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First total synthesis of two new diglycosides, neohancosides A and B, from *Cynanchum hancockianum*

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Abstract

Neohancosides A (**1**) and B (**2**) are monoterpene diglycosides isolated from *Cynanchum hancockianum*, which is a Chinese folk medicine having antitumor activity. First total synthesis of **1** and **2**, (3*R*)-linaloyl and (3*R*)-8-hydroxylinaloyl 3-*O*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranosides were achieved stereoselectively using fluoride **12b** as a glycosyl donor. The asymmetry of C-3 in **1** and **2** was introduced efficiently by separating diasteremers of (3*R*), (3*S*)-linaloyl and (3*R*), (3*S*)-8-benzoyloxylinaloyl 3-*O*-2,3,4-tri-*O*-benzoyl-β-D-glucopyranoside, **19** and **21** and **20** and **22**, respectively. Absolute configurations of **1** and **2** were determined by enzymatic degradation of synthetic intermediates **33** and **34**. © 1997 Elsevier Science Ltd.

Keywords: Terpene diglycosides; Linalool; 8-Hydroxylinalool; Absolute configuration

1. Introduction

Cynanchum hancockianum (Maxim) Al. Iljinski (Asclepiadaceae), distributed in Inner Mongolia, is known as a Chinese folk medicine that possesses antitumor activity. During the continuation of our work to search for bioactive compounds, our detailed examination of the constituents of this plant has led to the isolation and structure determination of various kinds of novel compounds such as triterpenes (hancockinol, hancolupenol) [1], a modified steroid (hancopregnane) [2], a steroid glycoside (hancoside) [3], and four diglycosides, neohancosides A (**1**), B (**2**), C, D [3,4], see Scheme 1. Although various monoterpene glycosides have been recently found in extracts from plants, their bioactivities have so far been scarcely reported to our knowledge. Furthermore, we could not determine the absolute configuration of the linaloyl moiety in **1** and **2** due to insufficient supplies from the natural source, which was the reason for our interest in their synthesis. This paper (for preliminary comunications see [5]) deals with the first total syntheses of these monoterpene diglycosides **1** and **2** that provided a supply of the com-

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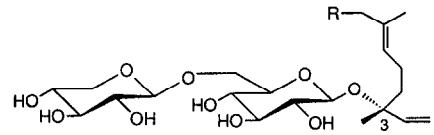
pounds to investigate their antitumor and other bioactivities and also enabled us to determine the absolute configuration of the linalool moiety of **1** and **2**. Furthermore, the stereostructure of disaccharides and their orthoester, which are important synthetic intermediates of **1** and **2**, were determined by NMR analysis.

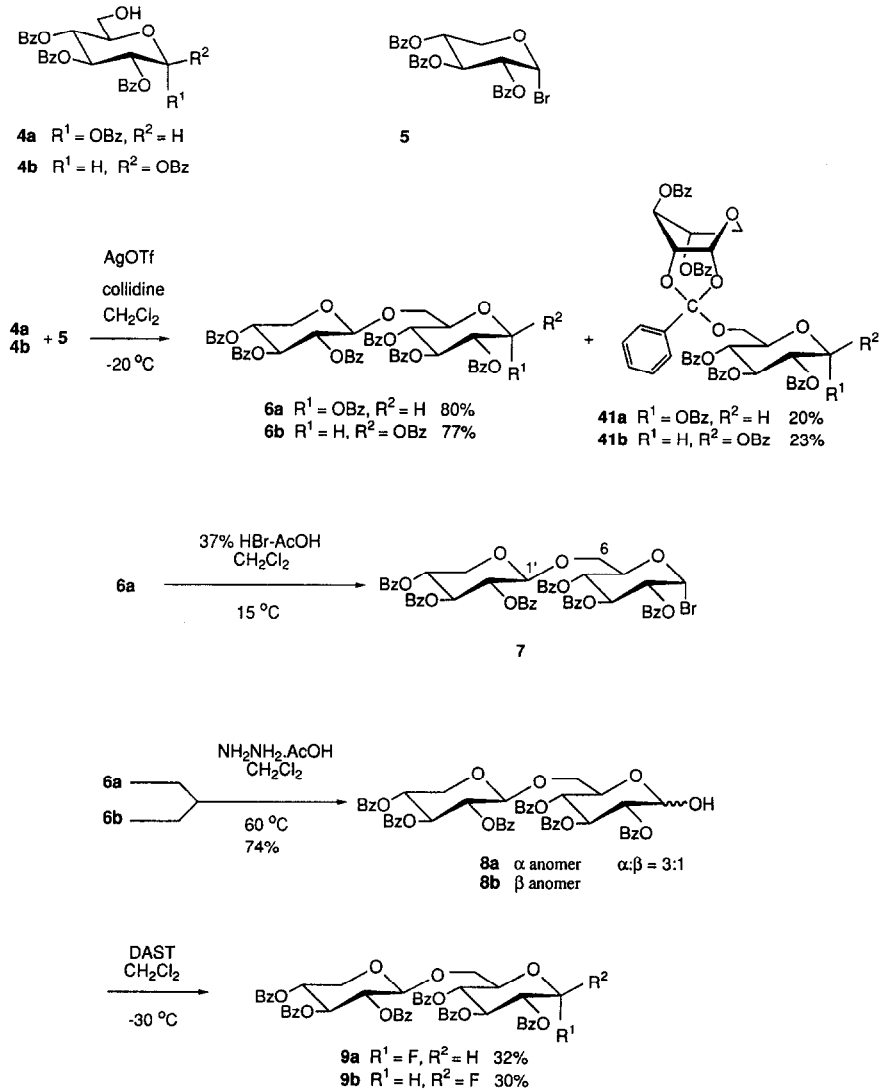


1 R = H Neohancoside A
2 R = OH Neohancoside B

Scheme 1.

2. Results and discussion

Synthesis of neohancoside A (**1**).—Neohancosides A (**1**) and B (**2**) are glycosides in which the disaccharide, β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranose, is linked at the position of the tertiary hydroxyl group of linalool and 8-hydroxylinalool by a glycosylic linkage. As *tert*-alcohols are much less reactive toward the glycosylation reaction than primary and secondary alcohols, it is important to select the most suitable reaction conditions in terms of the promoter and the glycosyl donor. We employed the benzoyl group as a protective group, because it generally suppresses the production of orthoesters more than does an acetyl group. We selected both a glucosyl bromide, which is popularly used for glycosylation



Scheme 2.

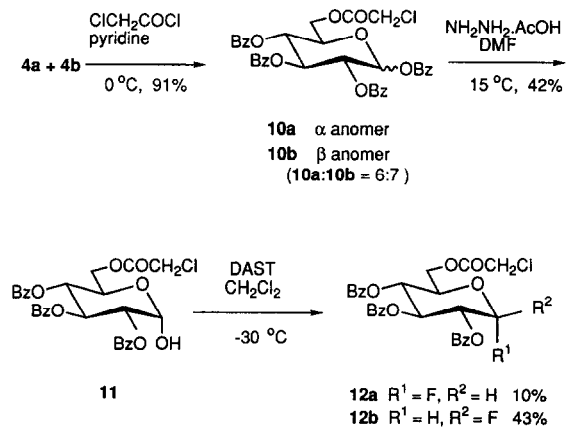
reactions by the Koenigs–Knorr method, and a glucosyl fluoride, which is most effective among the glycosyl halides for its stability in storage, purification and potent reactivity, even in the case of a tertiary alcohol, in combination with silver perchlorate and zirconocene dichloride [6].

We initially intended to synthesize the disaccharide, β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranosyl halide, and then construct **1** and **2** by glycosylation reactions of linalool and 8-hydroxylinalool directly with the resulting disaccharide. The desired disaccharyl bromide **7** and fluoride **9** were successively synthesized as shown in Scheme 2. Glycosylation reaction of **4a** and **4b** [7] with glycosyl bromide **5** using silver triflate and 2,4,6-collidine afforded disaccharides **6a** and **6b** in 80% and 77% yield, respectively. Compound **6a** was then treated with HBr–HOAc to afford glycosyl bromide **7**. Glycosyl fluoride **9** was prepared by treatment of both **6a** and **6b** with hydrazine acetate [8], affording the same anomeric mixture **8** ($\alpha:\beta = 3:1$) in 74% yield, followed by a fluorination of **8** with DAST [9] to give **9a** and **9b** in 32% and 30% yields, respectively. All attempts to glycosylate linalool with the glycosyl bromide **7** by treatment with silver triflate and 2,4,6-collidine under various temperatures (−20–20 °C) were unsuccessful, and an attempt to glycosylate linalool with the fluoride **9b** by treatment with silver perchlolate and zirconocene dichloride was also unsuccessful and only starting materials were recovered.

These results compelled us to modify the synthetic route. Our new synthetic strategy consists of glycosylation reaction of linalool with glucosyl fluoride along with $AgClO_4$ and zirconocene dichloride, followed by the selective deprotection of the 6′-*O*-protective group in the glucose unit, glycosylation reaction of the resulting monoglycoside with a xylosyl bromide by treatment of AgOTf and 2,4,6-collidine (Scheme 5). This synthetic route has the following two important features. (1) We chose Suzuki's method to glycosylate linalool with a glucosyl fluoride as the glycosyl donor and $AgClO_4$ and zirconocene dichloride as a promoter. (2) We chose a chloroacetyl group as the protective group for the 6-hydroxyl in the glucosyl fluoride, because the chloroacetyl group can be easily removed under mild conditions relative to a benzoyl group.

We prepared the key compound **12** by two methods. One method, outlined in Scheme 3, involves 6-*O*-chloroacetylation of an anomeric mixture of **4** (**4a**:**4b** = 4:5.4) to afford an anomeric mixture **10** (**10a**:**10b** = 6:7) in 91% yield, followed by debenzoylation at the anomeric position by hydrazine acetate affording **11** in 42% yield. The resulting sugar **11** was then treated with DAST to give the desired fluoride **12a** and **12b** in 10% and 43%, respectively. The other method is shown in Scheme 4. 6-*O*-Tritylation of D-glucose, followed by benzoylation, afforded an anomeric mixture **13** [1] (**13a**:**13b** = 5:6) in 46% yield. Benzoate **13** was converted to lactol **14** by treatment with hydrazine acetate in 83% yield, which was treated in turn with DAST to give fluoride **15** [1] as an anomeric mixture (**15a**:**15b** = 1:4.5) in 94% yield. Fluoride **15** was detritylated by treatment with HBF_4 to afford 6-hydroxyl fluoride **16** [1] (**16a**:**16b** = 1:4.5) in 92% yield. Protection of the fluoride **16** using chloroacetyl chloride provided **12a** and **12b** in 17% and 79% yield, respectively. Total yields of **12b** from D-glucose were 14% and 26%, respectively, by the former and latter methods.

The route for **1** is summarized in Scheme 5. Our important approach to **1** using key compound **12** is the introduction of asymmetry at the C-3 of linalool. We used racemic linalool in the glycosylation reaction with the monosaccharyl fluoride and to separate the resulting diastereomers. The reason for the use of racemic linalool, though enantiomerically pure linalool has already been reported [11], is described as follows. Since the absolute configuration of the linaloyl aglycone of **1** was not known, we must prepare both (*R*)- and (*S*)-linalools and need to complete the total synthesis using each linalool to get neohancoside A having same configuration as natural



Scheme 3.

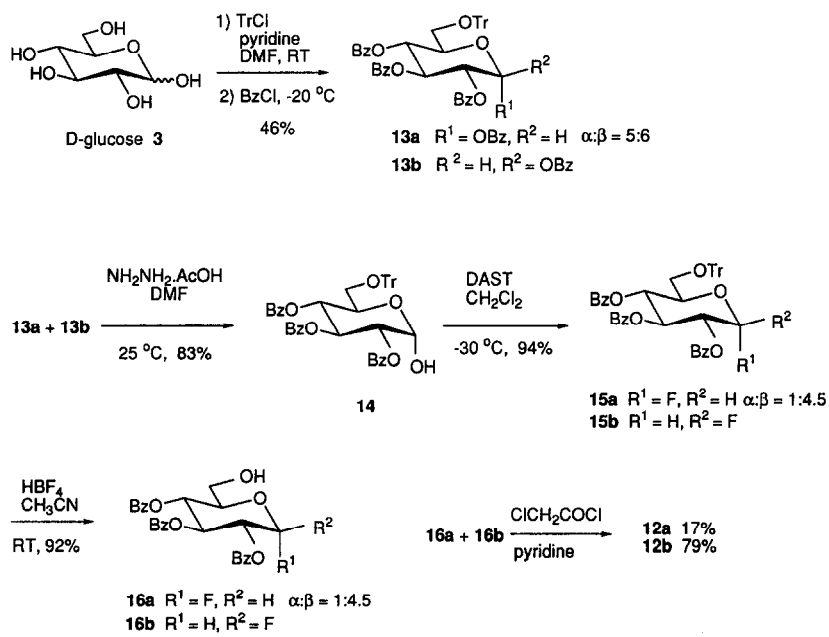
[1] Each anomeric mixture of **13**, **15** and **16** was separated by chromatography to afford **13a** and **13b**, **15a** and **15b**, **16a** and **16b** that were characterized by $[\alpha]_D$ NMR, and MS as described in the Experimental section.

compound, because our purpose of the total synthesis of **1** is mainly the investigation of the bioactivities of **1**. On the other hand, racemic linalool is commercially available, and, as we are interested in the utility of sugars as reagents for the diastereomeric resolution, the use of racemic linalool is justified.

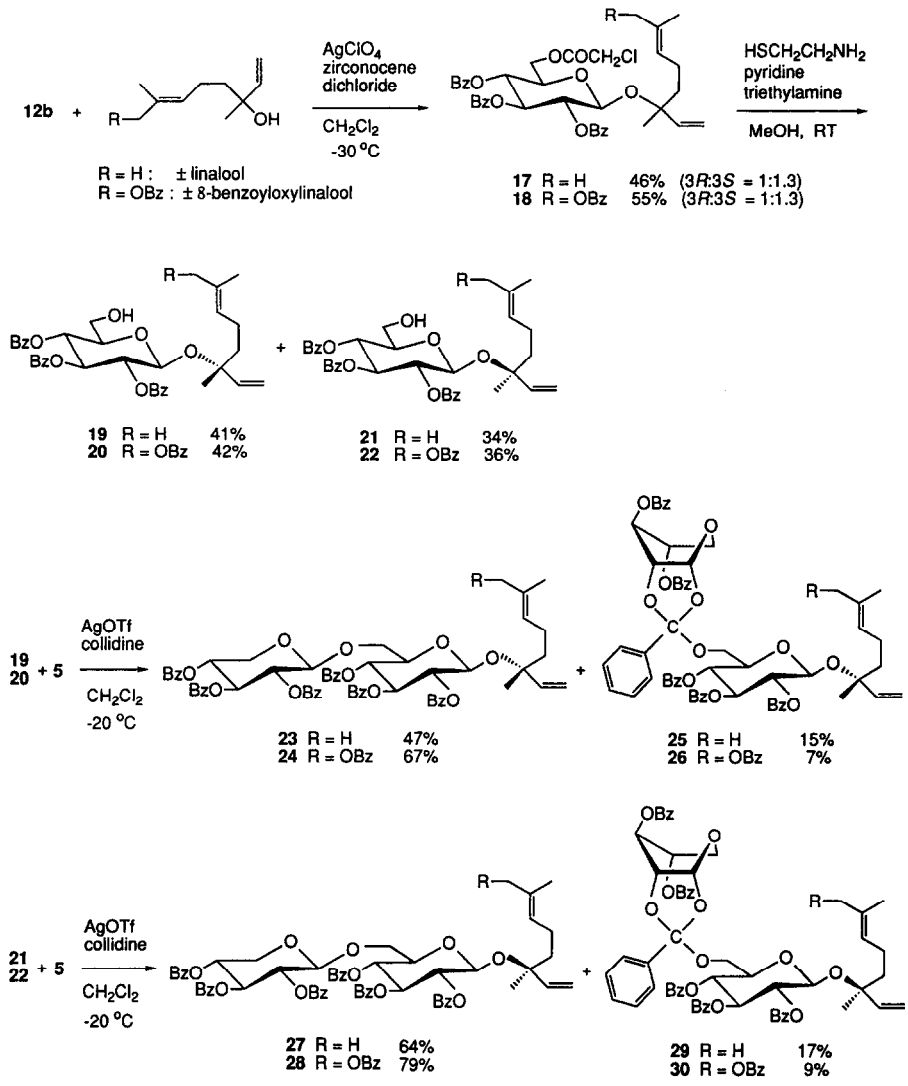
Glycosylation of linalool with fluoride **12b** was carried out by the application of Suzuki's procedure [6]. Thus, **12b** was successively linked with (±)-linalool by treatment with silver perchlorate and zirconocene dichloride in CH_2Cl_2 at −30 °C to give linaloyl glycoside **17** as a mixture of diastereomers in 46% yield. (3*R*:3*S* = 1:1.3). In this step, the diastereomers could not be separated by chromatography, but each signal of the ^1H NMR spectrum was distinguishable and served to characterize two diastereomers of **17**. On glycosylation of linalool with an anomeric mixture of **12a** and **12b**, it was clarified by monitoring with TLC that reaction rates of **12b** were much faster than **12a**. This is because **12a** is thermodynamically more stable than **12b**; accordingly, we employed **12b** as a glycosyl donor.

Selective deprotection of the chloroacetyl group in **17** using 2-aminoethanethiol [10] and pyridine triethylamine wad carried out carefully by monitoring the starting material with TLC to prevent further deprotection of the benzoyl group. The resulting 6′-hydroxyl compounds were successively separated by chromatography to afford diastereomer **19** (3*R*) and **21** (3*S*) in 41% and 34% yield, respectively. Alcohol **19** (3*R*) was glycosylated with glycosyl bromide **5** under the usual conditions using silver triflate and 2,4,6-collidine in CH_2Cl_2 at −20 °C to afford disaccharyl glycoside **23**, together with orthoester **25** in 47% and 15% yield, respectively. These two spectrometrically complicated products were fully characterized by ^1H NMR, ^1H–^1H COSY, ^{13}C NMR, HMQC, and HMBC as described later.

Debenzoylation of **23** using sodium methoxide in a THF–methanol mixture quantitatively gave completely deprotected compound **1** (Scheme 6). Synthetic **1** showed mp of 92–94 °C (EtOAc)), $[\alpha]_D^{25}$ −25.96° (MeOH). Compound **1** was identified in all respects (mp, $[\alpha]_D$, HRMS, ^1H NMR, and ^{13}C NMR) with natural neohancoside A [5]. ^1H and ^{13}C NMR spectra were superimposable to those of natural products as shown in Tables 1 and 2. Glycosylation reaction of **21** (3*S*) with bromide **5** by a similar procedure as above also afforded diglycoside **27** and orthoester **29**, in 64%, 17%, respectively. Compound **27** was deprotected in the same way to give **31**, a stereoisomer of neohancoside A (**1**), in 92% yield. Compound **31** showed mp of 75–77 °C (EtOAc), $[\alpha]_D$ −19.95° (MeOH) and its ^1H and ^{13}C NMR spectra were clearly distinguishable from **1** as described in Tables 1 and 2. These results show the diastereomer **19** has the same chirality at C-3 of linalool as natural neohancoside A (**1**). Thus, total synthesis of neohancoside A was achieved in 3.1% total yield from D-glucose in nine steps.

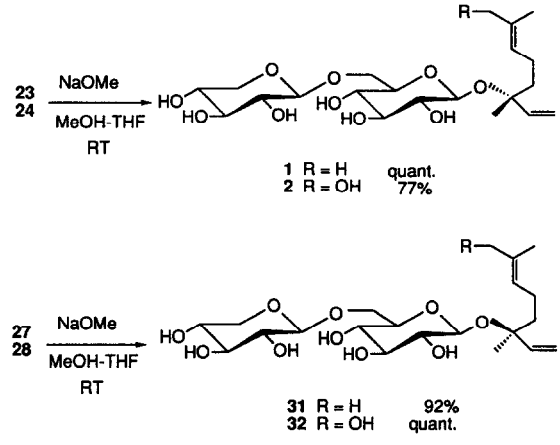


Scheme 4.



Scheme 5.

Determination of absolute configuration of **1**.— Our procedure to determinate the absolute configuration at C-3 of neohancoside A (**1**) involves cleavage of the glycosylic linkage of compound **19** and **21** to isolate chiral linalool as illustrated in Scheme 7. Debenzoylation of **19** and **21** using sodium methoxide in a solvent of THF–MeOH afforded glycosides **33** and **35**, in 94% and 94% yields, respectively. It is well known that linalool is easily isomerized to other compounds under acidic conditions. In fact, we failed in the hydrolysis of natural neohancoside A (**1**) to isolate linalool under the acidic conditions of 5% HCl–MeOH, which are the usual conditions for cleaving a glycosylic linkage, and alternatively, obtained an unknown compound from the chemical degradation of linalool. Therefore the glycosylic linkage of **33** and **35** was cleaved by enzymatic hydrolysis using β-glucosidase in Na_2HPO_4–citrate buffer under incubation at 37 °C for 53 h and 90 h, respectively, to give each chiral linalool **37** and **39** in 83% and 88% yield, respectively. Measurements of the



Scheme 6.

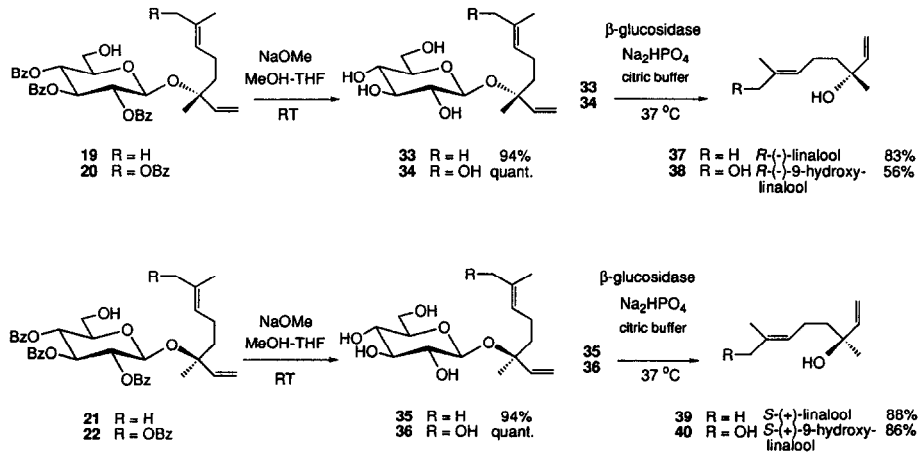
Table 1
Comparison of ^{1}H NMR data of neohancoside A, **1**, and **31**

Number	Neohancoside A [a] δ ^{1}H mult (J)	**1** [a] δ ^{1}H mult (J)	**31** [a] δ ^{1}H mult (J)
H-1a	5.19 dd (17.5, 1.5)	5.19 dd (17.5, 1.0)	5.23 dd (17.0, 1.0)
H-1b	5.12 dd (10.8, 1.5)	5.12 dd (11.0, 1.0)	5.18 dd (11.0, 1.0)
H-2	6.33 dd (17.5, 10.8)	6.32 dd (17.5, 11.0)	6.15 dd (17.0, 11.0)
H_2-4	1.73 t (8.3)	1.72 t (8.5)	1.64 m
H_2-5	2.18 m	2.19 m	2.11 m
H-6	5.11 m	5.11 m	5.04 t (7.0)
H_3-8	1.52 s	1.52 s	1.50 s
H_3-9	1.45 s	1.45 s	1.41 s
H_3-10	1.41 s	1.41 s	1.50 s
H-1′	4.80 d (7.8)	4.79 d (8.0)	4.82 d (8.0)
H-2′	3.83 dd (8.2, 7.8)	3.82 dd (8.5, 8.0)	3.84 dd (8.5, 8.0)
H-3′	4.07 t (8.2)	4.08 t (8.5)	4.05 t (8.5)
H-4′	4.06 t (8.2)	4.07 t (8.5)	4.04 t (8.5)
H-5′	3.86 m	3.86 m	3.87 m
H-6′a	4.21 dd (11.0, 4.5)	4.22 dd (11.0, 5.0)	4.19 dd (11.0, 5.5)
H-6′b	4.61 dd (11.0, 2.0)	4.60 dd (11.0, 2.0)	4.64 dd (11.0, 2.0)
H-1″	4.87 d (7.1)	4.87 d (7.0)	4.88 d (7.5)
H-2″	3.91 dd (8.5, 7.1)	3.90 dd (8.0, 7.0)	3.92 dd (8.0, 7.5)
H-3″	4.02 t (8.5)	4.01 t (8.0)	4.02 t (8.0)
H-4″	4.09 ddd (9.7, 8.5, 4.6)	4.09 ddd (10.0, 8.0, 4.0)	4.10 m
H-5″a	3.53 dd (11.0, 9.7)	3,55 dd (11.0, 10.0)	3.56 dd (11.0, 10.0)
H-5″b	4.21 dd (11.0, 4.6)	4.20 dd (11.0, 4.5)	4.22 dd (11.0, 5.0)

[a] Assignments were made by ^{1}H–^{1}H COSY and HOHAHA spectra. Spectra were taken at 400 MHz in pyridine-d_5.

optical rotation, **37**: $[\alpha]_D^{27}$ −3.04° (*c* 0.33, $CHCl_3$); **39**: $[\alpha]_D^{27}$ +8.00° (*c* 0.45, $CHCl_3$); revealed that **37** is (*R*)-(−)-linalool, lit. $[\alpha]_D^{20}$ −20.7° (*c* 0.18, $CHCl_3$) [11]; and **39** is (*S*)-(+)-linalool, lit. $[\alpha]_D^{23}$ +11.9° (*c* 2.29, $CHCl_3$) [12]; by comparison with the values in the literature. Both values of the optical rotations of **37** and **39** are smaller than the values in the literature. This is because that linalool is very volatile oil (bp 110 °C/12 torr), which makes it difficult to completely remove the solvent (CH_2Cl_2) from small amounts of oily compound. This result forced us to degrade both compounds **33** and **35** and to compare the signs of the $[\alpha]$ of the recovered linalools to the signs of the (*R*)- and (*S*)-linalool reported. Thus, the configuration of **19** and **21** at C-3 of linalool was determined to be 3*R* and 3*S*, respectively, and, hence, the configuration of neohancoside A (**1**) was determined to be 3*R*.

Synthesis of neohancoside B (**2**).—Neohancoside B (**2**) is a monoterpene diglycoside containing the



Scheme 7.

Table 2
Comparison of ^{13}C NMR data of neohancoside A, **1**, and **31**

Position	Neohancoside A [a]	**1** [a] δ_c	**31** [a]
C-1	114.29 t	114.26 t	115.00 t
C-2	144.52 d	144.49 d	144.52 d
C-3	80.21 s	80.18 s	80.27 s
C-4	40.99 t	40.97 t	42.32 t
C-5	23.22 t	23.20 t	23.16 t
C-6	125.68 d	125.65 d	125.48 d
C-7	131.14 s	131.10 s	131.16 s
C-8	25.91 q	25.89 q	25.85 q
C-9	17.91 q	17.89 q	17.81 q
C-10	24.40 q	24.39 q	23.75 q
C-1′	99.55 d	99.52 d	99.83 d
C-2′	75.26 d	75.23 d	75.37 d
C-3′	78.86 d	78.83 d	78.86 d
C-4′	71.74 d	71.76 d	71.82 d
C-5′	76.97 d	76.93 d	76.95 d
C-6′	70.02 t	70.01 t	70.13 t
C-1″	105.91 d	105.87 d	105.88 d
C-2″	75.02 d	74.96 d	75.00 d
C-3″	78.24 d	78.16 d	78.24 d
C-4″	71.29 d	71.25 d	71.28 d
C-5″	67.19 t	67.14 t	67.21 t

[a] Assignments were made by DEPT and HMQC spectra. Spectra were taken at 100.6 MHz in pyridine-d_5.

Table 3
Comparison of ^1H NMR data of neohancosidc B, **2**, and **32**

Position	Neohancoside B [a] δ ^1H (J)	**2** [a] δ ^1H (J)	**32** [a] δ ^1H (J)
H-1a	5.11 d (17.5)	5.11 dd (17.5, 1.5)	5.23 dd (17.5, 1.5)
H-1b	5.18 d (11.0)	5.18 dd (11.0, 1.5)	5.18 dd (11.0. 1.5)
H-2	6.31 dd (17.5, 11.0)	6.31 dd (17.5, 11.0)	6.15 dd (17.5, 11.0)
H_2-4	1.77 t (8.3)	1.77 t (8.5)	1.68 m
H_2-5	2.30 m	2.30 m	2.21 m
H-6	5.62 t (7.0)	5.62 t (7.0)	5.55 t (7.0)
H_3-8	4.15 s	4.15 s	4.13 s
H_3-9	1.66 s	1.66 s	1.62 s
H_3-10	1.41 s	1.41 s	1.51 s
H-1′	4.80 d (8.0)	4.80 d (7.5)	4.81 d (8.0)
H-2′	3.83 t (8.0)	3.83 dd (9.0, 7.5)	3.84 dd (9.0, 8.0)
H-3′	4.06 m	4.06 t (9.0)	4.05 t (9.0)
H-4′	4.06 m	4.06 t (9.0)	4.05 t (9.0)
H-5′	3.87 m	3.86 m	3.88 m
H-6′a	4.20 dd (11.0, 4.7)	4.19 dd (11.0, 5.0)	4.19 dd (11.5, 6.0)
H-6′b	4.62 dd (11.0, 2.0)	4.61 dd (11.0, 2.0)	4.63 dd (11.5, 2.0)
H-1″	4.88 d (8.5)	4.88 d (7.0)	4.88 d (7.5)
H-2″	3.91 t (8.5)	3.90 dd (8.5, 7.0)	3.91 dd (8.0, 7.5)
H-3″	4.02 t (8.5)	4.02 t (8.5)	4.02 t (8.0)
H-4″	4.09 ddd (10.0, 8.5, 4.0)	4.09 ddd (9.5, 8.5, 4.0)	4.09 ddd (9.5, 8.0, 4.5)
H-5″a	3.55 dd (11.0, 10.0)	3.55 dd (11.0, 9.5)	3.68 dd (10.5, 9.5)
H-5″b	4.21 dd (11.0, 4.0)	4.21 dd (11.0,4.0)	4.21 dd (10.5, 4.5)
OH-9	6.06 s	–	–

[a] Assignments were made by ^1H–^1H COSY and HOHAHA spectra. Spectra were taken at 400 MHz in pyridine-d_5.

same disaccharide as **1** but having 8-hydroxylinalool as the aglycone in place of linalool in **1**. Neohancoside **2** was totally synthesized using racemic 8-hydroxylinalool by essentially the same procedure as in the case of **1** (Scheme 5). The starting material, (±)-8-hydroxylinalool, was prepared by oxidation of (±)-linalool using SeO_2 as described [13]. (±)-8-Hydroxylinalool was converted to (±)-8-benzoyloxylinalool using the usual procedure. The glycosyl fluoride **12b** was linked to (±)-8-benzoyloxylinalool by a glycosylation reaction to afford a mixture of diastereomers **18** in 55% yield (3*R*:3*S* = 1.4:1). Removal of the chloroacetyl group and purification of the products by chromatography provided **20** (3*R*) and **22** (3*S*) in 42% and 36% yield, respectively. Glycosylation of **20** with **5** provided diglycoside **24** in high yield (67%), together with a small amount of orthoester **26** (7%). Deprotection of the benzoyl group of **24** provided neohancoside B (**2**) in 77% yield as shown in Scheme 6. Compound **2** showed mp 46–48° C (EtOAc) and $[\alpha]_D^{28}$ −27.3° (MeOH); and **2** was identical in all respects ($[\alpha]_D$, HRMS, and ^1H and ^{13}C NMR) with natural neohancoside B [5]. ^1H and ^{13}C NMR spectra of **2** were superimposable with those of the natural products (Tables 3 and 4). Another diastereomer **22** was similarly glycosylated to afford diglycoside **28** and orthoester **30** in 79% and 9% yield, respectively, followed by deprotection of **28** to quantitatively provide **32**. Compound **32** shows mp 33–35 °C and $[\alpha]_D^{21}$ of −28.6°. The ^1H and ^{13}C NMR spectra of **28** were clearly distinguishable from those of natural neohancoside B. Thus, a total synthesis of **2** was achieved in 4.0% total yield from D-glucose.

Absolute configuration of **2**.—The absolute configuration at C-3 of **2** was determined by the same procedure as for **1** (Scheme 7). Deprotection of **20** and **22** quantitatively gave **34** and **36**, followed by enzymatic hydrolysis to afford *R*-(−)-8-hydroxylinalool (**38**), $[\alpha]_D^{25}$ −5.95° (*c* 0.57, $CHCl_3$), lit. $[\alpha]_D^{22}$ −12.8° (*c* 0.05, MeOH) [14]; and *S*-(+)-8-hydroxylinalool (**40**), $[\alpha]_D^{26}$ +7.13° *c* 0.76, $CHCl_3$), lit. $[\alpha]_D^{24}$ +20.0° (*c* 0.20, MeOH) [12]; in 56% and 86% yield, respectively. From these results, the absolute configuration at C-3 of neohancoside B was also determined to be *R*.

NMR spectral analysis of disaccarides and their orthoesters.—As shown in Schemes 2 and 5, upon the glycosylation of **4a**, **4b**, **19**, **20**, **21** and **22**, we always obtained orthoesters **41a**, **41b**, **25**, **26**, **29** and **30** as byproducts, together with the desired disaccharyl glycosides **6a**, **6b**, **23**, **24**, **27** and **28**, respectively. The structures of these six disaccaryl glycosides and their corresponding orthoesters were determined by ^1H, ^{13}C, ^1H–^1H COSY, DEPT, HMQC, and HMBC spectral analysis. Each pair of **6a** and **41a**, **6b** and

Table 4
Comparison of ^{13}C NMR data of neohancoside B, **2**, and **32**

Position	Neohancoside B [a]	**2** [a] δ_c	**32** [a]
C-1	114.29 t	114.30 t	115.03 t
C-2	144.46 d	144.45 d	144.49 d
C-3	80.12 s	80.14 s	80.24 s
C-4	40.68 t	40.68 t	42.15 t
C-5	22.78 t	22.78 t	22.78 t
C-6	125.16 d	125.17 d	125.01 d
C-7	136.30 s	136.33 s	136.44 s
C-8	68.23 t	68.23 t	68.21 t
C-9	14.12 q	14.12 q	14.08 q
C-10	24.54 q	24.53 q	23.81 q
C-1′	99.55 d	99.53 d	99.84 d
C-2′	75.26 d	75.25 d	75.37 d
C-3′	78.85 d	78.84 d	78.86 d
C-4′	71.78 d	71.76 d	71.82 d
C-5′	77.02 d	77.01 d	77.00 d
C-6′	70.03 t	70.03 t	70.12 t
C-1″	105.87 d	105.85 d	105.86 d
C-2″	75.00 d	74.99 d	75.01 d
C-3″	78.20 d	78.20 d	78.25 d
C-4″	71.27 d	71.27 d	71.30 d
C-5″	67.16 t	67.15 t	67.22 t

[a] Assignments were made by DEPT and HMQC spectra. Spectra were taken at 100.6 MHz in pyridine-d_5.

Table 5
^{1}H NMR chemical shift data [a] of the sugar moiety of the disaccharides and their orthoesters

Position	6a δ_c	6b	23	24	27	28	41a	41b	25	26	29	30
H-1′	6.20	6.80	4.78	4.78	4.79	4.79	6.20	6.82	4.79	4.80	4.83	4.83
H-2′	5.76	5.49	5.44	5.45	5.44	5.45	5.82	5.66	5.49	5.50	5.50	5.51
H-3′	5.98	6.24	5.82	5.84	5.83	5.82	5.94	6.22	5.78	5.79	5.78	5.62
H-4′	5.62	5.68	5.38	5.42	5.43	5.38	5.76	5.84	5.57	5.58	5.54	5.54
H-5′	4.28	4.50	3.98	3.94	3.94	3.97	4.15	4.34	3.76	3.77	3.80	3.81
H-6′a	3.90	3.82	3.77	3.76	3.75	3.77	3.60	3.49	3.46	3.47	3.45	3.45
H-6′b	4.08	4.09	3.98	4.01	4.01	4.01	3.60	3.60	3.54	3.56	3.57	3.57
H-1″	4.94	4.89	4.90	4.88	4.88	4.89	5.94	5.91	5.89	5.90	5.90	5.94
H-2″	5.35	5.38	5.36	5.38	5.36	5.37	4.65	4.67	4.58	4.58	4.60	4.61
H-3″	5.70	5.73	5.72	5.72	5.72	5.72	5.64	5.66	5.64	5.65	5.67	5.67
H-4″	5.21	5.22	5.23	5.22	5.21	5.23	5.26	5.25	5.22	5.24	5.25	5.25
H-5″a	3.70	3.70	3.66	3.67	3.68	3.66	3.60	3.60	3.64	3.64	3.64	3.64
H-5″b	4.41	4.41	4.38	4.38	4.38	4.38	4.10	4.10	4.11	4.11	4.12	4.12

[a] Assignments were made by ^{1}H–^{1}H COSY, HMQC, and HMBC spectra. Spectra were taken at 400 MHz in pyridine-d_5.

41b, **23** and **25**, **24** and **26**, **27** and **29**, **28** and **30** had the same molecular formula by HRMS, indicating structural isomers, respectively. In the HMBC spectra of **6b** and **24** and **28**, the correlation of C-1″ in the xylose unit to 6′-Ha in the glucose unit was observed in each compound, whereas the HMBC spectrum of **41b**, **26**, and **30** showed correlation of benzylidene-C to H-6′a in the glucose unit, to H-1″ in the xylose unit and to phenyl proton of benzylidene. The HMBC spectrum of **26** also showed a correlation of the benzylidene-C to H-2″ in the xylose unit as shown in Fig. 1. From these results we determined the structure of the **6b**, **24** and **28** group as the desired disaccharides and the **41b**, **26**, and **30** groups as their orthoesters. Chemical shifts and *J*-values of these six disaccharides of **6a**, **6b**, **23**, **24**, **27**, and **28** and the six orthoesters of **41a**, **41b**, **25**, **26**, **29**, and **30** are provided in Tables 5 and 6.

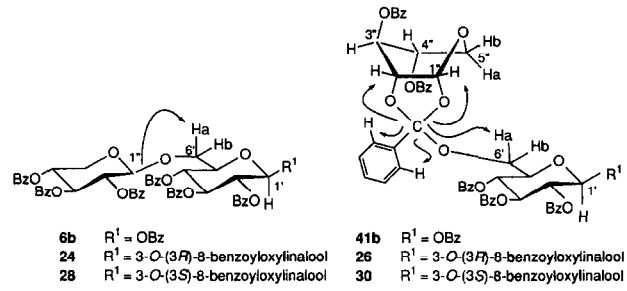


Fig. 1. The HMBC correlation of disaccharides **6b**, **24**, **28** and their orthoesters **41b**, **26**, **30** (arrows show the HMBC correlation).

The group of disaccharides shows common charac-

Table 6
Coupling constants of the sugar moieties for the disaccharides and their orthoesters

Position	6a *J* (Hz)	6b	23	24	27	28	41a	41b	25	26	29	30
$J_{1',2'}$	8.0	4.0	8.0	8.0	8.0	8.0	7.5	4.0	8.0	8.0	8.0	8.0
$J_{2',3'}$	10.0	10.0	10.0	9.5	9.5	9.5	10.0	10.0	9.5	9.5	10.0	9.5
$J_{3',4'}$	10.0	10.0	10.0	9.5	9.5	9.5	10.0	10.0	9.5	9.5	9.5	10.0
$J_{4',5'}$	10.0	10.0	10.0	9.5	9.5	9.5	10.0	10.0	9.2	9.5	10.0	9.5
$J_{5',6'Ha}$	6.0	5.0	7.0	7.0	1.0	7.0	3.5	3.0	3.0	3.0	3.0	2.5
$J_{5',6'Hb}$	2.0	2.5	m	2.0	2.0	2.0	3.5	4.0	4.5	4.5	5.0	5.0
$J_{6'Ha,b}$	12.0	12.0	11.0	11.0	10.5	11.0	m	11.0	10.5	10.5	11.0	10.5
$J_{1'',2'}$	4.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	4.5	5.0	5.0
$J_{2'',3''}$	6.0	6.5	7.0	6.5	6.5	7.0	3.0	3.5	3.0	3.0	3.0	3.0
$J_{3'',4''}$	6.0	6.5	7.0	6.5	6.5	7.0	3.0	3.5	3.0	3.0	3.0	3.0
$J_{4'',5''Ha}$	5.5	6.5	7.0	6.5	6.5	7.0	3.0	3.5	3.0	3.0	3.0	3.0
$J_{4'',5''Hb}$	4.0	4.0	4.0	4.0	4.0	4.0	4.0	7.5	7.0	7.0	7.0	7.0
$J_{5''Ha,b}$	13.0	12.0	12.0	12.5	12.0	12.0	13.5	12.0	12.0	12.0	12.5	12.0

teristics as described below.

(1) The chemical shift values of xylose units almost coincide with each other. (2) Considering the values of $J_{2',3'} = J_{3',4'} = J_{4',5'}$ Hz, it is assumed that the glucose unit takes the typical $^4C_1$ conformation. (3) The values of $J_{1'',2''} = 4.0–5.0$, $J_{2'',3''} = J_{3'',4''} = 6.0–7.0$ Hz in the xylose units indicate a somewhat flattened $^4C_1$ chair form arising from the repulsion between the 1-glycosyl group and 2-*O*-benzoyl, 2- and 3-*O*-benzoyl, and 3- and 4-*O*-benzoyl groups, respectively.

The group of orthoesters shows common characteristics as described below.

(1) The chemical shift values of xylose units almost coincide with each other. (2) The *J*-values show that glucose units assume the typical chair conformation of $^4C_1$. (3): The chemical shift of H-2 (δ 4.58–4.67) in the xylose units is found at higher field due to the benzylidene group present in the orthoester instead of a benzoyl group at C-2 as in the disaccharides, whereas the chemical shift of H-1 (δ 5.89–5.94) in xylose is found at lower field due to the anomeric effect. (4) The *J* values ($J_{2'',3''} = J_{3'',4''} = J_{4'',5''Ha} = 3.0$, $J_{4'',5''Hb} = 7.0$ Hz) for the xylose units indicate that H-2, H-3 and H-4 should be equatorial protons, and it is assumed that the xylose units assume a boat conformation as shown in Fig. 1.

From the above results, we can summarize that the stereostructure of **6a**, **6b**, **23**, **24**, **27**, and **28** resemble each other and are determined to be the desired disaccharide, and **41a**, **41b**, **25**, **26**, **29**, and **30** also assume a similar stereostructure and are determined to be the corresponding orthoester. The glucose unit assumes a typical $^4C_1$ chair conformation in both the disaccharide and orthoester, and the xylose unit assumes a somewhat flattened $^4C_1$ conformation in the disaccharide and a boat conformation in the orthoester as indicated by chemical shifts and *J* values in the ^{1}H NMR spectra.

In conclusion, total syntheses of two monoterpene diglycosides from *Cynanchum hancockianum*, neohancoside A (**1**) and B (**2**), were achieved for the first time, and their absolute stereostructures were determined. The conformations of the disaccharides and their orthoesters were determined by NMR spectral measurements.

3. Experimental

Acetonitrile, pyridine, MeOH, *N*,*N*-dimethylformamide (Me_2NCHO) were dried over molecular sieves. CH_2Cl_2 and tetrahydrofuran were dried by refluxing with CaH_2 and sodium, respectively, and AgOTf and $AgClO_4$ were dried over P_2O_5 for 1 h at 75 °C. Molecular sieves used in the glycosylation were dried by a heating mantle for 1 h. Flash column chromatography was performed on Silica Gel-60H (E. Merck). Thin-layer chromatography (TLC) was done on Silica Gel 60 PF_{254} (E. Merck). Melting points were taken on a Yanagimoto hot-stage and are uncorrected. Optical rotations were measured on a JASCO model DPI-181 polarimeter ^{1}H and ^{13}C NMR were recorded on Varian VXR-300 and XL-400 spectrometers ^{1}H NMR chemical shifts in pyridine-d_6 are set at δ 8.60 for reference. The signals were assigned by ^{1}H–^{1}H COSY, DEPT, HMQC, and HMBC experiments. Mass spectra were obtained on a JEOL-JMX-DX 300 mass spectrometer (low-resolution mass spectrometry) and a JEOL-JMS-AX505 HA mass spectrometer (high-resolution mass spectrometry).

2,3,4-Tri-O-benzoyl-β-D-xylopyranosyl-(1 → 6)-1,2,3,4-tetra-O-benzoyl-α and β-D-glucopyranoses (**6a** *and* **6b**).—(1) Compound **4a** (224 mg, 0.38 mmol), AgOTf (126 mg, 0.49 mmol) in dry toluene (0.2 mL), and 2,4,6-collidine (59.3 mg, 0.49 mmol) were added to a mixture of MS-4A (672 mg) and CH_2Cl_2 (5 mL) under argon at −20 °C, and the mixture was stirred for 15 min. Xylosyl bromide **5** (296 mg, 0.56 mmol) was then added and stirred for 42 h. The reaction mixture was filtered through a Celite pad. The filtrate was diluted with $CHCl_3$ (100 mL), washed with 10% aqueous $Na_2S_2O_4$ (10 mL), water (10 mL), 0.5 M H_2SO_4 (10 mL), saturated $NaHCO_3$ (10 mL), water (10 × 2 mL), dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) to give **6a** (312.7 mg, 80%) and **41a** (78.2 mg, 20%) as white crystals. **6a**: mp 100–102 °C. $[\alpha]_D^{27}$ +31.89° (*c* 1.04, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.24–8.14 (35 H, ArH); other signals are listed in Tables 5 and 6. ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 60.89 (t, C-5′), 67.13 (t, C-6), 68.67 (d, C-4), 68.89 (d, C-4′), 69.68 (d, C-3′), 69.72 (d, C-2′), 70.39 (d, C-3), 70.58 (d, C-2), 71.78 (d, C-5), 90.01 (d, C-1), 100.11 (d, C1′), 128.19–133.74 (ArC), 164.32–165.82 (CO). HRFABMS *m/z*: Calcd for $C_{60}H_{48}O_{17}$ + Na 1063.2789. Found: 1063.2844. Anal. Calcd for $C_{60}H_{48}O_{17}$: C, 69.23; H, 4.65. Found: C, 68.94; H, 4.89. **41a**: mp 104–106 °C. $[\alpha]_D^{28}$ +66.38° (*c* 2.57, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.11–8.02 (35 H, ArH), see Tables 5 and 6. ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 59.40 (t, C-5′), 62.25 (t, C-6), 68.00 (d, C-4′), 68.60 (d, C-4), 69.04 (d, C-3′), 70.46 (d, C-2), 70.66 (d, C-3), 70.98 (d,

C-5), 72.87 (d, C-2′), 90.08 (d, C-1), 97.34 (d, C-1′), 120.97 (s, benzylidene C), 128.28–134.54 (ArC), 164.39–165.87 (CO). HRFABMS *m/z*: Calcd for $C_{60}H_{48}O_{17}$ + Na 1063.2789. Found: 1063.2786.

(2) Compound **4b** (100 mg, 0.17 mmol), AgOTf (560 mg, 0.22 mmol) in dry toluene (0.2 mL), and 2,4,6-collidine (26.4 mg, 0.22 mmol) were added to a mixture of MS-4A (300 mg) and CH_2Cl_2 (5 mL) under argon at −20 °C and stirred for 15 min. Xylosyl bromide **5** (114.2 mg, 0.22 mmol) was then added and stirred for 42 h. The reaction mixture was filtered through a Celite pad. The filtrate was diluted with $CHCl_3$ (100 mL), washed with 10% aqueous $Na_2S_2O_4$ (10 mL), water (10 mL), 0.5 M H_2SO_4 (10 mL), saturated $NaHCO_3$ (10 × 2 mL), and water (10 × 2 mL), and then dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) to give **6b** (133.7 mg, 77%) and **41b** (40.8 mg, 23%) as white crystals, respectively. **6b**: mp 113–115 °C. $[\alpha]_D^{28}$ −14.63° (*c* 2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.22–8.06 (35 H ArH), see Tables 5 and 6. ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 60.46 (t, C-5′), 67.26 (t, C-6), 68.63 (d, C-4′), 69.22 (d, C-3′), 69.50 (d, C-2′), 69.09 (d, C-4), 70.91 (d, C-2), 72.80 (d, C-3), 74.91 (d, C-5), 92.85 (d, C-1), 99.79 (d, C-1′), 128.18–133.68 (ArC), 164.54–165.62 (CO). HRFABMS *m/z*: Calcd for $C_{60}H_{48}O_{17}$ + Na 1063.2789. Found: 1063.2789. Anal. Calcd for $C_{60}H_{48}O_{17}$: C, 69.23; H, 4.65. Found: C, 68.99; H, 4.72. **41b**: mp 109–111 °C. $[\alpha]_D^{24}$ +10.20 °C (*c* 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.16–8.24 (35 H, ArH), see Tables 5 and 6. ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 59.47 (t, C-5′), 62.58 (t, C-6), 67.93 (d, C-4′), 68.92 (d, C-4), 69.04 (d, C-3′), 70.82 (d, C-2), 72.99 (d, C-3), 73.73 (d, C-2′), 73.72 (d, C-5), 92.72 (d, C-1), 97.30 (d, C-1′), 120.84 (s, benzylidene-C), 126.49–134.51 (ArC), 164.53–165.62 (CO). HRFABMS *m/z*: Calcd for $C_{60}H_{48}O_{17}$ + Na: 1063.2789. Found: 1063.2755. Anal. Calcd for $C_{60}H_{48}O_{17}$: C, 69.23; H, 4.65. Found: C, 69.07; H, 4.80.

*2,3,4-Tri-*O*-benzoyl-β-*D*-xylopyranosyl-(1 → 6)-2,3,4-tri-*O*-benzoyl-α-*D*-glucopyranosyl bromide* (**7**).—Compound **6a** (20 mg, 0.02 mmol) was dissolved in dry CH_2Cl_2 at 15 °C under argon, 30% HBr–HOAc (0.3 mL) was added, and the mixture was stirred for 4 h. The reaction mixture was neutralized with saturated $NaHCO_3$ at 0 °C and diluted with $CHCl_3$ (50 mL), washed with water (10 mL), dried over Na_2SO_4 and concentrated in vacuo to afford crude product **7** (27.0 mg). **7**: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.87 (1 H, d, *J* 4.0 Hz, H-1).

*A mixture of 2,3,4-tri-*O*-benzoyl-β-*D*-xylopyranosyl-(1 → 6)-2,3,4-tri-*O*-benzoyl-α and β-*D*-glucopyranose* (**8a** *and* **8b**).—(1) Compound **6a** (20 mg, 0.02 mmol) was dissolved in dry Me_2NCHO (1 mL) under argon, and hydrazine acetate (2.3 mg, 0.025 mmol) was added. After the solution had stirred at 60 °C for 2 h, the reaction mixture was concentrated. Water (30 mL) was added to the residue, and the mixture was extracted with $CHCl_3$ (20 mL × 3). The organic layer was washed with water (10 mL), dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) to afford white crystals **8** (5.0 mg, 28%) as a mixture of anomers **8a** and **8b** (**8a**:**8b** = 3:1). Compound **8** was not separated, and NMR assignment of **8a** was carried out as an anomeric mixture. **8**: mp 253–255 °C, $[\alpha]_D$ −3.71° (*c* 0.70, $CHCl_3$). HRFABMS *m/z*: Calcd for $C_{53}H_{44}O_{16}$ + Na: 959.2527. Found: 959.2513. Anal. Calcd for $C_{53}H_{44}O_{16}$: C, 67.94; H, 4.73. Found: C, 67.55; H, 4.70. **8a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.11 (1 H, br, OH-1), 3.70 (1 H, dd, *J* 7.0, 12.0 Hz, H-5′a), 3.79 (1 H, dd, *J* 7.0, 12.0 Hz, H-6a), 4.01 (1 H, dd, *J* 2.0 12.0 Hz, H-6b), 4.41 (1 H, dd, *J* 4.0, 12.0 Hz, H-5b), 4.52 (1 H, m, H-5), 4.98 (1 H, d, *J* 5.0 Hz, H-1′), 5.16 (1 H, dd, *J* 3.5, 10.0 Hz, H-2), 5.28 (1 H, m, H-4′), 5.37 (1 H, dd, *J* 7.0, 5.0 Hz, H-2′), 5.39 (1 H, t, *J* 10.0 Hz, H-4), 5.48 (1 H, t, *J* 3.5 Hz, H-1), 5.76 (1 H, t, *J* 7.0 Hz, H-3′), 6.14 (1 H, t, *J* 10.0 Hz, H-3), 7.22–8.06 (30 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 61.06 (t, C-5′), 68.39 (t, C-6), 69.53 × 2 (each d, C-4, C-5), 68.93 (d, C-4′), 69.93 (d, C-3′), 70.55 (d, C-2′), 70.61 (d, C-3), 72.19 (d, C-2), 90.19 (d, C-1), 100.69 (d, C-1′), 128.20–133.70 (ArC), 164.70–164.80 (CO). HRFABMS *m/z*: Calcd for $C_{53}H_{44}O_{16}$ + Na: 959.2527. Found: 959.2513. (2) The reaction was carried out with **6b** under the same procedure as **6a** using **6b** (100 mg, 0.01 mmol), hydrazine acetate (11.5 mg, 0.013 mmol) in Me_2NCHO (3 mL) for 2 h to afford white crystals of **8** (66.6 mg, 74%) as a mixture of anomers **8a** and **8b** (**8a**:**8b** = 3:1).

*2,3,4-Tri-*O*-benzoyl-β-*D*-xylopyranosyl-(1 → 6)-2,3,4-tri-*O*-benzoyl-α and β-*D*-glucopyranosyl fluorides* (**9a** *and* **9b**).—Anomeric mixture **8** (50 mg, 0.05 mmol) was dissolved in dry CH_2Cl_2 (3 mL) at −30 °C under argon, DAST (0.1 mL, 0.76 mmol) was added, and the mixture was stirred for 10 min. The reaction mixture was neutralized with saturated $NaHCO_3$ (2 mL) at −30 °C, diluted with $CHCl_3$ (100 mL), washed with water (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) affording

light yellow crystals of **9** (36.5 mg, 72.9%) as a mixture of anomers. Compound **9** was separated by preparative TLC (3:1 n-hexane–EtOAc) to afford **9a** (11.6 mg, 32%) and **9b** (10.9 mg, 30%). **9a**: mp 232–234 °C. $[\alpha]_D^{28}$ +8.27° (*c* 0.87, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 3.71 (1 H, dd, *J* 6.5, 12.0 Hz, H-5'a), 3.80 (1 H, dd, *J* 5.5, 11.5 Hz, H-6a), 4.10 (1 H, dd, *J* 2.0, 11.5 Hz, H-6b), 4.42 (1 H, dd, *J* 4.0, 12.0 Hz, H-5'b), 4.46 (1 H, ddd, *J* 2.0, 5.5, 10.0 Hz, H-5), 5.90 (1 H, d, *J* 5.0 Hz, H-1'), 5.22 (1 H, ddd, *J* 3.0, 10.0, 23.5 Hz, H-2), 5.26 (1 H, dt, *J* 4.0, 6.5 Hz, H-4'), 5.42 (1 H, dd, *J* 5.0, 6.5 Hz, H-2'), 5.60 (1 H, t, *J* 10.0 Hz, H-4), 5.75 (1 H, t, *J* 6.5 Hz, H-3'), 5.92 (1 H, dd, *J* 3.0, 52.5 Hz, H-1), 6.12 (1 H, t, *J* 10.0 Hz, H-3), 7.26–8.06 (30 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 60.94 (t, C-5'), 67.01 (t, C-6), 68.12 (d, C-4), 68.86 (d, C-4'), 69.65 (d, C-3), 69.72 (d, C-2'), 69.72 (d, C-3'), 71.36 (d, $J_{C\text{-}2,F}$ 9.5 Hz, C-2), 71.55 (d, C-5), 100.26 (d, C-1'), 103.90 (d, $J_{C\text{-}1,F}$ 34.5 Hz, C-1), 128.27–133.62 (ArC), 164.91–165.58 (CO). HRFABMS *m/z*: Calcd for $C_{53}H_{43}FO_{15}$ + Na: 961.2484. Found: 961.2483. Anal. Calcd for $C_{53}H_{43}FO_{15}$: C, 67.80; H, 4.61. Found: C, 67.44; H, 4.73. **9b**: mp 252–254 °C. $[\alpha]_D^{28}$ −10.20° (*c* 1.02, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.68 (1 H, dd, *J* 7.0, 12.0, 5'-Ha), 3.90 (dd, *J* 6.5, 11.0 Hz, H-6a), 4.16 (2 H, m, H-5, H-6b), 4.40 (1 H, dd, *J* 4.0, 12.0 Hz, H-5'b), 4.92 (1 H, d, *J* 5.0, H-1'), 5.17 (t, *J* 9.0, H-4), 5.26 (dt, *J* 4.0, 7.0 Hz, H-4'), 5.37 (dd, *J* 5.0, 7.0 Hz, H-2'), 5.43 (dd, *J* 5.5, 47.0 Hz, H-1), 5.56 (ddd, *J* 5.5, 7.5, 9.0 Hz, H-2), 5.57 (t, *J* 9.0 Hz, H-3), 5.76 (t, *J* 7.0 Hz, H-3), 7.25–8.07 (30 H, ArH). ^{13}C NMR δ: 61.17 (t, C-5'), 68.17 (d, C-4), 68.17 (t, C-6), 69.00 (d, C-4'), 70.00 (d, C-3'), 70.04 (d, C-2'), 71.29 (d, $J_{C\text{-}3,F}$ 8.3 Hz, C-3), 72.78 (d, $J_{C\text{-}2,F}$ 29.0 Hz, C-2), 74.11 (d, $J_{C\text{-}5,F}$ 3.1 Hz, C-5), 100.78 (d, C-1'), 106.52 (d, $J_{C\text{-}1,F}$ 220.5 Hz, C-1), 128.29–123.55 (ArC), 164.82–165.49 (CO). HRFABMS *m/z*: Calcd for $C_{53}H_{43}FO_{15}$ + Na: 961.2484. Found: 961.2507. Anal. Calcd for $C_{53}H_{43}FO_{15}$: C, 67.80; H, 4.61. Found: C, 67.82; H, 4.78.

A mixture of 1, 2, 3, 4-tetra-O-benzoyl-6-O-chloroacetyl-α and β-D-glucopyranoses (**10a** *and* **10b**).—An anomeric mixture of **4** was dissolved in dry CH_2Cl_2 (15 mL) under argon. Pyridine (1 mL) was added, and then chloroacetyl chloride (102.8 mg, 0.91 mmol) was added dropwise at 0 °C over a 30 min period with stirring that was continued for 2.5 h. The reaction mixture was diluted with $CHCl_3$ (50 mL) and washed with 2% HCl (10 mL), saturated $NaHCO_3$ (10 mL), and brine (20 mL), and then dried over Na_2SO_4, and concentrated. The residue was purified by preparative TLC (10:1 benzene–acetone) affording **10** as an anomeric mixture of **10a** and **10b** (470.0 mg, 91.3%, **10a**:**10b** = 6:7). **10**: mp 122–124 °C. $[\alpha]_D^{24}$ +27.85° (*c* 3.86, $CHCl_3$). HRFABMS *m/z*: Calcd for $C_{36}H_{29}ClO_{11}$ + Na 697.1267, 695.1296. Found: 697.1314, 695.1321. Anal. Calcd for $C_{36}H_{29}ClO_{11}$: C, 64.24; H, 4.34. Found: C, 63.85; H, 4.44. ^1H NMR (300 MHz, $CDCl_3$) **10a**: δ 4.11, 4.14 (each 1 H, d, *J* 16.0 Hz, $COCH_2Cl$), 4.38 (1 H, dd, *J* 2.5, 12.0 Hz, H-6a), 4.47 (1 H, dd, *J* 5.0, 12.0 Hz, H-6b), 4.52 (1 H, m, H-5), 5.65 (1 H, dd, *J* 3.5, 10.0 Hz, H-2), 5.75 (1 H, t, *J* 10.0 Hz, H-4), 6.31 (1 H, t, *J* 10.0 Hz, H-3), 6.83 (1 H, d, *J* 3.5 Hz, H-1), 7.25–8.20 (20 H, ArH). **10b**: δ 4.11, 4.13 (each 1 H, d, *J* 16.0 Hz, $COCH_2Cl$), 4.29 (1 H, ddd, *J* 2.5, 5.0, 10.0 Hz, H-5), 4.38 (1 H, dd, *J* 2.5, 12.0 Hz, H-6a), 4.47 (1 H, dd, *J* 5.0, 12.0 Hz, H-6b), 5.71 (1 H, t, *J* 10.0 Hz, H-4), 5.84 (1 H, dd, *J* 8.0, 10.0 Hz, H-2), 6.03 (1 H, t, *J* 10.0 Hz, H-3), 6.25 (1 H, d, *J* 8.0 Hz, H-1), 7.25–8.06 (20 H, ArH).

2, 3, 4-Tri-O-benzoyl-6-O-chloroacetyl-α-D-glucopyranose (**11**).—An anomeric mixture of **10** (30 mg, 0.05 mmol) was dissolved in dry Me_2NCHO (1 mL) under argon, and hydrazine acetate (5.4 mg, 0.06 mmol) was added. After the solution was stirred at 15 °C for 5 h, the reaction mixture was concentrated. Water (10 mL) was added to the residue, and the mixture was extracted with $CHCl_3$ (30 mL × 3). The organic layer was washed with brine (6 mL), then water (6 mL), and the extracts were dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) to afford **11** as a white powder (8.9 mg, 42%). **11**: mp 60–62 °C. $[\alpha]_D^{26}$ +26.75° (*c* 2.31, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 3.08 (1 H, br, OH-1), 4.13, 4.14 (each 1 H, d, *J* 15.0 Hz, $COCH_2Cl$), 4.38 (1 H, dd, *J* 3.5, 11.O Hz, H-6a), 4.40 (1 H, dd, *J* 3.5, 11.0 Hz, H-6b), 4.57 (1 H, dt, *J* 3.5 10.0 Hz, H-5), 5.30 (1 H, dd, *J* 3.5, 10.0 Hz, H-2), 5.61 (1 H, t, *J* 10.0 Hz, H-4), 5.76 (1 H, d, *J* 3.5 Hz, H-1), 6.22 (1 H, t, *J* 10.0 Hz, H-3), 7.26–8.00 (15 H, ArH). HRFABMS *m/z*: Calcd for $C_{29}H_{25}ClO_{10}$ + Na: 593.1004, 591.1034. Found: 593.0989, 591.1039.

2,3,4-Tri-O-benzoyl-6-O-chloroacetyl-α and β-D-glucopyranosyl fluorides (**12a** *and* **12b**).—Compound **11** (10.0 mg, 0.02 mmol) was dissolved in dry CH_2Cl_2 (1 mL) at −30 °C under argon, then DAST (0.01 mL, 0.08 mmol) was added, and the mixture was stirred for 10 min. The mixture was then neutralized with saturated $NaHCO_3$ (3 mL), and extracted with $CHCl_3$ (20 mL). The organic layer was washed

with water (3 mL), dried over Na_2SO_4, and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) affording **12a** (1.0 mg, 9.6%) and **12b** (4.3 mg, 43.2%) as light yellow crystals. **12a**: mp 49–51 °C. $[\alpha]_D^{28}$ +31.74′ (*c* 0.76, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.15, 4.16 (each 1 H, d, *J* 15.0 Hz, $COCH_2Cl$), 4.41, 4.46 (each 1 H, dd, *J* 3.5, 12.5 Hz, H_2-6), 4.50 (1 H, dt, *J* 10.0, 3.5 Hz, H-5), 5.39 (1 H, ddd, *J* 3.0, 10.0, 24.0 Hz, H-2), 5.69 (1 H, t, *J* 10.0 Hz, H-4), 6.03 (1 H, dd, *J* 3.0, 48.0 Hz, H-1), 6.18 (1 H, t, *J* 10.0 Hz, H-3), 7.26–8.04 (15 H, ArH). HRFABMS *m/z*: Calcd for $C_{29}H_{24}ClFO_9$ + Na: 595.0961, 593.0990. Found: 595.1003, 593.1016. **12b**: mp 40–42 °C. $[\alpha]_D^{27}$ +22.35° (*c* 0.85, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.13, 4.14 (each 1 H, d, *J* 15.0 Hz, $COCH_2Cl$), 4.28 (1 H, dt, *J* 9.0, 4.5 Hz, H-5), 4.48, 4.50 (each 1 H, dd, *J* 4.5, 9.5 Hz, H_2-6, 5.67 (1 H, dd, *J* 5.0, 51.0 Hz, H-1), 5.67 (1 H, ddd, *J* 5.0, 7.5, 9.5 Hz, H-2), 5.70 (1 H, t, *J* 9.0 Hz, H-4), 5.84 (1 H, dd, *J* 7.5, 9.0 Hz, H-3), 7.26–8.04 (15 H, ArH). HRFABMS *m/z*: Calcd for $C_{29}H_{24}ClFO_9$ + Na: 595.0961, 593.0990. Found: 595.0956, 593.1016. Anal. Calcd for $C_{29}H_{24}ClFO_9$: C, 61.00; H, 4.24. Found: C, 60.78; H, 4.33.

*1,2,3,4-Tetra-*O*-benzoyl-6-*O*-triphenylmethyl-α and β-*D*-glucopyranoses* (**13a** *and* **13b**).—After a mixture of D-glucose (5 g, 27.8 mmol), 4-dimethylaminopyridine (1.7 g, 13.9 mmol), Et_3N (7.0 mL, 50.2 mmol) and triphenylmethyl chloride (9.2 g, 33.3 mmol) in Me_2NCHO (20 mL) was stirred for 18 h at room temperature, pyridine (83 mL) was added, then benzoyl chloride (25.8 mL, 223.7 mmol) was added in portions over a 30 min period −20 °C with stirring for addition 2 h. The reaction mixture was poured into ice-water (200 mL) and extracted with $CHCl_3$ (150 mL × 3). The combined organic layer was washed with 3N H_2SO_4 (50 mL × 2) and saturated $NaHCO_3$ (30 mL) and then dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (10:1 benzene–EtOAc) to afford **13** [15] as an anomeric mixture of **13a** and **13b** (10.60 g, 46%, **13a**:**13b** = 1:4). Compound **13** (30 mg) was separated by preparative TLC (toluene) to afford **13a** (5.1 mg) and **13b** (21.0 mg) as pale yellow crystals, respectively. **13a**: mp 94–96 °C, $[\alpha]_D^{26}$ +69.06° (*c* 1.37, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.22 (1 H, dd, *J* 2.0, 11.0 Hz, H-6a), 3.44 (1 H, dd, *J* 4.0, 11.0 Hz, H-6b), 4.37 (1 H, ddd, *J* 2.0, 4.0, 10.0 Hz, H-5), 5.72 (1 H, dd, *J* 3.5, 10.0 Hz, H-2), 5.89 (1 H, t, *J* 10.0 Hz, H-4), 6.20 (1 H, t, *J* 10.0 Hz, H-3), 6.93 (1 H, d, *J* 3.5 Hz, H-1), 6.90–8.20 (35 H, benzoyl × 4, trityl). HRFABMS *m/z*: Calcd for $C_{53}H_{42}O_{10}$ + Na: 861.2676. Found: 861.2684. Anal. Calcd for $C_{53}H_{42}O_{10}$: C, 75.88; H, 5.04. Found: C, 75.56; H, 5.34. **13b**: mp 82–84 °C. $[\alpha]_D^{26}$ −8.10° (*c* 0.42, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.24 (1 H, dd, *J* 4.0, 11.0 Hz, H-6a), 3.47 (1 H, dd, *J* 2.0, 11.0 Hz, H-6b), 4.10 (1 H, m, H-5), 5.84 (1 H, t, *J* 10.0 Hz, H-4), 5.85 (1 H, dd, *J* 7.0, 10.0 Hz, H-2), 5.87 (1 H, t, *J* 10.0 Hz, H-3), 6.25 (1 H, d, *J* 7.0 Hz, H-1), 7.00–8.10 (35 H, benzoyl × 4, trityl). HRFABMS *m/z*: Calcd for $C_{53}H_{42}O_{10}$ + Na: 861.2676. Found: 861.2671. Calcd for $C_{53}H_{42}O_{10}$: C, 75.88; H, 5.04. Found: C, 75.50; H, 5.21.

*2,3,4-Tri-*O*-benzoyl-6-*O*-triphenylmethyl-α-*D*-glucopyranose* (**14**).—Compound **13** (1.55 g, 1.85 mmol) was dissolved in dry Me_2NCHO under argon, and hydrazine acetate (221.6 mg, 2.41 mmol) was added. The solution was stirred at 25 °C for 2 h and then concentrated. Water (30 mL) was added to the residue, and the mixture was extracted with $CHCl_3$ (100 mL × 3). The organic layer was washed with water (30 mL × 2), dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) to afford white crystals **14** (982.1 mg, 82.6%). **14**: mp 112–114 °C. $[\alpha]_D^{25}$ +25.22° (*c* 1.01, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 3.06 (1 H, br, OH-1), 3.22 (1 H, dd, *J* 4.0, 10.0 Hz, H-6a), 3.37 (1 H, dd, *J* 2.0, 10.0 Hz, H-6b), 4.47 (1 H, ddd, *J* 2.0, 4.0, 10.0 Hz, H-5), 5.35 (1 H, dd, *J* 3.5, 19.0 Hz, H-2), 5.71 (1 H, t, *J* 10.0 Hz, H-4), 5.80 (1 H, d, *J* 3.5 Hz, H-1), 6.14 (1 H, t, *J* 10.0 Hz, H-3), 7.10–8.10 (30 H, benzoyl × 3, trityl). HRFABMS *m/z*: Calcd for $C_{46}H_{38}O_9$ + Na: 757.2314. Found: 757.2415. Anal. Calcd for $C_{46}H_{38}O_9$: C, 75.19; H, 5.21. Found: C, 75.21; H, 5.34.

*2,3,4-Tri-*O*-benzoyl-6-*O*-triphenylmethyl α- and β-*D*-glucopyranosyl fluorides* (**15a** *and* **15b**).—Compound **14** (962.1 mg, 1.31 mmol) was dissolved in dry CH_2Cl_2 (5 mL) at −30 °C under argon, DAST (1.5 mL, 11.35 mmol) was added, and the mixture was stirred for 10 min. The mixture was then neutralized with saturated $NaHCO_3$ (20 mL), extracted with $CHCl_3$ (100 mL), and the $CHCl_3$ layer was washed with saturated $NaHCO_3$ (20 mL × 2) and water (20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) affording light yellow crystals of **15** [16] as a mixture of anomers **15a** and **15b** (995.8 mg, 93.9%, **15a**:**15b** = 1:4.5). Compound **15** (30.0 mg) was separated by preparative TLC (toluene) to afford **15a** (4.5 mg) and **15b** (20.5 mg) as pale yellow

amorphous crystals. **15a**: mp 92–94 °C; $[\alpha]_D^{27}$ +7.78° (*c* 0.36, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.20 (1 H, dd, *J* 4.0, 10.5 Hz, H-6a), 3.41 (1 H, dd, *J* 2.5, 10.5 Hz, H-6b), 4.40 (1 H, ddd, *J* 2.5, 4.0, 10.0 Hz, H-5), 5.44 (1 H, ddd, *J* 2.5, 10.0, 24.0 Hz, H-2), 5.85 (1 H, t, *J* 10.0 Hz, H-4), 6.09 (1 H, t, *J* 10.0 Hz, H-3), 6.09 (1 H, dd, *J* 2.5, 53.0 Hz, H-1), 7.10–8.10 (30 H, benzoyl × 3, trityl). HRFABMS *m/z*: Calcd for $C_{46}H_{37}FO_8$ + Na: 759.2371. Found: 759.2393. **15b**: mp 85–87 °C; $[\alpha]_D^{26}$ +20.63° (*c* 1.05, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 3.33 (1 H, dd, *J* 4.5, 10.5 Hz, H-6a), 3.49 (1 H, dd, *J* 3.0, 10.5 Hz, H-6b), 4.07 (1 H, ddd, *J* 3.0, 4.5, 8.5 Hz, H-5), 5.61 (1 H, ddd, *J* 5.5, 7.0, 8.5 Hz, H-2), 5.66 (1 H, dd, *J* 5.5, 47.5 Hz, H-1), 5.75 (1 H, t, *J* 8.5 Hz, H-4), 5.82 (1 H, t, *J* 8.5 Hz, H-3), 7.08–8.14 (30 H, benzoyl × 3, trityl). HRFABMS *m/z*: Calcd for $C_{46}H_{37}FO_8$ + Na: 759.2371. Found: 759.2365.

2,3,4-Tri-O-benzoyl-α- and β-D-glucopyranosyl fluorides (**16a** *and* **16b**).—Compound **15** (30 mg, 0.04 mmol) was dissolved in acetonitrile (1 mL), and tetrafluoroboric acid (0.02 mL, 0.47 mmol) was added. The solution was stirred at room temperature for 15 min. The reaction mixture was neutralized with Et_3N (0.02 mL, 0.14 mmol) and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) affording white crystals of **16** [16] (18.5 mg, 91.9%) as a mixture of anomers **16a** and **16b** (**16a**:**16b** = 1:4). Compound **16** (18.5 mg) was separated by preparative TLC (3:1 hexane–EtOAc) to give **16a** (3.1 mg) and **16b** (14.1 mg). **16a**: mp 66–68 °C; $[\alpha]_D^{28}$ +32.89° (*c* 1.04, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 2.72 (1 H, br, 6-OH), 3.73, 3.90 (1 H, m, H_2-6), 4.25 (1 H, dt, *J* 10.0, 3.0 Hz, H-5), 5.29 (1 H, t, *J* 10.0 Hz, H-4), 5.40 (1 H, ddd, *J* 3.0, 10.0, 24.0 Hz, H-2), 6.04 (1 H, dd, *J* 3.0, 53.0 Hz, H-1), 6.26 (1 H, t, *J* 10.0 Hz, H-3), 7.25–8.05 (15 H, ArH). HRFABMS *m/z*: Calcd for $C_{27}H_{23}FO_8$ + Na: 517.1275, found: 517.1288. Anal. Calcd for $C_{27}H_{23}FO_8$: C, 65.58; H, 4.69. Found: C, 65.89; H, 4.32. **16b**: mp 135–137 °C; $[\alpha]_D^{28}$ +12.14° (*c* 1.17, $CHCl_3$) ^1H NMR (300 MHz, $CDCl_3$): δ 2.54 (1 H, br, OH-6), 3.83 (1 H, dt, *J* 12.5, 4.5 Hz, H-6a), 3.91 (1 H, ddd, *J* 2.5, 8.0, 12.5 Hz, H-6b), 4.01 (1 H, ddd, *J* 2.5, 4.5, 9.0 Hz, H-5), 5.61 (1 H, ddd, *J* 5 5, 6.5, 9.0 Hz, H-2), 5.64 (1 H, t, *J* 9.0 Hz, H-4), 5.66 (1 H, dd, *J* 5.5, 53.0 Hz, H-1), 5.92 (1 H, t, *J* 9.0 Hz, H-3), 7.26–8.04 (15 H, ArH). HRFABMS *m/z*: Calcd for $C_{27}H_{23}FO_8$ + Na: 517.1275. Found: 517.1261. Anal. Calcd for $C_{27}H_{23}FO_8$: C, 65.58; H, 4.69. Found: C, 65.21; H, 5.02.

2,3,4-Tri-O-benzoyl-6-O-chloroacetyl-α and β-D-glucopyranosyl fluorides (**12a** *and* **12b**).—Compound **16** (377 mg, 0.76 mmol) was dissolved in dry CH_2Cl_2 (2 mL) under argon, and pyridine (0.8 mL) was added. Chloroacetyl chloride (171 mg, 1.53 mmol) was then added dropwise at 0 °C over a 30 min period with stirring. The stirring was continued for 1 h, then the reaction mixture was diluted with $CHCl_3$ (100 mL) and washed with 2% HCl (20 mL), saturated $NaHCO_3$ (20 mL), and brine (20 mL), and the extract was dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) affording **12a** (74.1 mg, 17.0%) and **12b** (344.1 mg, 79.0%), respectively, as light yellow crystals. Compounds **12a** and **12b** were coincident to **12a** and **12b** obtained from **11** by comparison of ^1H NMR spectra.

(3R) and (3S)-Linaloyl 2,3,4-tri-O-benzoyl-6-O-chloroacetyl-β-D-glucopyranosides (**17a** *and* **17b**).—Zirconocene dichloride (307.6 mg, 1.05 mmol), $AgClO_4$ (569 mg, 2.10 mmol) were added to a mixture of MS-4A (900 mg) and dry CH_2Cl_2 (5 mL) under argon, and the mixture was stirred in the dark at room temperature for 10 min. After (±)-linalool (105.4 mg, 0.68 mmol) was added, glycosyl fluoride **12b** (300 mg, 0.53 mmol) was added at −30 °C and stirred for 3 h. The reaction mixture was filtered through a Celite pad, and the filtrate was diluted with $CHCl_3$ (200 mL). The solution was washed with saturated $NaHCO_3$ (20 mL × 2), water (20 mL), dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) affording **17** as a mixture of **17a** (3*R*) and **17b** (3*S*) (**17a**:**17b** = 1:1.3) as pale yellow oil (170.7 mg, 46%). **17**: $[\alpha]_D^{26}$ +8.94° (*c* 0.47, $CHCl_3$). HRFABMS *m/z*: Calcd for $C_{39}H_{41}ClO_{10}$ + Na: 729.2256, 727.2286. Found: 729.2258, 727.2264. Anal. Calcd for $C_{39}H_{41}ClO_{10}$: C, 66.39; H, 5.86. Found: C, 66.02; H, 5.73. **17a**: ^1H NMR (300 MHz, $CDCl_3$): δ 1.18 (3 H, s, H_3-10), 1.51 (3 H, s, H_3-9), 1.64 (3 H, s, H_3-8), 1.38–1.66 (2 H, m, H_2-4), 1.64–2.04 (2 H, m H_2-5, 3.96 (1 H, ddd, *J* 2.5, 6.0, 9.5 Hz, H-5′), 4.10, 4.11 (each 1 H, d, *J* 16.0 Hz, $COCH_2Cl$), 4.33 (1 H, dd, *J* 2.5, 11.5 Hz, H-6′a), 4.41 (1 H, dd, *J* 6.0, 11.0 Hz, H-6′b), 4.84 (1 H, d, *J* 8.0 Hz, H-1′), 4.98 (1 H, t, *J* 6.5 Hz, H-6), 5.17 (1 H, dd, *J* 1.0, 17.5 Hz, H-1a), 5.17 (1 H, dd, *J* 1.0, 10.5 Hz, H-1b), 5.48 (1 H, t, *J* 9.5 Hz, H-4′), 5.50 (1 H, dd, *J* 8.0, 9.5 Hz, H-2′), 5.86 (1 H, t, *J* 9.5 Hz, H-3′), 5.92 (1 H, dd, *J* 10.5, 17.5 Hz, H-2), 7.25–8.00 (15 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 17.49

(q, C-9), 22.13 (t, C-5), 22.92 (q, C-10), 25.61 (q, C-8), 40.22 (t, C-4), 40.62 (t, $COCH_2Cl$), 64.36 (t, C-6′), 69.63 (d, C-2′ or C-4′), 71.68 (d, C-4′ or C-2′), 71.68 (d, C-5′), 72.91 (d, C-3′), 77.20 (s, C-3), 96.21 (d, C-1′) 115.15 (t, C-1), 124.02 (d, C-6), 129.35 (s, C-7), 141.50 (d, C-2), 128.27–133.55 (ArC), 164.78, 165.27, 165.77, 166.96 (benzoyl × 3, $COCH_2Cl$). **17b**: ^1H NMR (300 MHz, $CDCl_3$): δ 1.36 (3 H, s, H_3-10), 1.46 (3 H, s, H_3-9), 1.32–1.58 (2 H, m, H_2-4), 1.60 (3 H, s, H_3-8), 1.68–2.04 (2 H, m, H_2-5), 3.96 (1 H, ddd, *J* 2.5, 6.0, 9.5 Hz, H-5′), 4.10, 4.11 (each 1 H, d, *J* 16.0 Hz, $COCH_2Cl$), 4.36 (1 H, dd, *J* 6.0, 11.5 Hz, H-6′a), 4.39 (1 H, dd, *J* 2.5, 11.5 Hz, H-6′b), 4.88 (1 H, d, *J* 8.0 Hz, H-1′), 4.93 (1 H, t, *J* 6.5 Hz, H-6), 5.19 (1 H, dd, *J* 1.0, 17.5 Hz, H-1a), 5.21 (1 H, 1.0, 10.5 Hz, H-1b), 5.48 (1 H, t, *J* 9.5 Hz, H-4′), 5.51 (1 H, dd, *J* 8.0, 9.5 Hz, H-2′), 5.63 (1 H, dd, *J* 10.5, 17.5 Hz, H-2), 5.86 (1 H, t, *J* 9.5 Hz, H-3′), 7.25–8.00 (15 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 17.59 (q, C-9), 22.13 (t, C-5), 22.92 (q, C-10), 25.57 (q, C-8), 40.62 (t, $COCH_2Cl$), 41.67 (t, C-4), 64.36 (t, C-6′), 69.66 (d, C-2′ or C-4′), 71.68 (d, C-4′ or C-2′), 71.68 (d, C-5′), 72.91 (d, C-3′), 80.96 (s, C-3), 96.54 (d, C-1′) 116.29 (t, C-1), 123.95 (d, C-6), 129.35 (s, C-7), 141.50 (d, C-2), 128.27–133.55 (ArC), 164.78, 165.27, 165.77, 166.96 (benzoyl × 3, $COCH_2Cl$).

*(3R) and (3S)-Linaloyl 2,3,4-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**19** *and* **21**).—Compound **17** (20 mg, 0.03 mmol) was dissolved in dry MeOH (2 mL), and dry pyridine (0.4 mL), Et_3N (0.2 mL, 1.44 mmol), and 2-aminoethanethiol (16.1 mg, 0.14 mmol) were added under argon at room temperature with stirring. The stirring was continued for 3 min. The reaction mixture was concentrated, and the residue was purified by preparative TLC (10:1 benzene–EtOAc) affording **19** (3*R*, 18.3 mg, 41%) and **21** (3*S*, 15.2 mg, 34%) as a colorless oil. **19**: $[\alpha]_D^{27}$ +7.18° (*c* 1.25, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 1.26 (3 H, s, H_3-10), 1.52 (3 H, s, H_3-9), 1.64 (3 H, s, H_3-8), 1.52–1.67 (2 H, m, H_2-4), 1.66–2.12 (2 H, m, H_2-5, 2.44 (1 H, br, OH-6′), 3.72 (1 H, m, H-5′), 3.72 (2 H, m, H_2-6′), 4.86 (1 H, d, *J* 8.0 Hz, H-1′), 5.00 (1 H, t, *J* 7.0 Hz, H-6), 5.18 (1 H, dd, *J* 1.0, 17.5 Hz, H-1a), 5.18 (1 H, dd, *J* 1.0, 10,5 Hz, H-1b), 5.40 (1 H, t, *J* 10.0 Hz, H-4′), 5.50 (1 H, dd, *J* 8.0, 10.0 Hz, H-2′), 5.90 (1 H, t, *J* 10.0 Hz, H-3′), 5.90 (1 H, dd, *J* 10.5, 17.5 Hz, H-2), 7.25–8.00 (15 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 17.66 (q, C-9), 22.16 (t, C-5), 22.41 (q, C-10), 25.61 (q, C-8), 39.95 (t, C-4), 61.92 (t, C-6′), 69.87 (d, C-4′), 71.90 (d, C-2′), 73.07 (d, C-3′), 74.64 (d, C-5′), 80.59 (s, C-3), 96.25 (d, C-1′) 114.97 (t, C-1), 124.08 (d, C-6), 131.92 (s, C-7), 142.69 (d, C-2), 128.27–133.55 (ArC), 164.82, 165.81, 165.84 (CO × 3). HRFABMS *m/z*: Calcd for $C_{37}H_{40}O_9$ + Na: 651.2570. Found: 651.2570. Anal. Calcd for $C_{37}H_{40}O_9$: C, 70.68; H, 6.41. Found: C, 70.28; H, 6.50. **21**: $[\alpha]_D^{27}$ +9.33° (*c* 0.30, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 1.38 (3 H, s, H_3-10), 1.27–1.42 (2 H, m, H_2-4), 1.48 (3 H, s, H_3-9), 1.61 (3 H, s, H_3-8), 1.70–2.00 (2 H, m, H_2-5), 2.43 (1 H, br, OH-6′), 3.75 (1 H, m, H-5′), 3.75 (2 H, m, H_2-6′), 4.90 (1 H, d, *J* 8.0 Hz, H-1′), 4.94 (1 H, t, *J* 7.0 Hz, H-6), 5.19 (1 H, dd, *J* 1.0, 17.5 Hz, H-1a), 5.20 (1 H, dd, *J* 1.0, 10.0 Hz, H-1b), 5.43 (1 H, t, *J* 9.5 Hz, H-4′), 5.52 (1 H, dd, *J* 8.0, 9.5 Hz, H-2′), 5.63 (1 H, dd, *J* 10.0, 17.5 Hz, H-2), 5.90 (1 H, t, *J* 9.5 Hz, H-3′), 7.25–8.00 (15 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 17.53 (q, C-9), 22.13 (t, C-5), 23.15 (q, C-10), 25.58 (q, C-8), 41.58 (t, C-4), 61.79 (t, C-6′), 69.83 (d, C-4′), 71.85 (d, C-2′), 72.99 (d, C-3′), 74.52 (d, C-5′), 80.75 (s, C-3), 96.53 (d, C-1′), 116.13 (t, C-1), 123.98 (d, C-6), 131.69 (s, C-7), 141.62 (d, C-2), 128.27–133.57, (ArC), 164.82, 165.81, 165.84 (CO × 3). HRFABMS *m/z* Calcd for $C_{37}H_{40}O_9$ + Na: 651.2570. Found: 651.2570. Anal. Calcd for $C_{37}H_{40}O_9$: C, 70.68; H, 6.41. Found: C, 70.57; H, 6.48.

(3R) - Linaloyl 2, 3, 4 - tri - O *- benzoyl - β -* D *- xylopyranosyl - (1 → 6) - 2, 3, 4 - tri -* O *- benzoyl - β -* D *- glucopyranoside* (**23**).—To a mixture of MS-4A (54 mg) and dry CH_2Cl_2 (1 mL) was added acceptor **19** (18 mg, 0.029 mmol), a solution of AgOTf (14.9 mg, 0.058 mmol) in toluene (0.2 mL), and 2,4,6-collidine (7.1 mg, 0.058 mmol) under argon at −20 °C with stirring. After the stirring was continued for 15 min, xylosyl bromide **5** (30.5 mg, 0.058 mmol) was added, and the mixture was stirred for an additional 4 h. The reaction mixture was filtered through a Celite pad, and the filtrate was diluted with $CHCl_3$ (50 mL), washed with 10% $Na_2S_2O_4$ (10 mL), water (10 mL), 0.5 M H_2SO_4 (10 mL), saturated $NaHCO_3$ (10 mL), and water (10 mL × 2). The extract was dried over Na_2SO_4, and the solvent was evaporated. The residue was purified by preparative TLC (3:1 hexane–EtOAc) affording glycoside **23** (14.3 mg, 46.5%) and orthoester **25** (4.7 mg, 15.3%) as white crystals. **23**: mp 156–158 °C; $[\alpha]_D^{27}$ −7.25° (*c* 0.80, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.10 (3 H, s, H_3-10), 1.34–1.40 (2 H, m, H_2-4, 1.46 (3 H, s, H_3-9), 1.62 (3 H, s, H_3-8), 1.60–1.90 (2 H, m, H_2-5), 4.89 (1 H, t, *J* 7.0 Hz, H-6), 5.04 (1 H, dd, *J* Hz, H-1a), 5.12 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.79 (1 H, dd, *J* 11.0, 17.0 Hz, H-2), 7.22–8.06 (30 H, ArH). Assignments

for the sugar moiety are given in Tables 5 and 6. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 17.51 (q, C-9), 22.19 (t, C-5), 22.23 (q, C-10), 25.58 (q, C-8), 40.38 (t, C-4), 60.73 (t, C-5″), 67.81 (t, C-6′), 68.85 (d, C-4″), 69.75 (d, C-3″), 69.82 (d, C-4′), 69.82 (d, C-2″), 71.91 (d, C-2′), 73.26 (d, C-3′), 73.41 (d, C-5′), 80.82 (s, C-3), 96.08 (d, C-1′), 99.83 (d, C-1″), 115.02 (t, C-1), 124.15 (d, C-6), 131.28 (s, C-7), 142.13 (d, C-2), 128.18–133.38 (ArC), 164.76, 164.97, 165.21, 165.30, 165.48, 165.7 (CO × 6). HRFABMS *m/z*: Calcd for $C_{63}H_{60}O_{16}$ + Na: 1095.3779. Found: 1095.3784. Anal. Calcd for $C_{63}H_{60}O_{16}$: C, 70.51; H, 5.64. Found: C, 70.12; H, 5.75. **25**: mp 66–68 °C; $[\alpha]_D^{27}$ +8.00° (*c* 0.38, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.16 (3 H, s, H_3-10), 1.48 (3 H, s, H_3-9), 1.46–1.60 (2 H, m, H_2-4), 1.61 (3 H, s, H_3-8), 1.54–1.98 (2 H, m, H_2-5, 4.96 (1 H, t, *J* 7.0 Hz, H-6), 5.07 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.12 (1 H, dd, *J* 1.0, 17.0 Hz, H-1a), 5.90 (1 H, dd, *J* 11.0, 17.0 Hz, H-2), 7.18–8.11 (30 H, ArH); see Tables 5 and 6. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 17.58 (q, C-9), 22.27 (t, C-5), 22.59 (q, C-10), 25.61 (q, C-8), 40.46 (t, C-4), 59.45 (t, C-5″), 62.94 (t, C-6′), 67.98 (d, C-4″), 69.03 (d, C-3″), 69.77 (d, C-4′), 71.95 (d, C-2′), 72.61 (d, C-5′), 73.05 (d, C-2″), 73.43 (d, C-3′), 80.65 (s, C-3), 96.12 (d, C-1′), 97.24 (d, C-1″), 114.75 (t, C-1), 120.94 (s, benzylidene C), 124.17 (d, C-6), 131.43 (s, C-7), 142.40 (d, C-2), 128.19–133.60 (ArC), 164.58, 164.80, 165.20, 165.33, 165.83 (CO × 5). HRFABMS *m/z*: Calcd for $C_{63}H_{60}O_{16}$ + Na: 1095.3779. Found: 1095.3785.

*(3S)-Linaloyl 2,3,4-tri-*O*-benzoyl-β-*D*-xylopyranosyl-(1 → 6)-2,3,4-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**27**).—To a mixture of MS-4A (24.1 mg) and dry CH_2Cl_2 (1 mL) was added acceptor **21** (8.2 mg, 0.01 mmol), a solution of AgOTf (6.7 mg, 0.03 mmol) in toluene (0.2 mL), and 2,4,6-collidine (3.2 mg, 0.03 mmol) under argon at −20 °C with stirring. After the stirring was continued for 15 min, xyloside bromide **5** (13.7 mg, 0.03 mmol) was added, and the mixture was stirred for an additional 18 h at −20 °C. The reaction mixture was filtered through a Celite pad, and the filtrate was diluted with $CHCl_3$ (50 mL), washed with 10% $Na_2S_2O_4$ (10 mL), water (10 mL), 0.5 M H_2SO_4 (10 mL), saturated $NaHCO_3$ (10 mL), and water (10 mL × 2). The extract was dried over Na_2SO_4, and the solvent was evaporated. The residue was purified by preparative TLC (3:1 hexane–EtOAc) affording glycoside **27** (9.0 mg, 64.0%) and orthoester **29** (2.4 mg, 17.0%) as white crystals. **27**: mp 144–146 °C; $[\alpha]_D^{27}$ −4.50° (*c* 0.39, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.14 (3 H, s, H_3-10), 1.30–1.46 (2 H, m, H_2-4) 1.44 (3 H, s, H_3-9), 1.58 (3 H, s, H_3-8), 1.56–1.86 (2 H, m, H_2-5) 4.87 (1H, t, *J* 7.0 Hz, H-6), 5.09 (1 H, dd, *J* 1.0, 17.0 Hz, H-1a), 5.12 (1 H, dd, *J* 1.0, 10.5 Hz, H-1b), 5.52 (1 H, dd, *J* 10.5, 17.0 Hz, H-2), 7.20–8.05 (30 H, ArH), see Tables 5 and 6. ^{13}C NMR (100. 6 MHz, $CDCl_3$): δ 17.48 (q, C-9), 22.03 (t, C-5), 22.73 (q, C-10), 25.55 (q, C-8), 41.75 (t, C-4), 61.05 (t, C-5″), 67.89 (t, C-6′), 69.02 (d, C-4″), 69.87 (d, C-4′ or C-2″), 70.07 (d, C-3″), 70.12 (d, C-2″ or C-4′), 71.85 (d, C-2′), 73.14 (d, C-3′), 73.53 (d, C-5′), 80.78 (s, C-3), 96.44 (d, C-1′), 100.00 (d, C-1″), 116.37 (t, C-1), 124.02 (d, C-6), 131.37 (s, C-7), 141.40 (d, C-2), 128.19–133.39 (ArC), 164.74, 164.97, 165.30, 165.34, 165.49, 165.78 (CO × 6). HRFABMS *m/z*: Calcd for $C_{63}H_{60}O_{16}$ + Na: 1095.3779. Found: 1095.3844. **29**: mp 69–71 °C. $[\alpha]_D^{26}$ +9.47° (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (3 H, s, H_3-10), 1.44 (3 H, s, H_3-9), 1.36–1.50 (2 H, m, H_2-4), 1.60 (3 H, s, H_3-8), 1.54–1.94 (2 H, m, H_2-5), 4.90 (1 H, t, *J* 7.0 Hz, H-6), 5.14 (1 H, dd, *J* 1.0, 17.0 Hz, H-1a), 5.16 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.67 (1 H, dd, *J* 11.0, 17.0 Hz, H-2), 7.20–8.10 (30 H, ArH); see Tables 5 and 6. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 17.49 (q, C-9), 22.09 (t, C-5), 22.99 (q, C-10), 25.58 (q, C-8), 41.85 (t, C-4), 59.43 (t, C-5″), 62.99 (t, C-6′), 67.96 (d, C-4″), 68.99 (d, C-3″), 69.73 (d, C-4′), 71.90 (d, C-2′), 72.63 (d, C-5′), 72.95 (d, C-2″), 73.32 (d, C-3′), 80.65 (s, C-3), 96.48 (d, C-1′), 97.23 (d, C-1″), 116.17 (t, C-1), 120.87 (s, benzylidene C), 124.07 (d, C-6), 131.46 (s, C-7), 141.62 (d, C-2), 128.21–133.60 (ArC), 164.58, 164.76, 165.20, 165.32, 165.81 (CO × 5). HRFABMS *m/z*: Calcd for $C_{63}H_{60}O_{16}$ + Na: 1095.3779. Found: 1095.3800.

*(3R)-Linaloyl β-*D*-xylopyranosyl-(1 → 6)-β-*D*-glucopyranoside* (**1**), *(neohancoside A)*.—To dry MeOH (0.5 mL) was added a solution of **23** (10 mg, 0.009 mmol) in THF (0.5 mL) and a methanolic solution of 2.8% NaOMe (0.18 mL, 0.84 mmol). The reaction was continued under stirring at room temperature for 1 h. The reaction mixture was neutralized with IR-120 (H^+), filtered, and the filtrate was evaporated. The residue was purified by preparative TLC (5:1 $CHCl_3$–MeOH) to give **1** (4.3 mg, 100%) as a light yellow oil. Crystallization with EtOAc afforded white crystals of **1**. **1**: mp 92–94 °C. (EtOAc), lit. 84–86 °C, MeOH [10]; $[\alpha]_D^{25}$ −25.96° (*c* 0.47, MeOH), lit. $[\alpha]_D^{23}$ −27.7° (*c* 0.62, MeOH) [10]. HRFABMS *m/z*: Calcd for $C_{21}H_{36}O_{10}$ + Na: 471.2206. Found: 471.2200.

(3S)-Linaloyl 3-O-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (**31**).—To dry MeOH (0.5 mL) was added a solution of **27** (6.8 mg, 0.006 mmol) in dry THF (0.5 mL) and a methanolic solution of 2.8% NaOMe (0.11 mL, 0.057 mmol), and the reaction was allowed to continue under stirring at room temperature for 1 h. The reaction mixture was then neutralized with Amberlite IR-120 (H^+) and filtered and the filtrate was evaporated. Benzene (0.5 mL) was added to the residue to remove the soluble portion in benzene. The insoluble portion was dried in vacuo to give **31** (2.6 mg, 91.6%) as a light yellow crystals. **31**: mp 75–77 °C (EtOAc); $[\alpha]_D^{26}$ −19.95° (*c* 0.37, MeOH). HRFABMS *m/z*: Calcd for $C_{21}H_{36}O_{10}$ + Na: 471.2206. Found: 471.2221.

(3R)-Linaloyl β-D-glucopyranoside (**33**).—To a 1:1 solution of dry MeOH–THF (2 mL) was added **19** (17.7 mg, 0.03 mmol) and a methanolic solution of 2.8% NaOMe (0.26 mL, 0.13 mmol). The reaction was carried out at room temperature for 1 h with stirring. The reaction mixture was neutralized with Amberlite IR-120 (H^+) and filtered. The filtrate was concentrated, and the residue was purified by preparative TLC (5:1 $CHCl_3$–MeOH) affording **33** (48.4 mg, 94.3%) as a light yellow oil. **33**: $[\alpha]_D^{27}$ −15.83° (*c* 0.74, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 1.33 (3 H, s, H_3-10), 1.60 (3 H, s, H_3-9), 1.66 (3 H, s, H_3-8), 1.56–1.68 (2 H, m, H_2-4) 2.04 (2 H, m, H_2-5) 3.15 (1 H, dd, *J* 8.0, 9.0 Hz, H-2′), 3.15 (1 H, m, 5′-H), 3.28 (1 H, t, *J* 9.0 Hz, H-4′), 3.33 (1 H, t, *J* 9.0 Hz, H-3′), 3.63 (1 H, dd, *J* 5.5, 11.0 Hz, 6′-Ha), 3.79 (1 H, dd, *J* 2.5, 11.0 Hz, 6′-Hb), 4.32 (1 H, d, *J* 8.0 Hz, 1′-H), 5.10 (1 H, t, *J* 7.0 Hz, H-6), 5.14 (1 H, dd, *J* 1.0, 18.0 Hz, H-1a), 5.23 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 6.09 (1 H, dd, *J* 11.0, 18.0 Hz, H-2). ^{13}C NMR (75.0 MHz, CD_3OD): δ 17.74 (q, C-9), 23.43 (t, C-5), 23.63 (q, C-10), 25.84 (q, C-8), 41.61 (t, C-4), 62.84 (t, C-6′), 71.73 (d, C-4′), 75.07 (d, C-2′), 77.57 (d, C-5′), 78.25 (d, C-3′), 81.37 (s, C-3), 99.22 (d, C-1′), 114.88 (t, C-1), 125.75 (d, C-6), 132.11 (s, C-7), 144.51 (d, C-2). HRFABMS *m/z*: Calcd for $C_{16}H_{28}O_6$ + Na: 339.1783. Found: 339.1793.

(3S)-Linaloyl β-D-glucopyranoside (**35**).—To a 1:1 solution of dry MeOH–THF (2.0 mL) was added **21** (16.8 mg, 0.027 mmol) and a methanolic solution of 2.8% NaOMe (0.25 mL, 0.12 mmol). The reaction was carried out at room temperature for 1 h with stirring. The reaction mixture was neutralized with Amberlite IR-120 (H^+) and filtered. The filtrate was concentrated and the residue was purified by preparative TLC. (5:1 $CHCl_3$–MeOH) affording **35** [12] (7.9 mg, 93.5%) as a light yellow oil. **35**: $[\alpha]_D^{27}$ −15.14° (*c* 0.72, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 1.38 (3 H, s, H_3-10), 1.60 (3 H, s, H_3-9), 1.66 (3 H, s, H_3-8), 1.56–1.66 (2 H, m, H_2-4, 2.04 (2 H, m H_2-5, 3.15 (1 H, dd, *J* 8.0, 9.0 Hz, H-2′), 3.15 (1 H, m, 5′-H), 3.27 (1 H, t, *J* 9.0 Hz, H-4′), 3.32 (1 H, t, *J* 9.0 Hz, H-3′), 3.63 (1 H, dd, *J* 5.5, 12.0 Hz, H-6′a), 3.80 (1 H, dd, *J* 2.5, 12.0 Hz, H-6′b), 4.35 (1 H, d, *J* 8.0 Hz, H-1′), 5.10 (1 H, t, *J* 7.0 Hz, H-6), 5.20 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.23 (1 H, dd, *J* 1.0, 18.0 Hz, H-1a), 5.93 (1 H, dd, *J* 11.0, 18.0 Hz, H-2). ^{13}C NMR (75.0 MHz, CD_3OD): δ 17.70 (q, C-9), 23.19 (t, C-5), 23.66 (q, C-10), 25.84 (q, C-8), 42.66 (t, C-4), 62.84 (t, C-6′), 71.76 (d, C-4′), 75.21 (d, C-2′), 77.60 (d, C-5′), 78.27 (d, C-3′), 81.43 (s, C-3), 99.54 (d, C-1′), 115.73 (t, C-1), 125.69 (d, C-6), 132.14 (s, C-7), 144.49 (d, C-2). HRFABMS *m/z*: Calcd for $C_{16}H_{28}O_6$ + Na: 339.1783. Found: 339.1783.

(R)-(−)-Linalool (**37**)*: Enzymatic hydrolysis of* **33**.—Compound **33** (5.7 mg, 0.018 mmol) was dissolved in NaH_2PO_4–citrate buffer (2 mL, pH = 4.0), and β-glucosidase (3.8 mg, 100 units, Sigma Chemical Company) was added. The mixture was incubated at 37 °C for 52 h. The reaction mixture was extracted with CH_2Cl_2 (5 mL × 2). The CH_2Cl_2 layer was dried over Na_2SO_4 and concentrated carefully at 0 °C to give **37** [11] (2.3 mg, 82.7%) as a colorless oil. **37**: $[\alpha]_D^{27}$ −3.04° (*c* 0.33, $CHCl_3$), lit. −20.7° (*c* 0.18, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28 (3 H, s, H_3-10), 1.60 (3 H, s, H_3-9), 1.64 (2 H, m, H_2-4) 1.68 (3 H, s, H_3-8), 2.02 (2 H, m, H_2-5) 5.06 (1 H, dd, *J* 1.5, 11.0 Hz, H-1b), 5.12 (1 H, t, *J* 7.0 Hz, H-6), 5.21 (1 H, dd, *J* 1.5, 17.0 Hz, H-1a), 5.91 (1 H, dd, *J* 11.0, 17.0 Hz, H-2). LREIMS *m/z*: $[2M + Na]^+$, 318.

(S)-(+)-Linalool (**39**)*: Enzymatic hydrolysis of* **35**.—Compound **35** (7.0 mg, 0.022 mmol) was dissolved in Na_2HPO_4–citrate buffer (pH 4.0, 2 mL), and β-glucosidase (3.8 mg, 100 units) was suspended. The mixture was incubated at 37 °C for 90 h. The reaction mixture was extracted with CH_2Cl_2 (5 mL × 2), and the CH_2CI_2 layer was dried over Na_2SO_4 The solution was concentrated carefully at 0 °C giving **39** [12] (3.4 mg, 88.2%) as a colorless oil. **39**: $[\alpha]_D^{27}$ +8.00° (*c* 0.45, $CHCl_3$), lit. +11.9° (*c* 2.29, $CHCl_3$) [12]. LREIMS *m/z*: $[2M + Na]^+$, 318. ^{1}H NMR (300 MHz, $CDCl_3$) data were superimposable to **37**.

A mixture of (3R) and (3S)-8-benzoyloxylinaloyl 2,3,4-tri-O-benzoyl-6-O-chloroacetyl-β-D-glucopyranoside (**18a** *and* **18b**).—Zirconocene dichloride

(230.4 mg, 0.79 mmol), and $AgClO_4$ (426.1 mg, 1.58 mmol) were added to a mixture of MS-4A (675 mg) and dry CH_2Cl_2 (5 mL) under argon, and the mixture was stirred in the dark at room temperature for 10 min. After that time, (±)-8-*O*-benzoyllinalool (140.4 mg, 0.51 mmol) and glycosyl fluoride **12b** (300 mg, 0.53 mmol) were added at −20 °C, and the mixture was stirred for 24 h. The reaction mixture was filtered through a Celite pad, and the filtrate was diluted with $CHCl_3$ (200 mL). The solution was washed with saturated $NaHCO_3$ (20 mL × 2) and water (20 mL), and the extract was dried over Na_2SO_4 and concentrated. The residue was purified by preparative TLC (10:1 benzene–EtOAc) affording **18** as a mixture of **18a** (3*R*) and **18b** (3*S*) (**18a**:**18b** = 1:1.3) (179.3 mg, 55.3%). **18**: $[\alpha]_D^{27}$ +5.17° (*c* 0.93, $CHCl_3$). HRFABMS *m/z*: Calcd for $C_{46}H_{45}ClO_{12}$ + Na: 849.2468, 847.2498, found: 849.2489, 847.2493. Anal. Calcd for $C_{46}H_{45}ClO_{12}$: C, 66.95; H, 5.50. Found: C, 67.34; H, 5.29. ^{1}H NMR (300 MHz, $CDCl_3$) **18a**: δ 1.20 (3 H, s, H_3-10), 1.60 (2 H, m, H_2-4), 1.64 (3 H, s, H_3-9), 1.66–2.16 (2 H, m, H_2-5), 3.99 (1 H, ddd, *J* 3.0, 5.5, 9.5 Hz, H-5′), 4.06, 4.08 (each 1 H, d, *J* 14.5 Hz, $COCH_2Cl$), 4.34 (1 H, dd, *J* 3.0, 11.5 Hz, H-6′a), 4.34 (1 H, dd, *J* 5.5, 11.5 Hz, H-6′b), 4.65 (2 H, s, H_2-8), 4.84 (1 H, d, *J* 8.0 Hz, H-1′), 5.19 (1 H, dd, *J* 1.0, 18.0 Hz, H-1a), 5.19 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.43 (1 H, t, *J* 7.0 Hz, H-6), 5.49 (1 H, t, *J* 9.5 Hz, H-4′), 5.50 (1 H, dd, *J* 8.0, 9.5 Hz, H-2′), 5.87 (1 H, t, *J* 9.5 Hz, H-3′), 5.96 (1 H, dd, *J* 11.0, 18.0 Hz, H-2), 7.25–8.07 (20 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 13.84 (q, C-9), 21.85 (t, C-5), 22.01 (q, C-10), 39.94 (t, C-4), 40.61 (t, $COCH_2Cl$), 64.33 (t, C-6′), 69.60 (d, C-4′), 70.44 (t, C-8), 71.71, (d, C-2′), 71.72 (d, C-5′), 72.94 (d, C-3′), 80.80 (s, C-3), 96.22 (d, C-1′) 115.33 (t, C-1), 128.47 (d, C-6), 130.26 (s, C-7), 142.07 (d, C-2), 128.27–133.59 (ArC), 164.82–166.43 (COC_6H_5, $COCH_2Cl$). **18b**: δ 1.38 (3 H, s, H_3-10), 1.56 (2 H, m, H_2-4), 1.60 (3 H, s, H_3-9), 1.66–2.16 (2 H, m, H_2-5), 3.96 (1 H, ddd, *J* 3.0, 5.5, 9.5 Hz, H-5′), 4.06, 4.08 (each 1 H, d, *J* 14.5 Hz, $COCH_2Cl$), 4.40 (1 H, dd, *J* 3.0, 11.5 Hz, H-6′a), 4.41 (1 H, dd, *J* 5.5, 11.5 Hz, H-6′b), 4.62 (2 H, s, H_2-8), 4.88 (1 H, d, *J* 8.0 Hz, H-1′), 5.21 (1 H, dd, *J* 1.0, 18.0 Hz, H-1a), 5.23 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.38 (1 H, t, *J* 7.0 Hz, H-6), 5.49 (1 H, t, *J* 9.5 Hz, H-4′), 5.52 (1 H, dd, *J* 8.0, 9.5 Hz, H-2′), 5.64 (1 H, dd, *J* 11.0, 18.0 Hz, H-2), 5.87 (1 H, t, *J* 9.5 Hz, H-3′), 7.25–8.07 (20 H, ArH). ^{13}C NMR (75.0 MHz, $CDCl_3$): δ 13.94 (q, C-9), 22.30 (t, C-5), 23.03 (q, C-10), 40.61 (t, $COCH_2Cl$), 41.24 (t, C-4), 64.33 (t, C-6′), 69.64 (d, C-4′), 70.44 (t, C-8), 71.71, (d, C-2′), 71.71 (d, C-5′), 72.88 (d, C-3′), 80.76 (s, C-3), 96.58 (d, C-1′) 116.53 (t, C-1), 129.00 (d, C-6), 129.93 (s, C-7), 141.27 (d, C-2), 128.27–133.59 (ArC), 164.82–165.85 (COC_6H_5, $COCH_2Cl$).

*(3R) and (3S)-8-benzoyloxylinaloyl 2,3,4-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**20** *and* **22**).—Compound **18** (21.0 mg, 0.03 mmol) was dissolved in dry MeOH (1 mL), and dry pyridine (0.14 mL, 1.73 mmol), triethylanimine (0.07 mL, 0.50 mmol), and 2-aminoethanethiol (5.8 mg, 0.05 mmol) were added under argon at room temperature with stirring for 3 min. The reaction mixture was evaporated, and the residue was purified by preparative TLC (10:1 benzene–EtOAc) affording **20** (8.0 mg, 42.0%) and **22** (7.0 mg, 36.0%) as a colorless oil. **20**: $[\alpha]_D^{26}$ +1.34° (*c* 2.21, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (3 H, s, H_3-10), 1.66 (3 H, s, H_3-9), 1.51–1.70 (2 H, m, H_2-4), 1.82–2.22 (2 H, m, H_2-5), 2.44 (1 H, br, OH-6′), 3.74 (1 H, m, H-5′) 3.74 (2 H, m, H_2-6′, 4.46 (2 H, s, H_2-8), 4.87 (1 H, d, *J* 8.0 Hz, H-1′), 5.19 (1 H, dd, *J* 1.0, 18.0 Hz, H-1a), 5.19 (1 H, dd, *J* 1.0, 10.5 Hz, H-1b), 5.42 (1 H, t, *J* 9.5 Hz, H-4′), 5.44 (1 H, t, *J* 7.0 Hz, H-6), 5.51 (1 H, dd, *J* 8.0, 9.5 Hz, H-2′), 5.91 (1 H, t, *J* 9.5 Hz, H-3′), 5.96 (1 H, dd, *J* 10.5, 18.0 Hz, H-2), 7.24–8.12 (20 H, ArH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.96 (q, C-9), 21.96 (t, C-5), 22.20 (q, C-10), 39.84 (t, C-4), 61.77 (t, C-6′), 69.81 (d, C-4′), 70.43 (t, C-8) 71.90 (d, C-2′), 73.03 (d, C-3′), 74.59 (d, C-5′), 80.44 (s, C-3), 96.24 (d, C-1′), 115.10 (t, C-1), 129.07 (d, C-6), 130.41 (s, C-7), 142.48 (d, C-2), 128.27–133.58 (ArC), 164.90–166.40 (CO). HRFABMS *m/z*: Calcd for $C_{44}H_{44}O_{10}$ + Na: 771.2781. Found: 771.2785. Anal. Calcd for $C_{44}H_{10}O_{10}$: C, 70.57; H, 5.92. Found: C, 70.19; H, 5.98. **22**: $[\alpha]_D^{27}$ −0.85° (*c* 5.68, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (3 H, s, H_3-10), 1.60 (3 H, s, H_3-9), 1.46–1.66 (2 H, m, H_2-4), 1.80–2.14 (2 H, m, H_2-5), 2.45 (1 H, br, OH-6′), 3.75 (1 H, m, H-5′), 3.75 (2 H, m, H_2-6′, 4.62 (2 H, s, H_2-8), 4.90 (1 H, d, *J* 8.0 Hz, H-1′), 5.21 (1 H, dd, *J* 1.0, 18.0 Hz, H-1a), 5.22 (1 H, dd, *J* 1.0, 10.5 Hz, H-1b), 5.38 (1 H, t, *J* 7.0 Hz, H-6), 5.44 (1 H, t, *J* 9.5 Hz, H-4′), 5.53 (1 H, dd, *J* 8.0, 9.5 Hz, H-2′), 5.65 (1 H, dd, *J* 10.5, 18.0 Hz, H-2), 5.91 (1 H, t, *J* 9.5 Hz, H-3′), 7.26–8.16 (20 H, ArH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.86 (q, C-9), 21.85 (t, C-5), 23.20 (q, C-10), 41.18 (t, C-4), 61.71 (t, C-6′), 69.79 (d, C-4′), 70.45 (t, C-8), 71.86 (d, C-2′), 72.95 (d, C-3′), 74.51 (d, C-5′), 80.55 (s, C-3), 96.57 (d, C-1′), 116.40 (t, C-1), 129.03 (d, C-6), 130.30 (s, C-7), 143.39 (d, C-2), 128.27–133.59 (ArC), 164.82,

165.85, 165.91, 166.43 (CO × 4). HRFABMS *m/z*: Calcd for $C_{44}H_{44}O_{10}$ + Na: 771.2781. Found: 771.2787. Anal. Calcd for $C_{44}H_{44}O_{10}$: C, 70.57; H, 5.92. Found: C, 70.22; H, 5.96.

(3R)-8-benzoyloxylinaloyl 2,3,4-tri-O-benzoyl-β-D-xylopyranosyl-(1 → 6)-2,3,4-tri-O-benzoyl-β-D-glucopyranoside (**24**).—To a mixture of MS-4A (105 mg) and dry CH_2Cl_2 (3 mL) was added acceptor **20** (35.0 mg, 0.05 mmol), a solution of AgOTf (15.7 mg, 0.06 mmol) in toluene (0.2 mL), and 2,4,6-collidine (7.4 mg, 0.06 mmol) under argon at −20 °C with stirring. After stirring was continued for 13 min, glycosyl bromide **5** (32.0 mg, 0.06 mmol) was added, and the mixture was stirred for an additional 15 h. The reaction mixture was filtered through a Celite pad, the filtrate was diluted with $CHCl_3$ (50 mL), washed with 10% $Na_2S_2O_4$ (10 mL), water (10 mL), 0.5 M H_2SO_4 (10 mL), saturated $NaHCO_3$ (10 mL), and water (10 mL × 2). The extract was dried over Na_2SO_4, and the solvent was evaporated. The residue was purified by preparative TLC (50:1 benzene–EtOAc) affording glycoside **24** (37.2 mg, 66.7%) and orthoester **26** (3.6 mg, 6.5%) as white crystals. **24**: mp 64–66 °C. $[\alpha]_D^{27}$ −10.65° (*c* 0.66, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.10 (3 H, s, H_3-10), 1.31–1.52 (2 H, m, H_2-4), 1.58 (3 H, s, H_3-9), 1.70–2.04 (2 H, m, H_2-5), 4.63 (2 H, s, H_2-8), 5.10 (1 H, dd, *J* 1.0, 17.0 Hz, H-1a), 5.14 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.32 (1 H, t, *J* 7.0 Hz, H-6), 5.80 (1 H, dd, *J* 11.0, 17.0, H-2), 7.20–8.08 (35 H, ArH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.93 (q, C-9), 21.93 (t, C-5), 22.09 (q, C-10), 40.03 (t, C-4), 60.89 (t, C-5″), 67.87 (t, C-6′), 68.93 (d, C-4″), 69.83 (d, C-4′), 69.93 (d, C-2″), 69.93 (d, C-3″), 70.48 (t, C-8), 71.88 (d, C-2″), 71.88 (d, C-2′), 73.22 (d, C-3′), 73.44 (d, C-5′), 80.67 (s, C-3), 96.07 (d, C-1′), 99.92 (d, C-1″), 115.28 (t, C-1), 129.21 (d, C-6), 133.44 (s, C-7), 141.93 (d, C-2), 128.21–133.39 (ArH), 164.79–165.80 (CO). HRFABMS *m/z*: Calcd for $C_{70}H_{64}O_{18}$ + Na: 1215.3990. Found: 1215.4001. Anal. Calcd for $C_{70}H_{64}O_{18}$: C, 70.41; H, 5.41. Found: C, 70.31; 5.57. **26**: mp 56–58 °C; $[\alpha]_D^{27}$ +1.15° (*c* 0.87, $CHCl_3$) ^1H NMR (400 MHz, $CDCl_3$): δ 1.18 (3 H, s, H_3-10), 1.64 (3 H, s, H_3-9), 1.48–1.64 (2 H, m, H_2-4), 1.88–2.12 (2 H, m, H_2-5), 4.63 (2 H, s, H_2-8), 5.15 (1 H, dd, *J* 1.0, 17.5 Hz, H-1a), 5.39 (1 H, t, *J* 7.0 Hz, H-6), 5.94 (1 H, dd, *J* 11.0, 17.5 Hz, H-2), 7.16–8.10 (35 H, ArH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.91 (q, C-9), 21.97 (t, C-5), 22.48 (q, C-10), 40.06 (t, C-4), 59.45 (t, C-5″), 62.85 (t, C-6′), 67.94 (d, C-4″), 69.01 (d, C-3″), 69.70 (d, C-4′), 70.53 (t, C-8), 71.92 (d, C-2′), 72.62 (d, C-5′), 73.07 (d, C-2″), 73.37 (d, C-3′), 80.47 (s, C-3), 96.13 (d, C-1′), 97.24 (d, C-1″), 114.94 (t, C-1), 120.94 (s, benzylidene C), 129.24 (d, C-6), 134.82 (s, C-7), 142.40 (d, C-2), 128.19–133.60 (ArC), 164.58–165.83 (CO). HRFABMS *m/z*: Calcd for $C_{70}H_{64}O_{18}$ + Na: 1215.3990. Found: 1215.3997. Anal. Calcd for $C_{70}H_{64}O_{18}$: C, 70.46; H, 5.41. Found: C, 70.25; H, 5.58.

(3S)-8-benzoyloxylinaloyl 2,3,4-tri-O-benzoyl-β-D-xylopyranosyl-(1 → 6)-2,3,4-tri-O-benzoyl-β-D-glucopyranoside (**28**).—To a mixture of MS-4A (150 mg) and dry CH_2Cl_2 (5 mL), was added acceptor **21** (50.0 mg, 0.07 mmol), a solution of AgOTf (22.4 mg, 0.09 mmol) in toluene (0.2 mL), and 2,4,6-collidine (10.6 mg, 0.09 mmol) under argon at −20 °C with stirring. After the stirring was continued for 15 min, glycosyl bromide **5** (45.7 mg, 0.09 mmol) was added, and the mixture was stirred for an additional 15 h at −20 °C. The reaction mixture was filtered through a Celite pad, and the filtrate was diluted with $CHCl_3$ (100 mL), washed with 10% $Na_2S_2O_4$ (10 mL), water (10 mL), 0.5 M H_2SO_4 (10 mL), saturated $NaHCO_3$ (10 mL), and water (10 mL × 2). The extract was dried over Na_2SO_4 and evaporated. The residue was purified by preparative TLC (3:1 benzene–EtOAc) affording glycoside **28** (62.7 mg, 78.7%) and orthoester **30** (7.41 mg, 9.3%) as white crystals. **28**: mp 144–146 °C; $[\alpha]_D^{28}$ −14.33° (*c* 0.61, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.16 (3 H, s, H_3-10), 1.30–1.48 (2 H, m, H_2-4), 1.60 (3 H, s, H_3-9), 1.78–2.06 (2 H, m, H_2-5), 4.61 (2 H, s, H_2-8), 5.04 (1 H, dd, *J* 1.0, 17.0 Hz, H-1a), 5.14 (1 H, dd, *J* 1.0, 11.0 Hz, H-1b), 5.31 (1 H, t, *J* 7.0 Hz, H-6), 5.52 (1 H, dd, *J* 11.0, 17.0 Hz, H-2), 7.22–8.10 (35 H, ArH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.83 (q, C-9), 21.76 (t, C-5), 22.88 (q, C-10), 41.28 (t, C-4), 61.10 (t, C-5″), 67.93 (t, C-6′), 69.04 (d, C-4″), 69.88 (d, C-2″), 70.10 (d, C-4′), 70.18 (d, C-3″), 70.48 (t, C-8), 71.85 (d, C-2′), 73.10 (d, C-3′), 73.54 (d, C-5′), 80.57 (s, C-3), 96.47 (d, C-1′), 100.04 (d, C-1″), 116.63 (t, C-1), 129.12 (d, C-6), 133.38 (s, C-7), 141.16 (d, C-2), 128.21–133.39 (ArC), 164.78–165.79 (CO). HRFABMS *m/z*: Calcd for $C_{70}H_{64}O_{18}$ + Na: 1215.3990. Found: 1215.4078. Anal. Calcd for $C_{70}H_{64}O_{18}$: C, 70.46; H, 5.41. Found: 70.26; H, 5.51. **30**: mp 65–65 °C. $[\alpha]_D^{26}$ +10.5 (*c* 0.29, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.36 (3 H, s, H_3-10), 1.59 (3 H, s, H_3-9), 1.40–1.59 (2 H, m, H_2-4), 1.80–2.08 (2 H, m, H_2-5), 4.61 (2 H, s, H_2-8), 5.17 (1 H, dd, *J* 1.0, 17.5 Hz, H-1a), 5.18 (1 H, dd, *J* 1.0, 10.5 Hz, H-1b), 5.35 (1 H, t, *J* 6.5 Hz, H-6), 5.62 (1 H, dd, *J* 10.5, 17.5 Hz, H-2), 7.18–8.12

(35 H, ArH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.84 (q, C-9), 21.82 (t, C-5), 23.13 (q, C-10), 41.41 (t, C-4), 59.45 (t, C-5″), 62.96 (t, C-6′), 67.96 (d, C-4″), 69.01 (d, C-3″), 69.70 (d, C-4′), 70.51 (t, C-8), 71.91 (d, C-2′), 72.66 (d, C-5′), 72.97 (d, C-2″), 73.23 (d, C-3′), 80.44 (s, C-3), 99.53 (d, C-1′), 97.24 (d, C-1″), 116.45 (t, C-1), 120.88 (s, benzylidene-C), 129.15 (d, C-6), 134.70 (s, C-7), (d, C-2), 128.21–133.63 (ArC), 164.59, 164.79, 165.21, 165.33, 165.82, 166.44 (CO × 6). HRFABMS *m/z*: Calcd for $C_{70}H_{64}O_{18}$ + Na: 1215.3990. Found: 1215.3954. Anal. Calcd for $C_{70}H_{64}O_{18}$: C, 70.46; H, 5.41. Found: C, 70.51; H, 5.50.

(3R)-8-Hydroxylinaloyl β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (**2**) *(neohancoside B).*—Compound **24** (10 mg, 0.009 mmol) was dissolved in 1:1 THF–MeOH (1 mL), and a methanolic solution of 2.8% NaOMe (0.16 mL, 0.08 mmol) was added. The reaction was allowed to continue under stirring at room temperature for 1 h. The reaction mixture was neutralized with Amberlite IR-120 (H^+) and filtered, and the filtrate was evaporated. The residue was purified by preparative TLC (3:1 $CHCl_3$–MeOH) to give **2** (3.0 mg, 77.1%) as a light-yellow oil. Crystallization with EtOAc afforded white crystals of **2**. **2**: mp 46–48 °C (EtOAc), $[\alpha]_D^{28}$ −27.3° (*c* 0.59, MeOH), lit., $[\alpha]_D^{27}$ −25.7°, (*c* 0.28, MeOH) [11]. HRFABMS *m/z*: Calcd for $C_{21}H_{36}O_{11}$ + Na: 487.2156. Found: 487.2171.

(3S)-8-Hydroxylinaloyl β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (**32**).—Compound **28** (20.0 mg, 0.02 mmol) was dissolved in 1:1 THF–MeOH (1.0 mL), a methanolic solution of 2.8% NaOMe (0.30 mL, 0.15 mmol) was added, and the reaction was allowed to continue under stirring at room temperature for 3 h. The reaction mixture was neutralized with Amberlite IR-120 (H^+) and filtered, and the filtrate was evaporated. The residue was purified by preparative TLC (3:1 $CHCl_3$–MeOH) to give **32** (8.9 mg, 100.0%) as a light-yellow crystals. **32**: mp 33–35 °C (EtOAc); $[\alpha]_D^{21}$ −28.64° (*c* 1.27, MeOH). HRFABMS *m/z*: Calcd for $C_{21}H_{36}O_{11}$ + Na: 487.2156. Found: 487.2171.

(3R)-8-Hydroxylinaloyl β-D-glucopyranoside (**34**).—To dry MeOH (2 mL) was added a solution of **20** (40 mg, 0.05 mmol) in dry THF (0.5 mL) and a methanolic solution of 2.8% NaOMe (0.57 mL, 0.28 mmol). The reaction was carried out at room temperature for 2.5 h with stirring. The reaction mixture was then neutralized with Amberlite IR-120 (H^+) and filtered. The filtrate was concentrated, and the residue was purified by preparative TLC (3:1 $CHCl_3$–MeOH) affording **34** (17.5 mg, 100.0%) as a light-yellow oil. **34**: $[\alpha]_D^{25}$ −10.58° (*c* 2.51, MeOH); ^{1}H NMR (300 MHz, pyridine-d_5): δ 1.40 (3 H, s, H_3-10), 1.67 (3 H, s, H_3-9), 1.58–1.86 (2 H, m, H_2-4), 2.28 (2 H, m, H_2-5), 3.73 (1 H, m, H-5′), 3.89 (1 H, dd, *J* 8.0, 9.0 Hz, H-2′), 4.10 (1 H, t, *J* 9.0 Hz, H-3′), 4.13 (1 H, t, *J* 9.0 Hz, H-4′), 4.15 (2 H, s, H_2-8), 4.21 (1 H, dd, *J* 5.0, 11.5 Hz, H-6′a), 4.35 (1 H, dd, *J* 3.0, 11.5 Hz, H-6′b), 4.83 (1 H, d, *J* 8.0 Hz, H-1′), 5.06 (1 H, dd, *J* 1.5, 11.0 Hz, H-1b), 5.19 (1 H, dd, *J* 1.5, 17.5 Hz, H-1a), 5.61 (1 H, t, *J* 7.0 Hz, H-6), 6.25 (1 H, dd, *J* 11.0, 17.5 Hz, H-2) ^{13}C NMR (75.0 MHz, pyridine-d_5): δ 14.13 (q, C-9), 22.76 (t, C-5), 24.34 (q, C-10), 40.82 (t, C-4), 63.09 (t, C-6), 68.25 (t, C-8), 71.95 (d, C-4′), 75.40 (d, C-2′), 78.24 (d, C-5′), 78.95 (d, C-3′), 80.10 (s, C-3), 99.58 (d, C-1′), 114.08 (t, C-1), 125.13 (d, C-6), 136.47 (s, C-7), 144.59 (d, C-2). HRFABMS *m/z*: Calcd for $C_{16}H_{28}O_7$ + Na: 355.1733. Found: 355.1729.

(3S)-8-Hydroxylinaloyl β-D-glucopyranoside (**36**).—To dry MeOH (2 mL) was added a solution of **22** (30.0 mg, 0.04 mmol) in dry THF and a MeOH solution of 2.8% NaOMe (0.43 mL, 0.21 mmol). The reaction was carried out at room temperature for 1 h with stirring. The reaction mixture was then neutralized with Amberlite IR-120 (H^+) and filtered. The filtrate was concentrated, and the residue was purified by preparative TLC (3:1 $CHCl_3$–MeOH) affording **36** (12.0 mg, 90.1%) as a light-yellow oil. **36**: $[\alpha]_D^{28}$ −17.04° (*c* 1.71, MeOH). ^{1}H NMR (300 MHz, pyridine-d_5): δ 1.46 (3 H, s, H_3-10), 1.63 (3 H, s, H_3-9), 1.48–1.82 (2 H, m, H_2-4), 2.23 (2 H, m, H_2-5), 3.74 (1 H, m, H-5′), 3.90 (1 H, dd, *J* 8.0, 9.0 Hz, H-2′), 4.12 (1 H, t, *J* 9.0 Hz, H-3′), 4.12 (1 H, t, *J* 9.0 Hz, H-4′), 4.14 (2 H, s, H_2-8), 4.21 (1 H, dd, *J* 5.0, 12.0 Hz, H-6′a), 4.37 (1 H, dd, *J* 2.5, 12.0 Hz, H-6′b), 4.85 (1 H, d, *J* 8.0 Hz, H-1′), 5.09 (1 H, dd, *J* 1.5, 11.0 Hz, H-1b), 5.26 (1 H, dd, *J* 1.5, 17.5 Hz, H-1a), 5.56 (1 H, t, *J* 7.0 Hz, H-6), 6.17 (1 H, dd, *J* 11.0, 17.5 Hz, H-2). ^{13}C NMR (75.0 MHz, pyridine-d_5): δ 14.07 (q, C-9), 22.75 (t, C-5), 23.71 (q, C-10), 42.10 (t, C-4), 63.09 (t, C-6′), 68.20 (t, C-8), 71.96 (d, C-4′), 75.50 (d, C-2′), 78.23 (d, C-5′), 78.96 (d, C-3′), 80.12 (s, C-3), 99.91 (d, C-1′), 114.91 (t, C-1), 124.98 (d, C-6), 136.49 (s, C-7), 144.61 (d, C-2). HRFABMS *m/z*: Calcd for $C_{16}H_{28}O_7$ + Na: 355.1733. Found: 355.1744.

(3R)-(−)-8-Hydroxylinalool (**38**)*: Enzymatic hydrolysis of* **34**.—Compound **34** (16.0 mg, 0.05 mmol) was dissolved in Na_2HPO_4–citrate buffer (2 mL, pH 4.0), and β-glucosidase (6.7 mg, 180 units) was added. The mixture was incubated at 37 °C for

136 h. The reaction mixture was extracted with CH_2Cl_2 (5 mL × 2). The CH_2Cl_2 layer was dried over Na_2SO_4 and concentrated carefully at 0 °C to give **38**: [14] (4.6 mg, 56.2%) as a light-yellow oil. **38**: $[\alpha]_D^{25}$ −5.95° (*c* 0.57, $CHCl_3$), lit., −12.8° (*c* 0.05, MeOH). ^1H NMR (300 MHz, $CDCl_3$): δ 1.30 (3 H, s, H_3-10), 1.60 (2 H, m, H_2-4), 1.66 (3 H, s, H_3-9), 2.08 (2 H, m, H_2-5), 3.99 (2 H, s, H_2-8), 5.07 (1 H, dd, *J* 1.5, 10.5 Hz, H-1b), 5.22 (1 H, dd, *J* 1.5, 17.5 Hz, H-1a), 5.41 (1 H, t, *J* 7.0 Hz, H-6), 5.91 (1 H, dd, *J* 10.5, 17.5 Hz, H-2). LREIMS *m/z*: $[M - H_2O]^+$, 152.

(3S)-(+)-8-Hydroxylinalool (**40**)*: Enzymatic hydrolysis of* **36**.—Compound **36** (12.0 mg, 0.04 mmol) was dissolved in Na_2HPO_4–citrate buffer (pH 4.0, 2 mL), and β-glucosidase (5.0 mg, 135 unit) was suspended. The mixture was incubated at 37 °C for 52 h, then extracted with CH_2Cl_2 (5 mL × 2), and the CH_2Cl_2 layer was dried over Na_2SO_4. The solution was concentrated carefully at 0 °C to give **40** [12] (5.3 mg, 86.3%) as a light-yellow oil. **40**: $[\alpha]_D^{26}$ +7.13° (*c* 0.76, $CHCl_3$), lit., +20.0° (*c* 0.20, MeOH). ^1H NMR (300 MHz, $CDCl_3$) data were superimposable on **38**. LREIMS *m/z*: $[M - H_2O]^+$ 152.

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