Phytochemistry, Vol 24, No 1, pp 139–146, 1985
Printed in Great Britain

0031–9422/85 $3.00 + 0.00

BITTER PHENYL PROPANOID GLYCOSIDES FROM *CAMPSIS CHINENSIS*

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(*Received* 12 *June* 1984)

Key Word Index—*Campsis chinensis*; Bignoniaceae; bitter phenyl propanoid glycosides, *R,S*-β-methoxy-β-(3',4'-dihydroxyphenyl)-ethyl alcohol; *R,S*-β-hydroxy-β-(3',4'-dihydroxyphenyl)-ethyl alcohol, caffeic acid; acteoside; campneoside I; campneoside II.

Abstract—A new bitter phenyl propanoid glycoside, campneoside I, was isolated, together with acteoside and campneoside II, from the leaves of *Campsis chinensis*. The stereostructure of campneoside I was established as *R,S*-β-methoxy-β-(3',4'-dihydroxyphenyl)-ethyl-*O*-α-L-rhamnopyranosyl(1 → 3)-β-D-(4-*O*-caffeoyl)-glucopyranoside on the basis of the spectroscopic studies and chemical evidence.

INTRODUCTION

Previously, we reported the structures of six iridoid glucosides, campenoside (**1**) [1], 5-hydroxycampenoside (**2**) [1, 3], cachineside I (**3**) [3], tecomoside (**4**) [3], campsiside (**5**) [2] and 5-hydroxycampsiside (**6**) [2], which were isolated from a methanol extract of the leaves of *Campsis chinensis* Voss. Further studies on this plant led to the isolation of a new bitter phenyl propanoid glycoside named campneoside I (**8**) together with acteoside (**7**) [4] and campneoside II (**9**, β-hydroxyacteoside) [5]. This paper describes the isolation and stereostructural elucidation of campneoside I (**8**) and campneoside II (**9**, β-hydroxyacteoside).

RESULTS AND DISCUSSION

From a methanol extract of the fresh leaves of *C. chinensis*, a new amorphous bitter phenyl propanoid glycoside named campneoside I (**8**) was isolated together with acteoside (**7**) [4] and campneoside II (**9**, β-hydroxyacteoside) [5] by the procedure described in the Experimental.

Acteoside (**7**) was isolated as an amorphous powder, $[\alpha]_D$ −57.5°, which was converted into a nonaacetate (**10**), descaffeoyl 3',4'-dimethyl acteoside (**11**) and descaffeoyl octa-*O*-methyl acteoside (**12**) as described in the Experimental. These compounds (**7**, **10** and **11**) were confirmed to be identical with authentic samples by direct comparison of their IR, ^{1}H NMR and ^{13}C NMR spectra and TLC. Campneoside I (**8**) was isolated as an amorphous powder, $C_{30}H_{38}O_{16}$ (fast atom bombardment mass spectrum (FABMS): *m/z* 677 $[M+Na]^+$), $[\alpha]_D$ −68.2°. Compound **8** gave a grey-green colour with ethanolic ferric chloride, suggesting the presence of a phenolic hydroxy group in the molecule. The presence of glucose and rhamnose moieties in **8** was suggested by acidic hydrolysis with 2N sulphuric acid. Acetylation of **8** with acetic anhydride–pyridine gave a nonaacetate (**13**). Alkaline hydrolysis of **13** with methanolic sodium hydroxide followed by treatment with methanol gave a descaffeoyl campneoside I (**14**) and methyl caffeate (**14'**). Methylation of the phenolic hydroxy groups in **8** and **14** with dimethyl sulphate gave a tetramethyl derivative (**15**) and a dimethyl derivative (**16**), respectively. The mass spectra of **13**, **15** and **16** showed the characteristic fragment peaks due to the caffeoyl (*m/z* 191 and 247), terminal rhamnose (*m/z* 273) and β-methoxy-β-(3',4'-dihydroxyphenyl)-ethyl (*m/z* 195) moieties as shown in Scheme 1. These findings indicated the presence of the partial structures **A**, **B** and **C** in **8** (see formulae). The bonding positions of these moieties were suggested by the ^{1}H NMR (see Experimental) and ^{13}C NMR (see Tables 1, 2 and 3) spectral data of **8**. In the ^{1}H NMR spectrum of **8**, irradiation at the frequency of H-1 (δ4.35 and 4.41, total 1H) collapsed a double-doublet of the signal at δ3.44 into a doublet ($J_{2,3}$ = 8.0 Hz), which was assigned as H-2. The assignments of H-3 at δ3.74 and H-4 at δ4.94 were deduced by irradiation of H-2 and H-3. Consequently, the caffeoyl group was located at C-4 in the glucose moiety. Comparison of ^{13}C NMR spectral data (Table 2) of **8** with those of **14** revealed that the signals due to C-3, C-4 and C-5 of the glucose moiety were shifted by −2.1 to −2.2, +0.4 and −1.8 ppm, respectively. These shifts indicated that the caffeoyl moiety is combined with the hydroxy group at C-4 (esterification shift [6, 7]). Downfield shifts (+3.1 and +5.3 ppm) of the signals of C-3 in the glucose moiety of **8** and **14**, respectively, relative to that of C-3 in methyl-β-D-glucopyranoside (**17**) indicated that the rhamnose moiety is combined with the hydroxy group at C-3 (glycosidation shift [8–10]).

Descaffeoyl octa-*O*-methyl campneoside I (**8**), which was prepared by per-*O*-methylation (Hakomori's method [11]) of **14**, was methanolysed with 9% methanolic hydrochloric acid to give the methyl 2,3,4-tri-*O*-methyl-L-rhamnopyranoside and methyl 2,4,6-tri-*O*-methyl-D-glucopyranoside. The stereochemistry of the glycoside linkage at C-1 of the glucose moiety was easily assigned to be β by observation of the large coupling constant (*J* = 7.8 Hz) of the anomeric hydrogen signal in the ^{1}H NMR spectrum of **8** and by the ^{13}C–^{1}H coupling

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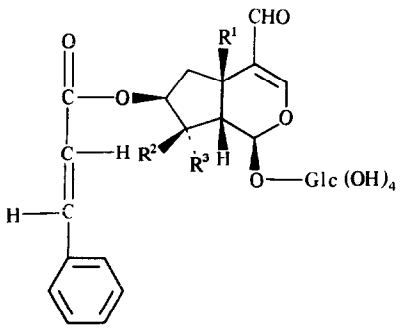
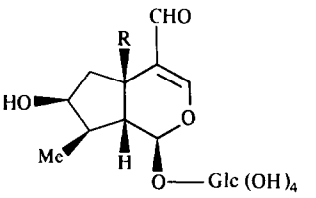
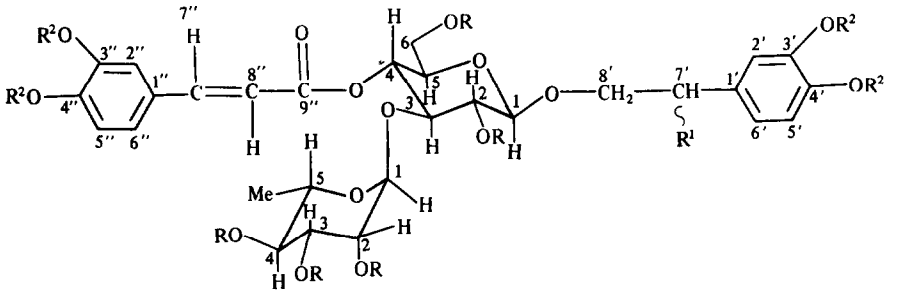


1 $R^1 = R^3 = H$, $R^2 = Me$
2 $R^1 = OH$, $R^2 = Me$, $R^3 = H$
5 $R^1 = H$, $R^2 = OH$, $R^3 = Me$
6 $R^1 = R^2 = OH$, $R^3 = Me$



3 R = H
4 R = OH

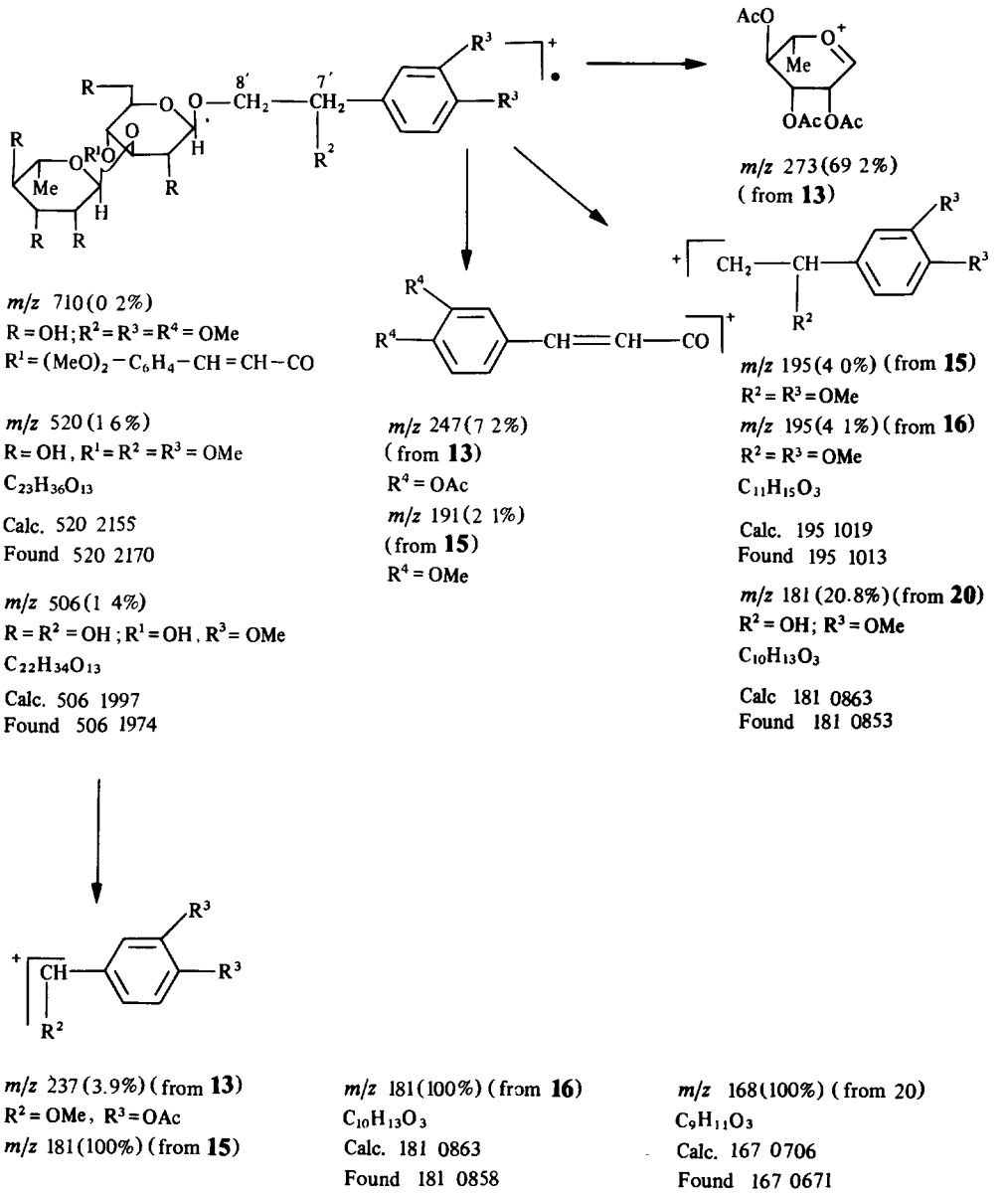


7 $R = R^1 = R^2 = H$
8 $R = R^2 = H$, $R^1 = OMe$
9 $R = R^2 = H$; $R^1 = OH$
10 $R = R^2 = Ac$, $R^1 = H$
13 $R = R^2 = Ac$, $R^1 = OMe$
15 $R = H$, $R^1 = OMe$, $R^2 = Me$

constant of 155 Hz of the anomeric carbon atom in the ^{13}C NMR spectrum of **8** [12]. Similarly, the stereochemistry of the glycoside linkage at C-1 of the rhamnose moiety was determined to be α from the ^{13}C–^{1}H coupling constant of 170 Hz of the anomeric carbon atom. Consequently, the structure of campneoside I was deduced to be **8**. The stereochemistry of C-7′ was determined as follows: although **8** gave one spot on TLC, the ^{1}H NMR and ^{13}C NMR spectral data of **8** and its derivatives (**13**, **16**) showed two kinds of chemical shifts for each proton, such as H-1 in the glucose moiety and MeO-7′ in the aglycone and each carbon such as C-1, C-2 and C-3 in the glucose moiety and C-1′, C-2′, C-6′, C-7′, MeO-7′ and C-8′ in the aglycone in the vicinity of the asymmetric C-7′. These findings suggested that campneoside I exists as epimers at C-7′ (*R,S*-β-OMe). The ratio of the epimers was deduced to be *ca* 5:7 from the intensities of the proton signals of the methoxy group at C-7′ and the carbon signals of C-1 in glucose [13].* For confirmation of the deduced structure (**8**), **14** was compared chemically with **11** prepared from **7**. Namely, **11** was methylated by Hakomori's method to give an octa-*O*-methyl derivative (**12**), which was oxidized by potassium persulphate–copper(II) sulphate, pentahydrate in methyl cyanide to give the ketone derivative (**19**). Reduction of **19** with lithium aluminium hydride gave a nona-*O*-methyl derivative (**18**), which was identified by its ^{1}H NMR, ^{13}C NMR and mass spectra and TLC with an authentic sample of **18** prepared from **14**. Consequently, the stereochemistry of campneoside I was established as *R,S*-β-methoxy-β-(3′,4′-dihydroxyphenyl)-ethyl-*O*-α-L-rhamno-pyranosyl(1 → 3)-β-D-(4-*O*-caffeoyl)-glucopyranoside.†

*This assignment was also suggested by comparison of molecular optical rotation differences ($\Delta[M]_D$) between **8** and **7** ($\Delta[M]_D = -87.4°$) and **18** and **12** ($\Delta[M]_D = +79.8°$ [13].

†This compound (**8**) was also isolated together with **7** and **9** from a water extract of the leaves of *C. chinensis*.

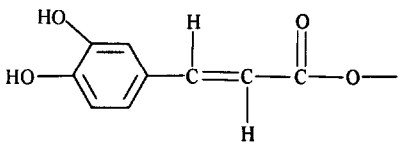


Scheme 1 Mass spectral fragmentation of **13**, **15**, **16** and **20**.

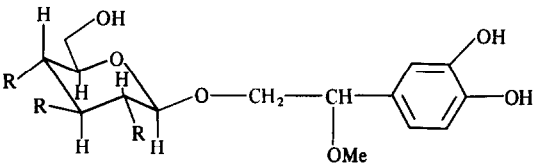
Campneoside II (**9**)‡ was isolated as an amorphous powder, $C_{29}H_{36}O_{16}$ (FABMS: *m/z* 663 $[M+Na]^+$), $[\alpha]_D$ −60.5°, which gave glucose and rhamnose on acidic hydrolysis. The ^1H NMR and ^{13}C NMR spectral data of **9** were very similar (except for the disappearance of the methoxy group) with those of **8**, as shown in the Experimental and Tables 1, 2 and 3. This means that **9** has the same moieties as **8**: a glucose, rhamnose and a caffeoyl group.

Furthermore, from the similarity of these spectral data, the linkage positions of the rhamnose and caffeoyl groups were concluded to be C-3 and C-4, respectively, in the glucose moiety of **9**. The stereochemistries of the glycoside linkage at C-1 of the glucose and rhamnose in **9** were deduced as β and α, respectively, from the coupling constants [^1H NMR: glucose (*d*, J = 7.8 Hz), rhamnose (*d*, J = 1.5 Hz); ^{13}C NMR: glucose (*d*, J = 159 Hz), rhamnose (*d*, J = 170 Hz)] of the anomeric hydrogen and carbon signals. Alkaline hydrolysis of **9** followed by methylation with diazomethane afforded **20**, mp 123–125°, whose mass spectrum showed the presence of the β-hydroxy-β-(3′,4′-dihydroxyphenyl)-ethyl moiety as an aglycone (see Scheme 1). This assignment was supported by the ^{13}C NMR spectral data of **9** and **20** as follows. The signals at C-7′ in the aglycones of **9** and **20** were 10.0 and 10.4 ppm higher field than those in **8** and **16**,

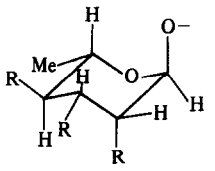
‡Nishibe *et al.* [13] have observed the single signals in the ^1H NMR and ^{13}C NMR spectra of β-hydroxyacteoside, and the ratio of the epimers of the hydroxy group at C-7′ was deduced to be *ca* 7:5 from the $\Delta[M]_D$ as shown in [5]. Hence, we use a different name (campneoside II) for the β-hydroxyacetoside



A Caffeoyl group



B R = OH or A or C



C Rhamnose moiety

respectively. The hydroxy group at C-7′ in the aglycone of **9** was deduced to be epimeric for similar reasons to those in the case of **8**. The epimers at C-7′ seem to exist in a ratio of *ca* 5:6 from the ^{13}C NMR and ^{1}H NMR spectral data of **9** and **20** as shown in the case of **8**. Consequently, the structure of campneoside II was assigned to be **9**. For confirmation of this assignment, campneoside II (**9**) was chemically correlated with authentic **18**. Compound **20**, which was prepared from **9**, was methylated by Hakomori's method to give a nona-*O*-methyl derivative (**18**), $[\alpha]_D$ −10.5°, which appeared identical with authentic **18** from its TLC, ^{1}H NMR and mass spectra.

Consequently, the stereochemistry of campneoside II was established as *R,S*-β-hydroxy-β-(3′,4′-dihydroxyphenyl)-ethyl-*O*-α-L-rhamnopyranosyl(1 → 3)-β-D-(4-*O*-caffeoyl)-glucopyranoside (**9**) or β-hydroxyacteoside [5].

EXPERIMENTAL

All mps are uncorr. NMR spectra were measured on a JEOL-JNN-PS-100 (^{1}H: 100 MHz) or an FX-200 (^{1}H: 200 MHz; ^{13}C: 50.10 MHz) spectrometer. Chemical shifts are given in δ values (ppm) with TMS as internal standard. TLC and prep. TLC were conducted on precoated silica gel 60 F_{254} and 60 PF_{254} plates (Merck), respectively, and the spots were located by UV illumination or by spraying with 1% $Ce(SO_4)_2$–10% H_2SO_4 soln followed by heating.

Plant materials. Leaves of *C. chinensis* were collected at the Botanic Garden of Tokushima University in September 1978. A voucher specimen has been deposited at the Botanic Garden of the Faculty of Pharmaceutical Sciences, Tokushima University

Isolation of phenyl propanoid glycosides from leaves of C. chinensis. The *n*-BuOH extract (95 g) of leaves of *C. chinensis*

Table 1. ^{13}C NMR peaks of aglycones of **8**, **9**, **11**, **14**, **16**, **18** and **20** (50.10 MHz, TMS as internal standard in CD_3OD)

	Aglycone								
	1′	2′	3′	4′	5′	6′	7′	8′	MeO-7′
8	130.6	115.0	146.4*	146.5*	116.3	119.9	83.5	75.0	56.7
	(131.1)	(115.2)				(120.0)	(84.4)	(75.5)	(56.8)
9	133.6	114.8	146.0*	146.3*	116.2	119.0	73.5	76.1	
	(133.9)					(119.1)	(74.2)	(76.7)	
11	132.9	113.1	148.8	150.1	114.1	122.1	36.5	71.6	
14	131.0	115.0	146.5*	146.5*	116.2	119.9	84.3	74.4	56.7
	(131.7)	(115.1)			(116.3)	(120.0)	(84.4)	(74.7)	(56.8)
16	132.4	111.9	150.6*	150.7*	113.1	121.0	83.6	74.3	56.6
	(132.7)	(112.1)					(84.4)	(74.8)	(56.9)†
18‡	131.3	109.7	148.9*	149.2*	111.1	119.5	84.3	73.5	56.8
	(131.7)	(110 0)				(119.8)	(84.4)	(74.4)	(56.9)†
20	135.2	111.9	150.1*	150.5*	113.3	120 1	73 4	76.0	†
	(135.4)	(112.0)					(74 0)	(76.5)	

*Interchangeable in the same horizontal column.

†Not assignable due to overlap with the signals of other methoxy groups.

‡In $CDCl_3$.

Table 2. ^{13}C NMR peaks of the sugar moieties of **7**, **8**, **9**, **11**, **14**, **16**, **17**, **18**, **20** and **21** (50.10 MHz, TMS as internal standard in CD_3OD)

	7	8	9	11	14	16	17	18*	20	21
Glucose moiety										
1	104.0	104.0 (104.5)	104 1 (104.6)	104.0	104.0 (104.5)	104.1 (104.6)	105.5	103.4 (104.0)	104.1 (104.7)	
2	75.8	76.0 (76.3)	76.1 (76.4)	75.3	75.4 (75.7)	75.5 (75.7)	74.9	79.8 (79.9)	75.3 (75.5)	
3	81.5	81.4 (81.5)	81.3 (81.4)	84.5	83.6	84.4	78.3	84.4	84.6	
4	70.5	70.5	70.5	70.1	70.1	70.2	71.4	74.7	70.3	
5	76.0	76.0	76.1	77.6	77.8	78.0	78.2	82.3	77.8	
6	62.3	62.3	62.3	62.6	62.7	62.8	62.2	71.2	62.7	
Rhamnose moiety										
1	102 8	102.9	102.9	102.5	102.6 (102.7)	102.7		97.5 (97.6)	102.7	102.4
2	72.1	72.3	72.4	72.1	72.3	72.3		77.9	72.3	72.6
3	72.0	72.1	72.1	72.1	72.2	72.3		78.4	72.3	72.0
4	73.7	73.8	73.8	73.8	74.0	74.0		81.0	74.0	73.7
5	70.2	70.4	70.4	69.9	70.0	70.1		68.1	70.1	69.4
Me-5	18.3	18.4	18.4	17.8	17.9	17.9		17.7	17.9	17.7

*In $CDCl_3$.

Table 3. ^{13}C NMR peaks of caffeoyl moieties of **7**, **8** and **9** (50 10 MHz, TMS as internal standard in CD_3OD)

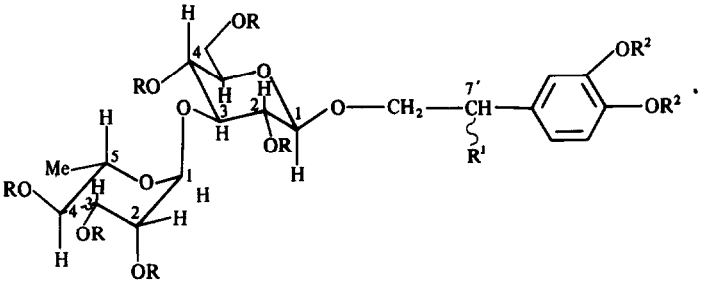
	Caffeoyl moiety								
	1″	2″	3″	4″	5″	6″	7″	8″	9″
7	127.5	114.5	146.6	149.5	116.2	123.0	147.9	115.2	168.1
8	127 6	114.1	146.8	149.7	116.5	123.2	148.0	115.3	168.3
9	127.7	114.7	146.8	149.8	116.5	123.2	148.0	115.3	168.3

described earlier [1, 3] was chromatographed over a charcoal (450 g)–celite 535 (450 g) column using MeOH (until fraction 60) and MeOH–Me_2CO (1:1, from fraction 61) as eluants, to yield 7 fractions: fraction I (fractions 5–7, 835 mg), fraction II (fractions 9–13, 2.5 g), fraction III (fractions 14–16, 1.3 g), fraction IV (fractions 18–28, 4.9 g), fraction V (fractions 29–42, 5.5 g), fraction VI (fractions 43–60, 2.5 g) and fraction VII (fractions 61–80, 7 0 g) (each fraction 500 ml). An aliquot (150 mg) of fraction III was chromatographed by prep. TLC ($CHCl_3$–MeOH–H_2O, 50:15:3, lower phase, triple development) to give an acteoside (**7**, 51 mg, R_f 0.14). An aliquot (80 mg) of fraction I was chromatographed by prep. TLC ($CHCl_3$–MeOH–H_2O, 7:3:0.5) to give a campneoside I (**8**, 35.0 mg, R_f 0.31) and campneoside II (**9**, 33.2 mg, R_f 0.20).

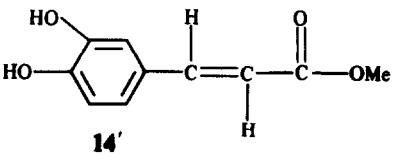
Acteoside (**7**). Amorphous yellow powder, $[\alpha]_D$ −57.5° (MeOH; *c* 0.53); IR ν_{max}^{KBr} cm^{-1}: 3400, 1690, 1630, 1600, 1520; ^1H NMR (CD_3OD): aglycone moiety: δ2.78 (2H, *t*-like, *J* = 7.3 Hz, H-7′), 3.71 (1H, *dt*, *J* = 7.3, 9.5 Hz, H-8′), 4.04 (1H, *dt*, *J* = 7.3, 9.5 Hz, H-8′), 6.54 (1H, *dd*, *J* = 2.0 Hz, H-6′), 6.66 (1H, *d*, *J* = 8.1 Hz, H-5′), 6.67 (1H, *d*, *J* = 2.0 Hz, H-2′); glucose moiety: δ4.40 (1H, *d*, *J* = 7.8 Hz, H-1), 3.84 (1H, *dd*, *J* = 9.0, 7.8 Hz, H-2), 3.80 (1H, *t*, *J* = 9.0 Hz, H-3), 4.88 (1H, *t*, *J* = 9.0 Hz, H-4); rhamnose moiety: δ1.09 (3H, *d*, *J* = 6.4 Hz, Me-5), 5.17 (1H, *d*, *J* = 1.7 Hz, H-1)]; and caffeoyl moiety: δ6.25 (1H, *d*, *J* = 16.0 Hz, H-8″), 7 57 (1H, *d*, *J* = 16.0 Hz, H-7″), 6.76 (1H, *d*, *J* = 8.0 Hz, H-5″), 6.93 (1H, *dd*, *J* = 8.0, 1.7 Hz, H-6″), 7.03 (1H, *d*, *J* = 1.7 Hz, H-2″). ^{13}C NMR (CD_3OD): aglycone moiety: δ131.3 (*s*, C-1′), 116.4 (*d*, C-2′), 144.4 (*s*, C-3′), 145.9 (*s*, C-4′), 117.0 (*d*, C-5′), 121.1 (*d*, C-6′), 71.9 (*d*, C-7′), 36.4 (*t*, C-8′); glucose moiety: see Table 3; rhamnose moiety: see Table 2; and caffeoyl moiety: see Table 3.

Campneoside I (**8**). Amorphous powder, $[\alpha]_D$ −68.2° (MeOH; *c* 0.43); IR ν_{max}^{KBr} cm^{-1}: 3400, 1700, 1630, 1610; ^1H NMR (CD_3OD): glucose moiety: δ4.35 and 4.41 (total 1H, each *d*, *J* = 7.8 Hz, H-1), 3.44 (1H, *dd*, *J* = 7.8, 8.0 Hz, H-2), 3.73 (1H, *t*, *J* = 8.0 Hz, H-3); rhamnose moiety: δ1.09 (3H, *d*, *J* = 6.1 Hz, Me-5), 5.19 (1H, *d*, *J* = 1.5 Hz, H-1); and caffeoyl group: δ6.26 (1H, *d*, *J* = 16.1 Hz, H-8″), 7.58 (1H, *d*, *J* = 16.1 Hz, H-7″), 6.76 (1H, *d*, *J* = 8.1 Hz, H-5″), 6.95 (1H, *dd*, *J* = 8.1, 1.7 Hz, H-6″), 7.04 (1H, *d*, *J* = 1.7 Hz, H-2″). ^{13}C NMR (CD_3OD): see Tables 1, 2 and 3; FABMS *m/z* (rel. int.): 677 $[C_{30}H_{38}O_{16}$ (M) + Na$]^+$ (88.7).

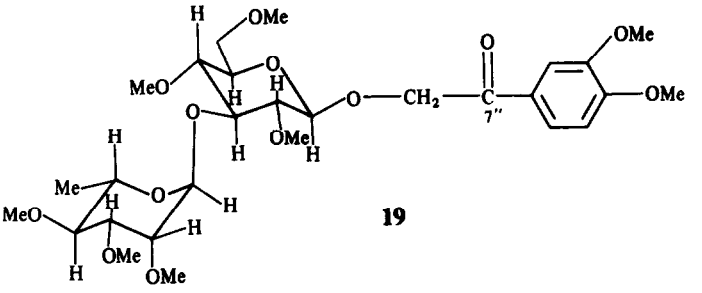
Campneoside II (**9**). Amorphous powder, $[\alpha]_D^{20}$ −45.8° (MeOH; *c* 0.45); IR ν_{max}^{KBr} cm^{-1}: 3400, 1700, 1630, 1600; ^1H NMR (CD_3OD): glucose moiety: δ4.41 and 4.42 (total 1H, each *d*, *J* = 7.8 Hz, H-1), 3.47 (1H, *dd*, *J* = 7.8, 8.0 Hz, H-2), 3.86 (1H, *dd*, *J* = 6.1 Hz, H-3), 4.94 (1H, *t*, *J* = 9.0 Hz, H-4); rhamnose moiety: δ1.10 (3H, *d*, *J* = 6.1 Hz, Me-5), 5.20 (1H, *d*, *J* = 1.5 Hz, H-1); and caffeoyl group: δ6.26 (1H, *d*, *J* = 15.9 Hz, H-8″), 7.59 (1H, *d*, *J* = 15.9 Hz, H-7″), 6.78 (1H, *d*, *J* = 8.1 Hz, H-5″), 6.95 (1H, *dd*, *J* = 8.1, 1.96 Hz, H-6″), 7.05 (1H, *d*, *J* = 1.96 Hz, H-2″). ^{13}C NMR



11 R = R¹ = H, R² = Me
12 R = R² = Me; R¹ = H
14 R = R² = H, R¹ = OMe
16 R = H, R² = Me, R¹ = OMe
18 R = R² = Me; R¹ = OMe
20 R = H; R² = Me, R¹ = OH



14'



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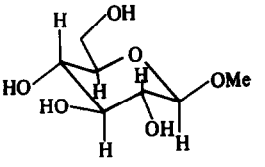

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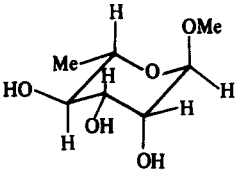

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(CD₃OD): see Tables 1, 2 and 3; FABMS *m/z* (rel. int.): 663 $[C_{29}H_{36}O_{16}\ (M)+Na]^+$ (100).

Acetylation of compound **7**. Compound **7** (200 mg) was acetylated with Ac_2O (5 ml) and pyridine (4 ml) to give a nonaacetate (**10**, 175 mg), which was identified with authentic **10** by direct comparison (IR, ^1H NMR and ^{13}C NMR, TLC). Amorphous powder, $[\alpha]_D^{19}$ −40.5° ($CHCl_3$; *c* 0.37); IR ν_{max}^{KBr} cm^{-1}: no OH, 1750, 1640, 1500; ^1H NMR ($CDCl_3$): glucose moiety: δ4.39 (1H, *d*, *J* = 8.0 Hz, H-1), 5.13 (1H, *t*, *J* = 8.0 Hz, H-2), 3.87 (1H, *t*, *J* = 8.0 Hz, H-3), 5.24 (1H, *t*, *J* = 8.0 Hz, H-4); rhamnose moiety: δ1.04 (3H, *d*, *J* = 6.3 Hz, Me-5), 4.84 (1H, *d*, *J* = 2.0 Hz, H-1); caffeoyl group: δ6.35 (1H, *d*, *J* = 16.0 Hz, H-8″), 7.64 (1H, *d*, *J* = 16.0 Hz, H-7″), 7.22 (1H, *d*, *J* = 8.2 Hz, H-5″), 7.40 (1H, *dd*, *J* = 8.2, 2.0 Hz, H-6″), 7.36 (1H, *d*, *J* = 2.0 Hz, H-2″); aglycone moiety: δ2.97 (2H, *t*, *J* = 7.0 Hz, H-7′), 7.03–7.04 (3H, aromatic H); and others 1.87–2.10 (15H, 5 × OAc), 2.29 and 2.30 (6H, each *s*, 4 × OAc)]. ^{13}C NMR ($CDCl_3$): aglycone moiety: δ137.5 (*s*, C-1′), 122.8 (*d*, C-2′), 141.9 (*s*, C-3′), 140.6 (*s*, C-4′), (*d*, C-5′), 126.4 (*d*, C-6′), 35.4 (*t*, C-7′), 69.7 (*t*, C-8′); glucose moiety: δ104.0 (*d*, C-1), 75.8 (*d*, C-2), 81.5 (*d*, C-3), 70.5 (*d*, C-4), 76.0 (*d*, C-5), 62.3 (*t*, C-6); rhamnose moiety: δ102.8 (*d*, C-1), 72.1 (*d*, C-2), 72.0 (*d*, C-3), 73.7 (*d*, C-4), 70.2 (*d*, C-5), 18.3 (*q*, C-6); and caffeoyl group: δ132.8 (*s*, C-1″), 118.1 (*d*, C-2″), 142.6 (*s*, C-3″), 143.9 (*s*, C-4″), 124.1 (*d*, C-5″), 127.2 (*d*, C-6″), 164.9 (*s*, C-9″), 123.1 (*d*, C-8″), 144.4 (*d*, C-7″).

Treatment of compound **7** *with* CH_2N_2. A solution of **7** (135 mg) in MeOH (15 ml) was treated with excess CH_2N_2 and left to stand overnight in a refrigerator. The mixture was concd to dryness under red. pres. and the residue was purified by prep. TLC ($CHCl_3$–MeOH–H_2O, 50:15:3, lower phase) to give **11** (55 mg, R_f 0.33), which was recrystallized from MeOH, mp 113–115°, $[\alpha]_D^{20}$ −45.8° (MeOH; *c* 0.53); MS *m/z* (rel. int.): 490 $[M]^+$ (9.5), 182 (23.2), 165 (100), 164 (96.2); (Found: 490.2071.

Calc. for $C_{22}H_{34}O_{12}$: 490.2051; Found: 182.0962. Calc. for $C_{10}H_{14}O_3$: 182.0492; Found: 165.0923. Calc. for $C_{10}H_{13}O_{12}$: 165.0915, Found: 164.0892. Calc. for $C_{10}H_{12}O_2$: 164.0837.) ^{1}H NMR (Me_2CO-d_6): δ1.25 (3H, *d*, *J* = 6.4 Hz, rhamnose Me-5), 3.77, 3.88 (3H, each *s*, 2 × OMe), 4.29 (1H, *dd*, *J* = 7.9 Hz, glucose H-1), 5.14 (1H, *d*, *J* = 1.7 Hz, rhamnose H-1), 6.75 (1H, *dd*, *J* = 8.1, 1.7 Hz, H-6′), 6.81 (1H, *d*, *J* = 8.1 Hz, H-5′), 6.85 (1H, *d*, *J* = 1.7 Hz, H-2′), 2.86 (2H, *t*, *J* = 7.3 Hz, H-7′), 3.68 (1H, *dt*, *J* = 9.5, 7.3 Hz, H-8′). ^{13}C NMR (CD_3OD): see Tables 1, 2 and 3.

Per-O-methylation of compound **11** *by Hakomori's method.* NaH (1 g, defatted with dry *n*-hexane) was warmed with DMSO (8 ml) at 65° for 2 hr with stirring under N_2 to give the DMSO carbanion. An aliquot (3 ml) of the DMSO carbanion was added to a soln of **11** (70 mg) in DMSO (3 ml), and the mixture was stirred at room temp. for 30 min under N_2, treated with MeI (3 ml) and stirred for a further 2.5 hr in the dark. The reaction mixture was poured into ice H_2O (50 ml) and extracted 3 × with Et_2O (each 50 ml). The combined Et_2O extract was washed with H_2O, 3% $Na_2S_2O_3$ soln and then H_2O, dried and concd under red. pres. The residue was purified by prep. TLC ($CHCl_3$–Me_2CO, 6·1; R_f 0.48) to give a descaffeoyl octa-*O*-methyl acteoside (**12**, 40 mg) as a colourless syrup. $[\alpha]_D^{20}$ −25.9° ($CHCl_3$; *c* 0.93); MS *m/z* (rel. int.): 574 $[M]^+$ (3.9), 189 (51.5), 165 (95 4), 164 (100); (Found: 574.3024. Calc. for $C_{28}H_{46}O_{12}$: 574.2989; Found: 189.1098. Calc. for $C_9H_{17}O_4$: 189.1120; Found: 165.0902 Calc. for $C_{10}H_{13}O_2$. 165.0913; Found: 164.0840. Calc for $C_{10}H_{12}O_2$: 164.0838) ^{1}H NMR ($CDCl_3$): δ1.28 (3H, each *s*, 6 × OMe), 3.47 (6H, *s*, 2 × OMe), 4.25 (1H, *d*, *J* = 7.8 Hz, glucose H-1), 5.31 (1H, *d*, *J* = 1.5 Hz, rhamnose H-1), 2.88 (2H, *t*, *J* = 6.8 Hz, H-7′), 4.12 (1H, *dt*, *J* = 6.8, 9.5 Hz, H-8′), 6.75–6.82 (3H, aromatic H) ^{13}C NMR ($CDCl_3$): aglycone moiety: δ131.2 (*s*, C-1′), 111.3 (*d*, C-2′), 147.6 (*s*, C-3′), 148.8 (*s*, C-4′), 112.4 (*d*, C-5′), 120.8 (*d*, C-6′), 70.8 (*t*, C-8′), 35.7 (*t*, C-7′); glucose moiety: δ103.4 (*d*, C-1), 79.7 (*d*, C-2), 84.5 (*d*, C-3), 74.7 (*d*, C-4), 82.2 (*d*, C-5), 71.1 (*t*, C-6); rhamnose moiety: δ97.5 (*d*, C-1), 77.8 (*d*, C-2), 78.3 (*d*, C-3), 80.9 (*d*, C-4), 68.0 (*d*, C-5), 17.6 (*q*, Me-5).

Acid hydrolysis of compound **8**. A soln of **8** (20 mg) in 2 N H_2SO_4 (3 ml) was refluxed for 2 hr Then H_2O was added to the soln, the mixture was washed with $CHCl_3$ and the aq. layer was neutralized with $BaCO_3$. The ppt. was filtered off, the filtrate was evapd *in vacuo*, and the residue was identified with authentic D-glucose and L-rhamnose by prep. PC and TLC.

Acetylation of compound **8**. Compound **8** (20 mg) was acetylated with Ac_2O (0 8 ml) and pyridine (0.8 ml) to give a nonaacetyl campneoside I (**13**, 30 mg) as an amorphous powder $[\alpha]_D^{19}$ −63.6° ($CHCl_3$; *c* 0 44); IR ν_{max}^{KBr} cm^{-1} 2935, 1750, 1640, 1500; ^{1}H NMR ($CDCl_3$)· δ1.04 and 1.05 (total 3H, each *d*, *J* = 6.1 Hz, rhamnose Me-5), 1.87–2.17 (5 × OAc), 2.28–2.30 (4 × OAc), 3 29 and 3.30 (total 3H, each *s* OMe-7′), 3.86 (1H, *t*, *J* = 8.0 Hz, glucose H-3), 4 39 and 4.56 (total 1H, each *d*, *J* = 8.0 Hz, glucose H-1), 5.10 (1H, *t*, *J* = 8.0 Hz, glucose H-2), 4.83 (1H, *d*, *J* = 2.0 Hz, rhamnose H-1), 6.35 (1H, *d*, *J* = 16.1 Hz, H-8″), 7.15–7 41 (6H, aromatic H), 7.66 (1H, *d*, *J* = 16.1 Hz, H-7″).

Alkaline hydrolysis of compound **13** A soln of **13** (204 mg) in MeOH (3 ml) and 1 N NaOH (3 ml) was stirred at 50° for 10 min. The reaction mixture was neutralized with 5% HCl and applied to a charcoal (4 g)–celite (4 g) column. The column was washed with H_2O (100 ml), and the product was eluted with MeOH (100 ml) and Me_2CO (100 ml). Concn of the MeOH eluate gave a descaffeoyl campneoside I (**14**, 70 mg) as an amorphous powder, and concn of the Me_2CO eluate gave a methyl caffeate (**14′**, 28 mg). **14**, $[\alpha]_D^{19}$ −62 0° (MeOH; *c* 0.29); IR ν_{max}^{KBr} cm^{-1}: 3400, 2938, 1617, 1525, 1450; ^{1}H NMR (CD_3OD): δ1.24 (3H, *d*, *J* = 6.1 Hz, rhamnose Me-5), 3.23 and 3.24 (total 3H, each *s*, OMe-7′), 4.31 and 4.39 (total 1H, each *d*, *J* = 7.8 Hz, glucose H-1), 4.37 (1H, *dd*, *J* = 9.0, 2.0 Hz, H-7′), 5 15 and 5.17 (total 1H, each *d*, *J* = 1.7 Hz, rhamnose H-1), 6.62 and 6.63 (total 1H, each *dd*, *J* = 8.3, 1.7 Hz, H-6′), 6.72 and 6.74 (total 1H, each *d*, *J* = 1.7 Hz, H-2′), 6.74 (1H, *d*, *J* = 8.3 Hz, H-5′). ^{13}C NMR (CD_3OD): see Tables 1, 2 and 3. **14′**, IR ν_{max}^{KBr} cm^{-1}: 3400, 2940, 1620, 1530, 1450, 1350; MS· *m/z* (rel. int.): 194 $[M]^+$ (24.4), 163 $[M-OMe]^+$ (26.6), 135 $[M-COOMe]^+$ (7.2).

Conversion of compound **8** *to compound* **15**. A soln of **8** (22 mg) in dry Me_2CO (10 ml) was refluxed wth Me_2SO_4 (0.2 ml) and dry K_2CO_3 (300 mg) for 1.5 hr. K_2CO_3 was removed by filtration and washed with Me_2CO (20 ml). The combined Me_2CO soln was concd and the residue was purified by prep. TLC ($CHCl_3$–MeOH, 6:1; R_f 0.71) to give **15** (15 mg) as an amorphous powder. $[\alpha]_D^{20}$ −26.0° (MeOH; *c* 0.53); IR ν_{max}^{KBr} cm^{-1}: 3450, 2940, 2850, 1710, 1630, 1600, 1520; ^{1}H NMR (Me_2CO-d_6): δ1.18 (3H, *d*, *J* = 6.1 Hz, rhamnose Me-5), 4.56 (1H, *d*, *J* = 7 6 Hz, glucose H-1), 4.75 (1H, *dd*, *J* = 9.5, 3.0 Hz, H-8′), 5.13 (1H, *t*, *J* = 9.0 Hz, glucose H-4), 5.24 (1H, *d*, *J* = 1.5 Hz, rhamnose H-1), 6.44 (1H, *d*, *J* = 15.9 Hz, H-8″), 6.95–7.35 (6H, aromatic H), 7.67 (1H, *d*, *J* = 15.9 Hz, H-7″). ^{13}C NMR (CD_3OD): aglycone moiety: δ131.1 (*d*, C-1′), 110.9 (*d*, C-2′), 150.1 (*s*, C-3′), 150.1 (*s*, C-4′), 112.0 (*d*, C-5′), 120.5 (*d*, C-6′), 83.8 (*d*, C-7′), 74.4 or 75.5 (*t*, C-8′), 56.8 (*s*, OMe); glucose moiety: δ130.9 (*d*, C-1), 75.5 (*d*, C-2), 80.6 (*d*, C-3), 69.9 (*d*, C-4), 78.5 (*d*, C-5), 61.9 (*t*, C-6); rhamnose moiety: δ102.2 (*d*, C-1), 71.6 (*d*, C-2), 71.6 (*d*, C-3), 73.3 (*d*, C-4), 70.1 (*d*, C-5), 18.1 (*q*, Me-5); caffeoyl moiety: δ128.0 (*s*, C-1″), 112.3 (*d*, C-2″), 152.3 (*s*, C-3″), 152.3 (*s*, C-4″), 123.8 (*d*, C-5″), 126.2 (*d*, C-6″), 147.1 (*d*, C-7″), 115.4 (*d*, C-8″), 167 7 (*s*, C-9″)]; MS: see Scheme 1

Conversion of compound **14** *to compound* **16**. A mixture of **14** (18 mg), K_2CO_3 (750 mg), Me_2SO_4 (0.1 ml) and dry Me_2CO (2.5 ml) was refluxed for 1 hr. The crude product was purified by prep. TLC ($CHCl_3$–MeOH, 5:1; R_f 0.31) to give **16** (8.2 mg) as an amorphous powder. $[\alpha]_D^{20}$ −12.0° (MeOH; *c* 0.25); IR ν_{max}^{KBr} cm^{-1}: 3400, 2930, 2850, 1610, 1590, 1520; ^{1}H NMR (CD_3OD): δ1.20 (3H, *d*, *J* = 5.6 Hz, rhamnose Me-5), 3.22 and 3.23 (total 3H, each *s*, OMe-7′), 3.80 and 3.81 (3H, each *s*, OMe-3′ and OMe-4′), 4.38 (1H, *dd*, *J* = 8.0, 4.0 Hz, H-7′), 4.37 and 4.42 (total 1H, each *d*, *J* = 7.6 Hz, glucose H-1), 5.18 (1H, *s*, rhamnose H-1), 6.89–6.92 (3H, aromatic H). ^{13}C NMR (CD_3OD): see Tables 1, 2 and 3; MS: see Scheme 1.

Per-O-methylation of compound **14**. A mixture of **14** (62 mg), DMSO (3 ml), DMSO carbanion (3 ml) and MeI (3 ml) was stirred for 2.5 hr in the dark The crude product was isolated in the usual manner as described for **12** and purified by prep. TLC ($CHCl_3$–Me_2CO, 6:1; R_f 0.39) to give **18** (29 mg) as a colourless syrup. $[\alpha]_D^{20}$ −11.4° ($CHCl_3$; *c* 0.53); IR ν_{max}^{KBr} cm^{-1}· 2980, 2930, 2830, 1610, 1600, 1510, 1460, 1420, 1370; ^{1}H NMR ($CDCl_3$): δ1.28 and 1.29 (total 3H, each *d*, *J* = 6 3 Hz, rhamnose Me-5), 3.38–3.58 (18H, 6 × OMe), 3.27 and 3 28 (total 3H, each *s*, OMe-7′), 3.87 and 3.88 (3H, each *s*, 2 × OMe), 4.24 and 4.35 (total 1H, each *d*, *J* = 7.8 Hz, glucose H-1), 4.10 (1H, *dd*, *J* = 7 3, 10.5 Hz, H-8′), 4.34 (1H, *m*, H-8′), 6.85–6.86 (3H, aromatic H) ^{13}C NMR ($CDCl_3$): see Tables 1 and 2; MS *m/z* (rel. int)· 604 $[M]^+$ (1 0), 195 (12.8), 189 (12.7), 181 (100). (Found· 604.3446. Calc. for $C_{29}H_{48}O_{13}$: 604.3456; Found· 195.1005 Calc. for $C_{11}H_{15}O_3$: 195.1018; Found: 189.1110. Calc. for $C_9H_{17}O_4$. 189 1125, Found: 181.0869. Calc. for $C_{10}H_{13}O_3$. 181.0864.)

Methanolysis of compound **18** *with* 9% *methanolic* HCl A soln of **18** (3 mg) in 9% methanolic HCl (1 ml) was refluxed for 2 hr The reaction mixture was neutralized with Ag_2CO_3 and filtered. The filtrate was concd to dryness *in vacuo*, and the residue was subjected to GC on a glass column (3 mm × 2 m) packed with 15% 1,4-butanediol succinate on Chromosorb W(AW) (60–80 mesh; column temp., 185°; inject. temp., 190°; carrier gas, N_2 at 210 ml/min). R_t in min. methyl 2,3,4-tri-*O*-methyl-(α,β)-L-rhamnopyranoside (**22**): 3.9, 5.8; methyl 2,4,6-tri-*O*-methyl-(α,β)-

D-glucopyranoside (**23**): 25.9, 37.2. TLC solvents (R_f): Et_2O, **22** (0.49), **23** (0.25); C_6H_6–Me_2CO (4:1), **22** (0.68), **23** (0.13, 0.09); C_6H_6–MeOH (10:1), **22** (0.58), **23** (0.34, 0.29).

Conversion of compound **12** *to compound* **18**. A soln of **12** (70 mg) in MeCN (2 ml) was added dropwise with stirring to a soln of $K_2S_2O_8$ (54 mg) and $CuSO_4 \cdot 5H_2O$ (5 mg) in H_2O (1 ml) at room temp. The mixture was stirred for 3 hr at 65–70° and then concentrated under red. pres. to remove MeCN, and H_2O was added to the residue. The reaction soln was extracted 3 × with $CHCl_3$ (30 ml each). The combined $CHCl_3$ extract was washed with H_2O, dried and concd. The residue was purified by prep. TLC ($CHCl_3$–Me_2CO, 10:1; R_f 0.29) to give **19** (11 mg). $LiAlH_4$ (15 mg) was added to the soln of **19** (11 mg) in dry THF (2 ml) and the mixture was refluxed for 1 hr. After usual work-up, the reduction product was methylated with DMSO carbanion (0.5 ml) and MeI (0.5 ml) as described for **12** to give the methylated product (**18**, 4.5 mg), which was identified with authentic **18** by TLC and ^1H NMR and ^{13}C NMR ($CDCl_3$) spectral data.

Acid hydrolysis of compound **9**. A mixture of **9** (20 mg) and 2 N H_2SO_4 (3 ml) was heated on a H_2O bath for 2 hr. The products (glucose and rhamnose) were isolated in the usual manner, as described for **8**, and identified with authentic samples of D-glucose and L-rhamnose by prep. PC and TLC as for **8**.

Conversion of compound **9** *to compound* **20**. A mixture of **9** (30 mg), 1 N NaOH (1 ml) and MeOH (1 ml) was stirred at 50° for 30 min. The reaction mixture was treated in the usual manner as described for **14**. The product was treated with excess CH_2N_2 in MeOH. The resulting residue was purified with prep. TLC ($CHCl_3$–MeOH–H_2O, 50:15:3, lower phase; R_f 0.21) to give **20** (8 mg) as colourless needles from MeOH, mp 123–126°, $[\alpha]_D^{20}$ −14.5° (MeOH, *c* 0.20). ^1H NMR ($CDCl_3$): δ1.25 (3H, *d*, J = 6.5 Hz, rhamnose Me-5), 3.81 and 3.84 (3H, each *s*, 2 × OMe), 4.32 and 4.33 (total 1H, each *d*, J = 7.8, 7.6 Hz, glucose H-1), 5.16 (1H, *s*, rhamnose H-1), 6.90–7.00 (3H, aromatic H). ^{13}C NMR ($CDCl_3$): see Tables 1 and 2; MS: see Scheme 1.

Per-O-methylation of compound **20**. Compound **20** (20 mg) was methylated with DMSO carbanion (2 ml) and MeI (2 ml) in DMSO (2 ml) as described for **12**. After usual work-up, the product was purified by prep. TLC ($CHCl_3$–Me_2CO, 6:1; R_f 0.39) to give a methylated product (**18**, 12 mg) as a colourless syrup, which was identified with an authentic sample of **18** by TLC and its mass and ^1H NMR ($CDCl_3$) spectral data.

Acknowledgements—We thank Professor T. Fugita and Assistant Professor Y. Takeda, Tokushima University, for a generous gift of acteoside, and Assistant Professor M. Kihara, Tokushima University, for helpful discussions.

REFERENCES

1. Kobayashi, S., Imakura, Y., Yamahara, Y and Shingu, T. (1980) *Heterocycles* **19**, 1475.
2. Imakura, Y., Kobayashi, S., Yamahara, Y., Kihara, M., Tagawa, M., Wakamatsu, K. and Murai, F. *Chem. Pharm. Bull. (Tokyo)* (submitted).
3. Imakura, Y., Kobayashi, S., Kida, K. and Kido, M. (1984) *Phytochemistry* **23**, 2263.
4. Birkofer, L., Kaizer, C. and Thomas, L. (1968) *Z. Naturforsch.* 1051.
5. Kitagawa, S., Tsukamoto, H., Hisada, S. and Nishibe, S. (1984) *Chem. Pharm. Bull. (Tokyo)* **32**, 1209.
6. Terui, Y., Tori, K. and Tsuji, N. (1976) *Tetrahedron Letters* 621.
7. Vingnon, M. R. and Vottero, P. J. A. (1976) *Tetrahedron Letters* 2445.
8. Tori, K., Seo, S., Yoshimura, Y., Nakamura, M., Tomita, Y. and Ishii, H. (1976) *Tetrahedron Letters* 4167.
9. Kasai, R., Suzuo, M., Asakawa, J. and Tanaka, O. (1977) *Tetrahedron Letters* 175.
10. Tori, K., Seo, S., Yoshimura, Y., Arita, H. and Tomita, Y. (1977) *Tetrahedron Letters* 179.
11. Hakomori, S. (1964) *J Biochem.* **55**, 205.
12. Bock, K., Lundt, I. and Pedersen, C. (1973) *Tetrahedron Letters* 1037.
13. Nishibe, S., Okabe, K., Tsukamoto, H., Sakushima, A., Hisada, S. Baba, H. and Akisada, T. (1982) *Chem. Pharm. Bull. (Tokyo)* **30**, 4548.