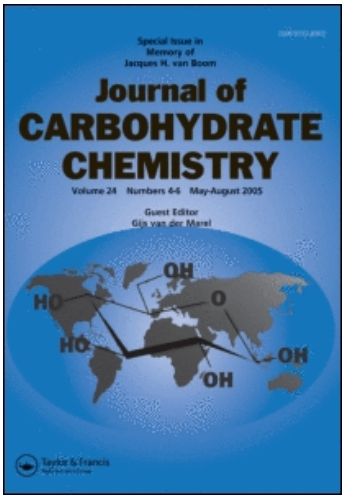

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GLYCOSYLATION WITH 1,2-ANHYDROMANNOFURANOSE BENZYL ETHER AS THE GLYCOSYL DONOR: A COMPARISON BETWEEN SUGAR PYRANOSE AND FURANOSE ACCEPTORS FOR THEIR PRIMARY HYDROXY ACTIVITY

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ABSTRACT

Some 1→5 and 1→6 α-linked furano-disaccharide derivatives were synthesized using 1,2-anhydromannofuranose as the glycosyl donor. Comparison of the glycosyl acceptors indicated that the activity of primary hydroxyl groups of glycofuranoses was much lower than that of glycopyranoses.

INTRODUCTION

Glycofuranosyl residues are widely distributed in natural oligosaccharides and many reports showed that some furanosides, as part of core oligosaccharides, have physiological activity. For example, ribofuranan and xylofuranan have high anti-HIV activity, low anticoagulant activity as well as low in vivo toxicities,[1,2] and they are considered to be potential anti-AIDs drugs. Some (1→5)-arabinofuranose oligomers, terminals of polysaccharide side chains, are responsible for the polysaccharide serological activity,[3,4] while some galactofuranosyl compounds are strongly antigenic.[5] Until now, there have

been only limited reports dealing with the synthesis of glycofuranosides. Procedures for 1,2-*trans*-glycofuranoside synthesis employing sugar 1,2-*O*-cyanoalkylidene and 1,2-thioorthoester derivatives as glycosyl donors have been developed by Kochetkov and coworkers.[6,7] More recently, (1→2), (1→3), and (1→5)-linked-α-L-arabinofuranosides were prepared from per-*O*-benzoyl-α-L-arabinofuranosyl chloride[8] and the (1→6)-linked-β-D-galactofuranoside disaccharide was conveniently synthesized from *n*-pentenyl galactofuranoside.[9] It is our interest to investigate new methods for the stereoselective formation of glycofuranosidic linkages, for instance, using 1,2-anhydrofuranose sugars for the synthesis of the corresponding 1,2-*trans*-related glycofuranosides. The syntheses of 1,2-anhydromanno-, gluco-, xylo-, lyxo-, arabino-, and ribofuranose benzyl ethers by an intramolecular S_N2 reaction of the corresponding C-1 alkoxide with C-2 bearing tosyloxy group have been reported.[10-12] Here, we wish to report the use of 1,2-anhydromannofuranose as the glycosyl donor for the synthesis of 1→5 and 1→6 linked furanosidic disaccharides.

RESULTS AND DISCUSSION

1,2-Anhydro-6-*O*-allyl-3,5-di-*O*-benzyl-β-D-mannofuranose (**7**) was chosen as the key intermediate in the present research as it can be used as the glycosyl donor and, after methanolysis and deallylation, as the glycosyl acceptor. We have reported that per-*O*-benzylated 1,2-anhydroglycofuranoses have excellent reactivity[10-12] as indicated from their coupling with methanol, trimethylsilylated thymine, and diacetone galactose. It was found that replacement of the 6-*O*-benzyl group with the allyl group did not affect the reactivity of **7**; its methanolysis gave the corresponding methyl α-D-mannofuranoside quantitatively, and its coupling with 1,2:3,4-di-*O*-isopropylidene-α-D-galacotopyranose (**17**) and methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (**18**) gave the corresponding 1→6 linked disaccharides (**19**, **20**) in high yields (87% and 83%, respectively) without the use of any catalyst. However, it was found that coupling of **7** with 3,5-di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**10**) in CH_2Cl_2 containing 4Å molecular sieves at room temperature did not give the disaccharide product (**21**) after 20 h. Even after an equivalent of $ZnCl_2$ was added to the reaction mixture, the 1→6 linked disaccharide was obtained in poor yield. A series of experiments (see Table 1) was carried out to optimize the coupling.

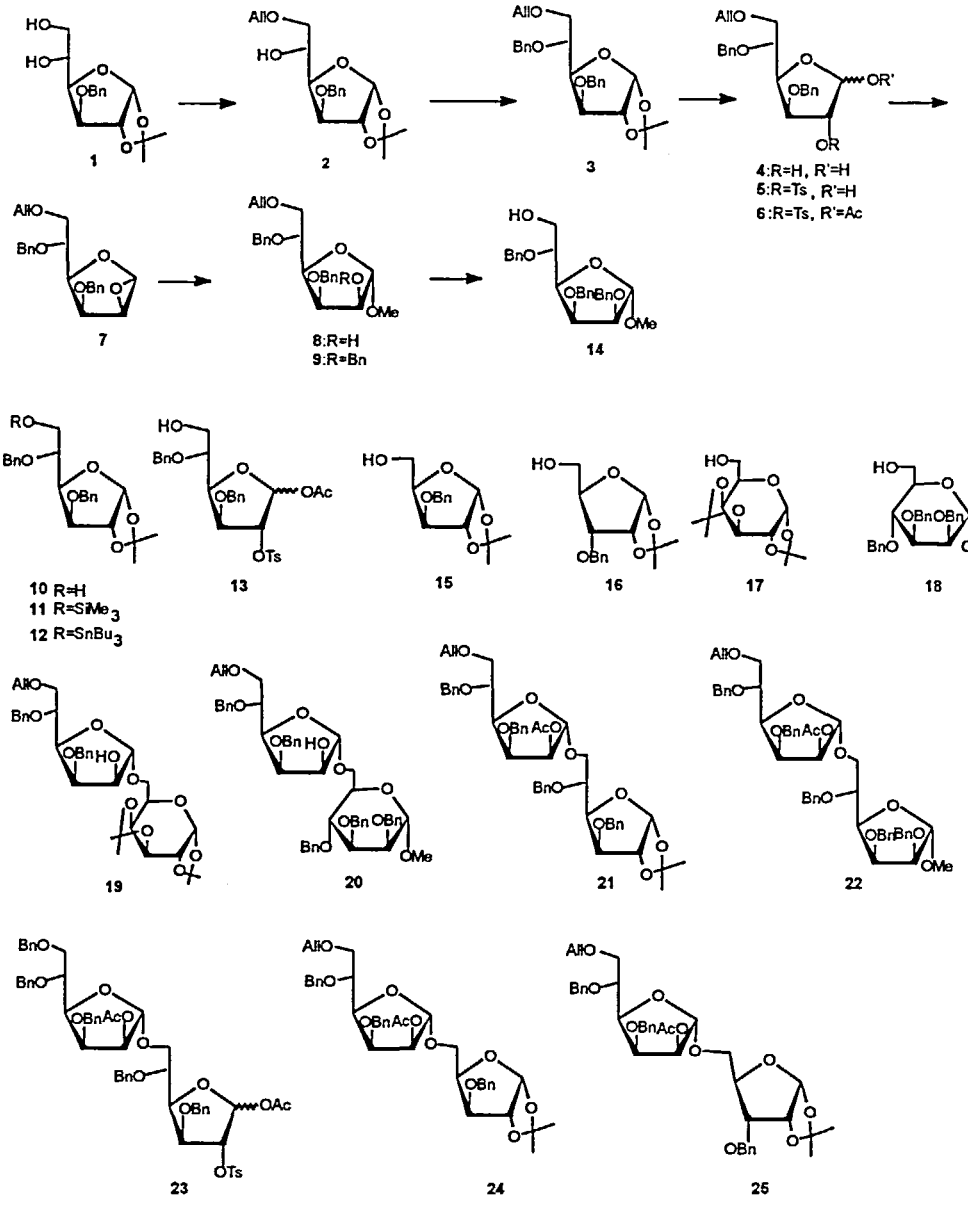

Table 1. Results for coupling of **7** with **10**

promoter	$ZnCl_2$	$BF_3.Et_2O$	AgOTf	TMSOTf	Bu_4NBr
yield% of **21**	30	37	65	Decomp.	20

The best result was obtained using AgOTf as the promoter while serious decomposition of both the donor and acceptor occurred when TMSOTf was used.

Furthermore, condensations of **7** and **10** using AgOTf as the promoter in CH_2Cl_2 at −15 °C, 0 °C, room temperature, and under refluxing were carried out, respectively, and the results (yields were 57%, 61%, 65%, and 68%, respectively) indicated that the favorable conditions were at room temperature and under refluxing. In attempts to change the reactivity of **10**, trimethylsilylation with trimethylsilyl chloride gave **11**, and tributylstannylation with bis(tributyltin)oxide gave **12**. Detrimethylsilylation of **11** occurred when coupling with **7** was attempted and no disaccharide was formed, whereas the disaccharide **21** was obtained from coupling **7** and **12** after acetylation in a slightly improved yield (71%). Moreover, the AgOTf promoted coupling of **7** or per-*O*-benzyl-1,2-anhydromannofuranose with the primary free hydroxyl of methyl 2,3,5-tri-*O*-benzyl-α-D-mannofuranoside (**14**), 1-*O*-acetyl-3,5-di-*O*-benzyl-2-*O*-tosyl-D-glucofuranose (**13**), 3-*O*-benzyl-1,2-di-*O*-isopropylidene-α-D-xylofuranose (**15**), and 3-*O*-benzyl-1,2-di-*O*-isopropylidene-α-D-ribofuranose (**16**) gave 1→6 or 1→5 linked disaccharide derivatives (**22-25**) in similar yields (60-70%) after acetylation. These results, together with our earlier reports regarding the coupling of 1,2-anhydroribofuranose benzyl ether with **17**[10] and **16**,[12] are a clear indication that in the glycosylation reactions the activity of the primary hydroxyl group of furanose sugars was much lower than that of pyranose sugars. The reason for this difference is not clear yet.

In summary, here we present the successful synthesis of 1→6 or 1→5 α-linked furano-disaccharides with 1,2-anhydromannofuranose as the glycosyl donor. In the glycosylation, the acceptor activity of 6-OH of furano-hexoses was similar to that of 5-OH of furano-pentoses but much lower than that of 6-OH of pyrano-hexoses.

EXPERIMENTAL

General methods. Optical rotations were determined at 20 °C with a Perkin-Elmer Model 241-Mc automatic polarimeter. ^{1}H NMR spectra were recorded with Varian XL-400 and Varian XL-200 spectrometers for solutions in $CDCl_3$. Chemical shifts are given in ppm downfield from internal Me_4Si. Thin-layer chromatography (TLC) was performed on silica gel HF with detection by charring with 30% (v/v) H_2SO_4 in MeOH or in some cases by a UV detector. Analytical LC was carried out with a Gilson HPLC set consisting of two pumps (Model 306), Dynamic Mixer (Model 811c), RI Detector (Model 132), UV/VIS Detector (Model 118), stainless steel column packed with silica gel (10 × 300 mm or 4.6 × 250 mm), and an IBM computer installed with system control software 712. Ethyl acetate - petroleum ether (bp 60-90 °C) was used as the eluent at a flow rate of 1 to 4 mL min^{-1}. Column chromatography was conducted by elution of a column (16 × 240 mm, 18 × 300 mm, 35 × 400 mm) of silica gel (100-200 mesh) with EtOAc - petroleum ether (60-90 °C) as the eluent. Solutions were concentrated at < 60 °C under diminished pressure.

6-*O*-Allyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (2). To a solution of 3-*O*-benzyl-1,2-di-*O*-isopropylidene-α-D-glucofuranose (**1**)[13] (3.1 g, 10 mmol) in CH_2Cl_2 (15 mL) was added Bu_4NBr (300 mg) and 15% NaOH solution (10 mL), the mixture was stirred for several minutes, then allyl bromide (0.85 mL,10 mmol) was added. The mixture was stirred at room temperature for 2 h, at the end of which time TLC (1:2 ethyl acetate - petroleum ether) indicated that the reaction was complete. The mixture was poured into water, the solution was extracted repeatedly with dichloromethane, and the combined extracts were concentrated to a syrup. Purification by column chromatography with 1:2 ethyl acetate -petroleum ether as the eluent afforded syrupy **2** (2.95 g, 84%). In order to identify **2**, its acetylation was carried out with Ac_2O in pyridine, and 5-*O*-acetyl-6-*O*-allyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose was obtained quantitatively: $[\alpha]_D$ −114.8° (*c* 4.0, $CHCl_3$); ^{1}H NMR δ 7.20–7.13 (m, 5H, Ph), 5.90 (d, 1H, $J_{1,2}$ = 3.7 Hz, H–1), 5.98–5.68 (m, 1H, $-CH$=CH_2), 5.32–5.09 (m, 3H, H–5, CH_2=CH–), 4.64–4.38 (m, 5H, H–3, $-CH_2$–CH=CH_2, CH_2Ph), 4.02 (dd, 1H, $J_{4,3}$ = 2.8 Hz, $J_{4,5}$ =

9.6Hz, H–4), 3.95 (d, 1H, H–2), 3.82 (dd, 1H, $J_{5,6}$ = 2.4 Hz, $J_{6,6'}$ = 11.5 Hz, H–6), 3.65 (dd, 1H, $J_{5,6'}$ = 4.9 Hz, H–6'), 1.92 (s, 3H, CO*CH*$_3$), 1.50, 1.32 (2s, 6H, *CH*$_3$*CCH*$_3$).

Anal. Calcd for $C_{21}H_{28}O_7$: C, 64.29; H, 7.14. Found: C, 64.40; H, 7.05.

6-*O*-Allyl-3,5-di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (3). Compound **2** (3.5 g, 10 mmol) was dissolved in *N,N*-dimethylformamide (20 mL) and subjected to benzylation with sodium hydride (80% in oil, 600 mg, 20 mmol) and benzyl bromide (1.8 mL, 15 mmol). The mixture was stirred at room temperature for 5 h, at the end of which time TLC (1:2 ethyl acetate - petroleum ether) indicated that the reaction was complete. The mixture was poured into water, the solution was extracted repeatedly with dichloromethane, and the combined extracts were dried over Na_2SO_4 and concentrated to a syrup. Purification by column chromatography with 1:2 ethyl acetate - petroleum ether as the eluent afforded syrupy **3** (4.32 g, 96%): $[\alpha]_D$ –33.8° (*c* 12.0, $CHCl_3$); ^{1}H NMR δ 7.40–7.18 (m, 10H, 2Ph), 5.92 (d, 1H, $J_{1,2}$ = 3.6 Hz, H–1), 6.00–5.80 (m, 1H, –*CH*=CH_2), 5.36–5.12 (m, 2H, *CH*$_2$=CH–), 4.72–4.34 (m, 7H, H–3, 2*CH*$_2$Ph, –*CH*$_2$–CH=CH_2), 4.28 (dd, 1H, $J_{4,3}$ = 2.6 Hz, $J_{4,5}$ = 8.8 Hz, H–4), 4.08 (d, 1H, H–2), 4.0–3.96 (m, 1H, H–5), 3.84 (dd, 1H, $J_{5,6}$ = 2.7 Hz, $J_{6,6'}$ = 12 Hz, H–6), 3.70 (dd, 1H, $J_{5,6'}$ = 5.2 Hz, H–6'), 1.51, 1.32 (2s, 6H, *CH*$_3$*CCH*$_3$).

Anal. Calcd for $C_{26}H_{32}O_6$: C, 70.91; H, 7.27. Found: C, 70.67; H, 7.31.

6-*O*-Allyl-3,5-di-*O*-benzyl-D-glucofuranose (4) and its acetate. To a solution of **3** (3.5 g, 8 mmol) in 1,4-dioxane (10 mL) was added 1M H_2SO_4 (1 mL). The mixture was boiled under reflux with stirring for 2 h, at the end of which time TLC (1:2 ethyl acetate - petroleum ether) showed that the hydrolysis was complete. The mixture was neutralized with $NaHCO_3$, filtered and concentrated to a syrup. Purification by column chromatography with 1:1 ethyl acetate - petroleum ether as the eluent afforded syrupy **4** (2.85 g, 89%). Since it was difficult to identify the product, **4** was acetylated with Ac_2O in pyridine quantitatively giving the diacetate as an α,β mixture in a ratio of 1:1: $[\alpha]_D$ –28.9° (*c* 8.3, $CHCl_3$); ^{1}H NMR δ 7.38–7.16 (m, 10H, 2Ph), 6.38 (d, 0.5H, $J_{1,2}$ = 3.4 Hz, H–1α), 6.12 (s, 0.5H, H–1β), 6.00–5.80 (m, 1H, –*CH*=CH_2), 5.34–5.11 (m, 3H, H–2, –CH=*CH*$_2$), 4.84–3.96 (m, 8H, H–3, H–4, 2*CH*$_2$Ph, –*CH*$_2$–CH=CH_2), 4.00 (m, 1H, H–5), 3.80 (m, 1H, H–6α,β), 3.60 (m, 1H, H–6'α,β), 2.12–2.02 (m, 6H, 2 CO*CH*$_3$).

Anal. Calcd for $C_{27}H_{32}O_8$: C, 66.94; H, 6.61. Found: C, 67.12; H, 6.47.

6-*O*-Allyl-3,5-di-*O*-benzyl-2-*O*-toluenesulfonyl-D-glucofuranose (5). To a solution of **4** (1.0 g, 2.5 mmol) in dichloromethane (5 mL) were added tetrabutylammonium hydrogen sulfate (TBAHS) (110 mg, 0.3 mmol), 5% NaOH (5 mL), and tosyl chloride (570 mg, 3.0 mmol). The mixture was stirred for about 24 h at room temperature and then diluted with dichloromethane and washed with cold water. The organic phase was dried over Na_2SO_4, concentrated, and the product was purified by column chromatography on silica gel with 1:3 ethyl acetate - petroleum ether as the eluent. Compound **5** (994 mg, 72%) was obtained as a syrupy α,β mixture in a ratio of 1:4: $[\alpha]_D$ −22.6° (*c* 3.0, $CHCl_3$); ^{1}H NMR δ 7.79 (d, 2H, Ph of Ts), 7.40–7.10 (m, 12H, Ph of Ts, 2Ph), 6.00–5.80 (m, 1H, −*CH*=CH_2), 5.46 (d, 0.2H, $J_{1,2}$ = 3.6 Hz, H–1α), 5.32–5.10 (m, 2H, *CH_2*=CH–), 5.08 (s, 0.8H, H–1β), 4.80 (s, 1H, H–2), 4.82–4.20 (m, 6H, H–3, H–4, 2*CH_2*Ph), 4.04–3.90 (m, 3H, H–5, −*CH_2*–CH=CH_2), 3.80 (dd, 1H, $J_{5,6}$ = 2.2 Hz, $J_{6,6'}$ = 11.9 Hz, H–6), 3.60 (dd, 1H, $J_{5,6'}$ = 4.7 Hz, H–6'), 2.44 (s, 3 H, Ph*CH_3*).

Anal. Calcd for $C_{30}H_{34}O_8S$: C, 64.98; H, 6.14. Found: C, 64.72; H, 6.08.

1-*O*-Acetyl-6-*O*-allyl-3,5-di-*O*-benzyl-2-*O*-toluenesulfonyl-D-glucofuranose (6). Compound **5** was acetylated with Ac_2O in pyridine, quantitatively giving **6** as a syrupy α,β mixture in a ratio of 1:2: $[\alpha]_D$ −13.0 (*c* 5.0, $CHCl_3$); ^{1}H NMR δ 7.78 (d, 2H, Ph of Ts), 7.40–7.10 (m, 12H, Ph of Ts, 2Ph), 6.20 (d, 1/3H, $J_{1,2}$ = 3.7 Hz, H–1α), 5.98 (s, 2/3H, H–1β), 6.00–5.78 (m, 1H, −*CH*=CH_2), 5.30–5.10 (m, 7/3H, H–2α, −CH=*CH_2*), 4.98 (S, 2/3H, H–2β), 4.76–4.20 (m, 6H, H–3, H–4, 2*CH_2*Ph), 4.06–3.90 (m, 3H, H–5, −*CH_2*–CH=CH_2), 3.76 (m, 1H, H–6), 3.58 (m, 1H, H–6'), 2.45, 2.42 (2s, 3H, *CH_3*Ph β,α), 2.00,1.94 (2s, 3H, CO*CH_3* β,α).

Anal. Calcd for $C_{32}H_{36}O_9S$: C, 64.43; H, 6.04. Found: C, 64.32; H, 5.98.

1,2-Anhydro-6-*O*-allyl-3,5-di-*O*-benzyl-β-D-mannofuranose (7). To a solution of **5** (100 mg, 0.18mmol) in THF (3 mL) was added potassium *tert*-butoxide (50 mg, 0.45 mmol) and the mixture was stirred at room temperature for 20 min. Concentration of the mixture gave a residue that was repeatedly extracted with 1:3 ethyl acetate - petroleum ether. The organic extracts were concentrated to afford **7** as a colorless syrup (67.5mg, 98%), which was used directly for the next reaction without purification: ^{1}H NMR δ 7.40-7.22 (m, 10H, 2Ph), 6.00-5.80 (m, 1H, *CH*=CH_2), 5.36-5.12 (m, 2H, *CH_2*=CH), 5.11 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.69 (s, 2H, Ph*CH_2*), 4.67, 6.51 (2d, 2H, J = 11.7 Hz, *CH_2*Ph),

4.48 (dd, 1H, $J_{3,4}$ = 7.5 Hz, $J_{4,5}$ = 8.3 Hz, H-4), 4.40 (dd,1H, $J_{2,3}$ = 2.0 Hz, H-3), 4.10-3.90 (m, 3H, CH_2-CH=CH_2, H-5), 3.80 (dd, 1H, $J_{5,6}$ = 2.6 Hz, $J_{6,6'}$ = 10.4 Hz, H-6),3.66 (dd, 1H, $J_{5,6'}$ = 5.5 Hz, H-6), 3.63 (t, 1H, H-2).

Methyl 6-*O*-Allyl-3,5-di-*O*-benzyl-α-D-mannofuranoside (8). A solution of 7 (100 mg, 0.26 mmol) in anhyd MeOH (10 mL) was stirred for 1 h and the mixture was concentrated giving **8** as a syrup (104 mg, 96%) which was used for further reaction. An analytical sample was obtained by HPLC purification using 1:2 ethyl acetate - petroleum ether as the eluent: $[\alpha]_D$ +13.0° (*c* 6.0, $CHCl_3$); ^{1}H NMR δ 7.39–7.20 (m, 10H, 2Ph), 5.98–5.78 (m, 1H, –*CH*=CH_2), 5.30–5.18 (m, 2H, CH_2=CH–), 4.86–4.42 (m, 5H, H–1, 2CH_2Ph), 4.38- –4.22 (m, 2H, H–3, H–4), 4.06–3.94 (m, 5H, H–2, H–5, OH, –CH_2–CH=CH_2), 3.84-3.64 (m, 2H, H–6, H–6'), 3.32 (s, 3H, OCH_3).

Anal. Calcd for $C_{24}H_{30}O_6$: C, 69.57; H, 7.25. Found: C, 69.91; H, 7.19.

Methyl 6-*O*-Allyl-2,3,5-tri-*O*-benzyl-α-D-mannofuranoside (9). Compound **8** (500 mg, 0.98 mmol) was benzylated using the same procedure as described in the preparation of **3**, and syrupy product **9** (578 mg, 95%) was obtained: $[\alpha]_D$ +29.2° (*c* 6.5, $CHCl_3$); ^{1}H NMR δ 7.35–7.23 (m, 15H, 3Ph), 5.95–5.78 (m, 1H, –*CH*=CH_2), 5.30–5.15 (m, 2H, CH_2=CH–), 4.95 (d, 1H, $J_{1,2}$ = 3.3 Hz, H–1), 4.88,4.63 (2d, 2H, J = 11.3 Hz, CH_2Ph), 4.68, 4.51 (2d, 2H, J = 10.6 Hz, CH_2Ph), 4.58, 4.52 (2d, 2H, J = 11.8 Hz, CH_2Ph), 4.25–4.00 (m, 4H, H–3, H–4, –CH_2–CH=CH_2), 3.99–3.87 (m, 2H, H–2, H–5), 3.82–3.62 (m, 2H, H–6, H–6'), 3.38 (s, 3H, OCH_3).

Anal. Calcd for $C_{31}H_{36}O_6$: C, 73.81; H, 7.14. Found: C, 73.51; H, 7.18.

Deallylation of compounds 3, 6, 9. To a solution of 6-*O*-allylated saccharide (**3**, **6**, or **9**, 0.5 mmol) in anhyd MeOH (10 mL) was added $PdCl_2$ (0.05 mmol). The mixture was stirred at room temperature for 5 h, TLC indicated that the reaction was complete. The mixture was filtered and concentrated to a syrup. Purification by column chromatography with 1:2 ethyl acetate - petroleum ether as the eluent afforded products with free primary hydroxyl groups respectively. For **10** (from **3**), syrup (76%); $[\alpha]_D$ –45.5° (*c* 11.0, $CHCl_3$); lit[14] $[\alpha]_D$ –50.5° (*c* 1.7, $CHCl_3$).

For **13** (*from* **6**), syrup (72%): $[\alpha]_D$ –52.7° (*c* 11.1, $CHCl_3$); ^{1}H NMR δ 7.80–7.77 (d, 2H, Ph of Ts), 7.38–7.12 (m, 12H, Ph of Ts, 2Ph), 6.20 (d, 0.25H, $J_{1,2}$ = 3.4 Hz, H–1α), 5.98 (s, 0.75H, H–1β), 5.15, 4.98 (d, s, 1H, H–2α,β), 4.80–4.24 (m, 6H, 2CH_2Ph,

H–3, H–4), 4.00–3.60 (m, 4H, H–5, H–6, 6', OH), 2.44, 2.42 (S, 3H, PhC*H*$_3$ α,β), 2.00, 1.96 (S, 3H, CO*CH*$_3$ α,β).

Anal. Calcd for $C_{28}H_{32}O_6$: C, 72.41; H, 6.90. Found: C, 72.19; H, 6.84.

For **14** (from **9**), syrup (78%): $[\alpha]_D$ +0.2° (*c* 4.8, $CHCl_3$); ^{1}H NMR δ 7.35–7.23 (m, 15H, Ph), 5.04 (d, 1H, $J_{1,2}$ = 3.3 Hz, H–1), 4.86, 4.61 (2d, 2H, J = 11.2 Hz, *CH*$_2$Ph), 4.65, 4.46 (2d, 2H, J = 11.9 Hz, *CH*$_2$Ph), 4.59, 4.50 (2d, 2H, J = 10.7Hz, *CH*$_2$Ph), 4.26–4.22 (m, 2H, H–3, H–4), 3.98–3.90 (m, 3H, H–2, H–5, OH), 3.95, 3.79 (m, 2H, H–6, H–6'), 3.38 (S, 3H, *CH*$_3$).

Anal. Calcd for $C_{29}H_{32}O_9S$: C, 62.59; H, 5.76. Found: C, 62.82; H, 5.71.

6-*O*-(6-*O*-Allyl-3,5-di-*O*-benzyl-α-D-mannofuranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (19). The 1,2-anhydro sugar **7** (220 mg, 0.58 mmol) was dissovled in anhyd dichloromethane (6 mL) containing 4 Å molecular sieves (300 mg). To the mixture was added a solution of **17** (88 mg, 0.36 mmol) in dichloromethane (2 mL) in one portion. The mixture was stirred at room temperature for 2 h, at the end of which time **7** had disappeared. The solution was concentrated to a syrup which was subjected to column chromatography on silica gel with 1:2 ethyl acetate - petroleum ether as the eluent, and **19** was obtained as a syrup (184 mg, 85%): $[\alpha]_D$ +6.3 ° (*c* 7.0, $CHCl_3$); ^{1}H NMR δ 7.35–7.18 (m, 10H, 2Ph), 5.96–5.70 (m, 1H, *CH*=CH$_2$), 5.50 (d, 1H, $J_{1,2}$ = 4.8 Hz, H–1), 5.30–5.08 (m, 2H, CH=*CH*$_2$), 4.96 (d, 1H, $J_{1',2'}$ = 1.4 Hz, H–1'), 4.83, 4.50 (2d, 2H, J = 11.4 Hz, *CH*$_2$Ph), 4.65, 4.61 (2d, 2H, J = 10.4 Hz, Ph*CH*$_2$), 4.57 (dd, 1H, $J_{2,3}$ = 2.5 Hz, $J_{3,4}$ = 7.8 Hz, H–3), 4.51, 4.49 (2d, 2H, J = 10.7 Hz, Ph*CH*$_2$), 4.37 (dd, 1H, $J_{2',3'}$ = 6.4 Hz, $J_{3',4'}$ = 4.6 Hz, H–3'), 4.32 (d, 1H, $J_{3',4'}$ = 4.6 Hz, H–4'), 4.30 (dd, 1H, $J_{1,2}$ = 4.8 Hz, $J_{2,3}$ = 2.5 Hz, H–2), 4.21 (dd, 1H, $J_{3,4}$ = 7.7 Hz, $J_{4,5}$ = 2.0 Hz, H–4), 4.12–4.08 (m, 1H, H–5'), 4.02–3.69 (m, 6H, H–2', 5, 6a, 6b, 6a', 6b'), 1.55, 1.46, 1.35, 1.34 (4s, 12H, 2 C(*CH*$_3$)$_2$).

Anal. Calcd for $C_{35}H_{46}O_{11}$: C, 65.42; H, 7.17. Found: C, 65.72; H, 7.25.

Methyl 6-*O*-(6-*O*-Allyl-3,5-di-*O*-benzyl-α-D-mannofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (20). Coupling of **7** with **18**[15] was carried out using the same procedure as described in the preparation of **19**, and **20** was obtained as a syrup (83%): $[\alpha]_D$ +29.4° (*c* 18.7, $CHCl_3$); ^{1}H NMR δ 7.40-7.10 (m, 25H, 5Ph), 6.00-5.80 (m, 1H, *CH*=CH$_2$), 5.36-5.12 (m, 3H, CH=*CH*$_2$, H-1), 4.97 (s, 1H, H-1'), 4.94-4.20 (m, 18H, 5*CH*$_2$Ph, *CH*$_2$-CH=CH$_2$, H-2, 2', 3, 3', 4, 4'), 4.10-3.60 (m, 6H, H-5, 5', 6a, 6a', 6b, 6b'), 3.30 (s, 3H, O*CH*$_3$), 2.64 (s, 1H, OH).

Anal. Calcd for $C_{51}H_{58}O_{11}$: C, 72.34; H, 6.86. Found: C, 72.58; H, 6.77.

3,5-Di-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-trimethylsilyl-α-D-glucofuranose (11). To a solution of compound **10** (140 mg, 0.35 mmol) in DMF (10 mL) was added chlorotrimethylsilane (1.3 mL, 10 mmol) and imidazole (820 mg, 12 mmol). The mixture was stirred at room temperature for 5 h, at the end of which time TLC (1:2 ethyl acetate - petroleum ether) indicated that the reaction was complete. The mixture was poured into water, the solution was extracted repeatedly with dichloromethane, and the combined extracts were dried over Na_2SO_4 and concentrated to a syrup. Purification by column chromatography with 1:3 ethyl acetate - petroleum ether as the eluent afforded syrupy trimethylsilylated **11** (144 mg, 87%).

3,5-Di-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-tributylstannyl-α-D-glucofuranose (12). Compound **10** (140 mg, 0.35 mmol) and bis(tributyltin)oxide (0.09 mL, 0.18 mmol) in 5 mL of toluene under N_2 was stirred at reflux for 30 h with azeotropic removal of water. The reaction mixture was cooled to 60 °C, and the solvents were removed by evaporation with a dry N_2 stream. Crude tributylstannylated **12** was dried in vacuo and used for further reaction without purification.

6-*O*-(2-*O*-Acetyl-6-*O*-allyl-3,5-di-*O*-benzyl-α-D-mannofuranosyl)-3,5-di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (21). To a solution of **10** (300 mg, 0.75 mmol) in dichloromethane (10 mL) containing 4 Å molecular sieves (500 mg) was added silver triflate (210 mg, 0.82 mmol) under N_2 atmosphere. The mixture was stirred at room temperature for several min, then 1,2-anhydro sugar **7** (440 mg, 1.15 mmol) was added. The mixture was stirred at room temperature for 1 h, TLC indicated that **7** disappeared. The mixture was filtered, concentrated to a syrup which was subjected to column chromatography on silica gel with 1:2 ethyl acetate - petroleum ether as the eluent. The product was obtained as a syrup (381 mg, 65%). Under the same conditions, coupling of **7** with **12** gave a higher yield of 71%. Acetylation with acetic anhydride in pyridine quantitatively gave **21**: $[\alpha]_D$ +3.6° (*c* 2.3, $CHCl_3$); ^{1}H NMR δ 7.38–7.18 (m, 20H, 4Ph), 5.88 (d, 1H, $J_{1,2}$ = 3.6 Hz, H–1), 6.00–5.80 (m, 1H, –*CH*=CH_2), 5.30–5.10 (m, 4H, H–1', H–2', CH=*CH_2*), 4.94–4.28 (m, 11H, 4*CH_2*Ph, H–3, H–3', H–4'), 4.20 (dd, 1H, $J_{3,4}$ = 2.7 Hz, $J_{4,5}$ = 9.0 Hz, H–4), 4.10 (d, 1H, $J_{1,2}$ = 3.6 Hz, H–2), 4.09–3.60 (m, 8H, –*CH_2*–CH=CH_2, H–5, 5', 6a, 6b, 6a', 6b'), 2.00 (s, 3H, CO*CH_3*), 1.44,1.30 (2s, 6H, *CH_3CCH_3*).

Anal. Calcd for $C_{48}H_{56}O_{12}$: C, 69.90; H, 6.80. Found: C, 69.95; H, 6.71.

Methyl 6-*O*-(2-*O*-Acetyl-6-*O*-allyl-3,5-di-*O*-benzyl-α-D-mannofuranosyl)-2,3,5-tri-*O*-benzyl-α-D-mannofuranoside (22). Condensation of **7** with **14** followed by acetylation using the same procedure as described in the preparation of **21** gave compound **22** as a syrup (67%): $[\alpha]_D$ +44.3° (*c* 8.5, $CHCl_3$); ^1H NMR δ 7.40-7.18 (m, 25H, 5Ph), 6.00-5.78 (m, 1H, *CH*=CH_2), 5.36-5.00 (m, 5H, CH_2=CH ,H-1 H-1', H-2'), 4.90-4.40 (m, 10H, 5CH_2Ph), 4.40 (m, 2H ,H-3, 3'), 4.30-4.20 (m, 2H, H-4, 4'), 4.10-4.00 (m, 5H, CH_2-CH=CH2, H-2, 5, 5'), 3.90 (m, 2H, H-6a, 6a'), 3.70-3.60 (m, 2H, H-6b, 6b'), 3.30 (s, 3H, OCH_3), 2.00 (s, 3H, COCH_3).

Anal. Calcd for $C_{53}H_{60}O_{12}$: C, 71.62; H, 6.76. Found: C, 71.85; H, 6.71.

6-*O*-(2-*O*-Acetyl-3,5,6-tri-*O*-benzyl-α-D-mannofuranosyl)-1-*O*-acetyl-3,5-di-*O*-benzyl-2-*O*-toluenesulfonyl-D-glucofuranose (23). Coupling of 1,2-Anhydro-3,5,6-tri-*O*-benzyl-β-D-mannofuranose[10] with **13** followed by acetylation using the same procedure as described in the preparation of **21** gave compound **23** as a syrup (61%): $[\alpha]_D$ –6.9° (*c* 10.2, $CHCl_3$); ^1H NMR δ 7.80-7.70 (d, 2H, Ph of Ts), 7.38-7.10 (m, 27H, Ph of Ts, 5Ph), 6.10 (d, 1/3H, $J_{1,2}$ = 3.4 Hz, H-1 α), 5.98 (s, 2/3H, H-1 β), 5.12-5.04 (m, 2H, H-2 α , β , H-2'), 4.98 (s, 1H, H-1'), 4.88-4.20 (m, 14H, 5CH_2Ph, H-3, 3', 4, 4'), 4.10-3.60 (m, 6H, H-5, 5', 6a, 6a', 6b, 6b'), 2.46, 2.44 (2s, 3H, PhCH_3 α , β), 204, 202, 200, 1.96 (4s, 6H, 2 COCH_3 α , β).

Anal. Calcd for $C_{58}H_{62}O_{15}S$: C, 67.57; H, 6.02. Found: C, 67.65; H, 6.01.

5-*O*-(2-*O*-Acetyl-6-*O*-allyl-3,5-di-*O*-benzyl-α-D-mannofuranosyl)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose (24). Coupling of **7** with **15**[16] folowed by acetylation using the same procedure as described in the preparation of **21** gave **24** as a syrup (61%): $[\alpha]_D$ –4.7° (*c* 3.2, $CHCl_3$); ^1H NMR δ 7.40-7.20 (m, 15H, 3Ph), 5.98-5.78 (m, 1H, *CH*=CH_2), 5.90 (d, 1H, $J_{1,2}$ = 3,4 Hz, H-1), 5.30-5.10 (m, 2H, CH=CH_2), 5.04 (s, 1H, H-1'), 4.97-4.40 (m, 9H, 3CH_2Ph, H-3, 3', 4), 4.24 (dd, 1H, $J_{3',4'}$ = 7.2 Hz, $J_{4',5''}$ = 8.0 Hz, H-4'), 4.09-3.90 (m, 5H, CH_2-CH=CH_2, H-2, 2', 5''), 3.90 (dd, 1H, $J_{5'',6}$ = 2.8 Hz, $J_{6,6'}$ = 10.2 Hz, H-6), 3.65 (dd, 1H, $J_{5'',6'}$ = 5.0 Hz, H-6'), 3.60 (dd, 1H, $J_{4,5}$ = 4.7 Hz, $J_{5,5'}$ 9.4 = Hz, H-5), 3.35 (dd, 1H, $J_{4,5'}$ = 7.0 Hz, H-5'), 1.55, 1.35 (2s, 6H, CH_3CCH_3).

Anal. Calcd for $C_{40}H_{48}O_{11}$: C, 68.18; H, 6.82. Found: C, 67.87; H, 6.76.

5-*O*-(2-*O*-Acetyl-6-*O*-allyl-3,5-di-*O*-benzyl-α-D-mannofuranosyl)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-ribofuranose (25). Coupling of **7** with **16**[17] followed by acetylation using the same procedure as described in the preparation of **21** gave **25** as a syrup (61%): $[\alpha]_D$ +11.3° (*c* 13.5, $CHCl_3$); ^1H NMR δ 7.38-7.18 (m, 15H, 3Ph), 6.00-5.80 (m, 1H, *CH*=CH_2), 5.84 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 5.30-5.10 (m, 2H, CH=*CH_2*), 4.98 (s, 1H, H-1'), 4.84-4.50 (m, 6H, 3*CH_2*Ph), 4.02-3.98 (m, 2H, H-3', 4), 4.26 (dd, 1H, $J_{3',4'}$ = 7.5 Hz, $J_{4',5''}$ = 8.3 Hz, H-4'), 4.02-3.90 (m, 5H, *CH_2*-CH=CH_2, H-2, 2', 5''), 3.90 (dd, 1H, $J_{5'',6}$ = 2.6 Hz, $J_{6,6'}$ = 10.4 Hz, H-6), 3.60 (dd, 1H, $J_{5'',6'}$ = 5.4 Hz, H-6'), 3.55 (dd, 1H, $J_{4,5}$ = 2.7 Hz, $J_{5,5'}$ = 11 Hz, H-5), 3.20 (dd, 1H, $J_{4,5'}$ = 4.3 Hz, H-5'), 1.60, 1.45 (2s, 6H, *CH_3CCH_3*).

Anal. Calcd for $C_{40}H_{48}O_{11}$: C, 68.18; H, 6.82. Found: C, 68.37; H, 6.89.

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