JOC The Journal of Organic Chemistry

Article

Synthesis of #-(1-2)-Linked 6-Deoxy-L-altropyranose Oligosaccharides via Gold(I)-Catalyzed Glycosylation of a ortho-Hexynylbenzoate Donor

Zhengnan Shen, Hani Mobarak, Wei Li, Göran Widmalm, and Biao Yu

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b00057 • Publication Date (Web): 23 Feb 2017

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Synthesis of β-(1→2)-Linked 6-Deoxy-L-altropyranose Oligosaccharides via Gold(I)-Catalyzed Glycosylation of a *ortho*-Hexynylbenzoate Donor

Zhengnan Shen,[†,‡] Hani Mobarak,[§] Wei Li,[‡] Göran Widmalm,[§]* and Biao Yu[‡]*

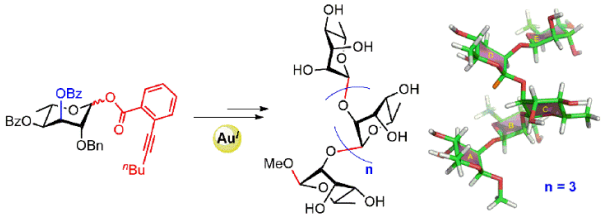
[†]School of Physical Science and Technology, ShanghaiTech University, 100 Haike Road, Shanghai 201210 (China)

[‡]State Key Laboratory of Bioorganic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032 (China)

[§]Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm (Sweden)

E-mail: byu@sioc.ac.cn Goran.Widmalm@su.se

Table of Contents



Abstract

The β-(1→2)-linked 6-deoxy-L-altropyranose di- to penta-saccharides **2**–**5**, relevant to the O-antigen of the infectious *Yersinia enterocolitica* O:3, were synthesized for the

first time. The challenging 1,2-*cis*-altropyranosyl linkage was assembled effectively via glycosylation with 2-*O*-benzyl-3,4-di-*O*-benzoyl-6-deoxy-L-altropyranosyl *ortho*-hexynylbenzoate (**7**) under the catalysis of PPh_3AuNTf_2. NMR and molecular modeling studies showed that the pentasaccharide (**5**) adopted a left-handed helical conformation.

Introduction

Yersinia enterocolitica, a coccobacillus widely spread in nature, can survive below 0 ^{o}C or above 40 ^{o}C in both invertebrates and vertebrates.[1] The Serotypes O:3, O:8, and O:9 are human pathogens that cause various intestinal and gastric infections.[2] Particularly, their tolerance to grow at 5 ^{o}C makes them life-threatening in the transfusion of contaminated blood.[3] In view of the important role of lipopolysaccharides (LPSs) in the invasion of bacteria to their host,[4] the structural analysis of *Y. enterocolitica* LPSs was conducted in the early 1970s, and a rare sugar 6-deoxy-L-altropyranose was isolated as one of the major components.[5] Further studies disclosed that 6-deoxy-L-Alt*p* assembled via a β-(1→2)-glycosidic linkage to form a homopolysaccharide in the O-antigen of *Y. enterocolitica* O:3.[6] It is of great interest to synthesize a series of the 6-deoxy-L-Alt*p* oligosaccharides (Figure 1) in order to study their potential biological functions in the bacteria-host interaction.

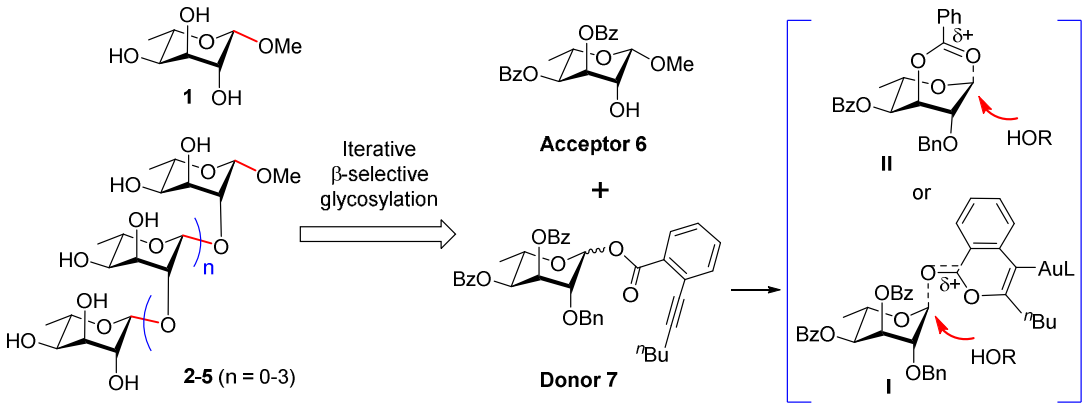


FIGURE 1. The synthetic 6-deoxy-β-L-Alt*p*-containing oligosaccharides **1**–**5** relevant to the O-antigen of *Y. enterocolitica* O:3 and the proposed β-selective glycosylation.

Relevant to the synthesis of β-glycosidic linkages in mannosides and rhamnosides, the construction of the equatorial 1,2-*cis*-β-linkages in 6-deoxy-β-L-Alt*p* (the C3-epimer of rhamnose) represents a synthetic challenge because of the α-favored anomeric and steric effects as well as the incapable of neighboring participation from a *trans*-oriented acyl group at O2.[7] Crich et al. have developed an effective β-selective mannosylation protocol[8] with substrates tethered with 4,6-*O*-benzylidene group that provides the torsional and electron withdrawing effects to favor the S_N2-like glycosylation via an intimate α-intermediate.[9] This protocol cannot be applied to the direct β-rhamnosylation due to the lack of an exo-cyclic hydroxymethyl group on rhamnosyl donors. Nevertheless, several methods for β-selective rhamnosylation have been developed employing donors equipped with a variety of protecting and leaving groups associated with varied glycosylation conditions.[10] However, to the best of our knowledge, the stereoselective β-glycosylation of 6-deoxy-L-Alt*p* has not been reported.

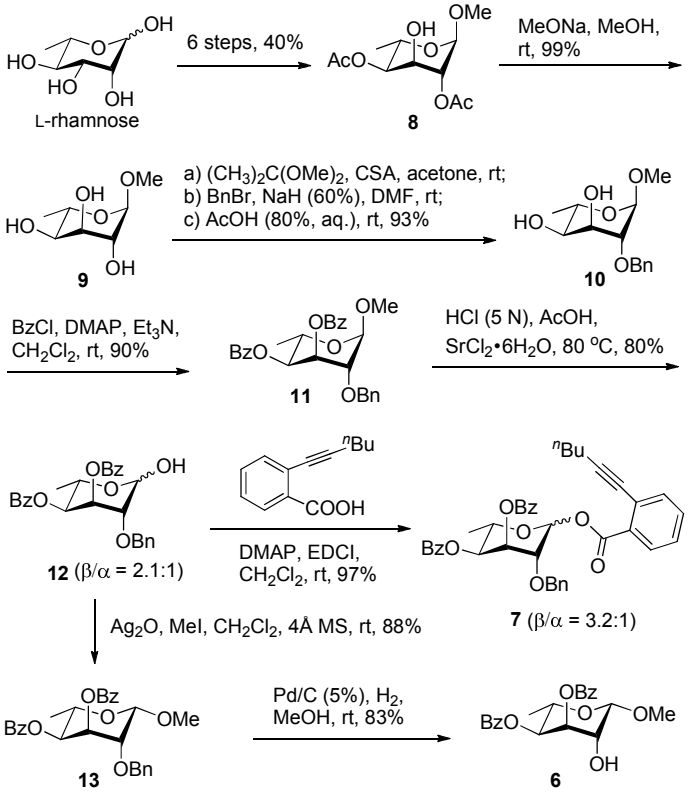
Recently, we discovered that glycosylation with both mannosyl and rhamnosyl *ortho*-alkynylbenzoate donors could provide good β-selectivity under the catalysis of $PPh_3AuBAr_4^F$ (BAr_4^F = tetrakis[3,5-bis-(trifluoromethyl)phenyl]borate) complex.[11,12] The β-stereoselective glycosylation could be attributed to a favorable 1-α-glycosyloxy-isochromenylium-4-gold(I) intermediate (e.g., **I**) that subsequently is displaced by nucleophilic substitution via an S_N2-like pathway.[11] As a consequence, we envisioned *ortho*-hexynylbenzoate donor **7** (Figure 1) installed with a non-participating benzyl group at O2 of 6-deoxy-L-Alt*p* as a choice to construct the desired glycosidic β-(1→2)-linkage. In addition, two benzoyl groups were installed at O3 and O4 that might enhance the β-selectivity via a putative remote participation (via intermediate **II**),[7d,11b,13] while the 2-*O*-benzyl group serves as a temporary protecting group at the position where glycan elongation will take place. Herein, we report the synthesis of 6-deoxy-β-L-Alt*p*-containing mono- to pentasaccharides **1**–**5** employing the gold(I)-catalyzed iterative glycosylation with *ortho*-hexynylbenzoate donor **7** and ^{1}H NMR analysis of the synthetic oligosaccharides.

Results and Discussion

Our synthesis commenced with the preparation of methyl 2,4-di-*O*-acetyl-6-deoxy-α-L-Alt*p* **8** from L-rhamnose (6 steps and 40% overall yield) employing modifications of literature transformations (Scheme 1).[14a] Treatment of **8** with a catalytic amount of MeONa in MeOH led to triol **9** (99%),[6b] which was then subjected to a regioselective isopropylidene protection of the *cis*-oriented 3-OH and 4-OH groups in the presence of $(CH_3)_2C(OMe)_2$ and CSA (camphorsulfonic acid) at rt. The residue was directly used in the benzylation of the axial 2-OH with BnBr and NaH in DMF, and the subsequent acidic hydrolysis of the isopropylidene group

provided diol **10** in an excellent 93% yield (3 steps from **9**). Benzoylation of the two free hydroxyl groups on **10** under the conditions of BzCl and Et_3N in a catalytic amount of DMAP provided **11** (90%).

SCHEME 1. Preparation of 6-deoxy-L-Alt*p* acceptor **6** and donor **7**.



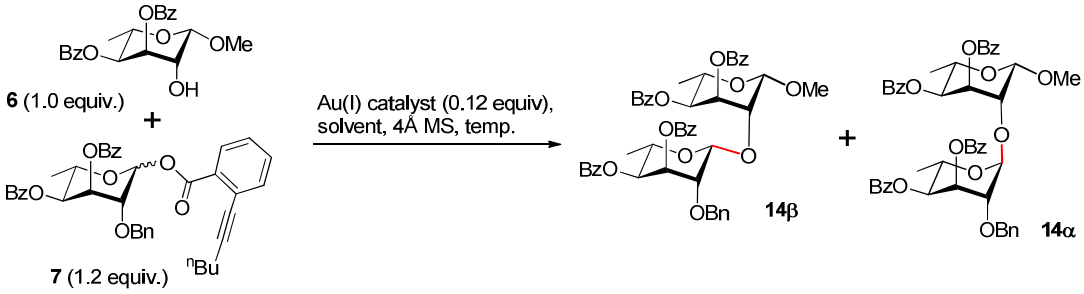
The subsequent cleavage of the anomeric methyl group on **11** turned out to be difficult, wherein the acidic conditions with AcOH, HCl, or H_2SO_4 at various temperatures failed to give the desired hemiacetal (See SI). Fortunately, addition of a catalytic amount of $SrCl_2 \cdot 6H_2O$ to a mixture of aqueous HCl (5 N) and AcOH at 80 ^oC succeeded in hydrolyzing the methyl glycoside to afford hemiacetal **12** in 80% yield (β/α = 2.1:1).[15] Condensation of **12** with *ortho*-hexynylbenzoic acid in the presence of DMAP and EDCI in CH_2Cl_2 provided the desired 6-deoxy-L-Alt*p* donor **7**

in an excellent 97% yield (β/α = 3.2:1). Furthermore, we capped hemiacetal **12** with a β-linked methyl group to provide **13** in 88% yield upon treatment with MeI and Ag_2O in CH_2Cl_2 at rt, wherein only a trace of the corresponding α-L-configured epimer **11** was isolated. This excellent β-selectivity could be attributed to the greater proportion of the β-OH at equilibrium on **12** as well as the significantly increased rate of equilibrium in the presence of Ag_2O prior to O-methylation.[16] Moreover, a presumable intramolecular hydrogen bonding of β-OH to O2 could make it a better nucleophile than the α-OH and therefore enhance the β-selectivity.[16a,16b] The resulting **13** was then subjected to the Pd/C-promoted hydrogenolysis in MeOH to selectively remove the benzyl group at O2, giving smoothly glycosyl acceptor **6** in 83% yield.

With the 6-deoxy-L-Alt*p* donor **7** and acceptor **6** at hand, we examined the gold(I)-catalyzed glycosylation with different counter anions (of the gold(I) catalyst), solvents, and temperatures. As depicted in Table 1, all the condensations of **7** (1.2 equiv.) with **6** (1.0 equiv.) under the activation of gold(I) species (0.12 equiv.) led to the desired disaccharide **14β** with good β-selectivity (from a β/α ratio of 7.3:1 to β only). The β-configuration was confirmed by the correlation observed between the *syn*-diaxial H1' and H5' in a NOESY spectrum. Lowering the temperature from 0 ^oC (entry 1) to -42 ^oC (entry 4) increased the β/α ratio from 7.3:1 to 15.2:1, but the yield dropped from 97% to 72%. The β-selectivity could also be improved by replacing the counter anion $^-NTf_2$ with the previously optimized $^-BAr_4^F$, used for β-mannosylation and β-rhamnosylation,[11] leading to a β-only selectivity in CH_2Cl_2 at -20 ^oC (entry 3); however, the reaction became sluggish and the yield dropped to 34%. Replacement of the solvent CH_2Cl_2 with PhCl in the presence of PPh_3AuNTf_2 at -42 ^oC decreased the

β-selectivity but improved the yield from 72% (entry 4) to 99% (entry 5). Interestingly, PhCl strongly weakened the effect of counter anion $^{-}BAr_4^F$, and therefore gave a yield of 90% and β/α ratio of 10.0:1 at -42 °C (entry 6), that was similar to those with $^{-}NTf_2$ (entries 2 and 5). Nevertheless, the most efficient and convenient glycosylation could be attained under the catalysis of PPh_3AuNTf_2 in CH_2Cl_2 at -20 °C (entry 2), leading to disaccharide **14β** in gram scale in a short time, excellent yield (98%), and high β-selectivity (β/α = 9.9:1).

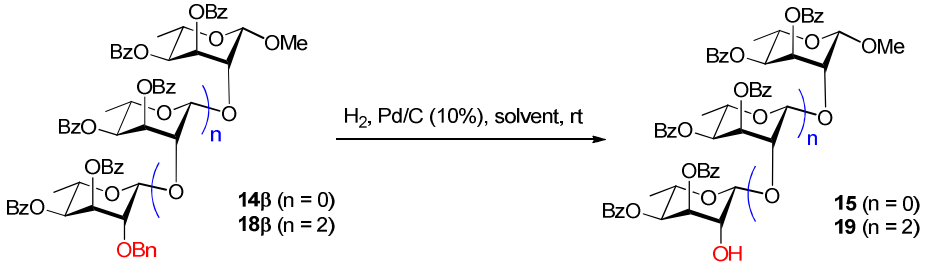
TABLE 1. Examination of the β-selective glycosylation of 6-deoxy-L-Alt*p* donor **7** with acceptor **6**.



Entry	Au(I) catalyst	Solvent	Temp. (°C)	Time (h)	Yield (%)	Ratio (β:α)
1	PPh_3AuNTf_2	CH_2Cl_2	0	2	97	7.3:1[a]
2	PPh_3AuNTf_2	CH_2Cl_2	-20	2	98	9.9:1[b]
3	$PPh_3AuBAr_4^F$	CH_2Cl_2	-20	8	34	β only[a]
4	PPh_3AuNTf_2	CH_2Cl_2	-42	8	72	15.2:1[a]
5	PPh_3AuNTf_2	PhCl	-42	8	99	9.2:1[a]
6	$PPh_3AuBAr_4^F$	PhCl	-42	14	90	10.0:1[a]

[a]Determined by ^1H NMR; [b]Determined by column isolation.

TABLE 2. Attempts at removal of the benzyl group on disaccharide **14β** (and tetrasaccharide **18β**) via hydrogenolysis.



Entry	Substrate	Solvent	H_2 (atm)	Time (h)	Yield
1	**14β**	MeOH	1	48	16%
2	**14β**	MeOH/EtOAc	1	48	21%
3[a]	**14β**	MeOH/EtOAc	1	48	12%
4	**14β**	MeOH/AcOH (5:1)	1	52	91%
5	**18β**	MeOH/AcOH (5:1)	1	48	26%
6	**18β**	MeOH/AcOH (2:1)	1	48	52%
7	**18β**	MeOH/THF	50	6	No reaction
8	**18β**	MeOH/AcOH (10:1)	50	24	9%
9[b]	**18β**	MeOH/AcOH (5:1)	50	24	Complex mixture

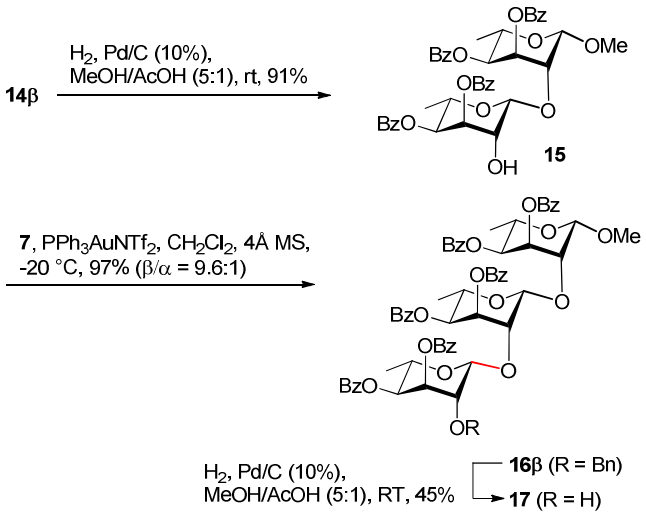
[a]$Pd(OH)_2/C$ (15%) was used. [b]at 50 °C.

Difficulty was encountered in the subsequent cleavage of the 2-*O*-benzyl group on disaccharide **14β** (Table 2). Due to the increased steric hindrance from the added sugar residue, hydrogenolysis of the 2-*O*-benzyl group turned out to be very sluggish with Pd/C (entries 1 and 2) or $Pd(OH)_2/C$ (entry 3) in neutral solvent (*cf.*, **13→6**). Delightfully, replacing the solvent with an acidic mixture of MeOH/AcOH (5:1) was

able to remove smoothly the benzyl group to give alcohol **15** in 91% yield in gram scale (entry 4).

Applying the optimized glycosylation conditions (PPh_3AuNTf_2 and 4Å MS in CH_2Cl_2 at -20 °C) to the condensation of disaccharide alcohol **15** with *ortho*-hexynylbenzoate donor **7** provided the desired trisaccharide **16β** in excellent yield (97%) and β-selectivity (β/α = 9.6:1) (Scheme 2). Although the Pd/C-promoted hydrogenolysis of the terminal benzyl group on **16β** was only partially successful even in the MeOH/AcOH (5:1) mixture, we isolated the desired trisaccharide alcohol **17** in an acceptable 45% yield and recovered the remaining **16β**.

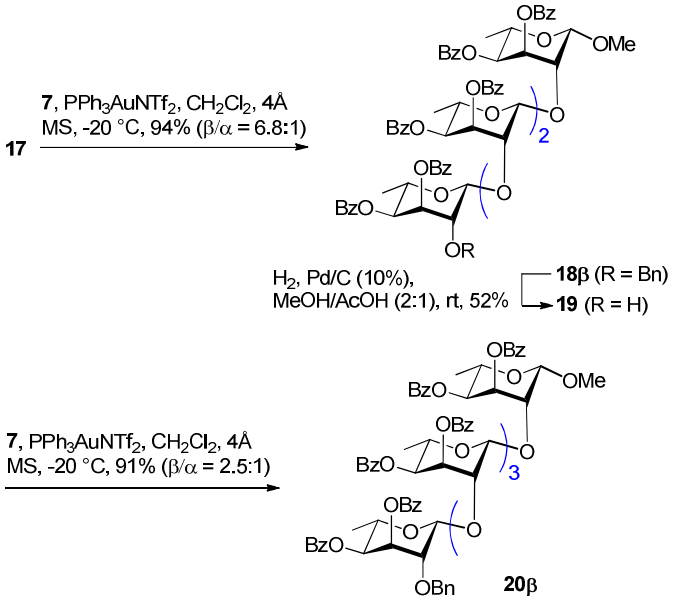
SCHEME 2. Synthesis of 6-deoxy-L-Alt*p* trisaccharide **16β**.



The same procedures were employed in the synthesis of tetra- (**18β**) and pentasaccharide (**20β**) (Scheme 3). Thus, treatment of trisaccharide alcohol **17** with donor **7** in the catalysis of PPh_3AuNTf_2 in CH_2Cl_2 at -20 °C led to tetrasaccharides **18β**/**18α** in comparably excellent yield (94%) but a decreased β/α ratio of 6.8:1 (*cf.*, **6**+**7**→**14β** and **15**+**7**→**16β**). The subsequent removal of the terminal benzyl group on

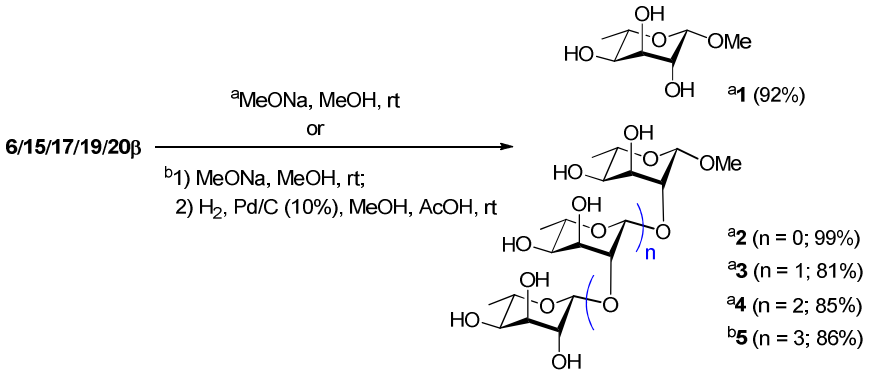
tetrasaccharide **18β** in a MeOH/AcOH (5:1) mixture via hydrogenolysis under 1-atm H_2 at rt, unsurprisingly, only gave the desired alcohol **19** in a poor 26% yield (Table 2, entry 5). Increasing the ratio of AcOH/MeOH from 1:5 to 1:2 improved the yield to an acceptable 52% (entry 6). Conducting the reaction at 50-atm H_2 or higher temperature was not able to offer a better result (entries 7-9). Nevertheless, tetrasaccharide alcohol **19** was able to be coupled with donor **7** under the conditions of PPh_3AuNTf_2 in CH_2Cl_2 at -20 °C, providing pentasaccharides **20β**/**20α** in 91% yield and a β/α ratio of 2.5:1. The poorer β-selectivity in the preparation of tetra- and pentasaccharide could be related to the weakened nucleophilicity of the terminal 2-OH on **17** and **19** due to their great bulkiness and multiple electron-withdrawing benzoyl groups.[11] Even so, the β-(1→2)-linked tetra- and pentasaccharide **18β** and **20β**, respectively, were still obtained in satisfactory yields.

SCHEME 3. Synthesis of 6-deoxy-L-Alt*p* tetrasaccharide **18β** and pentasaccharide **20β**.



The last stage of the synthesis involved the full cleavage of the benzoyl and benzyl groups (Scheme 4). Thus, treatment of compounds **6**, **15**, **17**, and **19** with MeONa in MeOH removed the benzoyl groups and furnished the desired 6-deoxy-β-L-Alt*p*-containing mono- to tetrasaccharides **1**-**4** in 81% to 99% yields. On the other hand, removing the benzoyl groups on pentasaccharide **20β** before hydrogenolysis was able to extricate the hindered terminal 2-*O*-benzyl group and therefore made the subsequent debenzylation smooth and highly efficient, furnishing pentasaccharide **5** in 86% yield (two steps).

SCHEME 4. Global deprotection in the synthesis of 6-deoxy-β-L-Alt*p*-containing mono- to pentasaccharides **1**–**5**.



The ^{1}H and ^{13}C NMR chemical shifts of compounds **1**–**5**, compiled in Table 3, were assigned using 1D and 2D NMR experiments suitable for carbohydrates.[17] The pyranoid sugar residues are present in the $^{1}C_{4}$ chair conformation based on vicinal $^{3}J_{HH}$ coupling constants (Table 3) where $J_{H2,H3} \approx 4$ Hz and $J_{H3,H4} \approx 3$ Hz are consistent with a synclinal arrangement between protons and $J_{H4,H5} \approx 10$ Hz arises from an antiperiplanar arrangement. The β-configuration of the 6-deoxy-L-Alt*p* sugar residues were determined based on the magnitude of the anomeric $^{1}J_{CH}$ coupling constants

being 160–165 Hz.[18] Chemical shift differences between sugar residues in an oligo- or polysaccharide compared to their constituent monosaccharides carry structural information and can be predicted employing computerized approaches, such as GODESS[19] and CASPER.[20] The monosaccharide chemical shift displacements take place as a result of various substitution effects, glycosylation or from steric influences between residues, notable in particular in di- and trisaccharides.[21]

TABLE 3. ^{1}H and ^{13}C NMR chemical shifts (ppm) and coupling constants (Hz) of compounds **1**–**5** in D_2O at 37 ºC.

Compound		1	2	3	4	5	6	OMe
		4.81 (1.06)	3.98	4.15	3.60	3.84	1.31	3.53
	A		(4.12)	(3.23)	(9.63)	(6.27)		
		100.48 [160]	77.97	70.65	70.72	70.85	17.90	57.85
		5.08 (0.82)	4.07	4.08	3.55	3.80	1.30	
	B		(3.99)	(3.20)	(9.84)	(6.26)		
		100.37 [163]	77.45	70.98	70.60	70.72	17.90	
		5.25 (0.93)	4.06	4.03	3.53	3.86	1.29	
5	C		(3.91)	(3.16)	(9.99)	(6.24)		
		100.09 [164]	77.24	71.01	70.68	70.59	17.85	
		5.29 (0.98)	4.02	4.10	3.55	3.87	1.30	
	D		(3.92)	(3.24)	(9.89)	(6.28)		
		99.89 [165]	78.20	70.82	70.60	70.59	17.85	
		5.16 (1.22)	3.92	4.03	3.57	3.88	1.30	
	E		(4.01)	(3.30)	(9.63)	(6.29)		
		100.43 [165]	71.49	71.11	70.53	70.78	18.10	
		4.80 (1.06)	3.98	4.13	3.58	3.84	1.31	3.53
	A		(4.14)	(3.20)	(9.64)	(6.26)		
		100.49 [160]	77.82	70.66	70.74	70.81	17.89	57.84
		5.08 (0.96)	4.08	4.03	3.52	3.79	1.29	
4	B		(3.91)	(3.07)	(9.86)	(6.22)		
		100.23 [163]	77.16	71.02	70.62	70.65	17.88	
		5.24 (1.01)	4.03	4.10	3.55	3.87	1.29	
	C		(3.89)	(3.19)	(9.93)	(6.24)		
		99.94 [165]	78.13	70.83	70.58	70.59	17.81	

	D	5.16 (1.20)	3.92 (3.96)	4.03 (3.24)	3.57 (9.62)	3.87 (6.30)	1.30	
		100.38 [165]	71.47	71.10	70.53	70.78	18.09	
3	A	4.80 (1.09)	3.98 (4.16)	4.09 (3.28)	3.55 (9.58)	3.83 (6.26)	1.29	3.53
		100.34 [160]	77.81	70.71	70.77	70.74	17.87	57.83
	B	5.06 (1.00)	4.06 (3.95)	4.10 (3.27)	3.54 (9.92)	3.81 (6.26)	1.29	
		100.18 [163]	77.98	70.80	70.52	70.71	17.85	
	C	5.12 (1.22)	3.92 (3.98)	4.03 (3.29)	3.56 (9.60)	3.87 (6.30)	1.30	
		100.42 [164]	71.47	71.11	70.51	70.76	18.05	
2	A	4.83 (1.31)	3.98 (4.48)	4.19 (3.24)	3.62 (9.21)	3.86 (6.38)	1.30	3.52
		100.09 [162]	78.58	70.17	70.74	71.12	17.94	57.59
	B	4.97 (1.21)	3.93 (4.08)	4.02 (3.29)	3.56 (9.52)	3.83 (6.31)	1.29	
		100.40 [163]	71.26	71.07	70.48	70.86	18.11	
1	A	4.76 (1.65)	3.87 (4.70)	4.01 (3.33)	3.61 (8.77)	3.86 (6.39)	1.31	3.52
		100.53 [161]	70.91	70.88	70.86	71.44	18.14	57.52

In the β-(1→2)-linked 6-deoxy-L-Alt*p* oligosaccharides synthesized herein glycosylation effects are pronounced in ^{1}H NMR spectra for the anomeric protons (Figure 2). The *O*-methyl monosaccharide glycoside **1** has the lowest anomeric ^{1}H NMR chemical shift compared to other residues in larger oligosaccharides. For compounds **3**–**5**, an essentially non-changing chemical shift at δ_H ~4.80 in residue A is evident. In disaccharide **2** the anomeric proton of the terminal residue B is displaced downfield towards a higher chemical shift, an effect that also occurs in trisaccharide **3**, where the terminal residue is denoted C. Notably, at the trisaccharide level and onwards the chemical shift of H1 in B, δ_H 5.06, only changes marginally in larger oligosaccharides, suggesting that this part of the oligosaccharides is not further perturbed once the length of the oligosaccharide increases. Similar to residue B, for larger oligosaccharides the terminal residue in tetrasaccharide **4** and in

pentasaccharide **5**, residues D and E, respectively, both occur at δ_H 5.16, thus implying that similar structural environments are present among residues at the terminal end when the length of the oligosaccharide reaches a certain point. In tetrasaccharide **4** the anomeric proton of residue C is shifted further downfield to 5.24 ppm whereas in pentasaccharide **5** the corresponding chemical shift is hardly altered, now at 5.25 ppm. However, in the latter saccharide the chemical shift of the anomeric proton of the penultimate residue D is shifted even further downfield to δ_H 5.29. The chemical shift of this resonance, which is similar to that of the anomeric proton of the adjacent residue C, indicates that the structural environment of residue D closely resembles that in the β-(1→2)-linked 6-deoxy-L-Alt*p*-containing polysaccharide of *Y. enterocolitica* O:3, since only a small chemical shift difference is present between the anomeric protons of these residues.

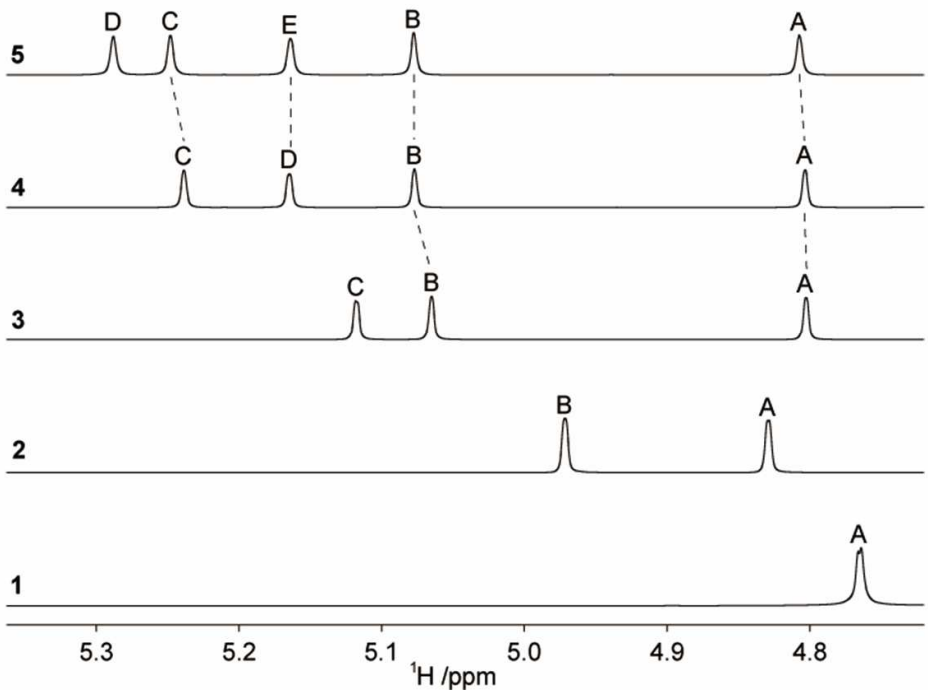


FIGURE 2. The anomeric region of ^{1}H NMR spectra of compounds **1**–**5** in D_2O at

37 °C with sugar residues labeled A–E starting from the reducing end of the oligosaccharides.

As the substitution pattern in the oligosaccharides contains β-(1→2)-linkages some sugar residues are destined to become proximate to each other.[22] A molecular model of pentasaccharide **5** was made using the CarbBuilder program[23] and is presented in Figure 3. The resulting structure of pentasaccharide **5** is a left-handed helix and this 3D structural arrangement may then form a highly specific epitope in the polysaccharide when present as an antigen in the bacterium.

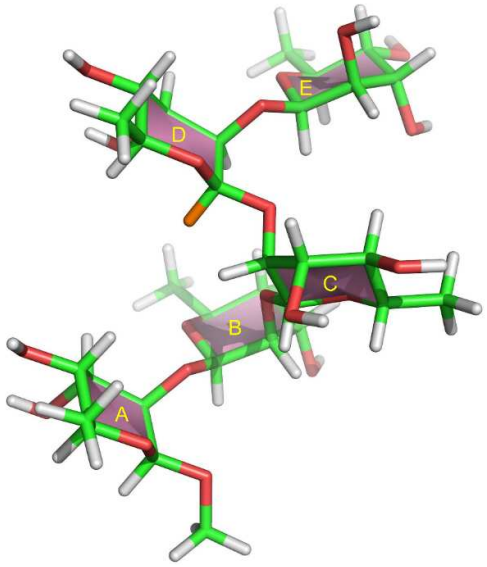


FIGURE 3. Molecular model of pentasaccharide **5**, 6-deoxy-β-L-Alt*p*-(1→2)-[6-deoxy-β-L-Alt*p*-(1→2)]$_3$-6-deoxy-β-L-Alt*p*-OMe, made by the computer program CarbBuilder and visualized using the PyMOL Molecular Graphics System, version 1.8.4 Schrödinger, LLC. Sugar residues are labeled A – E and the anomeric proton of residue D, which has the lowest ^{1}H NMR chemical shift in the pentasaccharide, is colored orange.

Interestingly, by noting that altrose is the C3-epimer of mannose the 3D structure of

the β-(1→2)-linked 6-deoxy-L-Alt*p*-containing oligosaccharides may be compared to the 3D structure of β-(1→2)-linked oligomannosides found in the cell wall of *Candida albicans*. Oligosaccharides having β-(1→2)-linked manosyl residues have been synthesized, including a reducing tetrasaccharide,[24] an octasaccharide with a hexyl group at the reducing end[25] and as propyl oligomannosides with up to six sugar residues.[26] These oligomannosides, including one with protecting groups,[25] have been described as having irregular, compact and/or contorted helical structures with approximately three residues per turn. Furthermore, β-(1→2)-linked oligomannosides bind to a monoclonal antibody in a helical conformation similar to that observed in absence of the protein, i.e., free in solution.[27] Notably, in the series of propyl glycosides the tri-, tetra-, and pentasaccharides show the exact same order of ^{1}H NMR chemical shifts of their anomeric protons, labeled A–E as herein, as those of the 6-deoxy-L-Alt*p*-containing oligosaccharides, i.e., for the trisaccharide the chemical shift increases in the order A–C, for the tetrasaccharide $\delta_{H1D} < \delta_{H1C}$ and for the pentasaccharide $\delta_{H1E} < \delta_{H1C} < \delta_{H1D}$. The conformational state at the glycosidic β-(1→2)-linkages deduced from the modeling and molecular simulation studies in conjunction with NMR spectroscopy experiments[24,26,27] can thus be described as an *exo*-anomeric *syn*-conformation.[28] Given these facts, a molecular model of β-D-Man*p*-(1→2)-[β-D-Man*p*]$_3$-β-D-Man*p*-OMe was built by CarbBuilder, in which the *exo*-anomeric *syn*-conformation was generated at the glycosidic linkages, forming a right-handed helix essentially the mirror image of that from 6-deoxy-β-L-Alt*p*-(1→2)-[6-deoxy-β-L-Alt*p*-(1→2)]$_3$-6-deoxy-β-L-Alt*p*-OMe

presented in Figure 3. Although the above analysis for the conformation of a pentasaccharide corresponding to the O-antigen of *Y. enterocolitica* O:3 is based on only a ^{1}H NMR chemical shift comparison and a pragmatic generation of the 3D structure of this oligomer, we judge it to be a reasonable model and description of its overall shape.

Conclusion

In summary, we have developed an efficient approach to the assembly of β-(1→2)-linked 6-deoxy-L-altropyranoside-containing oligosaccharides, which represent models of the O-antigen of *Yersinia enterocolitica* O:3. The synthesis employs an iterative gold(I)-catalyzed glycosylation approach with 2-*O*-benzyl-3,4-*O*-benzyol-6-deoxy-L-altropyranosyl *ortho*-hexynylbenzoate (**7**) as donor, which leads to excellent coupling yields and satisfactory β-selectivity. The synthetic mono- to pentasaccharides **1**–**5** were analyzed by NMR spectroscopy and molecular modeling of the pentasaccharide (**5**) shows that it adopts a left-handed helical structure; this may represent a 3D structural arrangement of a highly specific epitope in the bacterial lipopolysaccharide. Further studies on the 3D structure of these oligomers related to the lipopolysaccharide from *Y. enterocolitica* O:3 are underway and the results will be reported in due course.

Experimental Section

General Information. All reactions were carried out under nitrogen or argon atmosphere with anhydrous solvents in flame-dried glassware, unless otherwise noted.

All glycosylation reactions were performed in the presence of 4Å molecular sieves, which were flame-dried immediately before use in the reaction under high vacuum. Glycosylation solvents were dried using a solvent purification system and used directly without further drying. The chemicals used were reagent grade as supplied, except where noted. Analytical thin-layer chromatography was performed using silica gel 60 F254 glass plates. Compound spots were visualized by UV light (254 nm) and by heating with a solution of 10% H_2SO_4 in ethanol. Flash column chromatography was performed on silica gel. NMR chemical shifts were referenced using Me_4Si (0 ppm), residual $CHCl_3$ (^{1}H NMR δ = 7.26 ppm, ^{13}C NMR δ = 77.16 ppm) for compounds **6**–**20**. Peak and coupling constant assignments are based on ^{1}H NMR, COSY, HSQC, and NOESY spectral data. Splitting patterns were indicated as nr (not resolved), s (singlet), d (doublet), t (triplet), q (quartet), and br (broad resonance) for ^{1}H NMR data. High-resolution mass spectra were recorded on an ESI-TOF mass spectrometer. Optical rotations were measured on a polarimeter using either $CHCl_3$ or CH_3OH as solvent.

^{1}H, ^{13}C, and 2D NMR spectra for resonance assignments of compounds **1**–**5** in D_2O solution were carried out at 37 ^{o}C on an NMR spectrometer operating at a ^{1}H frequency of 600 MHz. The chemical shifts are reported in ppm using internal sodium 3-trimethylsilyl-(2,2,3,3-$^2H_4$)-propanoate (TSP, δ_H 0.00) or external 1,4-dioxane in D_2O (δ_C 67.40) as references. ^{1}H NMR chemical shifts and coupling constants of **1**–**5** were refined iteratively from ^{1}H NMR spectra by total-lineshape analysis using the PERCH NMR spin-simulation software.[29] For ^{13}C NMR spectra of compounds **1**–**5** an exponential line-broadening factor of only 0.1 Hz was applied to the FID prior to FT, such that peaks from nuclei with similar chemical shifts were resolved.

General Procedure for the Gold(I)-Catalyzed Glycosylation with *ortho*-hexynylbenzoate Donor 7.

To a solution of donor **7** (1.2 equiv.) and the acceptor (1.0 equiv.) in dry CH_2Cl_2 was added freshly activated 4Å molecular sieves (weight equaled the combined weight of the donor and acceptor). The mixture was stirred at the indicated temperature for 20 min under Ar. $Ph_3PAuNTf_2$ (0.12 equiv.) or a combination of Ph_3PAuCl (0.12 equiv.) and $AgBAr_4^F$ (0.028 M in Et_2O, 0.12 equiv.) was added. The stirring was continued at the same temperature until TLC showed complete conversion of the acceptor. The reaction was quenched by the addition of Ph_3P (0.15 equiv.). The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by silica gel column chromatography to provide the coupled glycosides.

General Debenzylation Procedure. To a solution of the benzylated compound in MeOH or a combination of MeOH/AcOH was added Pd/C, and the suspension was stirred under H_2. After complete consumption of the benzylated compound (TLC), the suspension was filtered through a pad of Celite and the filtrate was concentrated. The resulting residue was purified by column chromatography to provide the desired alcohol.

General Saponification Procedure. To a solution of the ester in MeOH was added MeONa, and the mixture was stirred at rt. After complete consumption of the ester (TLC), the mixture was concentrated. The resulting residue was purified by column chromatography to provide the desired alcohol.

Methyl 6-deoxy-α-L-altropyranoside (9). To a solution of 2,4-di-*O*-acetyl-6-deoxy-α-L-Alt*p* **8**[11a] (46 g, 175 mmol) in MeOH (400 mL) was

added MeONa (9.5 g, 17.5 mmol) at rt. After stirring at rt for 12 h, the solution was evaporated in vacuo to give a residue, which was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 10:1) to afford compound **9** (31 g, 99%) as a white solid: $[\alpha]_D^{28}$ = -49.8 (*c* 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.63 (nr, 1H), 3.95 (dd, *J* = 4.1, 2.0 Hz, 1H), 3.89 (d, *J* = 3.8 Hz, 1H), 3.75 (dq, *J* = 9.3, 6.3 Hz, 1H), 3.50 (dd, *J* = 9.3, 3.5 Hz, 1H), 3.43 (s, 3H), 1.35 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 101.1, 70.9, 69.7, 69.5, 65.4, 55.8, 17.7; HRMS (ESI) calcd for $C_7H_{14}O_5Na$ $[M + Na]^+$ 201.0733, found 201.0726.

Methyl 2-*O*-Benzyl-6-deoxy-α-L-altropyranoside (10). To a solution of **9** (30 g, 168 mmol) in acetone (1 L) was added $(CH_3)_2C(OMe)_2$ (207 mL, 1.68 mol) and camphorsulfonic acid (3.9 g, 16.8 mmol) at rt. After stirring for 1 h, Et_3N was added to quench the reaction. The mixture was concentrated in vacuo. The residue was used directly for the next step without further purification.

The residue was dissolved in dry DMF (600 mL), and stirred at 0 ^{o}C for 15 min. NaH (60% in mineral oil, 21 g, 504 mmol) and benzyl bromide (40 mL, 336 mmol) were slowly added under Ar. The mixture was allowed to stir at rt for 12h until TLC showed complete conversion of the starting materials. The mixture was quenched with MeOH, and then diluted with CH_2Cl_2, washed with saturated aq. NH_4Cl, dried over Na_2SO_4, and concentrated. The residue was used directly for the next step without further purification.

The residue above was dissolved in AcOH (80% aq. 400 mL). After stirring at 100 ^{o}C for 6 h, the mixture was evaporated in vacuo to give a residue, which was purified by silica gel column chromatography (petroleum ether/EtOAc, 4:1) to afford **10** (42 g, 93% over 3 steps) as a colorless syrup: $[\alpha]_D^{28}$ = -40.1 (c 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.28 (m, 5H), 4.70 (d, *J* = 1.4 Hz, 1H), 4.61 (s, 2H), 3.98–3.94

(m, 1H), 3.72–3.66 (m, 2H), 3.54–3.49 (m, 1H), 3.38 (s, 3H), 3.29 (d, J = 10.0 Hz, 1H), 2.53 (d, J = 10.2 Hz, 1H), 1.36 (d, J = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.6, 128.6, 128.1, 127.8, 99.4, 75.6, 72.3, 69.9, 68.9, 64.6, 55.4, 17.8; HRMS (ESI) calcd for $C_{14}H_{20}O_5Na$ $[M + Na]^+$ 291.1203, found 291.1203.

Methyl 2-*O*-Benzyl-3,4-di-*O*-benzoyl-6-deoxy-α-L-altropyranoside (11). To a solution of **10** (40.0 g, 149 mmol) in dry CH_2Cl_2/Et_3N (200 mL/207 mL) were added DMAP (1.8 g, 14.9 mmol) and BzCl (43 mL, 373 mmol) at 0 ^{o}C. After stirring overnight, the mixture was diluted with CH_2Cl_2, and was then washed with water and brine, respectively. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 5:1) to afford **11** (63.9 g, 90%) as a colorless syrup: $[\alpha]_D^{28}$ = -81.5 (*c* 4.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 7.9 Hz, 2H), 7.96–7.95 (m, 2H), 7.60–7.57 (m, 1H), 7.55–7.51 (m, 1H), 7.47–7.42 (m, 4H), 7.39–7.35 (m, 4H), 7.33–7.29 (m, 1H), 5.80–5.79 (m, 1H), 5.45 (dd, J = 9.0, 3.3 Hz, 1H), 4.87 (d, J = 11.9 Hz, 1H), 4.78–4.74 (m, 2H), 4.52 (dq, J = 8.6, 6.4 Hz, 1H), 3.88 (dd, J = 4.1, 1.8 Hz, 1H), 3.47 (s, 3H), 1.39 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 165.5, 137.5, 133.19, 133.17, 130.1, 129.9, 129.8, 129.7, 128.5, 128.44, 128.41, 128.1, 128.0, 100.1, 75.3, 72.7, 71.2, 68.1, 63.3, 55.5, 17.6; HRMS (ESI) calcd for $C_{28}H_{28}O_7Na$ $[M + Na]^+$ 499.1727, found 499.1728.

2-*O*-Benzyl-3,4-di-*O*-benzoyl-6-deoxy-L-altropyranose (12). A solution of compound **11** (7.1 g, 14.9 mmol), HCl (5 N aq., 6.3 mL), and $SrCl_2 \cdot 6H_2O$ (400 mg, 1.5 mmol) in AcOH (150 mL) was stirred at 80 ^{o}C for 8 h. The mixture was diluted with EtOAc, and washed with water, saturated aq. $NaHCO_3$, and brine, respectively. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 5:1) to

provide hemiacetal **12** (5.6 g, 81%, b/a = 2.1:1) as a colorless syrup: ^{1}H NMR (500 MHz, $CDCl_3$) *d* 8.05–8.00 (m, 2H), 7.93–7.89 (m, 2H), 7.59–7.28 (m, 11H), 5.95–5.94 (m, 0.68H), 5.82–5.81 (m, 0.32H), 5.41 (dd, *J* = 8.9, 3.3 Hz, 0.32H), 5.30 (dd, *J* = 10.0, 3.1 Hz, 0.68H), 5.26 (d, *J* = 5.3 Hz, 0.32H), 5.18 (d, *J* = 12.2 Hz, 0.68H), 5.00 (d, *J* = 11.6 Hz, 0.68H), 4.85 (d, *J* = 11.9 Hz, 0.32H), 4.74 (d, *J* = 12.0 Hz, 0.32H), 4.70 (d, *J* = 11.6 Hz, 0.68H), 4.67–4.62 (m, 0.32H), 4.30 (dq, *J* = 9.8, 6.2 Hz, 0.68H), 3.87 (dd, *J* = 4.3, 1.9 Hz, 0.32H), 3.77 (dd, *J* = 3.4, 1.6 Hz, 0.68H), 3.73 (d, *J* = 12.3 Hz, 0.68H), 3.17 (d, *J* = 5.7 Hz, 0.32H), 1.35–1.33 (m, 3H); ^{13}C NMR (125 Hz, $CDCl_3$) *d* 165.6, 165.5, 165.4, 165.2, 137.4, 136.7, 133.6, 133.3, 133.23, 133.15, 129.8, 129.7, 129.6, 129.5, 129.3, 128.7, 128.6, 128.47, 128.45, 128.44, 128.41, 128.40, 128.35, 128.0, 127.9, 93.4, 92.0, 75.7, 75.6, 73.2, 72.7, 71.2, 70.9, 68.4, 68.3, 67.9, 63.7, 18.0, 17.4; HRMS (ESI) calcd for $C_{27}H_{26}O_7Na$ $[M + Na]^+$ 485.1571, found 485.1576.

Methyl 2-*O*-Benzyl-3,4-di-*O*-benzoyl-6-deoxy-β-L-altropyranoside (13). To a solution of hemiacetal **12** (923 mg, 2.0 mmol) in dry CH_2Cl_2 (20 mL) were added Ag_2O (1.06 g, 4.6 mmol), 4Å MS (1.0 g), and MeI (335 μL, 4.6 mmol) at rt under Ar. The mixture was stirred until TLC showed the complete conversion of the hemiacetal. After being quenched with MeOH (1 mL), the mixture was filtered through Celite. The filtrate was concentrated and the residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 10:1) to provide **13** (839 mg, 88%) as a white foam: $[\alpha]_D^{22}$ = -3.2 (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00–7.99 (m, 2H), 7.92–7.90 (m, 2H), 7.61–7.58 (m, 1H), 7.54–7.51 (m, 1H), 7.47–7.44 (m, 4H), 7.38–7.34 (m, 4H), 7.31–7.27 (m, 1H), 5.82 (dd, *J* = 5.0, 3.2 Hz, 1H), 5.43 (dd, *J* = 8.5, 3.2 Hz, 1H), 4.91–4.82 (m, 3H), 4.23 (dq, *J* = 8.5, 6.4 Hz, 1H), 3.89 (dd, *J* = 5.0, 1.7 Hz, 1H), 3.60 (s, 3H), 1.42 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

165.5, 165.2, 137.9, 133.5, 133.3, 129.7, 129.7, 128.6, 128.5, 128.4, 128.1, 127.9, 100.5, 74.6, 73.5, 71.8, 69.6, 69.0, 57.1, 18.3; HRMS (ESI) calcd for $C_{28}H_{28}O_7Na$ [M + Na]$^+$ 499.1727, found 499.1729.

Methyl 3,4-Di-*O*-benzoyl-6-deoxy-β-L-altropyranoside (6). Compound **13** (3.7 g, 7.8 mmol) was subjected to the general debenzylation procedure with Pd/C (5%, 3.4 g) in MeOH (80 mL). The purification by silica gel column chromatography (petroleum ether/EtOAc, 4:1) provided **6** (2.5 g, 83%) as a white foam: $[\alpha]_D^{28}$ = -13.5 (*c* 3.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01–8.00 (m, 2H), 7.93–7.91 (m, 2H), 7.58–7.55 (m, 1H), 7.52–7.49 (m, 1H), 7.58–7.55 (m, 2H), 7.52–7.49 (m, 2H), 5.79 (dd, *J* = 5.6, 3.2 Hz, 1H), 5.45 (dd, *J* = 7.7, 3.2 Hz, 1H), 4.90 (d, *J* = 2.0 Hz, 1H), 4.32–4.19 (m, 1H), 4.14–4.11 (m, 1H), 3.59 (s, 3H), 2.79 (d, *J* = 5.1 Hz, 1H), 1.42 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 133.4, 133.2, 129.72, 129.68, 129.63, 129.61, 128.5, 128.4, 100.0, 71.5, 69.9, 69.8, 68.9, 56.6, 18.4; HRMS (ESI) calcd for $C_{21}H_{22}O_7Na$ [M + Na]$^+$ 409.1258, found 409.1267.

2-*O*-Benzyl-3,4-di-*O*-benzoyl-6-deoxy-β-L-altropyranosyl *ortho*-hexynylbenzoate (7). To a solution of hemiacetal **12** (4.6 g, 9.9 mmol), *ortho*-hexynylbenzoic acid (2.0 g, 11.9 mmol), and DMAP (605 mg, 5.0 mmol) in dry CH_2Cl_2 (50 mL) was added EDCI (2.3 g, 11.9 mmol) at rt. After stirring for 6 h, the mixture was diluted with CH_2Cl_2, and was then washed with saturated aq. $NaHCO_3$, water, and brine, respectively. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 10:1) to provide donor **7** (6.2 g, 97%, β/α = 3.2:1) as a colorless syrup: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03–8.91 (m, 5.74H), 7.75–7.73 (m, 0.26H), 7.61–7.27 (m, 12.74H), 7.00–6.97 (m, 0.26H), 6.50–6.50 (m, 0.74H), 6.45 (s, 0.26H), 5.95 (dd, *J* = 5.4, 3.1 Hz, 0.74H), 5.86–5.85 (m, 0.26H), 5.54–5.49 (m, 1H),

4.92–4.84 (m, 2H), 4.75–4.70 (m, 0.26H), 4.47–4.42 (m, 0.74H), 4.1 (dd, *J* = 5.5, 1.9 Hz, 0.74H), 4.06 (dd, *J* = 3.3, 1.3 Hz, 0.26H), 2.48 (t, *J* = 7.2 Hz, 1.48H), 2.41 (t, *J* = 7.1 Hz, 0.52H), 1.65–1.37 (m, 7H), 0.94–0.90 (m, 3H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 165.6, 165.5, 165.38, 165.37, 164.5, 164.2, 137.4, 137.2, 134.7, 134.5, 133.6, 133.4, 133.28, 133.25, 132.3, 131.8, 131.2, 130.7, 130.6, 130.3, 129.94, 129.89, 129.80, 129.77, 129.69, 129.65, 129.6, 129.5, 128.7, 128.53, 128.50, 128.4, 128.3, 128.2, 128.1, 128.0, 127.2, 126.9, 125.6, 125.1, 97.1, 96.9, 92.6, 92.1, 79.2, 79.1, 74.5, 73.9, 73.4, 72.9, 71.5, 71.0, 70.6, 68.5, 67.9, 65.1, 30.8, 30.7, 22.19, 22.15, 19.7, 19.6, 18.5, 17.8, 13.78, 13.76; HRMS (ESI) calcd for $C_{40}H_{38}O_8Na$ $[M + Na]^+$ 669.2459, found 669.2455.

Methyl 3,4-Di-*O*-benzoyl-6-deoxy-2-*O*-(2-*O*-benzyl-3,4-di-*O*-benzoyl-6-deoxy-β-L-altropyranosyl)-β-L-altropyranoside (14β) and Methyl 3,4-Di-*O*-benzoyl-6-deoxy-2-*O*-(2-*O*-benzyl-3,4-di-*O*-benzoyl-6-deoxy-α-L-altropyranosyl)-β-L-altropyranoside (14α). The general glycosylation procedure was used with donor **7** (2.72 g, 4.2 mmol), acceptor **6** (1.35 g, 3.5 mmol), and $Ph_3PAuNTf_2$ (311 mg, 0.42 mmol) in CH_2Cl_2 (60 mL) at -20 °C. The purification by silica gel column chromatography (petroleum ether/EtOAc, 10:1) afforded the disaccharide **14β** (2.58 g, 89%) and its α-anomer **14α** (261 mg, 9%), both as white foams.

14β: $[\alpha]_D^{28}$ = -4.4 (*c* 4.5, $CHCl_3$); mp = 87−90 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10–8.09 (m, 2H), 8.04–8.02 (m, 2H), 7.93–7.90 (m, 4H), 7.65–7.59 (m, 4H), 7.53–7.45(m, 6H), 7.43–7.4 (m, 2H), 7.37–7.33 (m, 4H), 7.32–7.29 (m, 1H), 6.00–5.98 (m, 1H), 5.84–5.82 (m, 1H), 5.52–5.50 (m, 2H), 5.45 (dd, *J* = 9.6, 3.2 Hz, 1H), 5.12 (d, *J* = 12.4 Hz, 1H), 5.01–4.94 (m, 2H), 4.39 (d, *J* = 4.4 Hz, 1H), 4.28–4.23 (m, 2H), 4.07 (d, *J* = 4.2 Hz, 1H), 3.53 (s, 3H), 1.43 (d, *J* = 6.3 Hz, 3H), 1.39 (d, *J* = 6.3 Hz, 3H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 165.4, 165.03, 164.97, 164.9, 138.3, 133.5, 133.4, 133.1, 129.8, 129.74, 129.69, 128.7, 128.5, 128.41, 128.37, 128.1, 127.6, 100.6, 100.0, 74.7, 73.9, 73.63, 73.61, 71.3, 71.0, 70.4, 69.6, 69.5, 69.4, 57.1, 18.2, 18.1; HRMS (ESI) calcd for $C_{48}H_{46}O_{13}Na$ $[M + Na]^+$ 853.2831, found 853.2833 .

14α: $[\alpha]_D^{28}$ = -25.6 (*c* 9.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.1, 1.4 Hz, 2H), 7.98 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.95–7.90 (m, 4H), 7.56–7.30 (m, 16H), 7.25–7.21 (m, 1H), 5.86–5.84 (m, 1H), 5.76 (dd, *J* = 6.1, 3.2 Hz, 1H), 5.40 (dd, *J* = 9.7, 3.2 Hz, 1H), 5.35 (dd, *J* = 7.3, 3.2 Hz, 1H), 5.13 (nr, 1H), 5.02 (d, *J* = 2.2 Hz, 1H), 4.84 (dq, *J* = 9.6, 6.4 Hz, 1H), 4.71 (dd, *J* = 60.6, 11.7 Hz, 2H), 4.30–4.26 (m, 2H), 3.92 (dd, *J* = 3.8, 1.2 Hz, 1H), 3.61 (s, 3H), 1.39 (d, *J* = 6.5 Hz, 3H), 1.30 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 165.6, 165.4, 165.1, 137.2, 133.5, 133.3, 133.04, 133.00, 130.6, 130.0, 129.83, 129.77, 129.6, 129.5, 128.6, 128.52, 128.47, 128.34, 128.30, 128.0, 127.9, 100.4, 98.8, 76.2, 73.3, 72.9, 72.0, 71.3, 70.1, 68.1, 67.4, 63.2, 56.7, 18.6, 17.5; HRMS (ESI) calcd for $C_{48}H_{50}O_{13}N$ $[M + NH_4]^+$ 848.3277, found 848.3273.

Methyl 3,4-Di-*O*-benzoyl-6-deoxy-2-*O*-(3,4-di-*O*-benzoyl-6-deoxy-β-L-altropyranosyl)-β-L-altropyranoside (15). Disaccharide **14β** (3.7 g, 7.8 mmol) was subjected to general debenzylation procedure with Pd/C (10%, 8.3 g) in MeOH/AcOH (100 mL/20 mL). The purification by silica gel column chromatography (petroleum ether/EtOAc, 4:1) provided **15** (2.90 g, 91%) as a white foam: $[\alpha]_D^{28}$ = +29.4 (*c* 1.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–8.03 (m, 2H), 8.01–7.99 (m, 2H), 7.97–7.95 (m, 2H), 7.92–7.90 (m, 2H), 7.64–7.61 (m, 1H), 7.57–7.47 (m, 5H), 7.43–7.34 (m, 6H), 5.98–5.91 (m, 1H), 5.93 (dd, *J* = 4.4, 3.2 Hz, 1H), 5.83 (dd, *J* = 7.0, 3.1 Hz, 1H), 5.53 (dd, *J* = 6.0, 3.1 Hz, 1H), 5.38–5.35 (m, 2H), 4.91 (d, *J* = 1.4 Hz, 1H), 4.32–4.29 (m,

2H), 4.26–4.23 (m, 2H), 3.58 (s, 3H), 3.19 (d, J = 6.3 Hz, 1H), 1.57 (d, J = 6.7 Hz, 3H), 1.40 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.54, 165.47, 165.3, 165.1, 133.7, 133.32, 133.27, 133.2, 129.89, 129.85, 129.82, 129.81, 129.77, 129.60, 129.59, 128.7, 128.49, 128.48, 128.46, 101.5, 99.8, 75.6, 72.1, 71.5, 71.1, 69.8, 69.6, 69.3, 68.5, 57.1, 19.4, 18.1; HRMS (ESI) calcd for $C_{41}H_{40}O_{13}Na$ $[M + Na]^+$ 758.2807, found 758.2803.

Trisaccharides 16β and 16α. The general glycosylation procedure was used with donor **7** (3.04 g, 4.7 mmol), acceptor **15** (2.90 g, 3.9 mmol), and $Ph_3PAuNTf_2$ (348 mg, 0.47 mmol) in CH_2Cl_2 (200 mL) at -20 ^{o}C. The purification by silica gel column chromatography (petroleum ether/EtOAc, 10:1) afforded the coupled trisaccharide **16β** (2.85 g, 88%) and its α-anomer **16α** (217 mg, 9%) as both white foams.

16β: $[\alpha]_D^{28}$ = +33.1 (*c* 1.8, $CHCl_3$); mp = 112−114 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11–8.09 (m, 2H), 8.03–8.01 (m, 2H), 7.91–7.89 (m, 4H), 7.87–7.85 (m, 2H), 7.75–7.73 (m, 2H), 7.64–7.58 (m, 4H), 7.51–7.40 (m, 8H), 7.35–7.27 (m, 10H), 7.17–7.13 (m, 1H), 6.00–5.99 (m, 1H), 5.94–5.93 (m, 1H), 5.78 (dd, J = 4.5, 3.0 Hz, 1H), 5.53 (dd, J = 9.7, 3.2 Hz, 1H), 5.50–5.43 (m, 2H), 5.43 (d, J = 1.3 Hz, 1H), 5.18 (d, J = 12.2 Hz, 1H), 5.10 (dd, J = 9.4, 3.0 Hz, 1H), 5.00 (d, J = 12.2 Hz, 1H), 4.86 (d, J = 1.2 Hz, 1H), 4.43 (d, J = 4.3 Hz, 1H), 4.38 (d, J = 4.4 Hz, 1H), 4.31–4.26 (m, 2H), 4.23 (dq, J = 9.7, 6.2 Hz, 1H), 4.11 (dq, J = 9.3, 6.2 Hz, 1H), 3.52 (s, 3H), 1.42 (d, J = 6.3 Hz, 3H), 1.38 (d, J = 6.2 Hz, 3H), 0.97 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, cdcl$_3$) δ 165.4, 165.2, 165.0, 164.9, 164.8, 164.4, 138.7, 133.5, 133.4, 133.04, 133.01, 132.97, 132.8, 130.3, 130.1, 130.0, 129.9, 129.82, 129.79, 129.77, 129.76, 129.6, 128.7, 128.6, 128.37, 128.36, 128.34, 128.31, 128.2, 127.4, 101.1, 100.5, 98.8, 74.8, 74.7, 74.4, 72.6, 71.6, 71.0, 70.9, 70.3, 69.7, 69.6, 69.1, 69.0, 57.3, 18.4, 18.1, 17.8; HRMS (ESI) calcd for $C_{68}H_{64}O_{19}Na$ $[M + Na]^+$ 1207.3934, found 1207.3937.

16α: $[\alpha]_D^{28}$ = -26.3 (*c* 0.4, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.32–8.30 (m, 2H), 8.18–8.16 (m, 2H), 8.11–8.09 (m, 2H), 8.04–8.02 (m, 2H), 7.87–7.85 (m, 2H), 7.66–7.60 (m, 2H), 7.55–7.30 (m, 17H), 7.27–7.19 (m, 6H), 5.96–5.94 (m, 1H), 5.89–5.87 (m, 1H), 5.67–5.66 (m, 1H), 5.51 (dd, *J* = 10.1, 3.2 Hz, 1H), 5.37 (d, *J* = 1.4 Hz, 1H), 5.23 (dd, *J* = 9.8, 3.2 Hz, 1H), 5.18 (dd, *J* = 10.0, 3.2 Hz, 1H), 5.15–5.12 (m, 2H), 4.93 (d, *J* = 11.7 Hz, 1H), 4.83–4.79 (m, 2H), 4.37 (dd, *J* = 3.8, 1.3 Hz, 1H), 4.27–4.21 (m, 2H), 4.07 (dq, *J* = 9.6, 6.2 Hz, 1H), 4.00 (d, *J* = 3.3 Hz, 1H), 3.49 (s, 3H), 1.38 (d, *J* = 6.3 Hz, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.15 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 166.1, 165.3, 165.0, 163.8, 137.5, 133.6, 133.5, 133.2, 132.83, 132.78, 132.7, 130.7, 130.6, 130.4, 130.2, 130.0, 129.9, 129.84, 129.82, 129.79, 129.73, 129.69, 129.6, 128.8, 128.73, 128.67, 128.5, 128.4, 128.24, 128.21, 128.12, 128.06, 100.7, 100.2, 97.5, 76.7, 76.3, 73.1, 72.5, 71.34, 71.31, 71.2, 70.3, 69.29, 69.26, 68.41, 67.39, 63.3, 56.9, 18.2, 18.1; HRMS (ESI) calcd for $C_{68}H_{64}O_{19}Na$ $[M + Na]^+$ 1207.3934, found 1207.3947.

Trisaccharide 17. Compound **16β** (1.8 g, 1.5 mmol) was subjected to the general debenzylation procedure with Pd/C (10%, 4.8 g) in MeOH/AcOH (30 mL/6 mL). The purification by silica gel column chromatography (petroleum ether/EtOAc, 4:1) recovered **16β** (711 mg, 40%) and provided the desired **17** (739 mg, 45%) as a white foam: $[\alpha]_D^{28}$ = +31.2 (*c* 0.3, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.05–8.00 (m, 4H), 7.98–7.89 (m, 6H), 7.82–7.80 (m, 2H), 7.62–7.58 (m, 2H), 7.52–7.44 (m, 8H), 7.36–7.29 (m, 8H), 5.96 (dd, *J* = 4.4, 3.2 Hz, 1H), 5.93–5.90 (m, 2H), 5.55 (dd, *J* = 7.2, 3.1 Hz, 1H), 5.45–5.40 (m, 3H), 5.26 (dd, *J* = 9.5, 3.1 Hz, 1H), 4.86 (d, *J* = 1.1 Hz, 1H), 4.48–4.46 (m, 1H), 4.40 (dd, *J* = 4.5, 1.3 Hz, 1H), 4.35–4.28 (m, 2H), 4.24 (dq, *J* = 9.3, 6.3 Hz, 1H), 4.17 (dq, *J* = 9.5, 6.3 Hz, 1H), 3.50 (s, 3H), 3.18 (d, *J* = 5.6 Hz, 1H), 1.53 (d, *J* = 6.6 Hz, 3H), 1.42 (d, *J* = 6.3 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.48, 165.46, 165.2, 165.0, 164.92, 164.87, 133.52, 133.50, 133.2, 133.1, 132.9, 130.2, 130.1, 129.91, 129.89, 129.86, 129.8, 129.73, 128.69, 128.66, 128.5, 128.4, 128.3, 101.2, 100.4, 99.0, 75.1, 73.5, 72.0, 71.1, 70.5, 70.2, 70.00, 69.99, 69.8, 69.2, 68.6, 57.3, 19.1, 18.3, 18.0; HRMS (ESI) calcd for $C_{61}H_{58}O_{19}Na$ $[M + Na]^+$ 1117.3465, found 1117.3464.

Tetrasaccharides 18β and 18α. The general glycosylation procedure was used with donor **7** (291 mg, 0.45 mmol), acceptor **17** (410 mg, 0.37 mmol), and $Ph_3PAuNTf_2$ (33 mg, 0.045 mmol) in CH_2Cl_2 (20 mL) at -20 ^{o}C. The purification by silica gel column chromatography (petroleum ether/EtOAc, 5:1) afforded the coupled glycoside **18β** (472 mg, 82%) and its α-anomer **18α** (69 mg, 12%) as both white foams.

18β: $[\alpha]_D^{28}$ = +23.5 (*c* 1.8, $CHCl_3$); mp = 133−136 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06–7.99 (m, 8H), 7.87–7.85 (m, 4H), 7.78–7.75 (m, 4H), 7.67–7.58 (m, 4H), 7.51–7.41 (m, 10H), 7.33–7.22 (m, 14H), 7.10–7.07 (m, 1H), 6.15–6.14 (m, 1H), 6.02–5.99 (m, 2H), 5.73 (dd, *J* = 4.3, 3.0 Hz, 1H), 5.61–5.58 (m, 2H), 5.51 (dd, *J* = 9.9, 3.2 Hz, 1H), 5.45 (nr, 1H), 5.36 (nr, 1H), 5.24–5.20 (m, 2H), 5.14 (dd, *J* = 9.6, 3.0 Hz, 1H), 5.08 (d, *J* = 12.4 Hz, 1H), 4.88 (nr, 1H), 4.65 (d, *J* = 3.9 Hz, 1H), 4.57 (dq, *J* = 9.7, 6.2 Hz, 1H), 4.49 (d, *J* = 4.3 Hz, 1H), 4.35 (d, *J* = 3.8 Hz, 1H), 4.26 (dd, *J* = 11.1, 5.3 Hz, 2H), 4.15 (dq, *J* = 9.6, 6.2 Hz, 1H), 4.04 (dq, *J* = 9.5, 6.3 Hz, 1H), 3.54 (s, 3H), 1.40 (d, *J* = 6.2 Hz, 6H), 1.06 (d, *J* = 6.2 Hz, 3H), 0.72 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.38, 165.37, 165.02, 164.97, 164.9, 164.8, 164.7, 164.3, 138.8, 133.6, 133.3, 133.1, 132.9, 132.84, 132.81, 132.7, 130.34, 130.25, 130.2, 130.1, 130.0, 129.94, 129.87, 129.82, 129.80, 129.77, 129.7, 129.6, 128.7, 128.6, 128.4, 128.33, 128.29, 128.26, 128.2, 127.3, 101.6, 100.4, 99.4, 99.0, 75.5, 75.0, 74.3, 73.4, 73.2, 71.9, 71.4, 71.2, 71.1, 71.0, 70.7, 70.3, 69.7, 69.01, 68.97, 68.8,

68.7, 57.3, 18.3, 18.1, 18.0, 17.4; HRMS (ESI) calcd for $C_{88}H_{82}O_{25}Na$ $[M + Na]^+$ 1561.5037, found 1561.5033.

18α: $[\alpha]_D^{28}$ = +0.4 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.33–8.30 (m, 2H), 8.23 (dd, *J* = 8.2, 1.4 Hz, 2H), 8.13–8.11 (m, 2H), 7.93–7.91 (m, 2H), 7.89–7.87 (m, 2H), 7.84–7.82 (m, 2H), 7.79–7.77 (m, 2H), 7.68–7.61 (m, 1H), 7.57–7.49 (m, 7H), 7.51–7.41 (m, 5H), 7.44–7.34 (m, 4H), 7.35–7.20 (m, 13H), 7.16–7.10 (m, 1H), 6.00–5.99 (m, 1H), 5.96–5.95 (m, 1H), 5.85–5.84 (m, 1H), 5.78 (dd, *J* = 5.3, 3.0 Hz, 1H), 5.50 (dd, *J* = 10.2, 3.1 Hz, 1H), 5.43 (d, *J* = 1.1 Hz, 1H), 5.38 (d, *J* = 1.4 Hz, 1H), 5.30 (dd, *J* = 9.9, 3.2 Hz, 1H), 5.24 (dd, *J* = 10.1, 3.0 Hz, 1H), 5.18–5.12 (m, 3H), 4.93 (d, *J* = 11.7 Hz, 1H), 4.88 (d, *J* = 1.4 Hz, 1H), 4.82 (d, *J* = 11.7 Hz, 1H), 4.60 (d, *J* = 3.8 Hz, 1H), 4.49 (dd, *J* = 5.3, 1.4 Hz, 1H), 4.33 (d, *J* = 4.0 Hz, 1H), 4.28 (dq, *J* = 9.9, 6.2 Hz, 1H), 4.12 (dq, *J* = 8.4, 6.4 Hz, 1H), 4.05 (dq, *J* = 9.6, 5.9 Hz, 1H), 4.00 (d, *J* = 3.3 Hz, 1H), 3.53 (s, 3H), 1.40 (d, *J* = 6.2 Hz, 3H), 1.33 (d, *J* = 6.2 Hz, 3H), 1.15 (d, *J* = 6.2 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.24, 166.22, 165.3, 165.0, 164.9, 164.7, 164.6, 163.4, 137.7, 133.5, 133.4, 133.0, 132.9, 132.8, 132.7, 132.6, 130.73, 130.69, 130.66, 130.3, 130.23, 130.19, 129.9, 129.84, 129.76, 129.72, 129.70, 129.62, 129.57, 128.70, 128.66, 128.6, 128.40, 128.38, 128.30, 128.26, 128.10, 128.07, 127.9, 101.6, 100.7, 97.4, 97.3, 72.9, 72.5, 71.7, 71.53, 71.45, 71.43, 71.41, 70.8, 70.1, 69.72, 69.67, 69.6, 68.9, 67.9, 67.4, 67.3, 63.2, 57.1, 18.26, 18.25, 18.2, 18.0; HRMS (ESI) calcd for $C_{88}H_{82}O_{25}Na$ $[M + Na]^+$ 1561.5037, found 1561.5045.

Tetrasaccharide 19. Tetrasaccharide **18β** (380 mg, 0.25 mmol) was subjected to the general debenzylation procedure with Pd/C (10%, 788 mg) in MeOH/AcOH (30 mL/15 mL). The purification by silica gel column chromatography (petroleum ether/EtOAc, 4:1) recovered **18β** (152 mg, 39%) and provided the desired **19** (185 mg,

52%) as a white foam: $[\alpha]_D^{28}$ = +28.8 (*c* 3.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–8.03 (m, 2H), 8.01–7.99 (m, 4H), 7.97–7.96 (m, 2H), 7.94–7.92 (m, 2H), 7.89–7.87 (m, 2H), 7.84–7.82 (m, 2H), 7.78–7.77 (m, 2H), 7.63–7.58 (m, 2H), 7.49–7.45 (m, 9H), 7.36–7.21 (m, 13H), 6.17–6.16 (m, 1H), 6.01 (dd, *J* = 5.9, 3.2 Hz, 1H), 5.96–5.92 (m, 2H), 5.65 (d, *J* = 2.1 Hz, 1H), 5.60 (dd, *J* = 7.4, 3.2 Hz, 1H), 5.51–5.43 (m, 3H), 5.33 (dd, *J* = 9.7, 3.1 Hz, 1H), 5.16 (dd, *J* = 9.7, 3.0 Hz, 1H), 4.89 (nr, 1H), 4.72 (d, *J* = 3.9 Hz, 1H), 4.58–4.56 (m, 1H), 4.54–4.50 (m, 1H), 4.47 (d, *J* = 4.4 Hz, 1H), 4.36 (d, *J* = 4.2 Hz, 1H), 4.33–4.29 (m, 1H), 4.16 (dq, *J* = 9.6, 6.2 Hz, 2H), 3.53 (s, 3H), 3.28 (d, *J* = 5.2 Hz, 1H), 1.54 (d, *J* = 6.6 Hz, 3H), 1.44 (d, *J* = 6.2 Hz, 3H), 1.06 (dd, *J* = 6.3, 2.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 165.4, 165.2, 165.0, 164.82, 164.79, 164.75, 133.5, 133.4, 133.04, 133.00, 132.94, 132.91, 132.90, 132.7, 130.2, 130.09, 130.07, 130.0, 129.89, 129.85, 129.82, 129.78, 129.76, 129.74, 129.71, 129.68, 129.5, 128.7, 128.6, 128.4, 128.30, 128.27, 128.23, 128.17, 101.5, 100.5, 99.8, 98.7, 75.6, 74.5, 72.9, 72.1, 71.3, 71.2, 71.0, 70.5, 70.23, 70.15, 70.03, 69.97, 69.2, 69.0, 68.82, 68.79, 57.3, 19.0, 18.0, 17.9, 17.8; HRMS (ESI) calcd for $C_{81}H_{76}O_{25}Na$ $[M + Na]^+$ 1471.4568, found 1471.4584.

Pentasaccharides 20β and 20α. The general glycosylation procedure was used with donor **7** (46 mg, 0.070 mmol), acceptor **19** (85 mg, 0.059 mmol), and $Ph_3PAuNTf_2$ (5.2 mg, 0.007 mmol) in CH_2Cl_2 (3 mL) at -20 °C. The purification by silica gel column chromatography (petroleum ether/EtOAc, 5:1) afforded the coupled glycoside **20β** (73 mg, 65%) and its α-anomer **20α** (29 mg, 26%) as both white foams.

20β: $[\alpha]_D^{28}$ = +26.9 (*c* 0.6, $CHCl_3$); mp = 137−141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08–8.00 (m, 8H), 7.96–7.95 (m, 2H), 7.86–7.80 (m, 6H), 7.76–7.69 (m, 6H), 7.64–7.60 (m, 2H), 7.50–7.47 (m, 4H), 7.46–7.40 (m, 5H), 7.35–7.19 (m, 21H), 7.09–7.06 (m, 1H), 6.17–6.16 (m, 1H), 6.03–6.02 (m, 1H), 5.98–5.97 (m, 2H),

5.93–5.91 (m, 1H), 5.65 (nr, 1H), 5.59–5.55 (m, 2H), 5.51 (dd, *J* = 10.0, 3.2 Hz, 1H), 5.41 (nr, 1H), 5.35 (nr, 1H), 5.31–5.27 (m, 2H), 5.20–5.13 (m, 3H), 4.89 (nr, 1H), 4.69–4.61 (m, 2H), 4.59 (d, *J* = 3.8 Hz, 1H), 4.55–4.50 (m, 1H), 4.41 (d, *J* = 4.1 Hz, 2H), 4.34 (d, *J* = 4.3 Hz, 1H), 4.18–4.10 (m, 2H), 4.09–4.02 (m, 1H), 3.53 (s, 3H), 1.39 (d, *J* = 6.2 Hz, 3H), 1.31 (d, *J* = 6.1 Hz, 3H), 1.05 (d, *J* = 6.2 Hz, 3H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.63 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.43, 165.40, 165.3, 165.0, 164.92, 164.86, 164.80, 164.75, 164.7, 164.3, 138.9, 134.0, 133.8, 133.6, 133.4, 133.1, 133.0, 132.81, 132.75, 132.7, 132.3, 132.2, 130.5, 130.3, 130.20, 130.16, 130.09, 130.06, 130.0, 129.92, 129.86, 129.85, 129.84, 129.81, 129.77, 129.71, 129.69, 129.6, 129.2, 128.8, 128.68, 128.65, 128.6, 128.52, 128.51, 128.47, 128.4, 128.31, 128.26, 128.2, 128.1, 127.3, 102.0, 100.4, 100.1, 99.5, 98.7, 76.3, 75.3, 74.4, 74.1, 73.2, 72.0, 71.6, 71.5, 71.3, 71.2, 71.0, 70.8, 70.4, 69.8, 68.77, 68.76, 68.7, 68.6, 68.3, 57.4, 18.2, 18.04, 17.97, 17.9, 17.3; HRMS (ESI) calcd for $C_{108}H_{100}O_{31}Na$ $[M + Na]^+$ 1916.6174, found 1916.6171.

20α: $[\alpha]_D^{28}$ = +8.8 (*c* 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37–8.35 (m, 2H), 8.27–8.25 (m, 2H), 8.04–7.98 (m, 8H), 7.87–7.85 (m, 2H), 7.80–7.78 (m, 4H), 7.65–7.62 (m, 1H), 7.56–7.54 (m, 3H), 7.51–7.39 (m, 14H), 7.34–7.16 (m, 19H), 6.14–6.13 (m, 1H), 6.03–6.00 (m, 2H), 5.98–5.96 (m, 1H), 5.79 (dd, *J* = 4.3, 3.0 Hz, 1H), 5.61 (d, *J* = 1.4 Hz, 1H), 5.51 (dd, *J* = 10.2, 3.1 Hz, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.38–5.35 (m, 2H), 5.32–5.29 (m, 2H), 5.26–5.16 (m, 3H), 4.94 (d, *J* = 11.6 Hz, 1H), 4.88–4.84 (m, 2H), 4.76 (d, *J* = 3.8 Hz, 1H), 4.65 (d, *J* = 3.8 Hz, 1H), 4.64–4.58 (m, 1H), 4.53 (d, *J* = 4.4 Hz, 1H), 4.28 (d, *J* = 4.2 Hz, 1H), 4.17–4.10 (m, 2H), 4.08–4.04 (m, 2H), 3.51 (s, 3H), 1.44 (d, *J* = 6.2 Hz, 3H), 1.35 (d, *J* = 6.1 Hz, 3H), 1.18 (d, *J* = 6.2 Hz, 3H), 1.02 (d, *J* = 6.2 Hz, 3H), 0.80 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 166.3, 165.39, 165.36, 165.2, 164.88, 164.85, 164.50, 164.49, 163.4,

137.8, 133.6, 133.2, 133.1, 133.0, 132.84, 132.79, 132.6, 130.70, 130.65, 130.5, 130.3, 130.1, 130.02, 129.95, 129.89, 129.88, 129.83, 129.81, 129.77, 129.72, 129.69, 129.6, 128.7, 128.6, 128.5, 128.4, 128.32, 128.29, 128.27, 128.22, 128.18, 128.1, 128.0, 127.8, 101.8, 100.5, 99.4, 98.9, 97.3, 73.6, 73.0, 72.8, 72.7, 71.9, 71.6, 71.4, 70.9, 70.8, 70.5, 70.2, 69.3, 69.1, 68.82, 68.78, 68.76, 68.1, 67.4, 63.1, 57.3, 18.19, 18.18, 18.1, 18.0, 17.7; HRMS (ESI) calcd for $C_{108}H_{100}O_{31}Na$ $[M + Na]^+$ 1916.6174, found 1916.6170.

Methyl 6-Deoxy-β-L-altropyranoside (1). Compound **6** (50 mg, 0.13 mmol) was subjected to the general saponification procedure with MeONa (1.4 mg, 0.026 mmol) in MeOH (5.0 mL). The purification by silica gel column chromatography (CH_2Cl_2/MeOH, 20:1) provided monosaccharide **1** (21 mg, 92%) as a white solid: $[\alpha]_D^{26}$ = +43.4 (*c* 0.2, MeOH); mp = 140−143 °C; ^1H and ^{13}C NMR data: see Table 3; HRMS (ESI) calcd for $C_7H_{14}O_5Na$ $[M + Na]^+$ 201.0733, found 201.0732.

Methyl 6-Deoxy-2-*O*-(6-deoxy-β-L-altropyranosyl)-β-L-altropyranoside (2). Compound **15** (63 mg, 0.085 mmol) was subjected to the general saponification procedure with MeONa (1.0 mg, 0.021 mmol) in MeOH (4.0 mL). The purification by silica gel column chromatography (CH_2Cl_2/MeOH, 10:1) provided disaccharide **2** (27 mg, 99%) as a white solid: $[\alpha]_D^{26}$ = +62.7 (*c* 0.9, MeOH); mp = 177−181 °C; ^1H and ^{13}C NMR data: see Table 3; HRMS (ESI) calcd for $C_{13}H_{24}O_9Na$ $[M + Na]^+$ 347.1313, found 347.1302.

Trisaccharide 3. Compound **17** (22 mg, 0.020 mmol) was subjected to the general saponification procedure with MeONa (1.1 mg, 0.021 mmol) in MeOH (5.0 mL). The purification by silica gel column chromatography (CH_2Cl_2/MeOH, 10:1) provided trisaccharide **3** (7.6 mg, 81%) as a white solid: $[\alpha]_D^{26}$ = +58.8 (*c* 4.6, MeOH); mp = 209−212 °C; ^1H and ^{13}C NMR data: see Table 3; HRMS (ESI) calcd for $C_{19}H_{34}O_{13}Na$

$[M + Na]^+$ 493.1892, found 493.1897.

Tetrasaccharide 4. Compound **19** (40 mg, 0.028 mmol) was subjected to the general saponification procedure with MeONa (1.5 mg, 0.028 mmol) in MeOH (5.0 mL). The purification by silica gel column chromatography (CH_2Cl_2/MeOH, 5:1) provided tetrasaccharide **4** (14.7 mg, 85%) as a white solid: $[\alpha]_D^{26}$ = +64.5 (*c* 3.6, MeOH); mp = 220−225 °C; ^1H and ^{13}C NMR data: see Table 3; HRMS (ESI) calcd for $C_{25}H_{44}O_{17}Na$ $[M + Na]^+$ 639.2471, found 639.2474.

Pentasaccharide 5. Compound **20β** (149 mg, 0.079 mmol) was subjected to the general saponification procedure with MeONa (4.2 mg, 0.079 mmol) in MeOH (2.0 mL). The filtration through a pad of silica gel (CH_2Cl_2/MeOH) and subsequent concentration gave a residue which was employed in the next step without further purification.

The residue above was subjected to the general debenzylation procedure with Pd/C (10%, 156 mg) in MeOH (10 mL). The purification by silica gel column chromatography (CH_2Cl_2/MeOH, 5:1) provided pentasaccharide **5** (51.3 mg, 86% over 2 steps) as a white solid: $[\alpha]_D^{26}$ = +67.9 (*c* 1.2, MeOH); ^1H and ^{13}C NMR data: see Table 3; HRMS (ESI) calcd for $C_{31}H_{54}O_{21}Na$ $[M + Na]^+$ 785.3050, found 785.3043.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (21611130029, 21432012, and 21621002), the Strategic Priority Research Program of the Chinese Academy of Sciences (XDB20020000), the Joint China-Sweden Mobility Programme funded by the Swedish Foundation for International Cooperation in

Research and Higher Education, the Swedish Academic Collaboration Forum, the Knut and Alice Wallenberg Foundation and the Swedish Research Council (grant no. 2013-4859).

Supporting Information

^{1}H and ^{13}C NMR spectra of new compounds (PDF)

References

(1) (a) Cover, T. L.; Aber, R. C. *N. Engl. J. Med.* **1989**, *321*, 16-24. (b) Muszyński, A.; Rabsztyn, K.; Knapska, K.; Duda, K. A.; Duda-Grychtol, K.; Kasperkiewicz, K.; Radziejewska-Lebrecht, J.; Holst, O.; Skurnik, M. *Microbiology* **2013**, *159*, 1782-1793.

(2) (a) Bottone, E. J. *Clin. Microbiol. Rev.* **1997**, *10*, 257-276. (b) Wren, B. W. *Nat. Rev. Microbiol.* **2003**, *1*, 55-64.

(3) (a) Al-Hendy, A.; Toivanen, P.; Skurnik, M. *Microb. Pathog.* **1991**, *10*, 81-86. (b) Goverde, R. L. J.; Huis in't Veld, J. H. J.; Kusters, J. G.; Mooi, F. R. *Mol. Microbiol.* **1998**, *28*, 555-569.

(4) (a) Raetz, C. R. H. *Annu. Rev. Biochem.* **1990**, *59*, 129-170. (b) Caroff, M.; Karibian, D. *Carbohydr. Res.* **2003**, *338*, 2431-2447.

(5) (a) Ellwood, D. C.; Kirk, G. R. A. *Proc. Biochem. Soc.* **1971**, *122*, 14p. (b) Beer, W.; Seltmann, G. *Z. Allg. Mikrobiol.* **1973**, *13*, 167-169.

(6) (a) Hoffman, J.; Lindberg, B.; Brubaker, R. R. *Carbohydr. Res.* **1980**, *78*, 212-214. (b) Gorshkova, R. P.; Kalmykova, E. N.; Isakov, V. V.; Ovodov, Y. S. *Eur. J. Biochem.*

1985, *150*, 527-531. (c) Ovodov, Y. S.; Gorshkova, R. P.; Tomshich, S. V.; Komandrova, N. A.; Zubkov, V. A.; Kalmykova, E. N.; Isakov, V. V. *J. Carbohydr. Chem.* **1992**, *11*, 21-35. (d) Bruneteau, M.; Minka, S. *Biochimie* **2003**, *85*, 145-152.

(7) (a) Paulsen, H. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 155-173. (b) Crich, D.; Hutton, T. K.; Banerjee, A.; Jayalath, P.; Picione, J. *Tetrahedron: Asymmetry* **2005**, *16*, 105-119. (c) El Ashry, E. S. H.; Rashed, N.; Ibrahim, E. S. I. *Tetrahedron* **2008**, *64*, 10631-10648. (d) Nigudkar, S. S.; Demchenko, A. V. *Chem. Sci.* **2015**, *6*, 2687-2704.

(8) (a) Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 4506-4507. (b) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217-11223. (c) Crich, D. *Acc. Chem. Res.* **2010**, *43*, 1144-1153.

(9) (a) Jensen, H. H.; Nordstrøm, L. U.; Bols, M. *J. Am. Chem. Soc.* **2004**, *126*, 9205-9213. (b) Aubry, S.; Sasaki, K.; Sharma, I.; Crich, D. *Top. Curr. Chem.* **2011**, *301*, 141-188. (c) Frihed, T. G.; Walvoort, M. T. C.; Codée, J. D. C.; van der Marel, G. A.; Bols, M.; Pedersen, C. M. *J. Org. Chem.* **2013**, *78*, 2191-2205. (d) Heuckendorff, M.; Bendix, J.; Pedersen, C. M.; Bols, M. *Org. Lett.* **2014**, *16*, 1116-1119.

(10) (a) Iversen, T.; Bundle, D. R. *Carbohydr. Res.* **1980**, *84*, c13-c15. (b) Backinowsky, L. V.; Balan, N. F.; Shashkov, A. S.; Kochetkov, N. K. *Carbohydr. Res.* **1980**, *84*, 225-235. (c) Srivastava, V. K.; Schuerch, C. *J. Org. Chem.* **1981**, *46*, 1121-1126. (d) Lichtenthaler, F. W.; Metz, T. W. *Tetrahedron Lett.* **1997**, *38*, 5477-5480. (e) Hodosi, G.; Kováč, P. *J. Am. Chem. Soc.* **1997**, *119*, 2335-2336. (f) Ikeda, T.; Yamada, H. *Carbohydr. Res.* **2000**, *329*, 889-893. (g) Crich, D.; Vinod, A. U.; Picione, J. *J. Org. Chem.* **2003**, *68*, 8453-8458. (h) Crich, D.; Picione, J. *Org. Lett.*

2003, *5*, 781-784. (i) Lee, Y. J.; Ishiwata, A.; Ito, Y. *J. Am. Chem. Soc.* **2008**, *130*, 6330-6331. (j) Christina, A. E.; van der Es, D.; Dinkelaar, J.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. *Chem. Commun.* **2012**, *48*, 2686-2688. (k) Heuckendorff, M.; Pedersen, C. M.; Bols, M. *J. Org. Chem.* **2012**, *77*, 5559-5568. (l) Elferink, H.; Pedersen, C. M. *Eur. J. Org. Chem.* **2017**, 53-59.

(11) (a) Zhu, Y.; Yu, B. *Chem. Eur. J.* **2015**, *21*, 8771-8780. (b) Zhu, Y.; Shen, Z.; Li, W.; Yu, B. *Org. Biomol. Chem.* **2016**, *14*, 1536-1539.

(12) (a) Li, Y.; Yang, Y.; Yu, B. *Tetrahedron Lett.* **2008**, *49*, 3604-3608. (b) Li, Y.; Yang, X.; Liu, Y.; Zhu, C.; Yang, Y.; Yu, B. *Chem. Eur. J.* **2010**, *16*, 1871-1882. (c) Zhu, Y.; Yu, B. *Angew. Chem. Int. Ed.* **2011**, *50*, 8329-8332. (d) Tang, Y.; Li, J.; Zhu, Y.; Li, Y.; Yu, B. *J. Am. Chem. Soc.* **2013**, *135*, 18396-18405.

(13) (a) Komarova, B. S.; Tsvetkov, Y. E.; Nifantiev, N. E. *Chem. Rec.* **2016**, *16*, 488-506 and references cited therein. (b) Baek, J. Y.; Lee, B.-Y.; Jo, M. G.; Kim, K. S. *J. Am. Chem. Soc.* **2009**, *131*, 17705-17713. (c) Demchenko, A. V.; Rousson, E.; Boons, G.-J. *Tetrahedron Lett.* **1999**, *40*, 6523-6526. (d) De Meo, C.; Kamat, M. N.; Demchenko, A. V. *Eur. J. Org. Chem.* **2005**, *2005*, 706-711. (e) Crich, D.; Sharma, I. *J. Org. Chem.* **2010**, *75*, 8383-8391. (f) Ma, Y.; Lian, G.; Li, Y.; Yu, B. *Chem. Commun.* **2011**, *47*, 7515-7517. (g) Kalikanda, J.; Li, Z. *J. Org. Chem.* **2011**, *76*, 5207-5218.

(14) (a) Yang, X.; Yu, B. *Chem. Eur. J.* **2013**, *19*, 8431-8434. (b) Ramesh, S.; Franck, R. W. *Tetrahedron: Asymmetry* **1990**, *1*, 137-140. (c) Han, O.; Liu, H.-w. *Tetrahedron Lett.* **1987**, *28*, 1073-1076. (d) Wang, H.-Y. L.; O'Doherty, G. A. *Chem. Commun.* **2011**, *47*, 10251-10253. (e) Frihed, T. G.; Pedersen, C. M.; Bols, M. *Eur. J. Org. Chem.*

2014, *2014*, 7924-7939. (f) Shan, M.; Xing, Y.; O'Doherty, G. A. *J. Org. Chem.* **2009**, *74*, 5961-5966. (g) Sanapala, S. R.; Kulkarni, S. S. *Org. Lett.* **2016**, *18*, 3790-3793.

(15) Shi, Y.-H.; Xie, Y.-F.; Liu, Y.-Q.; Wei, Q.-C.; Xu, W.-R.; Tang, L.-D.; Zhao, G.-L. *Chin. Chem. Lett.* **2014**, *25*, 561-566.

(16) (a) Haines, A. R. *Tetrahedron Lett.* **1969**, *10*, 1201-1202. (b) Haines, A. H.; Symes, K. C. *J. Chem. Soc. C.* **1971**, 2331. (c) Haines, A. H. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 11-109. (d) Schmidt, R. R. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 212-235 and references cited therein. (e) Box, V. G. S. *Heterocycles* **1990**, *31*, 1157-1181.

(17) Widmalm, G. In *Comprehensive glycoscience*; Kamerling, J. P., Ed.; Elsevier: Oxford, 2007; Vol. 2, pp 101-132.

(18) Bock, K.; Pedersen, C. *Acta Chem. Scand.* **1975**, *29B*, 258-264.

(19) Kapaev, R. R.; Toukach, P. V. *J. Chem. Inf. Model.* **2016**, *56*, 1100-1104.

(20) (a) Jansson, P.-E.; Kenne, L.; Widmalm, G. *J. Chem. Inf. Comput. Sci.* **1991**, *31*, 508-516. (b) Lundborg, M.; Widmalm, G. *Anal. Chem.* **2011**, *83*, 1514-1517.

(21) Söderman, P.; Jansson, P.-E.; Widmalm, G. *J. Chem. Soc., Perkin Trans. 2* **1998**, 639-648.

(22) (a) Adeyeye, A.; Jansson, P.-E.; Kenne, L.; Widmalm, G. *J. Chem. Soc., Perkin Trans. 2* **1991**, 963-973. (b) Yang, M.; Angles d'Ortoli, T.; Säwén, E.; Jana, M.; Widmalm, G.; MacKerell, A. D., Jr. *Phys. Chem. Chem. Phys.* **2016**, *18*, 18776-18794.

(23) Kuttel, M. M.; Ståhle, J.; Widmalm, G. *J. Comput. Chem.* **2016**, *37*, 2098-2105.

(24) Ekholm, F. S.; Sinkkonen, J.; Leino, R. *New J. Chem.* **2010**, *34*, 667-675.

(25) Crich, D.; Li, H.; Yao, Q.; Wink, D. J.; Sommer, R. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2001**, *123*, 5826-5828.

(26) Nitz, M.; Ling, C.-C.; Otter, A.; Cutler, J. E.; Bundle, D. R. *J. Biol. Chem.* **2002**, *277*, 3440-3446.

(27) Johnson, M. A.; Cartmell, J.; Weisser, N. E.; Woods, R. J.; Bundle, D. R. *J. Biol. Chem.* **2012**, *287*, 18078-18090.

(28) Dixon, A. M.; Venable, R.; Widmalm, G.; Bull, T. E.; Pastor, R. W. *Biopolymers* **2003**, *69*, 448-460.

(29) Pauli, G. F.; Chen, S.-N.; Lankin, D. C.; Bisson, J.; Case, R. J.; Chadwick, L. R.; Gödecke, T.; Inui, T.; Krunic, A.; Jaki, B. U.; McAlpine, J. B.; Mo, S.; Napolitano, J. G.; Orjala, J.; Lehtivarjo, J.; Korhonen, S.-P.; Niemitz, M. *J. Nat. Prod.* **2014**, *77*, 1473-1487.