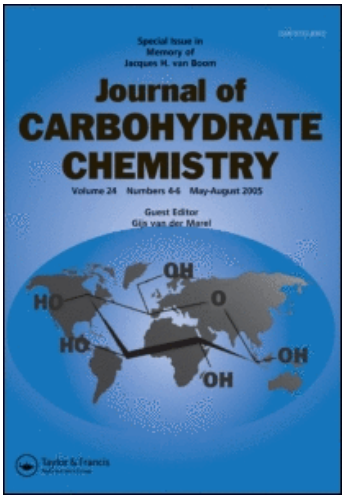

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REGIO- AND STEREOSELECTIVE SYNTHESIS OF OLIGOSACCHARIDES WITH ACETOBROMOLACTOSE AND ACETOBROMOMALTOSE AS GLYCOSYL DONORS VIA ORTHOESTER INTERMEDIATES

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ABSTRACT

Regio- and stereoselective synthesis of some trisaccharides was effected in high yields from coupling of acetobromolactose or acetobromomaltose as donors with partially protected glucoside acceptors through an orthoester formation-rearrangement strategy. Selective 1→6 or 1→3 with 1,2-*trans* glycosylation was achieved.

INTRODUCTION

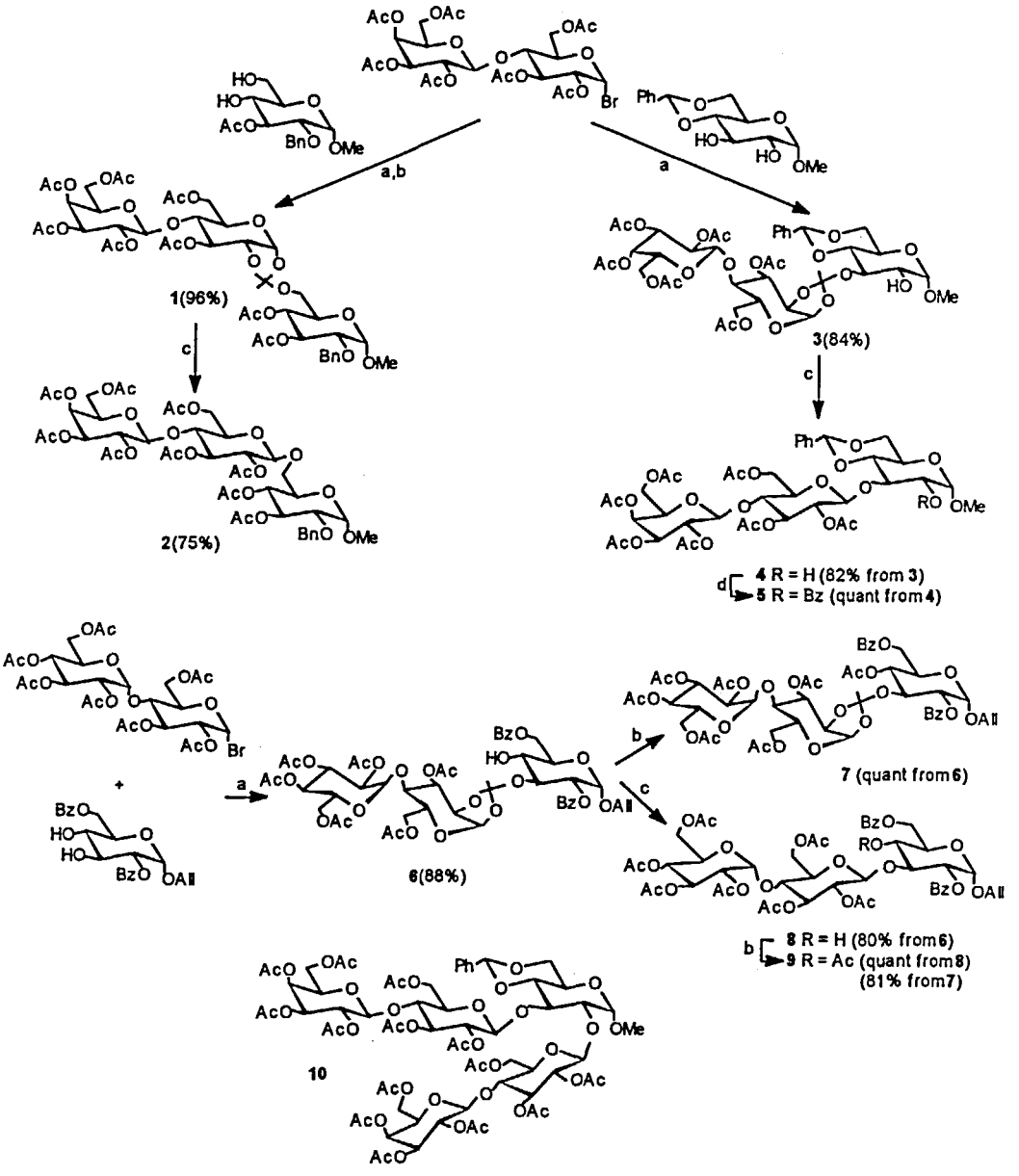
In our preceding communication,[1] we reported a new method for the regio- and stereoselective synthesis of oligosaccharides *via* orthoester intermediates using acetobromoglucose, -galactose, and -mannose as the glycosyl donors and unprotected or partially protected glycosides as the glycosyl acceptors. This method gave in very high yields the sugar-sugar orthoesters, rearrangement of which was carried out smoothly affording the desired oligosaccharides in satisfactory results. By the new method, a series of selective 1→6 or 1→3 glycosides was achieved. We suggested that the high regioselectivity, which cannot be achieved by direct coupling under normal

glycosylation conditions, was mainly the result of steric factors, i.e., the attack on the acyloxonium carbon of orthoester by a less hindered hydroxyl group, while the high regio- and stereoselectivity of the rearrangement resulted from the C-1 backside attack of the acyloxonium ion by the trimethylsilylated acceptor.[1] Now we report an important application of the method for the synthesis of oligosaccharides using acetobromolactose and acetobromomaltose as the glycosyl donors and partially protected glucopyranosides as the glycosyl acceptors.

RESULTS AND DISCUSSION

The preparation of disaccharide orthoesters from coupling of a disaccharide donor with an acceptor of alcohol aglycon were reported more than twenty years ago,[2b-d] but no significant use was found for those compounds. Danishefsky reported a trisaccharide orthoester[2a] as an undesired by-product in the coupling of a thiodisaccharide donor with a glucal acceptor. These represent the rarely reported works dealing with the orthoesters formed from disaccharide donors. Some examples for regioselective glycosylation using glycosyl fluorides[3a] and imidates[3b-d] as donors and partially protected glycosides as acceptors were reported recently. In our present research, highly regio- and stereoselective synthesis of trisaccharides with acetobromolactose and acetobromomaltose as the glycosyl donors and partially protected glucosides as the glycosyl acceptors was achieved through the orthoester formation–rearrangement strategy. That is: (1) preparation of trisaccharide orthoesters from coupling of acetobromolactose or acetobromomaltose with partially protected sugar acceptors in high yields and good selectivity; (2) rearrangement of either the partially protected or the fully protected trisaccharide orthoesters of diverse structure by catalytic TMSOTf giving satisfactory results.

As shown in the Scheme, coupling[1] of acetobromolactose with methyl 3-*O*-acetyl-2-*O*-benzyl-α-D-glucopyranoside[4] promoted by AgOTf (1 equiv) in the presence of 2,4-lutidine (1 equiv) in anhydrous dichloromethane followed by acetylation with Ac_2O in pyridine selectively afforded the orthoester **1** in nearly quantitative yield. Rearrangement[1,5] of **1** with a catalytic amount of TMSOTf selectively furnished **2** in a satisfactory yield (75%). The structure of **2** was unambiguously verified by its ^{1}H NMR spectrum showing seven signals at δ 5.41 – 4.82 for H-2'', H-3'', H-4'', H-2', H-3', H-3, and H-4, a normal region for the protons that are geminal to secondary *O*-acetyl, two



Scheme

Reagents and conditions: a. AgOTf (1 equiv), 2,4-lutidine (1 equiv), CH_2Cl_2 (anhydrous), M.S.(4 Å), RT, N_2, 2 h; b. Ac_2O, pyridine (dry); c. TMSOTf (0.1 equiv), CH_2Cl_2, M.S.(4 Å), -30 °C, N_2, 40 min; d. BzCl, pyridine (dry).

multiplets centered at δ 4.09 for the *O*-Ac-related H-6' and H-6'', and two upfield signals at δ 3.88, and 3.47 for H-6, a clear indication of 6-*O*-glycosylation. Coupling of the disaccharide bromides with secondary hydroxyl groups of partially protected sugars by the new method also showed excellent selectivity. For instance, coupling of acetobromolactose with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside gave orthoester **3** in a high yield (84%); further rearrangement selectively afforded 1→3 β-linked trisaccharide **4** with no change of the acid labile benzylidene group in a yield of 82%. In contrast, direct glycosylation of acetobromolactose with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside under similar conditions, but in the absence of 2,4-lutidine, yielded a bis-glycosylated pentasaccharide **10** even at a 1/1 ratio of donor/acceptor. Benzoylation of **4** gave **5**, the 1,3-linkage was easily identified, as the ^{1}H NMR spectrum of **5** gave a doublet of doublets at δ 5.12 for H-2 of the reducing end. Similar 3-regioselectivity was observed for coupling of acetobromomaltose with allyl 2,6-di-*O*-benzoyl-α-D-glucopyranoside[6] followed by rearrangement, and 1→3 linked trisaccharide **8** was obtained in an overall yield of 70%. The structure of **8** was verified as its acetate **9**, the 2D NMR spectrum of **9** showing a downfield chemical shift of H-4 (dd, δ 5.15) indicated 3-*O*-glycosylation. Alternatively, acetylation of the orthoester **6** (giving **7**) followed by rearrangement afforded a compound identical to **9**, confirming that both the orthoester formation and rearrangement are regioselective. It is interesting to note that with acetobromodisaccharides as the glycosyl donors, selective 3-*O*-glycosylation for the acceptors having either 2,3 or 3,4 free secondary hydroxyl groups was achieved. This is the same as in the case using acetobromomonosaccharides as the glycosyl donors[1] indicating that the regioselectivity of orthoester formation only depends on the acceptor structure rather than the donor structure.

In summary, we have presented a very effective method for regio- and stereoselective synthesis of 1,2-*trans*-linked oligosaccharides using disaccharide bromides as the glycosyl donors. The high regioselectivity of orthoester formation can result in a high yield synthesis of 1→6 and 1→3 linked oligosaccharides, while the high selectivity of rearrangement allows further modification at the unprotected hydroxyl groups of the rearrangement products. This new methodology will be very useful for the synthesis of complex oligosaccharides.[7] Further investigation of the application of this new method is in process.

EXPERIMENTAL

General methods. Optical rotations were determined with a Perkin-Elmer model 241-MC automatic polarimeter for solutions in a 1-dm, jacketed cell. ^{1}H NMR spectra were recorded with Varian XL-400 and XL-200 spectrometers, for solutions in $CDCl_3$ with tetramethylsilane (Me_4Si) as the internal standard. Chemical shifts are expressed in ppm downfield from the internal Me_4Si absorption. Thin-layer chromatography (TLC) was performed on silica gel HF, detection being affected by charring with 30% (v/v) sulfuric acid in methanol or sometimes by UV detection. Column chromatography was conducted by elution of a column (8/100 mm, 16/240 mm, 18/300 mm, and 35/400 mm) of silica gel (100-200 mesh) with EtOAc/petroleum ether (bp 60-90 °C) as the eluent. Solutions were concentrated at a temperature < 60 °C under diminished pressure.

3',6'-Di-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranose 1',2'-(Methyl 3,4-Di-*O*-acetyl-2-*O*-benzyl-α-D-glucopyranosid-6-yl Orthoacetate) (1). To a stirred solution of acetobromolactose (209 mg, 0.3 mmol), and 2,4-lutidine (45 μL, 0.39 mmol), and methyl 3-*O*-acetyl-2-*O*-benzyl-β-D-glucopyranoside (95 mg, 0.29 mmol) in dichloromethane (20 mL) under nitrogen atmosphere was added silver triflate (80 mg, 0.31 mmol) in a dark room, and the reaction was carried out at room temperature and monitored by TLC (1:1 petroleum ether/EtOAc). After completion of the reaction, the mixture was partitioned between dichloromethane and water. The organic phase was washed with 10% aq $Na_2S_2O_3$ and 10% aq Na_2CO_3, then concentrated, dried, and subjected to column chromatography with 1.5:1 petroleum ether/EtOAc as the eluent, giving the trisaccharide othoester. Acetylation of the trisaccharide orthoester with Ac_2O/pyridine followed by column chromatography with 2:1 petroleum ether/EtOAc as the eluent furnished the product **1** in almost quantitative yield (280 mg, 98% based on the acceptor) as a syrup: $[\alpha]_D$ +62.1° (*c* 1.1, $CHCl_3$); ^{1}H NMR δ 7.34-7.28 (m, 5H, Ph-H), 5.66 (d, 1H, $J_{1',2'}$ = 5.2 Hz, H-1'), 5.48 (m, 1H, H-4''), 5.41 (t, 1H, J = 9.6 Hz, H-3), 5.38-5.36 (m, 1H, H-3'), 5.17 (dd, 1H, $J_{1'',2''}$ = 8.0 Hz, $J_{2'',3''}$ = 10.4 Hz, H-2''), 5.01-4.95 (m, 2H, H-3'', 4), 4.66-4.56 (m, 4H, H-1, 1'', PhCH_2), 3.38 (s, 3H, CH_3O), 3.39-3.37 (m, 1H, H-2), 2.17-1.98 (8s, 24H, 8CH_3CO), 1.69 (s, 3H, CH_3CO_3).

Anal. Calcd for $C_{44}H_{58}O_{25}$: C, 53.55; H, 5.92. Found: C, 53.76; H, 6.01.

Methyl 3,4-Di-*O*-acetyl-2-*O*-benzyl-6-*O*-{2',3',6'-tri-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranosyl}-α-D-glucopyranoside (2). To a stirred solution of sugar-sugar orthoester **1** (162 mg, 0.16 mmol) in dichloromethane (10 mL) was added TMSOTf (3 μL, 0.1 equiv) under nitrogen atmosphere at -30°C, and the reaction was monitored by TLC (1:1 petroleum ether/EtOAc). After completion of the reaction, triethylamine (5 μL) was added to the mixture. The mixture was filtered, and the filtrate was washed with CH_2Cl_2. The combined solution was washed with N HCl (10 mL), sat aq $NaHCO_3$ (10 mL), and aq NaCl (2×10 mL), then dried over anhydrous Na_2SO_4, and concentrated. The residue was subjected to column chromatography with 1.5:1 petroleum ether/EtOAc as the eluent, giving the product **2** (121 mg, 75%) as an amorphous solid: $[\alpha]_D$ +45.2° (*c* 2.4, $CHCl_3$); ^1H NMR δ 7.36-7.29 (m, 5H, Ph-H), 5.41 (t, 1H, J = 9.6 Hz, H-3), 5.34 (d, 1H, $J_{3'',4''}$ = 3.0 Hz, H-4''), 5.18 (t, 1H, J = 9.3 Hz, H-3'), 5.10 (dd, 1H, $J_{1'',2''}$ = 7.9 Hz, $J_{2'',3''}$ = 9.3 Hz, H-2''), 4.96-4.82 (m, 3H, H-2'', 3'', 4), 4.65, 4.61 (ABq, 2H, J = 12.8 Hz, PhCH_2), 4.63 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 4.49 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.46 (d, 1H, $J_{1'',2''}$ = 8.0 Hz, H-1''), 4.14-4.04 (m, 4H, H-6', 6''), 3.90-3.84 (m, 3H, H-5'', 5', 6_a), 3.77 (t, 1H, J = 9.3 Hz, H-4'), 3.60-3.54 (m, 1H, H-5), 3.52 (dd, 1H, H-2), 3.46 (dd, 1H, $J_{5,6b}$ = 6.1Hz, $J_{6a,6b}$ = 12.7 Hz, H-6_b), 3.36 (s, 3H, CH_3O), 2.15-1.97 (9s, 27H, 9 CH_3CO).

Anal. Calcd for $C_{44}H_{58}O_{25}$: C, 53.55; H, 5.92. Found: C, 53.78; H, 6.03.

3',6'-Di-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranose 1',2'-(Methyl 4,6-*O*-Benzylidene-α-D-glucopyranosid-3-yl Orthoacetate) (3). Under the same conditions as described for the preparation of the trisaccharide orthoester **1** (without an acetylation step), coupling of acetobromolactose (300 mg, 0.43 mmol) and methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (120 mg, 0.43 mmol) in anhydrous dichloromethane (20 mL) promoted by AgOTf (110 mg, 1 equiv)/2,4-lutidine (50 μL, 1 equiv) furnished the trisaccharide orthoester **3** (325 mg) in a yield of 84%: $[\alpha]_D$ +88.5° (*c* 0.6, $CHCl_3$); ^1H NMR δ7.48-7.30 (m, 5H, Ph-H), 5.57 (d, 1H, $J_{1',2'}$ = 5.2 Hz, H-1'), 5.43 (s, 1H, PhC*H*), 5.42 (t, 1H, J = 1.3 Hz, H-3'), 5.32 (d, 1H, $J_{3'',4''}$ = 3.5 Hz, H-4''), 5.14 (dd, 1H, $J_{1'',2''}$ = 8.0 Hz, $J_{2'',3''}$ = 9.8 Hz, H-2''), 4.96 (dd, 1H, $J_{3'',4''}$ = 3.5 Hz, H-3''), 4.73 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.55 (d, 1H, $J_{1'',2''}$ = 8.0 Hz, H-1''), 3.43 (s, 3H, CH_3O), 2.14-1.94 (6s, 18H, 6CH_3CO), 1.71 (s, 3H, CH_3CO_3).

Anal. Calcd for $C_{40}H_{52}O_{23}$: C, 53.33; H, 5.82. Found: C, 53.50; H, 5.76.

Methyl 4,6-*O*-Benzylidene-3-*O*-{2',3',6'-tri-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranosyl}-α-D-glucopyranoside (4). The trisaccharide **4** (245 mg) was obtained in a yield of 82% through TMSOTf (0.1 equiv) catalyzed rearrangement of **3** (300 mg, 0.33 mmol) under the same conditions as described for the rearrangement of **1**: $[\alpha]_D$ +69.7° (*c* 1.5, $CHCl_3$); ^1H NMR δ 7.49-7.35 (m, 5H, Ph-H), 5.54 (s, 1H, PhC*H*), 5.32 (d, 1H, $J_{3'',4''}$ = 2.8 Hz, H-4''), 5.16 (t, 1H, J = 9.2 Hz, H-3'), 5.04 (dd, 1H, $J_{1'',2''}$ = 7.9 Hz, $J_{2'',3''}$ = 9.8 Hz, H-2''), 4.90 (dd, 1H, $J_{1',2'}$ = 7.9 Hz, $J_{2',3'}$ = 9.2 Hz, H-2'), 4.89 (dd, 1H, H-3''), 4.79 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 4.76 (d, 1H, $J_{1'',2''}$ = 7.9 Hz, H-1''), 4.35 (d, 1H, $J_{1',2'}$ = 7.9 Hz, H-1'), 3.45 (s, 3H, C*H*$_3$O), 2.15-1.96 (7s, 21H, 7C*H*$_3$CO).

Anal. Calcd for $C_{40}H_{52}O_{23}$: C, 53.33; H, 5.82. Found: C, 53.21; H, 5.77.

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-{2',3',6'-tri-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranosyl}-α-D-glucopyranoside (5). Benzoyl chloride (1.0 mL) was added dropwise to a solution of **4** (90 mg, 0.1 mmol) in pyridine (4 mL) at 0 °C and the mixture was stirred at room temperature overnight. Methanol was added to quench the reaction and the reaction mixture was concentrated and subjected to column chromatography with 1.5:1 petroleum ether/EtOAc as the eluent, quantitatively giving the product **5** as an amorphous solid: $[\alpha]_D$ +74.8° (*c* 0.8, $CHCl_3$); ^1H NMR δ 8.06 (d, 2H, J = 7.2 Hz, Bz-H), 7.75-7.30 (m, 8H, Bn, Bz-H), 5.60 (s, 1H, PhC*H*), 5.31 (d, 1H, $J_{3'',4''}$, = 2.9 Hz, H-4''), 5.12 (dd, 1H, $J_{1,2}$ = 3.4 Hz, $J_{2,3}$ = 9.6 Hz, H-2), 5.04 (dd, 1H, $J_{1'',2''}$ = 7.9 Hz, $J_{2'',3''}$ = 9.8 Hz, H-2''), 5.02 (t, 1H, J = 9.4 Hz, H-3'), 5.01 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.90 (dd, 1H, $J_{2'',3''}$ = 9.8 Hz, $J_{3'',4''}$ = 2.9 Hz, H-3''), 4.87 (dd, 1H, $J_{1',2'}$ = 7.9 Hz, $J_{2',3'}$ = 9.4 Hz, H-2'), 4.76 (d, 1H, $J_{1'',2''}$ = 7.9 Hz, H-1''), 4.35 (d, 1H, $J_{1',2'}$ = 7.9 Hz, H-1'), 3.39 (s, 3H, C*H*$_3$O), 2.15-1.54 (7s, 21H, 7C*H*$_3$CO).

Anal. Calcd for $C_{47}H_{56}O_{24}$: C, 56.17; H, 5.62. Found: C, 56.37; H, 5.51.

3',6'-Di-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl)-α-D-glucopyranose 1',2'-(Allyl 2,6-Di-*O*-benzoyl-α-D-glucopyranosid-3-yl Orthoacetate) (6). Coupling of acetobromomaltose (556 mg, 0.8 mmol) with allyl 2,6-di-*O*-benzoyl-α-D-glucopyranoside (348 mg, 0.81 mmol) under the same conditions as described for the preparation of **1** afforded the trisaccharide **6** (737 mg, 88%): $[\alpha]_D$ +72.1° (*c* 1.0, $CHCl_3$); ^1H NMR δ 8.09-7.46 (m, 10H, Bz-H), 5.88-5.78 (m, 1H,

CH_2=C*H*-CH_2-), 5.84 (d, 1H, $J_{1',2'}$ = 5.4 Hz, H-1'), 5.57 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 5.34 (t, 1H, J = 9.9 Hz, H-3'), 5.27-5.00 (m, 1H, H-1'', 3'', 4'', C*H*$_2$=CH-CH_2-), 4.87-4.52 (m, 4H, H-2, 2'', 6), 4.42-4.38 (m, 1H, H-2'), 2.10-1.92 (6s, 18H, 6 C*H*$_3$CO), 1.79 (s, 3H, C*H*$_3$CO$_3$).

Anal. Calcd for $C_{49}H_{58}O_{25}$: C, 56.21; H, 5.58. Found: C, 56.37; H, 5.67.

3',6'-Di-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl)-α-D-glucopyranose 1',2'-(Allyl 4-*O*-Acetyl-2,6-di-*O*-benzoyl-α-D-glucopyranosid-3-yl Orthoacetate) (7). Acetylation of compound **6** (300 mg, 0.29 mmol) with acetic anhydride (1 mL) in pyridine (2 mL) quantitatively afforded 7 (312 mg): $[\alpha]_D^{20}$ +101.1° (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 8.09-7.46 (m, 10H, Bz-H), 5.82-5.72 (m, 1H, CH_2=C*H*-CH_2-), 5.71 (d, 1H, $J_{1',2'}$ = 5.6 Hz, H-1'), 5.63 (d, 1H, $J_{1,2}$ = 4.1 Hz, H-1), 5.35 (t, 1H, J = 10.0 Hz, H-3'), 5.24-5.01 (m, 1H, H-1'', 2'', 4, 4'', C*H*$_2$=CH-CH_2-), 4.79-4.75 (m, 2H, H-2, 3'), 4.48-4.46 (m, 1H, H-6_a), 4.40-4.34 (m, 2H, H-2', 6_b), 2.14, 2.09, 2.07, 2.02, 2.02, 1.94, 1.26 (7s, 21H, 7C*H*$_3$CO), 1.75 (s, 3H, C*H*$_3$CO$_3$).

Anal. Calcd for $C_{51}H_{60}O_{26}$: C, 56.25; H, 5.55. Found: C, 56.11; H, 5.61.

Allyl 2,6-Di-*O*-benzoyl-3-*O*-{2',3',6'-tri-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranosyl}-α-D-glucopyranoside (8). Compound **8** (242 mg) was obtained in a yield of 80% from **6** (300 mg, 0.29 mmol) by TMSOTf (0.1 equiv) catalyzed rearrangement under the same conditions as described for the rearrangement of **1**: $[\alpha]_D^{20}$ +50.4° (*c* 1.7, $CHCl_3$); ^{1}H NMR δ 8.08-7.46 (m, 10H, Bz-H), 5.87-5.78 (m, 1H, CH_2=C*H*-CH_2-), 5.36 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 5.35 (dd, 1H, $J_{2',3'}$ = 10.4 Hz, $J_{3',4'}$ = 9.8 Hz, H-3'), 5.26-5.11 (m, 2H, C*H*$_2$=CH-CH_2-), 5.21 (t, 1H, J = 9.2 Hz, H-3''), 5.16 (d, 1H, $J_{1'',2''}$ = 3.9 Hz, H-1''), 5.09-5.02 (m, 2H, H-2'', 4''). 4.87-4.80 (m, 2H, H-2, 2'), 4.72 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.71-4.58 (m, 2H, CH_2=CH-C*H*$_2$-), 3.95 (t, 1H, J = 9.0 Hz, H-3), 3.74 (dd, 1H, $J_{3',4'}$ = 9.8 Hz, $J_{4',5'}$ = 8.6 Hz, H-4'), 2.15-1.34 (7s, 21H, 7C*H*$_3$CO).

Anal. Calcd for $C_{49}H_{58}O_{25}$: C, 56.21; H, 5.58. Found: C, 56.07; H, 5.41.

Allyl 4-*O*-Acetyl-2,6-di-*O*-benzoyl-3-*O*-{2',3',6'-tri-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranosyl}-α-D-glucopyranoside (9). Method A: Acetylation of compound **8** (100 mg, 0.1 mmol) with acetic anhydride in pyridine quantitatively afforded 9 (104 mg); Method B: Rearrangement of 7 (200 mg, 0.18 mmol) as described for the rearrangement of 6

gave the same compound **9** (162 mg, 81%): $[\alpha]_D^{20}$ +70.1° (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 5.86-5.78 (m, 1H, CH_2=C*H*-CH_2-), 5.34 (dd, 1H, $J_{2'',3''}$ = 10.4 Hz, $J_{3'',4''}$ = 9.6 Hz, H-3''), 5.31 (d, 1H, $J_{1'',2''}$ = 4.1 Hz, H-1''), 5.19 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.15 (dd, 1H, $J_{3,4}$ = 10.2 Hz, $J_{4,5}$ = 9.3 Hz, H-4), 5.12 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.2 Hz, H-2), 5.08 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, $J_{3',4'}$ = 11.1 Hz, H-3'), 5.05 (t, 1H, $J_{3'',4''}$ = $J_{4'',5''}$ = 9.6 Hz, H-4''), 5.02 (dd, 1H, $J_{1',2'}$ = 8.8 Hz, $J_{2',3'}$ = 10.5 Hz, H-2'), 4.84 (dd, 1H, $J_{1'',2''}$ = 4.1 Hz, $J_{2'',3''}$ = 10.4 Hz, H-2''), 4.74 (d, 1H, $J_{1',2'}$ = 8.8 Hz, H-1'), 4.52 (dd, 1H, $J_{5,6}$ = 2.4 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6_a), 4.40 (dd, 1H, $J_{5',6'a}$ = 2.5 Hz, $J_{6'a,6'b}$ = 12.1 Hz, H-6'$_a$), 4.40-4.30 (m, 2H, H-5, 6_b), 4.27 (dd, 1H, $J_{5'',6''a}$ = 3.9 Hz, $J_{6''a,6''b}$ = 13.8 Hz, H-6''$_a$), 4.20-4.117 (m, 3H, H-6'$_b$, CH_2=CH-CH_2-), 4.06-4.02 (m, 2H, H-6''$_b$, CH_2=CH-CH_2-), 4.00-3.91 (m, 2H, H-4', 5''), 3.74-3.70 (m, 1H, H-5'), 2.15, 2.10, 2.03, 2.03, 2.00, 2.00, 1.88, 1.58 (8s, 24H, 8CH_3CO).

Anal. Calcd for $C_{51}H_{60}O_{26}$: C, 56.25; H, 5.55. Found: C, 56.14; H, 5.47.

Methyl 4,6-*O*-Benzylidene-2,3-di-*O*-(β-D-acetolactopyranosyl)-α-D-glucopyranoside (10). A parallel experiment was carried out for comparison of the regioselectivity between the orthoester formation and the normal glycosylation,. Thus, coupling of acetobromolactose (119 mg, 0.17 mmol) with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (48 mg, 0.17 mmol) in anhydrous dichloromethane (10 mL) promoted by AgOTf (44 mg, 0.17 equiv) furnished the pentasaccharide **10** (32% based on the acceptor): ^{1}H NMR δ 7.50-7.36 (m, 10H, Ph-H), 5.52 (s, 1H, PhC*H*), 5.35, 5.29 (2d, 2H, $J_{3,4}$ = 2.9 Hz, H-4'', 4''), 4.69, 4.54 (2d, 2H, $J_{1',2'}$ = 7.9 Hz, H-1', 1'), 3.36 (s, 3H, CH_3O), 2.18-1.96 (14s, 42H, 14 CH_3CO).

Anal. Calcd for $C_{66}H_{86}O_{40}$: C, 52.17; H, 5.71. Found: C, 51.95; H, 5.86.

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