Six Secoiridoid Glucosides from *Adina racemosa*

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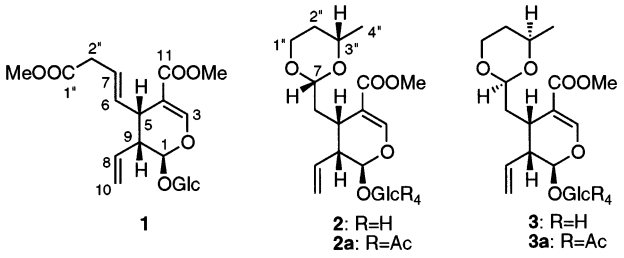
Six novel secoiridoid glucosides, adinosides A (**1**), B (**2**), C (**3**), D (**4**), E (**5**), and grandifloroside 11-methyl ester (**6**) were isolated, together with 27 known compounds, from the dried leaves, flowers, and twigs of *Adina racemosa*. The structures of the new compounds were determined by spectroscopic (NMR, MS) and chemical means.

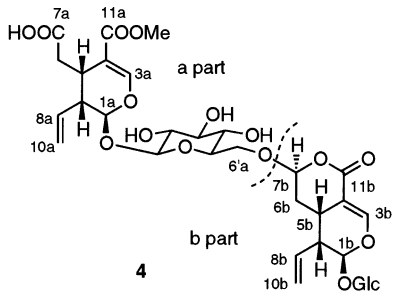
The genus *Adina* is well known to contain indole alkaloid glucosides, which are closely related to numerous bioactive monoterpenoid indole alkaloids.[1] On account of our interest in indole alkaloid glucosides and monoterpenoid indole alkaloids, we examined the glycosidic fraction of *Adina racemosa* (Sieb. et Zucc.) Miq. (Rubiaceae). The woody part of the plant has been used for building materials because of its termiticidal constituents.[2] Previous phytochemical studies reported the isolation of iridoid glucosides, coumarins, and chromones from its wood, bark, and leaves.[2−4] In this paper we describe the isolation and characterization of six new secoiridoid glucosides.



1

2: R=H
2a: R=Ac

3: R=H
3a: R=Ac



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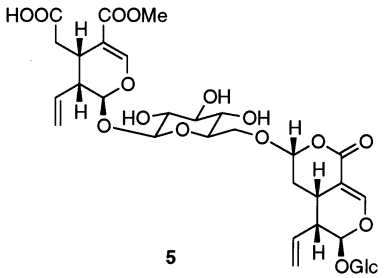

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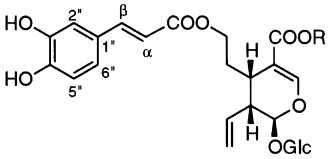
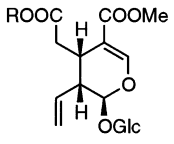


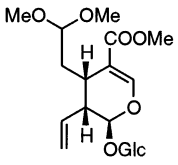
6: R=Me
11: R=H

Results and Discussion

The dried leaves, flowers, and twigs of *A. racemosa* collected in Taiwan were extracted with MeOH under reflux. The extract was successively partitioned between H_2O and $CHCl_3$ and between H_2O and *n*-BuOH. The *n*-BuOH-soluble fraction was separated by a combination of chromatographic procedures to afford six new compounds, **1**−**6**, along with 27 known compounds: secologanin,[3] sweroside,[3] secoxyloganin (**7**),[3] loganin,[3,4] noreugenin-7-*O*-*β*-D-glucoside,[4] secologanin dimethyl acetal (**8**),[5] secologanoside,[6] secologanoside 7-methyl ester,[7] secologanoside dimethyl ester (**9**),[6] secologanic acid (**10**),[8] grandifloroside (**11**),[9] vogeloside (**12**),[10] *epi*-vogeloside (**13**),[10] 8-epiloganin,[11] vincosamide,[12] strictosamide,[12] 1-*O*-feruloyl-*β*-glucose,[13] (6*S*,9*R*)-roseoside,[14] kaempferol,[15] quercetin,[15] trifolin,[16] hyperin,[15] chlorogenic acid,[17] methyl chlorogenate,[17] ethyl chlorogenate,[18] butyl chlorogenate,[19] and quinovic acid 3-*O*-*β*-D-quinovopyranosyl-28-*O*-*β*-D-glucopyranoside.[20] The last 22 compounds were isolated for the first time from this species. The structures of the six new glucosides **1**−**6** were determined as follows.



7: R=H
9: R=Me



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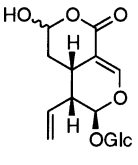

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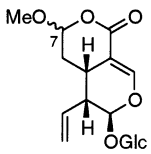

12: 7*R*
13: 7*S*

Adinoside A (**1**) was isolated as an amorphous powder. Its molecular formula was deduced as $C_{20}H_{28}O_{11}$ by HR-SIMS. It showed a UV maximum at 235 nm and IR bands at 3373, 1709, 1636, and 1074 cm^{-1}. Its ^1H NMR spectrum exhibited signals for an olefinic proton at δ 7.77 (s), two

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carbomethoxyl groups at δ 3.58 and 3.63 (each s), terminal vinyl protons at δ 5.13 (dd, J = 10.5 and 1.5 Hz), 5.23 (brd, J = 17.0 Hz), and 5.86 (ddd, J = 17.0, 10.5, and 8.0 Hz), and two acetal protons at δ 5.44 (d, J = 8.0 Hz) and 5.91 (d, J = 8.0 Hz). These spectral features were closely similar to those of secologanoside dimethyl ester (**9**)[6] except for the presence of the signals for *trans* olefinic protons at δ 5.62 (dd, J = 15.5 and 7.0 Hz) and 5.76 (dt, J = 15.5 and 7.0 Hz) and two olefinic carbons at δ 133.6 and 126.5. The double bond was situated between C-6 and C-7 in the secoiridoid skeleton by HMBC correlations between an olefinic proton signal [δ 5.62 (H-6)] and C-4 (δ 109.5), between H-5 (δ 3.62) and an olefinic carbon signal [δ 133.6 (C-6)], and between H-9 (δ 2.72) and an olefinic carbon signal [δ 133.6 (C-6)]. Furthermore, the HMBC experiments demonstrated correlations between the methoxyl signal (δ 3.58) and the carbonyl carbon signal [δ 174.0 (C-1″)] and between methylene signals [δ 3.04 and 3.08 (H_2-2″)] and the carbonyl carbon signal [δ 174.0 (C-1″)] and olefinic carbon signals [δ 126.5 (C-7) and 133.6 (C-6)], formulating the substituent at C-7 as a methoxycarbonyl methyl group. Thus, adinoside A was elucidated to be as shown in formula **1**.

Adinoside B (**2**) and adinoside C (**3**) revealed the same molecular formula, $C_{21}H_{32}O_{11}$. Both compounds showed closely similar UV and IR spectral features. Their ^{1}H and ^{13}C NMR spectra were similar to those of secologanin dimethyl acetal (**8**)[5] except that each compound showed signals for a secondary methyl group [**2**: δ 1.15 (d, J = 6.0 Hz, H_3-4″); **3**: δ 1.17 (d, J = 6.0 Hz, H_3-4″)], an oxymethine group [**2**: δ 3.69 (m, H-3″); **3**: δ 3.73 (dqd, J = 11.0, 6.0, 2.5 Hz, H-3″)], a methylene group [**2**: δ 1.44 and 1.54 (H_2-2″); **3**: δ 1.45 and 1.55 (H_2-2″)], and an oxymethylene group [**2**: δ 3.71 and 4.00 (H_2-1″); **3**: δ 3.69 and 3.99 (H_2-1″)] instead of signals for two methoxyl groups in secologanin dimethyl acetal (**8**). The COSY spectra of **2** and **3** suggested that these signals were due to a 1,3-butanediol unit. The HMBC correlations from H_2-1″ to C-7, from H-7 to C-1″, and from H-7 to C-3″ showed that **2** and **3** were two isomeric acetals formed from secologanin and 1,3-butanediol. The NOESY correlation between H-7 and H-3″ and a large coupling constant between H-2″ and H-3″ (J = 11.0 Hz) demonstrated *cis* diaxial orientation of H-7 and H-3″ in each compound. Finally, the absolute stereochemistry was confirmed by the preparation of **2** and **3**. Secologanin tetraacetate was condensed with (*S*)-1,3-butanediol[21] in the presence of *p*-toluenesulfonic acid in benzene, and subsequent deacetylation afforded a glucoside, which was identified with **2**. In the same manner, glucoside **3** was prepared from secologanin tetraacetate and (*R*)-1,3-butanediol.[21] Accordingly, adinosides B and C were characterized as **2** and **3**, respectively. Similar acetal derivatives of secologanin have recently been isolated from *Gentiana verna*[22] and *Lonicera japonica*.[23]

Adinoside D (**4**) was also obtained as an amorphous powder. The HRSIMS analysis established its molecular formula as $C_{33}H_{44}O_{20}$. Its ^{1}H NMR spectrum revealed two olefinic proton signals for H-3, signals for two sets of terminal vinyl groups, two acetal proton signals for H-1, and signals for two sets of β-glucopyranosyl units, indicating the presence of two secoiridoid glucoside units in the molecule. HMBC and COSY experiments allowed us to depict two units as secoxyloganin (**7**)[3] (part a) and secologanic acid (**10**)[8] (part b). The attachment of C-6′a of the secoxyloganin unit to C-7b of the secologanic acid unit was revealed by HMBC correlations between H_2-6′a (δ 3.97 and 4.03) and C-7b (δ 102.0) and between H-7b (δ 5.55) and C-6′a (δ 68.6). The *S*-configuration at C-7b of the secologanic acid unit was confirmed by the coupling constant between H_2-6b and H-7b ($J_{6b\alpha,7b}$ = 2.5 Hz, $J_{6b\beta,7b}$ = 1.5 Hz) and comparative studies of the chemical shifts of C-5b, C-6b, and C-7b with those of vogeloside (**12**) and *epi*-vogeloside (**13**).[10] Accordingly, the structure of adinoside D was determined to be **4**.

Adinoside E (**5**) was isolated as an amorphous powder and had the same molecular formula as **4**. Compound **5** showed spectral data closely similar to those of **4**. Significant differences were the ^{1}H−^{1}H coupling constants between H_2-6b and H-7b ($J_{6b\alpha,7b}$ = 9.5 Hz, $J_{6b\beta,7b}$ = 2.5 Hz) and the chemical shifts of C-5b, C-6b, and C-7b, which were comparable to those of vogeloside (**12**).[10] Therefore, adinoside E was a C-7b epimer of adinoside D as shown in formula **5**.

Compound **6** was obtained as an amorphous powder, $[\alpha]_D$ −94°, $C_{26}H_{32}O_{13}$. Its ^{1}H NMR spectrum showed a doublet for an olefinic proton [δ 7.49 (J = 0.5 Hz)], signals for a terminal vinyl group (δ 5.27−5.80), a singlet for a carbomethoxyl group (δ 3.68), signals for a β-glucopyranosyl moiety (δ 3.19−4.70), and signals for an acylated oxymethylene group (δ 4.17 and 4.23), which were correlated to H_2-6 in the COSY spectrum, suggesting a 7-*O*-acylated secologanol unit. Further ^{1}H NMR signals for an AMX spin system in the aromatic proton region [δ 6.78 (d, J = 8.0 Hz), 6.94 (dd, J = 8.0, 2.0 Hz), and 7.03 (d, J = 2.0 Hz)] and for *trans* olefinic protons [δ 6.22 and 7.53 (each d, J = 16.0 Hz)], together with a fragment ion peak at *m*/*z* 179 in its SIMS, showed the presence of a *trans*-caffeoyl moiety in **6**. These spectral data indicated **6** to be 7-*O*-*trans*-caffeoylsecologanol. This assumption was supported by HMBC correlations between H_2-7 (δ 4.17 and 4.23) and the carbonyl carbon (δ 169.2) and comparison of its NMR spectral data with those of grandifloroside (**11**).[9] Accordingly, compound **6** was determined to be grandifloroside 11-methyl ester.

Experimental Section

General Experimental Procedures. UV spectra were recorded on a Shimadzu UV-240 spectrophotometer and IR spectra on a Shimadzu FTIR-8200 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. ^{1}H (500 or 300 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on Varian VXR-500 or Varian Gemini-300 spectrometers with TMS as an internal standard. MS and HRMS were obtained with a Hitachi M-4100 mass spectrometer. Glycerol or 3-nitrobenzyl alcohol was used as the matrix for SIMS and HRSIMS. MPLC was carried out with Wakogel LP-40 C18. TLC was performed on precoated Kieselgel 60F_{254} plates (Merck).

Plant Material. The leaves, flowers, and twigs of *Adina racemosa* (Sieb. et Zucc.) Miq. were collected in Heng-Chun Tropical Botanical Garden, Taiwan, in May 1997. A voucher specimen (KPFY-972) is deposited in the laboratory of Kobe Pharmaceutical University.

Extraction and Isolation. Dried leaves, flowers, and twigs (1.27 kg) of *A. racemosa* were extracted with hot MeOH, the extracts were concentrated in vacuo, and the resulting residue (380 g) was resuspended in H_2O and extracted successively with $CHCl_3$ and *n*-BuOH. A part (83.0 g) of the residue (156.8 g) from the *n*-BuOH layer was fractionated over a silica gel column. Elution with $CHCl_3$−MeOH mixtures of the indicated MeOH content gave 17 fractions: 1 (7%, 1.33 g), 2 (7%, 14.57 g), 3 (7%, 5.83 g), 4 (7%, 1.85 g), 5 (7%, 0.99 g), 6 (7%, 2.62 g), 7 (7%, 1.42 g), 8 (7%, 1.04 g), 9 (7%, 4.25 g), 10 (7%, 3.17 g), 11 (7%, 2.62 g), 12 (10%, 0.42 g), 13 (10%, 0.88 g), 14 (10%, 4.03 g), 15 (10%, 0.77 g), 16 (10%, 2.16 g), and 17 (12%, 2.94 g). Fraction 1 was purified by reversed-phase MPLC with MeOH−H_2O (1:4−2:3) and preparative HPLC (μBondasphere

Table 1. ^{1}H NMR Spectral Data of **2**−**5** in CD_3OD at 500 MHz

H	**2**			**3**		
1	5.53	d	(6.5)	5.51	d	(5.5)
3	7.42	d	(0.5)	7.41	d	(1.0)
5	2.98	brq	(6.5)	2.98	brq	(6.5)
6	1.73	ddd	(13.5, 6.5, 4.5)	1.69	ddd	(13.5, 7.5, 4.5)
6	1.88	ddd	(13.5, 7.5, 6.0)	1.97	dt	(13.5, 6.5)
7	4.64	dd	(6.0, 4.5)	4.63	dd	(6.5, 4.5)
8	5.75	ddd	(17.5, 10.5, 8.5)	5.74	ddd	(17.5, 10.5, 8.5)
9	2.64	dt	(8.5, 6.5)	2.66	dt	(8.5, 5.5)
10	5.24	brd	(10.5)	5.25	brd	(10.5)
10	5.28	brd	(17.5)	5.29	brd	(17.5)
OMe	3.69	s		3.69	s	
1′	4.69	d	(7.5)	4.67	d	(8.0)
2′	3.19	dd	(9.0, 7.5)	3.19	dd	(9.0, 8.0)
3′	3.36	t	(9.0)	3.36	t	(9.0)
4′	3.28	t	(9.0)	3.27	t	(9.0)
5′	3.31	m		3.31	ddd	(9.0, 5.5, 2.0)
6′	3.67	dd	(12.0, 5.5)	3.66	dd	(11.5, 5.5)
6′	3.89	dd	(12.0, 2.0)	3.89	dd	(11.5, 2.0)
1″	3.71	ddd	(13.0, 11.0, 2.5)	3.69	ddd	(13.0, 11.0, 2.5)
1″	4.00	ddd	(11.0, 5.0, 1.5)	3.99	ddd	(11.0, 5.0, 1.5)
2″	1.44	dtd	(13.0, 2.5, 1.5)	1.45	dtd	(13.0, 2.5, 1.5)
2″	1.54	tdd	(13.0, 11.0, 5.0)	1.55	tdd	(13.0, 11.0, 5.0)
3″	3.69	m		3.73	dqd	(11.0, 6.0, 2.5)
4″	1.15	d	(6.0)	1.17	d	(6.0)

	4						**5**					
H	part a			part b			part a			part b		
1	5.39	d	(4.0)	5.56	d	(1.5)	5.35	d	(4.0)	5.56	d	(1.5)
3	7.45	d	(2.0)	7.61	d	(2.5)	7.45	d	(2.0)	7.59	d	(2.5)
5	3.27−3.40	m		3.43	m		3.28−3.33	m		3.10	dddd	(13.5, 5.5, 4.0, 2.5)
6	2.23	dd	(16.5, 9.0)	1.71	td	(13.5, 2.5)	2.19	dd	(16.0, 9.5)	1.52	td	(13.5, 9.5)
6	2.86	dd	(16.5, 5.0)	1.92	ddd	(13.5, 5.0, 1.5)	2.91	dd	(16.0, 5.0)	2.02	ddd	(13.5, 4.0, 2.5)
7				5.55	dd	(2.5, 1.5)				5.51	dd	(9.5, 2.5)
8	5.64	ddd	(17.0, 10.5, 9.0)	5.53	ddd	(17.0, 10.5, 9.5)	5.64	ddd	(17.0, 10.5, 9.5)	5.51	ddd	(17.0, 10.5, 9.5)
9	2.81	ddd	(9.0, 5.5, 4.0)	2.66	ddd	(9.5, 5.5, 1.5)	2.84	ddd	(9.5, 5.5, 4.0)	2.66	ddd	(9.5, 5.5, 1.5)
10	5.23[a]	dd	(10.5, 1.5)	5.27[a]	dd	(10.5, 1.5)	5.24[d]	dd	(10.5, 2.0)	5.28[d]	dd	(10.5, 2.0)
10	5.28[b]	dd	(17.0, 1.5)	5.31[b]	dd	(17.0, 1.5)	5.30	dd	(17.0, 2.0)	5.30	dd	(17.0, 2.0)
OMe	3.68	s					3.68	s				
1′	4.65	d	(8.0)	4.70	d	(8.0)	4.64	d	(8.0)	4.67	d	(8.0)
2′	3.19[c]	dd	(9.0, 8.0)	3.23[c]	dd	(9.0, 8.0)	3.20[e]	dd	(9.0, 8.0)	3.21[e]	dd	(9.0, 8.0)
3′	3.27−3.40	m		3.27−3.40	m		3.36	t	(9.0)	3.36	t	(9.0)
4′	3.27−3.40	m		3.27−3.40	m		3.27	brt	(9.5)	3.27	brt	(9.5)
5′	3.43	m		3.27−3.40	m		3.49	ddd	(9.5, 7.0, 2.0)	3.28−3.33	m	
6′	3.97	dd	(12.0, 2.0)	3.67	dd	(12.0, 5.5)	3.78	dd	(11.5, 7.0)	3.66	dd	(12.0, 6.0)
6′	4.03	dd	(12.0, 4.0)	3.89	dd	(12.0, 2.0)	4.26	dd	(11.5, 2.0)	3.89	dd	(12.0, 2.0)

[a−e] Values with the same superscript are interchangeable.

5μ C18−100 Å, MeOH−H_2O, 11:9, 1:1, 9:11) to afford **1** (4.9 mg), **2** (20.5 mg), **3** (24.3mg), **8** (3.8 mg), secologanin (9.0 mg), methyl chlorogenate (61.3 mg), butyl chlorogenate (48.3 mg), and ethyl chlorogenate (7.9 mg). In the same way, fractions 3−8 and 10−13 were purified by a combination of silica gel CC ($CHCl_3$−MeOH, 19:1−17:3), reversed-phase MPLC with MeOH−H_2O (3:17−4:1), preparative HPLC (μBondasphere 5μ C18−100 Å, MeOH−H_2O, 3:7−7:3), and preparative TLC ($CHCl_3$−MeOH, 7:3, 4:1; AcOEt−C_6H_6−EtOH, 4:1:1). Fraction 3 yielded **4** (28.2 mg), **5** (15.3 mg), **6** (12.2 mg), **7** (1752 mg), **10** (24.8 mg), **12** (41.4 mg), methyl chlorogenate (82.7 mg), chlorogenic acid (811 mg), 1-*O*-feruloyl-β-glucose (21.8 mg), (6*S*,9*R*)-roseoside (7.2 mg), and strictosamide (1.6 mg); fraction 4, **7** (480 mg), methyl chlorogenate (55.9 mg), sweroside (58.5 mg), chlorogenic acid (636 mg), trifolin (14.7 mg), and 1-*O*-feruloyl-β-glucose (13.5 mg); fraction 5, **7** (26.3 mg), methyl chlorogenate (10.3 mg), sweroside (69.1 mg), chlorogenic acid (455 mg), trifolin (14.9 mg), and vincosamide (6.0 mg); fraction 6, **7** (15.1 mg), **13** (10.6 mg), methyl chlorogenate (16.1 mg), chlorogenic acid (474 mg), and loganin (86.6 mg); fraction 7, **7** (1.8 mg), **11** (17.0 mg), methyl chlorogenate (38.3 mg), trifolin (3.0 mg), loganin (2.8 mg), hyperin (58.1 mg), and quercetin (5.4 mg); fraction 8, **11** (14.1 mg), methyl chlorogenate (136 mg), chlorogenic acid (162 mg), loganin (12.0 mg), hyperin (4.5 mg), and quercetin (15.2 mg); fraction 10, **9** (39.7 mg), methyl chlorogenate (169 mg), quercetin (31.8 mg), and kaempferol (11.6 mg); fraction 11, **9** (12.6 mg), **10** (11.9 mg), loganin (4.2 mg), noreugenin-7-*O*-β-D-glucoside (6.3 mg), (6*S*,9*R*)-roseoside (9.3 mg), quercetin (14.3 mg), secologanoside 7-methyl ester (30.9 mg), and secologanoside (10.4 mg); fraction 12, 8-epiloganin (2.0 mg), secologanoside 7-methyl ester (8.9 mg), and quinovic acid 3-*O*-β-D-quinovopyranosyl-28-*O*-β-D-glucopyranoside (16.8 mg); and fraction 13, **12** (9.6 mg), noreugenin-7-*O*-β-D-glucoside (1.5 mg), and quinovic acid 3-*O*-β-D-quinovopyranosyl-28-*O*-β-D-glucopyranoside (19.0 mg). Fractions 2 and 9 were not further purified because HPLC analyses showed fraction 2 consisted of chlorogenic acid and secoxyloganin (**7**) and fraction 9 consisted of methyl chlorogenate.

Adinoside A (1): amorphous powder; $[\alpha]^{26}_D$ −40° (*c* 0.5, MeOH); UV (MeOH) λ_{max} (log ϵ) 235 (4.07) nm; IR (KBr) ν_{max} 3373, 1709, 1636, 1074 cm^{-1}; ^{1}H NMR (pyridine-d_5, 500 MHz) δ 2.72 (1H, td, J = 8.0, 5.5 Hz, H-9), 3.04 (1H, dd, J = 16.5, 7.0 Hz, H-2″), 3.08 (1H, dd, J = 16.5, 7.0 Hz, H-2″), 3.58 (3H, s, OMe), 3.62 (1H, dd, J = 7.0, 5.5 Hz, H-5), 3.63 (3H, s, OMe), 3.99 (1H, ddd, J = 8.5, 5.5, 2.0 Hz, H-5′), 4.07 (1H, brt, J = 8.0 Hz, H-2′), 4.26 (1H, t, J = 8.5 Hz, H-4′), 4.29 (1H, t, J =

Table 2. ^{13}C NMR Spectral Data of **1**−**6** in CD_3OD at 125 MHz

				4		**5**		
C	**1**	**2**	**3**	part a	part b	part a	part b	**6**
1	97.4	97.7	97.7	97.9	98.4	97.9	97.9	97.7
3	154.2	153.3	153.2	153.4	154.3	153.3	154.1	153.6
4	109.5	111.8	111.8	110.5	105.6	110.6	105.1	111.5
5	39.6	30.2	29.7	29.2	22.9	28.8	25.3	31.6
6	133.6	36.1	35.8	36.1	30.3	36.1	31.7	30.2
7	126.5	102.2	102.0	177.3	102.0	177.4	105.2	64.1
8	135.8	135.9	135.9	134.6	133.3	134.6	133.0	135.7
9	46.3	45.4	45.3	45.3	43.5	45.2	43.8	45.4
10	118.9	111.5	119.7	120.5	121.0	120.7[c]	121.2[c]	119.6
11	168.8	169.3	169.3	169.0	167.4	168.9	167.6	169.2
OMe	51.8	51.7	51.7	51.6		51.6		51.8
1′	100.3	100.1	100.1	100.3	100.0	100.2	99.7	100.2
2′	74.7	74.7	74.7	74.5[a]	74.6[a]	74.5[d]	74.6[d]	74.7
3′	78.1	78.0	78.1	77.9[b]	78.1[b]	77.8[e]	78.0[e]	78.0
4′	71.6	71.6	71.6	71.0	71.5	71.6[f]	71.8[f]	71.6
5′	78.5	78.4	78.4	76.7	78.4	77.1	78.4	78.4
6′	62.8	62.8	62.8	68.6	62.7	70.5	62.7	62.8
1″	174.0	67.7	67.5					127.7
2″	38.3	34.2	34.2					115.1
3″		74.0	74.2					146.8
4″		22.0	22.0					149.6
5″								116.5
6″								122.9
OMe	52.4							
α								115.1
β								146.9
CO								169.2

[a−f] Values with the same superscript are interchangeable.

8.5 Hz, H-3′), 4.38 (1H, dd, J = 11.5, 5.5 Hz, H-6′), 4.54 (1H, dd, J = 11.5, 2.0 Hz, H-6′), 5.13 (1H, dd, J = 10.5, 1.5 Hz, H-10), 5.23 (1H, brd, J = 17.0 Hz, H-10), 5.44 (1H, d, J = 8.0 Hz, H-1′), 5.62 (1H, dd, J = 15.5, 7.0 Hz, H-6), 5.76 (1H, dt, J = 15.5, 7.0 Hz, H-7), 5.86 (1H, ddd, J = 17.0, 10.5, 8.0 Hz, H-8), 5.91 (1H, d, J = 8.0 Hz, H-1), 7.77 (1H, s, H-3); ^{13}C NMR, Table 2; HMBC, H-3 to C-11; H-5 to C-6; H-9 to C-6; H-6 to C-4; OMe (δ 3.63) to H-11; H-6 to C-7; H_2-2″ to H-6; H_2-2″ to C-7; H_2-2″ to C-1″; OMe (δ 3.58) to C-1″; negative-ion SIMS m/z 443 [M − H]$^-$, 281, 179; negative-ion HRSIMS m/z 443.1569 (calcd for $C_{20}H_{27}O_{11}$, 443.1554).

Adinoside B (2): amorphous powder; $[\alpha]^{31}_D$ −111° (c 0.93, MeOH); UV (MeOH) λ_{max} (log ϵ) 234 (4.07) nm; IR (KBr) ν_{max} 3422, 1705, 1636 cm^{-1}; ^1H NMR, Table 1; ^{13}C NMR, Table 2; NOESY, H-7 and H-3″; HMBC, H-3 to C-11; H-5 to C-7; H-5 to C-11; H_2-6 to C-7; H-7 to C-1″; H-7 to C-3″; OMe to C-11; H-1″ (δ 4.00) to C-7; H-1″ (δ 4.00) to C-3″; H_3-4″ to C-2″; H_3-4″ to C-3″; negative-ion SIMS m/z 459 [M − H]$^-$, 297, 183; negative-ion HRSIMS m/z 459.1887 (calcd for $C_{21}H_{31}O_{11}$, 459.1867).

Adinoside C (3): amorphous powder; $[\alpha]^{23}_D$ −134° (c 0.5, MeOH); UV (MeOH) λ_{max} (log ϵ) 233 (4.05) nm; IR (KBr) ν_{max} 3416, 1706, 1636, 1074 cm^{-1}; ^1H NMR, Table 1; ^{13}C NMR, Table 2; NOESY, H-7 and H-3″; HMBC, H-3 to C-11; H-5 to C-7; H-5 to C-11; H_2-6 to C-7; H-7 to C-1″; H-7 to C-3″; OMe to C-11; H_2-1″ to C-3″; H-1″ (δ 3.99) to C-7; H_3-4″ to C-2″; H_3-4″ to C-3″; negative-ion SIMS m/z 459 [M − H]$^-$, 297, 183; negative-ion HRSIMS m/z 459.1874 (calcd for $C_{21}H_{31}O_{11}$, 459.1867).

Adinoside D (4): amorphous powder; $[\alpha]^{28}_D$ −137° (c 1.0, MeOH); UV (MeOH) λ_{max} (log ϵ) 238 (4.24) nm; IR (KBr) ν_{max} 3405, 1701, 1620, 1016 cm^{-1}; ^1H NMR, Table 1; ^{13}C NMR, Table 2; HMBC, H-1a to C-1′a; H-3a to C-4a; H-3a to C-5a; H-3a to C-11a; H_2-6a to C-5a; H_2-6a to C-7a; OMe to C-11a; H_2-6′a to C-7b; H-7b to C-6′a; H-3b to C-4b; H-3b to C-5b; H-3b to C-11b; H-1b to C-1′b; negative-ion SIMS m/z 759 [M − H]$^-$, 403, 373; negative-ion HRSIMS m/z 759.2362 (calcd for $C_{33}H_{43}O_{20}$, 759.2349).

Adinoside E (5): amorphous powder; $[\alpha]^{28}_D$ −181° (c 1.0, MeOH); UV (MeOH) λ_{max} (log ϵ) 237 (4.23) nm; IR (KBr) ν_{max} 3405, 1697, 1624, 1074 cm^{-1}; ^1H NMR, Table 1; ^{13}C NMR, Table 2; HMBC, H-1a to C-1′a; H-3a to C-4a; H-3a to C-5a; H-3a to C-11a; H_2-6a to C-7a; H_2-6a to C-5a; OMe to C-11a; H_2-6′a to C-7b; H-7b to C-6′a; H-1b to C-1′b; H-3b to C-4b; H-3b to C-5b; H-3b to C-11b; negative-ion SIMS m/z 759 [M − H]$^-$, 403, 373; negative-ion HRSIMS m/z 759.2357 (calcd for $C_{33}H_{43}O_{20}$, 759.2349).

Grandifloroside 11-methyl ester (6): amorphous powder; $[\alpha]^{26}_D$ −94° (c 0.66, MeOH); UV (MeOH) λ_{max} (log ϵ) 222 (4.26), 234 (4.25), 302 (sh) (4.07), 328 (4.17) nm; IR (KBr) ν_{max} 3394, 1693, 1632, 1609, 1516, 1443, 1074 cm^{-1}; ^1H NMR (CD_3OD, 500 MHz) δ 1.87 (1H, td, J = 13.5, 7.0 Hz, H-6), 2.06 (1H, td, J = 13.5, 7.0 Hz, H-6), 2.67 (1H, dt, J = 8.5, 6.5 Hz, H-9), 2.93 (1H, brq, J = 6.5 Hz, H-5), 3.19 (1H, dd, J = 9.0, 8.0 Hz, H-2′), 3.26 (1H, t, J = 9.0 Hz, H-4′), 3.32 (1H, ddd, J = 9.0, 6.0, 2.0 Hz, H-5′), 3.36 (1H, t, J = 9.0 Hz, H-3′), 3.66 (1H, dd, J = 12.0, 6.0 Hz, H-6′), 3.68 (3H, s, OMe), 3.90 (1H, dd, J = 12.0, 2.0 Hz, H-6′), 4.17 (1H, dt, J = 11.0, 7.0 Hz, H-7), 4.23 (1H, dt, J = 11.0, 7.0 Hz, H-7), 4.70 (1H, d, J = 8.0 Hz, H-1′), 5.27 (1H, dd, J = 10.5, 1.5 Hz, H-10), 5.32 (1H, dd, J = 17.0, 1.5 Hz, H-10), 5.57 (1H, d, J = 6.5 Hz, H-1), 5.80 (1H, ddd, J = 17.0, 10.5, 8.5 Hz, H-8), 6.22 (1H, d, J = 16.0 Hz, H-α), 6.78 (1H, d, J = 8.0 Hz, H-5″), 6.94 (1H, dd, J = 8.0, 2.0 Hz, H-6″), 7.03 (1H, d, J = 2.0 Hz, H-2″), 7.49 (1H, d, J = 0.5 Hz, H-3), 7.53 (1H, d, J = 16.0 Hz, H-β); ^{13}C NMR, Table 2; HMBC, H-3 to C-11; H-5 to C-6; H-5 to C-7; H-5 to C-11; OMe to C-11; H_2-6 to C-7; H_2-7 to CO; H-α to CO; H-α to C-1″; H-β to CO; H-β to C-1″; H-β to C-2″; H-β to C-6″; negative-ion SIMS m/z 551 [M − H]$^-$, 179; negative-ion HRSIMS m/z 551.1766 (calcd for $C_{26}H_{31}O_{13}$, 551.1766).

Preparation of 2 and 3. To a solution of secologanin tetraacetate (74.4 mg, 0.13 mmol) and (*S*)-1,3-butanediol[21] (24.1 mg, 0.27 mmol) in dry benzene (1.0 mL) was added *p*-toluenesulfonic acid (1.9 mg), and the whole was stirred for 45 min under reflux. After addition of triethylamine (3 μL) and dilution with H_2O, the mixture was extracted with $CHCl_3$. Washed and dried organic layers were concentrated in vacuo to leave a residue (88.6 mg), which was subjected to preparative TLC (benzene−acetone, 7:3), giving rise to **2a** (72.1 mg, 85.8%): $[\alpha]^{25}_D$ −98° (c 1.0, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 232 (3.99) nm; IR (KBr) ν_{max} 1759, 1713, 1634 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19 (3H, d, J = 6.0 Hz, H_3-4″), 1.40 (1H, brd, J = 13.0 Hz, H-2″), 1.62 (1H, qd, J = 12.0, 5.0 Hz, H-2″), 1.75 (1H, ddd, J = 13.5, 7.0, 5.0 Hz, H-6), 1.89 (1H, dt, J = 13.5, 6.0 Hz, H-6), 1.96, 2.00, 2.03, 2.10 (12H, each s, 4 × Ac), 2.67 (1H, dt, J = 8.5, 5.5 Hz, H-9), 2.91 (1H, brq, J = 6.0 Hz, H-5), 3.63−3.76 (3H, m, H-5′, H-1″, H-3″), 3.70 (3H, s, COOMe), 4.05 (1H, dd, J = 11.5, 4.5 Hz, H-1″), 4.12 (1H, dd, J = 12.0, 2.0 Hz, H-6′), 4.29 (1H, dd, J = 12.0, 4.5 Hz, H-6′), 4.61 (1H, brt, J = 5.5 Hz, H-7), 4.90 (1H, d, J = 8.0 Hz, H-1′), 5.02 (1H, dd, J = 9.0, 8.0 Hz, H-2′), 5.10 (1H, t, J = 9.0 Hz, H-4′), 5.22 (1H, t, J = 9.0 Hz, H-3′), 5.22−5.30 (2H, m, H_2-10), 5.32 (1H, d, J = 5.5 Hz, H-1), 5.64 (1H, ddd, J = 18.0, 9.5, 8.5 Hz, H-8), 7.34 (1H, s, H-3); EIMS m/z 628 [M]$^+$, 627, 331, 169, 43; HREIMS m/z 628.2351 (calcd for $C_{29}H_{40}O_{15}$, 628.2369). A solution of **2a** (69.3 mg) in dry MeOH (2.7 mL) and 0.1 N NaOMe (0.3 mL) was stirred for 40 min at room temperature. The reaction mixture was neutralized with Amberlite IR-120 and evaporated in vacuo. The resulting residue (50.6 mg) was purified by preparative TLC ($CHCl_3$−MeOH, 8:2) and preparative HPLC (H_2O−MeOH, 1:1) to afford **2** (32.7 mg, 64.4%): $[\alpha]^{30}_D$ −128° (c 1.0, MeOH); SIMS m/z 459 [M − H]$^-$, 297. UV, IR, and ^1H NMR spectral data were identical to those of **2** from *A. racemosa*.

In a similar manner, condensation of secologanin tetraacetate (78.4 mg, 0.14 mmol) and (*R*)-1,3-butanediol[21] (25.4 mg, 0.28 mmol) gave **3a** (77.8 mg, 87.9%): $[\alpha]^{22}_D$ −94° (c 1.0, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 231 (3.99) nm; IR (KBr) ν_{max} 1759, 1713, 1634 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20 (3H, d, J = 6.0 Hz, H_3-4″), 1.39 (1H, brd, J = 13.0 Hz, H-2″), 1.60 (1H, ddd, J = 12.5, 11.0, 5.0 Hz, H-2″), 1.70 (1H, ddd, J = 13.5, 8.0, 4.5 Hz, H-6), 1.94, 2.00, 2.03, 2.10 (12H, each s, 4 × Ac), 1.98 (1H, ddd, J = 13.5, 6.5, 5.5 Hz, H-6), 2.69 (1H, dt, J = 8.5, 5.5 Hz, H-9), 2.91 (1H, dtd, J = 8.0, 5.5, 1.5 Hz, H-5), 3.65 (1H, ddd, J = 12.0, 11.5, 2.5 Hz, H-1″), 3.70 (1H, m, H-3″), 3.73 (1H, ddd, J = 9.5, 4.5, 2.5 Hz, H-5″), 4.04 (1H, ddd, J =

11.5, 5.0, 1.0 Hz, H-1″), 4.13 (1H, dd, J = 12.5, 2.5 Hz, H-6′), 4.30 (1H, dd, J = 12.5, 4.5 Hz, H-6′), 4.61 (1H, dd, J = 6.5, 4.5 Hz, H-7), 4.90 (1H, d, J = 8.0 Hz, H-1′), 5.01 (1H, dd, J = 9.5, 8.0 Hz, H-2′), 5.10 (1H, t, J = 9.5 Hz, H-4′), 5.22 (1H, t, J = 9.5 Hz, H-3′), 5.23−5.31 (2H, m, H_2-10), 5.64 (1H, ddd, J = 17.0, 10.0, 8.5 Hz, H-8), 7.31 (1H, d, J = 1.5 Hz, H-3); EIMS m/z 628 $[M]^+$, 627, 331, 169, 43; HREIMS m/z 628.2345 (calcd for $C_{29}H_{40}O_{15}$, 628.2369). Methanolysis of **3a** (75.9 mg, 0.12 mmol) yielded **3** (40.2 mg, 72.3%): $[\alpha]^{30}_D$ −123° (*c* 1.0, MeOH); SIMS m/z 459 $[M - H]^-$, 297. UV, IR, and ^{1}H NMR spectral data were identical to those of the isolated compound.

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