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Convergent synthesis of the tetrasaccharide repeating unit related to the *O*-antigenic polysaccharide of *Escherichia coli* 78

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ABSTRACT

A convergent synthesis of the tetrasaccharide repeating unit of the *O*-antigenic cell wall polysaccharide of *Escherichia coli* 78, as the corresponding methyl glycoside (**I**), is being reported. It involved stereoselective glycosidation of a β-linked mannodisaccharide acceptor with a β-linked glucosamine based disaccharide thioglycoside donor, which were prepared from the corresponding functionalised monosaccharide based glycosyl donors and acceptors. The resulting tetrasaccharide derivative was finally converted to (**I**) by selective deprotection and also by global protection and deprotection techniques.

1. Introduction

Escherichia coli, a group of gram negative bacteria generally confined to intestinal lumen, causes human gastroenteritis;[1] it may also infect immune-suppressed host.[2] Three general clinical syndromes effected by pathogenic clones of *E. coli* are urinary tract infection, sepsis or meningitis, and enteric or diarrheal disease.[3] About one third of isolated enterotoxic strains of *E. coli* (ETEC) include serogroups of O6, O8, and O78. ETEC are associated with pediatric diarrhea in developing countries, severe cholera like disease in epidemic cholera zones and 'travellers' diarrhea'.

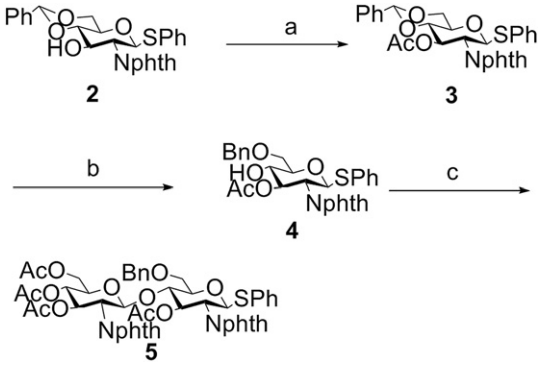
Structure of the *O*-antigenic cell wall polysaccharide of *E. coli* 78 (Fig. 1) was established by Jansson et al.[4] through methylation analysis, partial solvolysis with liquid hydrogen fluoride and also by 1D- and 2D-NMR spectroscopy.

→[4-β-D-GlcpNAc-(1→4)-β-D-GlcpNAc-(1→4)-β-D-Manp-(1→4)-α-D-Manp-1]$_n$→

Figure 1. Structure of the *O*-antigenic polysaccharide of *E. coli* 78.

Carbohydrates of bacterial cell wall play important role during host infection and subsequent immune response in the host. Substantial amounts of bacterial polysaccharides or oligosaccharides are necessary for extensive biological evaluation and biochemical studies of bacterial strains. Though, oligosaccharides can be isolated from the native sources, the meager amount obtained by isolation can not meet the quantity required for their detailed biological studies. Oligosaccharides or their modified forms are, however, obtainable in large quantities by chemical synthesis.

In continuation to our research based on carbohydrate synthesis,[5] and also as part of our ongoing research programme to the synthesis of oligosaccharides for developing serological markers toward a variety of bacterial strains, we present herein the convergent synthesis (Schemes 1–3) of the tetrasaccharide repeating unit, of the *O*-antigenic polysaccharide of *E. coli* 78 as its methyl glycoside (**I**). To the best of our knowledge, this is the first synthesis of the tetrasaccharide related to this strain.



Scheme 1. Reagents and conditions: (a) Ac_2O (1.2 equiv), pyridine, DMAP, CH_2Cl_2, rt, 1 h, 99%; (b) $NaCNBH_3$ (12 equiv), HCl/Et_2O, THF, 4 Å MS, 0 °C →20 °C, 40 min, 94%; (c) **1** (1.0 equiv), BSP, Tf_2O, TTBP, CH_2Cl_2, 4 Å MS, Ar, −78 °C, 30 min, 75%.

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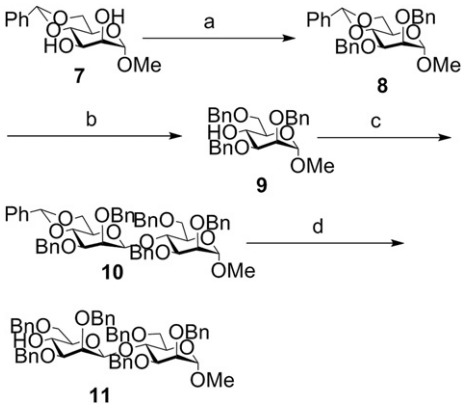
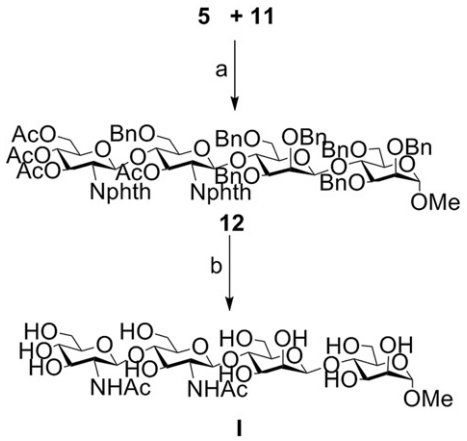


Scheme 2. Reagents and conditions: (a) NaH, DMF, 0 °C, BnBr (2.4 equiv), rt, 2 h, 92%; (b) $NaCNBH_3$ (9 equiv), HCl/Et_2O, THF, 4 Å MS, 0 °C, 10 min, 83%; (c) **6** (1.0 equiv), BSP, Tf_2O, TTBP, CH_2Cl_2, 4 Å MS, Ar, −78 °C, 1 h, 83%; (d) (i) Et_3SiH (16 equiv), $BF_3{\cdot}Et_2O$ (2 equiv), CH_2Cl_2, −5 °C, 2 h; (ii) TBDPSCl (1.5 equiv), Imidazole, DMF, 12 h, 65%.



Scheme 3. Reagents and conditions: (a) BSP (1.1 equiv), Tf_2O, TTBP, CH_2Cl_2, 4 Å MS, Ar, −70 °C, 1 h, 70%; (b) (i) $NH_2NH_2{\cdot}H_2O$, ethanol, reflux, 8 h; (ii) Ac_2O, Pyridine, rt, 12 h; (iii) 0.05 M CH_3ONa–CH_3OH, rt, 20 h; (iv) 10% Pd–C, CH_3OH/H_2O/AcOH (6:1:1 v/v), rt, 24 h; overall yield 96%.

2. Results and discussion

The convergent route depicted in Figure 2 was envisioned. The retrosynthetic analysis indicated that **I** could be synthesized through compound **12**, which could be assembled from the corresponding D-mannose disaccharide derived glycosyl acceptor **11** and glucosamine disaccharide based glycosyl donor **5**. Compound **11** could in turn be obtained by coupling reaction of the mannose-glycosyl donor **6** and acceptor **9**. Similarly, **5** was obtainable from its corresponding donor **1** and acceptor **4**. Throughout the synthesis we have used thioglycoside donors as these are sufficiently stable for protecting group manipulation and can tolerate a wide range of reaction conditions.

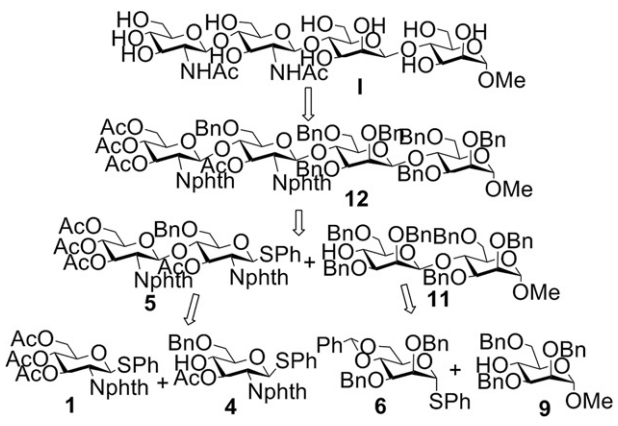


Figure 2. Retrosynthesis of **I**.

The actual synthesis of the tetrasaccharide methyl glycoside (**I**) was initiated from known phenyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **2**.[6] Acetylation of **2** followed by regioselective opening of the benzylidene acetal[7] of the resulting product **3** using $NaCNBH_3$ and ethereal hydrogen chloride afforded **4**[8] in excellent yield. The glucosamine derived glycosyl acceptors containing free 4-hydroxy group are known to have relatively low nucleophilicity.[9] Since Crich's glycosidation technique[10] has been successfully utilized for the synthesis of *N*-acetylglucosamine oligosaccharides involving less reactive glycosyl acceptors,[8] we have adopted Crich's glycosidation procedure. Preactivation of the known 2-phthalimidoglucosamine derived thioglycoside donor **1**[12] was done with 1-benzenesulfinylpiperidine (BSP)[13] and Tf_2O in the presence of 2,4,6-tri-*tert*-butylpyrimidine (TTBP) at −60 °C, and subsequent reaction of the in situ generated glucosaminyl triflate intermediate with acceptor **4** resulted in the formation of the corresponding disaccharide **5** in modest 55% yield, probably because of decomposition of the triflate intermediate as side reaction at this temperature. Similar decomposition has been observed by Hansen et al.[11] in such type of coupling reactions using related donors at −60 °C. It has also been mentioned by Yamago et al. that the α-glucosaminyl triflate intermediate generated in situ decomposes above −50 °C.[8] Preactivation of **1** at −60 °C and conducting the reaction with the acceptor **4** at −78 °C followed by quenching of the reaction mixture with triethylphosphite gave the desired β-disaccharide **5**[8] in good yield (75%, Scheme 1). Improvement of yield using triethylphosphite as quencher has also been mentioned for glycosidation of other glycosyl donors.[11,14] Although participation of the adjacent phthalimido group in such type of reaction was proposed earlier,[15] this point could not be proved by NMR.[8] Probably, O-glycosidation to give **5** proceeds by an S_N2 type reaction involving the triflate intermediate. Structure of **5** was confirmed by NMR (1D- and 2D-) spectroscopy. Although, the $^1J(C_{1'}, H_{1'})$ value (169.0 Hz) was higher than that expected for a β-linkage, but chemical shifts of H-1′ (δ 5.45) and C-1′ (δ 96.9) of **5** along with the corresponding high $^3J(H_{1'},H_{2'})$ value (8.4 Hz) and the $H_{1'}H_{5'}$ NOE correlation were indicative of a β-linkage between the two glucosamine units in this compound.

Synthesis of the mannose disaccharide acceptor (Scheme 2) was started from the known methyl 4,6-*O*-benzylidene-α-D-mannopyranoside **7**.[16] Benzylation followed by regioselective deprotection of **8** with $NaCNBH_3$ using ether moistened with hydrogen chloride[7] generated the mannose-glycosyl acceptor **9**. Preactivation of the known mannose derived thioglycoside donor **6**[5h,17] with BSP and Tf_2O generated in situ the corresponding α-mannosyl triflate,[10c,d,g,18] which subsequently reacted with **9** affording the corresponding crystalline β-mannoside **10**[19] in high yield (Scheme 2). Chemical shifts of H-1′ (δ 4.49, br s), H-5′ (δ 3.07, m, characteristic of H-5 of 4,6-O-benzylidenated β-mannoside[10c–f]) and C-1′ (δ 102.0) along with the corresponding $^1J(C_{1'}, H_{1'})$ (156.2 Hz) of compound **10** confirmed formation of the β-glycoside. It is worthy to mention here that synthesis of **10** has been made by Kim et al.,[19] via activation of the anomeric center through phthalic-triflic acid mixed anhydride, and compound **10** has been reported by this group to be a colorless oil showing $[\alpha]_D^{20}$ +5.2 in $CHCl_3$, whereas, in the present synthesis we have obtained crystalline **10** (having $[\alpha]_D^{20}$ −12.5 in $CHCl_3$), which was characterized by 1D- and 2D-NMR data. Regioselective opening of the benzylidene acetal of **10** was then effected by Et_3SiH in the presence of $BF_3{\cdot}Et_2O$,[20] which resulted in the formation of the desired glycosyl acceptor **11** (major) together with its 6-regioisomer (minor), but the mixture was chromatographically inseparable at

this stage. This problem was circumvented by selective silylation[21] of the primary hydroxyl group of the undesired regioisomer in the mixture followed by its facile chromatographic separation on silica gel column, which furnished **11** in 65% yield.

Preactivation of glucosamine derived disaccharide donor **5** with BSP and Tf_2O at −60 °C and its reaction with functionalized mannose disaccharide acceptor **11** in the presence of TTBP at −70 °C then afforded the corresponding tetrasaccharide derivative **12** in 70% yield (Scheme 3). The structure of **12** was confirmed by ^{1}H- and ^{13}C NMR using 1D- and 2D- (COSYGP, HMBCGP, HSQCGP, TOCSY, and ROESY) techniques. The anomeric protons of **12**, listed from the non-reducing end, appeared at δ 5.36 (d), 5.45 (d), 4.31 (br s), and 4.68 (d), and the corresponding anomeric carbons showed respective chemical shifts at δ 96.7, 97.7, 101.0, and 99.4. The $^1J(C_1, H_1)$ coupling constants from the non-reducing end were 167.0, 164.9, 156.9, and 168.3 Hz, respectively. Long-range coupling correlation (Fig. 3, vide Electronic Supplementary data) of the tetrasaccharide derivative **12**, together with the coupling constants $^1J(C_{1''}, H_{1''})$ (164.9 Hz) and $^3J(H''_1,H''_2)$ (8.5 Hz) corresponding to the new glycosidic bond unequivocally proved the new linkage to be (1→4)-β. Removal of the phthalimido groups of **12** with hydrazine hydrate followed by successive N-acetylation, Zémplen deacetylation and global debenzylation under catalytic hydrogenation conditions finally furnished the corresponding tetrasaccharide as its methyl glycoside (**I**). A comparison of the chemical shifts of anomeric protons and carbons along with the values of the $^1J(C_1, H_1)$ of the synthesized tetrasaccharide glycoside (**I**) recorded in D_2O at 22 °C, with those of *E. coli* 78 *O*-antigenic polysaccharide (taken in D_2O at 70 °C)[4] is given in Table 1. Compound **I** showed anomeric proton signals, listed from the non-reducing end at δ 4.53 (d, 7.8 Hz), 4.57 (d, 8.4 Hz), 4.72 (br s), and 4.76 (d, 3 Hz), respectively, and the corresponding anomeric carbons at δ 102.3 (162.9 Hz), 102.2 (162.9 Hz), 100.8 (163.3 Hz), and 101.5 (173.7 Hz). These chemical shifts and the respective $^1J(C_1, H_1)$ values are consistent with those of anomeric protons and carbons of the *O*-antigen of *E. coli* 78.[4] The observed NMR spectral data indicate the presence of two β-linked GlcpNAc residues, one β-linked Manp and one α-linked Manp residue in **I**.

Table 1
Comparison of chemical shifts and coupling constants of anomeric protons and carbons of compound **I** and *O*-antigen of *E. coli* 78

	H-1 (^3J)	H-1′ (^3J)	H-1″ (^3J)	H-1‴ (^3J)
Compound **I**	4.76 (3)	4.72	4.57 (8.4)	4.53 (7.8)
O-Antigen of *E.* coli 78[4]	5.25	4.70	4.63	4.55
	C-1 (^{1}J)	C-1′ (^1J)	C-1″ (^1J)	C-1‴ (^1J)
Compound **I**	101.5 (173.7)	100.8 (163.3)	102.2 (162.9)	102.3 (162.9)
O-Antigen of *E.* coli 78[4]	101.4 (174)	100.9 (162)	101.9 (164)	102.2 (164)

$^3J=^3J(H_1–H_2)$ Hz and $^1J=^1J(C_1–H_1)$ Hz; Chemical shifts in δ (ppm).

3. Conclusion

In summary, the first synthesis of the methyl glycoside of the tetrasaccharide repeating unit (**I**) of *O*-antigenic polysaccharide of *E. coli* 78 has been achieved following a convergent strategy that exploits Crich's glycosidation technique. The glycosidation steps proceeded well with generation of the corresponding glycosides in good yields and excellent β-selectivities.

4. Experimental

4.1. General methods

Unless otherwise stated, all the glass-wares were flame-or oven dried before use. All the commercial reagents were used as obtained without further purification. Solvents were purified and dried by standard methods prior to use. Melting points were determined on a Toshniwal melting apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed on glass plates precoated with silica gel or on Merck silica gel plates (60-F_{254}) to monitor the reactions. Visualization of spots was accomplished by spraying the chromatograms with 5% ethanolic solution of sulfuric acid and charring on a hot plate. Column chromatography was carried out on silica gel 60–120 mesh (SRL, India) and Flash chromatography was performed on Merck silica gel 60 (230–400 mesh). Proton and carbon chemical shifts (δ) are expressed in ppm. NMR spectra were recorded on a Brucker DPX-300 and AV 300 spectrometer at ambient temperature in $CDCl_3$ with tetramethylsilane as internal standard and D_2O [HOD (4.78 ppm, 298 °K)] with 1,4 Dioxan (67.4 ppm) as internal standard, respectively and assigned using 2D-methods (COSYGP, DEPT, HSQCGP, HBMCGP, TOCSYGP, NOESY, and ROESY). IR spectra were recoded on FTIR-8300 instrument and reported in cm^{-1}. Optical rotations were measured on a Jasco P-1020 polarimeter. Elemental analysis was done using 2400-Series II C,H,N-Analyzer, Perkin–Elmer, US from IACS, Kolkata 700032, India. HRMS measurements were made with a Q-tof-Micro (YA-263) mass spectrometer by electron spray ionization method.

4.2. Phenyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (3)

To a magnetically stirred solution of the phenyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**2**, 1.2 g, 2.45 mmol), DMAP (60 mg, 0.49 mmol), and pyridine (0.60 mL, 7.43 mmol) in dry CH_2Cl_2 (10 mL) was added acetic anhydride (0.347 ml, 3.68 mmol) at room temperature and the reaction mixture was stirred for 2 h. After completion of the reaction, the mixture was concentrated under reduced pressure and then diluted with CH_2Cl_2. The organic layer was successively washed with saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated under reduced pressure. The crude mass was purified by column chromatography (20% EtOAc/hexane) to furnish **3** (1.29 g, 99%) as white solid; R_f (30% EtOAc/hexane) 0.4; mp 114–115 °C (EtOAc/hexane) (lit.[22], 115 °C); $[\alpha]_D^{20}$ +23.0 (*c* 1.0, $CHCl_3$); lit.[22] $[\alpha]_D^{25}$ +18.3 (*c* 1.5, $CHCl_3$); ν_{max} (KBr plate) 3630, 2882, 1775, 1734, 1717, 1383, 1225, 1098, 1067, 725 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.87–7.74 (4H, m, ArH), 7.45–7.29 (10H, m, ArH), 5.90 (1H, t, *J* 9.5, 9.1 Hz, H-3), 5.84 (1H, d, *J* 10.6 Hz, H-1), 5.54 (1H, s, C*H*Ph), 4.44 (1H, d, *J* 5.9 Hz, H-4), 4.36 (1H, t, *J* 10.2, 10.1 Hz), 3.84–3.76 (3H, m, H-5, H-6a, H-6b), 1.88 (3H, s, COCH_3); δ_C (75 MHz, $CDCl_3$) 170.1 (C=O), 167.8 (C=O), 167.2 (C=O), 136.8, 134.4, 134.2, 133.0 (2C), 131.6, 131.1, 129.1, 129.0 (2C), 128.3, 128.2 (2C), 126.2 (2C), 123.7, 123.6, 101.6, 83.8, 79.0, 70.6, 70.5, 68.5, 54.3, 20.5.

4.3. Phenyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4)

To a solution of phenyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**3**, 1.7 g, 3.20 mmol) in freshly dried THF (40 mL) was added sodium cyanoborohydride (2.42 g, 38.42 mmol), 4 Å molecular sieves and a pinch of methyl orange. After stirring at 0 °C for 15 min, a saturated solution of hydrogen chloride in diethyl ether was added slowly until the color of the solution became permanently pink. The mixture was allowed to stir at 20 °C for another 40 min. Then the reaction mixture was diluted with CH_2Cl_2, filtered through a Celite bed and the filtrate was washed successively with saturated aqueous $NaHCO_3$ solution, brine and water. The organic layer was separated, dried and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (30% EtOAc/hexane) afforded **4** (1.6 g, 94%) as colorless foam; R_f (50% EtOAc/hexane) 0.41; $[\alpha]^{25}_D$

+22.5 (*c* 2.0, $CHCl_3$); ν_{max} (KBr plate) 3474, 2916, 1777, 1746, 1717, 1385, 1230, 1074, 719 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.87–7.82 (2H, m, ArH); 7.72–7.66 (2H, m, ArH), 7.43–7.38 (2H, m, ArH), 7.36–7.30 (5H, m, ArH), 7.26–7.20 (3H, m, ArH), 5.81 (1H, d, *J* 10.5 Hz), 5.71 (1H, dd, *J* 10.2, 8.3 Hz), 4.61 (2H, m), 4.31 (1H, t, *J* 10.3 Hz), 3.85 (2H, br s), 3.82 (2H, br s), 3.13 (1H, d, *J* 4.0 Hz), 1.9 (3H, s, $COCH_3$); δ_C (75 MHz, $CDCl_3$) 171.1 (C=O), 167.8 (C=O), 167.2 (C=O), 137.8, 134.4, 134.2, 132.7 (2C), 131.7, 131.6, 131.2, 128.8 (2C), 128.4 (2C), 128.0, 127.8, 127.7 (2C), 123.7, 123.6, 83.1, 78.5, 74.3, 73.7, 70.9, 70.1, 53.6, 20.6; HRMS (ESI-TOF) (*m*/*z*): $[M+Na]^+$, found 556.1403. $C_{29}H_{27}NO_7SNa$ requires 556.1406.

4.4. Phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (5)

A solution of donor **1** (525 mg, 0.996 mmol), BSP (229 mg, 1.096 mmol), TTBP[23] (495 mg, 1.99 mmol) and activated 4 Å powdered molecular sieves in dried CH_2Cl_2 (12 mL) was stirred at −60 °C under Ar atmosphere for 30 min, then was added Tf_2O (218 μL, 1.295 mmol). After 30 min, the temperature was brought down to −78 °C, and then a cold solution of acceptor **4** (796.5 mg, 1.49 mmol) in CH_2Cl_2 (3 mL) was slowly added. The reaction mixture was stirred at −78 °C for further 30 min and then quenched by the addition of triethylphosphite (0.52 mL, 3.03 mmol). The mixture was stirred at −78 °C for another 30 min, after which it was warmed up to room temperature. The molecular sieves were filtered off, and the filtrate was washed successively with saturated aqueous $NaHCO_3$ solution, brine and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure. Purification by silica gel column chromatography (32% EtOAc/hexane) afforded **5** (711.4 mg, 75%) as white foam, which on crystallization from EtOAc/hexane gave white crystals; R_f (50% EtOAc/hexane) 0.39; mp 193–194 °C; $[\alpha]_D^{25}$ +10.1 (*c* 2.0, $CHCl_3$); ν_{max} (KBr plate) 3480, 2936, 1778, 1748, 1717, 1389, 1233, 1071, 1042, 723 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.85–7.82 (7H, m, ArH), 7.74–7.71 (4H, m, ArH), 7.39–7.30 (7H, m, ArH), 7.21–7.12 (3H, m, ArH), 5.74–5.66 (2H, m, H-3, H-3′), 5.59 (1H, d, *J* 10.6 Hz, H-1), 5.45 (1H, d, *J* 8.4 Hz, H-1′), 5.09 (1H, t, *J* 9.7, 9.6 Hz, H-4′), 4.51 (1H, d, *J* 11.8 Hz, CH_2Ph), 4.44 (1H, d, *J* 11.8 Hz, CH_2Ph), 4.37 (1H, dd, *J* 12.4, 3.9 Hz, H-6a′), 4.23 (1H, t, *J* 10.5, 9.2 Hz, H-2), 4.20–4.09 (2H, m, H-2′, H-4), 3.93 (1H, dd, *J* 12.3, 1.7 Hz, H-6b′), 3.61–3.44 (4H, m, H-5, H-5', H-6a, H-6b), 2.03 (3H, s, $COCH_3$), 1.99 (3H, s, $COCH_3$), 1.90 (3H, s, $COCH_3$), 1.81 (3H, s, $COCH_3$); δ_C (75 MHz, $CDCl_3$) 170.5 (C=O), 170.1 (C=O), 169.9 (C=O), 169.4 (C=O), 167.7 (C=O, 2C), 167.2 (C=O, 2C), 138.3, 134.4, 134.1, 133.1, 131.7, 131.3, 131.2, 128.8, 128.3, 128.1, 127.5, 127.4, 123.6, 123.5, 96.9 [$^1J(C_1',H_1')$=169.0 Hz], 82.9 [$^1J(C_1,H_1)$=160.4 Hz], 78.5, 73.8, 72.7, 71.9, 71.6, 70.6, 68.4, 67.8, 61.4, 54.9, 53.9, 20.6, 20.5, 20.4, 20.3; HRMS (ESI-TOF) (*m*/*z*): $[M+Na]^+$, found 973.2463. $C_{49}H_{46}N_2O_{16}SNa$ requires 973.2466.

4.5. Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (8)

Sodium hydride (1.7 g, 60% suspension) was added to a solution of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside (**7**, 4.0 g, 14.18 mmol) in dry DMF (20 mL) at 0 °C with constant stirring followed by dropwise addition of benzyl bromide (4.05 mL, 34.0 mmol). The reaction mixture was allowed to warm gradually to room temperature, and stirred for 2 h. The excess of sodium hydride was decomposed with methanol, the mixture was evaporated to syrup, which was then dissolved in CH_2Cl_2, washed with water, dried over anhydrous Na_2SO_4, and concentrated. The crude product was then purified on a column of silica gel (10% EtOAc/hexane) to give methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (6.05 g, 92%) as colorless syrup; R_f (20% EtOAc/hexane) 0.50; $[\alpha]_D^{25}$ +28.5 (*c* 1.2, $CHCl_3$), lit.[24] $[\alpha]_D$ +29.6 (*c* 1.1, $CHCl_3$); ν_{max} (neat) 3030, 2909, 2866, 1454, 1126, 1101, 1057, 750, 698 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.53–7.50 (2H, m, ArH), 7.41–7.26 (13H, m, ArH), 5.65 (1H, s, *CH*Ph), 4.85–4.80 (2H, m), 4.76–4.64 (3H, m), 4.29–4.22 (2H, m), 3.97–3.83 (3H, m), 3.78 (1H, m), 3.37 (3H, s, OMe); δ_C (75 MHz, $CDCl_3$) 138.7, 138.2, 137.8, 128.8, 128.4 (2C), 128.3 (2C), 128.2 (2C), 128.1 (2C), 127.8, 127.5 (3C), 126.1 (2C), 101.5, 100.1, 79.2, 76.4, 73.6, 73.1, 68.9, 64.1, 54.8.

4.6. Methyl 2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (9)

To a solution of methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**8**, 2.3 g, 4.98 mmol) in freshly dried THF (70 mL) was added sodium cyanoborohydride (2.82 g, 44.87 mmol), 4 Å molecular sieves and a pinch of methyl orange. After stirring at 0 °C for 15 min, a saturated solution of hydrogen chloride in diethyl ether was added slowly until the color of the solution became permanently pink. The reaction mixture was stirred for 10 min at 0 °C. It was then diluted with CH_2Cl_2, filtered through Celite bed and the filtrate was washed successively with saturated aqueous $NaHCO_3$ solution, brine and water. The organic layer was separated, dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (14% EtOAc/hexane) afforded **9** (1.92 g, 83%) as colorless syrup; R_f (20% EtOAc/hexane) 0.38; $[\alpha]_D^{25}$ +5.1 (*c* 1.1, $CHCl_3$), lit.[24] $[\alpha]_D$ +4.5 (*c* 1.68, $CHCl_3$); ν_{max} (neat) 3462, 2910, 2872, 1454, 1138, 1109, 1057, 737, 698 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.38–7.27 (15H, m, ArH), 4.81 (1H, br s), 4.70 (1H, s), 4.69 (1H, s), 4.64–4.59 (3H, m,), 4.52 (1H, d, *J* 11.7 Hz), 4.06 (1H, dt, *J* 9.3, 1.5 Hz), 3.84–3.79 (3H, m), 3.76–3.70 (2H, m,), 3.37 (3H, s, OMe), 2.55 (1H, s, OH); δ_C (75 MHz, $CDCl_3$) 138.3, 138.2 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 127.9 (2C), 127.8, 127.75 (2C), 127.7, 127.6 (2C), 127.5, 99.2, 79.7, 73.9, 73.6, 72.7, 71.8, 71.5, 70.5, 67.8, 54.9.

4.7. Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (10)

To a stirred solution of donor **6** (1.44 g, 2.67 mmol), BSP (614 mg, 2.94 mmol), TTBP (1.33 g, 5.35 mmol), and 4 Å molecular sieves in CH_2Cl_2 (50 mL), at −60 °C under an Ar atmosphere, was added Tf_2O (0.54 mL, 3.21 mmol). After 30 min, the temperature was brought down to −78 °C, and then acceptor **9** (1.48 g, 0.60 mmol) in CH_2Cl_2 (3 mL) was slowly added. The reaction mixture was stirred for 1 h at −78 °C and then allowed to warm up over 1 h to 0 °C. The reaction mixture was poured into aq $NaHCO_3$ solution, diluted with CH_2Cl_2, and filtered through Celite. The organic layer was separated from the filtrate, washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash column chromatography (hexane/EtOAc/CH_2Cl_2, 6:2:1, v/v) on silica gel to give **10** (1.98 g, 83%) as white solid; R_f (hexane/EtOAc/CH_2Cl_2, 6:2:1, v/v) 0.30; mp 116–117 °C (EtOAc/hexane); $[\alpha]_D^{25}$ −12.5 (*c* 1.24, $CHCl_3$), lit.[19] $[\alpha]_D^{20}$ +5.2 (*c* 0.5, $CHCl_3$); ν_{max} (KBr plate) 3028, 2893, 2870, 1142, 1111, 1088, 1061, 735 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.52–7.17 (30H, m, ArH), 5.50 (1H, s, *CH*Ph), 4.84–4.74 (3H, m, CH_2Ph), 4.73 (1H, d, *J* 2.1 Hz, H-1), 4.71–4.63 (4H, m, CH_2Ph), 4.57–4.53 (2H, m, CH_2Ph), 4.49 (1H, s, H-1′), 4.40 (1H, d, *J* 12.0 Hz, CH_2Ph), 4.18 (1H, t, *J* 8.9 Hz, H-4), 4.09–4.00 (2H, m, H-4′, H-6a′), 3.84 (1H, dd, *J* 8.5, 3.0, Hz, H-3), 3.74 (1H, t, *J* 2.6, 2.5 Hz, H-2), 3.68 (1H, d, *J* 3.0 Hz, H-2′), 3.66–3.57 (4H, m, H-5, H-6a, H-6b, H-6b′), 3.39 (1H, dd, *J* 9.9, 2.9 Hz, H-3′), 3.34 (3H, s, OMe), 3.07 (1H, m, H-5′); δ_C (75 MHz, $CDCl_3$) 139.2, 138.7, 138.6, 138.4, 138.2, 137.7, 128.8, 128.4, 128.3, 128.23, 128.18, 128.14, 128.12, 128.0, 127.8, 127.7, 127.5, 127.4, 127.2, 127.1, 126.1, 102.0 [$^1J(C_1',H_1')$=156.2 Hz], 101.3, 99.5 [$^1J(C_1,H_1)$=167.5 Hz], 78.7, 78.4, 78.0, 77.2, 76.2, 75.8, 74.9, 73.5, 72.9, 72.6, 72.5, 71.2, 69.2, 68.6, 67.3, 54.9; HRMS (ESI-TOF) (*m*/*z*): $[M+Na]^+$, found 917.3880. $C_{55}H_{58}O_{11}Na$ requires 917.3877.

4.8. Methyl 2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (11)

To a mixture of **10** (614.4 mg, 0.687 mmol) and 4 Å molecular sieves in CH_2Cl_2 (14 mL) at 0 °C under Ar atmosphere triethylsilane (1.75 mL, 10.96 mmol) was added slowly, followed by boron trifluoride diethyletherate (0.175 mL, 1.38 mmol). After stirring the mixture for 2 h at −5 °C, molecular sieves were filtered off and the filtrate was poured into cold saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2 (3×30 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated.

The crude product was dissolved in DMF (6 mL) and stirred overnight with *tert*-butyldiphenylchlorosilane (TBDPSCl, 0.18 mL, 0.69 mmol) and imidazole (24 mg, 0.35 mmol). After removal of solvent, **11** (401 mg, colorless foam, 65%) was isolated by silica gel flash column chromatography (15% EtOAc/toluene); R_f (20% EtOAc/toluene) 0.25; $[\alpha]_D^{25}$ −22.1 (*c* 2.3, $CHCl_3$); ν_{max} (neat) 3030, 2916, 2868, 1452, 1105, 1061, 750, 739, 698 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.39–7.24 (30H, m, ArH), 4.87–4.79 (2H, m), 4.75 (1H, d, *J* 2.3 Hz), 4.71–4.66 (4H, m), 4.63–4.37 (7H, m), 4.24 (1H, t, *J* 8.8, 8.6 Hz), 3.97–3.89 (2H, m), 3.78–3.68 (5H, m), 3.66–3.57 (2H, m), 3.35 (3H, s, OMe), 3.24 (1H, m), 3.15 (1H, dd, *J* 9.4, 2.8 Hz), 2.71 (1H, s, OH); δ_C (75 MHz, $CDCl_3$) 139.2, 138.9, 138.4, 138.3, 138.1 (2C), 128.4 (2C), 128.34 (2C), 128.23 (2C), 128.18 (2C), 128.09 (2C), 128.03 (2C), 127.80 (2C), 127.7 (8C), 127.6 (2C), 127.5, 127.4, 127.3 (2C), 127.2, 127.1, 101.4, 99.5, 81.7, 78.1, 75.7, 75.6, 74.8, 74.7, 74.2, 73.7, 73.4, 72.7, 72.6, 71.4, 71.3, 71.1, 69.5, 68.7, 54.9; HRMS (ESI-TOF) (*m*/*z*): $[M+Na]^+$, found 919.4034. $C_{55}H_{60}O_{11}Na$ requires 919.4033.

4.9. Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (12)

A mixture of thioglycoside **5** (247.4 mg, 0.26 mmol), BSP (60 mg, 0.287 mmol), TTBP (130 mg, 0.52 mmol), and 4 Å molecular sieves in dry CH_2Cl_2 (10 mL) was stirred under Ar for 30 min. The mixture was cooled to −60 °C and trifluoromethanesulfonic anhydride (53 μL, 0.315 mmol) was added. After 30 min, the temperature was brought down to −70 °C, and then a cold solution of acceptor **11** (280 mg, 0.313 mmol) in CH_2Cl_2 (4 mL) was slowly added. The reaction mixture was stirred at −70 °C for further 1 h and then quenched by the addition of triethylamine (0.40 mL). The reaction mixture was warmed to room temperature, diluted with CH_2Cl_2 and filtered through a Celite bed. The organic phase was washed subsequently with saturated aqueous $NaHCO_3$ and brine, dried with anhydrous Na_2SO_4 and the solvent was evaporated to dryness. The crude product was purified by flash column chromatography (EtOAc/CH_2Cl_2/hexane, 3:1:4, v/v) over silica-gel to give **12** (317 mg, 70%) as colorless foam; [Found: C, 67.36; H, 5.67. $C_{98}H_{100}N_2O_{27}$ requires C, 67.73; H, 5.80%]; R_f (hexane/EtOAc/CH_2Cl_2, 3:1:4 v/v) 0.28; $[\alpha]_D^{25}$ +8.6 (*c* 1.98, $CHCl_3$); IR (KBr plate) 3474, 3428, 2872, 1777, 1749, 1719, 1387, 1368, 1229, 1051, 723, cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.90–7.87 (3H, m, ArH), 7.82–7.74 (3H, m, ArH), 7.61–7.59 (3H, m, ArH), 7.31–7.07 (28H, m, ArH), 6.98–6.96 (3H, m, ArH), 6.91–6.83 (3H, m, ArH), 5.66 (1H, dd, *J* 10.5, 9.1 Hz, H-3‴), 5.56 (1H, dd, *J* 10.5, 9.1 Hz, H-3″), 5.45 (1H, d, *J* 8.5 Hz, H-1″), 5.36 (1H, d, *J* 8.4 Hz, H-1‴), 5.06 (1H, t, *J* 9.8, 9.4 Hz, H-4‴), 4.68 (1H, d, *J* 2.1 Hz, H-1), 4.66–4.54 (6H, m, 3×C*H*$_2$Ph), 4.44, 4.42 (2H, d each, *J* 12.0 Hz, C*H*$_2$Ph), 4.38–4.32 (5H, m, H-6a‴, 2×C*H*$_2$Ph), 4.31 (1H, br s, H-1′), 4.15 (1H, m, H-2‴), 4.13 (1H, m, H-2″), 4.11–4.07 (4H, m, H-4, H-4′, H-4″, C*H*$_a$*H*$_b$Ph), 4.03 (1H, d, *J* 12.0 Hz, C*H*$_a$*H*$_b$Ph), 3.90 (1H, dd, *J* 12.4, 1.6 Hz, H-6b‴), 3.79 (1H, dd, *J* 8.4, 3.0 Hz, H-3), 3.66 (2H, m, H-2, H-5″), 3.59 (3H, m, H-2′, H-6a″, H-6b″), 3.43 (1H, m, H-5‴), 3.28 (5H, m, H-6a, H-6b, OMe), 3.18 (1H, dd, *J* 9.1, 2.7 Hz, H-3′), 3.00–2.91 (4H, m, H-5, H-5′, H-6a′, H-6b′), 2.03 (3H, s, COC*H*$_3$), 1.98 (3H, s, COC*H*$_3$), 1.81 (6H, s, 2×COC*H*$_3$); δ_C (75 MHz, $CDCl_3$) 170.6 (C=O), 170.1 (C=O), 169.9 (C=O), 169.4 (C=O), 168.0 (C=O), 167.8 (C=O), 139.0, 138.98, 138.7, 138.6, 138.5, 138.4, 138.3, 134.3, 134.1, 133.7, 131.7, 131.5, 131.4, 128.3 (2C), 128.19 (3C), 128.17 (3C), 128.0 (3C), 127.93 (2C), 127.88, 127.8 (2C), 127.7 (3C), 127.62 (2C), 127.55 (3C), 127.54 (3C), 127.4 (2C), 127.3, 127.2 (2C), 127.0 (2C), 126.8, 126.3 (2C), 123.6, 123.4, 123.1, 101.0 [^1J(C$_1$′,H$_1$′)=156.9 Hz], 99.4 [^1J(C$_1$,H$_1$)=168.3 Hz], 97.7 [^1J(C$_1$″,H$_1$″)=164.9 Hz], 96.7 [^1J(C$_1^{‴}$,H$_1^{‴}$)=167.0 Hz], 81.0, 77.9, 77.2, 75.6, 75.3, 75.2, 75.1, 74.1, 74.0, 73.5, 73.4, 73.3, 72.8, 72.63, 72.6, 72.4, 71.5, 71.2, 71.0, 70.7, 69.4, 68.5, 68.4, 66.7, 61.5, 55.8, 54.9, 54.8, 20.61, 20.55, 20.5, 20.4.

4.10. Methyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy -β-D-glucopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-α-D-mannopyranoside (I)

To a solution of **12** (155 mg, 0.089 mmol) in ethanol (10 mL) was added hydrazine hydrate (6 mL). The mixture was heated to reflux for 8 h and then concentrated under reduced pressure. The residual moisture was co-evaporated with toluene (3×5 mL) and the crude product was dissolved in pyridine (24 mL) and acetic anhydride (12 mL). After stirring at room temperature for 12 h, the solvent was removed under vacuum. The crude product was purified by silica gel column chromatography (EtOAc/hexane, 3:2). The resulting product was dissolved in dry methanol (19 mL), and NaOMe (1 M in MeOH, 1 mL) was added. The mixture was stirred for 20 h and then neutralized with DOWEX-50 W cation exchange resin (H^+). The resin was filtered off and the filtrate was evaporated under reduced pressure. A mixture of the residue, 10% Pd–C (100 mg) in AcOH (3 mL), MeOH (9 mL), and H_2O (1 mL) was stirred under H_2 atmosphere for 24 h. The catalyst was then removed by filtration through Celite bed and the filtrate, after passing through a 0.45 μm Millipore membrane, was lyophilized to give **I** (65.5 mg, 96%) as a white solid; R_f (30% H_2O/CH_3CN) 0.30; $[\alpha]_D^{25}$ +9.6 (*c* 1.62, H_2O); IR (KBr plate) 3397, 2938, 1651, 1559, 1377, 1317, 1065, 615 cm^{-1}; δ_H (300 MHz, D_2O) 4.76 (1H, d, *J* 3.0 Hz, H-1), 4.72 (1H, br s, H-1′), 4.57 (1H, d, *J* 8.4 Hz, H-1″), 4.53 (1H, d, *J* 7.8 Hz, H-1‴), 4.09 (1H, d, *J* 2.7 Hz, H-2), 3.98 (1H, br s, H-2′), 3.93–3.84 (6H, m), 3.76–3.68 (9H, m), 3.65–3.53 (4H, m), 3.47–3.45 (3H, m), 3.40 (3H, s, OMe), 2.06 (3H, s, NCOC*H*$_3$), 2.05 (3H, s, NCOC*H*$_3$); δ_C (75 MHz, D_2O) 175.4 (C=O), 174.1 (C=O), 102.3 [^1J(C$_1^{‴}$,H$_1^{‴}$)=162.9 Hz], 102.2 [^1J(C$_1$″,H$_1$″)=162.9 Hz], 101.5 [^1J(C$_1$,H$_1$)=173.7 Hz], 100.8 [^1J(C1′,H1′)=163.3 Hz], 80.1, 77.9, 77.4, 76.7, 75.8, 75.3, 74.2, 72.9, 72.4, 71.8, 70.8, 70.6, 70.3, 70.0, 61.4, 61.3, 60.9, 56.4, 55.8, 55.6, 23.0, 20.5; HRMS (ESI-TOF) (*m*/*z*): $[M+Na]^+$, found 785.2802. $C_{29}H_{50}N_2O_{21}Na$ requires 785.2804.

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Supplementary data

Copies of ^1H- and ^{13}C spectra (1D and 2D) and long-range coupling correlation of **12** (Fig. 3). Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.02.052.

References and notes

1. Stintzing, G. Medical Dissertation, Karolinska Institute, Stockholm, 1981.
2. Nataro, J. P.; James, B. K. *Clin. Microbiol. Rev.* **1998**, *11*, 142–201.
3. Ørskov, I.; Ørskov, F.; Jann, B.; Jann, K. *Bacteriol. Rev.* **1977**, *41*, 667–710.
4. Jansson, P.-E.; Lindberg, B.; Widmalm, G.; Leontein, K. *Carbohydr. Res.* **1987**, *165*, 87–92.

5. (a) Ghosh, R.; De, D.; Shown, B.; Maiti, S. B. *Carbohydr. Res.* **1999**, *321*, 1–3; (b) Ghosh, R.; Chakraborty, A.; Maiti, D. K. *Synth. Commun.* **2003**, *33*, 1623–1632; (c) Ghosh, R.; Chakraborty, A.; Maiti, S. *Arkivoc* **2004**, *xiv*, 1–9; (d) Ghosh, R.; Chakraborty, A.; Maiti, D. K.; Puranik, V. G. *Tetrahedron Lett.* **2005**, *46*, 8047–8050; (e) Ghosh, R.; Chakraborty, A.; Maiti, D. K.; Puranik, V. G. *Org. Lett.* **2006**, *8*, 1061–1064; (f) Das Sarma, M.; Ghosh, R.; Patra, A.; Chowdhury, R.; Chaudhuri, K.; Hazra, B. *Org. Biomol. Chem.* **2007**, *5*, 3115–3125; (g) Roy, S.; Chakraborty, A.; Ghosh, R. *Carbohydr. Res.* **2008**, *343*, 2523–2529; (h) Maity, S. K.; Maiti, S.; Patra, A.; Ghosh, R. *Tetrahedron Lett.* **2008**, *49*, 5847–5849.
6. (a) Ogawa, T.; Nakabayashi, S.; Sasajima, K. *Carbohydr. Res.* **1981**, *95*, 308–312; (b) de la Fuente, J. M.; Penadés, S. T. *Asymmetry* **2002**, *13*, 1879–1888.
7. Garegg, P. J. *Pure Appl. Chem.* **1984**, *56*, 845–858.
8. Yamago, S.; Yamada, T.; Maruyama, T.; Yoshida, J. I. *Angew. Chem., Int. Ed.* **2004**, *43*, 2145–2148.
9. Crich, D.; Dudkin, V. *J. Am. Chem. Soc.* **2001**, *123*, 6819–6825.
10. (a) Crich, D.; Sun, S. *J. Org. Chem.* **1997**, *62*, 1198–1199; (b) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217–11223; (c) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020; (d) Crich, D.; Vinogradova, O. *J. Org. Chem.* **2006**, *71*, 8473–8480; (e) Crich, D.; Li, H.; Yao, Q.; Wink, D. J.; Sommer, R. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2001**, *123*, 5826–5828; (f) Crich, D.; Banerjee, A.; Yao, Q. *J. Am. Chem. Soc.* **2004**, *126*, 14930–14934; (g) Crich, D.; Chadrasekera, N. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5386–5389; (h) Crich, D.; Li, W.; Li, H. *J. Am. Chem. Soc.* **2004**, *126*, 15081–15086; (i) Crich, D.; Wu, B.; Jayalath, P. *J. Org. Chem.* **2007**, *72*, 6806–6815; (j) Crich, D. *ACS Symposium Series*; American Chemical Society: Washington, 2007; Vol. 960, pp 60–72.
11. Hansen, S. G.; Skrydstrup, T. *Eur. J. Org. Chem.* **2007**, 3392–3401.
12. (a) Paulsen, H.; Paal, M. *Carbohydr. Res.* **1984**, *135*, 53–69; (b) Jain, R. K.; Matta, K. L. *Carbohydr. Res.* **1992**, *226*, 91–100; (c) Hernández-Torres, J. M.; Liew, S.-T.; Achkar, J.; Wei, A. *Synthesis* **2002**, 487–490.
13. Kice, J. L.; Liu, C.-C. A. *J. Org. Chem.* **1979**, *44*, 1918–1923.
14. (a) Codée, J. D. C.; Litjens, R. E. J. N.; den Heeten, R.; Overcleeft, H. S.; van Boom, J. H.; van der Marel, G. A. *Org. Lett.* **2003**, *5*, 1519–1522; (b) Codée, J. D. C.; van den Bos, L. J.; Litjens, R. E. J. N.; Overcleeft, H. S.; van Boeckel, C. A. A.; van Boom, J. H.; van der Marel, G. A. *Tetrahedron* **2004**, *60*, 1057–1064.
15. Zachara, N. E.; Hart, G. W. *Chem. Rev.* **2002**, *102*, 431–438.
16. Albert, R.; Dax, K.; Pleschko, R.; Stutz, A. E. *Carbohydr. Res.* **1985**, *137*, 282–290.
17. (a) Oshitari, T.; Shibasaki, M.; Yoshizawa, T.; Tomita, M.; Takao, K.-i.; Kobayashi, S. *Tetrahedron* **1997**, *53*, 10993–11006; (b) Crich, D.; Sun, S. *Tetrahedron* **1998**, *54*, 8321–8348.
18. Callam, C. S.; Gadikota, R. R.; Krein, D. M.; Lowary, T. L. *J. Am. Chem. Soc.* **2003**, *125*, 13112–13119.
19. Kim, K. S.; Fulse, D. B.; Baek, J. Y.; Lee, B.-Y.; Jeon, H. B. *J. Am. Chem. Soc.* **2008**, *130*, 8537–8547.
20. Oberli, M. A.; Bindschädler, P.; Werz, D. B.; Seeberger, P. H. *Org. Lett.* **2008**, *10*, 905–908.
21. Hsu, M. C.; Lee, J.; Kishi, Y. *J. Org. Chem.* **2007**, *72*, 1931–1940.
22. Tiwari, P.; Kumar, R.; Maulik, P. R.; Misra, A. K. *Eur. J. Org. Chem.* **2005**, 4265–4270.
23. Crich, D.; Smith, M.; Yao, Q.; Picione, J. *Synthesis* **2001**, 323–326.
24. Madiyalakan, R.; Chowdhary, M. S.; Rana, S. S.; Matta, K. L. *Carbohydr. Res.* **1986**, *152*, 183–194.