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Carbohydrate Research 265 (1994) 227–236

CARBOHYDRATE RESEARCH

Facile synthesis of the sugar cores from phenylpropanoid glycosides ☆

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Received 10 March 1994; accepted 30 May 1994

Abstract

Allyl 2-*O*-benzoyl-4, 6-*O*-benzylidene-α-D-glucopyranoside (**3**), obtained by selective benzoylation of allyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2**) with benzoyl chloride–imidazole in anhydrous chloroform, reacted with 2, 3, 4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide to give a disaccharide derivative (**4**), and an important intermediate (**5**) was obtained by cleavage of its acetal. Treatment of **5** with a series of glycopyranosyl bromides, protected by acetyl or benzoyl groups in benzene–nitromethane in the presence of $Hg(CN)_2$ as a catalyst afforded four trisaccharides (**6–9**). The disaccharide (**5**) and trisaccharides (**6–9**) constitute the sugar cores of phenylpropanoid glycosides. A new glycosyl anomeric leaving group, trichloroacetoxy, was employed to prepare the disaccharide (**4**) and trisaccharides residue (**8**) efficiently and with high stereoselectivity.

Keywords: Synthesis; Sugar cores; Phenylpropanoid glycosides

1. Introduction

Phenylpropanoid glycosides are widely distributed in medicinal plants [1]. Most of them possesses potent biological activities such as antiviral, antitumor, antifungal, and immunomodulatory agents [2–5]. More than eighty phenylpropanoid glycosides have thus far been isolated and identified with modern spectral techniques and chemical conversions, but their syntheses have not yet been reported. Here, we report the total synthesis of several trisaccharides, the carbohydrate moieties of phenylpropanoid glycosides, by using the Koenigs–Knorr and trichloroacetate methods.

☆ Part XVII of the series, Studies on Carbohydrates. For Part XVI, see *Carbohydr. Lett.*, (1994) submitted.

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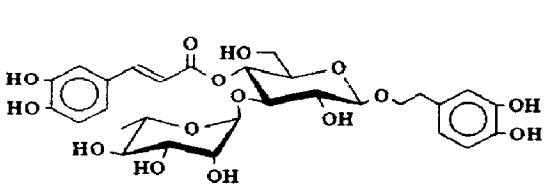
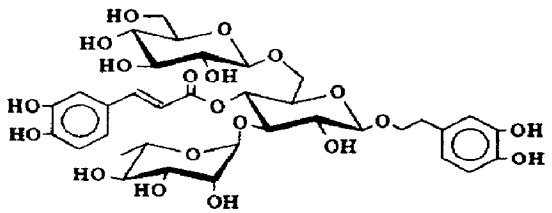
SSDI 0008-6215(94)00226-6



Verbascoside



Echinacoside

2. Results and discussion

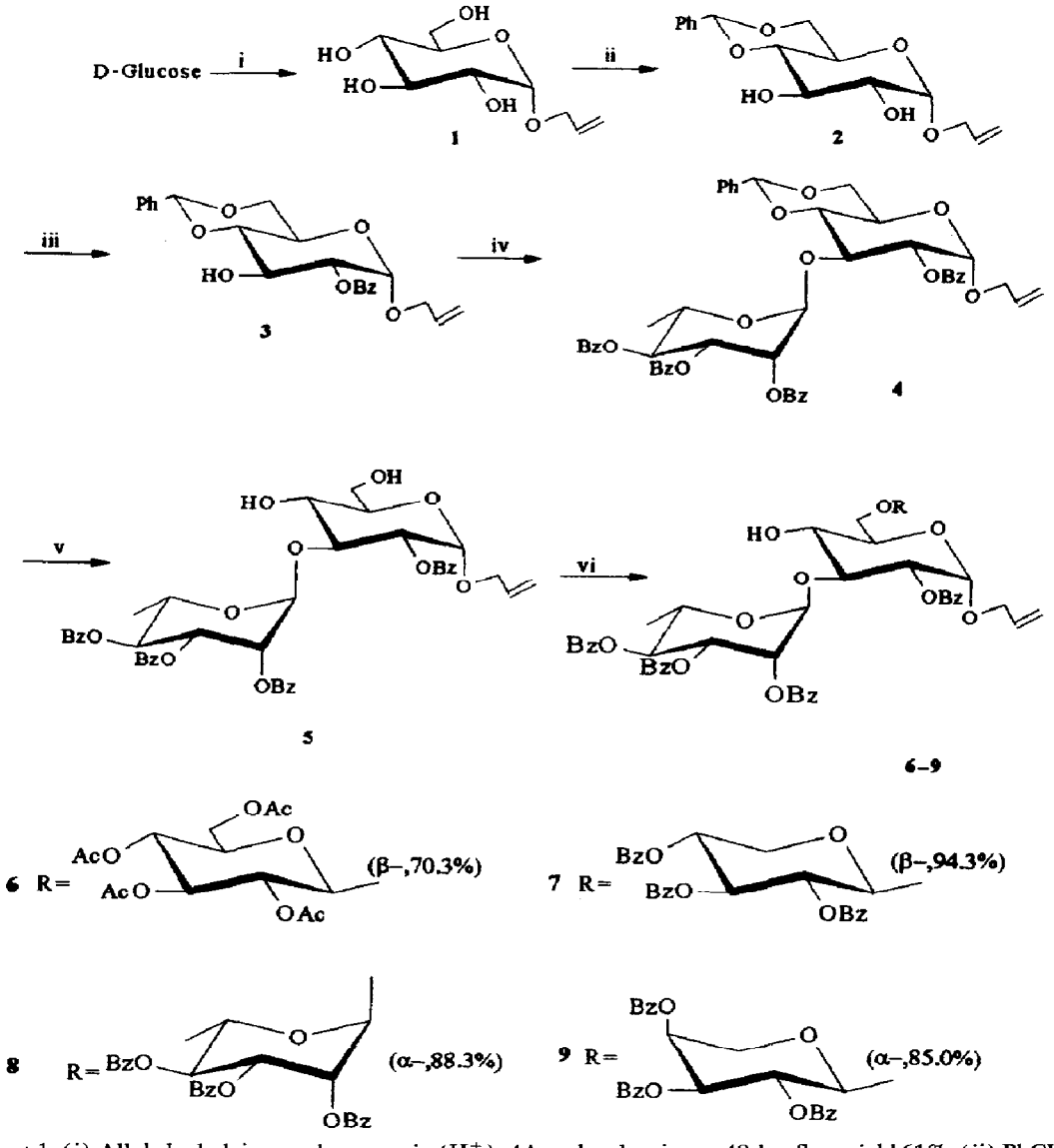
We used primarily the Koenigs–Knorr method [6] to synthesize one disaccharide and four trisaccharides.

Typical strategies are shown in Scheme 1. Allyl α-D-glucopyranoside (**1**) and allyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2**) were prepared as previously reported [7,8]. Compound **2** was treated with benzoyl chloride in boiling anhydrous chloroform for 7 h and the product was resolved by the column chromatography to afford the 2-*O*-benzoyl derivative (**3**) in 76% yield [9]. In the glycosylation reactions (step iv), $Hg(CN)_2$ was found to be the best among several catalysts used in the reaction of **3** with 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide. Compound **3** and the perbenzoylated rhamnosyl bromide in anhydrous toluene, with $Hg(CN)_2$ as a catalyst and powdered 4A molecular sieves as a dehydrating agent, were refluxed for 7 h to give **4** in 75.5% yield as a white solid.

Removal of the acetal group from compound **4** was readily accomplished by treatment with CF_3CO_2H or $TsOH \cdot H_2O$ in methanol–water to give the disaccharide derivatve **5** (82–84%). Compound **5** was a key intermediate, constituting itself the sugar core of many phenylpropanoid glycosides, such as verbascoside [10,11], cistanoside C.D. [12], β-hydroxyacetoside [13], and others. In the glycosylation reaction for the synthesis of the trisaccharides (compounds **6–9**), $Hg(CN)_2$ was likewise the best catalyst found. Treatment of **5** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in benzene–nitromethane gave a trisaccharide derivative **6** having the β configuration (the sugar core of echinacoside [14]), isolated by column chromatography in good yield (70.3%) and accompanied by a small amount of the α anomer(**6α**, 9.4%). Configurations of the anomers were readily assigned by ^{13}C NMR spectroscopy [α, $\delta_{C\text{-}1}$ Glc*p* = 100.9 ppm; β, $\delta_{C\text{-}1}$ Glc*p* = 96.8 ppm]. Similar reactions were adopted for the preparation of compounds **7**, **8**, and **9**. Thus, treatment of **5**, respectively with 2,3,4-tri-*O*-benzoyl-α-D-xylopyranosyl bromide, 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide and 2,3,4-tri-*O*-benzoyl-α-L-arabinopyranosyl bromide in benzene–nitromethane with $Hg(CN)_2$ as catalyst, gave compounds **7**, **8**, and **9** (the sugar cores of arenarioside [15], poliumose [16], and angoroside A [17]) as white solids in 94.3, 88.3, and 85.0% yields, respectively.

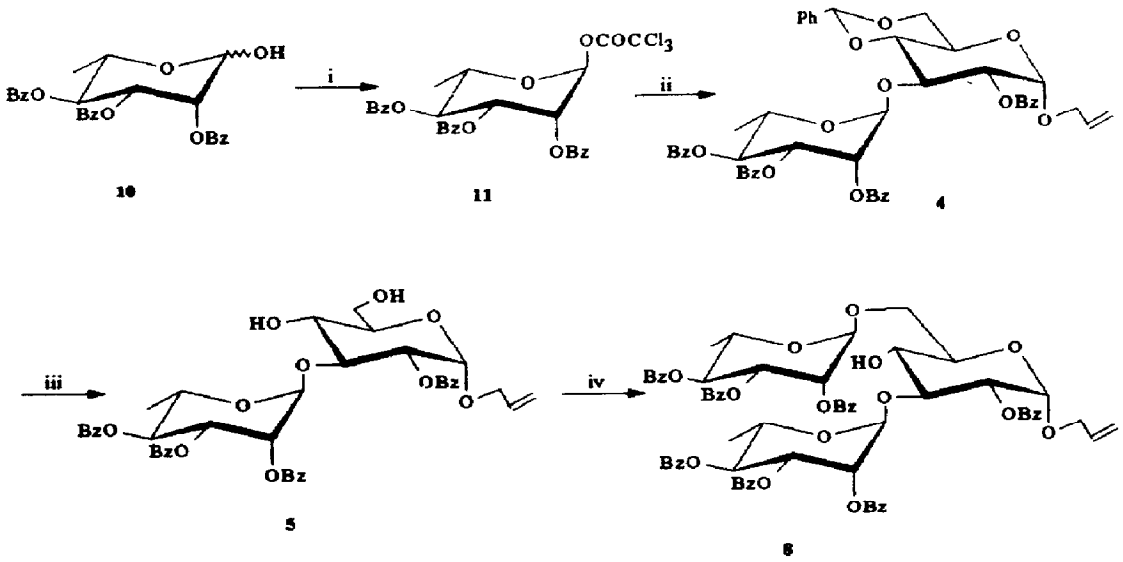
Trichloroacetoxy, a new glycosyl anomeric leaving group, has been used successfully in our laboratory to prepare some glycosides and oligosaccharides [18]. Compounds **5** and **8** were also prepared by this method, and the strategy is shown in Scheme 2.

2,3,4-Tri-*O*-benzoyl-L-rhamnopyranose (**10**) was obtained as described [19] and was then converted into trichloroacetyl 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranoside (**11**), an



Scheme 1. (i) Allyl alcohol, ion-exchange resin (H^+), 4A molecular sieves, 48-h reflux, yield 61%. (ii) PhCHO–ZnCl (anhyd), room temperature, 4.5 h, yield 78%. (iii) Benzoyl chloride (1 equiv), imidazole (2 equiv), $CHCl_3$ (anhyd), 7-h reflux, yield 76%. (iv) 2,3,4-Tribenzoyl rhamnosyl bromide (1.2 equiv), $Hg(CN)_2$(1.2 equiv), toluene, 4A molecular sieves, 4-h reflux, yield 75.5%. (v) CF_3CO_2H, MeOH–H_2O, 8-h reflux, yield 84%; or TsOH·H_2O, 80°C, 2 h, yield 82%. (vi) Protected glycosyl bromide (1.2 equiv), $Hg(CN)_2$, (1.2 equiv), benzene–$MeNO_2$, room temperature.

activated glycosyl donor, by treatment with trichloroacetyl anhydride in the presence of Cl_3CCO_2Na. Compound **11** reacted with **3** and **5**, respectively, to give the disaccharide **4** and the trisaccharide **8** in high yields (88.2 and 95.6%) and high stereoselectivity; Me_3SiOTf, a stronger Lewis acid, was used as the glycosylation catalyst. Addition of DBMP (2,6-di-*tert*-butyl-4-methylpyridine) as the neutralizing agent and 3A molecular sieves as the dehydrating agent favored this reaction. This is the first example of a synthesis of natural oligosaccharides by the trichloroacetate method.



Scheme 2. (i) $(Cl_3CO)_2O$, Cl_3CO_2Na, CH_2Cl_2, reflux, yield 96%. (ii) Me_3SiOTf, DBMP, 3A molecular sieves, CH_2Cl_2 (anhyd), −20°C → room temperature, 4 days, yield 88%. (iii) CF_3CO_2H, MeOH–H_2O, 8-h reflux, yield 84%; or TsOH·H_2O, 80°C, 2 h, yield 82%. (iv) Me_3SiOTf, DBMP, 3A molecular sieves, CH_2Cl_2 (anhyd), −20°C → room temperature, 4 days, yield 96%.

The structures (including the hydrogen and carbon shifts in all of the sugar rings, configurations, and the linkages) of each oligosaccharide synthesized here were assigned and determined by using ^{13}C and ^{1}H NMR and various 2D NMR techniques (COSY, HETCOR, NEOSY, LR-COSY, and others) (see Tables 1–3). These configurations were shown to be in full agreement with those of the natural products.

3. Experimental

General methods.—Melting points are uncorrected. Spectra were recorded with the following instruments, ^{1}H and ^{13}C NMR, Jeol FX-90Q (90 MHz), Varian VXR-300 (300 MHz), and Bruker AM-500 (500 MHz), ^{1}H–^{1}H COSY, HETCOR, NOESY, Bruker AM-500; mass spectra, VG 20-250 GLC–MS and VG ZAB GC GLC–MS. The ^{1}H NMR spectra were recorded with Me_4Si as the internal standard and ^{13}C NMR with $CDCl_3$ as solvent and internal standard. Optical rotations were measured at 22–25°C with a Polartronic-D polarimeter for $CHCl_3$ solutions. The progress of reactions was monitored by TLC on Silica Gel GF 254 (Hai Yang Chemical Factory, Qingdao, Shandong, P.R. China). Column chromatography was performed on silica gel H (10–40 mm), (Hai Yang Chemical Factory, Qingdao, Shandong, P.R. China). The solvent systems indicated are volume–volume ratios. Components were detected by spraying the plates with 20% concd H_2SO_4 in ethanol and heating. Elemental analyses were performed on Perkin–Elmer 240C instrument.

Allyl 2-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranoside (**3**).—Imidazole (5.44 g, 80 mmol) was dissolved in anhyd $CHCl_3$ (40 mL). The solution was stirred and cooled to 0°C. Benzoyl chloride (4.6 mL, 40 mmol) was added dropwise and the mixture was stirred for 30 min at 0°C, and then it was filtered and the white precipitate was washed with $CHCl_3$

Table 1
^{1}H NMR data of the synthetic sugar cores of phenylpropanoid glycosides

Compound No.	4	5	6	7	8	9
Allyl						
$-OCH_2-$	a:4.20(dd, 6.47, 14.33)	a:4.19(dd, 5.13, 13.13)	a:4.16(m)	a:4.06(dd, 5.64, 13.74)	a:4.29(m)	a:4.06(dd, 5.00, 13.26)
	b: 3.99(dd, 6.08, 13.14)	b:3.99(dd, 5.26, 13.09)	b:3.96(m)	b:3.84(dd, 5.73, 13.34)	b:4.08(m)	b:3.79(dd, 5.15, 13.41)
$-CH=$	5.81(dddd, 5.30, 6.03, 18.65, 10.52)	5.81(dddd, 5.15, 13.10, 17.33, 9.98)	5.78(m)	5.70(dddd, 5.62, 13.25, 10.45, 17.25)	5.85(m)	5.66(m)
$=CH_2$	a:5.26(dd, 1.58, 18.65)	a:5.25(dd, 1.26, 17.33)	a:5.27(m)	a:5.19(dd, 0.98, 10.45)	a:5.31(m)	a:5.18(dd, 0,99, 17,45)
	b:5.13(dd, 1.55, 10.50)	b:5.12(dd, 1.26, 9.98)	b:5.12(m)	b:5.06(dd, 0.96, 17.25)	b:5.17(m)	b:5.05(dd, 0.98, 10.40)
Glucose						
1	5.29(d, 3.69)	5.28(d, 3.57)	5.23(d, 3.88)	5.22(d, 3.60)	5.34(d, 3.40)	5.21(d, 3.39)
2	4.59(dd, 3.71, 9.81)	5.12(dd, 3.46, 8.24)	5.08(dd, 3.98, 8.92)	4.97(dd, 3.62, 9.62)	5.19(dd, 3.56, 9.90)	4.99(dd, 3.45, 9.82)
3	4.29(t, 9.62)	4.29(t,8.24)	4.42(t, 9.08)	4.21(t, 3.87, 9.23)	4.26(t, 10.03)	4.25(t, 9.69)
4	3.85(t, 10.31)	3.84(t, 8.25)	3.68(t, 9.19)	3.74(t, 9.07)	3.86(t, 9.89)	3.75(t, 9.69)
5	4.06(ddd, 5.75, 10.97, 10.42)	3.99(m)	3.87(m)	3.89(m)	3.99(dd, 4.31, 9.83)	3.95(m)
6	a:4.36(dd, 4.71, 10.28)	a:3.92(m)	a:4.29(m)	a:4.21(dd, 4.30, 13.17)	a:4.12(t, 10.27)	a:4.31(m)
	b:3.83(t, 4.85)	b:3.82(m)	b:4.18(m)	b:3.91(t, 4.47)	b:3.92(dd, 4.32, 10.22)	b:3.93(m)
Rhamnose						
1′	5.32(d, 1.62)	5.32(d, 1.62)	5.30(d, 1.62)	5.28(d, 1.56)	5.32(d, 1.83)	5.32(d, 1.64)
2′	5.49(dd, 1.61, 3.54)	5.49(dd, 1.60, 3.10)	5.44(dd, 1.64, 3.05)	5.46(dd, 1.56, 3.40)	5.49(dd, 1.82, 3.09)	5.51
3′	5.78(dd, 3.75, 9.85)	5.78(dd, 3.14, 10.02)	5.77(dd, 3.38, 9.85)	5.76(dd, 3.38, 10.04)	5.81(dd, 3.30, 10.07)	5.71
4′	5.51(t, 10.14)	5.65(t, 10.14)	5.63(t, 9.87)	5.64(t, 9.95)	5.68(t, 9.93)	5.68
5′	4.52(dd, 6.18, 10.01)	4.49(dd, 6.18, 10.14)	4.48(dd, 6.27, 9.70)	4.38(dd, 6.23, 9.74)	4.55(dd, 9.68, 6.21)	4.48
6′	0.92(d, 6.18)	1.37(d, 6.16)	0.94(d, 6.21)	1.34(d, 6.18)	1.36(d, 6.22)	1.36(d, 6.09)
Other siganls	5.69(s)		Glucose	Xylose	Rhamnose	Arabinose
			1″ 4.69(d, 7.97)	1″ 4.98(d, 4.90)	1″ 5.15(d, 1.65)	1″ 4.95(d. 5.86)
	(–CH, benzylidene)		2″ 5.06(dd, 9.82, 8.01)	2″ 5.46(dd, 4.76, 6.66)	2″ 5.75(dd, 1.66, 3.21)	2″ 5.84
			3″ 5.22(t, 9.54)	3″ 5.78(t, 6.80)	3″ 5.86(dd, 3.52, 3.21)	3″ 5.72
			4″ 5.10(m)	4″ 5.34(dd, 6.43, 10.64)	4″ 5.69(t, 9.86)	4″ 5.73
			5″ 3.74(m)	5″ a:4.55(dd, 3.97, 11.02)	5″ 4.30(dd, 6.36, 10.01)	5″ a:4.42
			6″ a: 4.28m, b: 4.20 m	b:3.79(t, 4.03)	6″ 1.38(d, 6.34)	b:3.97

Table 2
^{13}C NMR chemical shifts of the synthetic sugar cores of phenylpropanoid glycosides

Compound No.	4	5	6	7	8	9
Allyl						
$-OCH_2-$	68.8	68.6	68.3	68.1	68.8	68.1
$-CH=$	133.2	133.2	133.1	133.3	133.4	133.2
$=CH_2$	117.7	117.4	117.7	117.5	117.7	117.2
α-D-Glc*p*OAll						
C-1	96.0	95.3	95.0	95.0	95.3	94.9
C-2	74.8	72.7	72.8	72.7	72.5	72.8
C-3	79.6	81.8	81.2	82.0	82.9	81.5
C-4	73.0	71.5	70.1	69.9	69.7	69.7
C-5	63.0	62.3	70.6	70.3	70.9	70.4
C-6	69.0	69.0	68.6	68.2	67.1	68.6
α-L-Rha*p*						
C-1′	97.9	99.3	99.3	99.5	99.7	99.3
C-2′	70.4	70.8	70.8	70.8	70.8	70.7
C-3′	69.8	69.2	69.2	69.2	69.2	69.2
C-4′	71.7	71.2	71.6	71.5	71.5	71.5
C-5′	66.5	66.5	67.8	67.9	68.1	67.7
C-6′	16.8	17.7	17.6	17.6	17.7	17.5
Other signals	102.0 (benzylidene)		β-D-Glc*p* C-1″ 100.9 C-2″ 71.1 C-3″ 72.8 C-4″ 68.3 C-5″ 72.0 C-6″ 61.7	β-D-Xyl*p* C-1″ 100.2 C-2″ 70.0 C-3″ 69.6 C-4″ 68.9 C-5″ 60.9	α-L-Rha*p* C-1″ 98.2 C-2″ 70.7 C-3″ 70.0 C-4″ 71.8 C-5″ 66.9 C-6″ 17.8	β-L-Ara*p* C-1″ 101.0 C-2″ 69.9 C-3″ 70.3 C-4″ 68.1 C-5″ 62.4

(20 mL). The filtrate was added to anhyd $CHCl_3$ (150 mL) in which allyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2**; 12.32 g, 40 mmol) had been dissolved, and then the mixture was boiled under reflux for 7 h. The solution was washed with water (3×50 mL), aq NaCl (3×50 mL) and water (3×50 mL), dried, and evaporated in vacuo. The residue was purified by column chromatography with 8:1 petroleum ether (60–90°C)–EtOAc as eluent to give **3** as a colorless syrup (12.50 g, 75.9%); $[\alpha]_D^{25}$ +110° (*c* 0.88); ^1H NMR (300 MHz): δ (ppm) 7.31–8.10 (m, 10 H, arom), 5.85 (m, 1 H, =CH, allyl), 5.58 (s, 1 H, PhCH), 5.16 and 5.28 (2dd, 2×1 H, $=CH_2$, allyl), 5.22 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1, α), 5.06 (dd, 1 H, *J* 4.0, 10.3 Hz, H-2), 4.35 (m, 2 H, $-OCH_2$, allyl), 4.20 (ddd, 1 H, *J* 10.4 Hz, H-5), 3.92–4.05 (m, 2 H, H-6a,6b), 3.80 (t, 1 H, *J* 10.3, 10.5 Hz, H-3), 3.65 (t, 1 H, *J* 10.5, 10.4 Hz, H-4), 2.56 (br s, 3-OH, disappeared on D_2O exchange); ^{13}C NMR (300 MHz); $\delta_{C\text{-}1}$ 96.8 ppm.

Allyl 2-O-benzoyl-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-4,6-O-benzylidene-α-D-glucopyranoside (**4**).—A mixture of **3** (2.0 g, 4.85 mmol), 2,3,4-tri-*O*-benzoyl-α-D-rhamnopyranosyl bromide [19] (3.14 g, 5.82 mmol), $Hg(CN)_2$ (1.47 g, 5.82 mmol), and powdered 4A molecular sieves (2.0 g) in anhyd toluene was stirred under refluxed for 4 h. After cooling, the solid was removed by filtration and thoroughly washed with toluene. The filtrate and washings were combined and evaporated to dryness in vacuo. The residue was stirred in $CHCl_3$, the solid material that separated was filtered off, and the filtrate was

Table 3
Determination of the linkages and configurations of the synthetic sugar cores of phenylpropanoid glycosides

Compound No.	$^3J_{H-1,H-2}$ (Hz)	$^2J_{C-1,H-1}$ (Hz) [a]	NOE enhancement (NOESY, ROESY)	Linkage and configuration
4	Glc*p*: 3.69	Glc*p*: 172.9 (δ_{C-1} 96.0 ppm)	(1–2), (1′–2′), (1′–3),(1–8)	α-Rha*p*-(1→3)-α-Glc*p*
	Rha*p*: 1.62	Rha*p*: 174.4 (δ_{C-1} 97.9 ppm)		
5	Glc*p*: 3.57	Glc*p*: 172.8 (δ_{C-1} 95.2 ppm)	(1–2), (1′–2′), (1′–3),(1–8)	α-Rha*p*-(1→3)-α-Glc*p*
	Rha*p*: 1.62	Rha*p*: 173.8 (δ_{C-1} 99.3 ppm)		
6	Glc*p*: 3.88	Glc*p*: 171.5 (δ_{C-1} 95.2 ppm)	(1–2), (1′–2′), (1′–3),(1–7),	β-Glc*p*-(1→6)-[α-Rha*p*-(1→3)]α-Glc*p*
	Rha*p*: 1.62	Rha*p*: 172.9 (δ_{C-1} 99.3 ppm)	(1″–2″), (1″–3″), (1″–5″),	
	Glc*p*: 7.97	Glc*p*: 161.3 (δ_{C-1} 100.9 ppm)	(1″–6a,6b)	
7	Glc*p*: 3.60	Glc*p*: 171.5 (δ_{C-1} 95.0 ppm)	(1–2), (1–7), (1′–2′), (1′–3),	
	Rha*p*: 1.56	Rha*p*: 171.5 (δ_{C-1} 99.5 ppm)	(1″–2″), (1″–3″), (1″–5″),	β-Xyl*p*-(1→6)-[α-Rha*p*-(1→3)]α-Glc*p*
	Xyl*p*: 4.90	Xyl*p*: 163.7 (δ_{C-1} 100.2 ppm)	(1″–6a,6b)	
8	Glc*p*: 3.40	Glc*p*: 171.5 (δ_{C-1} 95.3 ppm)	(1–2), (1–7), (1′–2), (1′–3),	
	Rha*p*: 1.83	Rha*p*: 172.9 (δ_{C-1} 99.7 ppm)	(1″–2″), (1″–6a,6b)	α-Rha*p*-(1→6)-[Rha*p*-(1→3)]α-Glc*p*
	Rha*p*: 1.65	Rha*p*: 171.5 (δ_{C-1} 98.2 ppm)		
9	Glc*p*: 3.39	Glc*p*: 173.3 (δ_{C-1} 94.9 ppm)	(1–2), (1–7), (1′–2′), (1′–3),	
	Rha*p*: 1.64	Rha*p*: 172.3 (δ_{C-1} 99.3 ppm)	(1″–2″), (1″–3″), (1″–5″),	β-Ara*p*-(1→6)-[α-Rha*p*-(1→3)]α-Glc*p*
	Ara*p*: 5.86	Ara*p*: 162.4 (δ_{C-1} 101.0 ppm)	(1″–6a,6b)	

[a] These constants were measured by the broad-band decoupling technique.

evaporated to dryness. The residue was purified on a column of silica gel with 16:1 benzene–EtOAc as eluent to give **4** (3.20 g, 75.5%) as white needles; (MeOH); mp 184–185°C; $[\alpha]_D^{25}$ +146.2° (*c* 0.78); FABMS: 871 $(M+1)^+$. Anal. Calcd for $C_{50}H_{46}O_{14}$: C, 68.95; H, 5.32. Found: C, 69.01; H, 5.27

Allyl 2-O-benzoyl-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-D-glucopyranoside (**5**).—*Method A*. To a solution of **4** (1.50 g, 1.72 mmol) in CH_2Cl_2 (60 mL) was added dropwise aq CF_3CO_2H (0.9 mL, 90%). The mixture was stirred for 8 h under reflux. After the solution had been cooled, the mixture was washed succesively with water, aq $NaHCO_3$ and water, dried, and concentrated. The concentrate was applied to a column of silica gel and eluted with 2:1 petroleum ether (60–90°C)–EtOAc to give amorphous **5** (1.16 g, 83.9%).

Method B. This proceeded as Method A but using *p*-toluenesulfonic acid monohydrate (0.6 g) with **4** (4.70 g) in 95:5 MeOH–H_2O (200 mL) and stirring for 2 h at 80°C to afford **5** (3.50 g, 82.8%). Compound **5** was a white amorphous solid; mp 84–85°C; $[\alpha]_D^{25}$ +146.1° (*c* 0.78); IR (KBr) cm^{-1} 3443 (OH), 1726 (carbonyl group). Anal. Calcd for $C_{43}H_{42}O_{14}$: C, 65.97; H, 5.41. Found: C, 65.67; H, 5.24.

Allyl 2-O-benzoyl-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-6-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**6**) *and allyl 2-O-benzoyl-3-O- 48 points short (2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-6-O-(2,3,4,6-O-tetra-O-acetyl-α-D-glucopyranosyl)-α-D-glucopyranoside* (**6α**).—Compound **5** (150 mg, 0.192 mmol) and $Hg(CN)_2$ (65 mg, 0.250 mmol) were added to 1:1 benzene–$MeNO_2$ (20 mL). The mixture was stirred and heated to boiling, and 6 mL of the solvent was removed by distillation. After cooling to room temperature, 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide [20] (95 mg) and powdered 3A molecular sieves (200 mg) were added to the mixture and stirring was continued for 20 h at room temperature. The residue was stirred in $CHCl_3$ and the $Hg(CN)_2$ separated was filtered off and the filtrate was washed with water, dried, and evaporated to dryness. The residue, a yellow syrup, was purified by preparative TLC (silica gel GF 254) with 6:1 benzene–EtOAc as eluent to give **6** (150 mg, 70.3%) and **6α** (20 mg, 9.4%).

Compound **6** was a white, amorphous solid; mp 92–93°C; $[\alpha]_D^{25}$ +130.4° (*c* 2.30); IR (KBr) cm^{-1}: 3504 (OH), 2938 (CH_3–), 1728 (carbonyl group); FABMS: 1113 $(M+1)^+$. Anal. Calcd for $C_{57}H_{60}O_{23}$: C, 61, 51, H 5.43; Found: C, 61, 71, H, 5.36.

Compound **6α** was a white solid; mp 78.5–80.0°C; $[\alpha]_D^{25}$ +111.1° (*c* 0.1); IR (KBr) cm^{-1}: 3483 (OH), 2935 (CH_3–), 1729 (carbonyl group). ^1H NMR (500 MHz): dH (ppm) 0.90 (d, 3 H, Me of Rha), 1.50–1.80 (m, 12 H, 4 × CH_3COO–), 3.20–5.90 (24 H, protons of three sugar rings and allyl group), 6.70–7.60 (m, 20 H, ArH); ^{13}C NMR (500 MHz): $\delta_{C\text{-}1}$ Glc*p* 95.2 ppm (α), $\delta_{C\text{-}1}$ Glc*p* protected by four acetyl groups 96.8 ppm (α), $\delta_{C\text{-}1}$ Rha*p* 99.2 ppm.

Allyl 2-O-benzoyl-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-6-O-(2,3,4,-tri-O-benzoyl-β-D-xylopyranosyl)-α-D-glucopyranoside (**7**).—Glycosylation of compound **5** (2.0 g, 2.56 mmol) with 2,3,4-tri-*O*-benzoyl-α-D-xylopyranosyl bromide [21] (1.65 g, 3.07 mmol) and $Hg(CN)_2$ (850 mg, 3.32 mmol) as catalyst was performed in benzene–$MeNO_2$ as just described (see compound **6**); yield 2.96 g as an amorphous solid (94.3%); mp 111–113°C; $[\alpha]_D^{25}$ +71.8° (*c* 1.56); IR (KBr) cm^{-1}: 3448 (OH), 1727 (carbonyl group); FABMS: 1227$(M+1)^+$. Anal. Calcd for $C_{69}H_{62}O_{21}$: C, 67.53; H 5.09; Found: C, 67.45; H, 5.07.

Allyl 2-O-benzoyl-3,6-di-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-D-glucopyranoside (**8**).—Compound **8** was prepared as for the trisaccharide **6**. Compound **5** (150 mg, 0.192 mmol), $Hg(CN)_2$ (65 mg, 0.250 mmol), 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide (125 mg, 0.232 mmol), and powdered 3A molecular sieves (200 mg) were allowed to react for 15 h and the product was purified by preparative TLC (eluent, 4:1 benzene–EtOAc) to give **8** as a white, amorphous solid (210 mg, 88.3%); mp 106–107°C; $[\alpha]_D^{25}$ +162.3° (*c* 1.32); IR (KBr) cm^{-1}: 3448 (OH), 1727 (carbonyl group); FABMS: 1240 $(M)^+$. Anal. Calcd for $C_{70}H_{64}O_{21}$: C, 67.73; H, 5.16; Found: C, 67.82; H, 5.14.

Allyl 2-O-benzoyl-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-6-O-(2,3,4-tri-O-benzoyl-β-L-arabinopyranosyl)-α-D-glucopyranoside (**9**).—This trisaccharide was pre-

pared by the same synthetic procedure used for compound **6**. Compound **5** (150 mg, 0.192 mmol), $Hg(CN)_2$ (65 mg, 0.250 mmol), 2,3,4-tri-*O*-benzoyl-α-L-arabinopyranosyl bromide [22] (120 mg, 0.230 mmol), and powdered 3A molecular sieves (200 mg) were allowed to react for 24 h and the product was purified by preparative TLC (eluent, 8:1 benzene–EtOAc); yield 200 mg (85%) as a white, amorphous solid; mp 101–102°C; $[\alpha]_D^{25}$ +170.4° (*c* 0.54); IR (KBr) cm^{-1}: 3498 (OH), 1726 (carbonyl group); FABMS: 1227 $(M+1)^+$. Anal. Calcd for $C_{69}H_{62}O_{21}$: C, 67.54; H, 5.09. Found: C, 67.49; H, 5.00.

Trichloroacetyl 2,3,4-tri-O-benzoyl-α-L-rhamnopyranoside (**11**).—To a solution of 2,3,4-tri-*O*-benzoyl-L-rhamnopyranose (**10**) (800 mg) in anhyd CH_2Cl_2 (5 mL) were added trichloroacetyl anhydride (1.5 mL) and sodium trichloroacetate (200 mg). The solution was stirred and boiled under reflux for 30 min. After cooling to room temperature, the sodium trichloroacetate was filtered off and washed with CH_2Cl_2 (2×5 mL). The filtrate and washings were combined and washed with ice–water, aq $NaHCO_3$ and ice–water to pH 7.0, dried with anhyd Na_2SO_4, and evaporated to give **11** as a white solid (1.0 g, 95.7%); mp 57–58°C; $[\alpha]_D^{25}$ +123.1° (*c* 0.26); ^1H NMR (90 MHz): δ 1.50 (d, 3 H, *J* 6.40 Hz, CH_3 of rhamnopyranosyl), 4.00–4.60, 5.70–5.90 (m, 4 H, H-2,3,4,5), 6.52 (d, 1 H, *J* 1.65 Hz, H-1, α anomer), 7.20–8.30 (m, 15 H, arom); ^{13}C NMR (90 MHz): δ (ppm) 165.4 and 159.4 (C=O), 138.4, 133.4, 129.6, (arom), 94.98 (C-1), 70.5, 70.4, 69.2, 69.2, 68.7 (C-2,3,4,5, and $-CCl_3$), 17.6 (C-6).

Preparation of disaccharide **4** *by the glycosyl trichloroacetate method.*—A mixture of **11** (200 mg, 0.420 mmol), **3** (200 mg, 0.490 mmol), DBMP (50 mg), and powdered 3A molecular sieves (200 mg) in anhyd CH_2Cl_2 (10 mL) was stirred in an ice–salt bath (−20°C). After 10 min, 5 drops of Me_3SiOTf were added and the mixture was stirred for 4 days, during which time the temperature increased from −20°C to room temperature. The solid was filtered off and the filtrate was evaporated to dryness. The residue was separated by preparative TLC (eluent, 16:1 benzene–EtOAc) to give a white solid (210 mg, 88.2%). This compound was identified as disaccharide **4** synthesized earlier by TLC and ^1H and ^{13}C NMR spectra.

Preparation of trisaccharide **8** *by the glycosyl trichloroacetate method.*—The experimental procedure was the same as before. Compounds **11** (150 mg) and **5** (230 mg), DBMP (50 mg), and powdered 3A molecular sieves in anhyd CH_2Cl_2 (10 mL) were allowed to react for 4 days, and the product was purified by preparative TLC (eluent, 8:1 benzene–EtOAc); yield 280 mg (96.5%) as a white, amorphous solid. This compound was identified as the trisaccharide **8** already synthesized, by TLC and ^1H and ^{13}C NMR spectra.

Acknowledgements

This investigation was supported by the grant No. 29302008 from the National Natural Science Foundation of P.R. China

References

[1] P. Molgaard and H. Ravn, *Phytochemistry*, 27 (1988) 2411–2421.

[2] P.H. Chanh, Y. Koffi, and A.P.H. Chanh, *Planta Med.*, 54 (1988) 294–296.
[3] H. Ravn, S. Nishibe, M. Sasahara, and L. Xuebo, *Phytochemistry*, 29 (1990) 3627–3631.
[4] H. Sasaki and H. Nishimura, *Planta Med.*, (1989) 458–467.
[5] G.R. Pettit, A. Numate, T. Takemura, and R.H. Ode, *J. Nat. Prod.*, 53 (1990) 456–458.
[6] H. Paulsen, *Chem. Soc. Rev.*, 13 (1984) 15–45.
[7] R.T. Lee and Y.C. Lee, *Carbohydr. Res.*, 37 (1974) 193–201.
[8] P.M. Collins, V. Ranjit, N. Munasinghe, and N.N. Oparaeche, *J. Chem. Soc., Perkin Trans. 1*, (1977) 2423–2428.
[9] F.A. Carey and K.O. Hodgson, *Carbohydr. Res.*, 12 (1970) 463–468.
[10] H. Shimomura, Y. Sashida, and K. Ogawa, *Phytochemistry*, 26 (1987) 1981–1983.
[11] Z.D. He and C.R. Yang, *Phytochemistry*, 30 (1991) 701–702.
[12] H. Kobayashi, H. Karasaw, T. Miyase, and S. Fukushima, *Chem. Pharm. Bull.*, 32 (1984) 3880–3885.
[13] S. Kitagawa, H. Tsukamoto, S. Hisada, and S. Nishibe, *Chem. Pharm. Bull.*, 32 (1984) 1209–1213.
[14] H. Becler, *Z. Naturforsch.*, 37C (1982) 351–355.
[15] C. Andary, G. Privat, R. Wylde, and A. Heitz, *J. Nat. Prod.*, 48 (1985) 778–783.
[16] C. Andary, R. Wylde, A. Heitz, J.R. Rascol, J.L. Roussel, and C. Laffite, *Phytochemistry*, 24 (1985) 362–364.
[17] I. Calis, G.A. Gross, and O. Sticher, *Phytochemistry*, 26 (1987) 2057–2061.
[18] Z.J. Li and M.S. Cai, *Tetrahedron Lett.*, submitted.
[19] R.K. Ness, H.G. Fletcher, Jr., and C.S. Hudson, *J. Am. Chem. Soc.*, 73 (1951) 296–300.
[20] K.P. Ravindranathan Kartha and H.J. Jennings, *J. Carbohydr. Chem.*, 9 (1990) 777–781.
[21] G. Hewitt, H.G. Fletcher, Jr., and C.S. Hudson, *J. Am. Chem. Soc.*, 69 (1947) 921–924.
[22] G. Hewitt, *J. Am. Chem. Soc.*, 69 (1947) 1145–1147.