:4) eluate afforded known compounds **2**,[6] **3**,[7], **4** (verbascoside A),[8] **5**,[6] **8** (buddlejoside A_5),[8] **9** (buddlejoside A_3),[8] **10** (buddlejoside A_4),[8] **18** (pulverulentoside II),[9] **19** (acteoside),[10] **20** (jionoside D),[11] **21**,[12] **22** (angoroside A),[13] **23** (*cis*-acteoside),[14] **24**,[15] **26** (angoroside C),[16] and new compounds **6** (scrophuloside A_2), **7** (scrophuloside A_3), **14** (scrophuloside A_5), **17** (scrophuloside A_8), **25** (scrophuloside B_1), and **27** (scrophuloside B_2). The methanol eluate afforded known compounds **4** (verbascoside A),[8] **8** (buddlejoside A_5),[8] **9** (buddlejoside A_3),[8] **11** (scrovalentinoside),[18] **12** (scopolioside A),[17] and new compounds **1** (scrophuloside A_1), **13** (scrophuloside A_4), **15** (scrophuloside A_6), **16** (scrophuloside A_7), and **17** (scrophuloside A_8) (Chart 1). The known compounds were identified from NMR data.

The first of the eight new iridoid glycosides, scrophuloside A_1 (**1**), had a molecular formula of $C_{26}H_{32}O_{12}$ (FAMBS *m/z* 559 $[M + Na]^+$ and from elemental analysis). The UV spectrum showed absorption maxima at 227 (4.35), 298 (sh 4.31), and 309 (4.34) nm indicating the presence of an oxycinnamate structure. The ^{1}H NMR spectrum contained the signals of a methyl group at δ 1.23 (3H, d, J = 6 Hz), a trisubstituted olefinic proton at δ 7.43 (1H, br s), a *p*-methoxycinnamoyl and a glucopyranosyl group (see Table 1). Alkaline hydrolysis of compound **1** gave *p*-methoxycin-

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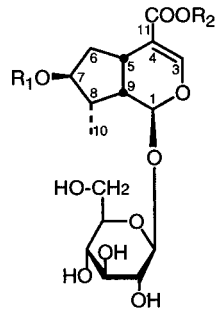
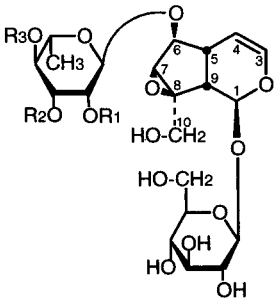
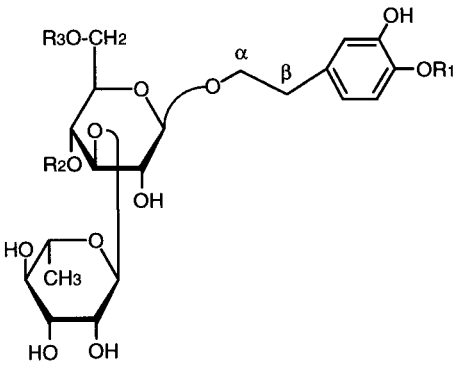
Chart 1



1 R_1= *p*-methoxycinnamoyl R_2= H
1a R_1= H R_2= H
1b R_1= H R_2= CH_3



	R_1	R_2	R_3
2	H	H	*p*-coumaroyl
2a	H	H	H
3	H	H	*cis*-*p*-coumaroyl
4	H	H	*p*-methoxycinnamoyl
5	H	H	isoferuloyl
6	acetyl	H	*p*-coumaroyl
7	H	acetyl	*p*-coumaroyl
8	acetyl	*p*-methoxycinnamoyl	H
9	acetyl	H	*p*-methoxycinnamoyl
10	H	acetyl	*p*-methoxycinnamoyl
11	acetyl	acetyl	*p*-methoxycinnamoyl
12	acetyl	*p*-methoxycinnamoyl	acetyl
13	acetyl	*p*-methoxycinnamoyl	*p*-methoxycinnamoyl
14	acetyl	*cis*-*p*-methoxycinnamoyl	H
15	acetyl	*cis*-*p*-methoxycinnamoyl	acetyl
16	acetyl	acetyl	*cis*-*p*-methoxycinnamoyl
17	acetyl	acetyl	isoferuloyl
18	acetyl	isoferuloyl	H



	R_1	R_2	R_3
19	H	caffeoyl	H
20	Me	caffeoyl	H
21	H	caffeoyl	xylosyl
22	H	caffeoyl	arabinosyl
23	H	*cis*-caffeoyl	H
24	H	*cis*-*p*-coumaroyl	H
25	H	feruloyl	arabinosyl
26	Me	feruloyl	arabinosyl
27	H	*cis*-feruloyl	arabinosyl

namic acid and compound **1a**. Methylation of compound **1a** with diazomethane afforded 8-epiloganin **1b**.[19] In the ^{1}H NMR spectrum of **1b**, H-7 was shifted upfield by 1.13 ppm compared with that of compound **1**. Therefore structure **1** may be assigned to scrophuloside A_1.

Scrophulosides A_2 (**6**, $C_{32}H_{40}O_{17}$) and A_3 (**7**, $C_{32}H_{40}O_{17}$) showed similar ^{1}H and ^{13}C NMR spectra to those of compound **26** except for the presence of an acetyl group (Tables 1 and 2). Alkaline hydrolysis of these two compounds yielded *p*-coumaric acid and 6-rhamnosyl catalpol (**2a**). In the ^{1}H NMR spectrum of **6**, H-2 of Rha [δ 5.11 (1H, dd, J = 3, 2 Hz)] was shifted downfield by 1.26 ppm and H-4 of Rha [δ 5.03 (1H, dd, J = 10, 10 Hz)] was shifted downfield by 1.54 ppm in comparison to those of 6-rhamnosyl catalpol (**2a**).[8] HMBC experiments established the binding site of the acetyl group at C-2 and the *p*-coumaroyl group at C-4 of the rhamnose. The ^{1}H NMR spectrum of **7** also showed two downfield-shifted rhamnosyl protons, i.e., H-3 [δ 5.22 (1H, dd, J = 10, 3 Hz)] and H-4 [δ 5.27 (1H, dd, J = 10, 10 Hz)]. The positions of an acetyl and a *p*-coumaroyl group were established as C-3 and C-4 in the rhamnosyl residue, respectively, by observation of the HMBC correlation. These results led to structures **6** and **7** for scrophulosides A_2 and A_3, respectively.

Scrophuloside A_4 (**13**, $C_{43}H_{50}O_{19}$) possessed an acetyl and two *p*-methoxycinnamoyl groups in a rhamnosyl residue. By comparing the ^{1}H NMR spectral data of **13** with those of **2a**, H-2 [δ 5.39 (1H, dd, J = 3, 2 Hz)], H-3 [δ 5.48 (1H, dd, J = 10, 3 Hz)], and H-4 of Rha [δ 5.28 (1H, dd, J = 10, 10 Hz)] of **13** were shifted downfield, suggesting that C-2, C-3, and C-4 in the rhamnose moiety were acylated. The HMBC correlation indicated the acetyl at C-2 and the two *p*-methoxycinnamoyl groups at C-3 and C-4 of the rhamnosyl residue.

The ^{1}H NMR spectral data of scrophuloside A_5 (**14**, $C_{33}H_{42}O_{17}$) was very similar to that of compound **8**,[8] showing acetyl, *cis*-*p*-methoxycinnamoyl, and 6-rhamnosyl catalpol residues. On alkaline hydrolysis compound **14** afforded *cis*-*p*-methoxycinnamic acid and 6-rhamnosyl catalpol (**2a**). The positions of two acyl groups were decided by the HMBC experiment to be as shown in the structure.

Scrophulosides A_6 (**15**, $C_{35}H_{44}O_{18}$) and A_7 (**16**, $C_{35}H_{44}O_{18}$) showed the presence of two acetyl and one *cis*-*p*-methoxycinnamoyl group in the ^{1}H NMR spectra. The three acyl groups were attached to C-2, C-3, and C-4 in the rhamnosyl moiety in both compounds. The HMBC correlation led to assignment of the structures **15** and **16** to scrophulosides A_6 and A_7, respectively.

Scrophuloside A_8 (**17**, $C_{35}H_{44}O_{19}$) also had three acyl groups in the rhamnosyl residue. Results from alkaline hydrolysis and the HMBC correlation established that the structure of scrophuloside A_8 was 6-(2,3-diacetyl-4-isoferuloyl)rhamnosyl catalpol.

The first of the two new phenylethanoid glycosides,

Table 1. ^{1}H NMR Spectral Data of Scrophulosides A_1−A_8 (**1**, **6**, **7**, and **13**−**17**)[a]

	1	**6**	**7**	**13**	**14**	**15**	**16**	**17**
aglycone								
1	5.55 d (5)	5.08 d (10)	5.10 d (10)	5.11 d (10)	5.09 d (10)	5.09 d (10)	5.08 d (10)	5.09 d (10)
3	7.43 br s	6.38 dd (6, 2)	6.40 dd (6, 2)	6.41 dd (6, 2)	6.38 dd (6, 2)	6.39 dd (6, 2)	6.38 dd (6, 2)	6.39 dd (6, 1.5)
4		5.06[b]	5.10[b]	5.12[b]	5.10[b]	5.07[b]	5.00 dd (6, 4)	5.08[b]
5	3.11 (m)	2.44 (m)	2.47 (m)	2.52 (m)	2.47 (m)	2.48 (m)	2.45 (m)	2.48 (m)
6	2.01 (m)	4.03 dd (8, 1)	4.05 dd (8, 1)	4.09 dd (8, 1)	4.04 dd (8, 1)	4.05 dd (8, 1)	4.03 dd (8, 1)	4.05 d (8)
6	2.26 (m)							
7	4.94 (m)	3.64 br s	3.67 br s	3.69 br s	3.65 br s	3.66 br s	3.65 br s	3.67 s
8	2.46 (m)							
9	2.60 (m)	2.57 dd (10, 7.5)	2.58 dd (10, 7.5)	2.61 dd (10, 7.5)	2.57 dd (9, 7.5)	2.58 dd (10, 7.5)	2.57 dd (10, 7.5)	2.59 dd (10, 7.5)
10	1.23 d (6)	3.81 d (13)	3.83 d (13)	3.84 d (13)	3.81 d (13)	3.81 d (13)	3.18 d (13)	3.82 d (13)
10		4.15 d (13)	4.15 d (13)	4.17 d (13)	4.14 d (13)	4.15 d (13)	4.14 d (13)	4.16 d (13)
sugar								
Glc-1	4.70 d (8)	4.77 d (7.5)	4.78 d (8)	4.79 d (8)	4.77 d (7.5)	4.77 d (8)	4.76 d (8)	4.79 d (8)
-2	3.20 d (9, 8)	3.26[b]	3.26[b]	3.27[b]	3.25[b]	3.26 dd (9, 8)	3.25[b]	3.28 dd (9, 8)
-3	3.37 dd (9, 9)	3.39 dd (9, 9)	3.40 dd (9, 9)	3.41 dd (9, 9)	3.39 dd (9, 9)	3.40 dd (9, 9)	3.39 dd (9, 9)	3.42 dd (9, 9)
-4	3.25 dd (9, 8.5)	3.26[b]	3.26[b]	3.27[b]	3.25[b]	3.25 dd (9, 9)	3.25[b]	3.27 dd (9, 9)
-5	3.31 (m)	3.32 (m)	3.31 (m)	3.33 (m)	3.32 (m)	3.25 (m)	3.29[b]	3.34 (m)
-6	3.65 dd (12, 6)	3.62 dd (12, 6)	3.92 dd (12, 2)	3.64 dd (12, 6)	3.61 dd (12, 6)	3.63 dd (12, 5)	3.62 dd (12, 6)	3.64 dd (12, 6)
-6	3.91 dd (12, 2)	3.91 dd (12, 2)	*c*	3.93 dd (12, 2)	3.91 dd (12, 2)	3.91 dd (12, 2)	3.91 dd (12, 2.5)	3.92 dd (12, 1)
Rha-1		5.02 d (2)	5.02 d (2)	5.11[b]	5.00 d (2)	5.05 d (2)	5.05 d (2)	5.07 d (1.5)
-2		5.11 dd (3, 2)	4.08 dd (3, 2)	5.39 dd (3, 2)	5.27 dd (3, 2)	5.31 dd (4, 2)	5.29 dd (4, 2)	5.31 dd (3, 1.5)
-3		4.12 dd (10, 3)	5.22 dd (10, 3)	5.48 dd (10, 3)	5.19 dd (10, 3)	5.35 dd (10, 4)	5.24 dd (10, 4)	5.36 dd (10, 3)
-4		5.03 dd (10, 10)	5.27 dd (10, 10)	5.28 dd (10, 10)	3.56 dd (10, 10)	5.08 dd (10, 10)	5.10 dd (10, 9.5)	5.17 dd (10, 10)
-5		3.93 (m)	4.12 (m)	4.13 (m)	3.86 (m)	4.01 (m)	3.94 (m)	4.07 (m)
-6		1.18 d (6)	1.20 d (6)	1.25 d (6)	1.31 d (6)	1.20 d (6)	1.18 d (6)	1.22 d (6)
ester	(at C-7)	(at Rha-4)	(at Rha-4)	(at Rha-4)	(at Rha-3)	(at Rha-3)	(at Rha-4)	(at Rha-4)
β	6.37 d (16)	6.38 d (16)	6.31 d (16)	6.34 d (16)	5.80 d (13)	5.70 d (13)	5.81 d (12.5)	6.31 d (16)
γ	7.62 d (16)	7.67 d (16)	7.63 d (16)	7.64d (16)	6.91 d (13)	6.92 d (13)	7.00 d (12.5)	7.61 d (16)
2	7.55 d (9)	7.48 d (9)	7.47 d (9)	7.48 d (9)	7.69 d (9)	7.69 d (9)	7.69 d (9)	7.09 d (2)
3	6.96 d (9)	6.81 d (9)	6.81 d (9)	6.89 d (9)	6.89 d (9)	6.90 d (9)	6.91 d (9)	
5	6.96 d (9)	6.81 d (9)	6.81 d (9)	6.89 d (9)	6.89 d (9)	6.90 d (9)	6.91 d (9)	6.94 d (8)
6	7.55 d (9)	7.48 d (9)	7.47 d (9)	7.48 d (9)	7.69 d (9)	7.69 d (9)	7.69 d (9)	7.07 dd (8, 2)
OMe	3.83 s			3.79 s (at Rha-3)	3.82 s	3.82 s	3.82 s	3.88 s
β				6.23 d (16)				
γ				7.55d (16)				
2				7.44 d (9)				
3				6.88 d (9)				
5				6.88 d (9)				
6				7.44 d (9)				
OMe				3.79 s				
		(at Rha-2)	(at Rha-3)	(at Rha-2)	(at Rha-2)	(at Rha-2)	(at Rha-2)	(at Rha-2)
OAc		2.16 s	2.00 s	2.17 s	2.02 s	2.01 s (at Rha-4)	2.15 s (at Rha-3)	2.16 s (at Rha-3)
OAc						2.06 s	1.96 s	1.93 s

[a] Coupling constants (Hz) in parentheses. [b] Superimposed signals. [c] Not assigned.

scrophuloside B_1 (**25**), presented a pseudomolecular ion peak at *m*/*z* 793 $[M + Na]^+$ in the FABMS, which, in combination with the elemental analysis, suggested a molecular formula of $C_{35}H_{46}O_{19}$. The UV spectrum showed absorption maxima at 231 (sh 4.17), 246 (sh 4.04), 291 (sh 4.13), and 330 (4.31) nm, indicating the presence of an oxycinnamate residue. The ^{1}H NMR spectrum of **25** displayed a signal pattern similar to that of angoroside A (**22**)[13] Alkaline hydrolysis afforded ferulic acid and desacyl compound. The latter afforded 3,4-dihydroxyphenethyl alcohol, D-glucose, L-arabinose, and L-rhamnose by acid hydrolysis. The ROE experiment on irradiating each anomeric proton signal in **25** determined the interglycosidic links to be as shown in the structure. The HMBC correlation placed the ferulic acid at the Glc C-4 and confirmed the glycosidic linkages.

Scrophuloside B_2 (**27**, $C_{35}H_{46}O_{19}$) showed a similar ^{1}H NMR spectrum to that of **25**, except for the presence of two doublets at δ 5.80 (1H, d, J = 13 Hz) and 6.94 (1H, d, J = 13 Hz) due to *cis*-1,2-disubstituted olefinic protons. Alkaline hydrolysis afforded *cis*-ferulic acid. The ROE experiment and the HMBC correlation showed connectivities between the H-1 of Glc (δ 4.35) and C-α of the aglycone (δ 72.3), H-1 of Rha (δ 5.16) and C-3 of Glc (δ 81.8), H-1 of Ara (δ 4.21) and C-6 of Glc (δ 68.9), and H-4 of Glc (δ 4.90) and C-α of the *cis*-feruloyl residue (δ 166.9).

The iridoid and phenylethanoid glycosides from *S. nodosa* are very similar to those found in *Verbascum* (Scrophulariaceae)[6] and *Buddleja* (Buddlejaceae).[8]

Experimental Section

General Experimental Procedures. The following instruments were used in this work: JASCO DIP-1000 digital polarimeter for optical rotation; JEOL α-400 FT-NMR spectrometer for NMR spectra (^{1}H, 400 MHz; ^{13}C, 100 MHz, in CD_3OD at 35 °C); JEOL JMS-SX102 mass spectrometer for positive mode FABMS (matrix: *m*-nitrobenzyl alcohol); Hitachi G-3000 gas chromatograph for GC; Hitachi U-3410 spectrometer for ultraviolet spectra; JASCO System 800 for HPLC.

Extraction and Isolation. The dried aerial parts of *S. nodosa* L. (1.36 kg) (cultivated in the botanical garden of University of Shizuoka in 1995 from seeds purchased from Chiltern Seeds, England) were extracted with ether (×3), and the residue was extracted with methanol (×3) for 12 h at room temperature. The methanolic extract was passed through an Amberlyst 27 (anion exchanger) column (6.5 × 13 cm). The methanolic eluate was suspended in water after evaporation of methanol under reduced pressure and chromatographed on a Mitsubishi Diaion HP-20 column (9 × 25 cm) and eluted with

Table 2. ^{13}C NMR Spectral Data of Scrophulosides A_1−A_8 (**1**, **6**, **7**, and **13**−**17**)[a]

	1	**6**	**7**	**13**	**14**	**15**	**16**	**17**
aglycone								
1	95.9	95.1	95.1	95.1	95.1	95.1	95.1	95.1
3	152.7	142.4	142.3	142.4	142.3	142.4	142.4	142.4
4	114.0	103.0	103.0	103.2	103.3	103.2	103.1	103.4
5	31.8	37.2	37.2	37.1	37.2	37.1	37.1	37.1
6	39.1	84.8	84.3	84.9	84.3	84.8	84.6	84.9
7	82.7	59.5	59.4	59.4	59.3	59.4	59.3	59.4
8	43.1	66.5	66.5	66.5	66.5	66.5	66.5	66.5
9	43.3	43.3	43.3	43.2	43.3	43.2	43.2	43.2
10	14.3	61.4	61.4	61.4	61.4	61.4	61.3	61.4
11	170.6							
sugar								
Glc-1	99.8	99.7	99.7	99.7	99.7	99.7	99.7	99.7
-2	74.8	75.1	74.8	74.8	74.8	74.8	74.8	74.8
-3	78.0	77.7	77.7	77.6	78.6	77.6	77.6	77.6
-4	71.7	71.8	71.8	71.7	71.8	71.7	71.7	71.7
-5	78.4	78.6	78.6	78.6	77.7	78.6	78.6	78.5
-6	62.9	62.9	62.9	62.9	62.9	62.9	62.9	62.9
Rha-1		97.7	100.3	97.7	97.5	97.6	97.6	97.7
-2		74.2	70.1	71.5	71.4	71.3	71.0	71.6
-3		68.4	73.1	70.6	71.6	70.2	70.7	70.6
-4		74.8	72.2	72.2	72.6	72.2	71.8	71.9
-5		68.3	68.3	68.3	70.3	68.1	68.1	68.2
-6		17.8	17.8	17.8	17.9	17.7	17.7	17.8
ester	(at C-7)	(at Rha-4)	(at Rha-4)	(at Rha-4)	(at Rha-3)	(at Rha-3)	(at Rha-4)	(at Rha-4)
α	168.8	168.6	168.2	168.0	167.3	166.7	166.7	167.9
β	116.4	114.9	114.3	115.0	117.1	116.3	116.5	115.0
γ	146.1	147.1	147.3	147.7	144.9	146.0	146.5	147.7
1	128.3	127.1	127.0	128.0	128.7	128.5	128.6	128.6
2	131.0	131.2	131.3	131.0	133.3	133.6	133.4	114.9
3	115.4	116.8	116.8	115.3	114.4	114.5	114.4	148.6
4	163.2	161.3	161.5	163.2	162.1	162.2	162.2	151.7
5	115.4	116.8	116.8	115.3	114.4	114.5	114.4	112.5
6	131.0	131.2	131.3	131.0	113.3	113.6	113.4	123.1
OMe	55.9			55.8	55.7	55.8	55.8	56.4
				(at Rha-3)				
α				167.7				
β				115.0				
γ				147.2				
1				128.0				
2				131.1				
3				115.3				
4				163.3				
5				115.3				
6				131.1				
OMe				55.8				
		(at Rha-2)	(at Rha-3)	(at Rha-2)	(at Rha-2)	(at Rha-2)	(at Rha-2)	(at Rha-2)
Ac		172.2	172.0	171.6	171.7	171.6	171.6	171.7
		20.8	20.8	20.7	20.6	20.6	20.6	20.7
						(at Rha-4)	(at Rha-3)	(at Rha-3)
Ac						171.7	171.5	171.6
						20.7	20.6	20.

[a] Assigned on the basis of HSQC and HMBC.

water, methanol−water (6:4), and methanol, successively. A 3.0 g amount of the methanol−water (6:4) eluate (62.8 g) was separated by preparative HPLC on a reversed phase (ODS, PhA) column using methanol−water system as eluent. A 3.0 g amount of the methanolic eluate (51.7 g) was also separated as mentioned above. The methanol−water (6:4) eluate gave compounds **2** (5 mg), **3** (29 mg), **4** (57 mg), **5** (11 mg), **6** (6 mg), **7** (7 mg), **8** (26 mg), **9** (32 mg), **10** (31 mg), **14** (5 mg), **17** (86 mg), **18** (4 mg), **19** (630 mg), **20** (12 mg), **21** (5 mg), **22** (5 mg), **23** (22 mg), **24** (5 mg), **25** (5 mg), **26** (77 mg), and **27** (22 mg). The methanolic eluate gave compounds **1** (7 mg), **4** (20 mg), **8** (30 mg), **9** (59 mg), **11** (398 mg), **12** (36 mg), **13** (504 mg), **15** (40 mg), **16** (6 mg), and **17** (58 mg).

Scrophuloside A_1 (1): Amorphous powder, $[\alpha]^{23}_D$ −67.8 ° (*c* 0.58, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 227 (4.35), 298 (sh 4.31), 309 (4.34). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m*/*z*: 559 $[M + Na]^+$; *anal.* C 56.44%, H 6.36%, calcd for $C_{26}H_{32}O_{12}\cdot H_2O$, C 56.31%, H 6.18%.

Scrophuloside A_2 (6): Amorphous powder, $[\alpha]^{23}_D$ −151.0° (*c* 0.15, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 226 (4.19), 301 (sh 4.28), 314 (4.34). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m*/*z*: 719 $[M + Na]^+$; *anal.* C 52.85%, H 6.16%, calcd for $C_{32}H_{40}O_{17}\cdot{}^3/_2H_2O$, C 53.11%, H 5.99%.

Scrophuloside A_3 (7): Amorphous powder, $[\alpha]^{23}_D$ −161.3° (*c* 0.19, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 228 (4 302 (sh 4.34), 315 (4.41). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m*/*z*: 719 $[M+Na]^+$; anal. C 52.20%, H 6.15%, calcd for $C_{32}H_{40}O_{17}\cdot 2H_2O$, C 52.46%, H 6.05%.

Scrophuloside A_4 (13): Amorphous powder, $[\alpha]^{23}_D$ +49.3° (*c* 0.74, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 227 (4.43), 300 (sh 4.69), 311 (4.73). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m*/*z*: 893 $[M + Na]^+$; *anal.* C 57.62%, H 5.78%, calcd for $C_{43}H_{50}O_{19}\cdot{}^3/_2H_2O$, C 57.52%, H 5.95%.

Scrophuloside A_5 (14): Amorphous powder, $[\alpha]^{23}_D$ −94.8° (*c* 0.30, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 225 (4.10), 300 (sh

Table 3. ^{1}H and ^{13}C NMR Spectral Data of Scrophulosides B_1 (**25**) and B_2 (**27**)[a]

	25			**27**		
	^{1}H	^{13}C	HMBC (C)	^{1}H	^{13}C	HMBC (C)
aglycone						
α	3.74[b]	72.4		3.75[b]	72.3	
α	4.03 (m)			4.03 (m)		
β	2.79 br t (7.5)	36.6		2.78 br t (7)	36.5	
1		131.6			131.5	
2	6.71 d (2)	116.3		6.71 d (2)	116.3	
3		146.1			146.0	
4		144.7			144.6	
5	6.67 d (8)	117.2	1,3,4 of agl.	6.67 d (8)	117.1	1,3,4 of agl.
6	6.57 dd (8, 2)	121.3		6.67 dd (8, 2)	121.3	
sugar						
Glc-1	4.38 d (8)	104.2	α of agl.	4.35 d (7)	104.0	α of agl.
-2	3.39 dd (9, 8)	76.2		3.38 dd (9, 7)	76.0	
-3	3.81 dd (9, 9)	81.5		3.77 dd (9, 9)	81.8	
-4	4.97 dd (9, 9)	70.4		4.90 dd (9, 9)	70.4	
-5	*c*	75.0		*c*	75.0	
-6	3.48[b]	69.0		3.58[b]	68.9	
-6	3.57[b]			3.84[b]		
Rha-1	5.19 d (2)	103.0	3 of Glc	5.16 d (1)	103.1	3 of Glc
-2	3.91 dd (3, 2)	72.4		3.92 dd (3, 1)	72.3	
-3	*c*	72.1		*c*	72.1	
-4	*c*	74.1		*c*	74.0	
-5	*c*	70.4		*c*	70.4	
-6	1.10 d (6)	18.4		1.16 d (6)	18.2	
Ara-1	4.23 d (7)	105.0	6 of Glc	4.21 d (7)	104.9	6 of Glc
-2	*c*	72.4		*c*	72.8	
-3	*c*	73.8		3.47 dd (9, 3.5)	72.1	
-4	*c*	69.5		*c*	74.0	
-5	*c*	66.7		*c*	70.4	
-5	*c*			*c*		
ester						
fer. CO		168.3	4 of Glc		166.9	4 of Glc
-α	6.37 d (16)	115.1		5.80 d (13)	115.6	
-*β*	7.66 d (16)	148.1		6.94 d (13)	147.7	
-1		127.7			127.9	
-2	7.20 d (2)	111.9		7.87 d (2)	115.6	
-3		149.4			148.2	
-4		150.9			149.8	
-5	6.81 d (8)	116.5		6.77 d (8)	115.4	
-6	7.08 dd (8, 2)	124.4		7.16 dd (8, 2)	127.4	
OMe	3.88 s	56.5		3.89 s	56.5	

[a] Assigned on the basis of HSQC and HMBC. Coupling constants (Hz) in parentheses. [b] Superimposed signals. [c] Not assigned.

4.26), 310 (4.29). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m/z*: 733 [M + Na]$^+$; *anal.* C 54.64%, H 6.16%, calcd for $C_{33}H_{42}O_{17}\cdot H_2O$, C 54.39%, H 6.09%.

Scrophuloside A_6 (15): Amorphous powder, $[\alpha]^{23}_D$ −77.5° (*c* 1.15, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 224 (sh 4.10), 291 (sh 4.09), 311 (4.19). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m/z*: 775 [M + Na]$^+$; *anal.* C 54.04%, H 6.11%, calcd for $C_{35}H_{44}O_{18}\cdot{}^3/_2H_2O$, C 53.91%, H 6.08%.

Scrophuloside A_7 (16): Amorphous powder, $[\alpha]^{23}_D$ −141.2° (*c* 0.70, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 224 (sh 4.07), 300 (sh 4.20), 311 (4.25). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m/z*: 775 [M + Na]$^+$; *anal.* C 54.46%, H 6.10%, calcd for $C_{35}H_{44}O_{18}\cdot H_2O$, C 54.54%, H 6.02%.

Scrophuloside A_8 (17): Amorphous powder, $[\alpha]^{23}_D$ −91.5° (*c* 0.56, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 216 (sh 4.29), 231 (sh 4.11), 243 (sh 4.03), 293 (4.18), 326 (4.15). ^{1}H and ^{13}C NMR: Tables 1 and 2. FABMS *m/z*: 791 [M + Na]$^+$; *anal.* C 54.39%, H 6.19%, calcd for $C_{35}H_{44}O_{19}\cdot{}^1/_4H_2O$, C 54.37%, H 5.90%.

Scrophuloside B_1 (25): Amorphous powder, $[\alpha]^{23}_D$ −68.4° (*c* 0.52, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 218 (sh 4.30), 231 (sh 4.17), 246 (sh 4.04), 291 (sh 4.13), 330 (4.31). ^{1}H and ^{13}C NMR: Table 3. FABMS *m/z*: 793 [M + Na]$^+$; *anal.* C 52.59%, H 6.20%, calcd for $C_{35}H_{46}O_{19}\cdot{}^3/_2H_2O$, C 52.69%, H 6.19%.

Scrophuloside B_2 (27): Amorphous powder, $[\alpha]^{23}_D$ −86.4° (*c* 0.21, MeOH); UV λ_{max}^{MeOH} nm (log ϵ): 217 (sh 4.40), 229 (sh 4.28), 246 (sh 4.11), 291 (sh 4.20), 330 (4.40). ^{1}H and ^{13}C NMR: Table 3. FABMS *m/z*: 793 [M + Na]$^+$; *anal.* C 52.22%, H 6.28%, calcd for $C_{35}H_{46}O_{19}\cdot 2H_2O$, C 52.11%, H 6.25%.

Alkaline Hydrolysis of Scrophuloside A_1 (1). Scrophuloside A_1 (**1**) (7 mg) was stirred in 2% aq. NaOH (5 mL) for 2 h under a N_2 atm at room temperature. The reaction mixture was passed through an Amberlyst 27 column (8 × 100 mm), and the eluate was partitioned between ether and water. The water layer was concentrated to dryness, and the residue was methylated with diazomethane in the usual manner. The methylated product was purified by preparative HPLC [column, YMC A-323 ODS, 10 × 250 mm; H_2O−CH_3CN (87.5:12.5)] to afford 8-epiloganin (**1b**) (0.7 mg) as amorphous powder. $[\alpha]^{23}_D$ −62.9° (*c* 0.07, MeOH). FABMS *m/z*: 413 [M + Na]$^+$. ^{1}H and ^{13}C NMR spectra were identical to the reported data.[18]

Acid and Sugar Analysis of Scrophulosides A_1−A_9 (1, 6, 7, and 13−17) and Scrophulosides B_1 (25) and B_2 (27). Each glycoside (1 mg) was stirred in 1% aq. NaOH (0.05 mL) for 1 h under a N_2 atm at room temperature. The reaction mixture was extracted with ether (×2) after acidification by 2 N HCl. From the ether extract, *p*-coumaric acid (6.6 min) (from **6** and **7**), *p*-methoxycinnamic acid (25.7 min) (from **1**, **11**, and **13**), *cis*-*p*-methoxycinnamic acid (21.4 min) (from **14**, **15**, and **16**), and isoferulic acid (7.6 min) (from **17**) were detected by HPLC [column, Develosil ODS-7 4.6 × 250 mm; H_2O−CH_3CN (75:25) + 0.05% trifluoroacetic acid (TFA), 1.0 mL/min; UV 320 nm] and ferulic acid (20.0 min) (from **25**), *cis*-ferulic

acid (22.2 min) (from **27**) were detected by HPLC [column, Develosil ODS-7 4.6 × 250 mm; H_2O-CH_3CN (85:15) + 0.05% TFA, 1.0 mL/min; UV 320 nm]. The water layer was passed through a Mitsubishi Diaion HP-20 column (8 × 100 mm), the column was washed with water, and the adsorbed material was eluted with methanol. From the methanolic eluate, 6-rhamnosyl catalpol (**6a**) (7.9 min) (from **6**, **7**, and **13**−**17**) was detected by HPLC [column, Develosil ODS-7 4.6 × 250 mm; H_2O-CH_3CN (97:3), 1.0 mL/min; UV 205 nm]. The methanolic eluate was hydrolyzed by 2 N HCl (0.05 mL) for 40 min at 100 °C. The reaction mixtures from compounds **25** and **27** were diluted with water and extracted with ethyl acetate. From the ethyl acetate extract, 3,4-dihydroxyphenethyl alcohol (7.0 min) was detected by HPLC [column, Develosil ODS-7 4.6 × 250 mm; H_2O-CH_3CN (85:15) + 0.05% TFA, 1.0 mL/min; UV 280 nm]. Acid hydrolysis products of **1**, **6**, **7**, and **13**−**17** and the water layer of **25** and **27** were passed through an Amberlite IRA-60E column (8 × 60 mm) and the eluate was concentrated. From the residue, D-glucose (from **1**); D-glucose, L-rhamnose (from **6**, **7**, and **13**−**17**); D-glucose, L-rhamnose, L-arabinose (from **25** and **27**) were detected by GC [column, Supelco SPB™-1 0.25 mm × 27 m; column temp. 230 °C; carrier gas N_2] as thiazolidine derivative described before.[20] t_R: D-glucose (18.1 min); L-glucose (17.3 min); D-rhamnose (12.1 min), L-rhamnose (12.5 min); D-arabinose (9.8 min), L-arabinose (10.9 min). The t_R of D-rhamnose was obtained from its enantiomer (L-rhamnose + L-cysteine).

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