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Secoiridoid and iridoid glucosides from *Syringa afghanica*

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Abstract

Phytochemical investigation of the dried leaves of *Syringa afghanica*, has led to the isolation of nine secoiridoid glucosides, safghanosides A–H and 2″-*epi*-frameroside, as well as an iridoid glucoside, syringafghanoside along with nineteen known compounds. The structures were elucidated by spectroscopic and chemical means.

Keywords: *Syringa afghanica*; Oleaceae; Secoiridoid glucosides; Iridoid glucoside; Oleoside; Safghanosides A–H; 2″-*Epi*-frameroside; Syringafghanoside

1. Introduction

Syringa afghanica C. K. Schneid. (= *S. persica* Aitch.) is a shrub found in Afghanistan and Pakistan (Kitamura, 1960). The bark of this plant species has been used as a tonic and antipyretic in folklore. In the course of our chemical studies on the glycosides of oleaceous plants (Tanahashi et al., 1999, Takenaka et al., 2000), we investigated the constituents of the dried leaves of *S. afghanica* and isolated seven monomeric and two dimeric secoiridoid glucosides as well as an iridoid glucoside. This paper deals with their structural determinations.

2. Results and discussion

The *n*-BuOH soluble fraction of the methanolic extract of the dried leaves of *S. afghanica* was fractionated by column chromatography on ODS and then purified by prep. HPLC, affording nine secoiridoid glucosides named safghanosides A–H (**1**–**8**) and 2″-*epi*-frameroside (**9**), and an iridoid glucoside, syringafghanoside (**10**) together with 19 known compounds, cinnamic acid, 1-*O*-*trans*- and *cis*-cinnamoyl-β-D-glucopyranose, syringin (Karasawa et al., 1986), acteoside (Imakura et al., 1985), poliumoside (Andary et al., 1985), lipedoside A-I (He et al., 1994), oleoside dimethyl ester (Kikuchi and Yamauchi, 1984), methyl glucooleoside (Kuwajima et al., 1989), isoligustroside (Kikuchi et al., 1987), isooleuropein (Kikuchi et al., 1987), ligstroside (Kikuchi and Yamauchi, 1984), oleuropein (Inoue et al., 1985), formoside (**11**) (Tanahashi et al., 1993), 1″-*O*-β-D-glucosylformoside (Tanahashi et al., 1993), fraxiformoside (**12**) (Tanahashi et al., 1992), 1‴-*O*-β-D-glucosylfraxiformoside (Tanahashi et al., 1993), rhoifolin (Kaneo and Matsuda, 1978), and luteolin (Markham et al., 1978).

Compound **1**, was obtained as a colorless amorphous powder, analysed for $C_{32}H_{40}O_{17}$ from its HR–SIMS. Its UV and IR spectra suggested the presence of an enol-ether system conjugated with a carbonyl group (241.5 nm, and 1716, 1635 cm^{-1}) that was typical of a secoiridoid nucleus. In addition, absorptions due to an aromatic ring (279.5 nm, 1448 cm^{-1}) were observed. The ^1H and ^{13}C NMR spectra of **1** exhibited typical signals of an oleoside 11-methyl ester (**13**) unit. Moreover, its ^1H NMR spectrum displayed resonances for an anomeric proton at δ 5.60 (*d*, $J = 8.0$ Hz), a pair of *trans*-olefinic protons at δ 6.58 and 7.81 (each *d*, $J = 16.0$ Hz), and five aromatic protons at δ 7.41–7.63, suggesting the presence of a 1-*O*-acyl-β-glucose moiety and a *trans*-cinnamic acid moiety. The HMBC experiments with **1** revealed significant ^3J interactions between H-3 and C-11, between OMe and C-11, between H_2-6 and C-7, between H_2-6″ and C-7 and between H-1″ and C-1‴. These findings suggested that in the structure of **1**, the C-7 carboxyl group of oleoside 11-methyl ester moiety was linked to

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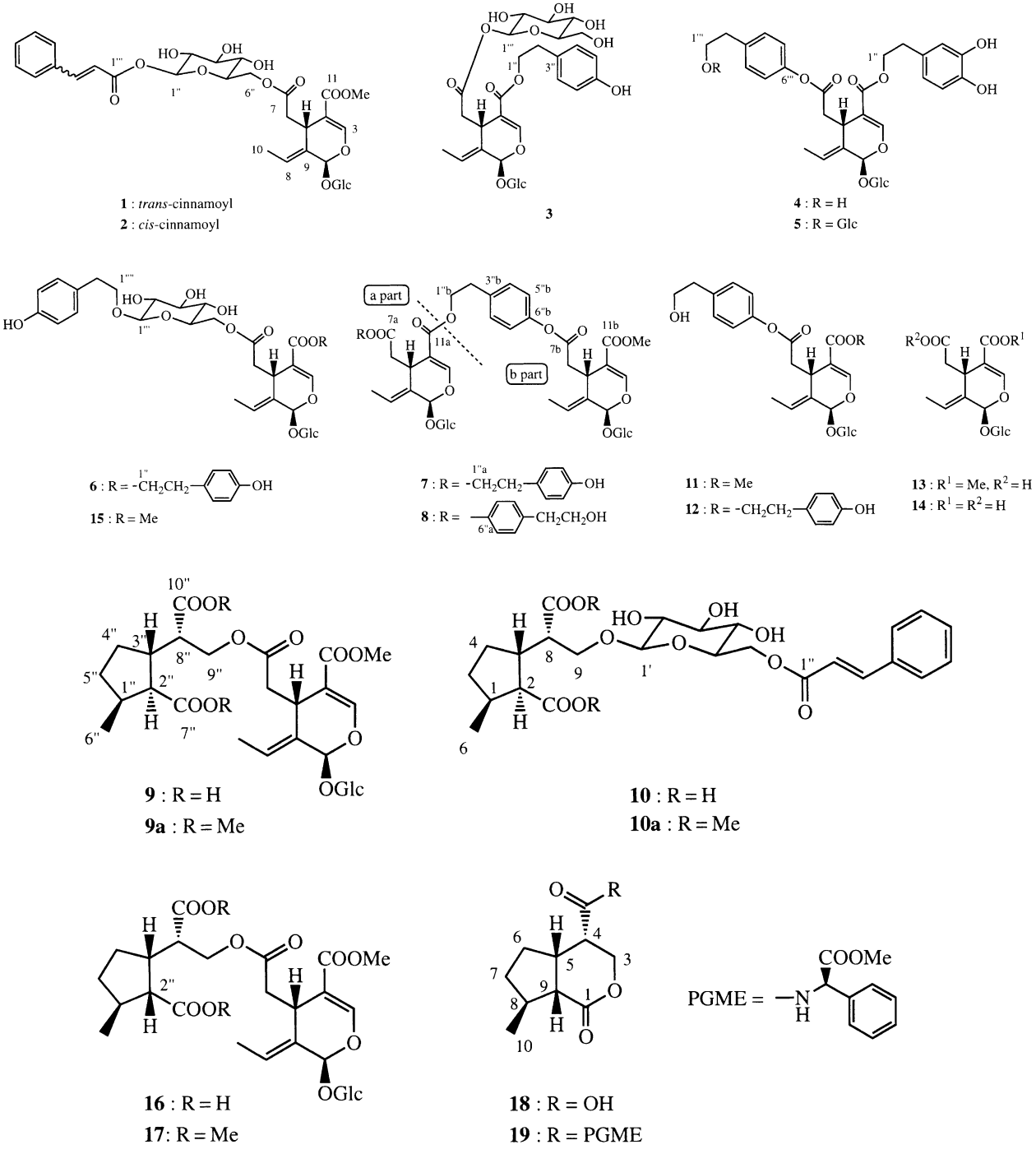

the C-6″ hydroxyl group of 1-*O*-*trans*-cinnamoyl-β-D-glucopyranose. Thus, **1** was established as depicted and given the trivial name safghanoside A.

Safghanoside B (**2**), $C_{32}H_{40}O_{17}$ was recognized to be an isomer of **1**. The only significant differences in their ^1H NMR spectra were the chemical shifts and the coupling constants of a pair of olefinic protons (**2**: δ 6.04 and 7.09, each *d*, $J = 12.5$ Hz), suggesting that **2** possessed a *cis*-cinnamoyl group instead of a *trans*-cinnamoyl group as in **1**. Accordingly, glucoside **2** was formulated as shown.

Compound **3** was isolated as an amorphous powder with the molecular formula $C_{30}H_{40}O_{17}$. The NMR spectra of **3** exhibited the signals assignable to an oleoside (**14**) moiety together with a *p*-hydroxyphenethyl alcohol moiety and an additional β-glucose unit. The ester linkages of oleoside with *p*-hydroxyphenethyl alcohol and glucose units were determined by HMBC experiments, which showed cross-peaks between H-1″ and C-11 and between H-1‴ and C-7. Consequently, the structure of the new compound was represented by **3** and designated safghanoside C.

The ^{1}H NMR spectrum (Table 1) of compound **4** was similar to that of fraxiformoside (**12**) (Tanahashi et al., 1992) except that the signals in the aromatic region were observed as an AA′BB′ and an ABX spin systems in **4** instead of two AA′BB′ spin systems as in **12**. The ^{13}C NMR spectral data (Table 2) of **4** were also superimposable on those of **12**, except for the aromatic carbon signals, which were in good agreement with those of the 3,4-dihydroxyphenyl moiety of oleuropein. These finding indicated that the glucoside **4** possessed an oleoside, a *p*-hydroxyphenethyl moiety and a 3,4-dihydroxyphenethyl moiety. The important HMBC correlation observed between H_2-1″ and conjugated carbonyl signal was indicative of an ester linkage of C-11 of an oleoside (**14**) unit with an alcoholic hydroxyl group of 3,4-dihydroxyphenethyl alcohol. Attachment of the *p*-hydroxyphenethyl alcohol unit at C-7 through a phenolic hydroxyl group was supported by comparative studies on the ^{13}C NMR spectra of formoside (**11**) (Tanahashi et al., 1993). Thus, compound **4** was formulated as shown and designated safghanoside D.

Glucoside **5**, named safghanoside E, on HR–SIMS exhibited a peak at *m*/*z* 807.2727 ([M–H]$^-$) consistent with a molecular formula of $C_{38}H_{48}O_{19}$. The ^{1}H and ^{13}C NMR spectral (Tables 1 and 2) features of **5** were similar to those of **4**, except for the presence of signals assignable to an extra β-glucopyranosyl unit and for the chemical shifts of the signals arising from the *p*-hydroxyphenethyl unit. The glycosidation shifts of C-1‴ (+7.4 ppm) and C-2‴ (−3.0 ppm), when compared with the corresponding signals of **4**, suggested the attachment of a glucose unit at the hydroxyl group on C-1‴. This was further confirmed by an HMBC experiment, which showed cross-peaks between H-1⁗ at δ 4.30 (*d*, J=8.0 Hz) and C-1‴ at δ 71.5 as well as between H_2-1″ and C-11. Accordingly, the structure of the new compound was represented by **5**.

Safghanoside F (**6**), $C_{38}H_{48}O_{18}$, was isolated as a colorless amorphous powder. The ^{1}H NMR spectrum (Table 1) of **6** revealed signals attributable to an oleoside unit and two *p*-hydroxyphenethyl moiety, with an additional signal of an anomeric proton at δ 4.28 (*d*, J=8.0 Hz). Its ^{13}C NMR spectrum (Table 2) was very similar to that of nuezhenide (**15**), except for the appearance of an additional set of signals assigned to a *p*-hydroxyphenethyl moiety. This unit was determined to be attached at C-11 by HMBC cross-peaks between H_2-1″ and C-11 as well as between H_2-6‴ and C-7 and between H-1‴ and C-1⁗. Thus, compound **6** was formulated as shown.

Compounds **7** and **8** were recognized as isomers, $C_{49}H_{60}O_{23}$, from their HR–SIMS. The NMR spectral features (Tables 1 and 2) demonstrated clearly the presence of two oleoside units, two *p*-hydroxyphenethyl moieties and a carbomethoxyl group in each compound. The HMBC experiments with **7** and **8** showed interactions between H_2-1″b and C-11a and between OMe and C-11b. Furthermore, the chemical shifts of C-3″b, C-5″b, C-7″b and C-7b suggested that the C-6″b hydroxyl group was esterified with the C-7b carboxyl group. The structural difference between **7** and **8** could be ascribed to the point of ester linkage of another *p*-hydroxyphenethyl moiety, which was discriminated by a combination of 2D-NMR experiments and the chemical shifts of carbon signals. The important ^3J correlation in **7**, observed between H_2-1″a and C-7a, was indicative of an ester linkage of C-7a of the oleoside unit with the C-1″a hydroxyl of the *p*-hydroxyphenethyl group. On the other hand, the chemical shifts of the aromatic carbons and C-7a in **8** suggested the attachment of the phenolic hydroxyl group at C-6″a to C-7a. Consequently, the glucosides were represented by **7** and **8**, and were designated safghanosides G and H, respectively.

The ^{13}C NMR spectrum of compound **9**, $C_{27}H_{38}O_{15}$ (HR–SIMS *m*/*z* 601.2155 [M−H]$^-$), indicated that **9** was composed of an oleoside 11-methyl ester unit and a monoterpene unit. The combination of 2D-NMR studies suggested that the planar structure of **9** was the same as frameroside (**16**) (Takenaka et al., 2000). The relative configurations of the cyclopentane moiety in **9** were suggested by its NOESY spectrum. The important NOE interaction was observed between H_3-6″ and H-3″ but not between H_3-6″ and H-2″, demonstrating that H-3″ exists on the same β face as the methyl group (H_3-6″), while H-2″ has α orientation.

Methylation of **9** with CH_2N_2–Et_2O yielded the methylated derivative **9a**, which exhibited ^{1}H NMR signals for two additional carbomethoxyl groups at δ 3.61 and 3.66, supporting the presence in **9** of two carboxyl groups. The ^{1}H NMR spectral data of **9a** was unexpectedly identical with those of a methylated compound of frameroside (**16**). This fact suggested that **9** has the same stereochemistry as **16**, apart from C-2″, which is epimerisable because of the adjacent carbomethoxyl group. Comparative studies of ^{1}H and ^{13}C NMR spectra of **9a**, **9** and **16** as well as the analysis of the NOESY spectrum of **9a** indicated that no epimerization had taken place in preparation of **9a** from **9**. By contrast, methylated compound of **16** was not the expected **17** (Takenaka et al., 2000) but a C-2″ epimer of **17**, i.e. **9a**. A similar epimerization has been reported for α-(2-formyl-3-methylcyclopentyl)acrylaldehyde (Pagnoni et al., 1976). Thus, compound **9** was determined to be 2″-*epi*-frameroside.

Compound **10** was obtained as a colorless amorphous powder. The HR–SIMS of **10** exhibited a strong [M−H]$^-$ at *m*/*z* 507.1866, indicating a molecular formula of $C_{25}H_{32}O_{11}$ for **10**. It showed UV maxima at 216, 222, and 276 nm and IR bands at 3393, 1712, 1637, and 1570 cm^{-1}. The ^{1}H NMR spectrum displayed, besides the signals corresponding to a *trans*-cinnamic acid and a β-glucose unit, signals for a secondary

Table 1
^{1}H NMR spectroscopic data of compounds **4**–**8** in CD_3OD

H	**4**						**5**						**6**					
1	6.01	*br s*					6.01	*br s*					5.90	*br s*				
3	7.52	*s*					7.52	*s*					7.46	*s*				
5	4.07	*dd*	(9.0, 4.0)				4.07	*dd*	(9.0, 5.0)				3.97	*dd*	(9.0, 4.0)			
6	2.66	*dd*	(14.0, 9.0)				2.66	*dd*	(14.0, 9.0)				2.43	*dd*	(14.0, 9.0)			
	2.87	*dd*	(14.0, 4.0)				2.87	*dd*	(14.0, 5.0)				2.69	*dd*	(14.0, 4.0)			
8	6.16	*br q*	(7.0)				6.17	*qd*	(7.0, 1.0)				6.08	*qd*	(7.0, 1.0)			
10	1.74	*dd*	(7.0, 2.0)				1.75	*dd*	(7.0, 2.0)				1.72	*dd*	(7.0, 1.0)			
1′, 1‴	4.82	*d*	(8.0)				4.81	*d*	(8.0)	4.30	*d*	(8.0)	4.79	*d*	(8.0)	4.28	*d*	(8.0)
3′, 3‴	3.41	*t*	(8.0)				3.41	*t*	(8.0)				3.40	*t*	(9.0)			
5′, 5‴													3.28	*m*		3.46	*m*	
6′, 6‴	3.63	*dd*	(12.0, 5.0)				3.63[a]	*dd*	(12.0, 5.0)	3.66[a]	*dd*	(12.0, 5.0)	3.66	*dd*	(12.0, 5.5)	4.20	*dd*	(12.0, 5.5)
	3.83	*dd*	(12.0, 1.0)				3.82[b]	*dd*	(12.0, 2.0)	3.86[b]	*dd*	(12.0, 2.0)	3.88	*dd*	(12.0, 1.5)	4.35	*dd*	(12.0, 2.0)
1″, 1‴	4.27	*dt*	(11.0, 6.5)	3.74	*t*	(7.0)	4.28	*m*		3.76	*dt*	(10.0, 7.0)	4.22	*dt*	(14.0, 7.0)	3.68	*ddd*	(9.5, 8.0, 6.5)
	4.30	*dt*	(11.0, 6.5)							4.09	*dt*	(10.0, 7.0)				3.94	*ddd*	(9.5, 8.0, 6.5)
2″, 2‴	2.80	*t*	(6.5)	2.81	*t*	(7.0)	2.81	*t*	(7.0)	2.94	*t*	(7.0)	2.83	*br t*	(7.0)	2.81	*m*	
4″, 4‴	6.67	*d*	(2.0)	7.24	*d*	(8.0)	6.67	*d*	(2.0)	7.29	*d*	(8.0)	7.03	*d*	(8.5)	7.05	*d*	(8.5)
5″, 5‴				6.99	*d*	(8.0)				6.98	*d*	(8.0)	6.68	*d*	(8.5)	6.70	*d*	(8.5)
7″, 7‴	6.68	*d*	(8.0)	6.99	*d*	(8.0)	6.68	*d*	(8.0)	6.98	*d*	(8.0)	6.68	*d*	(8.5)	6.70	*d*	(8.5)
8″, 8‴	6.56	*dd*	(8.0, 2.0)	7.24	*d*	(8.0)	6.56	*dd*	(8.0, 2.0)	7.29	*d*	(8.0)	7.03	*d*	(8.5)	7.05	*d*	(8.5)

H	**7**						**8**					
	a Part			b Part			a Part			b Part		
1	5.91	*br s*		6.02	*br s*		6.01[g]	*brs*		6.03[g]	*br s*	
3	7.50[c]	*s*		7.51[c]	*s*		7.51	*s*		7.57	*s*	
5	3.94	*dd*	(9.0, 4.0)	4.07	*dd*	(9.0, 4.0)	4.06	*dd*	(9.0, 4.0)	4.11	*dd*	(9.0, 4.0)
6	2.43	*dd*	(14.0, 9.0)	2.66	*dd*	(14.0, 9.0)	2.72	*dd*	(14.0, 9.0)	2.65	*dd*	(14.0, 9.0)
	2.72	*dd*	(14.0, 4.0)	2.87	*dd*	(14.0, 4.0)	2.95	*dd*	(14.0, 4.0)	2.85	*dd*	(14.0, 4.0)
8	6.05	*qd*	(7.0, 1.0)	6.16	*qd*	(7.0, 1.0)	6.17	*qd*	(7.0, 1.0)	6.17	*qd*	(7.0, 1.0)
10	1.59	*dd*	(7.0, 1.0)	1.74	*dd*	(7.0, 1.0)	1.74	*dd*	(7.0, 1.0)	1.74	*dd*	(7.0, 1.0)
OMe				3.71	*s*					3.72	*s*	
1′	4.82[d]	*d*	(8.0)	4.80[d]	*d*	(8.0)	4.82	*d*	(8.0)	4.82	*d*	(8.0)
3′	3.41	*t*	(8.5)	3.41	*t*	(8.5)	3.41	*t*	(8.5)	3.41	*t*	(8.5)
6′	3.63[e]	*dd*	(12.0, 5.5)	3.66[e]	*dd*	(12.0, 5.5)	3.63	*dd*	(12.0, 5.5)	3.63	*dd*	(12.0, 5.5)
	3.83[f]	*dd*	(12.0, 2.0)	3.88[f]	*dd*	(12.0, 2.0)	3.82	*dd*	(12.0, 2.0)	3.82	*dd*	(12.0, 2.0)
1″	4.16	*dt*	(11.0, 6.5)	4.29	*dt*	(11.0, 6.5)	3.74	*t*	(7.0)	4.36	*t*	(6.5)
	4.29	*dt*	(11.0, 6.5)									
2″	2.86	*t*	(6.5)	2.94	*t*	(6.5)	2.82	*t*	(7.0)	2.98	*t*	(6.5)
4″	7.06	*d*	(8.5)	7.28	*d*	(8.5)	7.25	*d*	(8.5)	7.29	*d*	(8.5)
5″	6.70	*d*	(8.5)	7.02	*d*	(8.5)	6.99	*d*	(8.5)	7.01	*d*	(8.5)
7″	6.70	*d*	(8.5)	7.02	*d*	(8.5)	6.99	*d*	(8.5)	7.01	*d*	(8.5)
8″	7.06	*d*	(8.5)	7.28	*d*	(8.5)	7.25	*d*	(8.5)	7.29	*d*	(8.5)

[a–g] Assignments may be interchangeable.

Table 2
^{13}C NMR spectroscopic data of compounds **4**–**8** in CD_3OD

C	**4**		**5**		**6**		**7**		**8**	
							a Part	b Part	a Part	b Part
1	95.3		95.4		95.2		95.2	95.4	95.4	95.4
3	155.3		155.3		155.2		155.3[j]	155.2[j]	155.3	155.4
4	109.5		109.5		109.6		109.5	109.4	109.4	109.4
5	31.8		31.8		31.7		31.9	31.8	31.8	31.8
6	41.0		41.1		41.2		41.3	41.1	41.1	41.1
7	171.7		171.7		173.0		173.2	171.6	171.6	171.7
8	125.1		125.1		125.0		125.0	125.2	125.2	125.2
9	130.6		130.7		130.7		130.4	130.6	130.7	130.6
10	13.8		13.8		13.8		13.6	13.9	13.9	13.9
11	168.2		168.2		168.2		168.2	168.7	168.1	168.7
OMe								52.0		52.0
1′, 1‴	101.0		101.1	104.4	100.9	104.5	101.0[k]	100.9[k]	101.1	101.1
2′, 2‴	74.8		74.8[a]	75.2[a]	74.8	75.0	74.8	74.8	74.8	74.8
3′, 3‴	77.9		78.0	78.0	78.0	78.0	78.0	78.0	78.0	78.0
4′, 4‴	71.4		71.5[b]	71.7[b]	71.5[e]	71.7[e]	71.5[l]	71.6[l]	71.5	71.5
5′, 5‴	78.4		78.2[c]	78.4[c]	78.5	75.3	78.5	78.5	78.4[n]	78.5[n]
6′, 6‴	62.7		62.7[d]	62.8[d]	62.7	65.1	62.7[m]	62.9[m]	62.7	62.7
1″, 1‴	66.4	64.1	66.4	71.5	66.5	72.3	66.5	66.5	64.1	66.0
2″, 2‴	35.5	39.6	35.6	36.6	35.3	36.4	35.4	35.3	39.6	35.5
3″, 3‴	131.0	138.2	131.0	138.0	130.5	130.3	130.3	137.2	138.3	137.5
4″, 4‴	116.4	131.0	116.4	131.0	131.1	131.1	131.1	131.0	131.0[o]	131.1[o]
5″, 5‴	146.3	122.6	146.3	122.5	116.3[f]	116.2[f]	116.4	122.8	122.6[p]	122.7[p]
6″, 6‴	144.9	150.5	145.0	150.6	156.8[g]	157.1[g]	157.1	150.8	150.6	150.8
7″, 7‴	117.0	122.6	117.0	122.5	116.3[h]	116.2[h]	116.4	122.8	122.6[q]	122.7[q]
8″, 8‴	121.3	131.0	121.3	131.0	131.1[i]	131.0[i]	131.1	131.0	131.0[r]	131.1[r]

[a–r] Assignments may be interchangeable.

methyl group, three pairs of methylene protons and four methine protons. The residual unit was formulated as the same cyclopentanoid monoterpene unit as in **9** by its ^{13}C NMR, COSY, HMBC and NOESY spectra. The linkage of these components were determined by an HMBC experiment, which revealed cross-peaks between H_2-9 and H-1′ and between H_2-6′ and C-1″, suggesting the structure of **10** as shown. Methylation of **10** with CH_2N_2–Et_2O yielded a methylate, whose spectral data were fully consistent with the structure **10a**. Finally, an (*R*)-PGME amide (Ohtani et al., 1991) was prepared from **10** in order to confirm the absolute configurations of the monoterpene unit. Compound **10** was subjected to alkaline hydrolysis and the resulting monoterpene lactone **18** was converted to the (*R*)-PGME amide **19** which was identical with a (*R*)-PGME amide derived from **16** (Takenaka et al., 2000). This unexpected result could be accounted for by the fact that the asymmetric center at C-9 was inverted in a similar manner as observed for the formation of *epi*-nepetalactone (Trave et al., 1968). Thus, the structure of the new compound was represented by **10** with the absolute stereochemistry 1*S*, 2*S*, 3*S* and 8*S* and designated as syringafghanoside.

Glucosides **1**–**9** are secoiridoid glucosides of the oleoside type, which have so far been isolated only from the oleaceous plants and structurally characterized by the esterified C-7 carboxyl group and the ethylidene group at C-9. Oleoside-type glucosides with C_6–C_2 unit(s) such as **4**–**8** represent common structures found in some genera of the family. However, glucoside **9** is the first example of oleoside-type secoiridoid glucoside esterified with a cyclopentane monoterpene unit isolated from the genus *Syringa*.

3. Experimental

3.1. General

^1H (300 or 500 MHz) and ^{13}C (75 or 125 MHz) NMR: TMS as int. standard. SIMS: glycerol or 3-nitrobenzyl alcohol as matrix. TLC: silica gel.

3.2. Plant material

Leaves of *Syringa afghanica* C. K. Schneid. were collected at the Nippon Shinyaku Institute for Botanical Research, Kyoto, Japan. A voucher specimen (KPU011) is deposited in the laboratory of Kobe Pharmaceutical University.

3.3. Isolation of glucosides

Dried leaves of *S. afghanica* (357.6 g) were extracted with hot MeOH. After concentration, the extract (64.6 g)

was suspended in H_2O and filtered through a celite layer. The filtrate and washings were combined and extracted successively with $CHCl_3$ and *n*-BuOH. The *n*-BuOH extract (23.5 g) was subjected to Wakogel LP-40C18 (Wako Pure Chemical Industries, Ltd., Osaka, Japan) chromatography. Elution with MeOH–H_2O mixtures of the indicated MeOH content gave 5 fractions I–V. Fraction I (1–15% MeOH eluent, 4.40 g) was further purified by chromatography on a Wakogel LP-40C18 column to give 3 subfractions I-1–I-3. Fraction I-1 (1% MeOH eluent, 380 mg) was further purified by preparative HPLC (μBondasphere 5 μ C18–100 Å, H_2O–MeOH, 3:2 or 13:7) and preparative TLC ($CHCl_3$–MeOH, 7:3 or acetone–$CHCl_3$–H_2O, 8:2:1), giving cinnamic acid (15 mg), 1-*O*-*trans*-cinnamoyl-β-D-glucopyranose (10 mg), 1-*O*-*cis*-cinnamoyl-β-D-glucopyranose (3.2 mg), syringin (22 mg), acteoside (20 mg), oleoside dimethyl ester (15 mg) and methyl glucooleoside (4.1 mg). Fr I-2 (7–10% MeOH eluent, 800 mg) was further purified by preparative HPLC (H_2O–MeOH, 11:9, 3:2 or H_2O–MeCN, 4:1) and preparative TLC ($CHCl_3$–MeOH, 7:3, acetone–$CHCl_3$–H_2O, 8:2:1 or *n*-BuOH–AcOH–H_2O, 8:2:1), giving isoligustroside (12 mg), isooleuropein (11 mg) and safghanoside C (**3**) (12 mg). Fr I-3 (20–50% MeOH eluent, 2.8 g) was purified by preparative HPLC (H_2O–MeOH, 9:11, 2:3, 3:7 or H_2O–MeCN, 3:1) and preparative TLC ($CHCl_3$–MeOH–AcOH, 7:3:0.1), giving rhoifolin (12.0 mg), poliumoside (21.0 mg), luteolin (15.0 mg), lipedoside A-I (2.4 mg) and 2″-*epi*-frameroside (**9**) (4.1 mg). The following fractions of the initial column chromatography were also purified by preparative HPLC (H_2O–MeOH, 3:7, 1:1, 11:9, 3:2, 73:27, 3:1 or H_2O–MeCN, 13:7, 7:3, 4:1) and preparative TLC ($CHCl_3$–MeOH, 7:3, acetone–$CHCl_3$–H_2O, 8:2:1 or *n*-BuOH–AcOH–H_2O, 8:2:1), Fr II (15–20% MeOH eluent, 480 mg): ligstroside (14 mg), formoside (**11**) (49 mg), 1″-*O*-β-D-glucosylformoside (6.8 mg) and safghanosode F (**6**) (3.0 mg); fr III (20–40% MeOH eluent, 2.31 g): oleuropein (13 mg), 1‴-*O*-β-D-glucosylfraxiformoside (41 mg), safghanoside A (**1**) (39 mg), safghanoside B (**2**) (12 mg), safghanoside D (**4**) (31 mg) and safghanoside E (**5**) (49 mg); fr IV (40–50% MeOH eluent, 3.85 g): fraxiformoside (**12**) (4.2 mg) and syringafghanoside (**10**) (78 mg); fr V (50–60% MeOH eluent, 344 mg): safghanoside G (**7**) (10 mg) and safghanoside H (**8**) (4.0 mg).

3.4. Safghanoside A (*1*)

Colourless amorphous powder, $[\alpha]_D^{27}$ −143° (*c* 0.96, MeOH); UV λ_{max}^{MeOH} nm (log ε): 218 (4.27), 223 (4.28), 241.5 (4.16), 279.5 (4.32); IR ν_{max}^{KBr} cm^{-1}: 3403, 1716, 1635, 1448, 1076; ^1H NMR (CD_3OD): δ 1.73 (3H, *dd*, *J* = 7.0, 2.0 Hz, H_3-10), 2.50 (1H, *dd*, *J* = 14.0, 9.0 Hz, H-6), 2.75 (1H, *dd*, *J* = 14.0, 5.0 Hz, H-6), 3.46 (1H, *t*, *J* = 8.0 Hz, H-3′), 3.68 (1H, *dd*, *J* = 12.0, 5.5 Hz, H-6′), 3.71 (3H, *s*, OMe), 3.87 (1H, *dd*, *J* = 12.0, 1.5 Hz, H-6′), 4.00 (1H, *dd*, *J* = 9.0, 5.0 Hz, H-5), 4.25 (1H, *dd*, *J* = 12.0, 5.0 Hz, H-6″), 4.32 (1H, *dd*, *J* = 12.0, 2.0 Hz, H-6″), 4.81 (1H, *d*, *J* = 8.0 Hz, H-1′), 5.60 (1H, *d*, *J* = 8.0 Hz, H-1″), 5.91 (1H, *br s*, H-1), 6.09 (1H, *qd*, *J* = 7.0, 1.0 Hz, H-8), 6.58 (1H, *d*, *J* = 16.0 Hz, H-2), 7.41–7.63 (5H, *m*, H-5‴–9‴), 7.51 (1H, *s*, H-3), 7.81 (1H, *d*, *J* = 16.0 Hz, H-3‴); ^{13}C NMR (CD_3OD): δ 13.7 (C-10), 31.8 (C-5), 41.2 (C-6), 52.0 (OMe), 62.8 (C-6′), 64.7 (C-6″), 71.2 (C-4′), 71.5 (C-4″), 74.0 (C-2′), 74.7 (C-2″), 76.1 (C-5″), 77.8 (C-5′), 78.0 (C-3′), 78.4 (C-3″), 95.2 (C-1), 95.8 (C-1″), 100.9 (C-1′), 109.4 (C-4), 118.3 (C-2‴), 125.0 (C-8), 129.5 ×2 (C-5‴, 9‴), 130.1 ×2 (C-6‴, 8‴), 130.5 (C-9), 131.9 (C-7‴), 135.6 (C-4‴), 147.8 (C-3‴), 155.2 (C-3), 167.0 (C-1‴), 168.8 (C-11), 173.0 (C-7); HMBC: H_2-6→C-7, H-1′→C-1, OMe→C-11, H-1″→C-1‴, H_2-6″→C-7; HR–SIMS found: 695.2183 $[M-H]^-$; $C_{32}H_{39}O_{17}$ requires 695.2188.

3.5. Safghanoside B (*2*)

Colourless amorphous powder, $[\alpha]_D^{26}$ −158° (*c* 0.33, MeOH); UV λ_{max}^{MeOH} nm (log ε): 217 *sh* (4.14), 225 (4.17), 240 (4.19), 277 (3.99); IR ν_{max}^{KBr} cm^{-1}: 3393, 1733, 1716, 1635, 1437, 1074; ^1H NMR (CD_3OD): δ 1.73 (3H, *dd*, *J* = 7.0, 1.5 Hz, H_3-10), 2.51 (1H, *dd*, *J* = 14.0, 8.0 Hz, H-6), 2.74 (1H, *dd*, *J* = 14.0, 5.0 Hz, H-6), 3.42 (1H, *t*, *J* = 8.0 Hz, H-3′), 3.67 (1H, *dd*, *J* = 12.0, 5.5 Hz, H-6′), 3.68 (3H, *s*, OMe), 3.87 (1H, *dd*, *J* = 12.0, 1.5 Hz, H-6′), 4.00 (1H, *dd*, *J* = 8.0, 5.0 Hz, H-5), 4.23 (1H, *dd*, *J* = 12.0, 5.0 Hz, H-6″), 4.32 (1H, *dd*, *J* = 12.0, 2.0 Hz, H-6″), 4.80 (1H, *d*, *J* = 8.0 Hz, H-1′), 5.53 (1H, *d*, *J* = 8.0 Hz, H-1″), 5.90 (1H, *br s*, H-1), 6.04 (1H, *d*, *J* = 12.5 Hz, H-2‴), 6.09 (1H, *br q*, *J* = 7.0 Hz, H-8), 7.09 (1H, *d*, *J* = 12.5 Hz, H-3‴), 7.33–7.65 (5H, *m*, H-5‴–9‴), 7.50 (1H, *s*, H-3); ^{13}C NMR (CD_3OD): δ 13.7 (C-10), 31.7 (C-5), 41.2 (C-6), 52.0 (OMe), 62.7 (C-6′), 64.7 (C-6″), 71.2 (C-4′), 71.5 (C-4″), 73.9 (C-2′), 74.7 (C-2″), 76.1 (C-5′), 77.9 (C-5″), 78.0 (C-3′), 78.4 (C-3″), 95.2 (C-1), 95.6 (C-1″), 100.9 (C-1′), 109.4 (C-4), 119.5 (C-2‴), 125.0 (C-8), 129.1×2 (C-6‴, 8‴), 130.4 (C-7‴), 130.5 (C-9‴), 131.3×2 (C-5‴, 9‴), 136.0 (C-4‴), 146.3 (C-3‴), 155.2 (C-3), 166.0 (C-1‴), 168.7 (C-11), 173.0 (C-7); HMBC: H-1′→C-1, H_2-6→C-7, OMe→C-11, H-1″→C-1‴, H_2-6″→C-7; HR–SIMS found: 695.2198 $[M-H]^-$; $C_{32}H_{39}O_{17}$ requires 695.2188.

3.6. Safghanoside C (*3*)

Colourless amorphous powder, $[\alpha]_D^{27}$ −102° (*c* 0.83, MeOH); UV λ_{max}^{MeOH} nm (log ε): 227 (4.18), 238 *sh* (4.11), 277 (3.26), 285 *sh* (3.15); IR ν_{max}^{KBr} cm^{-1}: 3393, 1740, 1716, 1635, 1517, 1076; ^1H NMR (CD_3OD): δ 1.76 (3H, *dd*, *J* = 7.0, 1.0 Hz, H_3-10), 2.54 (1H, *dd*, *J* = 15.0, 9.0 Hz, H-6), 2.73 (1H, *dd*, *J* = 15.0, 3.0 Hz, H-6), 2.86 (2H, *t*, *J* = 7.0 Hz, H_2-2″), 3.41 (1H, *t*, *J* = 9.0 Hz, H-3′), 3.66 (2H, *dd*, *J* = 12.0, 5.5 Hz, H-6′, 6‴), 3.81 (1H, *dd*, *J* = 12.0, 1.0 Hz, H-6′), 3.89 (1H, *dd*, *J* = 12.0, 2.0 Hz, H-6‴), 3.98 (1H, *dd*, *J* = 9.0, 3.0 Hz, H-5), 4.25, 4.28 (each 1H, *dt*, *J* = 10.0, 7.0 Hz, H_2-1″), 4.80 (1H, *d*, *J* = 8.0 Hz,

H-1′), 5.44 (1H, *d*, *J* = 8.0 Hz, H-1‴), 5.93 (1H, *br s*, H-1), 6.10 (1H, *br q*, *J* = 7.0 Hz, H-8), 6.71 (2H, *d*, *J* = 8.0 Hz, H-5″, 7″), 7.07 (2H, *d*, *J* = 8.0 Hz, H-4″, 8″), 7.45 (1H, *s*, H-3); ^{13}C NMR (CD_3OD): δ 13.9 (C-10), 31.3 (C-5), 35.4 (C-2″), 40.5 (C-6), 62.4 (C-6‴), 62.8 (C-6′), 66.5 (C-1″), 71.0 or 71.5 (C-4′ or C-4‴), 73.9 or 74.8 (C-2′ or C-2‴), 78.0 ×2 (C-5′, 5‴), 78.5 or 78.7 (C-3′ or C-3‴), 95.4 or 95.9 (C-1 or C-1‴), 100.9 (C-1′), 109.4 (C-4), 116.3×2 (C-5″, 7″), 125.5 (C-8), 130.2×2 (C-3″, 9), 131.0×2 (C-4″, 8″), 155.3 (C-3), 157.1 (C-6″), 168.3 (C-11), 171.9 (C-7); HMBC: H-1′→C-1, H-3→C-11, H_2-6→C-7, H-1″ (δ 4.27)→C-11, H_2-2″→C-1′, 4″, 8″, H-1‴ (δ 5.44)→C-7; HR–SIMS found: 671.2194 $[M–H]^-$; $C_{30}H_{39}O_{17}$ requires 671.2194.

3.7. Safghanoside D (**4**)

Colourless amorphous powder, $[\alpha]_D^{27}$ −129° (*c* 1.05, MeOH); UV λ_{max}^{MeOH} nm (log ε): 220 (4.26), 230 *sh* (4.24), 282.5 (3.49); IR ν_{max}^{KBr} cm^{-1}: 3389, 1743, 1697, 1635, 1508, 1074; ^{1}H and ^{13}C NMR (CD_3OD): see Tables 1 and 2; HMBC: H-1′→C-1, H-1→C-1′, H-3→C-11, H_2-6→C-7, H-1″ (δ 4.27)→C-11, 3″, H_2-2″→C-1″, 3″, H-4″→C-2″, 3″, 5″, H-7″→C-6″, H-8″→C-6″, H_2-1‴→C-2‴, H_2-2‴→C-1‴, 4‴, 8‴, H-4‴ and 8‴ (δ 7.24)→C-6‴, H-5‴ and 7‴ (δ 6.99)→C-6‴; HR–SIMS found: 645.2172 $[M–H]^-$; $C_{32}H_{37}O_{14}$ requires 645.2185.

3.8. Safghanoside E (**5**)

Colourless amorphous powder, $[\alpha]_D^{26}$ −104° (*c* 0.69, MeOH); UV λ_{max}^{MeOH} nm (log ε): 220 (4.23), 243 *sh* (4.08), 282 *sh* (3.44); IR ν_{max}^{KBr} cm^{-1}: 3383, 1740, 1697, 1522, 1074; ^{1}H and ^{13}C NMR (CD_3OD): see Tables 1 and 2; HMBC: H-1′→C-1, H-3→C-11, H_2-6→C-7, H_2-1″→C-11, 2″, H_2-2″→C-3″, 4″, 8″, H-4″→C-5″, H-7″→C-6″, H_2-1‴→C-1‴′, H_2-2‴→C-1‴, 3‴, 4‴, 8‴, H-4‴ and 8‴→C-6‴, H-5‴ and 7‴→C-3‴, 6‴, H-1‴′→C-1‴; HR–SIMS found: 807.2727 $[M–H]^-$; $C_{38}H_{47}O_{19}$ requires 807.2713.

3.9. Safghanoside F (**6**)

Colourless amorphous powder, $[\alpha]_D^{27}$ −101° (*c* 0.27, MeOH); UV λ_{max}^{MeOH} nm (log ε): 225.5 (4.27), 265 *sh* (3.43), 286.5 *sh* (3.33); IR ν_{max}^{KBr} cm^{-1}: 3407, 1749, 1734, 1635, 1508, 1078; ^{1}H and ^{13}C NMR (CD_3OD): see Tables 1 and 2; HMBC: H-3→C-11, H_2-6→C-7, H-1′→C-1, H_2-1″→C-11, H_2-2″→C-1″, 3″, 4″, 8″, H-4″ and 8″→C-6″, H-5″ and 7″→C-3″, 6″, H-1‴→C-1‴′, H_2-1‴′→C-1‴, H_2-2‴′→C-1‴′, 3‴′ 4‴′, 8‴′, H-4‴′ and 8‴′→C-6‴′, H-5‴′ and 7‴′→C-3‴′, 6‴′; HR–SIMS found: 791.2770 $[M–H]^-$; $C_{38}H_{47}O_{18}$ requires 791.2764.

3.10. Safghanoside G (**7**)

Colourless amorphous powder, $[\alpha]_D^{27}$ −182° (*c* 0.62, MeOH); UV λ_{max}^{MeOH} nm (log ε): 227 (4.35), 246.5 *sh* (4.24), 277 (3.64), 288 *sh* (3.54); IR ν_{max}^{KBr} cm^{-1}: 3413, 1739, 1705, 1634, 1508, 1076; ^{1}H and ^{13}C NMR (CD_3OD): see Tables 1 and 2; HMBC: H-1a (δ 5.91)→C-1′a (δ 101.0), 9a (δ 130.4), H-5a (δ 3.94)→C-6a (δ 41.3), 7a (δ 173.2), H_2-6a (δ 2.43, 2.72)→C-4a (δ 109.5), 7a (δ 173.2), 9a (δ 130.4), H-8a (δ 6.05)→C-9a (δ 130.4), 10a (δ 13.6), H_2-1″a (δ 4.16, 4.29)→C-7a (δ 173.2), H_2-1″a (δ 4.29)→C-3″a (δ 130.3), H-4″a and 8″a (δ 7.06)→C-2″a (δ 35.4), 6″a (δ 157.1), H-5″a and 7″a (δ 6.70)→C-3″a (δ 130.3), 6″a (δ 157.1), H-1b (δ 6.02)→C-1′b (δ 100.9), 9b (δ 130.6), H-5b (δ 4.07)→C-6b (δ 41.1), H_2-6b (δ 2.66, 2.87)→C-4b (δ 109.4), 7b (δ 171.6), 9b (δ 130.6), H-8b (δ 6.16)→C-9b (δ 130.6), 10b (δ 13.9), H_2-1″b (δ 4.29)→C-11a (δ 168.2), 2″b (δ 35.3), H_2-2″b (δ 2.94)→C-1″b (δ 66.5), 3″b (δ 137.2), H-4″b and 8″b (δ 7.28)→C-6″b (δ 150.8), H-5″b and 7″b (δ 7.02)→C-3″b (δ 137.2), 6″b (δ 150.8), OMe (δ 3.71)→C-11b (δ 168.7); HR–SIMS found: 1015.3454 $[M–H]^-$; $C_{49}H_{59}O_{23}$ requires 1015.3449.

3.11. Safghanoside H (**8**)

Colourless amorphous powder, $[\alpha]_D^{28}$ −142° (*c* 0.33, MeOH); UV λ_{max}^{MeOH} nm (log ε): 225.5 *sh* (4.22), 236 (4.28), 268 *sh* (3.22); ν_{max}^{KBr} cm^{-1}: 3397, 1751, 1701, 1631, 1508, 1074; ^{1}H and ^{13}C NMR (CD_3OD): see Tables 1 and 2; HMBC: H-1′a (δ 4.82)→C-1a (δ 95.4), H-3a (δ 7.51)→C-1a (δ 95.4), 11a (δ 168.1), H-5a (δ 4.06)→C-3a (δ 155.3), 4a (δ 109.4), 9a (δ 130.7), 11a (δ 168.1), H_2-6a (δ 2.72, 2.95)→C-5a (δ 31.8), 7a (δ 171.6), H-8a (δ 6.17)→C-9a (δ 130.7), H_3-10a (δ 1.74)→C-9a (δ 130.7), H_2-1″a (δ 3.74)→C-3″a (δ 138.3), H_2-2″a (δ 2.82)→C-1″a (δ 64.1), 3″a (δ 138.3), H-4″a and 8″a (δ 7.25)→C-2″a (δ 39.6), 6″a (δ 150.6), H-5″a and 7″a (δ 6.99)→C-3″a (δ 138.3), 6″a (δ 150.6), H-1′b (δ 4.82)→C-1b (δ 95.4), H-3b (δ 7.57)→C-1b (δ 95.4), 11b (δ 168.7), H-5b (δ 4.11)→C-3b (δ 155.4), 4b (δ 109.4), 9b (δ 130.6), 11b (δ 168.7), H_2-6b (δ 2.65, 2.85)→C-5b (δ 31.8), 7b (δ 171.7), H-8b (δ 6.17)→C-9b (δ 130.6), H_3-10b (δ 1.74)→C-9b (δ 130.6), H_2-1″b (δ 4.36)→C-11a (δ 168.1), H_2-2″b (δ 2.98)→C-1″b (δ 66.0), 3″b (δ 137.5), H-4″b and 8″b (δ 7.29)→C-2″b (δ 35.5), 6″b (δ 150.8), H-5″b and 7″b (δ 7.01)→C-3″b (δ 137.5), 6″b (δ 150.8), OMe (δ 3.72)→C-11b (δ 168.7); HR–SIMS found: 1015.3470 $[M–H]^-$; $C_{49}H_{59}O_{23}$ requires 1015.3449.

3.12. 2″-Epi-frameroside (**9**)

Colourless amorphous powder, $[\alpha]_D^{24}$ −116° (*c* 0.22, MeOH); UV λ_{max}^{MeOH} nm (log ε): 237 (3.98); ν_{max}^{KBr} cm^{-1}: 3413, 1717, 1636, 1580, 1078; ^{1}H NMR (CD_3OD): δ 1.09 (3H, *d*, *J* = 7.0 Hz, H_3-6″), 1.23 (1H, *m*, H-5″), 1.53 (1H, *tt*, *J* = 12.0, 8.0 Hz, H-4″), 1.74 (3H, *dd*, *J* = 7.0, 1.0 Hz, H-10), 1.83 (1H, *br dt*, *J* = 12.0, 6.0 Hz, H-4″), 2.03 (1H, *dt*, *J* = 12.0, 7.0 Hz, H-5″), 2.29 (1H, *m*, H-1″), 2.45 (1H, *m*, H- 2″), 2.48 (1H, *dd*, *J* = 14.0, 9.0 Hz, H-6), 2.59

(1H, *br dd*, $J=8.0$, 4.5 Hz, H-3″), 2.71 (1H, *dd*, $J=14.0$, 4.5 Hz, H-6), 2.90 (1H, *m*, H-8″), 3.41 (1H, *t*, $J=8.5$ Hz, H-3′), 3.71 (3H, *s*, OMe), 3.71 (1H, *dd*, $J=12.0$, 6.0 Hz, H-6′), 3.90 (1H, *dd*, $J=12.0$, 2.0 Hz, H-6′), 3.99 (1H, *dd*, $J=9.0$, 4.5 Hz, H-5), 4.27 (2H, *m*, H_2-9″), 4.81 (1H, *d*, $J=8.0$ Hz, H-1′), 5.92 (1H, *br s*, H-1), 6.11 (1H, *qd*, $J=7.0$, 1.0 Hz, H-8), 7.52 (1H, *s*, H-3); ^{13}C NMR (CD_3OD): δ 13.7 (C-10), 31.9 (C-5), 41.1 (C-6), 51.9 (OMe), 62.8 (C-6′), 71.6 (C-4′), 74.8 (C-2′), 78.0 (C-5′), 78.6 (C-3′), 94.9 (C-1), 100.6 (C-1′), 109.4 (C-4), 124.8 (C-8), 130.7 (C-9), 155.2 (C-3), 168.6 (C-11), 172.9 (C-7). See Table 3 for carbon signals due to cyclopentane monoterpene unit; HMBC: H-1→C-1′, H_3-10→C-8, 9, H-3→C-1, 4, 5, 11, H-5→C-7, 9, H_2-6→C-7, H-8→C-5, 9, 10, H-1′→C-1, OMe→C-11, H-1″→C-7″, H-2″→C-4″, H-4″ (δ 1.83)→C-3″, H-5″ (δ 1.23)→C-3″, 6″, H_3-6″→C-1″, 2″, 5″, H-8″→C-3″, H_2-9″→C-7, 10″; NOESY: H-3″↔H_3-6″, H_2-9″↔H-4″ (δ 1.83); HR–SIMS found: 601.2155 $[M-H]^-$; $C_{27}H_{37}O_{15}$ requires 601.2134.

3.13. Methylation of **9**

A solution of **9** (2.0 mg) in MeOH was treated with CH_2N_2–MeOH under ice-cooling. The reaction mixture was evaporated *in vacuo* to give **9a** (1.8 mg). ^{1}H NMR (CD_3OD): δ 1.07 (3H, *d*, $J=6.5$ Hz, H_3-6″), 1.24 (1H, *dddd*, $J=12.0$, 11.5, 8.5, 6.5 Hz, H-5″), 1.54 (1H, *m*, H-4″), 1.73 (3H, *dd*, $J=7.0$, 1.5 Hz, H_3-10), 1.87 (1H, *m*, H-4″), 2.02 (1H, *dtd*, $J=12.0$, 7.5, 1.5 Hz, H-5″), 2.24 (1H, *m*, H-1″), 2.47 (1H, *dd*, $J=14.5$, 9.0 Hz, H-6), 2.50 (2H, *m*, H-2″, 3″), 2.69 (1H, *dd*, $J=14.5$, 4.5 Hz, H-6), 2.79 (1H, *ddd*, $J=11.0$, 6.5, 4.0 Hz, H-8″), 3.61 (3H, *s*, OMe), 3.66 (3H, *s*, OMe), 3.72 (3H, *s*, OMe), 3.90 (1H, *dd*, $J=12.0$, 2.5 Hz, H-6′), 3.97 (1H, *dd*, $J=9.0$, 4.5 Hz, H-5), 4.21 (1H, *dd*, $J=11.0$, 6.5 Hz, H-9″), 4.26 (1H, *dd*, $J=11.0$, 4.0 Hz, H-9″), 4.81 (1H, *d*, $J=8.0$ Hz, H-1′), 5.91 (1H, *br s*, H-1), 6.11 (1H, *qd*, $J=7.0$, 1.0 Hz, H-8), 7.52 (1H, *s*, H-3). HR–SIMS found: 629.2463 $[M-H]^-$; $C_{29}H_{41}O_{15}$ requires 629.2447. This compound was identical with dimethyl ester derived from frameroside.

Table 3
^{13}C NMR spectroscopic data of the cyclopentane monoterpene unit of **9**, **9a**, **10**, **10a** and **16** in CD_3OD

C	**9**	**9a**	**16**	C	**10**	**10a**
1″	40.3	40.5	36.5	1	40.1	40.2
2″	55.2	54.8	57.2	2	55.3	54.9
3″	41.8	42.1	43.9	3	41.9	42.4
4″	30.9	31.2	30.6	4	30.8	31.2
5″	35.0	34.8	33.8	5	34.5	34.7
6″	21.9	21.4	22.8	6	22.0	21.5
7″	179.0	175.0[a]	180.0	7	179.2	177.4
8″	47.3	47.8	48.8	8	49.2	48.7
9″	66.0	65.6	66.6	9	71.3	71.2
10″	177.0	177.3[a]	180.0	10	178.1	176.1
OMe		51.9		OMe		51.9
OMe		52.5		OMe		52.2

[a] Assignments may be interchangeable.

3.14. Syringafghanoside (**10**)

Colourless amorphous powder, $[\alpha]_D^{28}$ −21° (*c* 1.01, MeOH); UV λ_{max}^{MeOH} nm (log ε): 216 (4.10), 222 *sh* (4.03), 276 (4.17); IR ν_{max}^{KBr} cm^{-1}: 3393, 1712, 1637, 1570, 1082; ^{1}H NMR (CD_3OD): δ 1.02 (3H, *d*, $J=7.0$ Hz, H_3-6), 1.14 (1H, *m*, H-5), 1.53 (1H, *m*, H-4), 1.85 (1H, *m*, H-4), 1.93 (1H, *m*, H-5), 2.25 (1H, *m*, H-1), 2.51 (2H, *m*, H-2, 3), 2.84 (1H, *m*, H-8), 3.35 (1H, *t*, $J=8.0$ Hz, H-3′), 3.70 (1H, *dd*, $J=10.0$, 7.0 Hz, H-9), 4.12 (1H, *dd*, $J=10.0$, 4.0 Hz, H-9), 4.25 (1H, *d*, $J=8.0$ Hz, H-1′), 4.36 (1H, *dd*, $J=12.0$, 6.0 Hz, H-6′), 4.50 (1H, *dd*, $J=12.0$, 2.0 Hz, H-6′), 6.57 (1H, *d*, $J=16.0$ Hz, H-2″), 7.35–7.44 (3H, *m*, H-6″, 7″, 8″), 7.55–7.62 (2H, *m*, H-5″, 9″), 7.72 (1H, *d*, $J=16.0$ Hz, H-3″); ^{13}C NMR (CD_3OD): δ 64.9 (C-6′), 71.9 (C-3′), 74.9 (C-2′), 75.4 (C-5′), 77.8 (C-4′), 105.0 (C-1′), 118.8 (C-2″), 129.3×2 (C-5″, 9″), 130.0×2 (C-6″, 8″), 131.6 (C-7″), 135.8 (C-4″), 146.5 (C-3″), 168.5 (C-1″). See Table 3 for carbon signals due to cyclopentane monoterpene unit; HMBC: H-1→C-2, H-2→C-7, H-3→C-2, 4, H-4 (δ 1.85)→C-2, H_2-4→C-3, H-5 (δ 1.93)→C-3, 4, H_3-6→C-1, 2, 5, H_2-9→C-3, 10, H-9 (δ 3.70)→C-1′, H-1′→C-9, 5′, H_2-6′→C-5′, 1″, H-2″→C-1″, 4″, H-3″→C-1″, 4″; NOESY: H-1↔H-4 (δ 1.53), H-3↔H_3-6, H-8↔H-4 (δ 1.53), H-9 (δ 4.12)↔H-4 (δ 1.85); HR–SIMS found: 507.1866 $[M-H]^-$; $C_{25}H_{31}O_{11}$ requires 507.1867.

3.15. Methylation of **10**

A solution of **10** (9.0 mg) in MeOH was treated with CH_2N_2–Et_2O under ice-cooling. The reaction mixture was evaporated *in vacuo* and the residue was subjected to preparative HPLC (μBondasphere 5μC18–100 Å, MeCN–H_2O, 9:11) to give **10a** (2.7 mg). Colourless amorphous powder, $[\alpha]_D^{26}$ −46° (*c* 0.18, MeOH); UV λ_{max}^{MeOH} nm (log ε): 214 *sh* (3.93), 216 (3.99), 221 (3.92), 276 (4.22); IR ν_{max}^{KBr} cm^{-1}: 3419, 1732, 1710, 1637, 1521, 1083; ^{1}H NMR (CD_3OD): δ 1.00 (3H, *d*, $J=7.0$ Hz, H_3-6), 1.12 (1H, *m*, H-5), 1.51 (1H, *m*, H-4), 1.85 (1H, *m*, H-4), 1.91 (1H, *m*, H-5), 2.19 (1H, *m*, H-1), 2.45 (1H, *m*, H-2), 2.51 (1H, *m*, H-3), 2.74 (1H, *ddd*, $J=10.0$, 7.0, 4.0 Hz, H-8), 3.59 (3H, *s*, OMe), 3.63 (3H, *s*, OMe), 3.70 (1H, *dd*, $J=10.0$, 7.0 Hz, H-9), 4.04 (1H, *dd*, $J=10.0$, 4.0 Hz, H-9), 4.22 (1H, *d*, $J=8.0$ Hz, H-1′), 4.35 (1H, *dd*, $J=12.0$, 6.0 Hz, H-6′), 4.50 (1H, *dd*, $J=12.0$, 2.0 Hz, H-6′), 6.58 (1H, *d*, $J=16.0$ Hz, H-2″), 7.40–7.42 (3H, *m*, H-6″, 7″, 8″), 7.61–7.63 (2H, *m*, H-5″, 9″), 7.73 (1H, *d*, $J=16.0$ Hz, H-3″); ^{13}C NMR (CD_3OD): δ 64.9 (C-6′), 71.8 (C-3′), 74.9 (C-2′), 75.4 (C-5), 77.9 (C-4′), 104.9 (C-1′), 118.8 (C-2″), 129.3×2 (C-5″, 9″), 130.1×2 (C-6″, 8″), 131.6 (C-7″), 135.8 (C-4″), 146.5 (C-3″), 168.5 (C-1″). See Table 3 for carbon signals due to cyclopentane monoterpene unit; HMBC: H-1→C-5, H-2→C-4, 7, H-3→C-7, H-4 (δ 1.85)→C-2, 3, H-4→C-5, H-5 (δ 1.91)→C-1, H_3-6→C-1, H-8→C-10, H_2-9→C-8, 10, 1′,

H-1′→C-9, 2′, 3′, 5′, H-2′→C-1′, 4′, H-3′→C-2′, 4′, H-6′ (δ 4.35)→C-5′, 1″, H-2″→C-1″, 4″, H-3″→C-1″, 2″, OMe (δ 3.56)→C-7, OMe (δ 3.63)→C-10; NOESY: H-3↔H_3-6, H-3↔H-9 (δ 3.70), H-4 (δ 1.85)↔H-9 (δ 3.70); HR–SIMS Found: 537.2345 $[M+H]^+$; $C_{27}H_{37}O_{11}$ requires 537.2337.

3.16. Alkaline hydrolysis of **10** followed by preparation of the (*R*)-PGME amide **18**

A solution of **10** (10.4 mg) in 0.2 M NaOH (1 ml) was stirred for 2 h at room temperature, neutralized with Amberlite IR-120 (H^+ form), following which the reaction mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was concentrated to give *trans*-cinnamic acid (2.3 mg). The H_2O layer was concentrated to give a residue (7.1 mg). This being hydrolysed with β-glucosidase (2 mg), 37 °C, pH 5.0, then added to Amberlite IR-120 (H^+ form) and stirred for 3 h at room temperature. The solution was applied to a Sephadex LH-20 column, eluted with H_2O. Evaporation of the eluate gave **18** (4.0 mg). **18**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.23 (3H, *d*, *J* = 6.0 Hz, H_3-10), 1.29 (1H, *m*, H-7), 1.54 (1H, *m*, H-6), 1.97 (1H, *m*, H-6), 1.97 (1H, *m*, H-7), 2.06 (1H, *m*, H-8), 2.53 (1H, *t*, *J* = 10.0 Hz, H-9), 2.96 (1H, *m*, H-5), 3.13 (1H, *ddd*, *J* = 10.0, 6.0, 4.0 Hz, H-4), 4.40 (2H, *m*, H_2-3).

To a solution of **18** (4.0 mg) in DMF (1 ml) were added (*R*)-PGME·HCl (4.6 mg), PyBOP (11.8 mg), HBT (3.1 mg) and TEA (0.02 ml), and whole was stirred at room temperature for 2 h. The reaction mixture was poured into dil. HCl and extracted with $CHCl_3$. The $CHCl_3$ layer was dried and concentrated in vacuo. The residue was purified by preparative HPLC (H_2O–CH_3CN, 1:1), to give **19** (2.9 mg). This compound was identical with the PGME amide derived from frameroside (^{1}H NMR, SIMS).

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References

Andary, C., Wylde, R., Heitz, A., Rascol, J.P., Roussel, J.L., Laffite, C., 1985. Poliumoside, a caffeic glycoside ester from *Teucrium belion*. Phytochemistry 24, 362–364.

He, Z.-D., Ueda, S., Akaji, M., Fujita, T., Inoue, K., Yang, C.-R., 1994. Monoterpenoid and phenylethanoid glycosides from *Ligustrum pedunculare*. Phytochemistry 36, 709–716.

Imakura, Y., Kobayashi, S., Mima, A., 1985. Bitter phenyl propanoid glycosides from *Campsis chinensis*. Phytochemistry 24, 139–146.

Inoue, K., Tanahashi, T., Inouye, H., 1985. Two secoiridoid glucosides from *Jasminum mesnyi*. Phytochemistry 24, 1299–1303.

Kanao, M., Matsuda, H., 1978. Studies on the constituents of the leaves of *Lespedeza thunbergii* (DC.) Nakai. I. The structure of miyaginin. Yakugaku Zasshi 98, 366–368.

Karasawa, H., Kobayashi, H., Takizawa, N., Miyase, T., Fukushima, S., 1986. Studies on the constituents of Cistanchis herba. VIII. Isolation and structure of a new phenylethanoid glycoside, cistanoside G. Yakugaku Zasshi 106, 721–724.

Kikuchi, M., Yamauchi, Y., Yanase, C., Nagaoka, I., 1987. Structures of new secoiridoid glycosides from the leaves of *Syringa vulgaris* Linn. Yakugaku Zasshi 107, 245–248.

Kikuchi, M., Yamauchi, Y., 1984. Studies on the constituents of Ligustrum species. IX. On the components of the fruits of *Ligustrum obtusifolium* Sieb. *et* Zucc. (3). Yakugaku Zasshi 104, 390–393.

Kitamura, S., 1955. Flora of Afghanistan. In: The Committee of the Kyoto University Scientific Expedition to the Karakoram and Hindukush. Results of the Kyoto University Scientific Expedition to the Karakoram and Hindukush, Vol. II. Kyoto University, Kyoto, p. 302.

Kuwajima, H., Matsuuchi, K., Takaishi, K., Inoue, K., Fujita, T., Inouye, H., 1989. A secoiridoid glucoside from *Ligustrum japonicum*. Phytochemistry 28, 1409–1411.

Markham, K.R., Ternai, B., Stanley, R., Geiger, H., Mabry, T.J., 1978. Carbon-13 NMR studies of flavonoids-III. Naturally occurring flavonoid glycosides and their acylated derivatives. Tetrahedron 34, 1389–1397.

Ohtani, I., Kusumi, T., Kashman, Y., Kakisawa, H., 1991. High-field FT NMR application of Mosher's method. The absolute configurations of marine terpenoids. Journal of the American Chemical Society 113, 4092–4096.

Pagnoni, U.M., Pinetti, A., Trave, R., Garanti, L., 1976. Monoterpenes of *Teucrium marum*. Australian Journal of Chemistry 29, 1375–1381.

Tanahashi, T., Watanabe, H., Itoh, A., Nagakura, N., Inoue, K., Ono, M., Fujita, T., Morita, M., Chen, C.-C., 1992. A secoiridoid glucoside from *Fraxinus formosana*. Phytochemistry 31, 2143–2145.

Tanahashi, T., Watanabe, H., Itoh, A., Nagakura, N., Inoue, K., Ono, M., Fujita, T., Morita, M., Chen, C.-C., 1993. Five secoiridoid glucosides from *Fraxinus formosana*. Phytochemistry 32, 133–136.

Tanahashi, T., Sakai, T., Takanaka, Y., Nagakura, N., Chen, C.-C., 1999. Structure elucidation of two secoiridoid glucosides from *Jasminum officinale* L. var. *grandiflorum* (L.). Chemical and Pharmaceutical Bulletin 47, 1582–1586.

Takenaka, Y., Tanahashi, T., Shintaku, M., Sakai, T., Nagakura, N., Parida, X., 2000. Secoiridoid glucosides from *Fraxinus americana*. Phytochemistry 55, 275–284.

Trave, R., Marchesini, A., Garanti, L., 1968. Sintesi dei quattro stereoisomeri del C_1 (S)-nepetalattone. Gazzetta Chimica Italiana 98, 1132–1151.