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STOLONIFERINS VIII–XII, RESIN GLYCOSIDES, FROM *IPOMOEA STOLONIFERA**

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Key Word Index—*Ipomoea stolonifera*; Convolvulaceae; resin glycoside; stoloniferins VIII–XII.

Abstract—Five new ether-soluble resin glycosides were isolated from whole plants of *Ipomoea stolonifera*. Their structures have been determined on the basis of chemical and spectral data. Similar to the resin glycosides previously isolated, all of them are monomers of a jalapinolic acid tetra- or penta-glycoside in which the sugar moiety is partially acylated by organic acids and also combined with the carboxy group of the aglycone to form a macrocyclic ester structure. © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

In the preceding paper [2], we reported on the structures of seven kinds of resin glycosides, stoloniferins I–VII, obtained from the whole plants of *Ipomoea stolonifera*. In a continuation of our systematic survey of the constituents of this plant, we have isolated and characterized five jalapins, stoloniferins VIII (**1**)–XII (**5**). This paper deals with the structure determination of these compounds.

RESULTS AND DISCUSSION

The ether-soluble resin glycoside fraction obtained previously [2] was subjected to a combination of silica gel, Sephadex LH-20 and Cosmosil 140 C_{18}–OPN CC with various solvent systems to yield two crude resin glycoside fractions, fr. 8 and fr. 9. On preparative HPLC these gave compounds **1**, **2** and **4** (from fr. 8) and **3** and **5** (from fr. 9).

Compound **1** was treated with 5% KOH to give an organic and a glycosidic acid fractions. Methylation of the former with CH_2N_2 yielded two methyl esters which were identified as (2*S*)-2-methylbutyrate [2] and *n*-octanoate by direct comparison (GC) with authentic samples. The glycosidic acid fraction, on purification (Diaion HP–20) followed by methylation, gave compound **6** which was identified by ^{1}H NMR spectroscopy as the methyl ester of simonic acid B [3]. The negative ion FAB mass spectrum of **1** exhibited a $[M-H]^-$ ion peak at *m/z* 1193, in addition to the characteristic fragment ion peaks at *m/z* 545 and 417, suggesting that the carboxyl group of jalapinolic acid was linked with the second sugar from the aglycone [4]. The ^{1}H NMR spectrum of **1** showed five anomeric protons (δ 4.72, 5.48, 5.59, 5.90, 6.15) and the non-equivalent H_2–2 of the jalapinolic acid moiety at δ 2.23 and 2.40, together with the signals due to one unit each of 2-methylbutyric and *n*-octanoic acid. All the proton signals arising from the sugar moieties of **1** were assigned with the aid of ^{1}H–^{1}H COSY and NOESY spectra. When compared with **6**, H–2 (1.30 ppm) of Rha, H–2 (1.12 ppm) of Rha′ and H–4 (1.56 ppm) of Rha‴ were shifted downfield due to acylation. These observations indicated that the carboxy group of the aglycone, jalapinolic acid, was intramolecularly linked with the second sugar (Rha) counted from the aglycone and that the two organic acids were attached at OH–2 of Rha' and OH–4 of Rha‴.

Acetylation of **1** gave the octaacetate (**1a**), whose EI mass spectrum showed diagnostic fragment ion peaks at *m/z* 273, 315, 569, 655 and 859 corresponding to the fragment ion peaks presented in Table 2. Thus, the sites of ester linkages of the organic acids were confirmed, that is, 2-methylbutyric and *n*-octanoic acids were located at OH–4 of Rha‴ and OH–2 of Rha′, respectively. Consequently, the structure of **1** is characterized as (*S*)-jalapinolic acid 11-*O*-α-L-rhamnopyranosyl-(1→3)-*O*-[4-*O*-(2*S*)-2-methylbutyryl-α-L-rhamnopyranosyl-(1→4)]-*O*-(2-*O*-*n*-octanoyl)-α-L-

* Part 24 in the series 'Resin Glycosides'. For Part 23 see ref.[1].

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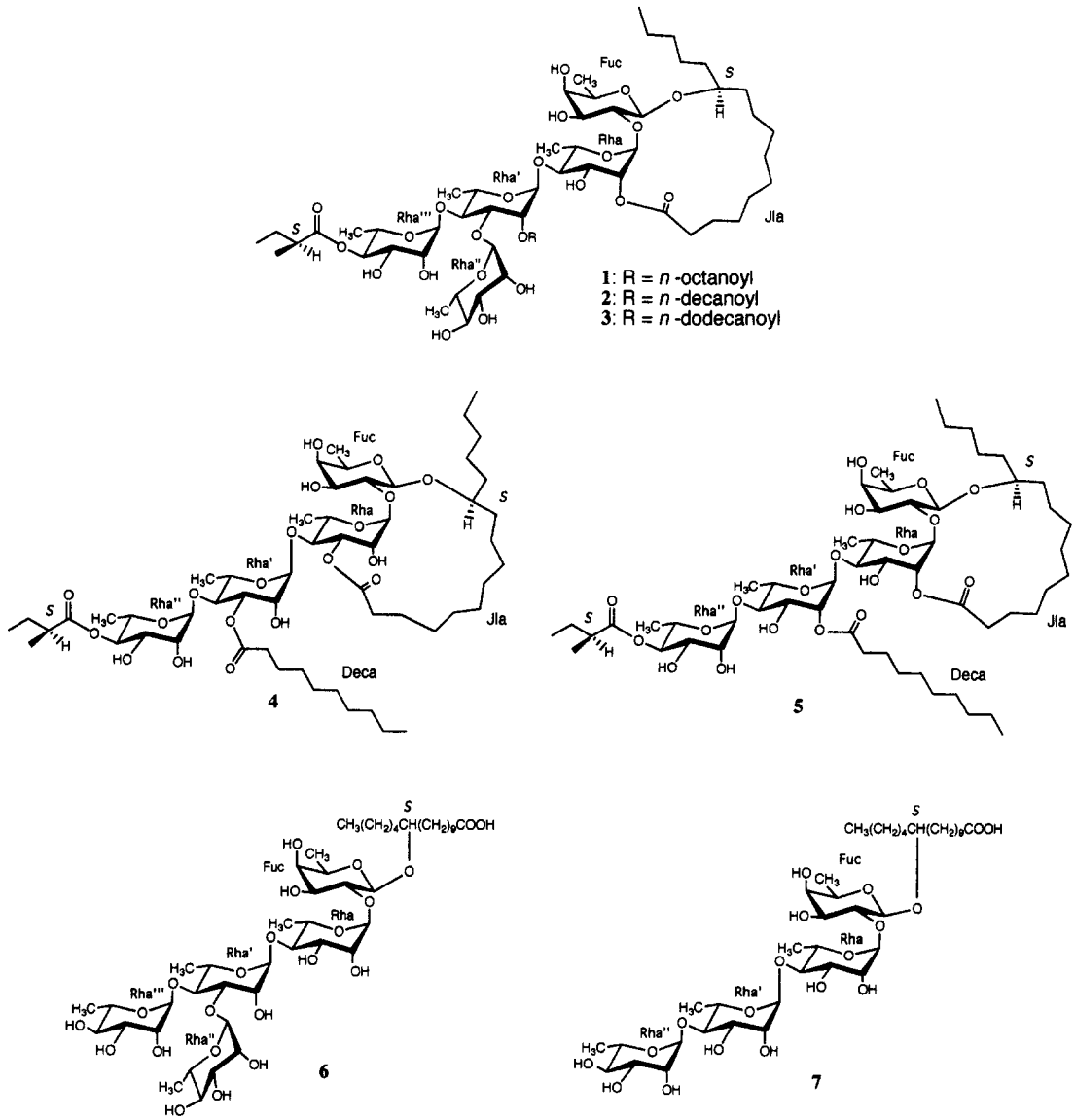
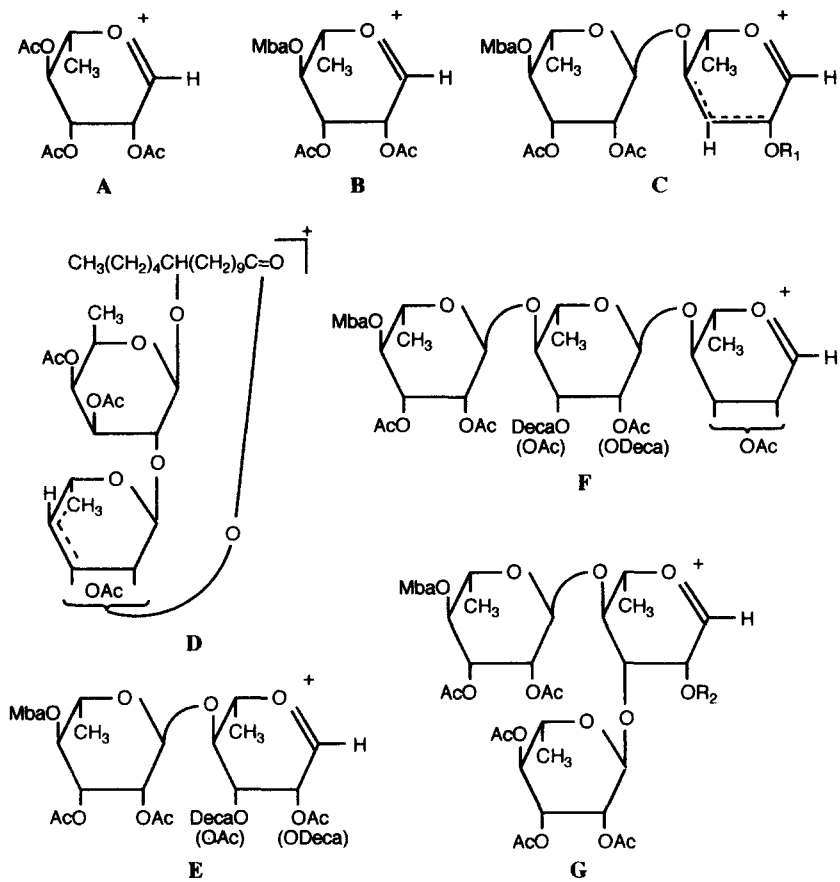


Fig. 1.

rhamnopyranosyl-(1→4)-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-fucopyranoside, intramolecular 1,2″-ester.

Compounds **2** (*m/z* 1221 $[M-H]^-$) and **3** (*m/z* 1249 $[M-H]^-$) each exhibited the same fragment ion peaks at *m/z* 545 and 417 as those of **1** in the negative ion FAB mass spectra. The ^1H NMR spectra of both compounds were closely correlated with that of **1**, including downfield shifts of H–2 of Rha, H–2 of Rha′ and H–4 of Rha‴. Both were treated in the same manner as described for **1**, and analyses of their chemical and spectral data revealed that they consisted of the same glycosidic acid (**6**) as **1**, and that **2** and **3** differed only in the fact that the *n*-octanoic acid at OH-2 of Rha′ in **1** is replaced by *n*-decanoic and *n*-dodecanoic acids, respectively. Figure 1 depicts their structures.

Compound **4**, in the negative ion FAB mass spectrum, gave a $[M-H]^-$ ion peak at *m/z* 1075 together with fragment ion peaks at *m/z* 545 and 417. On alkaline hydrolysis, **4** gave operculinic acid C (**7**) [5], 2-methylbutyric and *n*-decanoic acids. The ^1H NMR spectrum of **4** showed the signals of four anomeric protons, and when compared with that of **7**, it exhibited acylation shifts for H–3 of Rha, H–3 of Rha′ and H–4 of Rha″ (1.10, 1.19 and 1.54 ppm, respectively). On the other hand, compound **5** (*m/z* 1075 $[M-H]^-$) gave, on alkaline hydrolysis, the same units as those of **4**, and in the ^1H NMR spectrum, besides the acylation shift at H–4 of Rha″ (1.57 ppm), showed downfield shifts at H–2 (1.29 ppm) of Rha and H–2 (1.24 ppm) of Rha′, in place of H–3 of Rha and H–3 of Rha′ in **4**. Therefore, **5** was a positional isomer of **4**. The EI mass spectrum of their acetates (**4a** and **5a**) exhibited characteristic fragment ion peaks (Table 2),



showing the sites of ester linkage of the organic acids. Their structures were determined as shown in Fig. 1.

Five additional resin glycosides, stoloniferins VIII–XII, were isolated. All of them were ether-soluble (jalapins) consisted of known glycosidic acids [3, 5, 6].

EXPERIMENTAL

Mps: uncorr.; ^{1}H NMR (600 MHz): 30° using TMS as int. standard. The NOESY spectrum was obtained using a mixing time of 500 ms. EIMS: ionization voltage, 30 eV; accelerating voltage, 4–10 kv. Other instruments and materials used were the same as those cited in the previous report [2]. Optical rotations were measured at 20°.

Isolation of stoloniferins VIII-XII. I. stolonifera (cyrillo) J. F. Gmel (780 g) was collected in Guangdong (September 1990). Voucher specimens (#900923) are deposited at Kunming Institute of Botany. The MeOH extract (105 g) of the whole plants was treated as described in the preceding paper [2]. Fraction 8 was subjected to prep. HPLC with 95% MeOH to give **1** (24.4 mg), **2** (12.0 mg) and **4** (122 mg). Fraction 9 was separated by prep. HPLC with 98% MeOH to yield **3** (18.7 mg) and **5** (25.4 mg).

Stoloniferin VIII (**1**). Powder, mp 125–137°, $[\alpha]_D$ −76.6° (MeOH; *c* 1.2). Negative ion FABMS *m/z* (rel. int.): 1193 $[M-H]^-$ (91), 1067 (24), 965 (14), 837 (10), 691 (7), 545 (64), 417 (100), 271 (93); ^{1}H NMR (pyridine-d_5); Table 1. (Found: C, 57.97; H, 8.57. $C_{59}H_{102}O_{24}$ 3/2H_2O requires: C, 57.97; H, 8.66%.)

Stoloniferin IX. [(*S*)-*jalapinolic acid* 11-*O*-α-L-*rhamnopyranosyl*-(1→3)-*O*-[4-*O*-(2*S*)-2-*methylbutyryl*-α-L-*rhamnopyranosyl*-(1→4)]-*O*-(2-*O*-n-*decanoyl*)-α-L-*rhamnopyranosyl*-(1→4)-*O*-α-L-*rhamnopyranosyl*-(1→2)-β-D-*fucopyranoside*, *intramolecular* 1,2″-*ester*] (**2**). Powder, mp 132-139°, $[\alpha]_D$-53.7° (MeOH; *c* 1.3). Negative ion FABMS *m/z* (rel. int.): 1221 $[M-H]^-$(95), 1137 (5), 1067 (21), 965 (10), 837 (7), 691 (4), 545 (47), 417 (100), 271 (43). ^{1}H NMR (pyridine−d_5); Table 1. (Found: C, 58.91; H, 8.86. $C_{61}H_{106}O_{24}$ H_2O requires: C, 59.01; H, 8.79%.)

Stoloniferin X. [(*S*)-*jalapinolic acid* 11-*O*-α-L-*rhamnopyranosyl*-(1→3)-*O*-[4-*O*-(2*S*)-2-*methylbutyryl*-α-L-*rhamnopyranosyl*-(1→4)]-*O*-(2-*O*-*n*-*dodecanoyl*)-α-L-*rhamnopyranosyl*-(1→4)-*O*-α-L-*rhamnopyranosyl*-(1→2)-β-D-*fucopyranoside*, *intramolecular* 1,2″-*ester*] (**3**). Powder, mp 122–127°, $[\alpha]_D$−44.2° (MeOH; *c* 1.4). Negative ion FABMS *m/z* (rel. int.): 1249 $[M-H]^-$(96), 1105 (6), 1067 (21), 965 (10), 837 (10), 691 (5), 545 (48), 417 (100), 271 (78); ^{1}H NMR (pyridine-d_5); Table 1. (Found: C, 59.58; H, 8.85. $C_{63}H_{110}O_{24}$ H_2O requires: C, 59.60; H, 8.89%.)

Stoloniferin XI. [(*S*)-*jalapinolic acid* 11-*O*-[4-*O*-

Table 1. ^{1}H NMR spectra data for **1–5** (in pyridine–d_5, 600 MHz)

		1	2	3	4	5
Fuc	1	4.72 (*d*, 7.5)	4.72 (*d*, 7.3)	4.73 (*d*, 7.3)	4.80 (*d*, 7.9)	4.69 (*d*, 7.6)
	2	4.15 (*dd*, 7.5, 9.4)	4.15 (*dd*, 7.3, 9.8)	4.15 (*dd*, 7.3, 9.5)	4.55 (*dd*, 7.9, 9.2)	4.13 (*dd*, 7.6, 9.8)
	3	4.07 (*dd*, 9.4, 3.5)	4.06 (*dd*, 9.8, 3.4)	4.06 (*dd*, 9.5, 3.4)	4.20 (*dd*, 9.2, 3.4)	4.02 (*dd*, 9.8, 3.4)
	4	3.98 (*br. d*, 3.5)	3.98 (*br. d*, 3.4)	3.98 (*br. d*, 3.4)	3.94 (*br. d*, 3.4)	3.96 (*br. d*, 3.4)
	5	3.77 (*br. q*, 6.4)	3.76 (*br. q*, 6.1)	3.77 (*br. q*, 6.4)	3.83 (*br. q*, 6.4)	3.73 (*br. q*, 6.4)
	6	1.50 (*d*, 6.4)	1.52 (*d*, 6.1)	1.50 (*d*, 6.4)	1.53 (*d*, 6.4)	1.49 (*d*, 6.4)
Rha	1	5.48 (*d*, 1.8)	5.48 (*d*, 1.2)	5.48 (*d*, 1.5)	6.40 (*br. s*)	5.49 (*br. s*)
	2	5.94 (*dd*, 1.8, 3.3)	5.94 (*dd*, 1.2, 3.1)	5.94 (*dd*, 1.5, 3.4)	5.27 (*br. s*)	5.92 (*dd*, 1.5, 3.4)
	3	5.01 (*dd*, 3.3, 9.4)	5.00 (*dd*, 3.1, 9.5)	5.01 (*dd*, 3.4, 9.5)	5.68 (*dd*, 2.5, 10.1)	4.98 (*dd*, 3.4, 9.5)
	4	4.21 (*dd*, 9.4, 9.4)	4.20 (*dd*, 9.5, 9.5)	4.21 (*dd*, 9.5, 9.5)	4.72 (*dd*, 10.1, 9.5)	4.19 (*dd*, 9.5, 9.5)
	5	4.43 (*dq*, 9.4, 6.2)	4.43 (*dq*, 9.5, 6.1)	4.43 (*dq*, 9.5, 6.1)	5.09 (*dq*, 9.5, 6.7)	4.44 (*dq*, 9.5, 6.1)
	6	1.61 (*d*, 6.2)	1.61 (*d*, 6.1)	1.61 (*d*, 6.1)	1.60 (*d*, 6.7)	1.64 (*d*, 6.1)
Rha′	1	6.15 (*d*, 1.7)	6.14 (*d*, 1.5)	6.14 (*d*, 1.5)	5.90 (*br. s*)	6.02 (*br. s*)
	2	6.00 (*dd*, 1.7, 3.1)	6.00 (*dd*, 1.5, 3.1)	6.00 (*dd*, 1.5, 3.1)	4.72 (*br. s*)	5.98 (*dd*, 1.5, 3.7)
	3	4.59 (*dd*, 3.1, 9.2)	4.59 (*dd*, 3.1, 8.9)	4.58 (*dd*, 3.1, 8.9)	5.72 (*dd*, 2.8, 9.8)	4.66 (*dd*, 3.7, 9.5)
	4	4.28 (*dd*, 9.2, 9.2)	4.28 (*dd*, 8.9, 8.5)	4.28 (*dd*, 8.9, 8.5)	4.57 (*dd*, 9.8, 9.8)	4.28 (*dd*, 9.5, 9.5)
	5	4.34 (*dq*, 9.2, 6.1)	4.34 (*dq*, 8.5, 6.1)	4.34 (*dq*, 8.5, 6.1)	4.40 (*dq*, 9.8, 6.1)	4.36 (*dq*, 9.5, 6.1)
	6	1.64 (*d*, 6.1)	1.65 (*d*, 6.1)	1.64 (*d*, 6.1)	1.58 (*d*, 6.1)	1.69 (*d*, 6.1)
Rha″	1	5.59 (*br. s*)	5.59 (*br. s*)	5.59 (*br. s*)	5.69 (*br. s*)	6.18 (*br. s*)
	2	4.80 (*dd*, 1.4, 3.1)	4.80 (*dd*, 1.0, 2.9)	4.80 (*dd*, 1.5, 3.5)	4.48 (*br. s*)	4.79 (*dd*, 1.5, 3.4)
	3	4.47 (*dd*, 3.1, 9.0)	4.47 (*dd*, 2.9, 9.2)	4.48 (*dd*, 3.5, 9.5)	4.40 (*dd*, 3.7, 9.8)	4.53 (*dd*, 3.4, 9.8)
	4	4.22 (*dd*, 9.0, 9.0)	4.21 (*dd*, 9.2, 9.2)	4.22 (*dd*, 9.5, 9.5)	5.77 (*dd*, 9.8, 9.8)	5.80 (*dd*, 9.8, 9.8)
	5	4.28 (*dq*, 9.0, 6.1)	4.28 (*dq*, 9.2, 6.1)	4.29 (*dq*, 9.5, 6.1)	4.30 (*dq*, 9.8, 6.1)	4.43 (*dq*, 9.8, 6.4)
	6	1.59 (*d*, 6.1)	1.59 (*d*, 6.1)	1.59 (*d*, 6.1)	1.34 (*d*, 6.1)	1.43 (*d*, 6.4)
Rha‴	1	5.90 (*br. s*)	5.91 (*br. s*)	5.91 (*br. s*)		
	2	4.67 (*dd*, 1.5, 3.1)	4.66 (*dd*, 1.0, 3.1)	4.67 (*dd*, 1.5, 3.1)		
	3	4.46 (*dd*, 3.1, 9.7)	4.46 (*dd*, 3.1, 9.5)	4.46 (*dd*, 3.1, 9.5)		
	4	5.78 (*dd*, 9.7, 9.7)	5.77 (*dd*, 9.5, 10.1)	5.78 (*dd*, 9.5, 9.5)		
	5	4.36 (*dq*, 9.7, 6.2)	4.38 (*dq*, 10.1, 6.1)	4.36 (*dq*, 9.5, 6.1)		
	6	1.39 (*d*, 6.2)	1.39 (*d*, 6.1)	1.39 (*d*, 6.1)		
Jla	2	2.23 (*ddd*, 4.0, 8.1, 14.5)	2.26*	2.25*	2.16 (*m*)	2.23 (*ddd*, 4.3, 7.9, 14.7)
		2.40 (*ddd*, 3.9, 8.6, 14.5)	2.40*	2.40*	2.29 (*m*)	2.40 (*ddd*, 4.3, 8.2, 14.6)
	11	3.85 (*m*)	3.85 (*m*)	3.85 (*m*)	3.91 (*m*)	3.83 (*m*)
	16	0.82(*t*, 7.2)	0.85 (*t*, 7.0)	0.87 (*t*, 7.3)	0.86 (*t*, 6.7)	0.85 (*t*, 7.0)
Mba	2	2.50 (*tq*, 6.5, 7.0)	2.50 (*tq*, 7.0, 7.0)	2.50 (*tq*, 6.7, 6.7)	2.48 (*tq*, 7.0, 7.0)	2.51 (*tq*, 7.0, 7.0)
	4	0.93 (*t*, 7.3)	0.93 (*t*, 7.3)	0.93 (*t*, 7.3)	0.92 (*t*, 7.3)	0.94 (*t*, 7.3)
	5	1.20 (*d*, 7.0)	1.20 (*d*, 7.0)	1.20 (*d*, 6.7)	1.19 (*d*, 7.0)	1.20 (*d*, 7.0)
Octa	8	0.88 (*t*, 6.8)				
Deca	10		0.88 (*t*, 6.7)		0.89 (*t*, 7.0)	0.87 (*t*, 7.0)
Dodeca	12			0.88 (*t*, 7.0)		

δ in ppm from TMS (splitting patterns and coupling constants), J in Hz are given in parentheses. * Splitting patterns are complicated.

(2*S*)-2-*methylbutyryl*-α-L-*rhamnopyranosyl*-(1→4)]-*O*-(3-*O*-*n*-*octanoyl*)-α-L-*rhamnopyranosyl*-(1→4)-α-L-*rhamnopyranosyl*-(1→2)-β-D-*fucopyranoside*, *intramolecular* 1,3″-*ester*] (**4**). Powder, mp 105–110°, $[\alpha]_D$ −81.3° (MeOH; *c* 1.1). Negative ion FABMS *m/z* (rel. int.): 1075 $[M-H]^-$(64), 921 (28), 837 (8), 691 (10), 545 (38), 417 (100), 271 (90); ^{1}H NMR (pyridine-d_5); Table 1. (Found: C, 60.97; H, 9.04. $C_{55}H_{96}O_{20}$ $1/2H_2O$ requires C, 60.81; H, 9.00%.)

Stoloniferin XII. [(*S*)-*jalapinolic acid* 11-*O*-[4-*O*-(2*S*)-2-*methylbutyryl*-α-L-*rhamnopyranosyl*-(1→4)]-*O*-(2-*O*-*n*-*decanoyl*)-α-L-*rhammnopyranosyl*-(1→4)-α-L-*rhamnopyranosyl*-(1→2)-β-D-*fucopyranoside*, *intramolecular* 1,2″-*ester*] (**5**). Powder, mp 93–96° $[\alpha]_D$ −27.8° (MeOH; *c* 2.3). Negative ion FABMS *m/z* (rel. int.): 1075 $[M-H]^-$ (78), 921 (38), 837 (5), 691 (12), 545 (36), 417 (100), 271 (95); ^{1}H NMR (pyridine-d_5); Table 1. (Found: C, 61.27; H, 9.20. $C_{55}H_{96}O_{20}$ requires C, 61.32; H, 8.98%.)

Alkaline hydrolysis. Compounds **1–5** (12–20 mg) were suspended in 5% KOH (5 ml), and refluxed for 3 hr. The reaction mixture was acidified (pH 4) and extracted with Et_2O (5 ml × 2). A part of the Et_2O layer was subjected to GC (3.2 mm × 2 m glass column packed with 5% Unisol 30T; isothermal 120°; N_2, 1.5 kgcm^{-2}). R_t (min): 2.93 (2-methylbutyric acid). A part of the Et_2O layer was treated with CH_2N_2 and the reaction mixture was analyzed by GC (3.2 mm × 2 m glass column packed with Unisol 3000; isothermal 150°; N_2, 1.0 kgcm^{-2}). R_t (min): 2.64 (methyl *n*-octanoate) from **1**; 5.23 (methyl *n*-decanoate) from **2**, **4** and **5**; 11.03 (methyl *n*-dodecanoate) from **3**. The aq layer was desalted over Diaion HP-20, washed with excess H_2O then eluted with 1,4-dioxane-MeOH (1:1, 100 ml). After removal of the solvent, the residue was methylated with CH_2N_2 to give **6** from **1–3**, and **7** from **4** and **5**. The ^{13}C and ^{1}H NMR spectra of **6** and **7** were superimposable on those of methyl esters of simonic acid B [3] and operculinic acid C [4], respectively.

Table 2. Fragment ions (*m/z*) for **1a–5a**

	A	B	C (R_1)	D	E	F	G (R_2)
1a	273	315	567 (Octa)	655	—	—	859 (Octa)
2a	273	315	597 (Deca)	655	—	—	887 (Deca)
3a	273	315	625 (Dodeca)	655	—	—	915 (Dodeca)
4A	—	315	—	655	657	827	—
5A	—	315	—	655	657	827	—

Mba. (2*S*)-2-methylbutyryl; Octa, *n*-octanoyl; Deca, *n*-decanoyl; Dodeca, *n*-decanoyl.

Acetylation of **1–5**. Usual acetylation of each compound, **1–5**, (5–10 mg) in Ac_2O-pyridine (1:1, 2 ml) gave **1a–5a**, respectively. **1a**: mp 80–84°, EIMS *m/z* (rel. int.): 273 (69), 315 (100), 569 (10), 655 (6), 859 (9); ^{1}H NMR ($CDCl_3$): δ 1.95 (×2), 2.01, 2.05, 2.10, 2.11, 2.12, 2.17 (each *s*, OCOMe). **2a**: mp 77–79°; EIMS *m/z* (rel. int.): 273 (90), 315 (100), 597 (36), 655 (12), 887 (36); ^{1}H NMR ($CDCl_3$): δ 2.00, 2.01, 2.02, 2.06, 2.07, 2.08, 2.34, 2.36 (each *s*, OCOMe). **3a**: mp 58–62°, EIMS *m/z* (rel. int.): 273 (67), 315 (100), 625 (9), 655 (6), 915 (9). ^{1}H NMR ($CDCl_3$): δ 1.95 (×2), 2.01, 2.05, 2.10, 2.11, 2.12, 2.17 (each *s*, OCOMe). **4a**: mp 82–85°, EIMS *m/z* (rel. int.): 315 (100), 655 (6), 657 (12), 827 (5). ^{1}H NMR ($CDCl_3$): δ 1.94, 1.98, 2.05, 2.09, 2.13, 2.14 (each *s*, OCOMe). **5a**: syrup; EIMS *m/z* (rel. int.): 315 (100), 655 (5), 657 (12), 827 (3). ^{1}H NMR ($CDCl_3$): δ 2.00 (×2), 2.03, 2.23, 2.26, 2.37 (each, *s*, OCOMe) Table 2.

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