Automated Electrochemical Assembly of β-glucans and its applications to synthesis of cyclic oligosaccharides

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Declaration

I, Manmode Sujit Rajendra, declare that the thesis is an original report of my research, has been written by me and has been not submitted to any other degree. I confirm that the work submitted is my own, except where work which has formed part of jointly-authored publications have been included; the collaborative contributions have been indicated clearly and acknowledge. Due references have been provided on all supporting literatures and resources; moreover, I confirm that appropriate credit has been given within this thesis where reference has been made to the work of others.

I dually admit that, the work in this dissertation is performed in between October 2016 to January 2019 in the department of chemistry and biotechnology, graduate school of engineering, Tottori university under the supervision of Prof. Toshiyuki Itoh.

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List of Publications

1. Rational Optimization of the Mannoside Building Block for Automated Electrochemical Assembly of the Core Trisaccharide of GPI Anchor Oligosaccharides.
   S. Manmode, T. Sato, N. Sasaki, I. Notsu, S. Hayase, T. Nokami, T. Itoh,
   Carbohydr. Res., **2017**, *450*, 44-48.

2. Electrochemical Methods as Enabling Tools for Glycosylation.
   S. Manmode, Prof. K. Matsumoto, Prof. T. Nokami, Prof. T. Itoh,
   Asian J. Org. Chem. **2018**, *7*, 1719-1729.

3. Automated electrochemical assembly for the β-(1,3)-(1,6)-Glucan Hexasaccharide Using Thioglucoside Building Blocks.
   S. Manmode, M. Kato, T. Ichiyanagi, T. Nokami, T. Itoh,
   Asian J. Org. Chem. **2018**, *7*, 1802-1805.

4. Electrochemical Glycosylation as an Enabling Tool for the Synthesis of Cyclic β-1,6-Oligosaccharides.
   S. Manmode, S. Tanabe, T. Yamamoto, N. Sasaki, T. Nokami, T. Itoh,
   Manuscript in preparation.

Acronyms and Abbreviations

[α]: specific rotation expressed without units

Ac: acetyl

AEA: Automated Electrochemical Assembly

Ar: aryl

Bn: benzyl

Bu: butyl

br: broad (in NMR)

Bz: benzoyl

°C: degrees Celsius

ClAc: chloroaccetyl

CSA: camphorsulfonic acid

COSY: correlation spectroscopy

δ: chemical shift in parts per million downfield from tetramethylsilane

d: doublet (in NMR)

DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene

DCE: 1,2-dichloroethane

DCM: dichloromethane

DIC: *N*,*N*′-diisopropylcarbodiimide

DMAP: 4,4′-dimethylaminopyridine

DMF: dimethylformamide

DMSO: dimethyl sulphoxide

Et: ethyl

EtOAc: ethyl acetate

Fmoc: 9-fluorenylmethyloxycarbonyl

g: gram(s)

GPC: gel permeation chromatography

h: hour(s)

Hex: hexane

HMQC: Heteronuclear single quantum coherence spectroscopy

HRMS: high resolution mass spectrometry

Hz: hertz

J: coupling constant (in NMR)

Lev: levulinoyl

LevOH: levulinic acid

m: multiplet (in NMR)

Me: methyl

mol: mole(s)

MOM: methoxymethyl

MS: mass spectrometry

NIS: *N*-iodosuccinimide

NMR: nuclear magnetic resonance

PBB: 4-bromobenzyl

Ph: phenyl

PhthN: phthalimide

Piv: pivaloyl

py: pyridine

q: quartet (in NMR)

R_f: retention factor (in thin layer chromatography)

rt: room temperature

s: singlet (in NMR), second(s)

t: triplet (in NMR)

TBS: *tert*-butyldimethylsilyl

Tf: (trifluoromethyl)sulphonyl (triflyl)

TFA: trifluoroacetic acid

TfOH: triflic acid

THF: tetrahydrofuran

TLC: thin layer chromatography

TMSOTf: trimethylsilyl triflate

Tr: triphenylmethyl (trityl)

General Introduction

1. History of Cyclodextrin

It's been more than 120 years ago, when the first cyclic oligosaccharide, the so called cyclodextrins (CDs) was isolated by Villers[1] from a culture medium of *Bacillus amylobacter*. However, due to limited availability of technology, it took almost sixty years of devotion from profound scientists, to come at a fruitful product, in the form of structure elucidation, purification protocols and more significantly properties like formation of inclusion complex.[2]

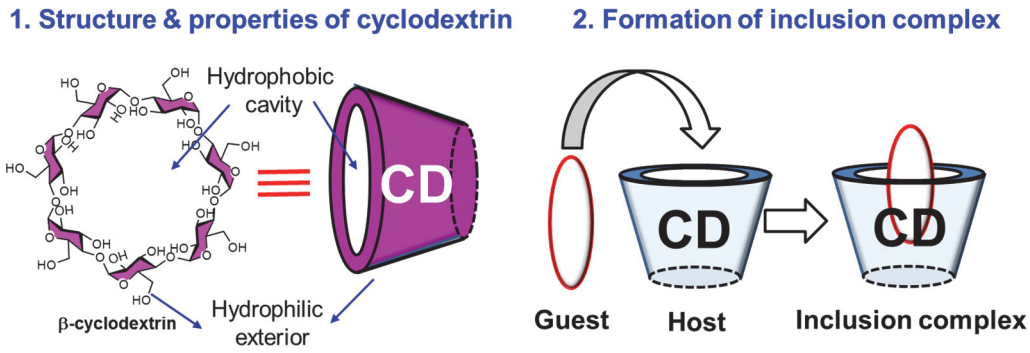
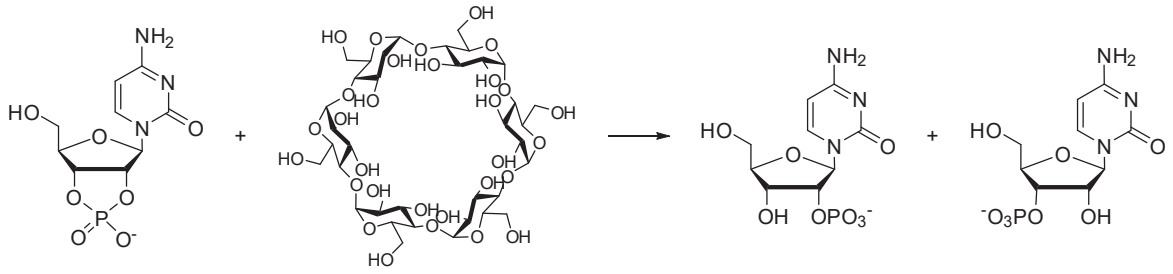


Figure 1. Structure, property and inclusion complex of cyclodextrin

Furthermore, highly innovative studies from Cramer[3] describe the application of CDs in supramolecular and/or host-guest chemistry. His continuous interest in the CDs, uncovered the characteristic properties such as; ability to induce chiral induction forming host-guest complex and catalysing the organic transformation to the effectiveness.

Table 1. Selectivity and rate constants for the cleavage of 2′,3′-cyclic monophosphate of cytidine in presence and absence of α-CD.



2',3'-cyclic monophosphates of cytidine + **α-cyclodextrin** → **(I) 2'-monophosphates of cytidine** + **(II) 3'-monophosphates of cytidine**

CDs	Conc. 10^{-2} M	Rate Constant 10^{-4} min^{-1}	Selectivity[b] %
α-CD	5.0	7.0	98
none		1.7	47

[a]at pH = 11.08, 20 °C, [b][II/(I+II)]

This enzyme mimicking property was then captured by Breslow[4], Komiyama[5] and others[6] to elaborate its utility in cyclic phosphate hydrolysis and non-covalent regioselective electrophilic aromatic substitution reactions. This finding opens new era of CDs as an artificial enzyme.

Till the mid 1980's all work performed with CDs is using the naturally available cyclodextrin, it was Ogawa and co-workers[7] who came up with the first chemical synthesis of "*manno- isomer"* of cyclodextrin; this first ever challenging chemical synthesis open up new class of torus-shaped cyclic oligosaccharides having a repeating unit other than glucose. Towards the end of 20th century, due to the advancement in the modern technique and emergence of new CD analogs[8] gain the phenomenal importance in the pharmaceuticals[9a], agrochemicals[9b], food[9c], cosmetics[9d] and glue industries[9e]; making considerable impact on daily life.

2. Synthetic cyclic oligosaccharides

Chemical synthesis of cyclic oligosaccharides unavoidably goes through the final cycloglycosylation event which possess quite different challenges from that of traditional oligosaccharide synthesis. Sugar hydroxyl group and appropriate leaving group at anomeric position are the desperate requirement of the precursor to undergo efficient cycloglycosylation. Chemical synthesis of cyclic oligosaccharides is broadly categorised into two categories as follows:

1. Intramolecular glycosylation of long chain linear precursor[10]

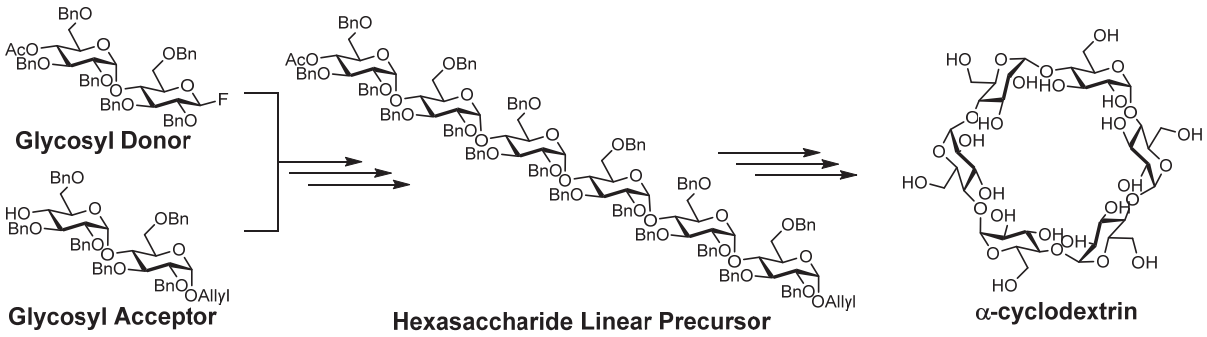


Figure 2. Synthesis of α-cyclodextrin using cycloglycosylation of linear precursor

In this approach appropriately protected maltose glycosyl donor was treated with another unit of maltose acceptor to form tetrasaccharide, the subsequent glycosylation of tetrasaccharide with another disaccharide furnish necessary hexasaccharide precursor for cyclization. This requires multistep procedure of protecting group manipulation and intramolecular glycosylation to form α-cyclodextrin. Efficiency of intramolecular glycosylation depended on the corresponding ring size and anmeric leaving group as well as promoter system. Irrespective of laborious stepwise elongation of linear precursor beauty of this protocol lies in the incorporation of varied sugar moiety in the cyclic oligosaccharide, hence this approach considered tobe overwhelming success of chemically synthesize cyclic oligosaccharides for the first time.

2. Intramolecular glycosylation (cyclic oligomarization) of functionalized disaccharide[11]

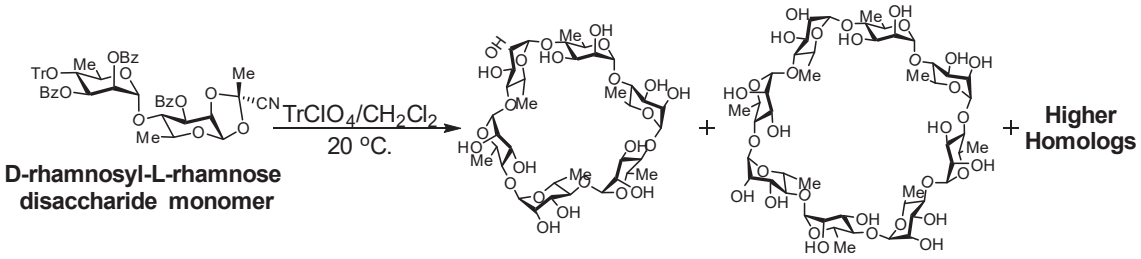
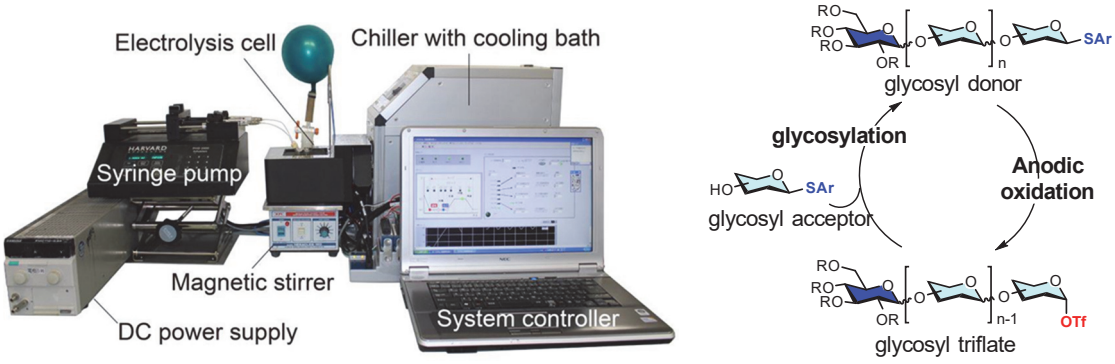


Figure 3. Synthesis of cyclic oligosaccharides using cyclic oligomerisation

In above mentioned approach, synthetically less laborious disaccharide was utilised in cyclic oligomerisation following traditional glycosylation procedures. Sufficiently reactive disaccharide enables production of series of cyclic oligosaccharides in acceptable yields. Hence this feature is considered as one of the advantages of this method over the other. However, both the methodologies are widely explored in the literature and are associated with their own merits and demerits.

3. Automated Electrochemical Assembly

Automated solution-phase electrochemical synthesizer[12a] is a state-of-art-way; dealing with time bound, cost effective, electrochemistry based instrument, design to address problem associated with oligosaccharide synthesis in significant amount. However, throughout the last two decade's variety of instruments have been developed to synthesized glycoconjugates purely for analytical purpose, such as "the first fully automated solid-phase oligosaccharide synthesizer" by Seeberger[12b] and HPLC-assisted automated electrochemical synthesizer by Denchenko[12c] and others.[12d]



Automated Electrochemical Synthesizer Principle of the Method

Figure 4. Automated electrochemical synthesizer and its principle

The highlights of automated electrochemical synthesizer are that works in solution phase, enabling relatively large-scale production of oligosaccharide. Besides that, it is a donor elongation method, which means it reduces the more common deprotection sequences predominantly used in solid-phase synthesizers to avail the acceptor for next consecutive glycosylation improving overall yield of the reaction. Hence, in recent years, this economically cost effective, user friendly, hazardous activator free and reliable instrument receiving the popularity and appreciation in the carbohydrate world.

4. Abstract of this thesis

Chapter 1

Continuing interest in the development of general methodology for synthesis of wide variety of oligosaccharides by electrochemical means, reveals that α-glycosyl triflate of 2-azido-2-deoxy thioglucosides can be generated and stabilised at -80 °C, allowing β-selective glycosylation with an acceptor, following S_N2 pathway, however similar approach with mannose derivatives found to be unsuccessful. Hence, herein this chapter, we report development of protecting group strategy for α-selective glycosylation of oligomannosides and effectively employed in synthesis of trimannoside as well as GPI anchor core trisaccharide. In addition, DFT calculation and measurement of oxidation potential thiomannoside building blocks were also performed.

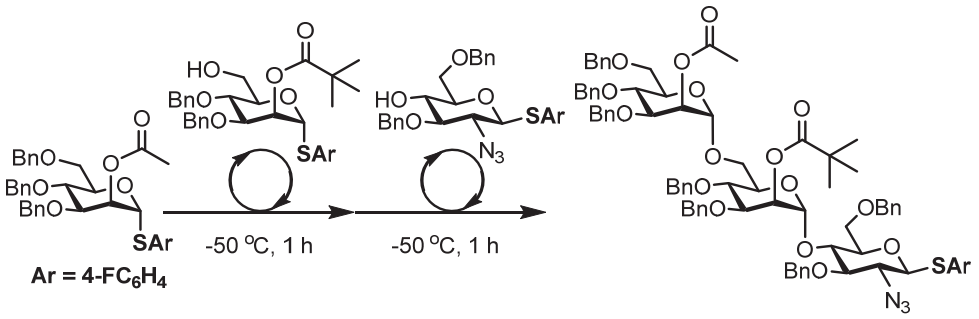


Figure 5. AEA for synthesis of GPI anchor core trisaccharide

Chapter 2

Design, synthesis and optimization of thioglucoside building blocks are described in this chapter for stereoselective glycosylation utilising automated electrochemical assembly. In company with that strategic attempts were also discussed for the development of rational protocol for synthesis of the hexasaccharide repeating unit found in macrocyclic β-glucan to facilitate its synthesis in preparative scale.

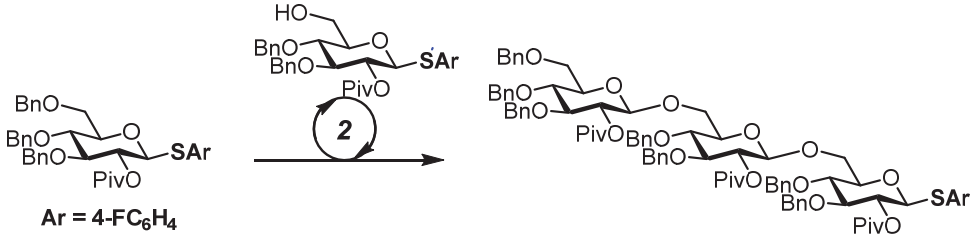


Figure 6. AEA for synthesis of β-1,6-linked triglucoside

Chapter 3

This chapter deals with a development of automated electrochemical assembly of thioglucosamine to form linear oligoglucosamine featuring one pot glycosylation followed by

intramolecular electrochemical glycosylasation of linear oligoglucosamine leading to cyclic oligoglucosamine. Alongside that, oligomer concentration effect has been studied to justify the intra-molecularity of the cyclisation. Additionally, parallel study was also commenced with respect to conventional chemical glycosylation for comparison.

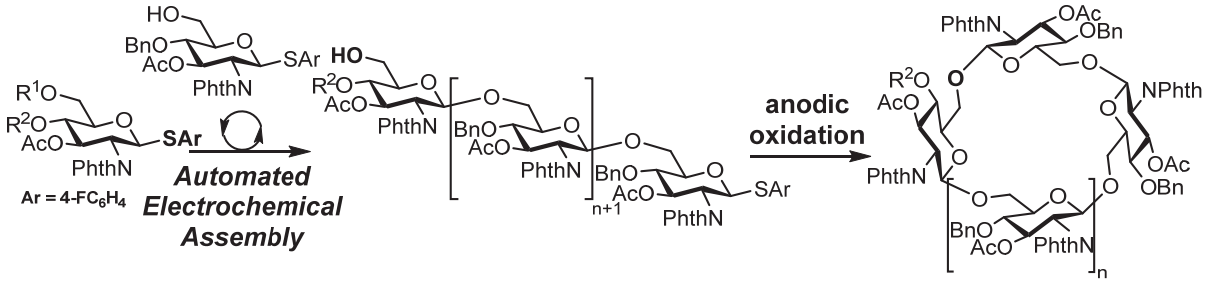


Figure 7. AEA for synthesis of oligoglucosamine and successive cyclization

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Chapter 1

Rational optimisation of the Mannoside Building Block for Automated Electrochemical Assembly of the Core Trisaccharide of GPI Anchor Oligosaccharides

Abstract

We have developed a carbohydrate building block of mannosides based on DFT calculations, electrochemical analysis, and automated solution-phase synthesis. The optimized building block in hand was used to prepare the core trisaccharide of GPI anchor oligosaccharides.

Introduction

Mannosides are abundant monosaccharides found in organisms including bacteria. For example, tuberculosis (TB) is a fatal disease caused by Mycobacterium tuberculosis, as the Global Burden of Disease Study 2013 (GBD 2013) indicates that TB caused 9.2 million deaths in 2013.[1] The mycobacterial cell wall consists of a highly dense network of glycoproteins including arabinogalactan (AG), lipoarabinomannan (LAM), mannose capped lipoarabinomannan (ManLAM), trehalose, glycosylphosphatidylinositol (GPI) and phosphatidylinositol mannoside (PIM). Glycans on the cell surface play a vital role in sustaining the lives of many fundamental processes.[2,3] Among these glycans PIM, GPI and LAM are found to be the most potent molecules for host immune response.[4] In the last few decades these oligosaccharides have become the molecules of particular interest for many chemist and biologist.

Oligomannosides are one of the most abundant oligosaccharides having the repeating unit of mannose residue with 1,2- or 1,6-glycosidic linkages and these oligosaccharides have been target structures to demonstrate benefits of novel strategy for oligosaccharide synthesis.[5,7] Automated solid-phase synthesis of oligomannosides up to 30mer has already been achieved, however, the quantity of the target oligosaccharides is limited.[8] Although iterative one-pot synthesis of oligosaccharides based on preactivation of glycosyl donors has already been applied for the synthesis of lipomannans, a tetramannoside with the same repeating structure is, to date, the only example of this method.[9,10]

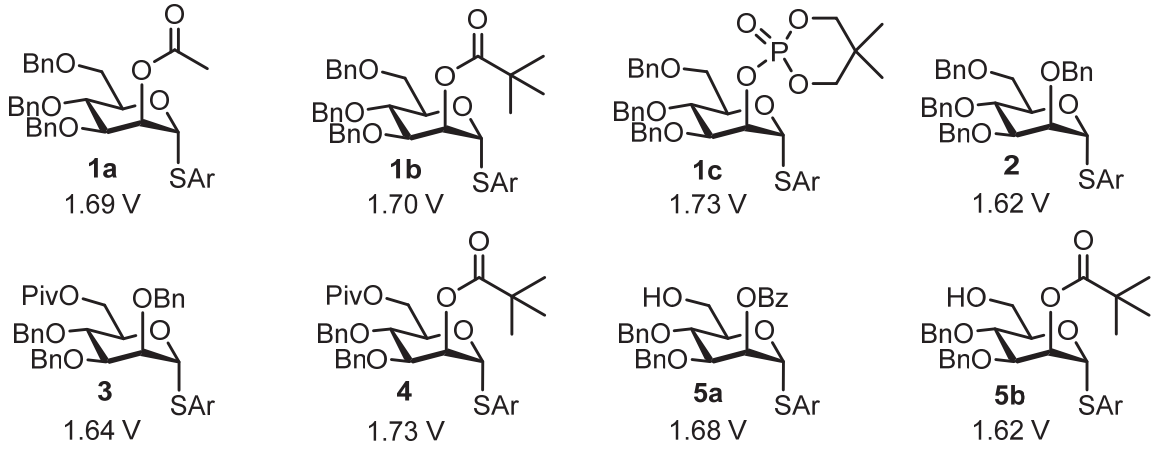
We have already reported automated electrochemical assembly of carbohydrate building blocks for the synthesis of the potential precursor of TMG-chitotriomycin tetrasaccharide by rational optimization of carbohydrate building blocks based on DFT calculation, and electrochemical measurements of their oxidation potentials.[11-13] Although α-glycosidic linkages of mannosides are thermodynamically favourable and can be selectively constructed by the neighbouring group participation, it is important to optimize the carbohydrate building blocks which can be converted to the corresponding storable glycosylation intermediates with reasonable reactivity for the subsequent glycosylation with a free OH of glycosides. Here we report optimization of carbohydrate building blocks for electrochemical automated solution-phase synthesis of oligomannosides with α-glycosidic linkages and its application to the synthesis of GPI anchor oligosaccharides.

Result and Discussion

We initiated our study on the evaluation of carbohydrate building blocks by preparing a variety of building blocks equipped with a neighbouring group such as pivaloyl and acetyl groups at the hydroxyl group of C-2 (2-OH) and/or C-6 (6-OH) (Fig. 1). Building blocks **1a-c** with a neighbouring group at 2-OH were easily accessible from the anomeric orthoester (See Supporting Information), whereas other building blocks **2-5** were synthesized by the conventional manipulations of protecting groups. Oxidation potentials of thus-obtained building blocks were measured by a standard technique of linear sweep voltammetry (LSV) using a rotation-desk electrode (RDE) (Table 1). These oxidation potentials were compared with that of 4-fluorophenyl 2,3,4,6-tetra-*O*-benzyl-α-D-thiomannoside **2**. Derivatization with an acetyl group at 2-OH increased the oxidation potential about 0.09 V. On the other hand, in the case of pivaloyl and phosphate, oxidation potentials were increased about 0.08 V and 0.11

V, respectively. Introduction of a pivaloyl group to 6-OH showed comparatively less change in oxidation potential (1.64 V), whereas pivaloyl functionalization of 2-OH as well as 6-OH increased the oxidation potential about 0.11 V. These results suggest that a structurally similar protecting group causes slightly different electronic behaviour which influences the electrochemical oxidation. To get a better understanding of this phenomenon we performed DFT calculations (B3LYP/6-31G(d)). Statistical data obtained by these calculations showed good correlation with oxidation potentials of glucosamine derivatives, however potential differences did not completely fit those obtained by measurements, especially in building blocks equipped with an acetyl or pivaloyl group at 2-OH. Therefore, further investigation is required for better prediction of oxidation potentials based on theoretical calculations.

Table 1. Oxidation potentials of building blocks



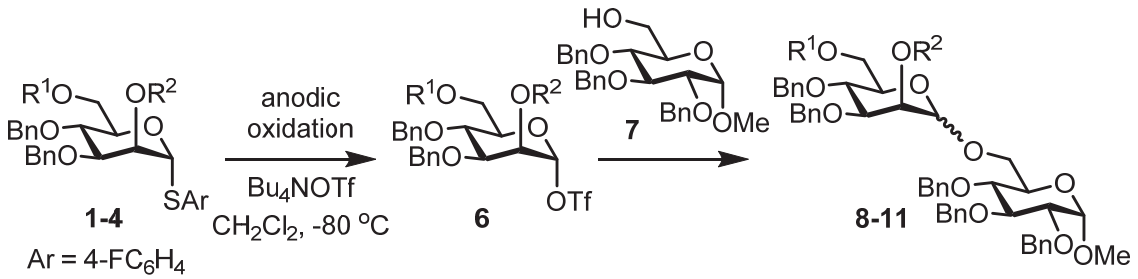
Building Block	Oxidation potential E_{ox} (V vs SCE)	ΔE_{ox} (V)	ΔE_{HOMO} (eV)[a]
1a	1.69	+0.07	+0.25
1b	1.70	+0.08	+0.21
1c	1.73	+0.11	+0.13
2	1.62	0.00	0.00
3	1.64	0.02	+0.11
4	1.73	+0.11	+0.15
5a	1.68	0.06	+0.07
5b	1.62	0.00	+0.03

[a]B3LYP/6-31G(d)

To confirm the stereoselectivity in glycosylation, we performed disaccharide synthesis based on the electrochemical pre-activation protocol (Table 2).[14] A building block was placed in the anodic chamber of a divided glass cell in the presence of Bu_4NOTf as an electrolyte (0.1M in CH_2Cl_2). Anodic oxidation was performed with a stoichiometric amount of electricity (1.0 F/mol) at -80 ºC and the subsequent glycosylation with a glycosyl accepter was carried out at-50 ºC for 1h (see Supporting Information for details). As a result, the building blocks

1a-c equipped with a neighbouring group at 2-OH afforded the corresponding disaccharides with desired α- glycosidic linkage in reasonable yields. Depending upon the reaction outcome, we hypothesized that there is a formation of glycosyl triflate which becomes more accumulated during the course of anodic oxidation. As the reaction progresses, the triflate is displaced by the neighbouring participating group to give acyloxonium ion, followed by the nucleophilic attack of a glycosyl acceptor at the anomeric carbon to secure α- selectivity in glycosylation. To check the validity of our hypothesis, comparative study was performed where the same reaction was carried out with a building block **2** without a participating group and a building block **3** equipped with a pivaloyl group at 6-OH. The building block without any participating group did not afford the corresponding disaccharide at all. Disappearance of the glycosyl donor spot on Thin Layer Chromatography (TLC) and the maximum amount of acceptor recovered after reaction suggested that the corresponding glycosyl triflate intermediate was not stable under the standard reaction condition and hence decomposed. Further investigation may be required, because this result was not consistent with those of pre-activation of 4-methylphenyl 2,3,4,6-tetra-*O*- benzyl-α-D-thiomannoside.[14,15] On the contrary, the building block equipped with a *O*-pivaloyl group at 6-OH afforded the corresponding disaccharide with complete α-selectivity. The neighbouring group participation of the protecting group at 6-OH has already been suggested by Kim;[16] however, this was the first example that clearly suggests the stabilizing effect of the protecting group at 6-OH of the glycosyl triflate intermediate.

Table 2. Pre-activation and the subsequent coupling with methylglycoside as an acceptor



Building Block	R^1	R^2	Product	Yield	Selectivity (α:β)
1a	Bn	Ac	**8a**	78%	α only
1b	Bn	Piv	**8b**	60%[b]	α only
1c	Bn	Phos[a]	**8c**	71% [b]	4:1
2	Bn	Bn	**9**	trace[c]	-
3	Piv	Bn	**10**	45% (41%)[b]	α only
4	Piv	Piv	**11**	47% (58%)[b]	α only

[a]$PO(OCH_2CMe_2CH_2O)$, [b]NMR yields, [c]Detected by MS.

We extended the scope of our methodology for synthesis of 1,6-α-linked trimannosides, where we choose substrate **1a** as a terminal building block (Fig. 1). The schedule of trisaccharide synthesis is also shown in Fig. 2. The first cycle of the process was initiated by anodic oxidation of building block **1a** at -80 °C, followed by the coupling with building block **5a** (R = Bz) or **5b** (R = Piv) which has a free 6-OH. The second cycle was performed in one pot and the subsequent purification of the crude product by preparative gel-permeation chromatography (GPC) afforded desired trisaccharides **14a** and **14b** in 15% and 24% yields, respectively.

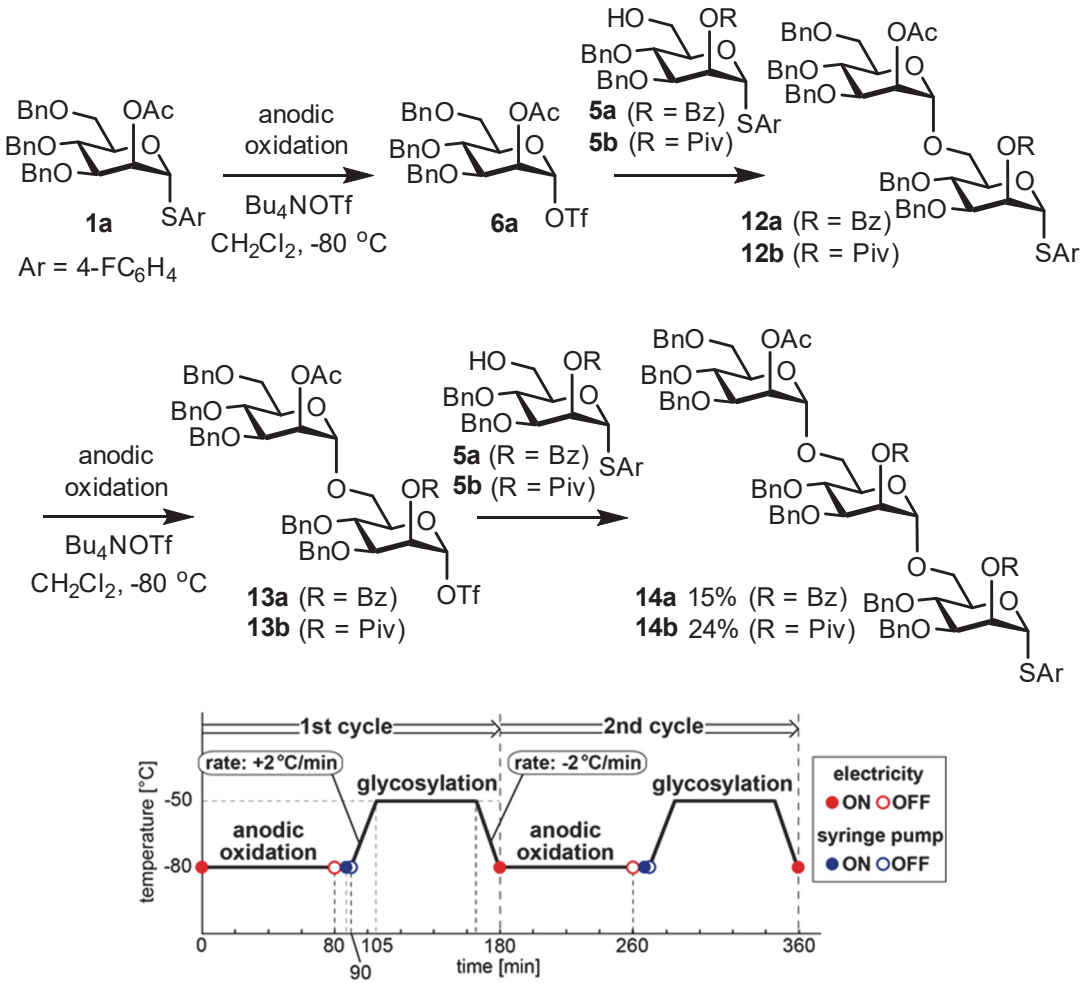


Figure 1. Synthesis of trimannoside

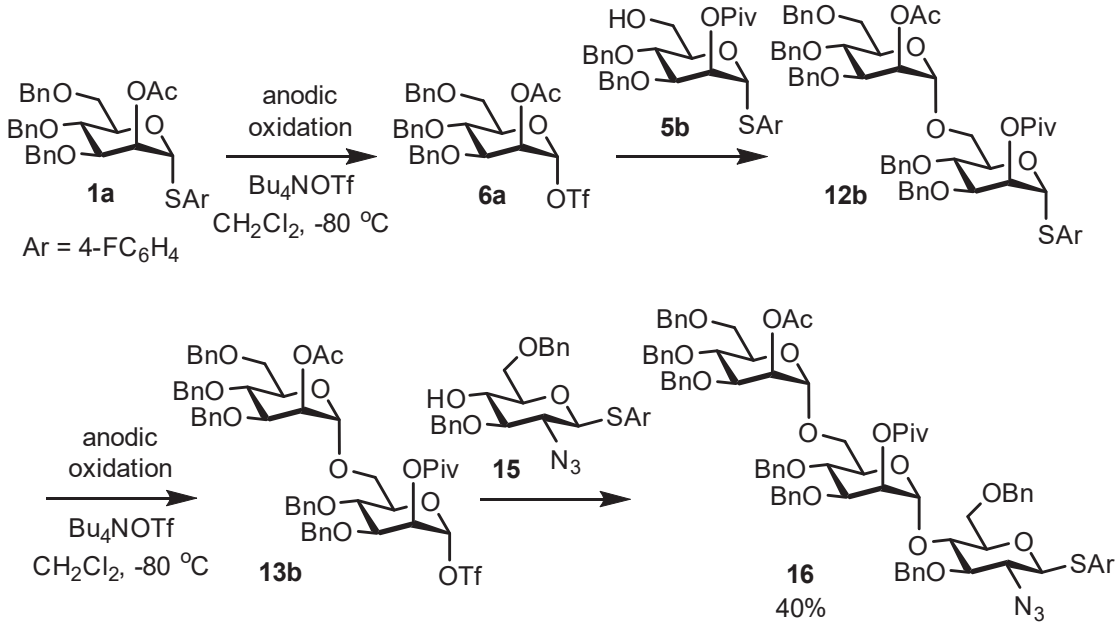


Figure 2. Synthesis of the core structure of the GPI anchor trisaccharide

To explore the efficacy of this method, we finally performed automated synthesis of the core trisaccharide of GPI anchor oligosaccharides (Fig. 2). In this case, we chose **1a** as the first building block, because installation of acid labile 2-O-acetyl group may enable us to perform selective cleavage of the group and elongation from trisaccharide **16**. The second building block **5b**, equipped with an orthogonal protecting group was added with exactly a 1.0 equivalent to prevent formation of undesired by-products. The third building block **15** having an azido group, which has frequently been chosen to perform a-selective glycosylation with an inositol as a glycosyl acceptor, was used in this synthesis, and finally, synthesis of core trisaccharide present in GPI anchor oligosaccharides was accomplished with 40% overall yield.

Conclusion

In summary, we have optimized the monosaccharide building block of mannosides for automated electrochemicalsolution-phase synthesis of oligosaccharides and exploited its application in the synthesis of a GPI anchor core trisaccharide. In order to synthesize biologically important oligomannosides on a preparative scale further optimization of reaction conditions using the automated synthesizer is in progress in our laboratory.

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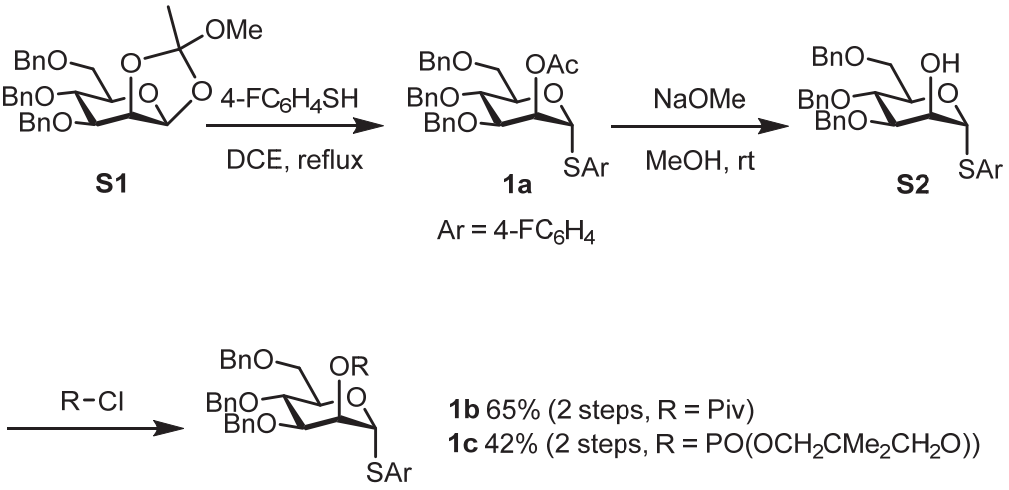
Experimental Section

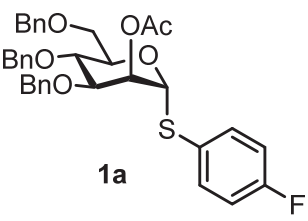
1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE II 600 (^{1}H 600 MHz, ^{13}C 150 MHz). NMR yields were based on 1,1,2,2-tetrachloroethane as an internal standard. Electrospray ionization mass spectra (ESI-TOF MS) were recorded on Thermo Scientific Exactive spectrometer. Preparative recycling gel permeation chromatography (PR-GPC) was performed on Japan Analytical Industry LC-918. Kanto silica gel (spherical, neutral, 100+69-210 μm) was used for column chromatography. Rotating-disk electrode voltammetry was carried out using BAS 700c analyzer and RRDE-3 rotating ring disk electrode. Measurements were carried out in 0.1 M Bu_4NOTf/CH_2Cl_2 using a glassy carbon disk working electrode, a platinum wire counter electrode, and a saturated calomel electrode (SCE) as a reference electrode with sweep rate of 10 mV/s at 3000 r.p.m. The automated synthesizer is consisting of the commercially available instruments such as the chiller with a cooling bath (UCR-150, Techno Sigma), the power suppy for constant current electrolysis (PMC 350-0.2 A, KIKUSUI), the syringe pump (PHD 2000 infusion, Harvard apparatus), and the system controller (LabVIEW, National Instruments). Optical rotation was recorded on JASCO DIP-1000 digital polarimeter in chloroform. Merck TLC (silica gel 60 F_{254}) was used for TLC analysis. Starting materials **S1**,[1] **S3**,[2] **S8**,[3] and **7**[4] were prepared according to the reported procedures. Spectra of known disaccharides **8a**[5] and **9**[6] were compared with those in the literature. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification.

2. Preparation of building blocks

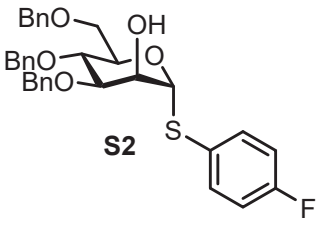


Scheme S1.



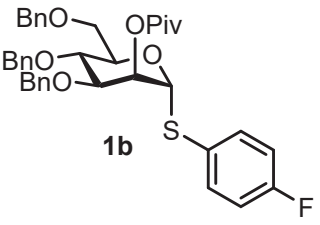
To a stirred solution of **S1** (0.77 g, 1.51 mmol) in dichloroethane (4 mL) 4-fluorothiophenol (0.20 mL, 1.8 mmol) was added. After the mixture was stirred at 120 °C over night, the solution was then concentrated and purified by silica gel chromatography to give **1a** as a white solid in 56% yield (0.51 g, 0.85 mmol). **4-Fluorophenyl 3,4,6-tri-*O*-benzyl-2-*O*-acetyl-1-thio-α-D-mannopyranoside (1a)**.

TLC (hexane/EtOAc 5:1): R_f 0.30. $[\alpha]_D$ = +10.0 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.45 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.35 – 7.27 (m, 13 H), 7.20 (dd, *J* = 7.8, 1.2 Hz, 2 H), 6.91 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.57 (s, 1 H) 5.41 (d, *J* = 1.2 Hz, 1 H), 4.88 (d, *J* = 10.8 Hz, 1 H), 4.72 (dd, *J* = 10.8 Hz, 1 H), 4.64 (d, *J* = 11.4 Hz, 1 H), 4.57 (d, *J* = 11.4 Hz, 1 H), 4.51 (d, *J* = 10.8 Hz, 1 H), 4.47 (d, *J* = 12.0 Hz, 1 H), 4.35 (dd, *J* = 6.4, 1.2 Hz, 1 H), 3.94 – 3.90 (m, 2 H), 3.83 (dd, *J* = 10.8, 6.4 Hz, 1 H), 3.73 (dd, *J* = 10.2, 1.8 Hz, 1 H), 2.14 (s, 3 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.3, 162.7 (d, *J* = 246.8 Hz), 138.2 138.1, 137.5, 134.7 (d, *J* = 8.3 Hz), 128.5, 128.4, 128.3, 128.2, 127.92, 127.88, 127.7, 127.6, 116.1 (d, *J* = 21.9 Hz), 86.7, 78.4, 75.3, 74.6, 73.4, 72.4, 71.9, 70.1, 68.9, 21.0. HRMS (ESI) *m/z* calcd for $C_{35}H_{35}FKO_6S$ $[M+K]^+$, 641.1775; found, 641.1785.



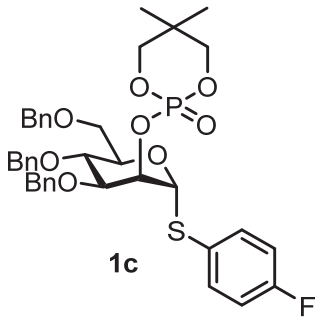
S2

Thioglycoside **1a** (1.3 g, 2.2 mmol) was dissolved in MeOH (18 mL) and treated with 0.5M NaOMe/MeOH solution (0.88 mL, 0.44 mmol) at rt for 20 h, and then most of solvent was removed. The reaction mixture was neutralized with Amberlite and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography to give **S2** in 93% yield (1.2 g, 2.1 mmol). **4-Fluorophenyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (S2)**. TLC (hexane/EtOAc 5:2): R_f 0.40. $[\alpha]_D$ = +1.7 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.44 (dd, *J* = 9.0, 5.4, 2 H), 7.37 – 7.26 (m, 13 H), 7.21 (d, *J* = 8.4 Hz, 2 H), 6.90 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.48 (d, *J* = 1.8 Hz, 1 H), 4.84 (d, *J* = 10.8 Hz, 1 H), 4.70 (s, 2 H), 4.60 (d, *J* = 12.0 Hz, 2 H), 4.52 (d, *J* = 12.0 Hz, 2 H), 4.46 (d, *J* = 12.0 Hz, 2 H), 4.32 (ddd, *J* = 9.0, 4.8, 1.8 Hz, 2 H), 4.22 (bs, 1 H), 3.90 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.85 (dd, *J* = 9.0, 3.6 Hz, 1 H), 3.77 (dd, *J* = 10.8, 5.4 Hz, 1 H), 3.69 (dd, *J* = 10.8, 1.8 Hz, 1 H), 2.71 (s, 1 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.6 (d, *J* = 246.2 Hz), 138.2, 138.1, 137.6, 134.6 (d, *J* = 8.4 Hz), 128.7, 128.6 (d, *J* = 3.3 Hz), 128.44, 128.37, 128.1, 128.02, 127.99, 127.9, 127.8, 127.7, 116.1 (d, *J* = 21.8 Hz), 87.9, 80.3, 75.2, 74.6, 73.5, 72.23, 72.19, 69.7, 69.0. HRMS (ESI) *m/z* calcd for $C_{33}H_{33}FKO_5S$ $[M+K]^+$, 599.1670; found, 599.1679.



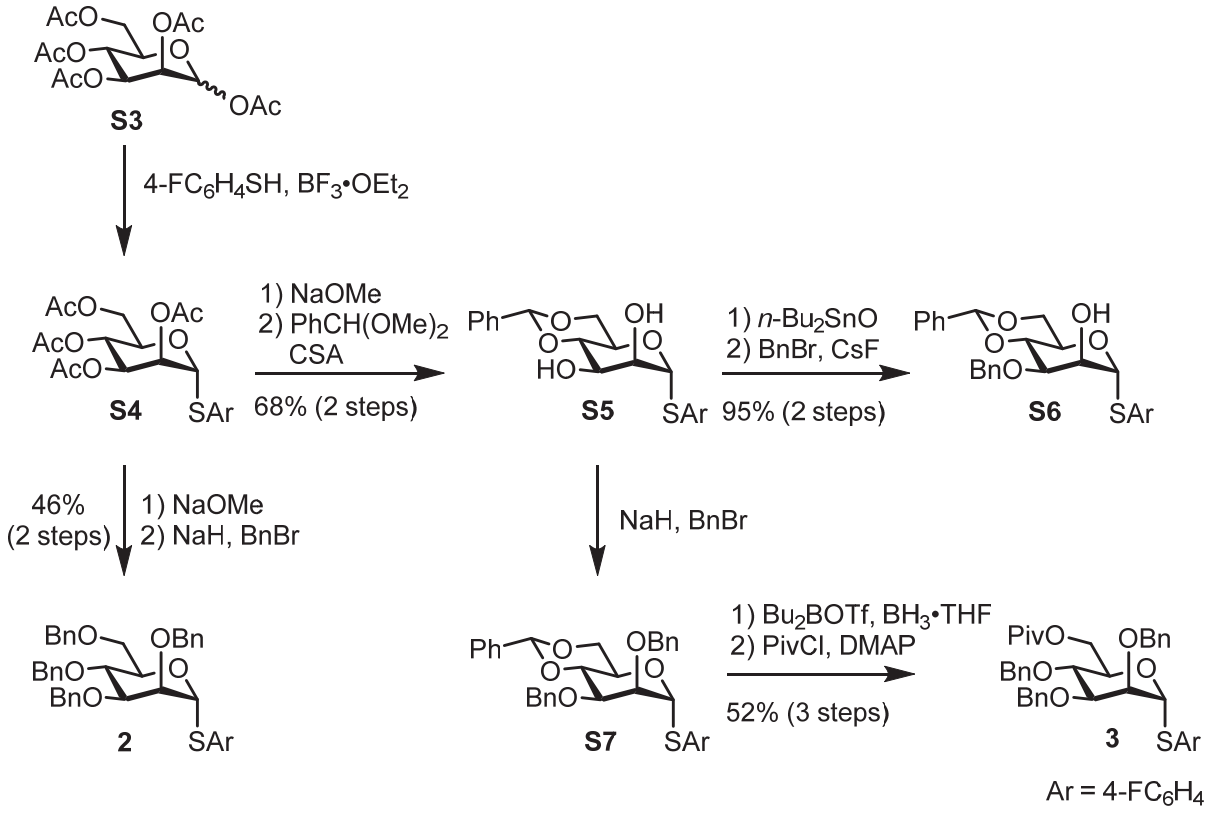
1b

To a stirred solution of **S2** (0.85 g, 1.5 mmol) in pyridine, DMAP (60 mg, 0.49 mmol) and pivaloyl chloride (0.56 mL, 4.5 mmol) were added. After stirring for 26 hour at 50 °C, the reaction was quenched by methanol and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography to give **1b** as colorless foam in 78% yield (0.76 g, 1.2 mmol). **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-1-thio-α-D-mannopyranoside (1b)**. TLC (hexane/EtOAc 5:1): R_f 0.60. $[\alpha]_D$ = +5.2 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.46 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.34 – 7.26 (m, 13 H), 7.20 (d, *J* = 6.6 Hz, 2 H), 6.90 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.58 (dd, *J* = 3.0, 1.8 Hz, 1 H) 5.38 (d, *J* = 1.8 Hz, 1 H), 4.87 (d, *J* = 10.8 Hz, 1 H), 4.70 (dd, *J* = 10.8 Hz, 1 H), 4.61 (d, *J* = 12.0 Hz, 1 H), 4.53 (d, *J* = 11.4 Hz, 1 H), 4.52 (d, *J* = 10.8 Hz, 1 H), 4.47 (d, *J* = 11.4 Hz, 1 H), 4.37 (ddd, *J* = 9.6, 4.8, 1.8 Hz, 1 H), 3.93 (dd, *J* = 9.6, 3.0 Hz, 1 H), 3.89 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.81 (dd, *J* = 10.8, 5.4 Hz, 1 H), 3.76 (dd, *J* = 10.2, 1.8 Hz, 1 H), 1.21 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.6, 162.9 (d, *J* = 246.9 Hz), 138.3 138.2, 137.8, 135.1 (d, *J* = 8.6 Hz), 128.41, 128.39, 128.3, 128.2, 128.1, 127.8 (d, *J* = 3.3 Hz), 127.6, 116.2 (d, *J* = 21.9 Hz), 86.8, 78.7, 75.3, 74.5, 73.3, 72.4, 71.6, 69.6, 69.2, 39.1, 27.1. HRMS (ESI) *m/z* calcd for $C_{38}H_{41}FNNaO_6S$ $[M+Na]^+$, 667.2500; found, 667.2473.

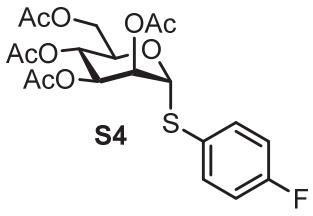


1c

To a stirred solution of **S2** (0.84 g, 1.50 mmol) in THF (5 mL) at rt, 60% NaH (0.24 g, 6.0 mmol) was added and stirred for 30 min. Then 2,2-dimethyltrimethylene phosphorochloridate (0.39 g, 2.2 mmol) was added in one portion. After stirring for 9 hours at rt, the reaction was quenched by saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with water and brine and dried over $MgSO_4$. After filtration, the reaction mixture was concentrated *in vacuo* and the crude product was purified by column chromatography to give **1c** as colorless foam in 85% yield (0.90 g, 1.3 mmol). **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-2-*O*-(2,2-dimethyltrimethylene phosphornoyl)-1-thio-α-D-mannopyranoside (1c)**. TLC (hexane/EtOAc 5:3): R_f 0.50. $[\alpha]_D$ = +76.8 (*c* = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.45 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.41 – 7.40 (m, 2 H), 7.35 – 7.27 (m, 11 H), 7.25 – 7.23 (m, 2 H), 6.94 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.59 (d, *J* = 1.8 Hz, 1 H), 5.11 (dt, *J* = 7.8, 2.4 Hz), 4.91 (d, *J* = 10.8 Hz, 1 H), 4.82 (d, *J* = 11.4 Hz, 1 H), 4.63 (d, *J* = 11.4 Hz, 1 H), 4.62 (d, *J* = 11.4 Hz, 1 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.48 (d, *J* = 12.0 Hz, 1 H), 4.33 (ddd, *J* = 5.4, 4.2, 3.0 Hz, 1 H), 4.14 (d, *J* = 10.8 Hz, 1 H), 4.09 (d, *J* = 10.8 Hz, 1 H), 3.96 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.91 – 3.85 (m, 2 H), 3.76 (ddd, *J* = 21.6, 10.8, 3.0 Hz, 1 H) 3.75 (dd, *J* = 10.8, 3.0 Hz, 1 H) 3.67 (ddd, *J* = 22.2, 11.4, 3.0 Hz, 1 H), 1.22 (s, 3 H), 0.63 (s, 3 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.8 (d, *J* = 246.9 Hz), 138.2, 138.0, 137.4, 134.9 (d, *J* = 8.1 Hz), 128.5, 128.4, 128.36, 128.34, 128.2 (d, *J* = 3.3 Hz), 128.1, 128.0, 127.9, 127.6, 116.2 (d, *J* = 21.9 Hz), 87.4, 79.1, 78.39, 78.35, 78.30, 78.25, 78.1, 75.2, 74.4, 74.3, 74.1, 73.4, 72.6, 71.9, 69.0, 32.0, 21.8, 20.1. HRMS (ESI) *m/z* calcd for $C_{38}H_{42}FNNaO_8PS$ $[M+Na]^+$, 731.2214; found, 731.2223.

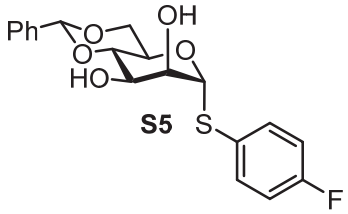


Scheme S2.



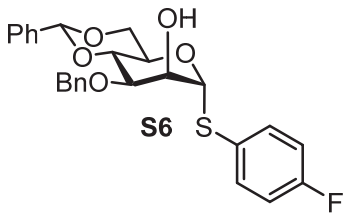
S4

The mixture of **S3** (19.6 g, 50 mmol), 4-fluorothiophenol (8.0 mL, 75 mmol) in CH_2Cl_2 (60 mL) was stirred at 0 °C, then BF_3•OEt_2 (9.4 mL, 75 mmol) was added, and stirred overnight at rt. The reaction mixture was quenched with aqueous solution of $NaHCO_3$, washed with H_2O and brine, and dried over anhydrous Na_2SO_4. The solution was then concentrated and purified by silica gel chromatography to give **S4** as colorless oil (20.9 g, 45.5 mmol, 91% yield). **4-Fluorophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-mannopyranoside S4** TLC (hexane/EtOAc 1:1): R_f 0.30. $[\alpha]_D$ = +9.7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.47 (dd, *J* = 8.4, 4.8 Hz, 2 H), 7.02 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.48 (dd, *J* = 3.0, 1.8 Hz, 1 H), 5.38 (d, *J* = 0.6 Hz, 1 H), 5.32 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 5.29 (dd, *J* = 10.2, 3.0 Hz, 1 H), 4.52 (ddd, *J* = 9.6, 6.0, 2.4 Hz, 1 H), 4.29 (dd, *J* = 12.0, 6.0 Hz, 1 H), 4.11 (dd, *J* = 12.6, 2.4 Hz, 1 H), 2.21 (s, 3 H), 2.09 (s, 3 H), 2.05 (s, 3 H), 1.99 (s, 3 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.5, 169.9, 169.8, 169.7, 162.9 (dd, *J* = 248.0 Hz), 134.8 (d, *J* = 8.0 Hz), 127.5 (d, *J* = 3.3 Hz), 116.4 (dd, *J* = 21.9 Hz), 86.1, 70.7, 69.5, 69.3, 66.3, 62.5, 20.7. HRMS (ESI) *m/z* calcd for $C_{20}H_{23}FNaO_9S$ $[M+Na]^+$, 481.0945; found, 481.0916.



S5

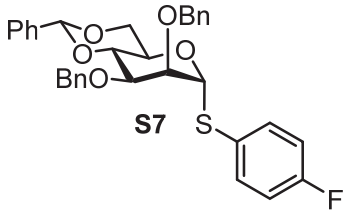
To a stirred solution of **S4** (59.6 g, 130 mmol) in methanol (220 mL) was added 0.5 M NaOMe (5.2 mL, 2.6 mmol). After stirring for 24 hours, the reaction mixture was neutralized with Amberlite and solvent was removed under reduced pressure to obtain the crude product of the intermediate. The crude product was dissolved into CH_3CN (300 mL) and camphor sulfonic acid (10.1 g, 43.5 mmol) and benzaldehyde dimethylacetal (29 mL, 194 mmol) were added. After stirring 24 hours, the reaction was quenched with Et_3N and solvent was removed under reduced pressure. The crude product was dissolved into EtOAc and washed with water and brine. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to obtain **S5** as colorless oil in 68% yield (89 mmol). **4-Fluorophenyl-4,6-*O*-benzylidene-1-thio-β-D-mannopyranoside (S5)**. TLC (hexane/EtOAc 1:1): R_f 0.30. $[\alpha]_D$ = +21.3 (*c* = 1.0, MeOH). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.51 (dd, *J* = 7.2, 3.6 Hz, 2 H), 7.46 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.42–7.36 (m, 3 H), 7.03 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.59 (s, 1 H), 5.49 (s, 1 H), 4.36–4.29 (m, 2 H), 4.21 (dd, *J* = 10.2, 4.8 Hz, 1 H), 4.12 (dt, *J* = 9.6, 3.0 Hz, 1 H), 4.01 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.84 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 2.84 (d, *J* = 2.4 Hz, 1 H), 2.77 (d, *J* = 3.0 Hz, 1 H). ^{13}C NMR (DMSO-d_6, 150 MHz) δ 161.8 (d, *J* = 243.9 Hz), 137.8, 134.4 (*pseudo*-t, *J* = 7.7 Hz), 128.9 (d, *J* = 3.0 Hz), 128.8, 128.0, 126.4, 116.3 (d, *J* = 21.8 Hz), 116.2 (d, *J* = 21.6 Hz), 101.2, 89.7, 78.4, 72.2, 68.0, 67.5, 65.2. HRMS (ESI) *m/z* calcd for $C_{19}H_{19}FNaO_5S$ $[M+Na]^+$, 401.0829; found, 401.0809.



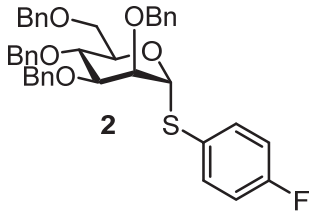
S6

Substrate **S5** (5.0 g, 13.2 mmol) and dibutyl tinoxide (4.2 g, 16.9 mmol) were placed in a round bottle flusk and dry toluene (100 mL) was added. The reaction mixture was refluxed for 22 hours and then evaporated to remove solvent. The crude product was again dissolved in DMF (100 mL) and CsF (2.5 g, 16.4 mmol) and BnBr (2.0 mL, 16.7 mmol) were added subsequently. Additional stirring at rt for 24 hours, the reaction was quenched with water and extracted with EtOAc. The organic layer was washed with water and dried with Na_2SO_4. Subsequent filteration and evaporation gave the crude product. Further purification by silica gel column chromatography afforded **S6** (5.05 g, 10.8 mmol) in 81% yield. **4-Fluorophenyl 3-*O*-benzyl-**

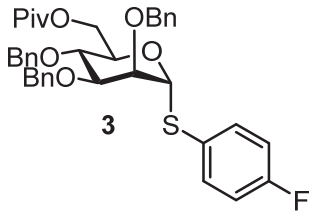
4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (S6). TLC (hexane/EtOAc 3:7): R_f 0.30. $[\alpha]_D$ = +15.6 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.51 (d, *J* = 7.8 Hz, 2 H), 7.43 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.41 – 7.31 (m, 8 H), 7.02 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.62 (s, 1 H), 5.49 (s, 1 H), 4.91 (d, *J* = 11.4 Hz, 1 H), 4.75 (d, *J* = 11.4 Hz, 1 H), 4.32 (td, *J* = 9.6, 4.8 Hz, 1 H), 4.26 (d, *J* = 3.0 Hz, 1 H), 4.20 (dd, *J* = 10.2, 4.8 Hz, 1 H), 4.18 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.95 (dd, *J* = 9.6, 3.6 Hz, 1 H), 3.86 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 2.86 (d, *J* = 8.4 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.7 (dd, *J* = 247.2 Hz), 137.7, 137.4, 134.5 (d, *J* = 8.0 Hz), 129.0, 128.6, 128.3, 128.1, 127.9, 126.1, 116.3 (dd, *J* = 21.8 Hz), 101.6, 88.3, 79.0, 75.6, 73.2, 71.3. HRMS (ESI) *m/z* calcd for $C_{26}H_{25}FKO_5S$ $[M+K]^+$, 507.1038; found, 507.1024.



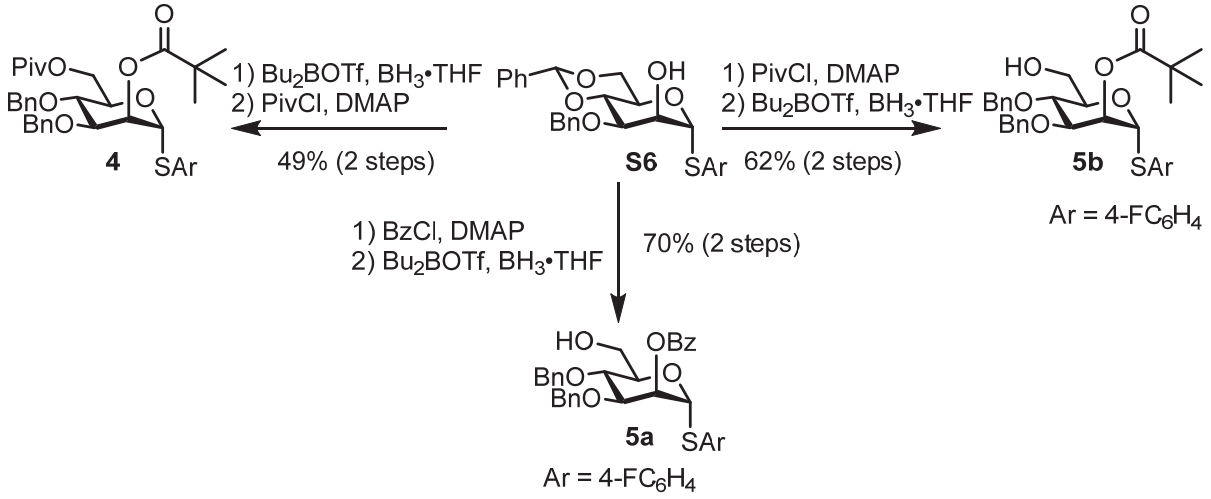
60% NaH (1.92 g, 48 mmol) was washed with dry hexane (50 mL) and dissolved in DMF (80 mL) at 0 ºC. Then **S5** (3.03 g, 8.0 mmol) was added. After 10 min, benzyl bromide (5.7 mL, 48 mmol) was added and stirred at rt for overnight. Standard procedure for quench the reaction and purification by silica gel column chromatography afforded **S7** (3.70 g, 6.62 mmol) in 83% yield. **4-Fluorophenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D–mannopyranoside (S7)**. TLC (hexane/EtOAc 5:1): R_f 0.60. $[\alpha]_D$ = +8.9 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.52 (d, *J* = 8.4 Hz, 2 H), 7.39 – 7.27 (m, 15 H), 6.97 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.64 (s, 1 H), 5.37 (d, *J* = 1.2 Hz, 1 H), 4.83 (d, *J* = 12.0 Hz, 1 H), 4.73 (d, *J* = 12.0 Hz, 1 H), 4.69 (d, *J* = 12.0 Hz, 1 H), 4.65 (d, *J* = 12.0 Hz, 1 H), 4.31 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.26 (td, *J* = 9.6, 4.8 Hz, 1 H), 4.21 (dd, *J* = 10.2, 4.8 Hz, 1 H), 4.00 (dd, *J* = 3.6, 1.2 Hz, 1 H), 3.95 (dd, *J* = 9.6, 3.0 Hz, 1 H), 3.88 (*pseudo*-t, *J* = 10.2 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.7 (d, *J* = 247.2 Hz), 138.4, 137.8, 137.6, 134.5 (d, *J* = 7.8 Hz), 129.0, 128.54, 128.3, 128.2, 128.0, 127.8, 126.2, 116.4 (d, *J* = 21.9 Hz), 101.6, 87.8, 79.2, 78.0, 76.2, 73.2, 68.5, 65.6. HRMS (ESI) *m/z* calcd for $C_{33}H_{31}FNaO_5S$ $[M+Na]^+$, 581.1768; found, 581.1746.



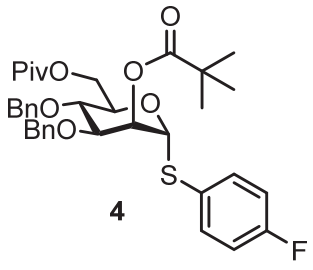
Removal of acetyl groups of **S4** gave a tetraol as an itermediate. Subsequent benzyl protection of the intermediate (1.42 g, 4.9 mmol) and purification by silica gel column chromatography afforded **2** (1.67 g, 2.58 mmol) in 52% yield. **4-Fluorophenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-mannopyranoside (2)**. TLC (hexane/EtOAc 5:2): R_f 0.70. $[\alpha]_D$ = +6.9 (*c* = 1.0, $CHCl_3$). E_{ox} = 1.62 V vs. SCE. ^1H NMR ($CDCl_3$, 600 MHz) δ 7.40 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.36 – 7.27 (m, 18 H), 7.21 (d, *J* = 7.8 Hz, 2 H), 6.89 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.46 (d, *J* = 1.8 Hz, 1 H), 4.90 (d, *J* = 10.8 Hz, 1 H), 4.71 (d, *J* = 12.6 Hz, 1 H), 4.64 – 4.59 (m, 4 H), 4.53 (d, *J* = 10.8 Hz, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.29 (ddd, *J* = 9.6, 5.4, 1.8 Hz, 1H), 4.01 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.96 (dd, *J* = 2.4, 1.8 Hz, 1 H), 3.84 (dd, *J* = 9.0, 3.0 Hz, 1 H), 3.81 (d, *J* = 10.8, 5.4 Hz, 1 H), 3.76 (d, *J* = 10.8, 1.8 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.7 (d, *J* = 246.3 Hz), 138.5, 138.4, 138.3, 138.0, 134.7 (d, *J* = 8.3 Hz), 129.2, 129.1, 128.51, 128.49, 128.4, 128.1, 128.04, 127.97, 127.85, 127.80, 127.6, 116.2 (d, *J* = 21.9 Hz), 86.4, 80.2, 76.2, 75.3, 75.2, 73.4, 72.8, 72.3, 72.1, 69.4. HRMS (ESI) *m/z* calcd for $C_{40}H_{39}FNaO_5S$ $[M+Na]^+$, 673.2394; found, 673.2369.



Cleavage of 4,6-*O*-benzylidene acetal of **S7** (1.54 g, 2.75 mmol) followed by installation of a pivaloyl group at the C6-hydroxyl group afforded **5b** (1.11 g, 1.72 mmol) in 62% yield. **4-Fluorophenyl-2,3,4-tri-*O*-benzyl-6-*O*-pivaloyl-1-thio-β-D-mannopyranoside (3)**. TLC (hexane/EtOAc 10:1): R_f 0.45. $[\alpha]_D$ = +6.1 (*c* = 1.0, $CHCl_3$). E_{ox} = 1.64 V vs. SCE. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.39 – 7.27 (m, 17 H), 6.98 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.43 (d, *J* = 1.8 Hz, 1 H), 4.96 (d, *J* = 10.2 Hz, 1 H), 4.67 (d, *J* = 12.6 Hz, 1 H), 4.66 – 4.62 (m, 3 H), 4.59 (d, *J* = 10.2 Hz, 1 H), 4.41 (d, *J* = 10.2 Hz, 1 H), 4.00 – 3.97 (m, 2 H), 3.85 (dd, *J* = 9.6, 3.0 Hz, 1 H), 1.18 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.2, 162.6 (d, *J* = 246.8 Hz), 138.0, 137.8, 137.7, 133.9 (d, *J* = 7.8 Hz), 129.3, 129.1 (d, *J* = 3.2 Hz), 128.9, 128.4, 128.3, 128.0, 127.9, 127.77, 127.72, 127.68, 116.2 (d, *J* = 21.9 Hz), 86.2, 79.9, 75.3, 74.7, 72.06, 71.99, 71.3, 63.3, 38.9, 27.3. HRMS (ESI) *m/z* calcd for $C_{38}H_{41}FKO_6S$ $[M+K]^+$, 683.2239; found, 683.2251.

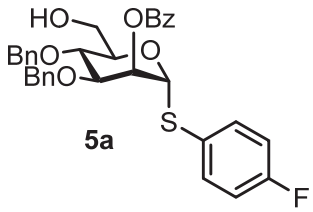


Scheme S3.



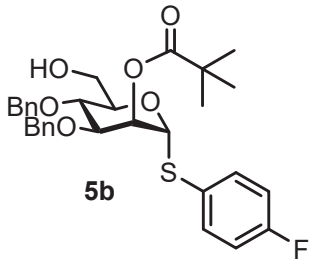
1.0 M Bu_2BOTf solution in CH_2Cl_2 (2.7 mL, 2.7 mmol) and **S6** (1.1 g, 2.3 mmol) were stirred at 0 °C. Then 1.0 M BH_3•THF (15.8 mL, 15.8 mmol) was added dropwise at 0 °C and stirred for 1.5 hours. The reaction was quenched with Et_3N and concentrated under reduced pressure. Purification by silica gel chromatography afforded the diol as an intermediate (0.91 g, 1.9 mmol) in 85% yield. To the stirred solution of the intermediate (0.91 g, 1.9 mmol) in dry pyridine (20 mL) pivaloyl choride (1.0 mL, 8.2 mmol) was added at rt. After the mixture was stirred for another 22 hours at 30 °C, the reaction was quenched by methanol. The solution was then concentrated and purified by silica gel chromatography to give **4** (0.73 g, 1.1 mmol) in 58% yield (49% in 2 steps). **4-Fluorophenyl 3,4-di-*O*-benzyl-2,6-*O*-pivaloyl-1-thio-β-D-mannopyranoside (4)**. TLC (hexane/EtOAc 5:1): R_f 0.55. $[\alpha]_D$ = +7.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.45 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.35 – 7.27 (m, 10 H), 6.98 (*psuedo*-t, *J* = 9.0 Hz, 2 H), 5.63 (dd, J = 3.0, 1.8 Hz, 1 H), 5.36 (d, *J* = 1.2 Hz, 1 H), 4.92 (d, *J* = 10.8 Hz, 1 H), 4.71 (d, *J* = 10.8 Hz, 1 H), 4.57 (d, *J* = 10.2 Hz, 1 H), 4.53 (d, *J* = 10.8 Hz, 1 H), 4.41 (dt, *J* = 9.6, 3.6 Hz, 1 H), 4.35 (d, *J* = 3.0 Hz, 1 H), 3.95 (dd, *J* = 8.0, 3.0 Hz, 1 H), 3.84 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 1.23 (s, 3 H), 1.21 (s, 3 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.0, 177.3, 162.6 (d, *J* = 246.9 Hz), 137.8, 138.6, 134.5 (d, *J* = 8.0 Hz), 128.4, 128.28, 128.25, 128.20, 128.1, 128.0, 127.8, 127.7, 116.2 (d, *J* = 21.9 Hz), 86.8, 78.5, 75.3, 74.1, 71.4,

70.7, 69.3, 63.3, 38.9, 38.7, 27.1. HRMS (ESI) *m/z* calcd for $C_{36}H_{43}FKO_7S$ $[M+K]^+$, 677.2345; found, 677.2349.



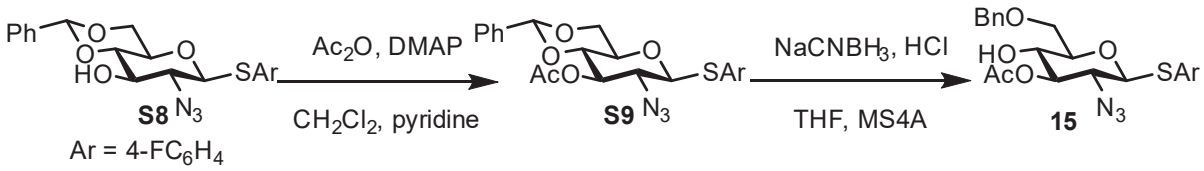
5a

To a stirred solution of **S6** (2.5 g, 5.3 mmol) and DMAP (0.25 g, 2.0 mmol) in dry pyridine (10 mL) at rt, benzoyl choride (1.0 mL, 8.6 mmol) was added. After the mixture was stirred for overnight at rt, the reaction was quenched with methanol. The solution was then concentrated and purified by silica gel chromatography to give the intermediate in 90% yield (2.8 g, 4.9 mmol). The intermadiate was dissolved in THF (40 mL) together with 0.9 M BH_3•THF (40.0 mL, 36.0 mmol) and stirred at 0 °C. Then CH_2Cl_2 solution of Bu_2BOTf (6.0 mL) was added dropwise at 0 °C and stirred at rt for 3 hours. The reaction was quenched with Et_3N and concentrated under reduced pressure. Purification by silica gel chromatography afforded **5a** (2.15 g, 3.7 mmol) in 78% yield (70% in 2 steps). **4-Fluorophenyl-3,4-di-*O*-acetyl-2-*O*-benzoyl-1-thio-β-D-mannopyranoside (5a)**. TLC (hexane/ EtOAc 3:1): R_f 0.25. $[\alpha]_D$ = +8.4 (*c* = 1.0, $CHCl_3$). E_{ox} = 1.68 V vs. SCE. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.05 (d, *J* = 7.8 Hz, 2 H), 7.58 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 7.47 – 7.43 (m, 4 H), 7.36 – 7.26 (m, 10 H), 7.00 (*psuedo*-t, *J* = 9.0 Hz, 2 H), 5.81 (s, 1 H), 5.48 (d, *J* = 1.2 Hz, 1 H), 4.94 (d, *J* = 10.8 Hz, 1 H), 4.79 (d, *J* = 11.4 Hz, 1 H), 4.68 (d, *J* = 11.4 Hz, 1 H), 4.61 (d, *J* = 11.4 Hz, 1 H), 4.26 – 4.21 (m, 1 H), 4.06 – 4.05 (m, 2 H), 3.85 (bs, 2 H), 1.86 (bs, 1 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.6, 162.9 (d, *J* = 247.2 Hz), 138.1, 137.6, 135.0 (d, *J* = 8.1 Hz), 133.5, 129.8, 129.6, 128.48, 128.41, 128.38, 128.13, 128.10, 128.05, 127.9, 127.8, 116.4 (d, *J* = 21.8 Hz), 86.9, 78.4, 75.4, 74.1, 73.1, 71.8, 70.6, 62.0. HRMS (ESI) *m/z* calcd for $C_{33}H_{31}FNaO_6S$ $[M+Na]^+$, 597.1723; found, 597.1696.

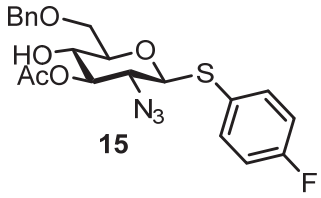


5b

To a stirred solution of **S6** (2.5 g, 5.3 mmol) and DMAP (0.30 g, 2.5 mmol) in dry pyridine (11 mL) at rt, pivaloyl choride (1.0 mL, 8.2 mmol) was added. After the mixture was stirred for another 18 hours at 40 °C, the reaction was quenched with methanol. The solution was then concentrated and purified by silica gel chromatography to give the intermediate in 80% yield (2.35 g, 4.3 mmol). The intermadiate (2.35 g, 4.3 mmol) was dissolved in THF (40 mL) together with 0.9 M BH_3•THF (40 mL, 36 mmol) and stirred at 0 °C. Then 1.0 M CH_2Cl_2 solution of Bu_2BOTf (5.2 mL, 5.2 mmol) was added dropwise at 0 °C and stirred at rt for 3 hours. The reaction was quenched with Et_3N and concentrated under reduced pressure. Purification by silica gel chromatography afforded **5a** (1.85 g, 3.34 mmol) in 78% yield (62% in 2 steps). **4-Fluorophenyl-3,4-di-*O*-acetyl-2-*O*-pivaloyl-1-thio-β-D-mannopyranoside (5b)**. TLC (hexane/EtOAc 5:1): R_f 0.25. $[\alpha]_D$ = +9.3 (*c* = 1.0, $CHCl_3$). E_{ox} = 1.62 V vs. SCE. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.34 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.25 – 7.18 (m, 10 H), 6.89 (*psuedo*-t, *J* = 9.0 Hz, 2 H), 5.50 (*psuedo*-t, *J* = 1.2 Hz, 1 H), 5.23 (s, 1 H), 4.81 (d, *J* = 10.8 Hz, 1 H), 4.60 (d, *J* = 11.4 Hz, 1 H), 4.56 (d, *J* = 10.8 Hz, 1 H), 4.44 (d, *J* = 11.4 Hz, 1 H), 4.10 (d, *J* = 9.6 Hz, 1 H), 3.86 (dd, *J* = 9.6, 3.0 Hz, 1 H), 3.78 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.72 (dd, *J* = 12.0, 2.4 Hz, 1 H), 3.67 (*pseudo*-t, *J* = 12.0, 4.2 Hz, 1 H), 1.12 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.5, 162.9 (d, *J* = 247.5 Hz), 138.1, 137.8, 135.2 (d, *J* = 8.0 Hz), 128.5, 128.4, 128.3, 128.2 (d, *J* = 3.3 Hz), 128.1, 128.0, 127.9, 116.4 (d, *J* = 21.8 Hz), 87.0, 78.6, 75.3, 74.0, 72.9, 71.6, 69.6, 62.0, 39.1, 27.2. HRMS (ESI) *m/z* calcd for $C_{31}H_{35}FKO_6S$ $[M+K]^+$, 593.1770; found, 593.1774.



Scheme S4.



To a stirred solution of **S8** (2.0 g, 5.1 mmol) and DMAP (63 mg, 0.51 mmol) in CH_2Cl_2 (16 mL) at room temperature (rt), acetic anhydride (1.5 mL) and dry pyridine (6.0 mL) were added. After the mixture was stirred for another 24 hours at rt, the reaction was quenched by methanol. The solution was then concentrated and purified by silica gel chromatography to give **S9** as white solid in 79% yield (1.8 g, 4.0 mmol). To a stirred solution of **S9** (1.7 g, 3.8 mmol), activated MS4A (1.1 g), and $NaCNBH_3$ (2.4 g, 40 mmol) in THF (40 mL) at 0 °C, HCl in ether (25 mL) was added dropwise. After the mixture was stirred for another 26 hours at rt, the reaction mixture was diluted with CH_2Cl_2 and filterated with a short column filled with celite. The solution was then concentrated and washed with saturated aqueous solution of $NaHCO_3$ and then water. Thus obtained organic layer was dride over $NaSO_4$. Removal of drying agent and solvent under reduced pressure gave a crude product. The crude product was purified by silica gel chromatography to give **15** as colorless oil in 75% yield (1.8 g, 4.0 mmol). **4-Fluorophenyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-azido-1-thio-β-D-glucopyranoside (15)**. TLC (hexane/EtOAc 1:1): R_f 0.65. $[\alpha]_D$ = -58.3 (*c* = 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.57 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.37 – 7.30 (m, 5 H), 6.97 (*psuedo*-t, *J* = 9.0 Hz, 2 H), 4.92 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.59 (d, *J* = 12.0 Hz, 1 H), 4.55 (d, *J* = 12.0 Hz, 1 H), 4.41 (d, *J* = 9.6 Hz, 1 H), 3.77 (d, *J* = 4.2 Hz, 1 H), 3.60 (td, *J* = 9.6, 4.2 Hz, 1 H), 3.48 (dt, *J* = 9.0, 4.2 Hz, 1 H), 3.29 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 3.01 (d, *J* = 4.8 Hz, 1 H), 2.14 (s, 3 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.4, 163.2 (d, *J* = 248.1 Hz), 137.7, 136.3 (d, *J* = 8.6 Hz), 128.5, 128.0, 127.7, 125.7 (d, *J* = 3.2 Hz), 116.2 (d, *J* = 21.9 Hz), 85.9, 78.6, 77.4, 73.7, 70.1, 69.7, 62.6, 20.9. HRMS (ESI) *m/z* calcd for $C_{21}H_{22}FN_3NaO_5S$ $[M+Na]^+$, 470.1156; found, 470.1158.

3. Automated synthesis of disaccharides

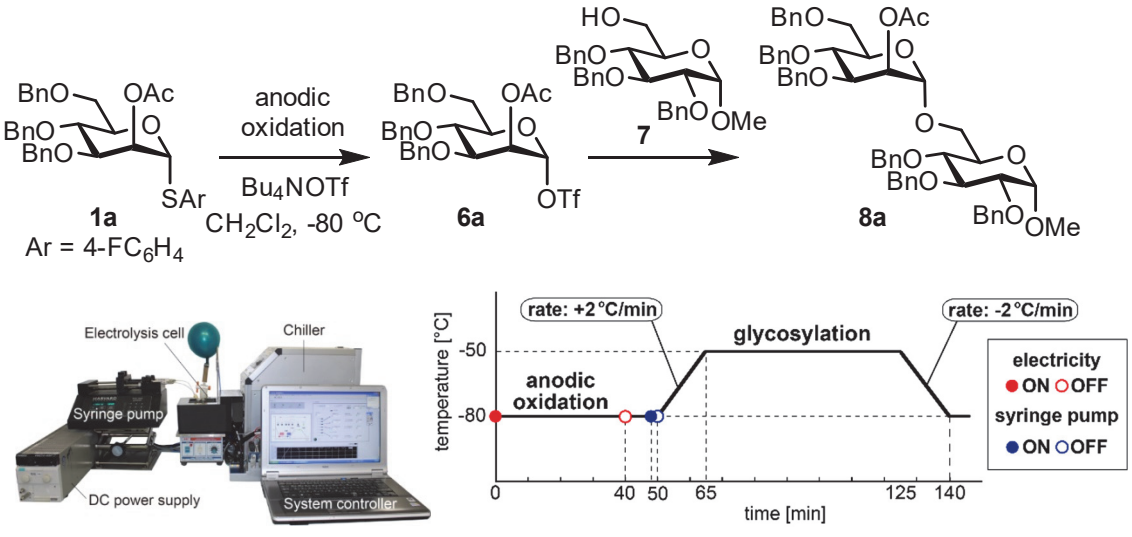
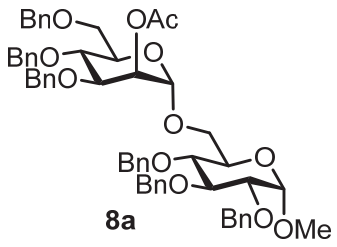
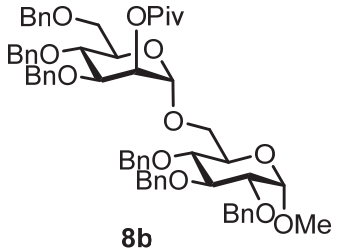


Figure S1.



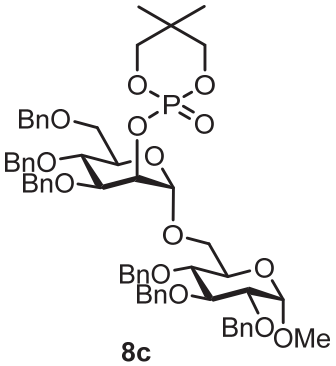
8a

The automated synthesis of disaccharide **8a** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm × 20 mm). In the anodic chamber were placed building block **1a** (121 mg, 0.20 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (10.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (18 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (10.0 mL). The constant current electrolysis (8.0 mA) was carried out at -80 °C with magnetic stirring until 1.0 F/mol of electricity was consumed. After the electrolysis, building block **7** (112 mg, 0.24 mmol) dissolved in CH_2Cl_2 (1.2 mL) was subsequently added by the syringe pump (1.0 mL, 0.20 mmol) under an argon atmosphere at -80 °C, and then the temperature was raised to -50 °C and kept for 60 min. The reaction temperature was cooled down to -80 °C and Et_3N (0.3 mL) was added at -80 °C. After additional stirring at rt for 30 min the reaction mixture was filtered through a short column (4 × 3 cm) of silica gel to remove Bu_4NOTf. The removal of the solvent under reduced pressure and column chromatography (silica gel, hexane/EtOAc 5:2 as an eluent) afforded disaccharide **8a** in 78% isolated yield (146 mg, 0.155 mmol). **Methyl-2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)- 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (8a)**. ^1H NMR ($CDCl_3$, 600 MHz) δ 7.37 (d, *J* = 7.2 Hz, 2 H), 7.34 – 7.19 (m, 26 H), 7.13 (dd, *J* = 7.8, 2.4 Hz, 2 H), 5.39 (*psuedo*-t, *J* = 1.8 Hz, 1 H), 4.99 (d, *J* = 10.2 Hz, 1 H), 4.90 (s, 1 H), 4.87 (d, *J* = 10.8 Hz, 1 H), 4.85 (d, *J* = 10.8 Hz, 1 H), 4.79 (d, *J* = 10.8 Hz, 1 H), 4.78 (d, *J* = 12.6 Hz, 1 H), 4.69 (d, *J* = 12.0 Hz, 1 H), 4.68 (d, *J* = 12.0 Hz, 1 H), 4.62 (d, *J* = 12.0 Hz, 1 H), 4.58 (d, *J* = 4.8 Hz, 1 H), 4.51 (d, *J* = 11.4 Hz, 1 H), 4.49 (d, *J* = 10.8 Hz, 1 H), 4.44 (d, *J* = 10.8 Hz, 1 H), 4.41 (d, *J* = 12.0 Hz, 1 H), 3.98 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.91 (dd, *J* = 9.6, 3.0 Hz, 1 H), 3.87 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.80 (dd, *J* = 11.4, 6.4 Hz, 1 H), 3.72 – 3.70 (m, 2 H), 3.66 (dd, *J* = 10.8, 5.6 Hz, 1 H), 3.62 (d, *J* = 11.4 Hz, 1 H), 3.56 – 3.52 (m, 2 H), 3.43 (pseudo-t, *J* = 9.0 Hz, 1 H), 3.32 (s, 3 H), 2.14 (s, 3 H).



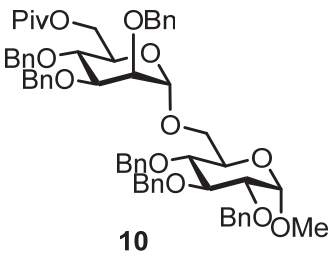
8b

Glycosylation of building blocks **1b** (129 mg, 0.20 mmol) with **7** (112 mg, 0.24 mmol) afforded **8b** (0.12 mmol) in 60% yield (NMR yield). **Methyl-3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (8b)**. TLC (hexane/ EtOAc 5:2): R_f 0.50. $[\alpha]_D$ = +3.7 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.38 (d, *J* = 8.4 Hz, 2 H), 7.35 – 7.20 (m, 26 H), 7.14 (dd, *J* = 7.8, 1.8 Hz, 2 H), 5.39 (dd, *J* = 2.4, 1.8 Hz, 1 H), 4.99 (d, *J* = 10.8 Hz, 1 H), 4.884 (d, *J* = 10.8 Hz, 1 H), 4.881 (d, *J* = 1.8 Hz, 1 H), 4.83 (d, *J* = 11.4 Hz, 1 H), 4.80 (d, *J* = 10.8 Hz, 1 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 4.682 (d, *J* = 12.6 Hz, 1 H), 4.680 (d, *J* = 10.8 Hz, 1 H), 4.591 (d, *J* = 12.0 Hz, 1 H), 4.588 (d, *J* = 3.6 Hz, 1 H), 4.51 (d, *J* = 11.4 Hz, 1 H), 4.47 (*pseudo*-t, *J* = 11.4 Hz, 2 H), 4.41 (d, *J* = 12.0 Hz, 1 H), 3.99 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.92 (dd, *J* = 9.0, 3.0 Hz, 1 H), 3.85 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.84 (dd, *J* = 11.4, 4.2 Hz, 1 H), 3.74 – 3.72 (m, 2 H), 3.65 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.64 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.59 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.55 (dd, *J* = 9.6, 3.6 Hz, 1 H), 3.45 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.32 (s, 3 H), 1.20 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.6, 138.7, 138.5, 138.4, 138.23, 138.16, 138.09, 128.5, 128.43, 128.40, 128.3, 128.25, 128.22, 128.1, 128.05, 127.97, 127.66, 127.65, 127.59, 127.43, 127.40, 98.1, 97.9, 82.1, 80.1, 77.9, 77.7, 75.8, 75.1, 75.0, 74.1, 73.4, 73.1, 71.5, 71.2, 69.6, 68.9, 67.9, 66.1, 55.1, 39.0, 27.2. HRMS (ESI) *m/z* calcd for $C_{60}H_{68}KO_{12}$ $[M+K]^+$, 1019.4342; found, 1019.4373.



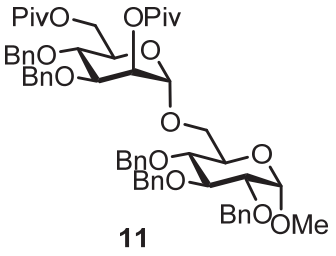
8c

Glycosylation of building blocks **1c** (143 mg, 0.20 mmol) with **7** (113 mg, 0.24 mmol) afforded **8c** (163 mg, 0.12 mmol) in 71% yield (NMR yield, α/β = 4:1). **Methyl-3,4,6-tri-*O*-benzyl-2-*O*-(2,2-dimethyltrimethylenephosphornoyl)-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (8c)**. TLC (hexane/EtOAc 5:2): R_f 0.20. $[\alpha]_D$ = +0.54 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.44 (d, *J* = 6.6 Hz, 2 H), 7.38 – 7.21 (m, 26 H), 7.20 (d, *J* = 7.8 Hz, 2 H), 4.99 (d, *J* = 10.8 Hz, 1 H), 4.95 (d, *J* = 11.4 Hz, 1 H), 4.90 (pseudo-t, *J* = 10.8 Hz, 1 H), 4.84 – 4.82 (m, 2 H), 4.80 (d, *J* = 12.0 Hz, 1 H), 4.66 (d, *J* = 12.6 Hz, 1 H), 4.60 (d, *J* = 11.4 Hz, 1 H), 4.59 (d, *J* = 12.6 Hz, 1 H), 4.54 – 4.48 (m, 4 H), 4.20 (dd, *J* = 9.0, 3.0 Hz, 1 H), 4.17 (s, 1 H), 4.11 (dd, *J* = 10.8, 1.8 Hz, 1 H), 4.08 (dd, *J* = 10.8, 2.4 Hz, 1 H), 3.99 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.81 – 3.72 (m, 2 H), 3.60 (ddd, *J* = 18.0, 9.6, 2.4 Hz, 1 H), 3.54 – 3.51 (m, 2 H), 3.47 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.46 (dd, *J* = 9.6, 3.6 Hz, 1 H), 3.38 (s, 3 H), 3.36 (ddd, *J* = 9.6, 5.6, 1.8 Hz, 1 H), 1.19 (s, 3 H), 0.63 (s, 3 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.7, 138.5, 138.30, 138.26, 138.22, 137.7, 128.50, 128.49, 128.38, 128.35, 128.32, 128.1, 128.0, 127.9, 127.7, 127.62, 127.59, 127.54, 127.53, 99.0, 98.0, 82.3, 80.1, 79.7, 77.8, 75.7, 75.4, 75.2, 74.9, 73.7, 73.31, 73.26, 71.0, 69.8, 69.0, 68.8, 55.2, 53.4, 31.9, 22.0, 20.2. HRMS (ESI) *m/z* calcd for $C_{60}H_{69}NaO_{14}P$ $[M+Na]^+$, 1067.4317; found, 1067.4277.



10

Glycosylation of building blocks **3** (129 mg, 0.20 mmol) with **7** (112 mg, 0.24 mmol) afforded **10** (89 mg, 0.091 mmol) in 45% yield (NMR yield 41%). **Methyl-2,3,4-tri-*O*-benzyl-6-*O*-pivaloyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (10)**. TLC (hexane/ EtOAc 5:2): R_f 0.35. $[\alpha]_D$ = +0.22 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.33 (d, *J* = 7.2 Hz, 2 H), 7.30 – 7.11 (m, 28 H), 4.93 (d, *J* = 10.8 Hz, 1 H), 4.86 (d, *J* = 10.8 Hz, 1 H), 4.83 (d, *J* = 12.6 Hz, 1 H), 4.75 (dd, *J* = 11.4, 3.0 Hz, 1 H), 4.69 (*pseudo*-t, *J* = 11.4 Hz, 2 H), 4.58 (d, *J* = 12.6 Hz, 1 H), 4.49 (d, *J* = 7.2, 3.0 Hz, 1 H), 4.48 (d, *J* = 12.0 Hz, 1 H), 4.42 (*pseudo*-t, *J* = 10.8 Hz, 2 H), 4.35 (dd, *J* = 12.0, 2.4 Hz, 1 H), 4.11 (dd, *J* = 11.4, 6.6 Hz, 1 H), 4.05 (s, 1 H), 4.03 (dd, *J* = 10.2, 1.8 Hz, 2 H), 3.93 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.74 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.70 (ddd, *J* = 9.6, 3.6, 1.8 Hz, 1 H), 3.65 (d, *J* = 3.0 Hz, 1 H), 3.42 (dd, *J* = 10.2, 3.6 Hz, 1 H), 3.39 (dd, *J* = 10.2, 5.4 Hz, 1 H), 3.37 – 3.31 (m, 3 H), 3.23 (s, 3 H), 1.08 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.2, 137.7, 137.6, 137.2, 137.01, 137.00, 136.95, 127.45, 127.42, 127.38, 127.35, 127.2, 127.14, 127.11, 126.9, 126.8, 126.69, 126.68, 126.6, 126.4, 100.5, 96.7, 81.09, 81.07, 78.8, 76.7, 74.7, 74.2, 73.8, 73.7, 72.8, 72.7, 72.5, 72.3, 71.2, 70.5, 68.7, 67.1, 62.6, 54.0, 37.7, 26.1. HRMS (ESI) *m/z* calcd for $C_{60}H_{68}NaO_{12}$ $[M+Na]^+$, 1003.4603; found, 1003.4564.



11

Glycosylation of building blocks **4** (128 mg, 0.20 mmol) with **7** (112 mg, 0.24 mmol) afforded **11** (92 mg, 0.094 mmol) in 47% yield (58% NMR yield). **Methyl-3,4-di-*O*-benzyl-2,6-di-*O*-pivaloyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (11)**. TLC (hexane/ EtOAc 4:1): R_f 0.55. $[\alpha]_D$ = +3.6 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.39 – 7.20 (m, 25 H), 5.40 (dd, *J* = 3.6, 1.8 Hz, 1 H), 4.99 (d, *J* = 10.8 Hz, 1 H), 4.90 (d, *J* = 11.4 Hz, 1 H), 4.87 (d, *J* = 10.8 Hz, 1 H), 4.80 – 4.78 (m, 3 H), 4.69 (d, *J* = 12.6 Hz, 1 H), 4.68 (d, *J* = 10.8 Hz, 1 H), 4.58 (d, *J* = 3.6 Hz, 1 H), 4.50 (d, *J* = 11.4 Hz, 1 H), 4.482 (d, *J* = 12.0 Hz, 1 H), 4.476 (d, *J* = 10.8 Hz, 1 H), 4.23 (dd, *J* = 12.0, 1.8 Hz, 2 H), 4.18

(dd, J = 7.8, 4.2 Hz, 1 H), 3.99 (*pseudo*-t, J = 9.6 Hz, 1 H), 3.90 (dd, J = 9.0, 3.0 Hz, 1 H), 3.80 – 3.71 (m, 4 H), 3.61 (dd, J = 11.4, 1.8 Hz, 1 H), 3.54 (dd, J = 9.6, 3.6 Hz, 1 H), 3.41 (*pseudo*-t, J = 9.0 Hz, 1 H), 3.32 (s, 3 H), 1.22 (s, 9 H), 1.19 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.0, 177.4, 138.6, 138.05, 138.02, 137.8, 128.4, 128.33, 128.28, 128.2, 128.02, 127.97, 127.91, 127.86, 127.7, 127.64, 127.60, 127.58, 127.4, 97.9, 97.7, 82.0, 80.0, 77.8, 77.7, 75.7, 75.1, 74.9, 73.9, 73.3, 71.2, 69.7, 69.5, 67.7, 66.0, 63.0, 55.0, 27.2, 27.1. HRMS (ESI) *m/z* calcd for $C_{58}H_{70}KO_{13}$ $[M+K]^+$, 1013.4448; found, 1019.4494.

4. Automated synthesis of trisaccharides

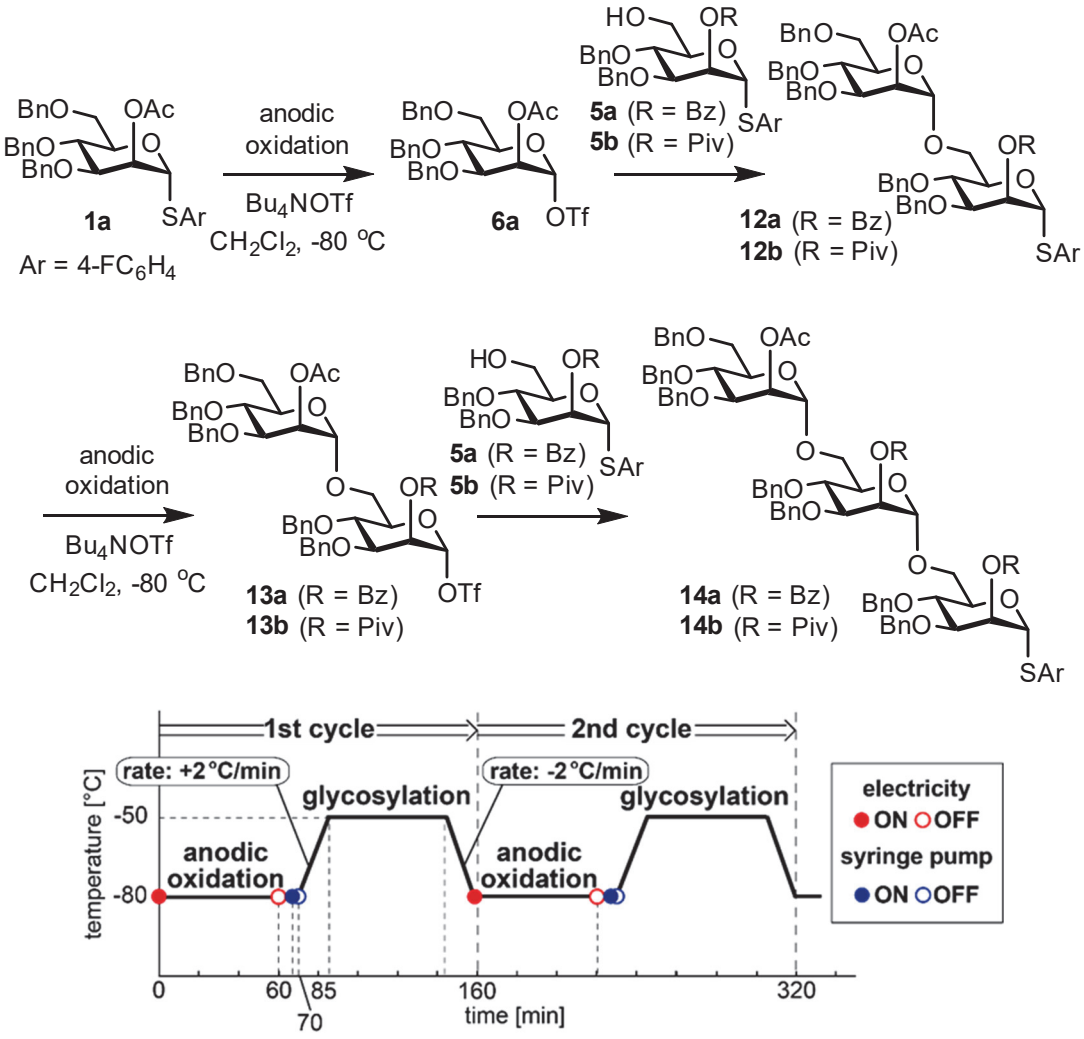
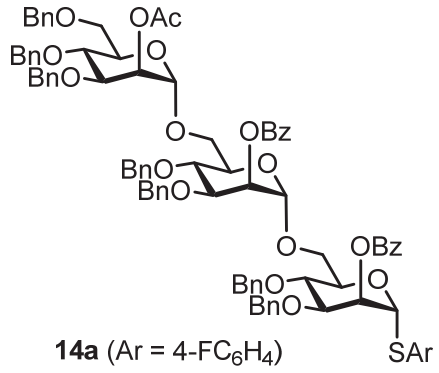
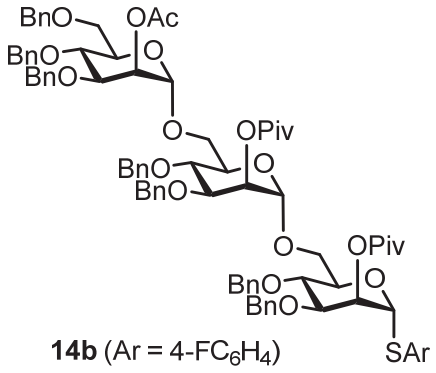


Figure S2.



14a (Ar = 4-FC_6H_4)

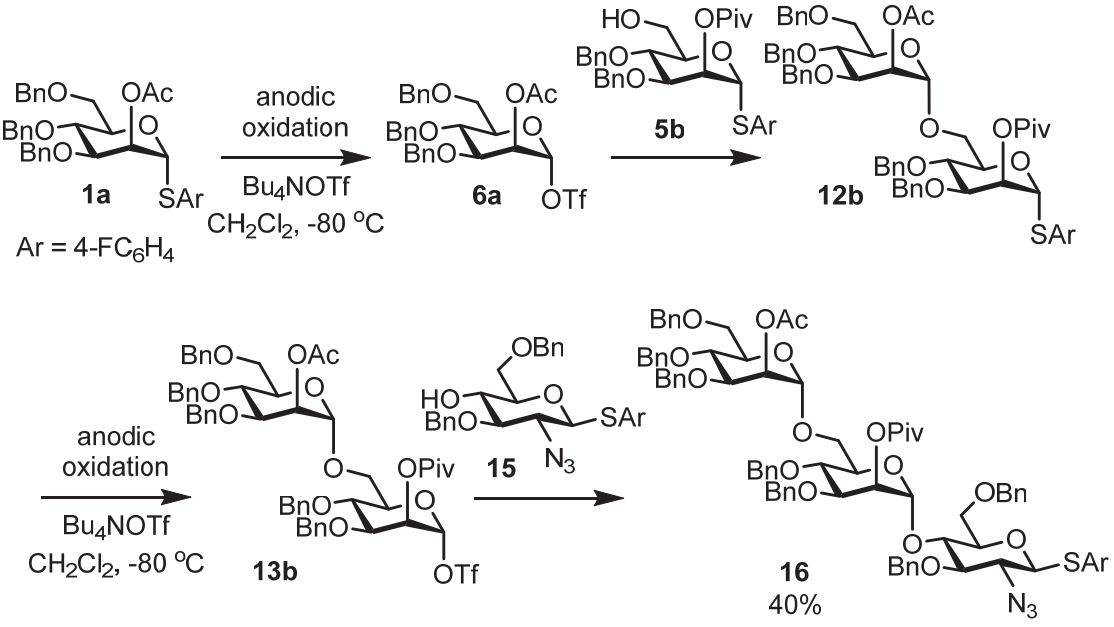
The automated synthesis of trisaccharide **14a** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm × 20 mm). In the anodic chamber were placed terminal building block **1a** (181 mg, 0.30 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.5 mL). In the cathodic chamber were placed trifluoromethane sulfonic acid (55 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.5 mL). The constant current electrolysis (8.0 mA) was carried out at -80 °C with magnetic stirring until 1.0 F/mol of electricity was consumed. After the electrolysis, building block **5a** (362 mg, 0.63 mmol) dissolved in CH_2Cl_2 (2.1 mL) was subsequently added by the syringe pump (1.0 mL (0.30 mmol) for one cycle) under an argon atmosphere at -80 °C, and then the temperature was raised to -50 °C and kept for 60 min. The reaction temperature was cooled down to -80 °C and the second cycle starts automatically. After the 2nd cycle, Et_3N (0.3 mL) was added and the mixture was filtered through a short column (4 × 3 cm) of silica gel to remove Bu_4NOTf. Removal of the solvent under reduced pressure and short column (silica gel, hexane/EtOAc 1:1 as an eluent) afforded a mixture of oligosaccharides. The crude product was purified by PR-GPC with $CHCl_3$ as an eluent and trisaccharide **14a** was obtained in 15% isolated yield (65 mg, 0.043 mmol). **4-Fluorophenyl-2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-α-D-mannopyranoside (14a)**. TLC (hexane/EtOAc 4:1): R_f 0.25. $[\alpha]_D$ = +6.3 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 8.11 (td, *J* = 8.4, 1.8 Hz, 4 H), 7.51 – 7.43 (m, 8 H), 7.35 – 7.08 (m, 35 H), 6.99 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.88 (dd, *J* = 3.0, 1.8 Hz, 1 H), 5.74 (dd, *J* = 3.0, 2.4 Hz, 1 H), 5.53 (dd, *J* = 3.0, 2.4 Hz, 1 H), 5.50 (d, *J* = 1.8 Hz, 1 H), 5.01 (d, *J* = 1.8 Hz, 1 H), 4.98 (d, *J* = 1.8 Hz, 1 H), 4.92 (d, *J* = 10.8 Hz, 1 H), 4.86 (d, *J* = 11.4 Hz, 1 H), 4.84 (d, *J* = 10.8 Hz, 1 H), 4.83 (d, *J* = 10.8 Hz, 1 H), 4.77 (d, *J* = 10.8 Hz, 1 H), 4.65 (d, *J* = 10.8 Hz, 1 H), 4.61 (d, *J* = 12.0 Hz, 1 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.50 (d, *J* = 11.4 Hz, 1 H), 4.43 (d, *J* = 10.8 Hz, 1 H), 4.42 (d, *J* = 12.0 Hz, 1 H), 4.41 – 4.37 (m, 4 H), 4.04 (dd, *J* = 3.0, 1.2 Hz, 1 H), 4.03 (dd, *J* = 3.0, 1.8 Hz, 1 H), 3.98 (dd, *J* = 11.4, 5.4 Hz, 1 H), 3.95 – 3.91 (m, 3 H), 3.88 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.85 (dd, *J* = 11.4, 3.0 Hz, 1 H), 3.75 (d, *J* = 9.6 Hz, 1 H), 3.72 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.66 (ddd, *J* = 9.6, 4.2, 1.8 Hz, 1 H), 3.62 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.59 (dd, *J* = 10.8, 1.2 Hz, 1 H), 3.50 (dd, *J* = 10.2, 1.2 Hz, 1 H), 2.15 (s, 3 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.3, 165.7, 165.6, 162.7 (d, *J* = 246.6 Hz), 138.5, 138.4, 138.2, 138.1, 137.66, 137.63, 137.5, 134.2 (d, *J* = 8.6 Hz), 133.5, 133.3, 129.95, 129.88, 129.80, 128.7, 128.63, 128.48, 128.45, 128.43, 128.36, 128.34, 128.31, 128.23, 128.17, 127.9, 127.82, 127.79, 127.76, 127.74, 127.72, 127.6, 127.5, 127.4, 116.4 (d, *J* = 21.9 Hz), 98.24, 98.21, 87.0, 78.8, 78.3, 77.8, 75.3, 75.2, 75.1, 74.4, 74.1, 73.9, 73.4, 72.0, 71.8, 71.7, 71.5, 71.4, 71.0, 70.5, 68.6, 68.5, 68.3, 66.6, 65.8, 21.2. HRMS (ESI) *m/z* calcd for $C_{89}H_{87}FKO_{18}S$ $[M+K]^+$, 1517.5495; found, 1517.5422.



14b (Ar = 4-FC_6H_4)

Glycosylation of building blocks **1a** (182 mg, 0.30 mmol) with **5b** (351 mg, 0.63 mmol) afforded **14b** (102 mg, 0.070 mmol) in 24% yield. **4-Fluorophenyl-2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-ma-nnopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-α-D-mannopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivalo-yl-1-thio-α-D-mannopyranosde (14b)**. TLC (hexane/ EtOAc 4:1): R_f 0.25. $[\alpha]_D$ = +6.6 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.43 (dd, *J* = 7.2, 5.4 Hz, 2 H), 7.32 (d, *J* = 4.2 Hz, 4 H), 7.30 – 7.21 (m, 27 H), 7.19 – 7.18 (m, 2 H), 7.10 (dd, *J* = 6.0, 1.8 Hz 2 H), 7.00 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.59 (dd, *J* = 2.4, 1.8 Hz, 1 H), 5.46 (dd, *J* = 2.4, 1.8 Hz, 1 H), 5.46 (dd, *J* = 2.4, 1.8 Hz, 1 H), 5.42 (dd, *J* = 3.0, 2.4 Hz, 1 H), 5.34 (d, *J* = 1.8 Hz, 1 H), 4.96 (d, *J* = 1.8 Hz, 1 H), 4.95 (d, *J* = 10.8 Hz, 1 H), 4.92 (d, *J* = 11.4 Hz, 1 H), 4.83 (d, *J* = 9.6 Hz, 1 H), 4.82 (d, *J* = 1.8 Hz, 1 H), 4.70 (d, *J* = 10.8 Hz, 1 H), 4.67 (d, *J* = 10.8 Hz, 1 H), 4.65 (d, *J* = 9.6 Hz, 1 H), 4.63 (d, *J* = 12.0 Hz, 1 H), 4.55 (d, *J* = 10.8 Hz, 1 H), 4.52 (d, *J* = 11.4 Hz, 1 H), 4.50 (d, *J* = 11.4 Hz, 1 H), 4.424 (d, *J* = 10.8 Hz, 1 H), 4.420 (d, *J* = 10.8 Hz, 1 H), 4.41 (d, *J* = 12.0 Hz, 1 H), 4.39 (d, *J* = 10.8 Hz, 1 H), 4.31 (dd, *J* = 9.6, 2.4 Hz, 1 H), 3.95 – 3.89 (m, 4 H), 3.86 (d, *J* = 9.6 Hz, 1 H), 3.83 – 3.80 (m, 3 H), 3.68 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.64 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.63 (dd, *J* = 10.2, 3.6 Hz, 1 H), 3.55 (dd, *J* = 11.4, 1.2 Hz, 1 H), 3.52 (dd, *J* = 10.8, 1.8 Hz, 1 H), 2.13 (s, 3 H), 1.23 (s, 9 H), 1.21 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.5, 177.4, 170.2, 162.8 (d, *J* = 247.1 Hz), 138.6, 138.4, 138.2, 138.1, 137.93, 137.89, 137.7, 134.4 (d, *J* = 8.1 Hz), 128.69, 128.67, 128.47, 128.46, 128.44, 128.33, 128.29, 128.27, 128.17, 128.16, 128.07, 127.9, 127.84, 127.82, 127.79, 127.7, 127.62, 127.55, 116.4 (d, *J* = 21.9 Hz), 98.2, 98.0, 86.8, 78.80, 78.76, 78.5, 75.23, 75.18, 75.15, 74.2, 74.1, 73.8, 73.4, 71.74, 71.72, 71.5, 71.4, 70.9, 69.5, 68.6, 68.2, 67.6, 66.4, 65.5, 39.1, 39.0, 27.28, 27.25, 21.2. HRMS (ESI) *m/z* calcd for $C_{85}H_{95}FKO_{18}S$ $[M+K]^+$, 1477.6121; found, 1477.6129.

5. Automated synthesis of the core trisaccharide of a GPI anchor oligosaccharide



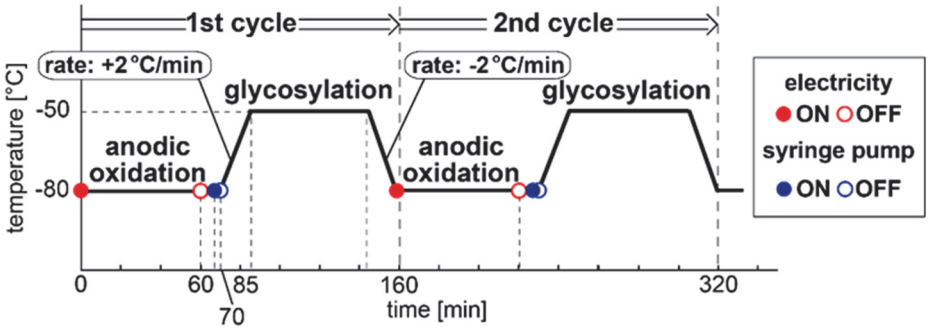
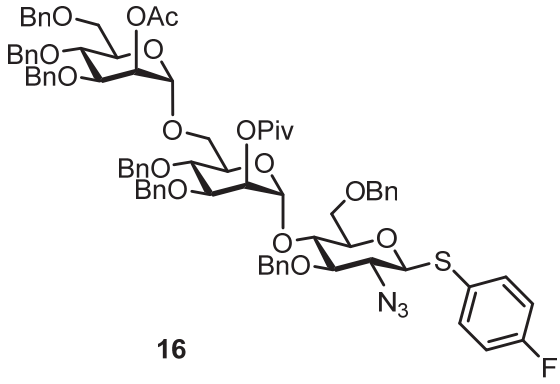


Figure S3.



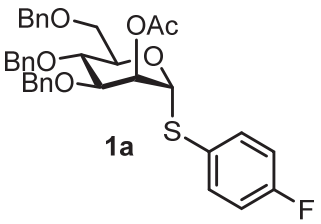
16

The automated synthesis of tetrasaccharide **16** (Ar = 4-FC_6H_4) was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm × 20 mm). In the anodic chamber were placed terminal building block **1a** (182 mg, 0.30 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.5 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (55 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.5 mL). The constant current electrolysis (8.0 mA) was carried out at -80 °C with magnetic stirring until 1.0 F/mol of electricity was consumed. After the electrolysis, the second building block **5b** (167 mg, 1.0 mmol) dissolved in CH_2Cl_2 (1.0 mL) was subsequently added by the syringe pump under an argon atmosphere at -80 °C, and then the temperature was raised to -50 °C and kept for 60 min. The reaction temperature was cooled down to -80 °C and the second cycle starts automatically. The second building block **15** (164 mg, 1.1 mmol) dissolved in CH_2Cl_2 (1.1 mL) was subsequently added by the syringe pump under an argon atmosphere at -80 °C, and then the temperature was raised to -50 °C and kept for 60 min. After the 2nd cycle, the reaction was quenched by adding Et_3N (0.3 mL) at -80 °C. Removal of the solvent under reduced pressure and column chromatography (silica gel, hexane/EtOAc 1:1 as an eluent) afforded a mixture of oligosaccharides (201 mg). The crude product was purified by PR-GPC with $CHCl_3$ as an eluent and trisaccharide **16** was obtained in 40% isolated yield (168 mg, 0.12 mmol). **4-Fluorophenyl-2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*- pivaloyl-α-D-mannopyranosyl-(1→6)-3,6-di-*O*-benzyl-2-*O*-deoxyl-2-azido-1-thio-α-D-glucopyranoside (16)**. TLC (hexane/EtOA-c 3:1): R_f 0.40. $[\alpha]_D$ = +1.2 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.55 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.34 – 7.20 (m, 33 H), 7.11 (dd, *J* = 7.2, 3.6 Hz 2 H), 6.89 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.44 – 5.43 (m, 2 H), 5.30 (d, *J* = 1.8 Hz, 1 H), 4.89 – 4.87 (m, 3 H), 4.84 (d, *J* = 11.4 Hz, 1 H), 4.78 (d, *J* = 10.8 Hz, 1 H), 4.68 (d, *J* = 10.8 Hz, 1 H), 4.63 (d, *J* = 12.0 Hz, 1 H), 4.60 (d, *J* = 10.8 Hz, 1 H), 4.55 (d, *J* = 11.4 Hz, 1 H), 4.51 – 4.49 (m, 2 H), 4.45 (d, *J* = 10.8 Hz, 1 H), 4.44 (d, *J* = 10.8 Hz, 1 H), 4.42 (d, *J* = 12.0 Hz, 1 H), 4.39 (d, *J* = 10.8 Hz, 1 H), 4.34 (d, *J* = 10.2 Hz, 1 H), 3.91 (dd, *J* = 9.0, 3.0 Hz, 1 H), 3.87 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.86 (dd, *J* = 9.0, 3.0 Hz, 1 H), 3.81 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.78 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 3.76 (dd, *J* = 11.4, 3.6 Hz, 1 H), 3.74 – 3.72 (m, 2 H), 3.68 (ddd, *J* = 9.0, 3.6, 1.2 Hz, 1 H), 3.65 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.54

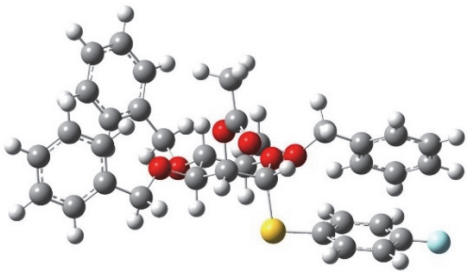
– 3.49 (m, 2 H), 3.46 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.42 (dt, *J* = 10.2, 3.6 Hz, 1 H), 3.28 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 2.11 (s, 3 H), 1.11 (s, 9 H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.2, 170.1, 163.2 (d, *J* = 247.5 Hz), 138.6, 138.29, 138.27, 138.1, 137.9, 137.26, 136.3 (d, *J* = 9.0 Hz), 128.55, 128.48, 128.38, 128.36, 128.3, 128.2, 127.97, 127.95, 127.91, 127.86, 127.82, 127.76, 127.74, 127.67, 127.64, 127.58, 127.50, 125.78, 125.76, 116.2 (d, *J* = 21.0 Hz), 98.7, 98.3, 86.2, 85.2, 78.74, 78.68, 78.4, 75.23, 75.21, 75.17, 74.2, 73.7, 73.6, 73.5, 72.0, 71.8, 71.6, 71.4, 69.1, 68.7, 68.2, 68.0, 65.7, 65.2, 38.9, 27.2, 21.2. HRMS (ESI) *m/z* calcd for $C_{80}H_{86}FN_3NaO_{16}S$ $[M+Na]^+$, 1418.5611; found, 1418.5614.

6. DFT calculations of building blocks

Calculations of the building blocks **1-5** were carried out with the three-parameter functional of Becke,[7] the correlation functional of Lee, Yang, and Parr (B3LYP),[8] and the 6-31G* basis set.[9] Geometries were optimized and vibrational analyses were performed at the B3LYP/6-31G* level of theory. The vibrational analyses were used to confirm energetic stability of the optimized structures. All of the calculations were carried out with the Gaussian 09 suite of programs.[10] Cartesian coordinates and energies of computationally characterized species are as follows:



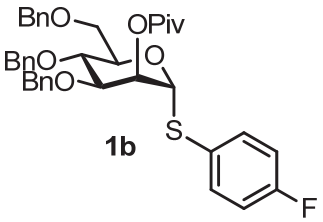
HOMO energy: $\mathbf{E_{HOMO}(1a)}$ = -0.23002 hartree (-6.259 eV)



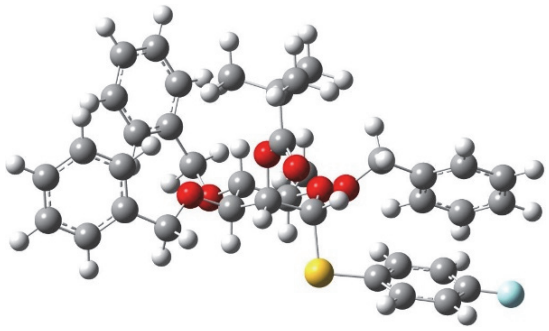
(white: H, gray: C, blue: N, red: O, yellow, S, light blue: F)

Ato	X	Y	Z	Ato	X	Y	Z
C	0.6727	-	0.3253	C	7.1109	1.9097	1.0667
C	-	-	0.3950	C	7.5675	2.5558	-
C	-	-	-	C	6.6453	3.0489	-
C	-	0.8834	-	C	5.2751	2.9041	-
C	0.5317	0.8573	-	H	1.1194	-	1.1896
O	1.0750	-	0.3935	H	-	-	0.2937
O	-	1.6039	-	H	-	-	-
C	-	3.1131	-	H	-	1.3148	0.3986
S	1.2834	-	-	H	0.8187	0.4733	-
O	-	-	-	H	0.8296	2.8920	-
C	1.1913	2.2212	-	H	0.9160	2.6444	0.5471
C	3.0168	-	-	H	2.8185	-	-
O	2.6022	2.1558	-	H	5.2536	-	0.1133
C	3.5026	-	-	H	5.9462	-	-
C	4.8560	-	-	H	3.5313	-	-
C	5.7050	-	-	H	-	3.3146	-2.424
C	5.2510	-	-	H	-	3.5669	-
C	3.8988	-	-	H	-	4.6936	0.6482
C	-	2.9484	-	H	-	5.0664	2.1021
C	-	4.0893	0.5107	H	-	-	-
C	-	4.3021	1.3299	H	-	-	-
C	-	-	-	H	-	-	1.1096

C	-	-	-	H	-	-	1.6789
C	-	-	0.3710	H	-	-	-
C	-	-	0.6823	H	-	-	-
C	-	-	-	H	-	-	-
C	-	-	-	H	-	-	4.2538
C	-	-	-	H	-	-	3.8053
F	7.0142	-	0.0751	H	-	-	4.7714
O	-	-	1.6839	H	-	3.6872	1.7969
C	-	-	2.7062	H	-	1.9247	0.0392
C	-	-	3.9704	H	-	1.5599	-
O	-	-	2.5965	H	3.1292	1.1946	1.1988
C	-	3.5275	1.1593	H	3.0003	2.9598	1.2915
C	-5.419	2.5416	0.1688	H	5.3913	1.2397	2.1763
C	-	2.3382	-	H	7.8203	1.5156	1.7897
C	3.3314	2.1233	0.6510	H	8.6338	2.6695	-
C	4.8104	2.2560	0.3651	H	6.9929	3.5482	-
C	5.7411	1.7566	1.2850	H	4.5559	3.2788	-



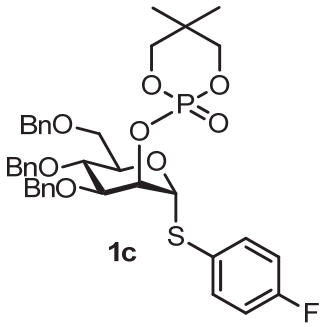
HOMO energy: $\mathbf{E_{HOMO}(1b)}$ = -0.22858 hartree (-6.220 eV)



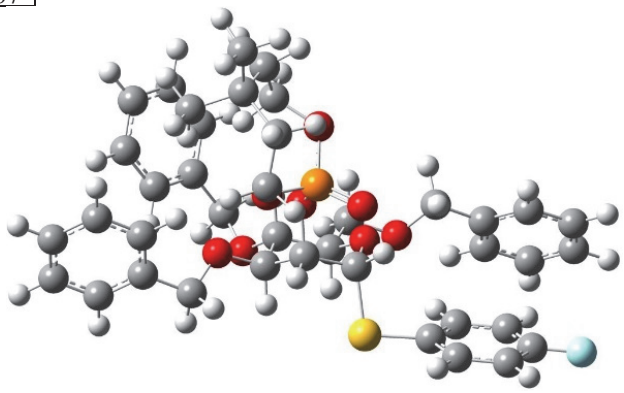
(white: H, gray: C, blue: N, red: O, yellow, S, light blue: F)

Atom	X	Y	Z	Atom	X	Y	Z
C	-0.78967	1.31083	-0.08153	C	-6.83922	-3.08481	-0.77531
C	0.742043	1.413059	-0.05943	C	-5.45738	-2.94614	-0.63281
C	1.377683	0.430057	-1.05434	H	-1.21054	1.874648	0.751512
C	0.86068	-0.99932	-0.81937	H	1.052333	2.442386	-0.24963
C	-0.69081	-0.96672	-0.84529	H	1.066591	0.721152	-2.06986
O	-1.19936	-0.02196	0.107456	H	1.221024	-1.35664	0.152556
O	1.359484	-1.80871	-1.87851	H	-1.00702	-0.66385	-1.85257
C	2.915541	-3.26066	-0.5697	H	-1.02769	-3.03728	-1.27026
S	-1.43248	2.118735	-1.64209	H	-1.03023	-2.65764	0.469972
O	2.789693	0.448412	-0.9626	H	-2.97897	4.483143	-1.07697
C	-1.34903	-2.30622	-0.52252	H	-5.40688	4.834757	-0.56877
C	-3.15917	2.338706	-1.21142	H	-6.061	0.599044	-0.73266
O	-2.7647	-2.24122	-0.60158	H	-3.655	0.235384	-1.28334
C	-3.65324	3.635087	-1.01065	H	2.063207	-3.55613	-2.5264
C	-5.00278	3.839902	-0.72495	H	0.921544	-3.73833	-1.19471
C	-5.83891	2.733213	-0.63074	H	1.938239	-4.77818	0.608844
C	-5.37591	1.435591	-0.81929	H	3.840265	-5.07884	2.166647
C	-4.02861	1.241041	-1.12301	H	3.170899	1.240995	-2.84475
C	1.770049	-3.13975	-1.55586	H	3.025652	2.431656	-1.54152
C	2.84096	-4.18382	0.479837	H	4.780993	1.01722	0.533497
C	3.913207	-4.35594	1.358199	H	7.240243	1.054347	0.883332
C	3.412728	1.428293	-1.7871	H	8.765999	1.439837	-1.04329
C	4.908542	1.392952	-1.57884	H	7.815928	1.786813	-3.31636
C	5.449924	1.196222	-0.30203	H	5.364416	1.744734	-3.65587
C	6.831915	1.210019	-0.11206	H	5.905531	-3.72054	1.883723

C	7.689718	1.427467	-1.19332	H	6.042104	-2.05404	0.037328
C	7.156782	1.624484	-2.46765	H	4.135687	-1.76009	-1.51161
C	5.773903	1.601454	-2.65817	H	-3.19136	-1.13778	1.110347
F	-7.14393	2.926361	-0.3468	H	-3.07865	-2.89248	1.335185
O	1.204187	1.026599	1.253019	H	0.688208	-0.45034	3.318582
C	1.262458	1.999853	2.200472	H	-0.22392	0.798139	4.188884
C	1.768396	1.44816	3.537672	H	1.11928	-0.03385	4.990874
O	0.937419	3.148138	1.985797	H	3.884607	1.561642	2.977422
C	5.070245	-3.59306	1.199905	H	3.132211	-0.00445	2.613362
C	5.149328	-2.66084	0.161294	H	3.532995	0.425458	4.28972
C	4.081596	-2.49879	-0.72008	H	0.870085	3.069949	4.695966
C	-3.43197	-2.10315	0.648418	H	2.538052	3.380647	4.208419
C	0.774428	0.372803	4.03324	H	2.201479	2.224732	5.514922
C	3.163636	0.816625	3.334611	H	-5.39804	-1.09735	2.218794
C	1.848188	2.60238	4.548771	H	-7.84644	-1.36148	1.977911
C	-4.92501	-2.23421	0.448075	H	-8.78088	-2.63052	0.050928
C	-5.80009	-1.66448	1.381665	H	-7.23956	-3.63458	-1.62334
C	-7.18102	-1.81099	1.245489	H	-4.78201	-3.37608	-1.36473
C	-7.7055	-2.5215	0.163467				



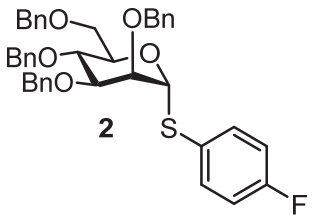
HOMO energy: $E_{HOMO(1c)}$ = -0.22578 hartree (-6.144 eV)



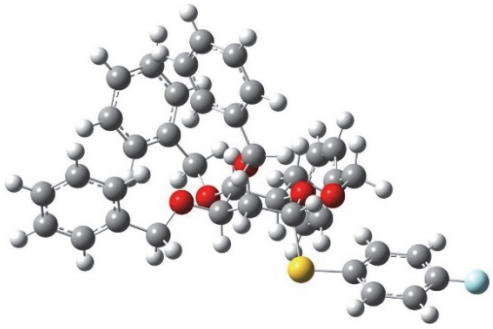
(white: H, gray: C, blue: N, red: O, yellow, S, light blue: F)

Atom	X	Y	Z	Atom	X	Y	Z
C	1.30257	0.70389	0.872596	C	-5.47585	4.324653	-3.11048
C	-0.21529	0.531747	1.032451	C	-5.64459	2.469685	-1.44087
C	-0.57311	-0.91982	1.385237	H	1.515657	1.686614	0.451225
C	0.031492	-1.88712	0.353752	H	-0.59858	1.219634	1.791781
C	1.555713	-1.61131	0.266609	H	-0.11508	-1.15827	2.357524
O	1.81056	-0.23415	-0.04218	H	-0.44639	-1.71815	-0.61814
O	-0.20676	-3.21151	0.819494	H	1.999506	-1.84923	1.243044
C	-1.89375	-3.95967	-0.86258	H	2.13685	-3.49555	-0.56729
S	2.098426	0.658287	2.565803	H	1.853963	-2.22962	-1.78925
O	-1.97372	-1.09956	1.454142	H	3.212322	3.236318	3.221944
C	2.279361	-2.43485	-0.79591	H	5.459068	4.261906	2.805513
C	3.68869	1.399821	2.197824	H	6.676439	0.744302	0.674999
O	3.679472	-2.20155	-0.78943	H	4.45788	-0.3072	1.115981
C	3.971557	2.687358	2.674055	H	-0.61261	-5.12166	0.421615
C	5.218929	3.267045	2.445056	H	0.220774	-4.31432	-0.90709
C	6.16583	2.546503	1.726309	H	-1.08121	-4.32783	-2.82461
C	5.911976	1.270015	1.236934	H	-3.25123	-4.07325	-3.99171
C	4.667489	0.691135	1.485043	H	-2.09711	-1.64586	3.457189
C	-0.57223	-4.19057	-0.15539	H	-2.25476	0.092085	3.136285
C	-1.97859	-4.09959	-2.25251	H	-4.23077	0.492862	1.203885
C	-3.20172	-3.95726	-2.912	H	-6.70761	0.291505	1.073353
C	-2.52074	-0.90866	2.758507	H	-7.89502	-1.37706	2.484957
C	-4.02067	-1.05148	2.684287	H	-6.59737	-2.83968	4.022006
C	-4.75819	-0.22986	1.820698	H	-4.13007	-2.63544	4.139874
C	-6.14472	-0.34909	1.747693	H	-5.30674	-3.54411	-2.69315

C	-6.81329	-1.28725	2.540657	H	-5.16631	-3.2622	-0.22244
C	-6.086	-2.10648	3.40391	H	-2.99563	-3.52237	0.93298
C	-4.69499	-1.98997	3.470919	H	3.731077	-0.29599	-1.62555
F	7.372269	3.106324	1.496621	H	3.789646	-1.64183	-2.77708
O	-0.84069	0.813623	-0.24349	H	-2.45199	0.843234	-3.46409
P	-1.26777	2.314077	-0.63179	H	-3.20727	0.866271	-1.86471
O	-2.71138	2.415227	0.093783	H	-4.28452	3.507225	0.719718
O	-0.30835	3.390443	-0.30819	H	-2.76681	4.421108	0.620545
C	-4.35343	-3.65929	-2.1835	H	-4.50283	1.93067	-3.83501
C	-4.27626	-3.50591	-0.79621	H	-3.25942	3.170499	-3.87879
C	-3.05631	-3.66024	-0.14045	H	-2.8934	4.576114	-1.80038
C	4.143309	-1.29907	-1.7886	H	-4.35822	5.153069	-1.03909
O	-1.60016	2.178765	-2.18812	H	5.743821	0.716301	-2.63906
C	-2.79495	1.496098	-2.65696	H	8.216248	0.790568	-2.71356
C	-3.40024	3.691136	0.105935	H	9.548454	-1.13362	-1.86502
C	-3.80579	2.499491	-3.2026	H	8.379892	-3.13044	-0.95177
C	-3.79148	4.239117	-1.26932	H	5.896726	-3.2018	-0.89625
C	5.654855	-1.25764	-1.77494	H	-6.06024	3.777374	-3.85995
C	6.320707	-0.13342	-2.27983	H	-4.82025	5.024539	-3.6427
C	7.714903	-0.08976	-2.31983	H	-6.1753	4.914348	-2.50605
C	8.46246	-1.16862	-1.84229	H	-6.31128	1.938613	-2.13096
C	7.805232	-2.28886	-1.33033	H	-6.27574	3.073314	-0.77664
C	6.410349	-2.33593	-1.3002	H	-5.1335	1.721778	-0.82695
C	-4.65846	3.358024	-2.22382				



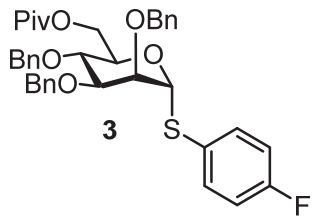
HOMO energy: $\mathbf{E_{HOMO(2)}}$ = -0.22098 hartree (-6.013 eV)



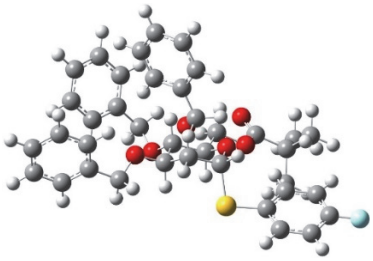
(white: H, gray: C, blue: N, red: O, yellow, S, light blue: F)

Atom	X	Y	Z	Atom	X	Y	Z
C	-1.06026	1.933052	-0.17857	C	-4.74023	-5.77851	1.154475
C	0.444473	1.722692	-0.44524	C	-4.89507	-5.98665	-0.21635
C	0.688679	0.379481	-1.15883	C	-4.88541	-4.89407	-1.08775
C	0.056637	-0.76931	-0.35661	C	-4.72952	-3.60142	-0.58942
C	-1.4482	-0.43982	-0.1839	H	-1.20635	2.772023	0.504889
O	-1.61415	0.823274	0.475164	H	0.834768	2.548345	-1.05819
O	0.217845	-1.96978	-1.10471	H	0.190083	0.401699	-2.13974
C	1.957284	-3.1009	0.27969	H	0.549781	-0.84006	0.619225
S	-1.9255	2.409877	-1.77072	H	-1.90248	-0.39277	-1.18375
O	2.076125	0.150498	-1.33012	H	-2.04777	-2.45887	0.243661
C	-2.22788	-1.45156	0.637156	H	-1.8981	-1.41621	1.687814
C	-3.45409	3.091903	-1.12555	H	-3.10567	5.012406	-2.04288
O	-3.60895	-1.12795	0.543551	H	-5.27086	5.988589	-1.25399
C	-3.78964	4.414242	-1.44865	H	-6.22232	2.303355	0.714395
C	-4.99267	4.968193	-1.01136	H	-4.08814	1.294616	-0.09911
C	-5.84035	4.188253	-0.23404	H	0.546428	-3.93794	-1.11919
C	-5.52895	2.877147	0.107935	H	-0.16714	-3.37725	0.394327
C	-4.33565	2.320193	-0.3519	H	1.235471	-3.73382	2.209016

C	0.587518	-3.13974	-0.3693	H	3.477718	-3.76597	3.261511
C	2.111283	-3.46238	1.622727	H	2.085304	-0.03967	-3.39957
C	3.375098	-3.48195	2.217378	H	2.343839	1.605272	-2.79114
C	2.576259	0.542813	-2.60521	H	4.440876	1.378759	-0.80283
C	4.070024	0.327019	-2.64609	H	6.89718	1.074209	-0.89484
C	4.890987	0.847153	-1.63606	H	7.931274	-0.16604	-2.78847
C	6.272406	0.668037	-1.68608	H	6.48618	-1.0978	-4.58651
C	6.853766	-0.02934	-2.74933	H	4.03015	-0.79005	-4.4874
C	6.043872	-0.55006	-3.75853	H	0.81514	3.481735	1.753224
C	4.658893	-0.37497	-3.70267	H	2.047444	3.487294	0.481583
F	-7.00215	4.720504	0.201591	H	5.484812	-3.1408	1.930804
O	1.136674	1.658299	0.789099	H	5.22427	-2.46853	-0.45302
C	1.62583	2.885018	1.305158	H	2.980261	-2.44044	-1.49405
C	2.694357	2.601944	2.338904	H	-5.42435	-1.47265	1.316187
C	4.499517	-3.12846	1.471533	H	-4.0987	-1.99427	2.369447
C	4.354782	-2.75665	0.131368	H	3.288913	0.729638	1.46499
C	3.093051	-2.74673	-0.46004	H	5.095433	0.317062	3.11499
C	-4.4468	-1.96912	1.324283	H	5.524443	1.963195	4.934454
C	3.484556	1.449113	2.253275	H	4.122086	4.012174	5.094552
C	4.496981	1.221629	3.18669	H	2.312852	4.408867	3.453038
C	4.735861	2.14299	4.20834	H	-4.44539	-4.32584	2.719083
C	3.949952	3.293464	4.29747	H	-4.73964	-6.62334	1.838344
C	2.930977	3.516879	3.370513	H	-5.01888	-6.99388	-0.60525
C	-4.57451	-3.38318	0.786151	H	-5.00147	-5.05023	-2.15717
C	-4.57452	-4.48308	1.64997	H	-4.71612	-2.75003	-1.26445



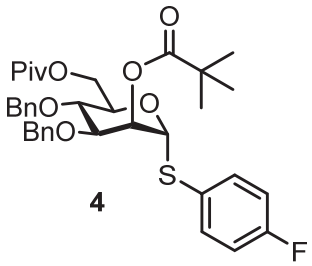
HOMO energy: $\mathbf{E_{HOMO}(3)}$ = -0.22482 hartree (-6.118 eV)



(white: H, gray: C, blue: N, red: O, yellow, S, light blue: F)

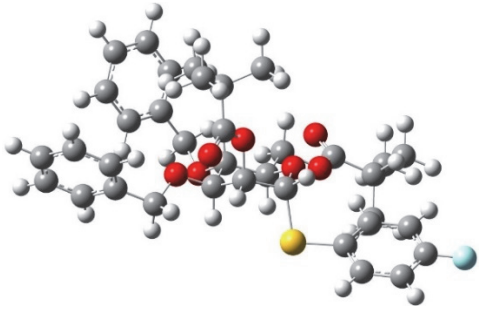
Atom	X	Y	Z	Atom	X	Y	Z
C	-1.2037	1.399655	-0.202	C	-5.81842	-2.49203	-0.82229
C	0.328936	1.429956	-0.36937	C	-6.12975	-4.37128	0.837339
C	0.808471	0.200895	-1.16542	H	-1.52272	2.16699	0.506289
C	0.319835	-1.08796	-0.48657	H	0.623989	2.354942	-0.88628
C	-1.22362	-1.00175	-0.34579	H	0.360434	0.230395	-2.17131
O	-1.62041	0.18159	0.359754	H	0.793262	-1.17145	0.498126
O	0.655283	-2.1919	-1.31899	H	-1.65322	-0.98502	-1.35735
C	2.604496	-3.15685	-0.10321	H	-1.49272	-3.11818	-0.02442
S	-2.02356	1.834237	-1.82711	H	-1.52044	-2.14823	1.466624
O	2.219426	0.18106	-1.26836	H	-3.51289	4.219594	-2.38435
C	-1.81642	-2.17303	0.412482	H	-5.79418	4.994817	-1.71294
C	-3.63341	2.382433	-1.26025	H	-6.30724	1.462719	0.658664
O	-3.25305	-2.08717	0.323811	H	-4.0484	0.647471	-0.04431
C	-4.12607	3.607865	-1.72963	H	1.219436	-4.10221	-1.45702
C	-5.39539	4.050281	-1.35764	H	0.542668	-3.70419	0.124071
C	-6.1511	3.263401	-0.49675	H	2.087184	-3.90931	1.848833
C	-5.6832	2.048541	-0.00851	H	4.383084	-3.70461	2.756424
C	-4.42395	1.599013	-0.40529	H	2.356996	0.389418	-3.33199
C	1.211481	-3.34073	-0.66903	H	2.368342	1.908556	-2.41866
C	2.885632	-3.52552	1.21675	H	4.372635	1.771517	-0.44005

C	4.180469	-3.41217	1.729378	H	6.848056	1.769647	-0.39534
C	2.727577	0.866029	-2.4116	H	8.130446	0.830173	-2.3098
C	4.236394	0.84242	-2.3797	H	6.913973	-0.10722	-4.26697
C	4.929703	1.368375	-1.28103	H	4.436265	-0.10428	-4.30394
C	6.322897	1.361004	-1.25467	H	0.200383	2.925342	2.054378
C	7.043782	0.832174	-2.32963	H	1.432859	3.367131	0.862216
C	6.36188	0.307607	-3.42774	H	6.214056	-2.82418	1.319707
C	4.964638	0.310969	-3.44856	H	5.723655	-2.13859	-1.02275
F	-7.37542	3.691226	-0.12368	H	3.426945	-2.35228	-1.92084
O	0.951646	1.357522	0.899567	H	3.199712	0.803753	1.613922
C	1.136936	2.58609	1.584141	H	5.010073	0.594235	3.300716
C	2.212898	2.416867	2.635146	H	5.042911	2.093905	5.287849
C	5.205866	-2.91714	0.923929	H	3.24697	3.791063	5.578098
C	4.932641	-2.53756	-0.39379	H	1.439654	3.985088	3.898671
C	3.642	-2.66078	-0.9031	H	-5.39818	-1.0275	1.510249
C	-3.93018	-3.20635	0.686962	H	-5.63811	-2.35283	2.664301
C	3.223799	1.461537	2.476427	H	-6.97005	-1.84994	1.609027
C	4.236257	1.346459	3.430445	H	-5.49626	-3.1895	-1.60424
C	4.253951	2.185758	4.545955	H	-5.36184	-1.51952	-1.02427
C	3.24695	3.139244	4.708299	H	-6.90657	-2.38343	-0.89925
C	2.2291	3.248717	3.760098	H	-5.86785	-4.76684	1.822673
C	-5.44835	-3.01757	0.5813	H	-5.82752	-5.11418	0.092403
O	-3.37192	-4.21571	1.06123	H	-7.21811	-4.2538	0.7855
C	-5.88467	-1.99647	1.657565				



4

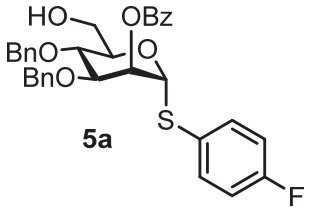
HOMO energy: $\mathbf{E_{HOMO(4)}}$ = -0.22635 hartree (-6.159 eV)



(white: H, gray: C, blue: N, red: O, yellow, S, light blue: F)

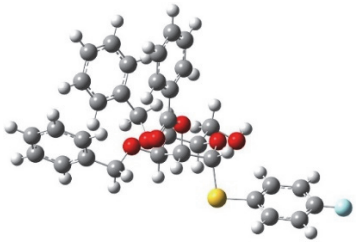
Atom	X	Y	Z	Atom	X	Y	Z
C	1.133575	-1.43924	0.080113	C	6.022729	4.436414	-0.01341
C	-0.38801	-1.53642	-0.07163	H	1.463857	-2.07908	0.899932
C	-0.94568	-0.43188	-0.99218	H	-0.67761	-2.52676	-0.42487
C	-0.44297	0.950874	-0.54189	H	-0.56499	-0.60231	-2.0127
C	1.106447	0.900498	-0.45995	H	-0.86647	1.179308	0.443043
O	1.5332	-0.13824	0.431614	H	1.497656	0.699719	-1.46699
O	-0.85402	1.904641	-1.51219	H	1.384506	3.036886	-0.54449
C	-2.59051	3.116086	-0.18761	H	1.445887	2.362952	1.099563
S	1.935601	-2.11149	-1.47084	H	3.453083	-4.52894	-1.68583
O	-2.35842	-0.44069	-0.99342	H	5.760904	-5.15919	-0.95692
C	1.718735	2.188765	0.053066	H	6.255315	-1.30305	0.845728
C	3.563082	-2.54109	-0.85522	H	3.969656	-0.63648	0.075788
O	3.152589	2.085828	-0.05012	H	-1.51468	3.734308	-1.94997
C	4.068094	-3.816	-1.14526	H	-0.54863	3.699765	-0.47474
C	5.352337	-4.17787	-0.73917	H	-1.75965	4.307222	1.40549
C	6.110048	-3.25899	-0.02303	H	-3.84121	4.321236	2.749717
C	5.629358	-1.99194	0.287799	H	-2.58109	-1.12807	-2.93925
C	4.354867	-1.62609	-0.14483	H	-2.63102	-2.38906	-1.68146
C	-1.3327	3.166825	-1.03059	H	-4.62031	-2.57689	-0.17379
C	-2.64183	3.784149	1.041249	H	-7.09235	-2.35961	-0.02336

C	-3.81555	3.794642	1.799216	H	-8.31344	-0.90701	-1.62977
C	-2.93934	-1.36443	-1.92605	H	-7.05502	0.318558	-3.39091
C	-4.4412	-1.24751	-1.856	H	-4.58909	0.09499	-3.53414
C	-5.15813	-1.93965	-0.87088	H	-5.86222	3.127862	1.924668
C	-6.54526	-1.81505	-0.78864	H	-5.77658	1.91214	-0.24912
C	-7.23215	-0.99908	-1.69128	H	-3.69253	1.902698	-1.57974
C	-6.52606	-0.31034	-2.67959	H	-0.64295	-0.93677	3.732678
C	-5.13772	-0.43684	-2.75966	H	-0.93899	-2.63656	4.148668
F	7.348894	-3.60666	0.38309	H	-1.82424	-1.35423	4.990623
O	-0.94089	-1.34283	1.247895	H	-3.95923	-0.31629	2.034687
C	-1.98035	-2.13813	1.617553	H	-2.4481	0.440037	2.55432
C	-2.54926	-1.71532	2.975254	H	-3.66365	-0.02305	3.760339
O	-2.38634	-3.06026	0.940623	H	-3.18942	-3.74465	3.485209
C	-4.94818	3.124425	1.336381	H	-4.43755	-2.78015	2.689001
C	-4.90264	2.445503	0.114852	H	-4.01974	-2.45663	4.383558
C	-3.73318	2.445778	-0.6425	H	5.327281	1.271415	1.278408
C	3.830359	3.2543	0.094264	H	5.575352	2.788424	2.163598
C	-1.41379	-1.65655	4.020377	H	6.894021	2.105127	1.19696
C	-3.19185	-0.31749	2.815667	H	5.356495	2.819457	-2.18318
C	-3.61248	-2.73826	3.40602	H	5.248602	1.285271	-1.30119
C	5.347421	3.055475	-0.00309	H	6.786338	2.167996	-1.36686
O	3.271467	4.311853	0.29348	H	5.770885	5.008351	0.884091
C	5.808574	2.25319	1.235984	H	5.706595	5.025742	-0.88002
C	5.698668	2.281332	-1.29156	H	7.111109	4.316097	-0.05698



5a

HOMO energy: $\mathbf{E_{HOMO(5a)}}$ = -0.22333 hartree (-6.077 eV)



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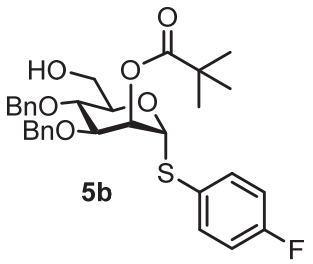
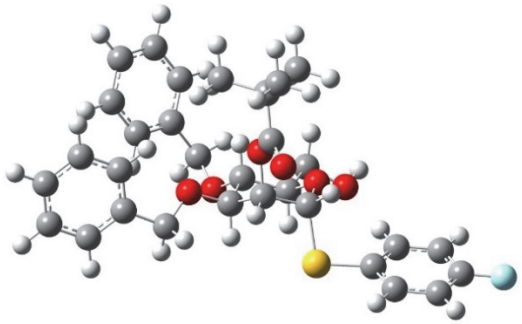
C	-2.183677	-0.2903	0.312901	C	2.117007	4.211679	0.497397
C	-0.74408	0.491674	-0.80176	C	2.691228	4.987444	1.500807
C	0.037289	-0.8381	-0.8569	C	2.440895	4.689189	2.842938
C	-0.0886	-1.60195	0.474302	C	1.614224	3.614504	3.179128
C	-1.59799	-1.75793	0.787031	C	1.03708	2.835271	2.178304
O	-2.22062	-0.46865	0.866745	H	-2.6198	1.256501	-0.05434
O	0.521115	-2.87628	0.304994	H	-0.72608	0.996501	-1.76863
C	2.554122	-2.57377	1.722489	H	-0.41781	-1.46952	-1.63794
S	-3.21655	-0.39704	-1.71415	H	0.41009	-1.02834	1.264753
O	1.401229	-0.61981	-1.14533	H	-2.05923	-2.33591	-0.02605
C	-1.91805	-2.46398	2.093202	H	-1.36466	-3.41101	2.128296
C	-4.86406	-0.02287	-1.11148	H	-1.59671	-1.83327	2.936336
O	-3.3216	-2.70239	2.123416	H	-3.54588	-3.06376	2.993575
C	-5.68363	0.818951	-1.8763	H	-5.29708	1.260056	-2.78986
C	-6.98901	1.096394	-1.47117	H	-7.63954	1.743127	-2.05077
C	-7.45058	0.535751	-0.28629	H	-7.05988	-0.71537	1.411093
C	-6.65653	-0.29631	0.494874	H	-4.7363	-1.2462	0.671523
C	-5.35953	-0.58934	0.073643	H	1.577913	-4.38218	1.072559
C	1.307038	-3.36969	1.393298	H	0.697495	-3.47411	2.302981
C	2.843416	-2.23722	3.049752	H	2.144847	-2.51258	3.83798
C	4.020079	-1.55793	3.374011	H	4.231645	-1.30493	4.409809
C	1.697285	-0.49769	-2.54347	H	1.319466	-1.38421	-3.07463

C	3.191105	-0.37958	-2.71339	H	1.19953	0.390308	-2.9541
C	3.836702	0.833969	-2.44143	H	3.244609	1.689153	-2.1272
C	5.220571	0.942356	-2.57499	H	5.711399	1.888907	-2.3636
C	5.975822	-0.15989	-2.98548	H	7.053781	-0.07247	-3.09486
C	5.340088	-1.3713	-3.26247	H	5.920205	-2.23097	-3.58771
C	3.954244	-1.47781	-3.12523	H	3.45951	-2.42211	-3.34235
F	-8.70967	0.807044	0.117942	H	5.827554	-0.66236	2.613099
O	-0.11686	1.353885	0.173328	H	5.313255	-1.23279	0.243259
C	0.695888	2.33883	-0.28166	H	3.229612	-2.43989	-0.31525
C	1.288851	3.131035	0.831118	H	2.293991	4.42829	-0.5509
O	0.89502	2.561758	-1.46183	H	3.332283	5.824496	1.238536
C	4.914395	-1.1977	2.365977	H	2.889027	5.29472	3.626367
C	4.628811	-1.52096	1.036374	H	1.419185	3.383398	4.222664
C	3.459643	-2.2089	0.718287	H	0.39291	2.001036	2.431508



HOMO energy: $\mathbf{E_{HOMO}(5b)}$ = -0.22179 hartree (-6.035 eV)



(white: H, gray: C, blue: N, red: O, yellow, S, light blue: F)

Atom	X	Y	Z	Atom	X	Y	Z
C	-1.95133	0.37188	-0.03629	C	2.091725	1.591548	3.080884
C	-0.50319	0.869841	-0.15851	C	0.399121	3.20781	4.03626
C	0.347677	-0.09233	-1.00111	H	-2.4773	0.950961	0.723546
C	0.241541	-1.5301	-0.46307	H	-0.48451	1.885162	-0.55951
C	-1.26415	-1.89879	-0.40883	H	-0.05936	-0.10459	-2.02404
O	-1.98396	-0.96153	0.403287	H	0.688987	-1.57536	0.536623
O	0.929858	-2.38231	-1.37167	H	-1.65638	-1.86898	-1.435
C	2.905685	-2.98654	0.030106	H	-0.94707	-4.01863	-0.34392
S	-2.85212	0.686162	-1.64491	H	-1.3313	-3.27937	1.237464
O	1.701552	0.319094	-1.03004	H	-3.18332	-4.35206	0.402032
C	-1.57175	-3.2721	0.163314	H	-5.01045	2.576408	-1.66066
C	-4.55378	0.546426	-1.09507	H	-7.42215	2.408189	-1.01
O	-2.95178	-3.53647	-0.06621	H	-6.80567	-1.64154	0.248987
C	-5.40376	1.649536	-1.25487	H	-4.40827	-1.51075	-0.43462
C	-6.74779	1.566399	-0.89171	H	2.070061	-3.98696	-1.68595
C	-7.21825	0.375406	-0.35189	H	1.102608	-4.11792	-0.21608
C	-6.39457	-0.73049	-0.17385	H	2.425981	-4.2957	1.673372
C	-5.05683	-0.65007	-0.56029	H	4.411449	-3.66772	3.016356
C	1.723	-3.42968	-0.80838	H	1.847571	0.677247	-3.07013
C	3.13034	-3.56176	1.286038	H	1.344243	2.067557	-2.09594
C	4.249896	-3.21008	2.043757	H	3.467961	1.69829	0.141571
C	2.014341	1.191216	-2.11069	H	5.796385	2.55174	0.294032
C	3.45059	1.648277	-2.00625	H	7.106097	2.973088	-1.77874
C	4.039107	1.894615	-0.75974	H	6.07249	2.533297	-3.99886
C	5.349805	2.366437	-0.67962	H	3.753304	1.680845	-4.14047
C	6.086029	2.603704	-1.84289	H	6.022856	-1.98704	2.139882
C	5.50543	2.359224	-3.08817	H	5.621372	-0.93345	-0.08003
C	4.197206	1.879012	-3.16707	H	3.635169	-1.56749	-1.41296

F	-8.51588	0.289538	0.010755	H	0.031875	-0.22262	3.511284
O	0.082307	0.884358	1.161882	H	-1.15016	0.911586	4.191671
C	-0.08399	2.013291	1.901028	H	0.383407	0.625712	5.03203
C	0.587802	1.887694	3.272838	H	2.585149	2.401213	2.530082
O	-0.70057	2.977604	1.501153	H	2.251249	0.65784	2.535164
C	5.152086	-2.26667	1.552389	H	2.578114	1.508989	4.05984
C	4.930333	-1.67882	0.303531	H	-0.66131	3.439961	4.172144
C	3.817002	-2.03887	-0.45351	H	0.853966	4.045456	3.498652
C	-0.07997	0.725875	4.043758	H	0.868187	3.134737	5.024027

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Chapter 2

Automated Electrochemical Assembly of the β-(1,3)-β-(1,6)-Glucan Hexasaccharide Using Thioglucoside Building Block

Abstract

This study deals with the design, synthesis, and rational optimization of carbohydrate building blocks of glucosides for automated electrochemical assembly of β-glucans. Oxidation potentials of building blocks with various types of protecting groups of hydroxyl groups were measured to estimate their reactivity under anodic oxidation conditions. Building blocks for both β-1,3- and β-1,6-glycosidic linkages were optimized by automated electrochemical assembly of disaccharides and trisaccharides. Several synthetic attempts were also made for the synthesis of the hexasaccharide repeating unit in a macrocyclic β-glucan tridecasaccharide.

Introduction

β-Glucans are abundant oligosaccharides found in fungi and bacteria and their biological activities have attracted researchers for many years.[1,2] Usually β-glucans contain both β-(1,3)- and β-(1,6)-linkages in their structures and the fungal β-glucans can modulate the immune system[3] and exhibit anti-tumor activities.[4] The immunomodulatory properties of β-glucans are influenced by the structural complexity such as the distribution of β-(1,6) branching.[5,6] Thus, structurally well-defined β-glucans with different branching patterns and chain lengths would be useful to reveal the effects of β-glucan structures on their biological activities.

Although the convergent synthesis of oligosaccharides based on solution-phase synthesis has been an enabling method to provide β-glucans in preparative scale, the strategy limits a variety of accessible structures of β-glucans.[7] Utilizing the solid-phase synthesis as an alternative approach, syntheses of linear dodecasaccharides of β-(1,3)-glucans have already been reported.[8a-d] A sophisticated automated solid-phase synthesis has also been demonstrated for the preparation of a linear β-(1,3)-glucan up to dodecasaccharide by Seeberger and co-workers.[8e] Previously reported electrochemical synthesis of disaccharides of glucose suffers from problem of stereoselectivity, giving a mixture of (α:β) anomers.[8f] Hence, rational optimization of glucoside building blocks for electrochemical synthesis of oligosaccharides is highly desirable. In our laboratory, continuous efforts have been taken towards long lasting problem of stereoselective oligosaccharides synthesis in time and cost-effective manner, combining the concept of automation,[9] electrochemistry,[10] and pre-activation protocol.[11] The automated electrochemical synthesizer was successfully employed in the syntheses of oligoglucosamine,[12a] TMG-chitotriomycin,[12b-c] and GPI anchor trisaccharide.[12d] In this study, we carried out rational design, synthesis, and measurement of oxidation potential of thioglucosides as carbohydrate building blocks, alongside that strategic approaches towards automated electrochemical assembly of the hexasaccharide repeating unit present in the macrocyclic β-glucans are discussed.

Results and Discussion

To begin with our study, we have synthesized a variety of thioglucosides as carbohydrate building blocks where an ester protecting group was selectively introduced at the 2-OH position to ensure the stereochemical outcome and temporary protecting groups were introduced in other positions (Figure 1). We also measured the oxidation potentials of synthesized building blocks. The closer look at building blocks **3** and **4** equipped with two benzyl protecting groups and one protecting group free hydroxyl group, their protecting groups do not cause any significant change in oxidation potentials. On the other hand, oxidation potential of building block **10** found to be 1.67 V, which is 0.05 V higher than its 6-OH analogue **3**. Replacement of benzoyl group of 2-OH of building block **7** (1.64 V) with acetyl group and pivaloyl group slightly increases the oxidation potential by 0.02 V (building block **8**) and 0.03 V (building block **10**), respectively. As we go on increasing the number of the electron withdrawing groups, the oxidation potential goes on increasing significantly from 1.66 – 1.72 V. Comparison of closely related building blocks, such as building block **9** (1.66V) with that of building block **1** (1.55 V), **15** (1.72 V) and **16** (1.72 V) shows a distinct effect of protecting group on the oxidation potential and introduction of allyl group at the 3-OH position lowers the oxidation potential (1.55 V), whereas introduction of acetyl (Ac) or chloroacetyl (ClAc) group at the same position increases the oxidation potential to 1.72 V.

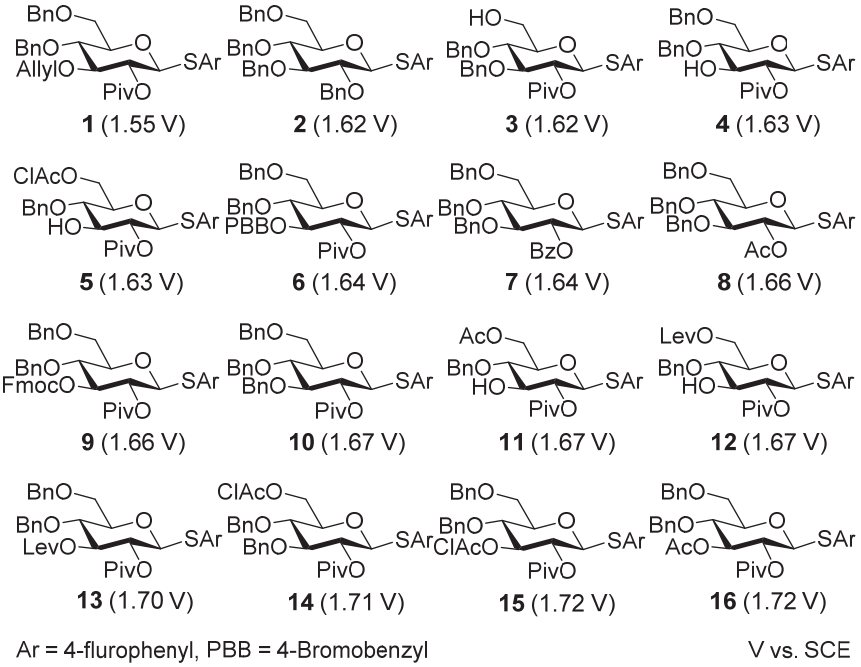
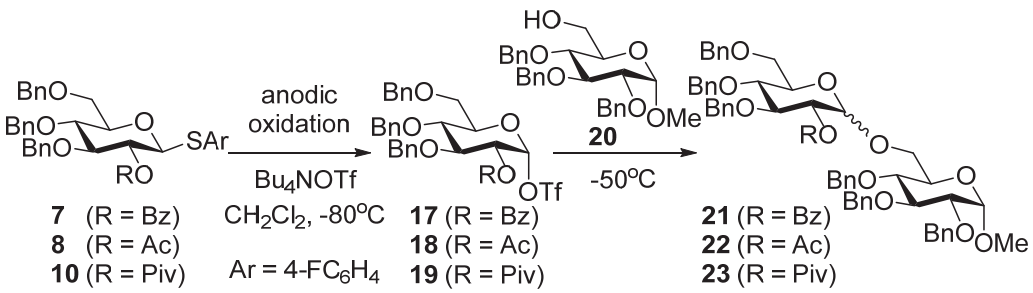


Figure 1. Oxidation potentials of glucoside building blocks

Having done with oxidation potential measurement, we then verified our hypothesis (Table 1). We chose the thioglucosides having an ester protecting group R^1 = Bz (**7**), Ac (**8**), and Piv (**10**) at the 2-OH position and benzyl groups at remaining hydroxyl groups. Thioglucosides are then electrochemically activated to form the corresponding glucosyl triflates at -80 ºC and accumulated.[8f,13] In the glycosylation step, the subsequent addition of solution of glycosyl acceptor afforded a desired disaccharide β selectively. Stereoselectivity of glycosylation was controlled by the protecting group of 2-OH. The donor **8** having the 2-OAc gave 69% of the desired disaccharide **21** whereas glycosyl donors **7** (R = Bz) and **10** (R = Piv) gave 75% and 86% of disaccharides **22** and **23**, respectively.

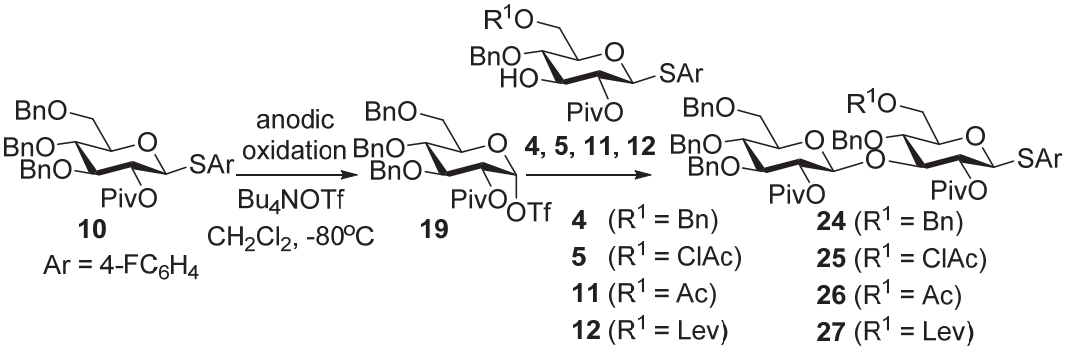
Table 1. Electrochemical pre-activation and the subsequent coupling with methyl glycoside as a glycosyl acceptor



Building Block	R	Product	Yield	Selectivity (α:β)
7	Bz	**21**	78%	β only
8	Ac	**22**	60%	β only
10	Piv	**23**	47%	β only

Next, we investigated the electrochemical glycosylation protocol for the comparatively less reactive secondary hydroxyl group, where we used building block **10** as a glycosyl donor (Table 2). We have synthesized a variety of thioglycoside acceptors with free 3-OH (**4**, **5**, **11** and **12**), along with that protecting groups were introduced at other hydroxyl groups by conventional method and screened these acceptors for electrochemical glycosylation. Stereoselectivity of glycosylation was again controlled by 2-OPiv. Depending upon the yields of the reaction, it can be concluded that protecting group of glycosyl acceptors play a crucial role, because building block **4** with two benzyl groups at 4-OH and 6-OH formed disaccharide **24** in 64% and building blocks **5** and **11** with ClAc and Ac groups, the yields of disaccharide **25** and **26** dropped down to 58% and 45%, respectively. Contrary the surprising result was obtained, when we tested building block **12** having levulinoyl group (Lev) at the 6-OH position as a glycosyl acceptor, significant increase in the yield of disaccharide **27** was observed (83%). It was not clear why the significant increase of the glycosylation yield by introducing an electron withdrawing group to the glycosyl acceptor; however, a hydrogen bonding of 6-OLev might increase the reactivity of 3-OH as a nucleophile.[14]

Table 2. Optimization of secondary sugar hydroxyl acceptors.



Building Block	R^1	Product	Yield	Selectivity (α:β)
4	Bn	**24**	64%	β only
5	ClAc	**25**	58%	β only
11	Ac	**26**	45%	β only
12	Lev	**27**	83%	β only

Further we tested a standard protocol of automated electrochemical assembly for trisaccharide synthesis (Figure 2). The first cycle initiated with anodic oxidation of glycosyl donor **10** at -80ºC under the constant current condition, after that solution of acceptor **3** with a 3-OPiv was added to the cell and the reaction temperature was raised to -50ºC and kept for 1 h to enhance the rate of glycosylation. After the completion of glycosylation, the bath temperature was then decreased to -80ºC and the second cycle was started subsequently. The entire process including temperature control was carried out automatically. As the result of the process, the desired trisaccharide **30** was obtained in 61% overall yield.

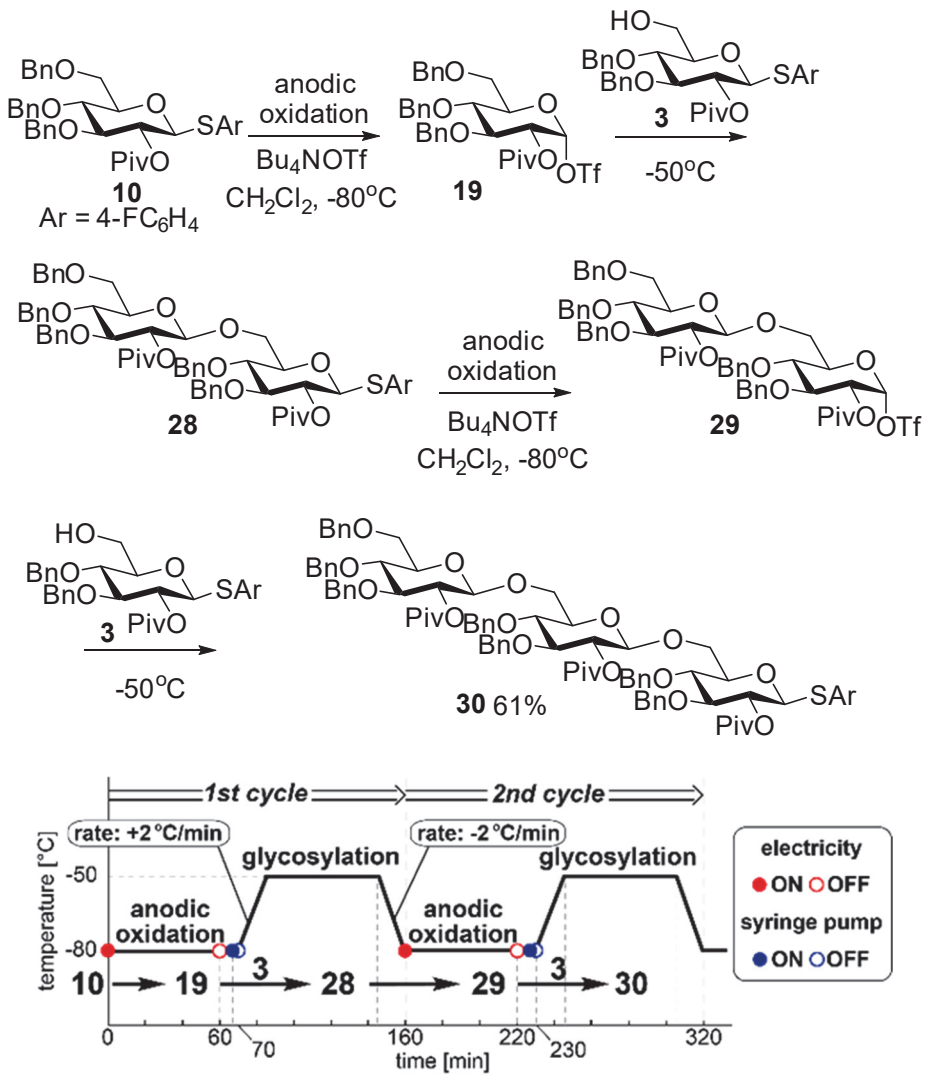
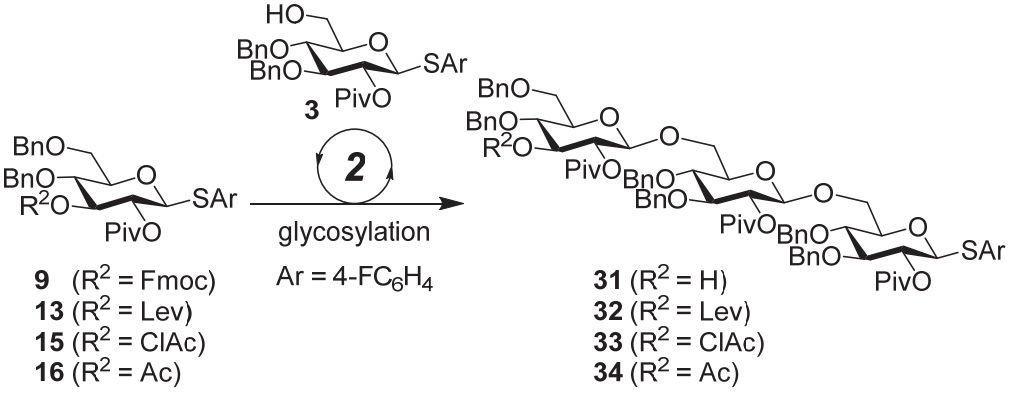


Figure 2. Automated Electrochemical Assembly of a β-1,6-trisaccharide

Successful optimization of building blocks encouraged us to utilize this protocol for the synthesis of biologically important oligoglucosides. During our literature search, we come to know about an interesting molecule present in the fungal cell wall. The molecule has a cyclic β-glucan structure having β-(1,3)- and β-(1,6)-linkages repeated after every trisaccharide.[15] As this molecule possesses both β-(1,3)- and β-(1,6)-linkages, we initiated with optimization of donor having a selectively removable protecting group at 3-OH (Table 3). Various protecting groups were tested for the synthesis of trisaccharide using a standard protocol for automated electrochemical assembly. As a result of this trisaccharide synthesis, we found that glycosyl donor **15**, having the ClAc group as a temporary protecting group at 3-OH gave the best yield of trisaccharide **31** in 44% yield, whereas **9** (R^2 = Fmoc), **16** (R^2 = Ac) and **13** (R^2 = Lev) gave relatively lower yields of trisaccharide **32-34** in 41%, 38% and 24% yields, respectively.

Table 3. Optimization of temporary protecting group R^2 at the 3-OH position



Building Block	R^2	Product	R^2	Yield	Selectivity (α:β)
9	Fmoc	**31**	Fmoc	64%	β only
13	Lev	**32**	Lev	58%	β only
15	ClAc	**33**	ClAc	45%	β only
16	Ac	**34**	Ac	83%	β only

To achieve automated electrochemical assembly of the hexasaccharide repeating unit, we investigated two model strategies (Figure 3). Firstly, we tested the [3+1+2] (**33**+**3**+**35**) strategy as a model strategy for hexasaccharide synthesis, trisaccharide donor **33** was coupled with glycosyl acceptor **3** with free 6-OH in the first cycle and the resulted tetrasaccharide was coupled with disaccharide glycosyl acceptor **35**, having 3-OH in the second cycle. When we employed the [3+1+2]; (**33**+**3**+**35**), strategy, unfortunately we did not obtain a trace amount of hexasaccharide **36** and ended up with hydration of a glycosyl triflate intermediate and unreacted glycosyl acceptor **35**. These results were quite disappointing; however, a glycosyl triflate of tetrasaccharide formed in the second cycle of the activation step might be least reactive towards disaccharide glycosyl acceptor **35**.[16] One of the reasons might be a trisaccharide unit at the 6-OH position covered the anomeric center from the top face, moreover the 3-OH of disaccharide acceptor **35** seemed to be sterically crowded and not easily accessible for glycosylation. To overcome this problem, we modified our strategy from [3+1+2]; (**33**+**3**+**35**) to [3+2+1] (**33**+**37**+**12**), where we thought that the problematic β-(1,3)-linkages should be synthesized in advance and more reactive 6-OH primary alcohol **37** was allowed to react in the first cycle, followed by the reaction with the 3-OH of glycosyl acceptor **12**, in the second cycle. The strategy seemed to be promising; however, we got a trace amount of the desired hexasaccharide **36** (<6 mg).

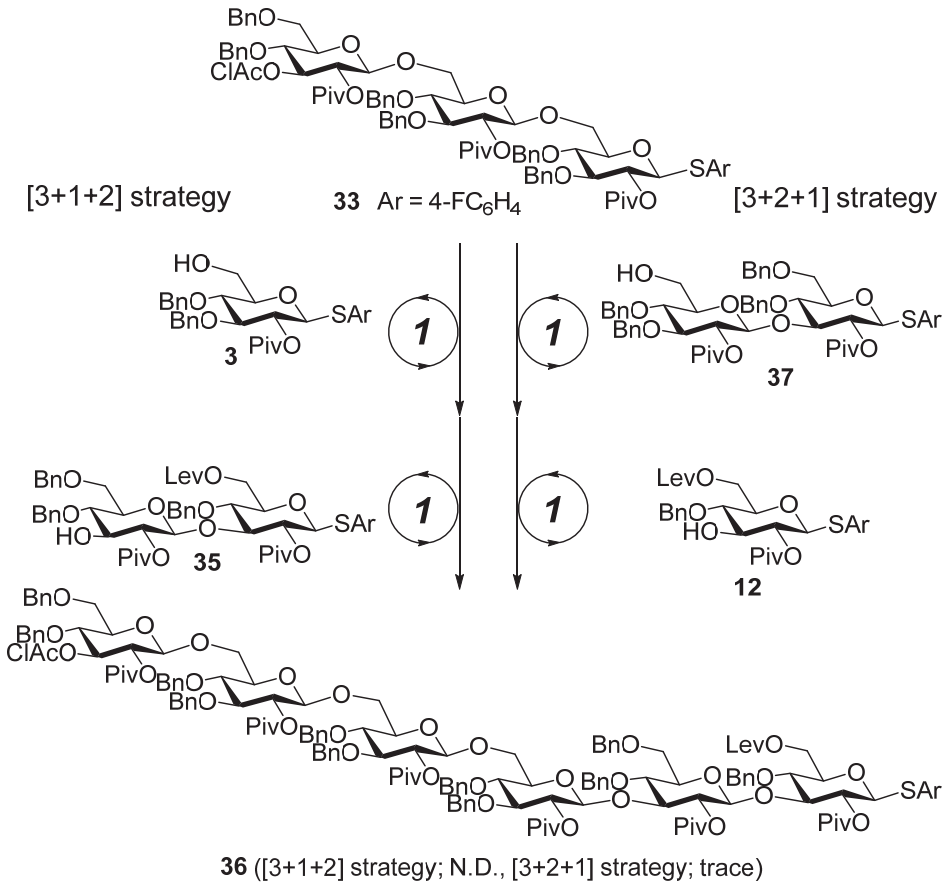
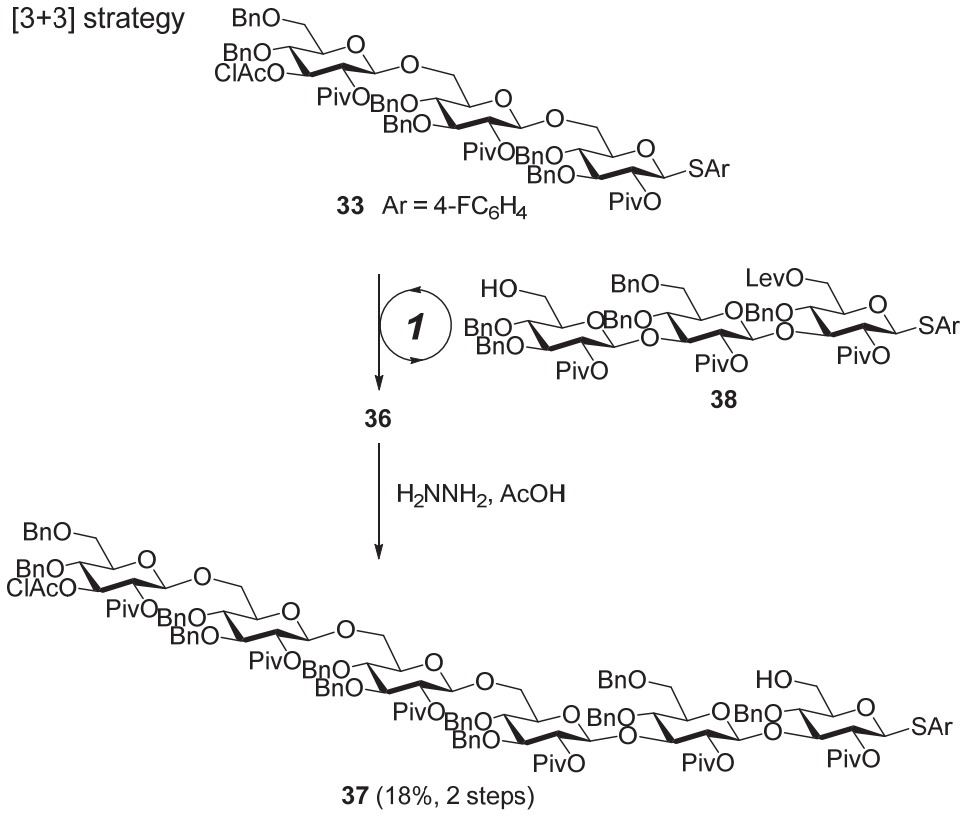


Figure 3. [3+1+2] and [3+2+1] strategies for hexasaccharide synthesis

Finally, [3+3] strategy was employed to obtain sufficient quantity of desired hexasaccharide **36**, where trisaccharide glycosyl donor **33** activated electrochemically followed by the coupling with trisaccharide glycosyl acceptor **38** (Scheme 2). At this stage, ^{1}H NMR along with mass spectral analysis clearly shows the presence of desired hexasaccharide **36**. Several attempts using column chromatographic purification found to be unsuccessful to obtain hexasaccharide **36** with high purity.[17] To obtain pure compound, the crude product was treated with hydrazine acetate to deprotect levulinoyl group at 6-OH of **36** selectively and the desired hexasaccharide **39** was obtained in high purity with 18% overall yield over two steps.

Conclusion

In summary, we have designed, synthesized and optimized carbohydrate building blocks of thioglucosides for automated electrochemical assembly of β-glucans. Along with that systematic strategic attempts were made to developed rational protocol for the synthesis of the hexasaccharide repeating unit present in macrocyclic β-glucans to facilitate the preparative scale synthesis. Further optimization of reaction conditions for total synthesis of macrocyclic β-glucans is underway in our laboratory.



Scheme 2. [3+3] strategy for hexasaccharide synthesis and subsequent levulinoyl ester deprotection

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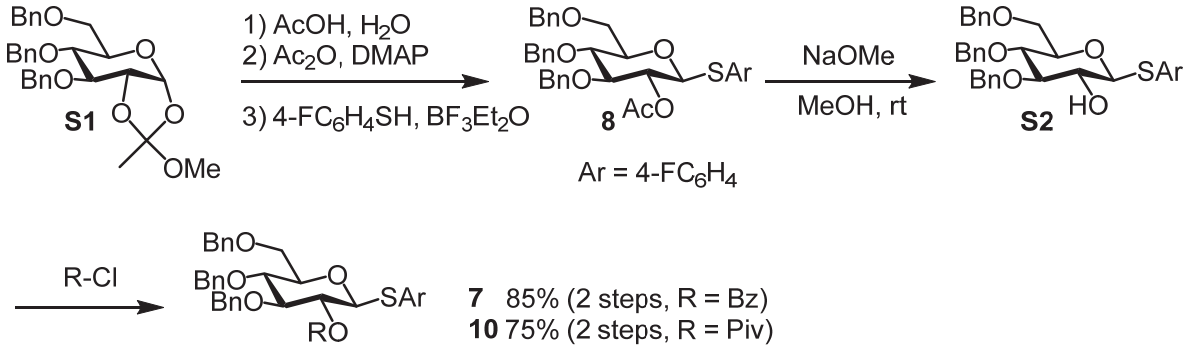
16 We observed the corresponding molecular ion peak of hydroxyl suger of tetrasaccharide (HRMS (ESI) *m/z* calc. for $C_{102}H_{123}ClNaO_{26}$ $[M+Na]^+$, 1822.7922; found, 1822.7874), which was formed by hydrolysis of the corresponding glycosyl triflate of tetrasaccharide.

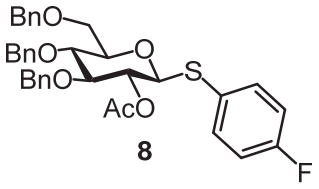
17 It was hard to purify hexasaccharide **36** because of the presence of a by-product, which might be a homo-coupling product of trisaccharide **33** (a trehalose-type pseudo-hexasaccharide). After deprotection of the Lev group at 6-OH **36** it was easy to purify by silica-gel chromatography

Experimental Section

Preparation of buiding block

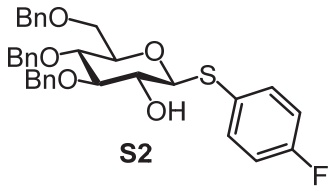


Scheme S1



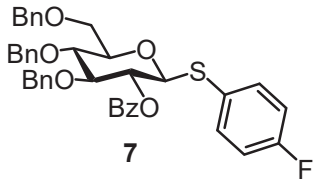
A solution of 3,4,6-tri-*O*-benzyl-(1,2-*O*-methoxyethylidene)-α-D-glucopyranose **(S1)**[1] (38.0 g, 75.0 mmol) in acetic acid (300 mL) and water (200 mL) was stirred at r.t. for 4 h whereupon TLC analysis (EtOAc/Hexane 1:1) indicated the complete consumption of the starting material (R_f = 0.62) and formation of three products (R_f = 0.24, 0.36, 0.51). The mixture was concentrated in vacuo and partitioned between water (400 mL) and ethyl acetate (400 mL). The layers were separated and the aqueous phase was extracted with ethyl acetate (2 × 175 mL). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate solution (2 × 200 mL) and brine (200 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to give a yellow oil which was dissolved in dry pyridine (250 mL) under an atmosphere of nitrogen. The resulting solution was cooled to 0 ºC and acetic anhydride (100 mL) was added dropwise over 30 min. The mixture was stirred for 16 h, slowly warming to room temperature. TLC analysis (Hexane/EtOAc 1:1) indicated the complete consumption of the starting materials (R_f = 0.24, 0.36, 0.51) and formation of a single product (R_f = 0.88). The mixture was concentrated in vacuo to give a pale-yellow oil (39.0 g). The resulting yellow oil was purified by flash column chromatography. Boron trifluoride diethyl etherate (4.62 mL, 37.4 mmol) was added dropwise to a solution of 1,2-di-*O*-Acetyl-3,4,6-tri-*O*-benzyl-D-glucopyranose (10.0 g, 18.7 mmol) and 4-fluorothiophenol (2.40 ml, 22.5 mmol) in dry dichloromethane (250 mL) at room temperature under an atmosphere of argon. The reaction mixture was stirred at room temperature for 19 h by which time TLC analysis (Hexane/EtOAc 4:1) indicated that all starting material was consumed. The reaction mixture was diluted with dichloromethane (150 mL) and washed with saturated aqueous sodium hydrogen carbonate solution (3 × 200 mL) and brine (200 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to give a pale-yellow oil. The resulting yellow oil was purified by flash column chromatography, to get **8** as a white solid in 69%. **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-2-*O*-acetyl-1-thio-β-D-glucopyranoside (8)**. TLC (Hexane /EtOAc 4:1) R_f = 0.66; $[\alpha]_D$ = 0.71 (*c* = 1.0, $CHCl_3$); *E*ox = 1.66 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50 (m, 2 H), 7.31 (m, 13 H), 7.19 (d, *J* = 6.6 Hz, 2 H), 6.89 (*pseudo*-t, *J* = 8.6 Hz, 2 H), 4.94 (dd, *J* = 9.8, 8.9 Hz, 1 H), 4.78 (*pseudo*-t, *J* = 10.8 Hz, 2 H), 4.66 (d, *J* = 11.4 Hz, 1 H), 4.57 (dd, *J* = 11.4, 5.5 Hz, 2 H), 4.51 (m, 2 H), 3.76 (dd, *J* = 10.8, 1.5 Hz, 1 H), 3.71 (dd, *J* = 10.3, 4.3 Hz, 1 H), 3.65 (m, 2

H), 3.51 (m, 1 H), 2.00 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.4, 162.9 (d, *J* = 247.05 Hz), 138.1, 138.0, 137.8, 135.5 (d, *J* = 8.4 Hz), 128.4, 128.3, 128.0, 127.9, 127.85, 127.80, 127.6, 127.02, 127.00, 115.8 (d, *J* = 21.6 Hz), 85.6, 84.3, 79.2, 77.7, 75.3, 75.1, 73.4, 71.6, 68.9, 21.0. HRMS (ESI) *m/z* calc. for $C_{35}H_{35}FO_6S$ [M+K]$^+$, 641.1770; found, 641.1768.



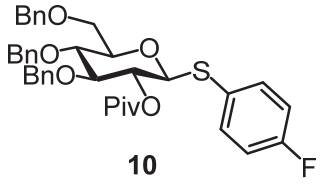
S2

Thioglycoside **8** (4.0 g, 6.64 mmol) was dissolved in MeOH (21.5 mL) and treated with 0.5 M NaOMe/MeOH solution (0.66 mL, 3.32 mmol) at rt for 20 h, and then most of solvent was removed. The reaction mixture was neutralized with Amberlite and concentrated in vacuo. The crude product was purified by silica gel column chromatography to give **S2** in 91% yield (1.2 g, 2.1 mmol). **4-Fluoro-phenyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (S2).**[2] TLC (Hexane/EtOAc 4:1) R_f = 0.37; $[\alpha]_D$ = -0.11 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.35 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.29 (m, 13 H), 7.19 (d, *J* = 6.7 Hz, 2 H), 6.87 (*pseudo*-t, *J* = 8.6 Hz, 2 H), 4.89 (d, *J* = 11.3 Hz, 1 H), 4.83 (d, *J* = 11.2 Hz, 1 H), 4.81 (d, *J* = 10.9 Hz, 1 H), 4.57 (dd, *J* = 11.0, 9.3 Hz, 2 H), 4.51 (d, *J* = 11.9 Hz, 1 H), 4.40 (d, *J* = 9.7 Hz, 1 H), 3.75 (d, *J* = 9.7 Hz, 1 H), 3.70 (dd, *J* = 10.8, 4.5 Hz, 1 H), 3.56 (dd, *J* = 8.7, 6.5 Hz, 2 H), 3.49 (bs, 1 H), 3.42 (m, 1 H), 2.58 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.9 (d, *J* = 247.5 Hz), 138.6, 138.3, 138.2, 135.7 (d, *J* = 8.0 Hz), 128.7, 128.6, 128.5, 128.1, 128.0, 127.9, 127.79, 127.75, 126.68, 126.66, 116.1 (d, *J* = 21 Hz), 87.9, 86.0, 79.4, 77.5, 75.5, 75.2, 73.5, 72.6, 69.1. HRMS (ESI) *m/z* calc. for $C_{33}H_{33}FO_5S$ [M+K]$^+$, 599.1664; found, 599.1666.



7

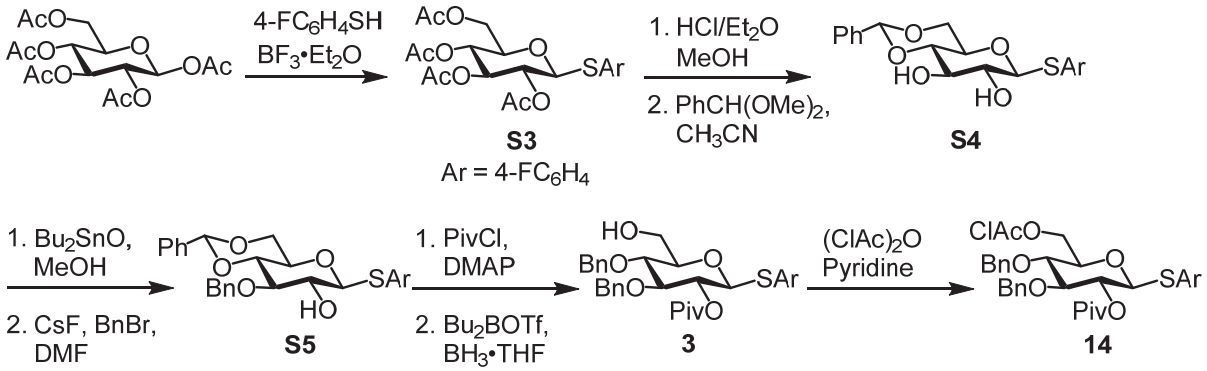
To a stirred solution of **S2** (1.00 g, 1.78 mmol) in pyridine, DMAP (65.4 mg, 0.53 mmol) and benzoyl chloride (0.25 mL, 0.21 mmol) were added. After stirring for 26h at rt, the reaction was quenched by methanol and concentrated in vacuo. The crude product was purified by silica gel column chromatography to give **7** as colorless foam in 80% yield (0.76 g, 1.2 mmol). **4-Fluorophenyl- 3,4,6-tri-*O*-benzyl-2-*O*-benzoyl-1-thio-β-D-glucopyranoside (7)**. TLC(Hexane/EtOAc 4:1) R_f = 0.68; $[\alpha]_D$ =2.61 (*c* = 1.0, $CHCl_3$); *E*ox = 1.64 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04 (dd, *J* = 7.2, 1.2 Hz, 2 H), 7.47 (m, 4 H), 7.31 (m, 9 H), 7.20 (dd, *J* = 7.6, 1.6 Hz, 2 H), 7.11 (m, 5 H), 6.87 (*pseudo*-t, *J* = 8.6 Hz, 2 H), 5.26 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.80 (d, *J* = 10.9 Hz, 1 H), 4.72 (d, *J* = 11.0 Hz, 1 H), 4.67 (d, *J* = 10.0 Hz, 1 H), 4.62 (d, *J* = 11.0 Hz, 1 H), 4.60 (d, *J* = 9.1 Hz, 1 H), 4.58 (d, *J* = 8.1 Hz, 1 H), 4.54 (d, *J* = 11.4 Hz, 1 H), 3.82 (dd, *J* = 18.0, 9.0 Hz, 1 H), 3.79 (d, *J* = 12.0 Hz, 1 H), 3.74 (dd, *J* = 10.9, 4.9 Hz, 1 H), 3.59 (m, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 163.0 (d, *J* = 248.3 Hz), 138.2, 137.9, 137.7, 135.8 (d, *J* = 7.5 Hz), 133.7, 133.3, 130.2, 129.9, 128.6, 128.51, 128.48, 128.43, 128.3, 128.1, 128.0, 127.9, 127.71, 127.66, 127.01, 126.99, 115.9 (d, *J* = 22.5 Hz), 85.9, 84.3, 79.5, 77.8, 75.4, 75.2, 73.6, 72.4, 69.0. HRMS (ESI) *m/z* calc. for $C_{40}H_{37}FO_6S$ [M+K]$^+$, 703.1926; found, 703.1924.



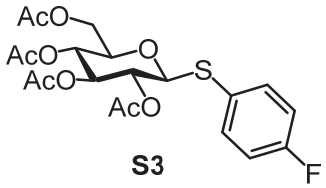
10

To a stirred solution of **S2** (1.00 g, 1.5 mmol) in pyridine, DMAP (65.4 mg, 0.53 mmol) and pivaloyl chloride (0.26 mL, 2.14 mmol) were added. After stirring for 24 h at 50 °C, the reaction was quenched by methanol and concentrated in vacuo. The crude product was purified by silica gel column chromatography to give **10** as colorless foam in 71% yield (0.82 g, 1.27 mmol). **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-**

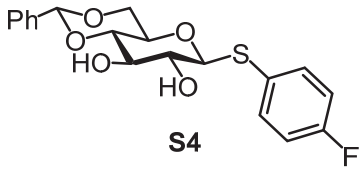
2-*O*-pivaloyl-1-thio-β-D-mannopyranoside (10). TLC (Hexane/ EtOAc 4:1) R_f =0.62; $[\alpha]_D$ = -0.83 (*c* = 1.0, $CHCl_3$); *E*ox = 1.67 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50 (m, 2 H), 7.29 (m, 13 H), 7.17 (m, 2 H), 6.90 (*pseudo*-t, *J* = 9.0 Hz), 5.03 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.76 (d, *J* = 6.8 Hz, 1 H), 4.74 (d, *J* = 6.7 Hz, 1 H), 4.68 (d, *J* = 11.0 Hz, 1 H), 4.57 (d, *J* = 11.9 Hz, 1 H), 4.54 (m, 3 H), 3.77 (dd, *J* = 10.9, 1.8 Hz, 1 H), 3.71 (m, 2 H), 3.65 (*pseudo*-t, *J* = 9.3 Hz, 1 H), 3.53 (ddd, *J* = 9.7, 4.9, 1.8 Hz, 1 H), 1.24 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.6, 162.9 (d, *J* = 246.6 Hz), 138.1, 138.0, 137.9, 135.5 (d, *J* = 8.0 Hz), 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7 (d, *J* = 2.0 Hz), 127.6, 127.5, 127.46, 127.38, 115.9 (d, *J* = 21.6 Hz), 86.2, 84.7, 79.3, 77.6, 75.3, 75.2, 75.1, 73.6, 73.5, 71.5, 69.0, 30.8, 27.2. HRMS (ESI) *m/z* calc. for $C_{38}H_{41}FO_6S$ $[M+K]^+$, 683.2239; found, 683.2236.



Scheme S2

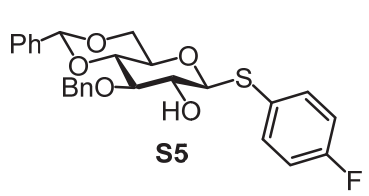


The mixture of penta-*O*-acetyl-β-D-glucopyranose (10.0 g, 25.6 mmol), 4-fluorothiophenol (3.27 mL, 30.7 mmol) in CH_2Cl_2 (70 mL) was stirred at 0 °C, then BF_3•OEt_2 (6.3 mL, 51.2 mmol) was added, and stirred overnight at rt. The reaction mixture was quenched with aqueous solution of $NaHCO_3$, washed with H_2O and brine, and dried over anhydrous Na_2SO_4. The solution was then concentrated and purified by silica gel chromatography to give **S3** as white solid (9.46 g, 20.6 mmol, 81% yield). **4-Fluorophenyl-2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (S3).**[3] TLC (Hexane/ EtOAc 1:1) R_f = 0.73; $[\alpha]_D$ = 2.17 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50 (m, 2 H), 7.02 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.20 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 5.00 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 4.90 (dd, *J* = 10.2, 9.6 Hz, 1 H), 4.60 (d, *J* = 10.2 Hz, 1 H), 4.19 (m, 2 H), 3.70 (m, 1 H), 2.10 (s, 3 H), 2.07 (s, 3 H), 2.01 (s, 3 H), 1.98 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.5, 170.1, 169.3, 169.2, 163.3 (d, *J* = 247.8 Hz), 136.5 (d, *J* = 8.1 Hz), 125.7, 116.0 (d, *J* = 21.7 Hz), 85.3, 75.8, 73.9, 69.7, 68.0, 62.0, 20.7, 20.7, 20.5, 20.5. HRMS (ESI) *m/z* calc. for $C_{20}H_{23}FO_9S$ $[M+K]^+$, 497.0678; found, 497.0675.



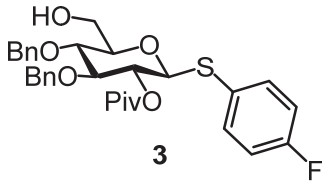
To a stirred solution of **S3** (24.5 g, 53.4 mmol) in methanol (100 mL) was added 2 N HCl in Et_2O (110 mL, 107 mmol). After stirring for 24 h, solvent was removed under reduced pressure to obtain the crude product of the intermediate. The crude product was dissolved into CH_3CN (150 mL) and benzaldehyde dimethylacetal (24.5 mL, 160 mmol) were added. After stirring for 24 h, the reaction was quenched with Et_3N and solvent was removed under reduced pressure. The crude product was then purified using flash chromatography to obtain pure product in 60% (32.0 mmol) as a

colourless solid. **4-Fluorophenyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside (S4).**[4] TLC (Hexane/EtOAc 1:1) R_f = 0.20; $[\alpha]_D$ = -3.41 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.52 (dd, *J* = 8.4, 4.8 Hz, 2 H), 7.46 (dd, *J* = 7.2, 3.6 Hz, 2 H), 7.35 (m, 3 H), 7.02 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.49 (s, 1 H), 4.49 (d, *J* = 9.6 Hz, 1 H), 4.33 (dd, *J* = 10.2, 4.2 Hz, 1 H), 3.77 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 3.72 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 3.44 (m, 2 H), 3.37 (td, *J* = 9.6, 1.8 Hz, 1 H), 3.15 (s, 1 H), 2.94 (d, *J* = 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 163.2 (d, *J* = 247.8 Hz), 138.8, 135.9 (d, *J* = 8.4 Hz), 129.4, 128.4, 128.4, 126.3, 126.0 (d, *J* = 3.2 Hz), 116.2 (d, *J* = 21.7 Hz), 101.9, 88.4, 80.1, 74.5, 72.5, 70.5, 68.5. HRMS (ESI) *m/z* calc. for $C_{19}H_{19}FO_5S$ $[M+K]^+$, 417.0569; found, 417.0570.



S5

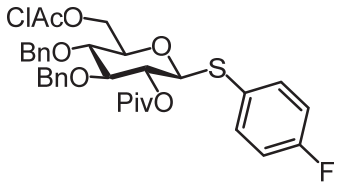
Substrate **S4** (0.60 g, 1.59 mmol) and dibutyl tinoxide (0.493 g, 1.98 mmol) were placed in a round bottle flask and dry MeOH (10 mL) was added. The reaction mixture was refluxed for 22 h and then evaporated to remove solvent. The crude product was again dissolved in DMF (15 mL) and CsF (0.301 g, 1.98 mmol) and BnBr (0.235 mL, 1.98 mmol) were added subsequently. Additional stirring at rt for 24 h, the reaction was quenched with water and extracted with EtOAc. The organic layer was washed with water and dried with Na_2SO_4. Subsequent filtration and evaporation gave the crude product. Further purification by silica gel column chromatography afforded **S5** (0.451 g, 0.96 mmol) in 61% yield. **4-Fluorophenyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (S5).**[5] TLC (Hexane/EtOAc 4:1) R_f = 0.28; $[\alpha]_D$ = -3.67 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.54 (dd, *J* = 8.4, 4.8 Hz, 2 H), 7.49 (dd, *J* = 7.2, 1.2 Hz, 2H), 7.28 (m, 8 H), 7.03 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.57 (s, 1 H), 4.97 (d, *J* = 11.4 Hz, 1 H), 4.78 (d, *J* = 12.0 Hz, 1 H), 4.54 (d, *J* = 9.6 Hz, 1 H), 4.38 (dd, *J* = 10.8, 4.8 Hz, 1 H), 3.78 (*pseudo*-t, *J* = 10.1 Hz, 1 H), 3.67 (dd, *J* = 17.4, 9.0 Hz, 1 H), 3.63 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.48 (m, 2 H), 2.68 (d, *J* = 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 163.1 (d, *J* = 247.6 Hz), 138.1, 137.1, 136.1 (d, *J* = 8.4 Hz), 129.0, 128.59, 128.55, 128.3, 128.1, 127.9, 127.6, 127.0, 126.0, 126.0, 116.1 (d, *J* = 21.6 Hz), 101.2, 88.3, 81.6, 81.1, 74.8, 72.0, 70.7, 68.6, 65.3. HRMS (ESI) *m/z* calc. for $C_{26}H_{25}FO_5S$ $[M+K]^+$, 507.1038; found, 507.1042.



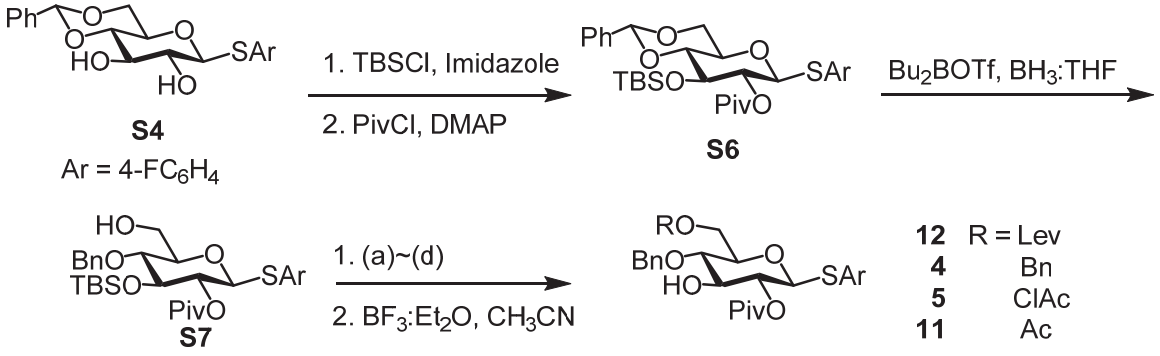
3

To a stirred solution of **S5** (2.0 g, 4.27 mmol) and DMAP (0.15 g, 1.28 mmol) in dry pyridine (18 mL) at rt, pivaloyl chloride (0.8 mL, 6.40 mmol) was added. After the mixture was stirred for another 18 h at 55 ºC, the reaction was quenched with methanol. The solution was then concentrated and purified by silica gel chromatography to give the intermediate in 76% yield (1.80 g, 3.26 mmol). The intermediate (1.80 g, 3.26 mmol) was dissolved in THF (26.4 mL) together with 0.9 M BH_3•THF (26 mL, 23.1 mmol) and stirred at 0 ºC. Then 1.0 M CH_2Cl_2 solution of Bu_2BOTf (3.9 mL, 3.91 mmol) was added dropwise at 0 ºC and stirred at rt for 6 h. The reaction was quenched with Et_3N and concentrated under reduced pressure. Purification by silica gel chromatography afforded **3** (1.30 g, 2.34 mmol) in 72% yield (55% in 2 steps). **4-Fluorophenyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (3).** TLC (Hexane/EtOAc 3:1) R_f = 0.67; $[\alpha]_D$ = -1.33 *(c* = 1.0, $CHCl_3$); *E*ox = 1.62 V vs. SCE; ^1H NMR (CDCl3, 600 MHz) δ 7.46 (m, 2 H), 7.28 (m, 10 H), 7.01 (*pseudo*-t, *J* = 8.6 Hz, 2 H), 5.02 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.78 (d, *J* = 10.8 Hz, 2 H), 4. 70 (d, *J* = 11.2 Hz, 1 H), 4.60 (*pseudo*-t, *J* = 1.2 Hz, 2 H), 3.88 (d, *J* = 11.9 Hz, 1 H), 3.72 (m, 2 H), 3.61 (*pseudo*-t, *J* = 9.4 Hz, 1 H), 3.42 (m, 1 H), 1.96 (s, 1 H), 1.25 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 163.0 (d, *J* = 247.6 Hz), 138.0, 137.8, 135.4 (d, *J* = 8.1 Hz), 128.6, 128.5, 128.1, 128.1, 127.8, 127.4, 116.2 (d, *J*

= 21.6 Hz), 86.5, 84.5, 79.6, 77.3, 75.2, 71.6, 62.1, 38.9, 27.3. HRMS (ESI) *m/z* calc. for $C_{31}H_{35}FO_6S$ $[M+Na]^+$, 577.2031; found, 577.2037.

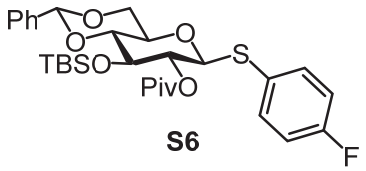


To a stirred solution of **3** (3.0 g, 5.4 mmol) and pyridine (0.55 mL, 6.5 mmol) in dry dichloromethane (50 mL) at 0 °C, chloroacetic anhydride (1.12 g, 6.5 mmol) was added. After the mixture was stirred for 2 h at 0 °C, the reaction was quenched with aq. 2 N HCl. After normal workup procedure purification by silica gel chromatography afforded **14** (2.8 g, 4.4 mmol) in 82% yield. **4-Fluorophenyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-gluco-pyranoside (14).** TLC (Hexane/ EtOAc 17:3) R_f = 0.40; $[\alpha]_D$ = 0.40 *(c* = 1.0, $CHCl_3$); *E*ox = 1.71 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.46 (*pseudo*-dd, *J* = 8.4, 5.4 Hz, 2 H), 7.33-7.22 (m, 10 H), 7.00 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.00 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.79 (d, *J* = 11.4 Hz, 1 H), 4.75 (d, *J* = 11.4 Hz, 1 H), 4.71 (d, *J* = 10.8 Hz, 1 H), 4.54 (*pseudo*-t, *J* = 11.4 Hz, 1 H), 4.23 (dd, *J* = 12.0, 4.2 Hz, 1 H), 3.98 (d, *J* = 15.0, Hz, 1 H), 3.95 (d, *J* = 15.0, Hz, 1 H), 3.74 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 3.58-3.53 (m, 2 H), 1.25 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 163.0 (d, *J* = 247.6 Hz), 162.2, 138.0, 137.8, 135.5, 135.5, 128.6, 128.5, 128.1, 128.1, 127.8, 127.4, 116.2 (d, *J* = 21.6 Hz), 86.5, 84.5, 79.6, 77.3, 75.2, 71.6, 62.1, 38.9, 27.3. HRMS (ESI) *m/z* calc. for $C_{33}H_{36}ClFKO_7S$ $[M+K]^+$, 669.1486; found, 669.1468.



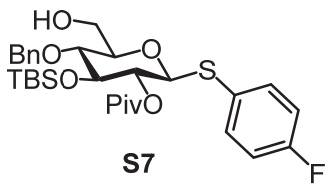
(a) LevOH, DIC, DMAP, CH_2Cl_2, rt, 3 h.
(b) NaH, BnBr, DMF, rt, 3 h.
(c) $(ClCH_2CO)_2O$, DMAP, pyridine,CH_2Cl_2, rt, overnight.
(d) Ac_2O, DMAP, pyridine,CH_2Cl_2, rt, overnight.

Scheme S3



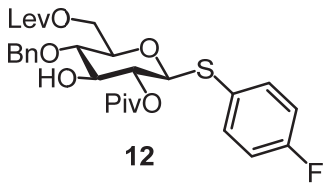
To a solution of compound **S4** (0.880 g, 2.33 mmol) in anhydrous DCM (5.0 mL) were added TBSCl (0.42 g, 2.79 mmol) and imidazole (0.22 g, 3.3 mmol) at 0 °C, and the mixture was stirred for 12 h at room temperature. Reaction mixture is then quenched with MeOH and partitioned between saturated aqueous $NaHCO_3$ and DCM. DCM layered is dried over $MgSO_4$ and evaporated in vacuo to obtain crude product. To a solution of crude product in anhydrous DCM (2.0 mL) were added pivaloyl chloride (PivCl) (0.34 mL, 2.77 mmol), pyridine (6.0 mL, 73.9 mmol), and DMAP (0.22 g, 1.85 mmol) at 0 °C and the mixture was stirred at 55 °C until completion. After the

reaction mixture was quenched by MeOH and subsequent workup with 1N HCl and saturated sodium bicarbonate. Then the organic layer was dried over $MgSO_4$, and the solvent was evaporated in vacuo. The crude product was purified by column chromatography on silica gel to afford **4-Fluorophenyl-2-*O*-pivaloyl-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (S6).**[6] (0.782 g, 1.36 mmol, 60% over two steps). TLC (Hexane/EtOAc 19:1) R_f = 0.59; $[\alpha]_D$ =-4.50 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50-7.45 (m, 4 H), 7.37-7.36 (m, 3 H), 7.03 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.49 (s, 1 H), 4.96 (dd, *J* = 10.2, 8.4 Hz, 1 H), 4.60 (d, *J* = 9.6 Hz, 1 H), 4.35 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.94 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 3.78-3.74 (m, 1 H), 3.52-3.49 (m, 2 H), 1.30 (s, 9 H), 0.00 (s, 3 H), -0.06 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.6, 163.0 (d, *J* = 247.2 Hz), 136.9. 135.6, 129.2, 128.1, 126.4, 116.0 (d, *J* = 21.7 Hz), 102.1, 86.9, 81.3, 77.2, 77.0, 76.8, 74.1, 72.8, 70.3, 68.5, 38.9, 27.4, 25.8, 18.1, -3.8, -4.8. HRMS (ESI) *m/z* calc. for $C_{30}H_{41}FKO_6SSi$ $[M+K]^+$, 615.2009; found, 615.1989.



S7

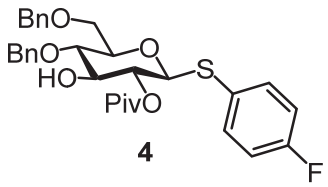
The compound **S6** (3.20 g, 5.55 mmol) was dissolved in THF (45 mL) together with 0.9 M BH_3•THF (45.0 mL, 44.4 mmol) and stirred at 0 ºC. Then CH_2Cl_2 solution of Bu_2BOTf (6.66 mL, 6.66 mmol) was added dropwise at 0 ºC and stirred at room temperature for 6 h. The reaction was quenched with Et_3N and concentrated under reduced pressure. Purification by silica gel chromatography afforded **S7** (2.41 g, 4.15 mmol) in 75% yield. **4-Fluorophenyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (S7)**.[7] TLC (Hexane/EtOAc 9:1) R_f = 0.20; $[\alpha]_D$ =-0.72 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.45 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.34-7.27 (m, 5 H), 7.01 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 4.09 (dd, *J* = 2.4 Hz, 1 H), 4.81 (d, *J* = 11.4 Hz, 1 H), 4.61 (d, *J* = 11.4 Hz, 1 H), 4.55 (d, *J* = 9.6 Hz, 1 H), 3.85 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 3.82 (d, *J* = 12.0 Hz, 1 H), 3.64 (d, *J* = 9.6 Hz, 1 H), 3.47 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.42-3.39 (m, 1 H), 1.83 (bs, 1 H), 1.29 (s, 9 H), 0.86 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.2, 162.9 (d, *J* = 247.0 Hz), 137.9, 135.1, 135.0, 128.3, 127.6, 127.2, 116.0 (d, *J* = 21.7 Hz), 86.4, 79.3, 78.3, 75.9, 74.6, 73.0, 62.0, 39.0, 27.6, 25.8, 17.9, -3.7, -4.2. HRMS (ESI) *m/z* calc. for $C_{30}H_{43}FO_6SSi$ $[M+K]^+$, 617.2165; found, 617.2167.



12

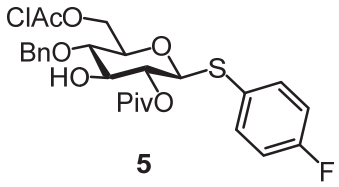
To a solution of **S7** (2.12 g, 3.63 mmol) in anhydrous CH_2Cl_2 (25.0 mL) were added DMAP (0.66 g, 5.4 mmol) and DIC (0.85 mL, 5.44 mmol) at 0 ºC. After 5 min at 0 ºC, levulinic acid (0.59 mL, 5.80 mmol) was added, and the mixture was stirred at room temperature for 2 h. The suspension was diluted with DCM and washed with brine, followed by drying over Na_2SO_4 and filtration, and finally the solvents were evaporated. To the solution of crude product in CH_3CN (190 mL), BF_3•Et_2O was added at 0 ºC. After the completion of the reaction determined by TLC (Hexane/EtOAc 8:2). The reaction was quenched with sat. aqueous $NaHCO_3$. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure resulted crude product. Purification by flash silica gel column chromatography afforded **12** (2.31 g, 3.40 mmol) in 74% yield. **4-Fluorophenyl-4-*O*-benzyl-6-*O*-levulinoyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (12).** TLC (Hexane/ EtOAc 4:1) R_f = 0.10; $[\alpha]_D$ = -0.65 (*c* = 1.0, $CHCl_3$); *E*ox = 1.67 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.40 (dd, *J* = 5.4, 2.4 Hz, 2 H), 7.26-7.19 (m, 5 H), 6.92 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 4.74 (d, *J* = 11.4 Hz, 1 H), 4.64 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.58 (d, *J* = 11.4 Hz, 1 H), 4.45 (d, *J* = 10.2

Hz, 1 H), 4.33 (dd, *J* = 12.0, 1.8 Hz, 1 H), 4.12 (dd, *J* = 12.0, 5.4 Hz, 1 H), 3.71 (td, *J* = 9.0, 4.8 Hz, 1 H), 3.43 (ddd, *J* = 12.0, 4.8, 1.8 Hz, 1 H), 3.34 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 2.66 (*pseudo*-t, *J* = 6.6 Hz, 2 H), 2.59 (d, *J* = 4.8 Hz, 1 H), 2.49 (d, *J* = 7.2 Hz, 1 H), 2.48 (dd, *J* = 6.6, 1.8 Hz, 1 H), 2.18 (s, 3 H), 1.20 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 205.4,177.0, 171.3,162.0 (d, *J* = 247.0 Hz), 136.6, 134.8 (d, *J* = 8.0 Hz), 127.5, 127.1, 127.0, 125.9, 125.9, 114.8 (d, *J* = 21.4 Hz), 84.5, 76.6, 76.4, 75.8, 73.8, 71.0, 62.1, 37.8, 36.7, 28.8, 26.7, 26.1; HRMS (ESI) *m/z* calc. for $C_{29}H_{35}FO_8S$ $[M+K]^+$, 601.1668; found 601.1646.



4

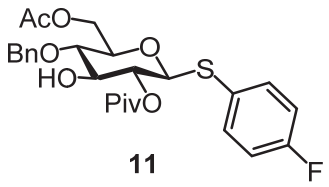
To the solution of **S7** (10.4 mmol, 6.00 g) in DMF (1.30 mmol, 100 mL), and BnBr (37.3 mmol, 4.43 mL), NaH (37.3 mmol, 1.49 g) were added at 0ºC and the reaction mixture was stirred at room temperature for another 3 h. After the completion of the reaction determined by TLC (Hexane/EtOAc 19:1). The reaction was quenched with MeOH. The aqueous phase was extracted with EtOAc. The reaction mixture was washed with H_2O and brine for three times and dried over Na_2SO_4 and evaporated to obtain crude product. To the solution of crude product in CH_3CN (190 mL), BF_3•Et_2O was added at 0 ºC. After the completion of the reaction determined by TLC (Hexane/EtOAc 4:1) the reaction was quenched with sat. aqueous $NaHCO_3$. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure the crude product was purified with silica gel chromatography to obtain **4** in 78% yield (4.49 g, 8.11 mmol). **4-Fluorophenyl-4,6-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (4).** TLC (Hexane/EtOAc 17:3) R_f = 0.23; $[\alpha]_D$ = -0.23 (*c* = 1.0, $CHCl_3$); *E*ox = 1.63 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50-7.48 (m, 2 H), 7.24-7.36 (m, 10 H), 6.90 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 4.76 (dd, *J* = 18.0, 9.0 Hz, 1 H), 4.74 (d, *J* = 6.6 Hz, 1 H), 4.63 (d, *J* = 10.8 Hz, 1 H), 4.59 (d, *J* = 12.0 Hz, 1 H), 4.55 (d, *J* = 12.6 Hz, 1 H), 4.54 (d, *J* = 10.2 Hz, 1 H), 3.80-3.74 (m, 2 H), 3.72 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.52 (pseudo-t, *J* = 10.2 Hz, 1 H), 3.49-3.47 (m, 1 H), 2.42 (d, *J* = 4.2 Hz, 1 H), 1.27 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.0, 162.9 (d, *J* = 247.0 Hz), 138.1, 137.9, 135.5, 135.5, 128.5, 128.4, 128.0, 128.0, 127.7, 127.7, 127.2, 127.2, 115.9 (d, *J* = 21.6 Hz), 85.6, 78.9, 77.9, 77.3, 74.9, 73.4, 72.2, 68.9, 38.9, 27.1; HRMS (ESI) *m/z* calc. for $C_{31}H_{35}FO_6S$ $[M+K]^+$, 593.1770; found 593.1775.



5

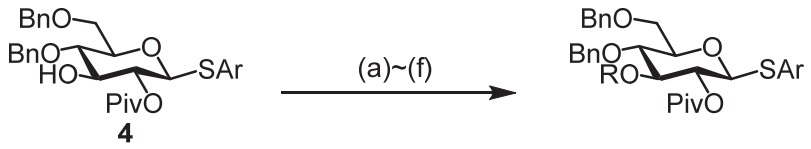
To the solution of **S7** (5.91 mmol, 3.42 g) in CH_2Cl_2 (56.6 mL), and pyridine (8.9 mmol, 0.71 mL) were added at room temperature. $(ClCH_2CO)_2O$ (8.86 mmol, 1.52 g) was added at -10 ºC and the reaction mixture was stirred for another 2 h. After the completion of the reaction determined by TLC (Hexane/EtOAc 9:1), the reaction was quenched with 1 N HCl. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. Solid was removed by filtration and the reaction mixture was evaporated to obtain crude product. To the solution of crude product in CH_3CN (108 mL), BF_3•Et_2O was added at 0 ºC. After the completion of the reaction determined by TLC (Hexane/EtOAc 8:2). The reaction was quenched with sat. aqueous $NaHCO_3$. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure the crude product was purified with silica gel chromatography to obtain **5** in 86% yield (2.75 g, 5.08 mmol). **4-Fluorophenyl-4-*O*-benzyl-6-*O*-chloroacetyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (5).** TLC (Hexane/EtOAc 4:1) R_f = 0.24; $[\alpha]_D$ = 0.35 (*c* = 1.0, $CHCl_3$); *E*ox = 1.63 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ

7.45 (*pseudo*-dd, *J* = 8.4, 5.4 Hz, 2 H), 7.36-7.30 (m, 5 H), 7.01 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 4.85 (d, *J* = 11.4 Hz, 1 H), 4.78-4.71 (m, 2 H), 4.54 (d, *J* = 10.2 Hz, 1 H), 4.52 (dd, *J* = 12.0, 1.8 Hz, 1 H), 4.27 (dd, *J* = 12.0, 5.4 Hz, 1 H), 4.01 (d, *J* = 15.0 Hz, 1 H), 3.97 (d, *J* = 15.0 Hz, 1 H), 3.82 (td, *J* = 9.0, 4.8 Hz, 1 H), 3.54 (ddd, *J* = 9.6, 4.8, 1.8 Hz, 1 H), 3.43 (dd, *J* = 9.6, 0.6 Hz, 1 H), 2.50 (d, *J* = 4.2 Hz, 1 H), 1.29 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.2, 167.0, 163.1 (d, *J* = 247.2 Hz), 137.6, 135.9 (d, *J* = 8.25 Hz), 128.6, 128.3, 128.2, 126.8, 116.8 (d, *J* = 21.8 Hz), 128.2, 126.8, 116.0 (d, *J* = 21.8 Hz), 85.7, 77.5, 77.1, 76.6, 74.8, 72.1, 64.5, 40.7, 38.9, 27.2; HRMS (ESI) *m/z* calc. for $C_{26}H_{30}ClFO_7S$ [M+K]$^+$, 579.1022; found 579.1016.



11

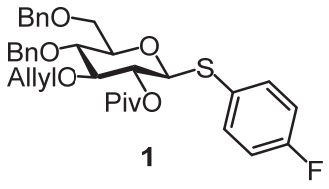
To the solution of **S7** (2.00 g, 3.46 mmol) in CH_2Cl_2 (23 mL), DMAP (126 mg, 1.04 mmol), pyridine (11.1 mL, 138 mmol), and Ac_2O (0.425 mL, 4.49 mmol) were added at 0 °C and the reaction mixture was stirred at room temperature overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 4:1), the reaction was quenched with 1 N HCl. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. Solid was removed by filtration and the reaction mixture was evaporated to obtain crude product. To the solution of crude product in CH_3CN (66.1 mL), BF_3•Et_2O was added at 0 °C. After the completion of the reaction determined by TLC (eluent: Hexane/EtOAc 8:2). The reaction was quenched with sat. aqueous $NaHCO_3$. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure the crude product was purified with silica gel chromatography to obtain **11** in 93% yield (1.63 g, 3.22 mmol). **4-Fluorophenyl-6-*O*-acetyl-4-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (11).** TLC (Hexane/EtOAc 9:1) R_f = 0.10; $[\alpha]_D$ = -0.41 (*c* = 1.0, $CHCl_3$); *E*ox = 1.67 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.47 (*pseudo*-dd, *J* = 9.0, 5.4 Hz, 2 H), 7.36-7.29 (m, 5 H), 7.00 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 4.82 (d, *J* = 10.8 Hz, 1 H), 4.72 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.67 (d, *J* = 11.4 Hz, 1 H), 4.54 (d, *J* = 9.6 Hz, 1 H), 4.43 (dd, *J* = 12.0, 1.8 Hz, 1 H), 4.19 (dd, *J* = 12.0, 5.4 Hz, 1 H), 3.81 (td, *J* = 9.0, 4.8 Hz, 1 H), 3.52 (ddd, *J* = 10.0, 5.4, 2.4 Hz, 1 H), 3.44 (dd, *J* = 9.6, 9.0 Hz, 1 H), 2.49-2.47 (m, 1 H), 2.06 (s, 3 H), 1.29 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.2, 170.6, 163.1 (d, *J* = 247.4 Hz), 137.6, 135.9 (d, *J* = 7.5 Hz), 128.6, 128.24, 128.19, 126.8, 126.8, 115.9 (d, *J* = 21.8 Hz), 85.5, 77.6, 77.6, 75.0, 72.1, 63.0, 38.9, 27.2, 20.9; HRMS (ESI) *m/z* calc. for $C_{26}H_{31}FO_7S$ [M+K]$^+$, 545.1406; found 545.1385.



1 R = allyl
6 4-BrBn
9 Fmoc
13 Lev
15 ClAc
16 Ac

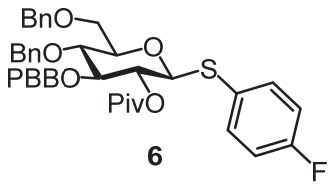
(a) NaH, allylBr, DMF, 0 °C~rt, 3 h.
(b) NaH, 4-BrBnBr, DMF, 0 °C~rt, 3 h.
(c) FmocCl, pyridine, CH_2Cl_2, rt, 2 days.
(d) LevOH, DIC, DMAP, CH_2Cl_2, rt, 3 h.
(e) $(ClCH_2CO)_2O$, DMAP, pyridine,CH_2Cl_2, rt, overnight.
(f) Ac_2O, DMAP, pyridine,CH_2Cl_2, rt, overnight.

Scheme S4



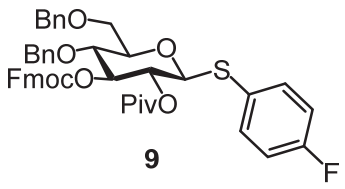
1

To the solution of **4** (1.0 g, 1.8 mmol) in DMF (18 mL) NaH (161 mg, 6.5 mmol) was added at 0 ºC. Then allyl bromide (0.60 mL, 6.5 mmol) was added and the reaction mixture was stirred at room temperature for 3 h. After the completion of the reaction determined by TLC (Hexane/EtOAc 9:1), the reaction was quenched with MeOH. The reaction mixture was extracted with EtOAc and the organic layer washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure, the crude product was purified with silica gel chromatography to afford **1** in 68% yield (727 mg, 1.22 mmol). **4-Fluorophenyl-3-*O*-allyl-4,6-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (1).** TLC (Hexane/EtOAc 9:1) R_f 0.30; $[\alpha]_D$ = -13.2 (*c* = 1.0, $CHCl_3$); *E*ox = 1.55 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.56 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.38-7.24 (m, 8 H), 7.16 (d, *J* = 8.4 Hz, 2 H), 6.93 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.90-5.83 (m, 1 H), 5.32 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 5.25 (dd, *J* = 17.4, 1.8 Hz, 1 H), 5.15 (dd, *J* = 10.8, 1.8 Hz, 1 H), 4.60-4.57 (m, 3 H), 4.52 (d, *J* = 12.0 Hz, 1 H), 4.49 (d, *J* = 10.8 Hz, 1 H), 4.38 (ddt, *J* = 12.0, 5.4, 1.8 Hz, 1 H), 4.02 (ddt, *J* = 11.4, 5.4, 1.2 Hz, 1 H), 3.72 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.69 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.67 (pseudo-t, *J* = 9.6 Hz, 1 H), 3.51 (ddd, *J* = 9.6, 4.2, 1.8 Hz, 1 H), 1.20 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.0, 162.7 (d, *J* = 246.9 Hz), 138.0, 137.6, 134.8 (d, *J* = 7.8 Hz), 134.1, 128.40, 128.34, 128.26, 127.78, 127.74, 127.71, 127.4, 117.0, 116.0 (d, *J* = 21.6 Hz), 87.6, 78.9, 78.6, 76.1, 74.2, 73.4, 73.3, 68.7, 38.8, 27.2; HRMS (ESI) *m/z* calc. for $C_{34}H_{39}FKO_6S$ $[M+K]^+$, 633.2083; found 633.2075.



6

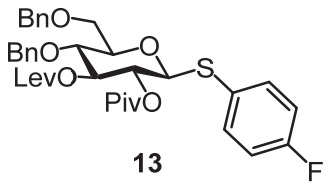
To the solution of **4** (1.0 g, 1.8 mmol) in DMF (18 mL), NaH (158 mg, 6.5 mmol) was added at 0 ºC. Then 4-bromobenzyl bromide (1.63 g, 6.5 mmol) was added to the reaction mixture and the reaction mixture was stirred at room temperature for 3 h. After the completion of the reaction determined by TLC (Hexane/EtOAc 9:1) the reaction was quenched with water. The reaction mixture was extracted with EtOAc and thus-obtained organic layer washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure the crude product was purified with silica gel chromatography to afford **6** in 90% yield (1.17 g, 1.62 mmol). **4-Fluorophenyl-4,6-di-*O*-benzyl-3-*O*-*para*-bromobenzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (6).** TLC (Hexane/EtOAc 9:1) R_f 0.30; $[\alpha]_D$ = 4.20 (*c* = 1.0, $CHCl_3$); *E*ox = 1.64 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.53 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.45 (d, *J* = 7.8 Hz, 2 H), 7.38-7.25 (m, 8 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.17 (d, *J* = 7.8 Hz, 2 H), 6.93 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.41 (pseudo-t, *J* = 9.0 Hz, 1 H), 4.85 (d, *J* = 10.2 Hz, 1 H), 4.64 (d, *J* = 10.2 Hz, 1 H), 4.61- 4.56 (m, 2 H), 4.53 (d, *J* = 12.0 Hz, 1 H), 4.52-4.48 (m, 2 H), 3.75-3.69 (m, 3 H), 3.54 (ddd, *J* = 9.6, 3.6, 1.8 Hz, 1 H), 3.45 (pseudo-t, *J* = 9.0 Hz, 1 H), 1.14 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.1, 162.7 (d, *J* = 246.6 Hz), 138.0, 137.6, 136.7, 134.8 (d, *J* = 8.0 Hz), 131.4, 128.9, 128.41, 128.36, 128.0 (d, *J* = 3.3 Hz), 127.78, 127.76, 127.74, 127.3, 121.5, 116.0 (d, *J* = 21.8 Hz), 87.4, 79.2, 78.6, 76.7, 76.1, 74.3, 73.4, 73.2, 68.6, 38.8, 27.2; HRMS (ESI) *m/z* calc. for $C_{38}H_{40}BrFKO_6S$ $[M+K]^+$, 761.1345; found 761.1333.



9

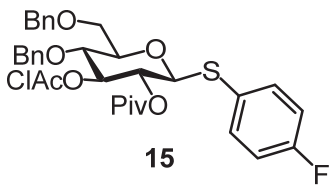
To the solution of **4** (378 mg, 0.68 mmol) in CH_2Cl_2 (5.0 mL), FmocCl (427.7 mg, 1.65 mmol), and pyridine (1.00 mL, 12.4 mmol) were added at 0 ºC and the reaction mixture was stirred at room temperature for 2 days. After the completion of the reaction determined by TLC (Hexane/EtOAc 4:1) the reaction was

quenched with 1 N HCl. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure the crude product was purified with silica gel chromatography to obtain **9** in 89% yield (469 mg, 0.604 mmol). **4-Fluorophenyl-4,6-di-*O*-benzyl-3-*O*-(9-fluorenylme-thyloxycarbonyl)-2-*O*-pivaloyl-1-thio-β-D-gluco-pyranoside (9).** TLC (hexane/EtOAc 9:1) R_f = 0.27; $[\alpha]_D$ =-0.62 (*c* = 1.0, $CHCl_3$); *E*ox = 1.66 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.74, (dd, *J* = 7.8, 3.6 Hz, 2 H), 7.55 (d, *J* = 7.8 Hz, 2 H), 7.50 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.39-7.21 (m, 14 H), 7.15 (dd, *J* = 7.2, 1.2 Hz, 2 H), 6.92 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.13 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.98 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.63-4.52 (m, 5 H), 4.27 (qd, *J* = 10.8, 7.3 Hz, 2 H), 4.15 (t, *J* = 7.2 Hz, 1 H), 3.79-3.76 (m, 2 H), 3.73 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.57 (ddd, *J* = 9.6, 4.2, 1.8 Hz, 1 H), 1.16 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.6, 163.1 (d, *J* = 247.2 Hz), 154.6, 143.2, 141.2, 138.1, 137.5, 135.9 (d, *J* = 8.6 Hz), 128.44, 128.37, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.3, 127.2, 126.8, 126.8, 125.2, 120.0, 120.0, 116.0 (d, *J* = 21.8 Hz), 85.8, 80.6, 79.1, 75.7, 74.9, 73.5, 70.3, 69.6, 68.6, 46.6, 38.7, 27.0; HRMS (ESI) *m/z* calc. for $C_{46}H_{45}FO_8S$ $[M+K]^+$, 815.2456; found 815.2437.



13

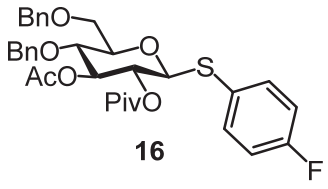
To the solution of **4** (1.00 g, 1.80 mmol) in CH_2Cl_2 (11.5 mL, 180 mmol), DMAP (330 mg, 2.70 mmol), *N*, *N'*-diisopropyl carbodiimide (0.42 mL, 2.7 mmol) and LevOH (0.293 mL, 2.88 mmol) were added at 0 °C and the reaction mixture was stirred at room temperature 3 h. After the completion of the reaction determined by TLC (Hexane/EtOAc 8:2) the reaction was quenched. After normal workup procedure the crude product was purified with silica gel chromatography to obtain **13** in 98% (1.19 g, 1.82 mmol). **4-Fluorophenyl-4,6-di-*O*-benzyl-3-*O*-levulinoyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (13).** TLC (hexane/EtOAc 8:2) R_f = 0.22; $[\alpha]_D$ = -2.85 (*c* = 1.0, $CHCl_3$); *E*ox = 1.70 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (*pseudo*-dd, *J* = 9.0, 5.4 Hz, 2 H), 7.39-7.27 (m, 8 H), 7.21-7.19 (m, 2 H), 6.92 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.27 (t, *J* = 9.6 Hz, 1 H), 4.85 (t, *J* = 9.6 Hz, 1 H), 4.60-4.51 (m, 5 H), 3.77-3.68 (m, 3 H), 3.54 (ddd, *J* = 9.6, 4.2, 1.8 Hz, 1 H), 2.59 (dt, *J* = 12.6, 6.0 Hz, 2 H), 2.41 (*pseudo*-t, *J* = 7.2 Hz, 2 H), 2.14 (s, 3 H), 1.21 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 205.9, 176.8, 171.7, 163.0 (d, *J* = 247.1 Hz), 138.1, 137.8, 135.8 (d, *J* = 8.4 Hz), 128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 126.9, 126.8, 116.0 (d, *J* = 21.8 Hz), 85.7, 79.1, 76.1, 75.7, 74.6, 73.5, 69.8, 68.6, 60.4, 38.8, 37.6, 29.8, 27.9, 27.1, 21.1, 14.2; HRMS (ESI) *m/z* calc. for $C_{36}H_{41}FO_8S$ $[M+K]^+$,691.2143; found 691.2126.



15

To the solution of **4** (928 mg, 1.67 mmol) in CH_2Cl_2 (11.5 mL), DMAP (68.1 mg, 0.541 mmol), pyridine (0.436 mL, 5.41 mmol), and $(ClCH_2CO)_2O$ (401 mg, 2.34 mmol) were added at 0 °C and the reaction mixture was stirred at room temperature for overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 8:2), the reaction was quenched with 1 N HCl. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure, the crude product was purified with silica gel chromatography to afford **15** in 93% yield (982 mg, 1.56 mmol). **4-Fluorophenyl-4,6-di-*O*-benzyl-3-*O*-chloroacetyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (15).** TLC (Hexane/EtOAc 8:2) R_f 0.55; $[\alpha]_D$ = -4.75 (*c* = 1.0, $CHCl_3$); *E*ox = 1.72 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (dd, *J* = 5.4, 1.4 Hz, 2 H), 7.39-7.24 (m, 8 H), 7.16-7.15 (m, 2 H), 6.93 (*pseudo*-

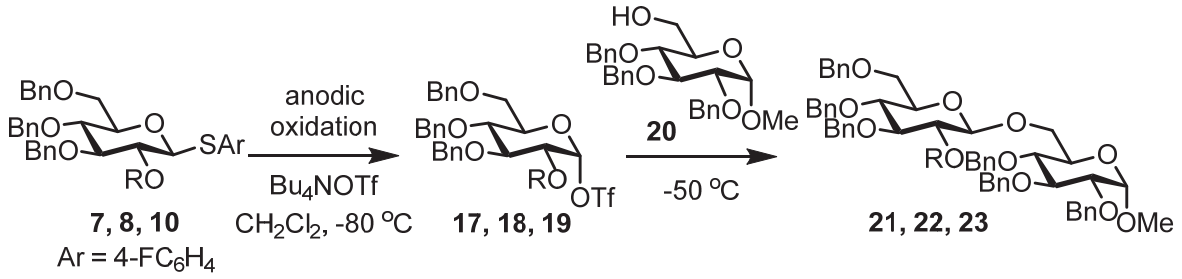
t, *J* = 9.6 Hz, 2 H), 5.27 (t, *J* = 9.6 Hz, 1 H), 4.83 (t, *J* = 9.6 Hz, 1 H), 4.63- 4.46 (m, 5 H), 3.80-3.72 (m, 3 H), 3.72 (d, *J* = 15.0 Hz, 1 H), 3.58 (d, *J* = 15.0 Hz, 1 H), 3.54 (dt, *J* = 10.2, 3.6 Hz, 1 H), 1.20 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.9, 171.2, 166.5, 163.1 (d, *J* = 247.2 Hz), 138.0, 137.7, 136. 0 (d, *J* = 8.1 Hz), 128.6, 128.5, 128.0, 127.9, 127.8, 126.5, 126.5, 116.0 (d, *J* = 21.8 Hz), 85.6, 79.2, 77.5, 75.4, 74.7, 73.6, 69.6, 68.4, 60.4, 40.4, 38.8, 27.1, 21.1, 14.2; HRMS (ESI) *m/z* calc. for $C_{33}H_{36}ClFO_7S$ $[M+K]^+$, 669.1491; found 669.1475.



16

To the solution of **4** (1.00 g, 1.80 mmol) in DMAP (66.1 mg, 0.541 mmol), CH_2Cl_2 (11.5 mL, 180 mmol), pyridine (0.436 mL, 5.41 mmol) and Ac_2O (0.22 mL, 2.34 mmol) were added at 0 °C and the reaction mixture was stirred at room temperature for overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 9:1), the reaction was quenched with 1 N HCl. The reaction mixture was washed with H_2O for three times and dried over Na_2SO_4. After filtration and removal of solvent under reduced pressure the crude product was purified with silica gel chromatography to obtain **16** in 97% yield (1.05 g, 1.75 mmol). **4-Fluorophenyl-3-*O*-acetyl-4,6-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (16).** TLC (hexane/EtOAc 9:1) R_f = 0.26; $[\alpha]_D$ = -3.67 (*c* = 1.0, $CHCl_3$); *E*ox = 1.72 V vs. SCE; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (*pseudo*-dd, *J* = 8.4, 4.8 Hz, 2 H), 7.39-7.28 (m, 8 H), 7.17 (d, *J* = 7.2 Hz, 2 H), 6.92 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.27 (t, *J* = 9.6 Hz, 1 H), 4.85 (t, *J* = 9.6 Hz, 1 H), 4.61-4.53 (m, 5 H), 3.78-3.68 (m, 3 H), 3.55 (dt, *J* = 10.2, 2.4 Hz, 1 H), 1.87 (s, 3 H), 1.21 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.9, 169.9, 163.0 (d, *J* = 247.1 Hz), 138.0, 137.7, 135.8 (d, *J* = 8.1 Hz), 128.5, 128.4, 127.91, 127.88, 127.8, 127.7, 126.8 (d, *J* = 3.3 Hz), 116.0 (d, *J* = 21.8 Hz), 79.2, 75.7, 74.6, 73.5, 69.8, 68.6, 38.8, 27.0, 20.8; HRMS (ESI) *m/z* calc. for $C_{33}H_{37}FO_7S$ $[M+K]^+$, 635.1881; found 635.1868.

3. Automated synthesis of disaccharide

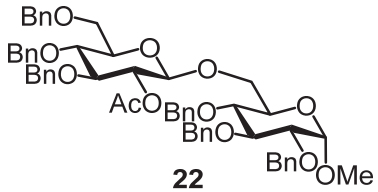


7, 8, 10
Ar = 4-FC_6H_4

17, 18, 19

21, 22, 23

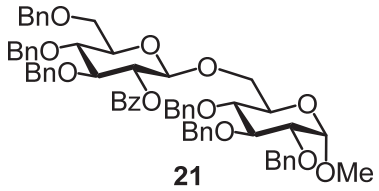
Scheme S5



22

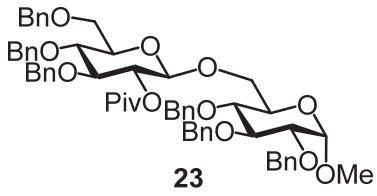
The automated synthesis of disaccharide **22** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm × 20 mm). In the anodic chamber were placed building block **8** (241 mg, 0.40 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (35.3 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). The constant current electrolysis (8.0 mA) was carried out at -80 °C with magnetic stirring until 1.0

F/mol of electricity was consumed. After the electrolysis, Methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **20** (223 mg, 0.48 mmol) dissolved in CH_2Cl_2 (1.2 mL) was subsequently added by the syringe pump (1.0 mL, 0.20 mmol) under an argon atmosphere at -80 ºC, and then the temperature was raised to -50 ºC and kept for 60 min. The reaction temperature was cooled down to -80 ºC and Et_3N (0.3 mL) was added at -80 ºC. After additional stirring at rt for 30 min the reaction mixture was filtered through a short column (4 × 3 cm) of silica gel to remove Bu_4NOTf. The removal of the solvent under reduced pressure and column chromatography (silica gel, Hexane/EtOAc 5:2) afforded disaccharide **22** in 69% isolated yield (260 mg, 0.28 mmol). **Methyl-3,4,6-tri-*O*-benzyl-2-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-gluco-pyranoside (22)**. TLC (Hexane/EtOAc 7:3) R_f = 0.26. $[\alpha]_D$ = 0.89 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.29 (m, 28 H), 7.18 (m, 2 H), 5.05 (dd, *J* = 9.0, 8.2 Hz, 1 H), 4.96 (d, *J* = 11.0 Hz, 1 H), 4.83 (d, *J* = 10.8 Hz, 1 H), 4.79 (d, *J* = 3.0 Hz, 1 H), 4.77 (d, *J* = 6.6 Hz, 1 H), 4.77 (s, 1 H), 4.76 (s, 1 H), 4.65 (s, *J* = 4.6 Hz, 1 H), 4.63 (d, *J* = 5.3 Hz, 1 H), 4.56 (s, 1 H), 4.55 (dd, *J* = 1.9 Hz, 1 H), 4.53 (s, 1 H), 4.52 (d, *J* = 12.0 Hz, 1 H), 4.39 (d, *J* = 8.0 Hz, 1 H), 4.09 (dd, *J* = 10.7, 1.7 Hz, 1 H), 3.96 (t, *J* = 9.3 Hz, 1 H), 3.75 (ddd, *J* = 10.1, 4.6, 1.6 Hz, 1 H), 3.72 (dd, *J* = 10.9, 1.9 Hz, 1 H), 3.65 (m, 4 H), 3.52 (dd, *J* = 9.6, 3.6 Hz, 1 H), 3.48 (m, 1 H), 3.44 (t, *J* = 9.2 Hz, 1 H), 3.34 (s, 3 H), 1.86 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 163.9, 138.9, 138.3, 138.2, 138.2, 137.9, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 101.1, 98.1, 83.1, 82.1, 79.9, 78.1, 77.8, 75.7, 75.4, 75.1, 75.1, 74.9, 73.5, 73.5, 73.0, 69.8, 68.9, 68.0, 55.1, 21.0; HRMS (ESI) *m/z* calc. for $C_{57}H_{62}O_{12}$ $[M+K]^+$,977.3873; found 977.3874. The NMR data were in good agreement with those reported in the literature.[10]



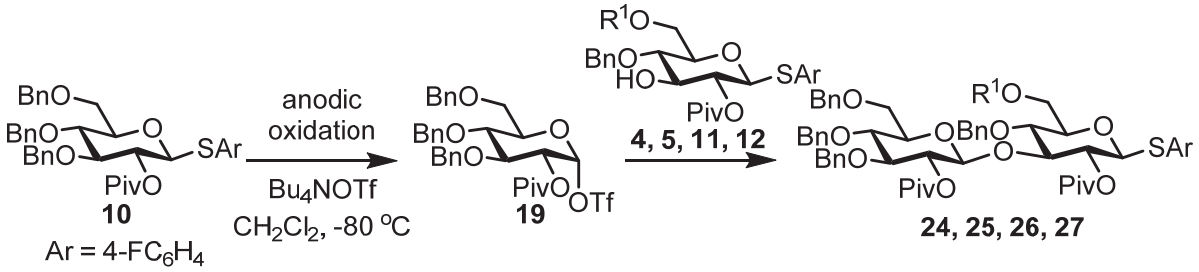
21

Automated electrochemical glycosylation of building blocks **7** (130 mg, 0.20 mmol) with Methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **20** (113 mg, 0.24 mmol) afforded **21** (147 mg, 0.14 mmol) in 75% yield, following the same procedure as that of compound **22**. **Methyl-3,4,6-tri-*O*-benzyl-2-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (21)**. TLC (Hexane/EtOAc 3:1) R_f = 0.39. $[\alpha]_D$ = 2.19 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.92 (m, 2 H), 7.42 (m, 1 H), 7.24 (m, 25 H), 7.12 (s, 5 H), 7.01 (dd, *J* = 6.9, 2.1 Hz, 2 H), 5.35 (dd, *J* = 9.2, 8.2 Hz, 1 H), 4.87 (d, *J* = 11.0 Hz, 1 H), 4.81 (d, *J* = 10.7 Hz, 1 H), 4.73 (d, *J* = 6.8 Hz, 1 H), 4.71 (d, *J* = 7.8 Hz, 1 H), 4.67 (d, *J* = 7.5 Hz, 1 H), 4.65 (d, *J* = 7.7 Hz, 1 H), 4.58 (m, 4 H), 4.53 (d, *J* = 8.0 Hz, 1 H), 4.47 (d, *J* = 3.5 Hz, 1 H), 4.43 (d, *J* = 11.0 Hz, 1 H), 4.27 (d, *J* = 11.0 Hz, 1 H), 4.14 (d, *J* = 9.4 Hz, 1 H), 3.87 (t, *J* = 9.3 Hz, 1 H), 3.81 (t, *J* = 9.2 Hz, 1 H), 3.76 (dd, *J* = 10.8, 1.5 Hz, 1 H), 3.68 (m, 4 H), 3.56 (ddd, *J* = 9.7, 5.2, 1.6 Hz, 1 H), 3.43 (dd, *J* = 9.7, 3.5 Hz, 1 H), 3.37 (t, *J* = 9.4 Hz, 1 H), 3.19 (s, 3 H)); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 139.1, 138.5, 138.5, 138.4, 138.1, 138.0, 133.2, 130.1, 130.0, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.1, 128.1, 127.9, 127.9, 128.8, 128.7, 128.7, 101.5, 98.2, 83.1, 82.2, 80.0, 78.3, 77.4, 75.7, 75.7, 75.3, 75.3, 75.3, 74.9, 73.9, 73.7, 73.6, 69.7, 69.1, 68.3, 55.2; HRMS (ESI) *m/z* calc. for $C_{62}H_{64}O_{12}$ $[M+K]^+$, 1039.4029; found 1039.4023. The NMR data were in good agreement with those reported in the literature.[11]

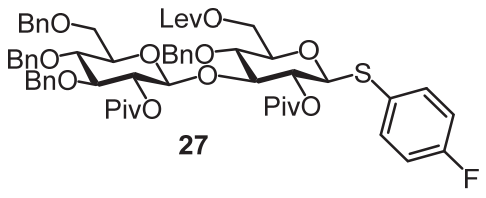


23

Automated electrochemical glycosylation of building blocks **10** (130 mg, 0.20 mmol) with Methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **20** (113 mg, 0.24 mmol) afforded **23** (147 mg, 0.14 mmol) in 86% yield, following the same procedure as that of compound **22**. **Methyl-3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (23)**. TLC (Hexane/EtOAc 7:3) R_f = 0.64. $[\alpha]_D$ = 1.75 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.92 (m, 28 H), 7.14 (m, 2 H), 5.10 (dd, *J* = 8.8, 8.1 Hz, 1 H), 4.97 (d, *J* = 11.0 Hz, 1 H), 4.84 (d, *J* = 11.0 Hz, 1 H), 4.79 (d, *J* = 11.0 Hz, 1 H), 4.75 (m, 3 H), 4.67 (d, *J* = 10.9 Hz, 1 H), 4.64 (d, *J* = 12.1 Hz, 1 H), 4.57 (dd, *J* = 11.6, 8.6 Hz, 2 H), 4.55 (m, 2 H), 4.49 (d, *J* = 12.2 Hz, 1 H), 4.41 (d, *J* = 7.9 Hz, 1 H), 4.04 (dd, *J* = 10.6, 1.8 Hz, 1 H), 3.98 (t, *J* = 9.2 Hz, 1 H), 3.81 (ddd, *J* = 10.1, 6.1, 1.7 Hz, 1 H), 3.68 (m, 4 H), 3.56 (dd, *J* = 10.6, 6.1 Hz, 1 H), 3.49 (dd, *J* = 9.6, 3.6 Hz, 1 H), 3.48 (m, 1 H), 3.37 (dd, *J* = 9.6, 3.0 Hz, 1 H), 3.35 (s, 3 H), 1.15 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.7, 138.9, 138.3, 138.2, 138.2, 138.0, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.4, 101.1, 83.4, 82.1, 80.0, 78.1, 77.8, 75.7, 75.4, 75.0, 74.8, 74.8, 73.6, 73.3, 72.9, 69.9, 68.9, 68.1, 55.3, 38.8, 27.2; HRMS (ESI) *m/z* calc. for $C_{60}H_{68}O_{12}$ $[M+K]^+$, 1019.4342; found 1019.4343. The NMR data were in good agreement with those reported in the literature.[12]



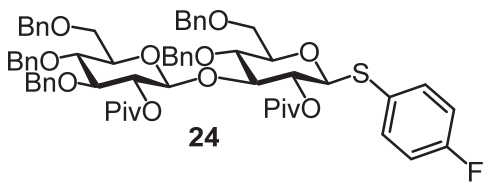
Scheme S6



27

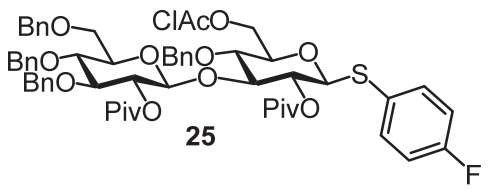
The automated synthesis of disaccharide **27** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm × 20 mm). In the anodic chamber were placed building block **10** (194 mg, 0.300 mmol), Bu_4NOTf (589 mg, 1.50 mmol) and CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (26 μL), Bu_4NOTf (589 mg, 1.50 mmol) and CH_2Cl_2 (15.0 mL). The constant current electrolysis (12 mA) was carried out at -80 °C with magnetic stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, building block **12** (203 mg, 0.361 mmol) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump (1.0 mL/min) under an argon atmosphere at -80 °C, and then the temperature was raised to -50 °C and kept for 60 min. The reaction temperature was cooled down to -80 °C and Et_3N (0.5 mL) was added at -80 °C. After additional stirring at rt for 30 min the reaction mixture was filtered through a short column (4 × 3 cm) of silica gel to remove Bu_4NOTf. The removal of the solvent under reduced pressure

and column chromatography (silica gel, Hexane/EtOAc 9:1 as an eluent) afforded disaccharide **27** in 83% isolated yield (269 mg, 0.249 mmol). **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranocyl-(1→3)-4-*O*-benzyl-6-*O*-levulinoyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (27).** TLC (Hexane/EtOAc 8:2) R_f = 0.20; $[\alpha]_D$ = 0.37 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.44 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.21-7.34 (m, 17 H), 7.16 (m, 3 H), 6.98 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.09 (dd, *J* = 9.6, 8.4 Hz, 1 H), 4.98 (d, *J* = 10.8 Hz, 1 H), 4.88 (t, *J* = 9.0 Hz, 1 H), 4.73 (ABq, *J* = 52.2, 10.8 Hz, 2 H), 4.73 (dd, *J* = 15.0, 8.4 Hz, 2 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.55 (d, 10.8 Hz 1 H), 4.52 (ABq, *J* = 31.8, 12.6 Hz, 2 H), 4.38 (d, *J* = 10.2 Hz, 1 H), 4.35 (d, *J* = 10.8 Hz, 1 H), 4.22 (m, 1 H), 4.10 (m, 1 H), 3.81 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.68 (t, *J* = 9.0 Hz, 1 H), 3.61 (t, *J* = 9.6 Hz, 1 H), 3.59 (dd, *J* =11.4, 5.4 Hz, 1 H), 3.49 (m, 1 H), 3.38 (s, 1 H), 3.37 (d, *J* = 1.2 Hz, 1 H), 2.65 (m, 2 H), 2.52 (m, 2 H), 2.17 (s, 3 H), 1.31 (s, 9 H), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 206.3, 177.3, 176.1, 172.3, 162.9 (d, *J* = 247.0 Hz), 138.5, 137.9, 137.9, 137.7, 135.1, 135.1, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 127.4, 127.3, 127.3, 115.8 (d, *J* = 21.9 Hz), 99.4, 86.7, 83.2, 78.6, 78.2, 76.9, 75.9, 75.2, 75.2, 75.1, 74.8, 73.4, 73.3, 72.5, 68.9, 63.4, 38.9, 38.7, 37.8, 29.8, 27.8, 27.3, 27.2; HRMS (ESI) *m/z* calc. for $C_{61}H_{71}FO_{14}S$ $[M+K]^+$, 1068.9278; found 1101.4421.



24

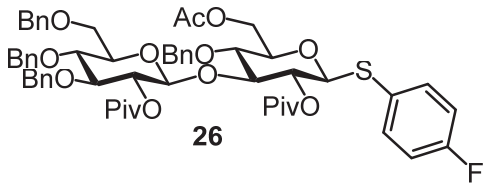
Automated electrochemical glycosylation of building blocks **10** (194 mg, 0.300 mmol) with building block **4** (175 mg, 0.315 mmol) afforded **24** (206 mg, 0.19 mmol) in 64% yield, following the same procedure as that of compound **27**. **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (24).** TLC (Hexane/EtOAc 17:3) R_f = 0.50; $[\alpha]_D$ = 0.37 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.46 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.26-7.38 (m, 17 H), 7.23-7.26 (m, 2 H), 7.16-7.22 (m, 6 H), 6.88 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.08 (dd, *J* = 7.8, 9.6Hz, 1 H), 4.99 (d, *J* = 10.8 Hz, 1 H), 4.94 (t, *J* = 9.6 Hz, 1 H), 4.77 (t, *J* = 11.4 Hz, 2 H), 4.73 (d, *J* = 7.8 Hz, 1 H), 4.69 (d, *J* = 10.8 Hz, 1 H), 4.55 (d, *J* = 7.8 Hz, 1 H), 4.54 (s, 1 H), 4.52 (s, 1 H), 4.52 (d, *J* = 2.4 Hz, 2 H), 4.47 (d, *J* = 12.0 Hz, 1 H), 4.42 (d, *J* = 10.2 Hz, 1 H), 4.23 (t, *J* = 8.4 Hz, 1 H), 3.81 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.73 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.69 (t, *J* = 9.6 Hz, 1 H), 3.62 (t, *J* = 9.6 Hz, 1 H), 3.59 (m, 2 H), 3.49 (m, 1 H), 3.46 (t, *J* = 8.4 Hz, 1 H), 3.40 (m, 1 H), 1.31 (s, 9 H), 1.21 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.3, 176.2, 162.7 (d, *J* = 246.1 Hz), 138.5, 138.4, 138.2, 137.9, 137.7, 134.7, 134.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.1, 128.0, 127.7, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 115.8 (d, *J* = 21.6 Hz), 99.4, 86.9, 83.3, 79.0, 78.8, 78.3, 75.8, 75.7, 75.2, 75.2, 74.9, 73.4, 73.4, 73.3, 72.7, 69.3, 68.9, 38.9, 38.7, 27.3, 27.2; HRMS (ESI) *m/z* calc. for $C_{63}H_{71}FO_{12}S$ $[M+K]^+$, 1009.4282; found 1109.4238.



25

Automated electrochemical glycosylation of building blocks **10** (194 mg, 0.30 mmol) with building block **5** (171 mg, 0.315 mmol) afforded **25** (186 mg, 0.176 mmol) in 58% yield, following the same procedure as that of compound **27**. **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-4-*O*-benzyl-6-*O*-chloroacetyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (25).** TLC (Hexane/EtOAc 7:3) R_f = 0.68; $[\alpha]_D$ = 1.01 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 7.42 (m, 2 H), 7.23-7.34 (m, 17 H), 7.17 (m, 3 H), 6.98 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.10 (dd, *J* = 9.6,

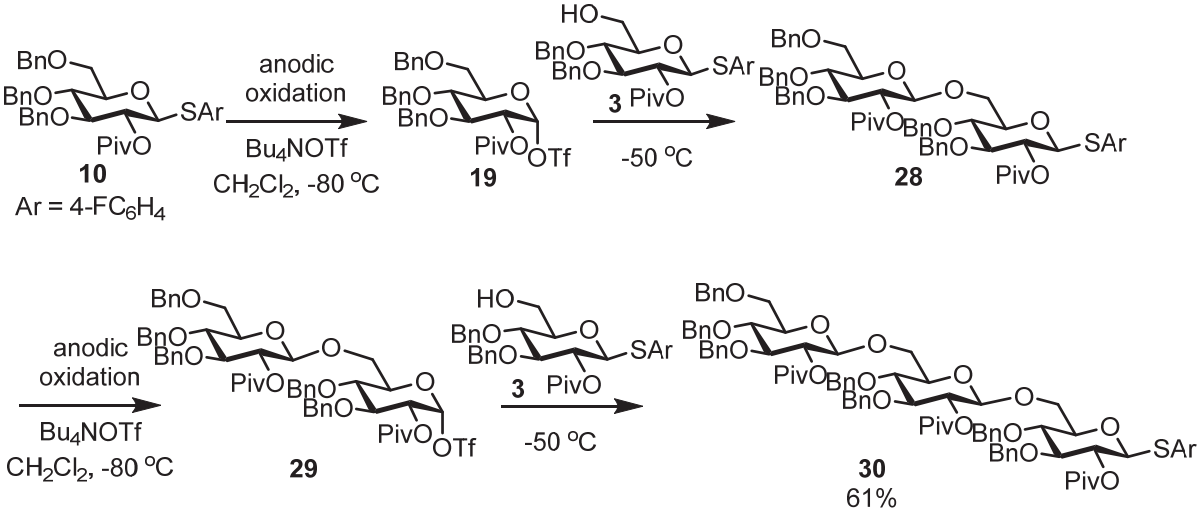
7.8 Hz, 1 H), 4.96 (d, *J* = 11.4 Hz, 1 H), 4.87 (t, *J* = 9.6 Hz, 1 H), 4.78 (d, *J* = 10.8, 1 H), 4.75 (d, *J* = 10.8 Hz, 1 H), 4.73 (d, *J* = 8.4 Hz, 1 H), 4.69 (d, *J* = 10.8 Hz, 1 H), 4.62 (d, *J* = 10.8 Hz, 1 H), 4.57 (d, *J* = 12.6 Hz, 1 H), 4.55 (d, *J* = 10.8 Hz, 1 H), 4.53 (d, *J* = 12.6 Hz, 1 H), 4.41 (d, *J* = 11.4 Hz, 1 H), 4.38 (d, *J* = 10.2 Hz, 1 H), 4.28 (m, 1 H), 4.19 (m, 1 H), 3.96 (d, *J* = 15.0 Hz, 1 H), 3.89 (d, *J* = 15.0 Hz, 1 H), 3.82 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.69 (t, *J* = 9.0 Hz, 1 H), 3.62 (m, 2 H), 3.50 (ddd, *J* = 9.6, 4.8, 1.2 Hz, 1 H), 3.38 (m, 2 H), 1.31 (s, 9 H),1.20 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.3, 176.1, 166.8, 162.9 (d, *J* = 247.2 Hz), 138.5, 137.9, 137.7, 137.6, 135.3, 135.2, 128.8, 128.5, 128.4, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.4, 127.3, 127.3, 115.9 (d, *J* = 21.6 Hz), 99.4, 86.7, 83.2, 78.6, 78.2, 76.6, 75.9, 75.2, 74.7, 74.3, 73.4, 73.3, 72.4, 68.8, 64.6, 40.6, 38.9, 38.7, 27.3, 27.2; HRMS (ESI) *m/z* calc. for $C_{58}H_{66}ClFO_{13}S$ $[M+K]^+$, 1095.3528; found 1095.3475.



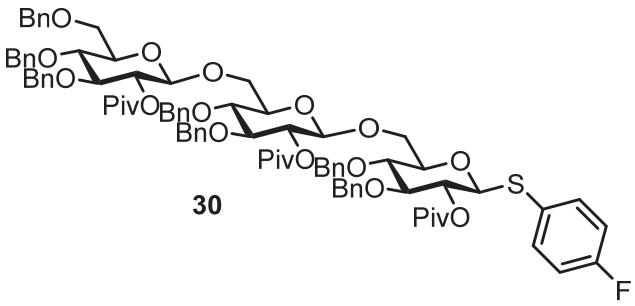
26

Automated electrochemical glycosylation of building blocks **10** (194 mg, 0.30 mmol) with building block **11** (160 mg, 0.315 mmol) afforded **26** (138 mg, 0.135 mmol) in 45% yield, following the same procedure as that of compound **24**. **4-Fluorophenyl-3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D- glucopyranosyl-(1→3)-4-*O*-benzyl-6-*O*-acetyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (27).** TLC (Hexane/EtOAc 7:3) R_f = 0.63; $[\alpha]_D$ = 0.53 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.45 (m, 2 H), 7.18-7.42 (m, 17 H), 7.16 (m, 3 H), 6.98 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.09 (dd, *J* = 9.6, 8.4 Hz, 1 H), 4.98 (d, *J* = 11.4, 1 H), 4.89 (d, *J* = 9.6 Hz, 1 H), 4.78 (d, *J* = 10.8 Hz, 1 H), 4.75 (d, *J* = 10.8 Hz, 1 H), 4.73 (d, *J* = 7.8 Hz, 1 H), 4.69 (d, *J* = 10.8 Hz, 1 H), 4.58 (d, *J* = 10.8 Hz, 1 H), 4.55 (d, *J* = 12.6 Hz, 1 H), 4.54 (d, *J* = 10.2 Hz, 1 H), 4.49 (d, *J* = 12.6 Hz, 1 H), 4.38 (d, *J* = 9.6 Hz, 1 H), 4.32 (d, *J* = 12.0, 1.8 Hz, 1 H), 4.22 (t, *J* = 9.0 Hz, 1 H), 4.11 (dd, *J* = 12.0, 5.4 Hz, 1 H), 3.80 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.68 (t, *J* = 9.6 Hz, 1 H), 3.62 (d, *J* = 9.6 Hz, 1 H), 3.58 (dd, *J* = 12.0, 6.0 Hz, 1 H), 3.49 (ddd, *J* = 9.6, 5.4, 1.8 Hz, 1 H), 3.40 (dd, *J* = 8.4 Hz, 1 H), 3.37 (m, 1 H), 2.00 (s, 3 H), 1.31 (s, 9 H), 1.21 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.3, 176.1, 170.6, 162.9 (d, *J* = 247.0 Hz), 138.5, 137.9, 137.9, 137.6, 135.2, 135.1, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.7, 127.7, 127.4, 127.3, 127.3, 115.8 (d, *J* = 21.7 Hz), 99.4, 86.8, 83.2, 78.7, 78.2, 75.8, 75.2, 75.2, 75.0, 74.8, 73.4, 73.3, 72.5, 68.9, 63.1, 38.9, 38.7, 27.3, 27.2, 20.8; HRMS (ESI) *m/z* calc. for $C_{58}H_{67}FO_{13}S$ $[M+K]^+$, 1061.3871; found 1061.3918.

4. Automated synthesis of trisaccharide

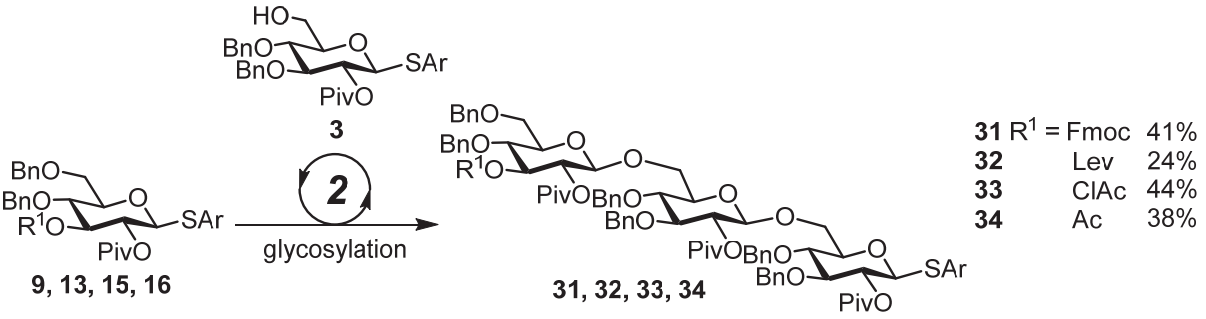


Scheme S7

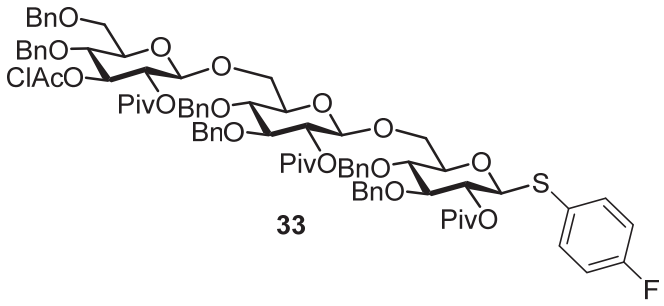


The automated synthesis of trisaccharide **30** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm × 20 mm). In the anodic chamber were placed terminal building block **10** (194 mg, 0.30 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.5 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (55 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.5 mL). The constant current electrolysis (8.0 mA) was carried out at -80 °C with magnetic stirring until 1.0 F/mol of electricity was consumed. After the electrolysis, building block **3** (352 mg, 0.63 mmol) dissolved in CH_2Cl_2 (2.1 mL) was subsequently added by the syringe pump (1.0 mL (0.30 mmol) for one cycle) under an argon atmosphere at -80 °C and then the temperature was raised to -50 °C and kept for 60 min. The reaction temperature was cooled down to -80 °C and the second cycle starts automatically. After the 2nd cycle, Et_3N (0.3 mL) was added and the mixture was filtered through a short column (4 × 3 cm) of silica gel to remove Bu_4NOTf. Removal of the solvent under reduced pressure and short column (silica gel, Hexane/EtOAc 1:1 as an eluent) afforded a mixture of oligosaccharides. The crude product was purified by PR-GPC with $CHCl_3$ as an eluent and trisaccharide **30** was obtained in 61% isolated yield (275.7 mg, 0.184 mmol). **4-Fluorophenyl-2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl-(1→6)-2-*O*-pivaloyl-3,4-di-*O*-benzy-l-β-D-glucopyranosyl-(1→6)-2-*O*-pivaloyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (30).** TLC (Hexane/EtOAc 4:1) R_f = 0.34; $[\alpha]_D$ = -0.55 (*c* = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.49 (m, 2 H), 7.26 (m, 3 H), 7.19 (m, 2 H), 7.12 (m, 2 H), 7.03 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.08 (m, 2 H), 4.99 (t, *J* = 9.6 Hz, 1 H), 4.76 (d, *J* = 11.0 Hz, 1 H), 4.73 (d, *J* = 3.2 Hz, 1 H), 4.72 (dd, *J* = 7.2, 3.9 Hz, 3 H), 4.69 (d, *J* = 8.3 Hz, 2 H), 4.66 (d, *J* = 3.0 Hz, 1 H), 4.64 (s, 1 H), 4.62 (d, *J* = 6.2 Hz, 1 H), 4.59 (d, *J* = 4.0 Hz, 1 H), 4.56 (d, *J* = 5.5 Hz, 1 H), 4.51 (d, *J* = 10.1 Hz, 1 H), 4.47 (d, *J* = 7.7 Hz, 1 H), 4.45 (m, 2 H), 4.43 (d, *J* = 5.4 Hz, 1 H), 3.97 (dd, *J* = 11.4, 1.6 Hz, 1 H), 3.91 (dd, *J* = 11.4, 1.6 Hz, 1 H), 3.71 (m, 2 H), 3.67 (m, 3 H), 3.64 (dd, *J* = 5.7, 3.6 Hz, 2 H), 3.61 (ddd, *J*

= 9.6, 5.7, 1.7 Hz, 2 H), 3.59 (s, 1 H), 3.57 (m, 1 H), 3.46 (m, 1 H), 3.39 (t, *J* = 9.4 Hz, 1 H), 1.23 (s, 9 H), 1.15 (s, 9 H), 1.13 (s, 9 H) ; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 176.7, 176.6, 162.9 (d, *J* = 246.1 Hz), 138.3, 138.2, 138.1, 138.1, 138.1, 137.8, 135.3, 135.2, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6, 127.4, 127.4, 127.3, 116.1 (d, *J* = 21.6 Hz), 101.7, 101.0, 86.5, 84.7, 83.3, 83.3, 79.0, 78.1, 78.0, 78.0, 75.3, 75.2, 75.1, 75.1, 74.9, 74.9, 74.9, 74.8, 73.5, 73.1, 72.9, 71.4, 69.0, 68.7, 68.1, 38.8, 38.8, 38.8, 27.2, 27.2, 27.2; HRMS (ESI) *m/z* calc. for $C_{58}H_{67}FO_{13}S$ $[M+K]^+$, 1535.6324; found 1535.6309.

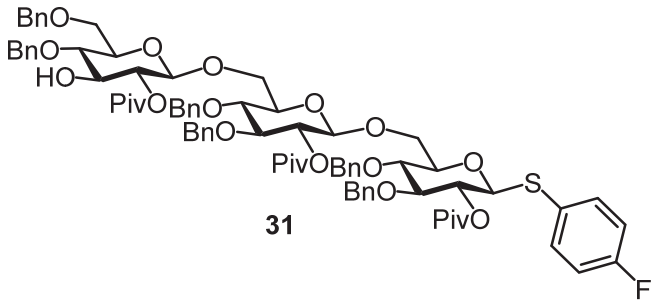


Scheme S8



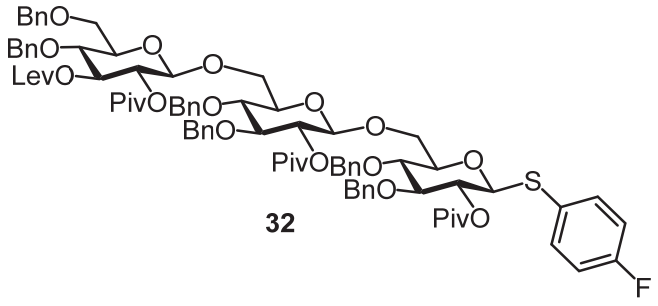
The automated synthesis of trisaccharide **33** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm × 20 mm). In the anodic chamber were placed terminal building block **15** (190 mg, 0.300 mmol), Bu_4NOTf (589 mg, 1.50 mmol) and CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (26.6 μL), Bu_4NOTf (589 mg, 1.50 mmol) and CH_2Cl_2 (15.0 mL). The constant current electrolysis (12.0 mA) was carried out at -80 ºC with magnetic stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, building block **3** (350 mg, 0.630 mmol) dissolved in CH_2Cl_2 (4.0 mL) was subsequently added by the syringe pump (1.0 mL (0.315 mmol) for one cycle) under an argon atmosphere at -80 ºC, and then the temperature was raised to -50 ºC and kept for 60 min. The reaction temperature was cooled down to -80 ºC and the second cycle starts automatically. After the 2nd cycle, Et_3N (0.5 mL) was added and the mixture was filtered through a short column (4 × 3 cm) of silica gel to remove Bu_4NOTf. Removal of the solvent under reduced pressure and short column (silica gel, Hexane/EtOAc 8:2 as an eluent) afforded a mixture of oligosaccharides. The crude product was purified by preparative GPC with $CHCl_3$ as an eluent and trisaccharide **33** was obtained in 44% isolated yield (180 mg, 0.133 mmol). **4-Fluorophenyl-4,6-di-*O*-benzyl-3-*O*-chloroacetyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-gluco-pyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pi-valoyl-1-thio-β-D-gluco-pyranoside (33)**. TLC (hexane/EtOAc 4:1) R_f = 0.36; $[\alpha]_D$ = -1.77 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (*pseudo*-dd, *J* = 9.0, 5.4 Hz, 2 H), 7.34-7.21 (m, 28 H), 7.13 (dd, *J* = 7.2, 1.2 Hz, 2 H), 7.06 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.21 (t, *J* = 9.6 Hz, 1 H), 5.06 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 4.96 (t, *J* = 9.6 Hz, 1 H), 4.91 (dd, *J* = 9.6 Hz, 1 H), 4.78-4.46 (m, 16 H), 3.97 (dd, *J* = 27.0, 12.0 Hz, 1 H), 3.96 (dd, *J* = 27.0, 12.0 Hz, 1 H), 3.79-3.42 (m, 10 H), 3.66 (ABq, *J* = 94.2, 15.0 Hz, 2 H), 3.40 (t, *J* = 9.0 Hz, 1 H), 1.23 (s, 9 H), 1.12 (s, 9 H), 1.12 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.9, 176.7, 176.6, 176.5, 162.9 (d, *J* = 246.9 Hz), 138.1, 138.1, 137.9, 137.9, 137.8, 135.3 (d, *J* = 8.1 Hz), 128.5 (d, *J* = 1.4 Hz), 128.4,

128.4, 128.4, 128.0, 128.0, 128.0, 127.9, 127.9, 127.7, 127.7, 127.7, 127.6, 127.5, 127.3, 127.3, 116.2 (d, *J* = 21.3 Hz), 101.3, 100.8, 86.4, 84.5, 83.1, 79.3, 77.8, 77.6, 76.7, 75.8, 75.2, 75.2, 75.1, 74.9, 74.9, 74.8, 74.5, 73.7, 72.8, 71.6, 71.3, 68.8, 68.3, 67.6, 40.5, 38.8, 38.8, 38.7, 27.2, 27.2, 27.2, 27.1, 27.1; HRMS (ESI) *m/z* calc. for $C_{83}H_{96}ClFO_{19}S$ $[M+K]^+$,1521.5576; found 1521.5496.



31

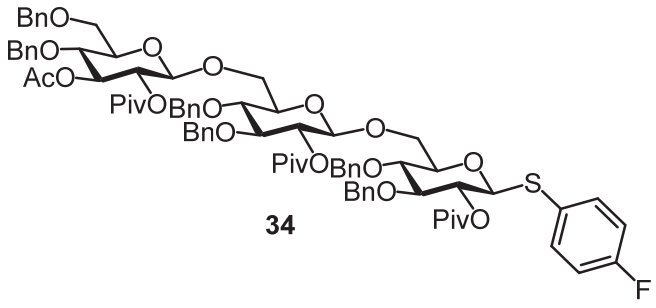
Automated electrochemical synthesis of trisaccharide **31** using terminal building blocks **9** (194 mg, 0.30 mmol) with building block **3** (349 mg, 0.63 mmol) afforded **31** (165 mg, 0.12 mmol) in 41% yield, following the same procedure as that of compound **33**. **4-Fluorophenyl-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-gluco-pyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (31)**. TLC (Hexane/EtOAc 4:1) R_f = 0.16; $[\alpha]_D$ =-1.58 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.32-7.20 (m, 30 H), 7.05 (t, *J* = 8.4 Hz, 2 H), 5.23 (s, 1 H), 5.09 (t, *J* = 8.4 Hz, 1 H), 4.99 (t, *J* = 9.6 Hz, 1 H), 4.79-4.44 (m, 16 H), 3.98 (dd, *J* = 11.4, 5.4 Hz, 1 H), 3.98 (dd, *J* = 11.4, 6.0 Hz, 1 H), 3.77-3.51 (m, 11 H), 3.43-3.39 (m, 2 H), 1.23 (s, 1 H), 1.20 (s, 1 H), 1.13 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.6, 176.7, 162.9 (d, *J* = 246.8 Hz), 138.3, 138.0, 137.9, 135.2 (d, *J* = 8.1 Hz), 128.5, 128.5, 128.4, 128.4, 128.1 (d, *J* = 3.0 Hz), 128.0, 128.0, 127.9, 127.9, 127.9, 127.7, 127.6, 127.4, 116.2 (d, *J* = 21.8 Hz), 101.2, 101.0, 86.6, 84.6, 83.2, 79.1, 78.5, 77.9, 77.9, 76.4, 75.3, 75.1, 75.0, 74.9, 74.8, 74.7, 74.5, 73.6, 72.9, 71.4, 68.9, 68.6, 67.9, 53.5, 39.0, 38.8, 38.8, 27.2; HRMS (ESI) *m/z* calc. for $C_{77}H_{93}FO_{18}S$ $[M+K]^+$,1445.5860; found 1445.5820.



32

Automated electrochemical synthesis of trisaccharide **32** using terminal building blocks **13** (196 mg, 0.30 mmol) with building block **3** (349 mg, 0.63 mmol) afforded **32** (98.8 mg, 0.072 mmol) in 24% yield, following the same procedure as that of compound **33**. **4-Fluorophenyl-4,6-di-*O*-benzyl-3-*O*-levulinoyl-2-*O*-pivaloyl-β-D-gluco-pyranocyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-gluco-pyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (32)**. TLC (Hexane/EtOAc 4:1) R_f = 0.21; $[\alpha]_D$ = -1.29 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.47 (*pseudo*-dd, *J* = 8.4, 4.8 Hz, 2 H), 7.32-7.20 (m, 28 H), 7.16 (*pseudo*-d, *J* = 6.6 Hz, 2 H), 7.05 (t, *J* = 8.4 Hz, 2 H), 5.21 (t, *J* = 9.6 Hz, 1 H), 5.05 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 4.92 (t, *J* = 9.0 Hz, 1 H), 4.92 (dd, *J* = 9.6, 8.4 Hz, 1 H), 4.77-4.44 (m, 16 H), 3.96 (dd, *J* = 28.2, 12.0 Hz, 1 H), 3,96 (dd, *J* = 28.2, 12.0 Hz, 1 H), 3.77-3.51 (m, 9 H), 3.43 (dt, *J* = 9.6, 3.0 Hz, 1 H), 3.39 (t, *J* = 9.6 Hz, 1 H), 2.60-2.55 (m, 2 H), 2.42 (*pseudo*-t, *J* = 6.0 Hz), 2.11 (s, 3 H), 1.23 (s, 9 H), 1.14 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 205.9, 176.8, 176.7, 176.6, 171.7, 162.9 (d, *J* = 246.2 Hz), 138.1, 138.0, 137.8, 135.4 (d, *J* = 31.8 Hz), 128.5, 128.4, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.3, 116.1 (d, *J* = 21.6 Hz), 101.3, 100.8, 86.4, 84.6, 83.1, 79.3, 77.9, 77.7, 76.0, 75.2, 75.2, 75.1, 74.9, 74.9, 74.8, 74.5, 73.6, 72.8, 71.6, 71.3, 68.7, 68.5,

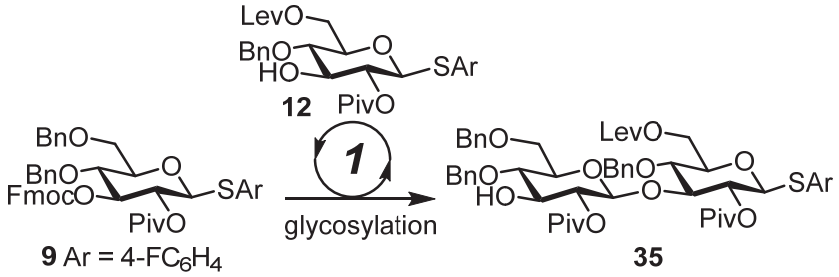
67.7, 46.3, 38.8, 38.7, 37.6, 29.8, 28.0, 27.2, 27.2, 27.1, 27.1, 11.5; HRMS (ESI) *m/z* calc. for $C_{86}H_{101}FO_{20}S$ $[M+K]^+$, 1543.6228; found 1543.6173.



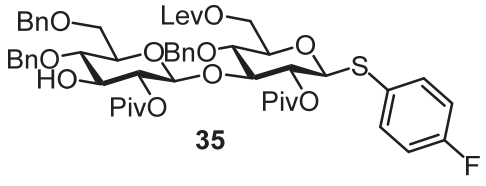
34

Automated electrochemical synthesis of trisaccharide **34** using terminal building blocks **16** (179 mg, 0.300 mmol) with building block **3** (349 mg, 0.630 mmol) afforded **34** (153 mg, 0.112 mmol) in 38% yield, following the same procedure as that of compound **33**. **4-Fluorophenyl-3-*O*-acetyl-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-gluco-pyranoside (34)**. TLC (Hexane/EtOAc 4:1) R_f = 0.38; $[\alpha]_D$ =-1.88 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.49 (*pseudo*-dd, *J* = 8.4, 1.8 Hz, 2 H), 7.34-7.22 (m, 30 H), 7.15 (*pseudo*-d, *J* = 6.0 Hz, 2 H), 7.06 (t, *J* = 9.0 Hz, 2 H), 5.23 (t, *J* = 9.6 Hz, 1 H), 5.07 (td, *J* = 7.8, 2.4 Hz, 1 H), 4.97 (t, *J* = 9.6 Hz, 1 H), 4.94 (dd, *J* = 9.6, 7.8 Hz, 1 H), 4.79-4.45 (m, 16 H), 3.98 (dd, *J* = 25.8, 12.0 Hz, 1 H), 3.98 (dd, *J* = 25.8, 11.4 Hz, 1 H), 3.79-3.52 (m, 9 H), 3.47 (dt, *J* = 9.6, 3.0 Hz, 1 H), 3.41 (t, *J* = 9.6 Hz, 1 H), 1.88 (s, 3 H), 1.24 (s, 9 H), 1.15 (s, 9 H), 1.13 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 176.7, 176.6, 169.9, 162.9 (d, *J* = 246.3 Hz), 138.1, 138.1, 138.0, 137.9, 137.8, 135.4 (d, *J* = 7.8 Hz), 128.5, 128.4, 128.4 (d, *J* = 1.7 Hz), 128.1, 128.0, 127.8, 127.8, 127.3, 116.1 (d, *J* = 21.8 Hz), 101.4, 100.8, 86.3, 84.6, 83.1, 79.3, 77.9, 77.7, 76.0, 75.2, 75.1, 74.9, 74.9, 74.8, 74.7, 74.5, 73.6, 72.8, 71.6, 71.3, 68.7, 68.5, 67.6, 38.8, 38.7, 27.3, 27.2, 27.1, 27.1, 20.8; HRMS (ESI) *m/z* calc. for $C_{83}H_{97}FO_{19}S$ $[M+K]^+$,1487.5966; found 1487.5898.

5. Preparation of disaccharide and trisaccharide acceptors



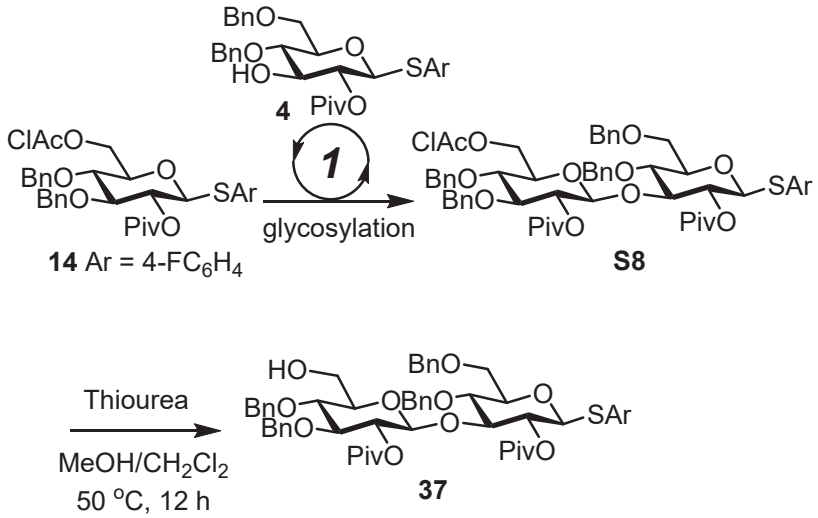
Scheme S9



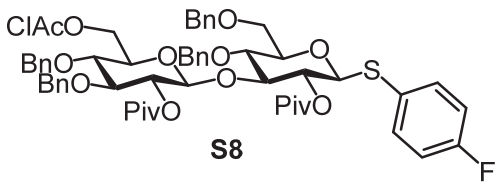
35

The automated synthesis of disaccharide **(35)** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm×20 mm). In the anodic chamber were placed building block **(9)** (233.0 mg, 0.30 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (35.3 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). The constant current electrolysis (12.0 mA) was carried out at -80 ºC with magnetic stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, 4-Fluorophenyl-4-*O*-benzyl-6-*O*-levulinoyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside **(12)** (202.0 mg, 0.36 mmol)

dissolved in CH_2Cl_2 (1.2 mL) was subsequently added by the syringe pump (1.0 mL, 0.20 mmol) under an argon atmosphere at -80 °C, and then the temperature was raised to -50 °C and kept for 60 min. The reaction temperature was cooled down to -80 °C and Et_3N (0.3 mL) was added at -80 °C. After additional stirring at rt for 30 min the reaction mixture was filtered through a short column of silica gel to remove Bu_4NOTf. The removal of the solvent under reduced pressure and column chromatography (silica gel, Hexane/EtOAc 5:2 as an eluent) afforded disaccharide **(35)** in 30% isolated yield (89 mg, 0.089 mmol). **4-Flurophenyl-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-6-*O*-levunilyl-4-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (35)**. TLC (Hexane/ EtOAc 3:1) R_f = 0.21; $[\alpha]_D$ = 0.41 (c = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.44 (m, 2 H), 7.28 (m, 14 H), 7.17 (m, 1 H), 6.98 (*pseudo-t*, *J* = 9.0 Hz, 2 H), 4.94 (d, *J* = 11.4 Hz, 1 H), 4.89 (t, *J* = 9.0 Hz, 1 H), 4.81 (d, *J* = 10.8 Hz, 1 H), 4.73 (m, 2 H), 4.62 (d, *J* = 10.8 Hz, 1 H), 4.56 (d, *J* = 11.4 Hz, 1 H), 4.54 (d, *J* = 11.4 Hz, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.39 (d, *J* = 9.6 Hz, 1 H), 4.36 (d, *J* = 11.4 Hz, 1 H), 4.19 (t, *J* = 8.4 Hz, 1 H), 4.10 (dd, *J* = 11.4, 4.8 Hz, 1 H), 3.82 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.69 (m, 1 H), 3.57 (dd, *J* = 11.4, 5.4 Hz, 1 H), 3.52 (t, *J* = 9.6 Hz, 1 H), 3.45 (m, 1 H), 3.38 (m, 2 H), 2.69 (m, 2 H), 2.53 (m, 2 H), 2.16 (s, 3 H), 1.28 (s, 9 H), 1.24 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 206.0, 179.0, 176.0, 176.0, 172.2, 162.9 (d, *J* = 246.9 Hz), 138.5, 138.0, 137.9, 135.1, 135.1, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.7, 127.4, 127.3, 115.8 (d, *J* = 21.6 Hz), 99.1, 86.6, 78.9, 78.8, 76.9, 76.4, 75.6, 75.4, 74.9, 74.8, 74.5, 73.4, 72.5, 69.0, 63.4, 39.0, 38.6, 37.8, 29.7, 27.8, 27.3, 27.1; HRMS (ESI) *m/z* calc. for $C_{54}H_{65}FO_{14}S$ $[M+K]^+$,1027.3711; found 1027.3640.

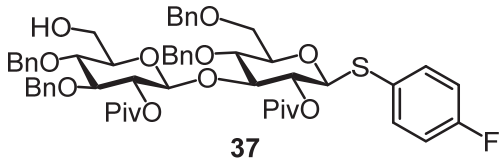


Scheme S10



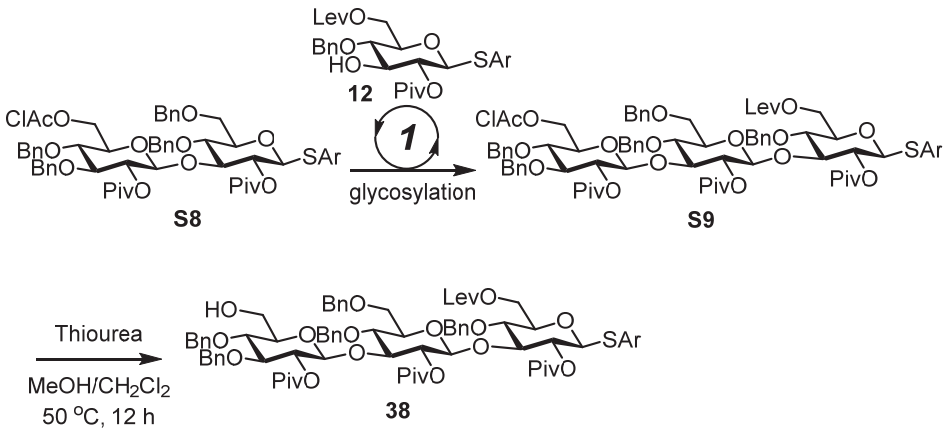
The automated synthesis of disaccharide **(S8)** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm×20 mm). In the anodic chamber were placed building block **(14)** (379.0 mg, 0.60 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (50.9 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). The constant current electrolysis (12.0 mA) was carried out at -80 °C with magnetic stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, 4- Fluorophenyl-4-

O-benzyl-6-*O*-levulinoyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside **(4)** (399.6 mg, 0.72 mmol) dissolved in CH_2Cl_2 (1.2 mL) was subsequently added by the syringe pump (1.0 mL, 0.20 mmol) under an argon atmosphere at -80 ºC, and then the temperature was raised to -50 ºC and kept for 60 min. The reaction temperature was cooled down to -80 ºC and Et_3N (0.3 mL) was added at -80 ºC. After additional stirring at rt for 30 min the reaction mixture was filtered through a short column of silica gel to remove Bu_4NOTf. The removal of the solvent under reduced pressure and column chromatography (silica gel, Hexane/EtOAc 5:2 as an eluent) afforded disaccharide **(S8)** in 43% isolated yield (89 mg, 0.255 mmol). **4-Flurophenyl-6-*O*-chloroacetyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-gluco-pyr-anoside (S8)**. TLC (Hexane/EtOAc 4:1) R_f = 0.45; $[\alpha]_D$ = -0.55 (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.46 (m, 2 H), 7.27 (m, 20 H), 6.86 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.04 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 4.95 (d, *J* = 11.4 Hz, 1 H), 4.90 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.73 (m, 4 H), 4.49 (m, 5 H), 4.39 (dd, *J* = 12.0, 1.8 Hz. 1 H), 4.22 (m, 2H), 3.69 (m, 1 H), 3.65 (d, *J* = 4.8 Hz, 1 H), 3.60 (m, 4 H), 3.47 (m, 3 H), 1.31 (s, 9 H), 1.20 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.2, 176.1, 166.9, 162.8 (d, *J* = 246.9 Hz), 138.5, 138.1, 137.6, 137.2, 134.8, 134.8, 128.6, 128.4, 128.3, 128.3, 128.2, 128.2, 127.8, 127.7, 127.7, 127.6, 127.5, 127.4, 115.9 (d, *J* = 21.9 Hz), 99.2, 86.6, 83.2, 79.0, 79.0, 75.7, 75.2, 75.0, 74.5, 73.4, 73.1, 73.9, 69.2, 64.2, 40.4, 38.9, 38.7, 27.3, 27.2; HRMS (ESI) *m/z* calc. for $C_{58}H_{66}ClFO_{13}S$ $[M+K]^+$,1095.3812; found 1095.3517.

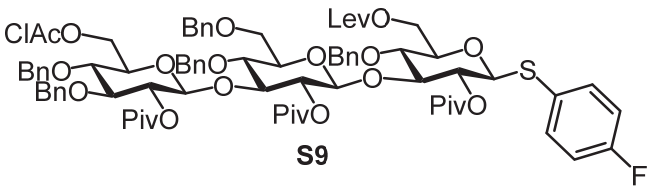


37

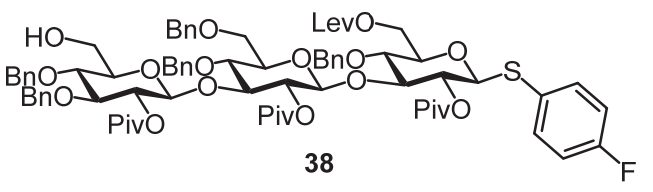
To a solution of 4-Flurophenyl-6-*O*-chloroacetyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside **(S8)** (462mg, 0.775 mmol) in CH_2Cl_2 (10.0 mL) and MeOH (9.0 mL) thiourea (590.5 mg, 7.76 mmol) was added. The solution is then allowed to stir at 50 ºC for 12 h. TLC analysis (7:3 Hexane/EtOAc) indicated the complete consumption of the starting materials and formation of a single product (R_f = 0.21). The reaction mixture is then diluted with excess amount of CH_2Cl_2 and washed with brine and dried over Na_2SO_4. Removal of solvent under reduced pressure afford a crude product which will further purified using silica gel chromatography to obtain **(37)** (590 mg, 0.601 mmol) in 77.5%.). **4-Flurophenyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (37)**. TLC (Hexane/EtOAc 7.5:2.5) R_f = 0.21; $[\alpha]_D$ = -1.53 (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.47 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.26-7.35 (m, 18 H), 7.23 (d, *J* = 7.8 Hz, 2 H), 6.88 (*pseudo-t*, *J* = 8.4 Hz, 2 H), 5.04 (dd, *J* = 9.6, 8.4 Hz, 1 H), 4.93 (*pseudo-t*, *J* = 9.6 Hz, 1 H), 4.90 (d, *J* = 10.8 Hz, 1 H), 4.78 (d, *J* = 11.4 Hz, 1 H), 4.75 (d, *J* = 10.8 Hz, 1 H), 4.70 (d, *J* = 8.4 Hz, 1 H), 4.69 (d, *J* = 11.4 Hz, 1 H), 4.49-4.58 (m, 5 H), 4.18 (*pseudo-t*, *J* = 8.4 Hz, 1 H), 3.73-3.76 (m, 2 H), 3.66 (dd, *J* = 10.8, 5.4 Hz, 1 H), 3.58-3.62 (m, 2 H), 3.52 (t, *J* = 9.0 Hz, 1 H), 3.46-3.49 (m, 2 H), 3.29-3.32 (m, 2 H), 1.30 (s, 9 H), 1.20 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.3, 176.0, 162.7 (d, *J* = 246.8 Hz), 138.1, 138.0, 137.8, 137.6, 134.8 (d, *J* = 8.1 Hz), 128.5, 128.3, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 127.6, 127.3, 115.8 (d, *J* = 21.9 Hz), 99.5, 86.8, 82.9, 79.2, 79.0, 77.9, 75.6, 75.5, 75.1, 75.1, 74.8, 73.4, 73.1, 72.5, 69.0, 61.6, 38.8, 38.6, 27.2, 27,1; HRMS (ESI) *m/z* calc. for $C_{56}H_{65}FO_{12}S$ $[M+K]^+$,1019.3812; found 1019.3806.



Scheme S11



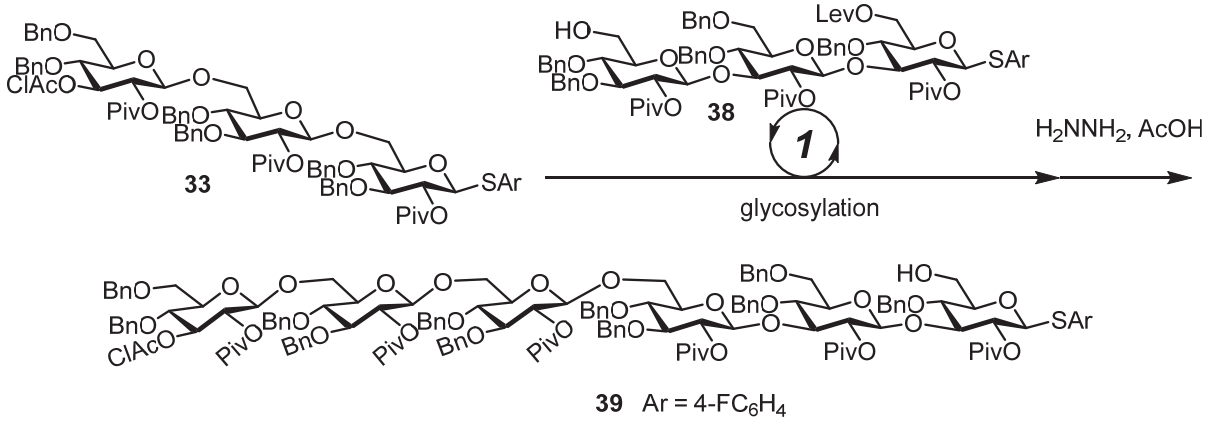
Automated electrochemical synthesis of trisaccharide **S9** using thus-obtained disaccharide building block **S8** (319 mg, 0.30 mmol) and building block **12** (206 mg, 0.36 mmol) afforded **S9** (163 mg, 0.11 mmol) in 37% yield. **4-Fluorophenyl-6-*O*-chloroacetyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranocyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-6-*O*-levulinoyl-4-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-gluco-pyranoside (S9)**. TLC (Hexane/EtOAc 3:1) R_f = 0.32; $[\alpha]_D$ = 0.59 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.44 (m, 2 H), 7.35 (d, *J* = 1.8 Hz, 1 H), 7.32 (m, 6 H), 7.27 (ddd, *J* = 6.6, 4.8, 1.8, 6 H), 7.23 (m, 11 H), 7.15 (ddd, *J* = 8.6, 4.3, 2.0, 1 H), 6.99 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.07 (m, 1 H), 4.93 (d, *J* = 6.6 Hz, 1 H), 4.91 (d, *J* = 6.6 Hz, 1 H), 4.90 (m, 1 H), 4.83 (t, *J* = 8.4 Hz, 1 H), 4.79 (d, *J* = 10.8 Hz, 1 H), 4.77 (d, *J* = 4.9 Hz, 1 H), 4.76 (d, *J* = 1.5 Hz, 1 H), 4.72 (d, *J* = 10.8 Hz, 1 H), 4.63 (d, *J* = 7.8 Hz, 1 H), 4.56 (d, *J* = 10.8 Hz, 1 H), 4.53 (dd, *J* = 15.0, 7.8 Hz, 2 H), 4.46 (d, *J* = 6.6 Hz, 1 H), 4.44 (d, *J* = 5.4 Hz, 1 H), 4.39 (dd, *J* = 12.0, 1.8 Hz, 1 H), 4.35 (s, 1 H), 4.34 (m, 1 H), 4.26 (dd, *J* = 12.0, 4.8 Hz, 1 H), 4.22 (t, *J* = 8.4 Hz, 1 H), 4.12 (m, 2 H), 3.72 (m, 1 H), 3.70 (s, 1 H), 3.69 (s, 1 H), 3.65 (dd, *J* = 7.2, 2.5 Hz, 2 H), 3.53 (m, 1 H), 3.46 (m, 3 H), 3.34 (m, 2 H), 2.71 (m, 2 H), 2.54 (m, 2 H), 2.17 (s, 3 H), 1.29 (s, 9 H), 1.27 (s, 9 H), 1.16 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 206.2, 177.2, 176.4, 176.3, 172.3, 166.9, 162.9 (d, *J* = 246.7 Hz), 138.6, 138.3, 138.0, 137.6, 137.3, 135.2, 135.2, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 127.8, 127.7, 127.4, 127.4, 127.3, 115.9 (d, *J* = 21.4 Hz), 99.3, 98.5, 86.5, 83.2, 77.9, 77.7, 76.1, 75.5, 75.4, 75.3, 75.0, 74.8, 74.6, 74.6, 73.3, 73.1, 72.9, 72.5, 69.0, 64.2, 63.4, 40.4, 38.9, 38.8, 38.7, 37.8, 29.8, 27.8, 27.3, 27.3, 27.1; HRMS (ESI) *m/z* calc. for $C_{81}H_{96}FO_{21}S$ $[M+Na]^+$, 1513.5730; found 1513.5696.



To a solution of **S9** (462 mg, 0.30 mmol) in CH_2Cl_2 (4.0 mL) and MeOH (4.0 mL) thiourea (235 mg, 3.10 mmol) was added. The solution is then allowed to stir at 50 °C for 12 h. TLC analysis (Hexane/EtOAc 7:3) indicated the complete consumption of the starting materials and formation of a single product (R_f = 0.21). The reaction mixture is

then diluted with excess amount of CH_2Cl_2 and washed with brine and dried over Na_2SO_4. Removal of solvent under reduced pressure afford a crude product which will further purified using silica gel chromatography to obtain **38** (312 mg, 0.22 mmol) in 71%. **4-Fluorophenyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranocyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-6-*O*-levulinoyl-4-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (38).** TLC (Hexane/EtOAc 7:3) R_f = 0.21; $[\alpha]_D$ = 0.15 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.43 (m, 2 H), 7.35-7.21 (m, 24 H), 7.16 (m, 1 H), 6.98 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.05 (t, *J* = 8.4 Hz, 1 H), 4.92 (d, *J* = 10.8 Hz, 1 H), 4.92 (d, *J* = 7.8 Hz, 1 H), 4.87 (d, *J* = 10.8 Hz, 1 H), 4.82 (t, *J* = 9.6 Hz, 1 H), 4.80 (d, *J* = 4.2 Hz, 1 H), 4.77 (d, *J* = 3.6 Hz, 1 H), 4.73 (d, *J* = 8.4 Hz, 1 H), 4.69 (d, *J* = 10.8 Hz, 1 H), 4.61 (t, *J* = 9.0 Hz, 1 H), 4.57 (d, *J* = 11.4 Hz, 1 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.51 (d, *J* = 10.2 Hz, 1 H), 4.50 (d, *J* = 12.6 Hz, 1 H), 4.36 (d, *J* = 10.2 Hz, 1 H), 4.34 (dd, *J* = 12.0, 2.4 Hz, 1 H), 4.22 (t, *J* = 8.4 Hz, 1 H), 4.11 (t, *J* = 5.4 Hz, 1 H), 4.09 (m, 1 H), 3.77 (m, 2 H), 3.66 (t, *J* = 9.0 Hz, 1 H), 3.62 (t, *J* = 9.6 Hz, 1 H), 3.57 (dd, *J* = 12.0, 4.2 Hz, 1 H), 3.54 (dd, *J* = 11.4, 5.4 Hz, 1 H), 3.48 (m, 2 H), 3.35 (m, 1 H), 3.32 (m, 2 H), 2.69 (m, 2 H), 2.55 (m, 2 H), 2.18 (s, 3 H), 1.87 (bs, 1 H), 1.27 (s, 9 H), 1.26 (s, 9 H), 1.16 (s, 9 H)); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 206.2, 177.3, 176.4, 176.3, 172.3, 162.9 (d, *J* = 247.0 Hz), 138.4, 138.0, 138.0, 137.8, 137.6, 135.2, 135.1, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.7, 127.7, 127.4, 127.4, 127.3, 115.9 (d, *J* = 21.7 Hz), 99.4, 98.8, 86.5, 82.9, 77.9, 77.8, 76.9, 76.1, 75.6, 75.6, 75.3, 75.2, 75.0, 74.8, 74.3, 73.4, 73.1, 72.5, 68.9, 63.4, 61.6, 38.8, 38.7, 37.8, 29.8, 27.8, 27.3, 27.3, 27.1; HRMS (ESI) *m/z* calc. for $C_{79}H_{95}FO_{20}S$ $[M+Na]^+$, 1437.6014; found 1437.5984.

6. Automated synthesis of Hexasaccharide



Scheme S12

The automated synthesis of hexasaccharide **39** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm×20 mm). In the anodic chamber were placed building block **33** (420.0 mg, 0.282 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (30 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). The constant current electrolysis (12.0 mA) was carried out at -80 °C with magnetic stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, building block **38** (316.4 mg, 0.223 mmol) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump (2.0 mL) under an argon atmosphere at -80 °C, and then the temperature was raised to -50 °C and kept for 60 min.

The reaction temperature was cooled down to -80 ºC and Et_3N (0.30 mL) was added at -80 ºC. After additional stirring at rt for 30 min the reaction mixture was filtered through a short column (4 × 3 cm) of silica gel to remove Bu_4NOTf. The removal of the solvent under reduced pressure afford a crude hexasaccharide. The crude hexasaccharide is dissolved in CH_2Cl_2, and mixture of pyridine and acetic acid (0.20 mL:0.10 mL) was added to the same solution. Finnaly hydrazine acetate (0.032 mg, 0.329 mmol) is added to the reaction flask and allowed it to stirr for 24 h. TLC analysis (Hexane/EtOAc 7:3) indicated the complete consumption of the starting materials and formation of a new spot at (R_f = 0.40). The reaction mixture is then diluted with excess amount of CH_2Cl_2 and washed with brine and dried over Na_2SO_4. Removal of solvent under reduced pressure afford a crude product which will further purified using silica gel chromatography to obtain **39** (77.6 mg, 0.028 mmol) in 18% over two steps. **Methyl-4,6-di-*O*-benzyl-3-*O*-chloroacetyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-gluco-pyranosyl-(1→6)-3,4-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-gluco-pyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-4-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-gluco-pyranoside. (39)**. TLC (Hexane/EtOAc 7:3) R_f = 0.40; $[\alpha]_D$ = -1.89 (*c* = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.38 (m, 2 H), 7.32-7.19 (m, 52 H), 7.15 (m, 1 H), 7.20 (m, 2 H), 6.98 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.16 (t, *J* = 9.6 Hz, 1 H), 5.05 (dd, *J* = 9.0, 8.4 Hz, 1 H), 5.02, (s, 1 H), 5.00 (t, *J* = 8.4 Hz, 1 H), 4.93 (d, *J* = 11.4 Hz, 1 H), 4.89 (d, *J* = 9.6 Hz, 1 H), 4.87 (s, 1 H), 4.86 (d, *J* = 2.4 Hz, 1 H), 4.80 (dd, *J* = 9.6, 7.8 Hz, 1 H), 4.74 (d, *J* = 2.4 Hz, 1 H), 4.73 (d, *J* = 7.8 Hz, 1 H), 4.72 (s, 2 H), 4.70 (d, *J* = 4.8 Hz, 1 H), 4.69 (t, *J* = 6.6Hz, 2 H), 4.66 (d, *J* = 2.4 Hz, 1 H), 4.64 (d, *J* = 6.6 Hz, 1 H), 4.64 (s, 1 H), 4.62 (d, *J* = 4.2 Hz, 1 H), 4.58 (d, *J* = 1.8 Hz, 1 H), 4.56 (d, *J* = 10.8 Hz, 2 H), 4.52 (d, *J* = 9.6 Hz, 1 H), 4.50 (s, 1 H), 4.49 (d, *J* = 3.6 Hz, 1 H), 4.48 (s, 1 H), 4.48 (s, 1 H), 4.46 (s, 1 H), 4.43 (d, *J* = 7.8 Hz, 1 H), 4.40 (t, *J* = 12.6 Hz, 2 H), 4.37 (d, *J* = 7.8 Hz, 1 H), 4.27 (d, *J* = 7.8 Hz, 1 H), 4.19 (d, *J* = 7.8 Hz, 1 H), 4.13 (d, *J* = 8.4 Hz, 1 H), 4.01 (dd, *J* = 11.4, 3.0 Hz, 1 H), 3.92 (dd, *J* = 11.4, 3.0 Hz, 1 H), 3.86 (dd, *J* = 11.4, 3.0 Hz, 1 H), 3.77 (d, *J* = 4.2 Hz, 1 H), 3.75 (d, *J* = 4.2 Hz, 1 H), 3.72 (d, *J* = 15.0 Hz, 1 H), 3.71 (d, *J* = 5.4 Hz, 1 H), 3.70 (d, *J* = 3.6 Hz, 1 H), 3.68 (d, *J* = 2.4 Hz, 1 H), 3.67 (t, *J* = 2.4 Hz, 1 H), 3.67 (s, 1 H), 3.65 (d, *J* = 1.8 Hz, 1 H), 3.63 (s, 1 H), 3.60 (m, 2 H), 3.56 (d, *J* = 15.0 Hz, 1 H), 3.52 (s, 1 H), 3.51 (s, 1 H), 3.51 (s, 1 H), 3.50 (s, 1 H), 3.48 (m, 2 H), 3.45 (m, 1 H), 3.42 (d, *J* = 9.0 Hz, 1 H), 3.39 (dd, *J* = 15.6, 1.2 Hz, 1 H), 3.35 (dd, *J* = 10.2, 4.2 Hz, 1 H), 3.31 (m, 1 H), 3.26 (m, 1 H), 1.82 (bs, 1 H), 1.25 (s, 9 H), 1.23 (s, 9 H), 1.13 (s, 18 H), 1.11 (s, 9 H), 1.10 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.2, 176.9, 176.6, 176.4, 176.4, 165.5, 162.8 (d, *J* = 247.0 Hz), 138.6, 138.1, 138.1, 138.0, 138.0, 137.9, 137.8, 134.7, 134.7, 129.0, 128.6, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5, 127.5, 127.3, 127.3, 127.2, 127.1, 116.1 (d, *J* = 21.9 Hz), 101.3, 100.9, 100.5, 99.3, 98.6, 86.5, 83.0, 83.0, 82.9, 79.1, 78.1, 78.0, 77.8, 77.6, 76.6, 75.8, 75.6, 75.5. 75.4, 75.2, 75.0, 74.8, 74.7, 74.6, 74.5, 74.4, 74.4, 73.6, 73.2, 73.1, 72.6, 72.4, 71.5, 69.2, 68.9, 68.2, 67.9, 66.7, 62.5, 40.5, 38.8, 38.8, 38.7, 38.7, 38.7, 27.4, 27.3, 27.2, 27.2, 27.0; HRMS (ESI) *m/z* calc. for $C_{156}H_{186}FO_{39}S$ $[M+K]^+$, 2711.1262; found 2712.1067.

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Chapter 3

Electrochemical Glycosylation as an Enabling Tool for the Synthesis of Cyclic β-1,6-Oligosaccharides

Abstract

Due course of study deals with a comprehensive automated electrochemical assembly of carbohydrate entities to form linear oligoglucosamine featuring one pot glycosylation followed by intramolecular electrochemical glycosylasation of linear oligoglucosamine leading to cyclic oligoglucosamine. Alongside that, oligomer concentration effect has been studied to justify the intra-molecularity of the cyclisation. Additionally, parallel study was also commenced with respect to conventional chemical glycosylation for comparison.

Introduction

Cyclic oligosaccharides such as cyclodextrins (CDs) which involve α–D–(1→4) glycosidic linkages of D-glucopyranose have attracted researchers more than a century because of their unique structures and properties.[1,2] Both chemical[3] and enzymatic[4] approaches have been developed to prepare natural and unnatural CDs. Moreover, chemical modification in the exocyclic hydroxyl groups of CDs show fundamental alterations in host-guest features of cyclic oligosaccharides.[5] Other cyclic oligosaccharides involving other monosaccharides have also investigated intensively; however, cyclic oligosaccharides of glucosamines are rare.[6-11]

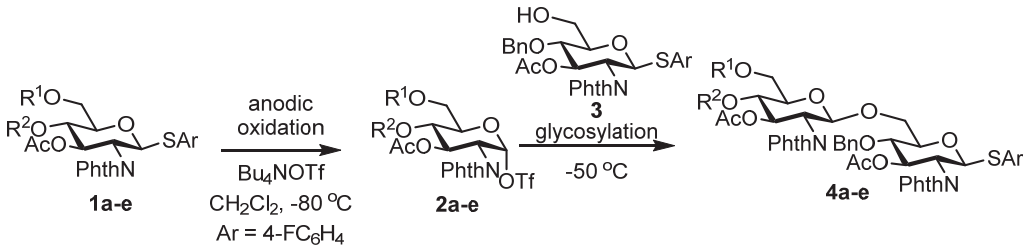
Recently, Nifantiev and co-workers[12] reported synthesis of cyclic oligo-(1→6)-β-D-glucosamine utilizing thioglycoside as precursor and NIS/TfOH as promoter system. The scope of aforementioned system was found to be limited only for di- and trisaccharide and unable to give stereochemically pure β-isomer of oligosaccharide as a single product even in the presence of *N*-phthalimide at C-2 position which secures β stereoselectivity in glycosylation. To address the problem of stereoselectivity and yield of cyclic oligosaccharides, further improvement of synthetic methodology is desirable.

In the course of our study of electrochemical glycosylation we have developed automated electrochemical assembly which is a method for automated electrochemical solution-phase synthesis of oligosaccharides. The method has already been successfully applied to synthesis of linear oligoglucosamines,[13a] TMG-Chitotriomycin,[13b,c] GPI anchor trisaccharide[13d] and β-(1→3)-(1→6) linked oligoglucosides.[13e] Thus, we envisioned that precursors of cyclic oligosaccharides will be easily prepared using the method and subsequent electrochemical glycosylation might be an alternative method for chemical synthesis of cyclic oligosaccharides. Here we demonstrate that electrochemical glycosylation is useful for not only intermolecular glycosylation but also intramolecular glycosylation to synthesize cyclic oligosaccharides.

Results and Discussion

We initiated our study with development of the terminal building block with a temporary protecting group. Thus, a series of thioglycosides **1a-e** equipped C-2 N-phthalimide group to ensure stereochemical outcome in the glycosylation and various substituents at remaining hydroxyl groups. With thioglycosides in hand, building blocks were evaluated by synthesis of disaccharide (Table 1). The electrochemical glycosylation of terminal building block **1a-e**, with building block **3**, was performed under the same condition as the previously reported synthesis of oligoglucosamines.[13a] To our delight, glycosylation of **1b** afforded desired product **4b** in 59% yield (entry 2); however, the yield is much lower than that with **1a** (entry 1). Building block **1c** with MOM protection at 6-OH and benzyl protection at 4-OH equipped donor did not afford detectable amount of desired disaccharide **4c**. Further, building block **1d**, bearing chloroacetyl (ClAc) and benzyl (Bn) groups at 6-OH and 4-OH, respectively; lowers the glycosylation yield to 45% (entry 4). Moreover, building block **1e** bearing chloroacetyl and benzyl group at 6-OH and 4-OH afforded disaccharide **4e** in 57% yield (entry 5). Influence of protecting group at 6-OH is still remains an unsolved puzzle, these results may be attributed to tolerance of protecting group under the electrochemical condition and stability of glycosyl triflate formed in the reaction.

Table 1. Optimization of terminal building block

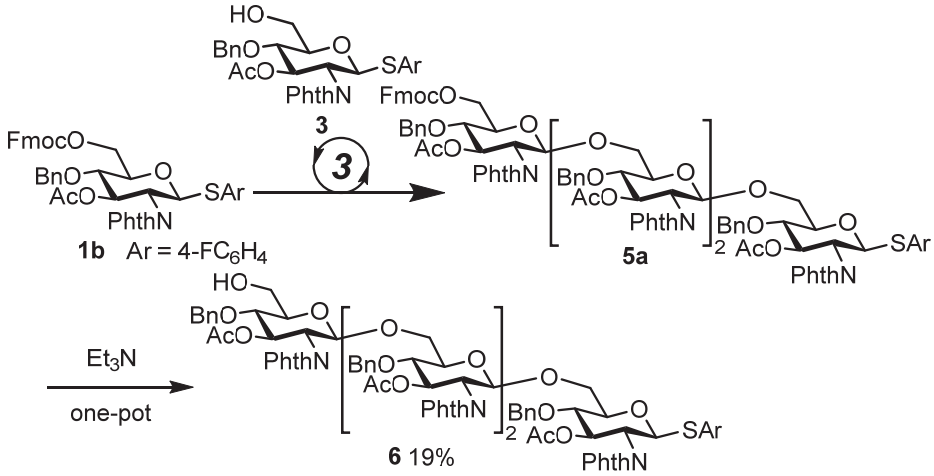


Building Block	R^1	R^2	Product	Yield (%)	Selectivity (α:β)
1a	Ac	Ac	**4a**	92[a]	β only
1b	Fmoc	Bn	**4b** (R^1 = H)	59[b]	β only
1c	MOM	Bn	**4d**	ND[c]	–
1d	ClAc	Bn	**4c**	45	β only
1e	ClAc	Ac	**4e**	57	β only

[a]Reference 13a. [b] Glycosylation at -40 °C and yield after Fmoc deprotection (R^1 = H).
[c]Product was not detected.

The best performing building block **1b** with Fmoc at 6-OH, was then employed in the automated electrochemical assembly with building block **3** for chain elongation for the synthesis of tetrasaccharide (Scheme 1). Subsequent one-pot deprotection of Fmoc group afforded desired tetrasaccharide **5b** in 19% overall yield, which is intern much less than that of disaccharide assembled from building block **1a**.[13a] Therefore, strategic improvement in the methodology is highly desirable to address necessity of oligosaccharides in sufficient quantity.

Scheme 1. Automated electrochemical assembly and subsequent one-pot Fmoc deprotection for synthesis of the precursor of cyclic tetrasaccharide

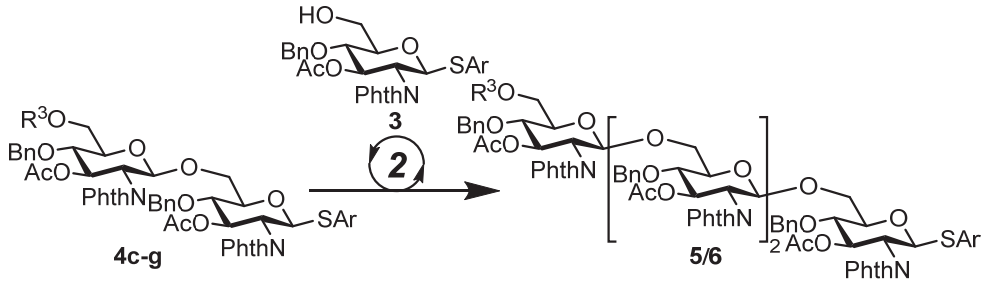


After the detailed investigation of glycosylation sequence (Table 1), glycosyl donor was not detected in ^{1}H NMR analysis of crude reaction mixture, which is in another way states that there is complete oxidation of donor, however, protecting group at C-6 position possess a destabilizing effect towards glycosyl triflate and not allowing it to get accumulate. Taking this fact into consideration, a strategic modification in the methodology was made, where instead

of monosaccharide; disaccharide was chosen as a terminal building block. Thus, terminal building block equipped with variety of orthogonal protecting group at non-reducing end were synthesized and automated electrochemical assembly was investigated (Table 2).

Pleasurably, our understanding of reaction found to be worthy and automated electrochemical assembly starting from disaccharide building block was able to furnished desired tetrasaccharides over two repetitive cycles in reasonable yield. Results listed in Table 2 concludes that Fmoc and Ac have relatively less influence on stability of glycosyl triflate intermediate as indicated by their glycosylation efficiency, whereas ClAc, MOM and Lev possess more pronounced effect leading to less or no product formation. Encouraged by the results of tetrasaccharides starting from disaccharide building block **4f**, we also synthesized pentasaccharide **7** and hexasaccharide **8** which were precursor of cyclic oligosaccharides (See supporting information for details).

Table 2. Optimization of disaccharide terminal building block

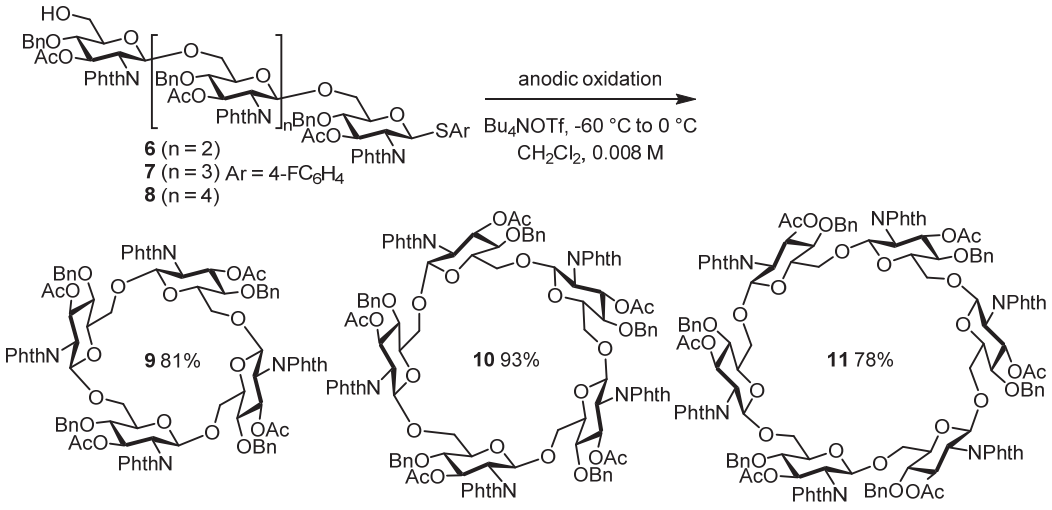


Building Block	R^3	Product	Yield (%)	Selectivity (α:β)
4f	Fmoc	**6**	47	β only
4c	ClAc	**5c**	ND[a]	–
4d	MOM	**5d**	7	β only
4g	Ac	**5g**	38	β only
4h	Lev	**5h**	12	β only

[a]Not detected

Next intramolecular cyclization under anodic oxidation conditions was investigated (Table 3). As a model reaction, electrochemical cell charged with 0.008 M linear tetrasaccharide **5b** was electrochemically activated at -60 ºC by means of 1.6 F/mol electricity and further the reaction temperature gradually brought to 0 ºC over a period of 2.5 h and finally quench with Et_3N (see supporting information for detailed procedure). Purification of compound by simple extraction with EtOAc avoiding tedious chromatographic methods, resulted cyclic tetrasaccharide **9** in 81% as a single compound. Further, increasing the concentration of substrate four times higher than that of the ordinary condition did make a significant change in the glycosylation yield, suggesting only intramolecular reaction are favored at low concentration (Table 3). Similarly, cyclic pentasaccharide **10** and hexasaccharide **11** were also efficiently synthesized exploiting generality of methodology with 93% and 78% yields, respectively.

Table 3. Intramolecular cyclization under anodic oxidation condition



Oligosaccharide	Conc. [M]	Product	Yield (%)	Selectivity (α:β)
6 (n = 2)	0.008	**9**	81	β only
6 (n = 2)	0.032	**9**	78	β only
7 (n = 3)	0.008	**10**	93	β only
8 (n = 4)	0.008	**11**	78	β only

Excellent results of electrochemical cyclization encouraged us for detailed investigation of reactivity based selective cyclization in the presence of both primary and secondary sugar alcohols (Figure 1).[13a] We prepared tetrasaccharide 5h from **1a** and successive treatment of hydrochloric acid resulted partially protected tetrasaccharide **5i** in quantitative yield.[14a,b] Aforementioned electrochemical protocol was then employed for partially protected tetrasaccharide **5i**, followed by acetylation afforded cyclic tetrasaccharide **12** with complete β selectivity in 84% yield (2 steps). To confirm the selectivity in the cyclization is solely govern with the primary alcohol, global deprotection have was carried out. Deprotection of phthaloyl group using 1,2-diamino ethane followed by acetylation gave *N*-acetyl version of cyclic tetrasaccharide **13** in one pot with good yield. Successively, acid mediated acetate hydrolysis followed by conventional hydrogenation over $Pd(OH)_2/C$ gave fully deprotected cyclic tetrasaccharide **14** in good yield. The ^1H and mass spectral analysis is in total agreement in those of literature report **12a** not only confirms identity of the molecule but also concludes that the selectivity in cyclization is govern by the primary alcohol.

For comparison, we also carried out intramolecular cyclization of tetrasaccharide **6** under conventional chemical glycosylation conditions.[15] Tetrasaccharide **6** which was treated with *N*-iodosuccimide (NIS) and triflic acid (TfOH) at -15 °C afforded both α- and β-isomers of cyclic oligoglucosamine **15** and **9** in 12% and 30% yields, respectively. This result is consistent with that obtained by Nifantiev and co-workers,[12a] therefore choice of protecting groups of 3-OH and 4-OH is not crucial to obtain cyclic oligoglucosamine stereoselectively. Although it is still not clear the reason why electrochemical glycosylation afforded cyclic oligoglucosamine in stereoselective manner, we assume that both activation and glycosylation at lower temperature are critical.

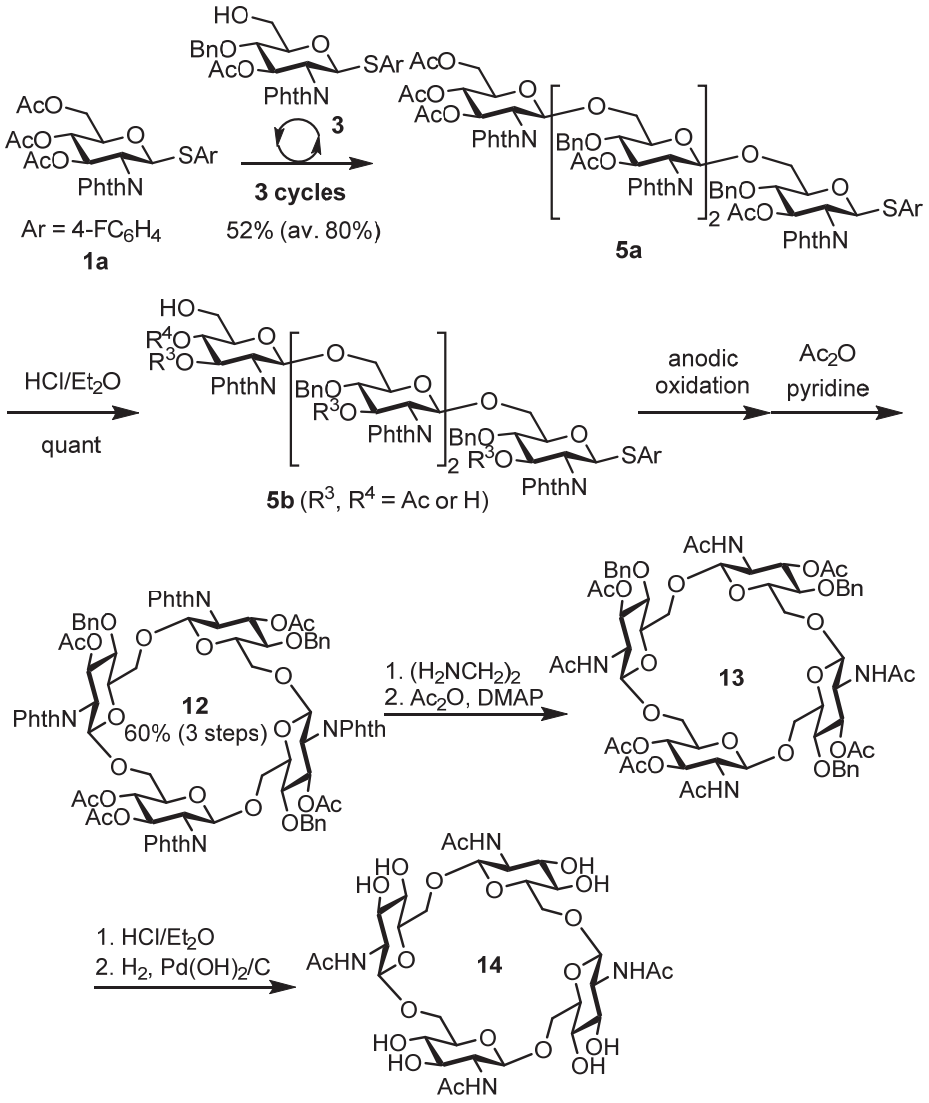
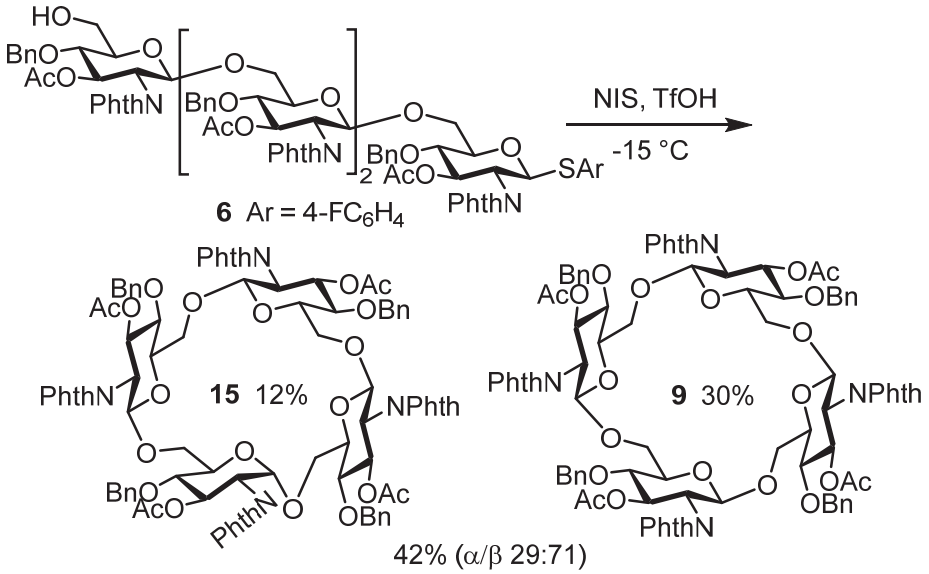


Figure 1. Selective intramolecular cyclization of primary alcohol and global deprotection.

Scheme 2. Conventional intramolecular chemical glycosylation.



Conclusion

In summary, we have developed a comprehensive automated electrochemical protocol for stereoselective synthesis of cyclic oligoglucosamine in an excellent glycosylation yield. Furthermore, reactivity based regioselective glycosylation independent of number of secondary alcohols has been explore to justify dominance of intramolecularity in cyclization. Comparative study of conventional glycosylation and electrochemical glycosylation were also performed exploring silent features of electrochemical glycosylation.

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14. a) HCl/Et2O mediated hydrolysis of acetate resulted mixture of mono, di- and tri-acetate protected tetrasaccharide detected by ESI-MS. The rate of hydrolysis of the acetyl group of the primary hydroxyl group is faster than that of secondary hydroxyl group, thus we considered that the primary alcohol was fully hydrolyzed. b) Zemplén's condition gave complete deacetalised product; however, insolubility of the compound in CH_2Cl_2 renders its use for cyclization.
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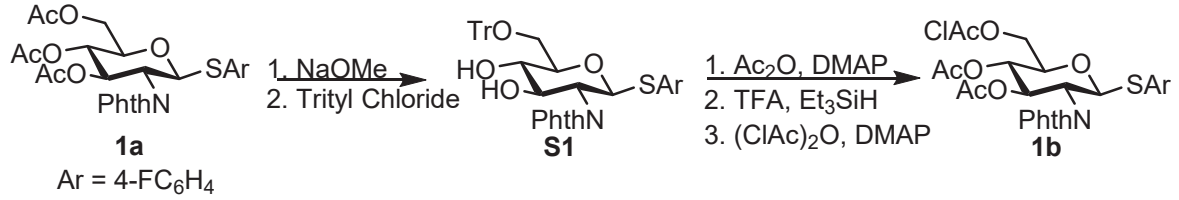
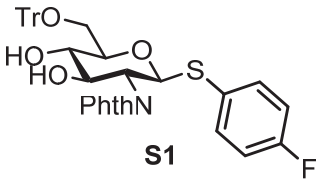
Experimental section

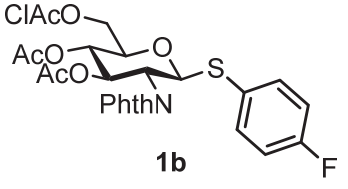
Preparation of building block



Scheme S1

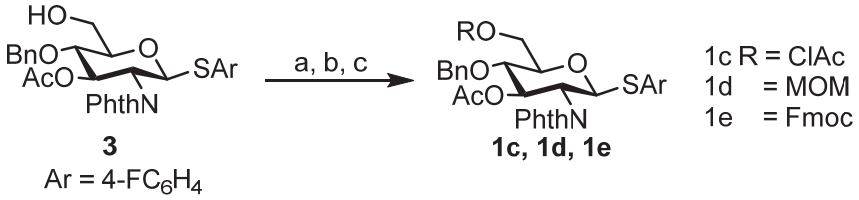


To a solution of **1a** (10.60 g, 19.4 mmol) in methanol (43 mL) was added NaOMe (3.88 mL, 19.4 mmol) dropwise over a period of 15 min and allowed reaction to stir at room temperature for overnight. Completion of reaction monitored by TLC analysis, following addition of amberlite IR 120 resin to neutralised sodium methoxide and evaporated under reduced pressure and dried under vacuum. The same crude product is then treated with trityl chloride (3.56 g, 13.0 mmol) in pyridine (31.4 mL) maintaining dry and dark condition for 4 days. TLC analysis ($CHCl_3$/MeOH = 10:1) suggest completion of reaction and crude product evaporated to dryness. Purification using silica gel chromatography furnished the pure compound **S1** as a white solid (6.58 g, 9.95 mmol) in 52 % yield over two steps.**4-fluorophenyl-6-*O*-trityl-3,4-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (S1).** TLC (hexane/ethyl acetate = 1:1) $[\alpha]_D = 4.66$ (c = 1.03 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.62 (bs, 2H, 2 X OH), 3.41 (dd, *J* = 10.2, 4.2 Hz, 1H, H-6), 3.51 (m, 2H, H-5 & H-6), 3.57 (*pseudo*-t, *J* = 9.0 Hz, 1H, H-4), 4.15 (t, *J* = 10.2 Hz, 1H, H-2), 4.26 (dd, *J* = 10.2, 9.0 Hz, 1H, H-3), 5.50 (d, *J* = 10.2 Hz, 1H, H-1), 6.91 (*pseudo*-t, *J* = 9.0 Hz, 2H, aromatic CH), 7.26 (m, 2H, aromatic CH), 7.31 (*pseudo*-t, *J* = 5.4 Hz, 6H, aromatic CH), 7.45 (m, 9H, aromatic CH), 7.73 (dd, *J* = 6.0, 3.0 Hz, 2H, aromatic CH), 7.83 (bs, 1H), 7.86 (bs, 1H, aromatic CH); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.9 (d, *J* = 247.5 Hz, aromatic-C), 143.5 (aromatic-C), 135.8 (d, *J*= 7.5 Hz)(aromatic-C), 134.3(aromatic-C), 128.6(aromatic-C), 128.0(aromatic-C), 127.2(aromatic-C), 115.9 (d, *J* = 21.0 Hz)(aromatic-C), 87.0(O-C(Ph)$_3$), 83.3(C-1), 78.2(C-5), 72.9(C-3), 72.7(C-4), 63.5(C-6), 55.2(C-2).



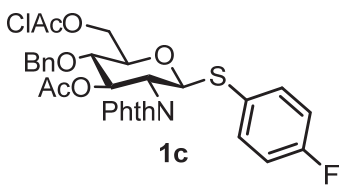
To a solution of **S1** (6.58 g, 9.95 mmol) in the mixture of pyridine (11 mL) and CH_2Cl_2 (32 mL) was added acetic anhydride (6.1 mL, 59.7 mmol) following 4-Dimethylaminopyridine (0.13 g, 1.09 mmol) at 0 ^{0}C and allowed the reaction to stir at room temperature for 12h. TLC analysis monitoring suggest that completion of reaction. The crude product is then evaporated to dryness under reduced pressure to remove volatile impurities. Crude product is then dissolved in CH_2Cl_2 (100 mL) and washed three times with 1N HCl followed by brine. Further the product was dried over Na_2SO_4 and filtered successively. Filtrate is then evaporated under reduced pressure and dried under vacuum. The portion of above obtained product (1.5 g, 2.01 mmol) is then treated with Triethylsilane (7.1 mL, 44.2 mmol) and allowed the reaction flask to stir at 0 ^{0}C for 15 min and trifluoroacetic acid (6.78 mL, 88.5 mmol) was added dropwise. After stirring at same temperature for next 5min TLC analysis shows completion of reaction and 10% $NaHCO_3$ was added successively

to quenched the reaction. Further reaction mixture is diluted with CH_2Cl_2 (25 mL) and washed three times with brine (3 x 20 mL) followed by dried over Na_2SO_4 and filtered. Filtrate is then evaporated under reduced pressure to furnished desired product. The portion of above obtained product (0.495 g, 0.98 mmol) is then dissolved in the mixture of pyridine (0.1 mL) and CH_2Cl_2 (8.0 mL) and allowed the reaction to stir at -10 ^{0}C for 30 min, after which chloroacetic anhydride (0.21 g, 1.18 mmol) was added portion wise to the reaction mixture. After stirring the reaction at same temperature for next 3h, TLC analysis shows completion of reaction. Reaction is then diluted with CH_2Cl_2 (25 mL) and washed successively with 1N HCL for three times (3 X 20 mL) and finally with brine. The crude product is then dried over Na_2SO_4 and filtered. Filtrate was evaporated under reduced pressure to furnished desired product. Finally, the crude product is purified using silica gel chromatography to get desired product **1b** in 36% yield over three steps. **4-fluorophenyl-6-*O*-chloroacetyl-3,4-di-*O*-acetyl-2-deoxy-2-phthalimido-1-thio- β-D-glucopyranoside (1b).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.62, $[\alpha]_D$ = 33.99 (c = 1.0 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.84 (s, 3H, O=C-C<u>H</u>$_3$), 2.03 (s, 3H, O=C-C<u>H</u>$_3$), 3.93 (ddd, *J* = 10.2, 4.8, 2.4 Hz, 1H, H-5), 4.12 (s, 2H, ClC<u>H</u>$_2$=CO), 4.28 (t, *J* = 10.8 Hz, 1H, H-2), 4.34 (dd, *J* = 12.0, 1.8 Hz, 1H, H-6), 4.40 (dd, *J* = 12.6, 4.8 Hz, 1H, H-6), 5.10 (t, *J* = 9.6 Hz, 1H, H-4), 5.65 (d, *J* = 10.8 Hz, 1H, H-1), 5.79 (t, *J* = 10.2 Hz, 1H, H-3), 7.00 (t, *J* = 9.0 Hz, 2H, aromatic C<u>H</u>), 7.42 (m, 2H, aromatic C<u>H</u>), 7.78 (m, 2H, aromatic C<u>H</u>), 7.89 (m, 2H, aromatic C<u>H</u>); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.0(O=C-<u>C</u>H$_3$), 169.4(O=C-<u>C</u>H$_3$), 167.8(O=<u>C</u>-, phthalimido), 166.9(O=<u>C</u>-CH$_2$Cl), 166.9(O=<u>C</u>-, phthalimido), 163.2 (*J* = 248.1 Hz)(aromatic-<u>C</u>), 136.5(aromatic-<u>C</u>), 136.4(aromatic-<u>C</u>), 134.6(aromatic-<u>C</u>), 134.4(aromatic-<u>C</u>), 131.5(aromatic-<u>C</u>), 131.0(aromatic-<u>C</u>), 125.1(aromatic-<u>C</u>), 125.1(aromatic-<u>C</u>), 123.7(aromatic-<u>C</u>), 116.0 (*J* = 21.75 Hz)(aromatic-<u>C</u>), 82.8(C-1), 75.7(C-5), 71.4(C-3), 68.4(C-4), 63.5(C-6), 53.4(C-2), 40.6(O=C-<u>C</u>H$_2$Cl), 20.5(O=C-<u>C</u>H$_3$), 20.3(O=C-<u>C</u>H$_3$); HRMS (ESI) m/z calcd for $C_{26}H_{23}ClFNO_9S$ $[M+Na]^+$, 602.0658; found, 602.0643.



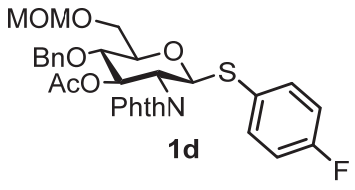
a = $(ClCH_2CO)_2O$, DMAP, Pyridine, CH_2Cl_2, rt, overnight
b = MOMCl, NaI, DIPEA, $CH_3OCH_2CH_2OCH_3$, 90 ^{o}C, 4h
c = FmocCl, pyridine, CH_2Cl_2, rt, 4h

Scheme S2



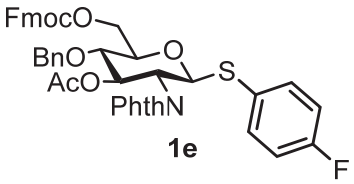
The compound **3** (1.10 g, 2.0 mmol) is dissolved in the mixture of pyridine (0.2 mL) and CH_2Cl_2 (17.0 mL) and allowed the reaction to stir at -10 ^{0}C for 30 min, after which chloroacetic anhydride (0.41 g, 2.40 mmol) was added portion wise to the reaction mixture. After stirring the reaction at same temperature for next 3h, TLC analysis shows completion of reaction. Reaction is then diluted with CH_2Cl_2 (25 mL) and washed successively with 1N HCL for three times (3 x 20 mL) and then with brine. The crude product is then dried over Na_2SO_4 and filtered. Filtrate was evaporated under reduced

pressure to furnished desired product. Finally, the crude product is purified using silica gel chromatography to get desired product **1c** (1.10 g, 1.77 mmol) in 89% yield. **4-Fluorophenyl-6-*O*-chloroacetyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (1c).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.72, $[\alpha]_D$ = 30.28 (c = 1.04 %, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 1.78 (s, 3H, O=C-C<u>H</u>$_3$), 3.65 (*pseudo*-t, *J* = 9.6 Hz, 1H, H-4), 3.80 (ddd, *J* = 10.2, 4.8, 2.4 Hz, 1H, H-5), 4.02 (dd, *J* = 19.2, 15.0 Hz, 2H, O=C-C<u>H</u>$_2$Cl), 4.16 (t, *J* = 10.2 Hz, 1H, H-2), 4.30 (dd, *J* = 12.0, 4.8 Hz, 1H, H-6), 4.55 (dd, *J* = 12.0, 1.8 Hz, 1H, H-6), 4.57 (d, *J* = 11.4 Hz, 1H, Ph-C<u>H</u>$_2$), 4.64 (d, *J* = 11.4 Hz, 1H, Ph-C<u>H</u>$_2$), 5.64 (d, *J* = 10.2 Hz, 1H, H-1), 5.78 (dd, *J* = 10.2, 9.0 Hz, 1H, H-3), 6.99 (*pseudo*-t, *J* = 6.6 Hz, 2H, aromatic C<u>H</u>), 7.23 (d, *J* = 6.6 Hz, 2H, aromatic C<u>H</u>), 7.29 (m, 2H, aromatic C<u>H</u>), 7.32 (m, 2H, aromatic C<u>H</u>), 7.39 (m, 2H, aromatic C<u>H</u>), 7.76 (m, 2H, aromatic C<u>H</u>), 7.88 (dd, *J* = 13.2, 6.6 Hz, 2H, aromatic C<u>H</u>); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.9(O=C-<u>C</u>H$_3$), 167.8(O=<u>C</u>-, phthalimido), 167.3(O=-<u>C</u>-CH$_2$Cl), 166.7(O=<u>C</u>-; phthalimido), 163.2 (d, *J* = 247.9 Hz) (aromatic-<u>C</u>), 137.2(aromatic-<u>C</u>), 136.5(aromatic-<u>C</u>), 136.4(aromatic-<u>C</u>), 134.5(aromatic-<u>C</u>), 134.3(aromatic-<u>C</u>), 131.7(aromatic-<u>C</u>), 131.1(aromatic-<u>C</u>), 128.6(aromatic-<u>C</u>), 128.1(aromatic-<u>C</u>), 127.9(aromatic-<u>C</u>), 125.4(aromatic-<u>C</u>), 125.4(aromatic-<u>C</u>), 123.7(aromatic-<u>C</u>), 123.6(aromatic-<u>C</u>), 115.9 (d, *J* = 21.6 Hz)(aromatic-<u>C</u>), 82.6(C-1), 76.8(C-5), 75.8(C-3), 74.6(C-4), 74.1, 64.1(C-6), 53.8(C-2), 40.6(O=C-<u>C</u>H$_2$Cl), 20.5(O=C-<u>C</u>H3); HRMS (ESI) m/z calcd for $C_{31}H_{27}ClFNO_8S$ $[M+K]^+$, 666.0762; found, 666.0743.



1d

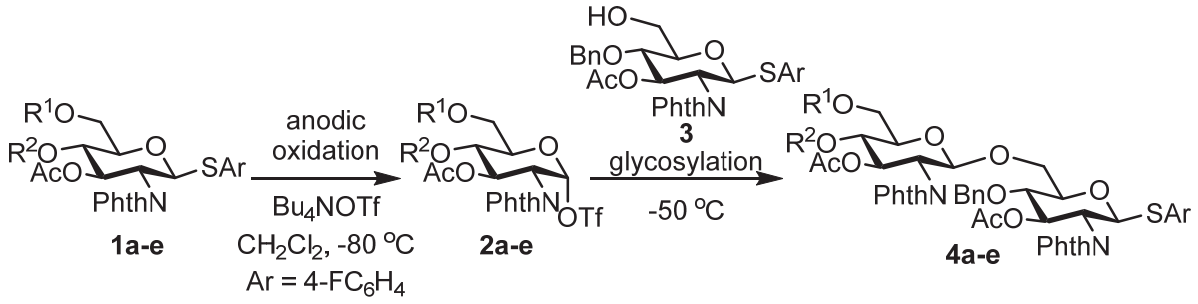
To a stirred solution of **3** (1.03 g, 1.87 mmol) in dimethoxyethane (7.5 mL) was added NaI (1.12 g, 7.48 mmol), chloromethyl methyl ether (0.71 mL, 9.37 mmol), *N*,*N*′-Diisopropylethylamine (1.63 mL, 9.37 mmol) and allowed the reaction to reflux at 90 ^{0}C for 4h. after which TLC analysis shows completion of reaction. The reaction is then diluted with CH_2Cl_2 (25 mL) and washed successively with 10% $NaHCO_3$ (3 X 25 mL) and brine. The product is then dried over Na_2SO_4 and filtered. After evaporation of filtrate under reduced pressure the product was purified using silica gel chromatography to furnished desired product **1d** (0.97 g, 1.63 mmol) in 87 % yield. **4-Fluorophenyl-6-*O*-methoxymethyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (1c).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.71, $[\alpha]_D$ = 27.79 (c = 1.01 %, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 1.73 (s, 3H, O=C-C<u>H</u>$_3$), 3.40 (s, 3H, -O-C<u>H</u>$_3$), 3.73 (m, 1H, H-6), 3.76 (dd, *J* = 18.0, 9.6 Hz, 1H, H-4), 3.81 (dd, *J* = 10.8, 3.6 Hz, 1H, H-5), 3.88 (d, *J* = 10.8 Hz, 1H, H-6), 4.21 (t, *J* = 10.8 Hz, 1H, H-2), 4.62 (d, *J* = 11.4 Hz, 1H, -O-C<u>H</u>$_2$-Ph), 4.67 (d, *J* = 12.0 Hz, 1H, O-C<u>H</u>$_2$-Ph), 4.70 (d, *J* = 5.4 Hz, 1H, -O-C<u>H</u>$_2$-OCH$_3$), 4.71 (d, *J* = 6.0 Hz, 1H, -O-C<u>H</u>$_2$-OCH$_3$), 5.65 (d, *J* = 10.8 Hz, 1H, H-1), 5.78 (dd, *J* = 9.6, 9.0 Hz, 1H, H-3), 6.95 (t, *J* = 8.4 Hz, 2H, aromatic CH), 7.25 (m, 3H, aromatic CH), 7.30 (t, *J* = 7.2 Hz, 2H, aromatic CH), 7.42 (dd, *J* = 6.0, 5.4 Hz, 2H, aromatic CH), 7.73 (m, 2H, aromatic CH), 7.85 (m, 2H, aromatic CH); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.0(O=<u>C</u>-CH$_3$), 167.8(O=<u>C</u>-; phthalimido), 167.3(O=-<u>C</u>; phthalimido), 163.1 (d, *J* = 247.3 Hz) (aromatic-<u>C</u>), 137.8(aromatic-<u>C</u>), 136.1(aromatic-<u>C</u>), 136.0(aromatic-<u>C</u>), 134.4(aromatic-<u>C</u>), 134.1(aromatic-<u>C</u>), 131.7(aromatic-<u>C</u>), 131.2(aromatic-<u>C</u>), 128.4(aromatic-<u>C</u>), 127.8(aromatic-<u>C</u>), 127.6(aromatic-<u>C</u>), 126.0(aromatic-<u>C</u>), 126.0(aromatic-<u>C</u>), 123.6(aromatic-<u>C</u>), 123.5(aromatic-<u>C</u>), 115.9 (d, *J* = 21.4 Hz) (aromatic-<u>C</u>), 96.8(-O-<u>C</u>H$_2$-OCH$_3$), 82.8(C-1), 78.8(C-4), 76.4(C-5), 74.6(-O-<u>C</u>H$_2$-Ph), 74.1(C-3), 66.1(C-6), 55.3(C-2), 54.1(-O-CH$_2$-O<u>C</u>H$_3$), 20.4(O=C-<u>C</u>H3); HRMS (ESI) m/z calcd for $C_{31}H_{30}FNO_8S$ $[M+K]^+$, 634.1308; found, 634.1322.



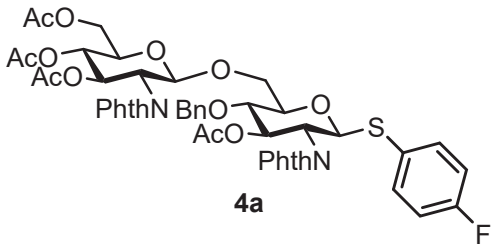
1e

The compound **3** (1.65 g, 3.0 mmol) is dissolved in the mixture of pyridine (3.1 mL) and CH_2Cl_2 (15.0 mL) and allowed the reaction to stir at 0 ^{0}C for 30 min, after which chloroacetic anhydride (1.16 g, 4.5 mmol) was added portion wise to the reaction mixture. After stirring the reaction at room temperature for next 24h, TLC analysis shows completion of reaction. Reaction is then diluted with CH_2Cl_2 (25 mL) and washed successively with 1N HCL for three times (3 X 20 mL) and then with brine. The crude product is then dried over Na_2SO_4 and filtered. Filtrate was evaporated under reduced pressure to furnished desired product. Finally, the crude product is purified using silica gel chromatography to get desired product **1e** (1.59 g, 2.07 mmol) in 69% yield. **4-Fluorophenyl-6-*O*-(9-fluorenylmethoxycarbonyl)-3-acetyl-4-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (1e).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.55. $[\alpha]_D$ = 24.64 ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.77 (s, 3H, O=C-C<u>H</u>$_3$), 3.73 (t, *J* = 9.6 Hz, 1H, H-4), 3.84 (ddd, *J* = 10.2, 4.8, 1.8 Hz, 1H, H-5), 4.20 (*pseudo*-t, *J* = 10.2 Hz, 1H, H-2), 4.30 (*pseudo*-t, *J* = 7.2 Hz, 1H, Fmoc; -CH$_2$-C<u>H</u>(Ar)), 4.34 (dd, *J* = 12.0, 4.8 Hz, 1H, H-6), 4.47 (m, 2H Fmoc; -C<u>H</u>$_2$-CH(Ar)), 4.55 (dd, *J* = 11.4, 1.8 Hz, 1H, H-6), 4.62 (s, 2H), 5.67 (d, *J* = 10.2 Hz, 1H, H-1), 5.79 (dd, *J* = 10.2, 9.0 Hz, 1H, H-3), 6.93 (*pseudo*-t, *J* = 8.4 Hz, 2H, aromatic C<u>H</u>), 7.23-7.24 (m, 3H, aromatic C<u>H</u>), 7.28-7.32 (m, 2H, aromatic C<u>H</u>), 7.35-7.37 (m, 2H, aromatic C<u>H</u>), 7.40-7.45 (m, 4H, aromatic C<u>H</u>), 7.66 (pseudo-t, *J* = 7.8 Hz, 2H, aromatic C<u>H</u>), 7.75-7.77 (m, 2H, aromatic C<u>H</u>), 7.80 (dd, *J* = 7.2, 3.0 Hz, 2H, aromatic C<u>H</u>), 7.86-7.89 (m, 2H, aromatic C<u>H</u>); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.0(O=C-<u>C</u>H$_3$), 167.8(O=<u>C</u>-; phthalimido), 167.3(O=-<u>C</u>-; phthalimido), 162.3 (d, *J* = 247.7 Hz) (aromatic-<u>C</u>), 154.9(aromatic-<u>C</u>), 143.3(aromatic-<u>C</u>), 143.2(aromatic-<u>C</u>), 141.3(aromatic-<u>C</u>), 137.3(aromatic-<u>C</u>), 136.2 (d, *J* = 8.4 Hz) (aromatic-<u>C</u>), 134.5(aromatic-<u>C</u>), 134.2(aromatic-<u>C</u>), 131.7(aromatic-<u>C</u>), 131.1(aromatic-<u>C</u>), 128.5(aromatic-<u>C</u>), 128.0(aromatic-<u>C</u>), 128.0(aromatic-<u>C</u>), 127.8(aromatic-<u>C</u>), 127.2(aromatic-<u>C</u>), 127.2(aromatic-<u>C</u>), 125.6 (d, *J* = 3.0 Hz) (aromatic-<u>C</u>), 125.1(aromatic-<u>C</u>), 125.1(aromatic-<u>C</u>), 123.7(aromatic-<u>C</u>), 123.6(aromatic-<u>C</u>), 120.1(aromatic-<u>C</u>), 116.0 (d, *J* = 21.6 Hz) (aromatic-<u>C</u>), 82.7(-C-1), 77.0(C-4), 76.1(Fmoc; -C<u>H</u>$_2$-CH(Ar)), 74.7(-O-CH2-Ph), 74.0(C-5), 70.0(C-3), 66.3(C-6), 53.8(C-2), 46.7(Fmoc; -CH$_2$-<u>C</u>H(Ar)), 20.5(O=C-<u>C</u>H3); HRMS (ESI) m/z calcd for $C_{44}H_{36}FNO_9S$ $[M+Na]^+$, 796.1987; found, 796.1978.

Synthesis of disaccharide

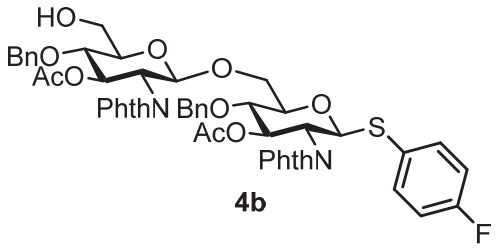


Scheme S3



4a

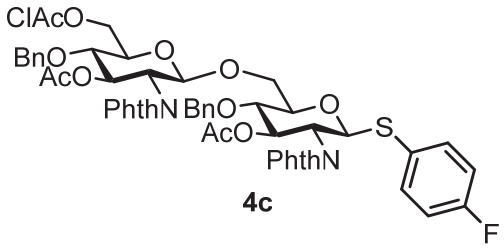
The automated synthesis of disaccharide **4a** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (20 mm×20 mm). In the anodic chamber were placed building block **1a** (0.164 g, 0.30 mmol) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (26.0 μL) and 0.1 M Bu_4NOTf in CH_2Cl_2 (15.0 mL). The constant current electrolysis (8.0 mA) was carried out at -80 ^{0}C with magnetic stirring until 1.0 F/mol of electricity was consumed. After the electrolysis, 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** (0.165 g, 0.30 mmol) dissolved in CH_2Cl_2 (1.0 mL) was subsequently added by the syringe pump (1.0 mL, 0.30 mmol) under an argon atmosphere at -80 ^{0}C, and then the temperature was raised to -50 ^{0}C and kept for 60 min. The reaction temperature was cooled down to -80 ^{0}C and Et_3N (0.3 mL) was added at -80 ^{0}C. After additional stirring at rt for 30 min the reaction mixture was filtered through a short column (4×3 cm) of silica gel to remove Bu_4NOTf. The removal of the solvent under reduced pressure and column chromatography (silica gel, hexane/EtOAc 1:1 as an eluent) afforded **4-Fluorophenyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranos-yl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4a)** in 91% isolated yield (0.265 mg, 0.273 mmol).[S1]



4b

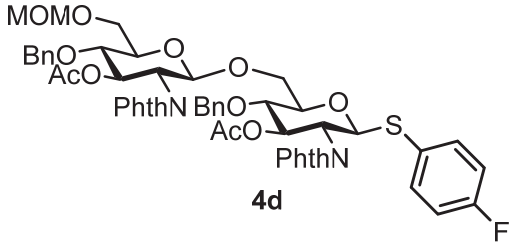
Preparation of glycosyl triflate **2b** from thioglycoside **1b** (0.232 g, 0.40 mmol) and its reaction with 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** (0.231 g, 0.42 mmol) afforded disaccharide **4b** as white foam in 57% isolated yield after silica gel chromatography (0.229 g, 0.228 mmol). **4-Fluorophenyl 6-*O*-chloroacetyl-3,4-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4b).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.41. $[\alpha]_D$ =20.79 (c = 1.02 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.65 (s, 3H, O=C-C<u>H</u>$_3$), 1.89 (s, 3H, O=C-C<u>H</u>$_3$), 2.06 (s, 3H, O=C-C<u>H</u>$_3$), 3.48 (t, *J* = 9.6 Hz, 1H, H-4), 3.70 (dd, *J* = 9.0, 5.6 Hz, 1H, H-5), 3.80 (dd, *J* = 10.8, 4.8 Hz, 2H, H-5 & H-6), 4.05 (t, *J* = 10.2 Hz, 1H, H-2), 4.08 (d, *J* = 1H, H-6), 4.13 (s, 2H, O=C-C<u>H</u>$_2$Cl), 4.33 (dd, *J* = 7.8, 7.2 Hz, 2H, H-6 & Ph-C<u>H</u>$_2$-O), 4.39 (m, 3H, H-2, H-6 & Ph-C<u>H</u>$_2$-O), 5.18 (t, *J* = 9.6 Hz, 1H, H-4), 5.55 (t, *J* = 10.2 Hz, 2H, H-1 & H-1), 5.67 (t, *J* = 9.6 Hz, 1H, H-3), 5.78 (t, *J* = 9.6 Hz, 1H, H-3), 7.03 (m, 4H, aromatic C<u>H</u>), 7.23 (s, 3H, aromatic C<u>H</u>), 7.36 (t, *J* = 7.2 Hz, 2H, aromatic C<u>H</u>), 7.65 (bs, 2H, aromatic C<u>H</u>), 7.78 (bs, 2H, aromatic C<u>H</u>), 7.78 (bs, 2H, aromatic C<u>H</u>), 7.83 (bs, 2H, aromatic C<u>H</u>); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.1(O=<u>C</u>-CH$_3$), 169.9(O=<u>C</u>-CH$_3$), 169.5(O=<u>C</u>-CH$_3$), 167.7(O=<u>C</u>-; phthalimido), 167.2(O=<u>C</u>-CH$_2$Cl), 162.9 (d, *J* = 247.2 Hz) (aromatic-C), 137.4(aromatic-C), 135.9 (d, *J* = 8.55 Hz) (aromatic-C), 134.4(aromatic-C), 134.3(aromatic-C), 134.1(aromatic-C), 131.6(aromatic-C), 131.2(aromatic-C), 131.1(aromatic-C), 128.4(aromatic-C), 127.8(aromatic-C), 127.4(aromatic-C), 125.7 (d, *J* = 3.00 Hz) (aromatic-C), 123.7(aromatic-C), 123.5(aromatic-C), 116.0 (d, *J* = 21.6 Hz) (aromatic-C), 98.1(C-1), 82.1(C-1), 78.4(C-5), 76.5(C-4), 74.5(Ph-<u>C</u>H$_2$-O), 73.8(C-3), 71.8(C-5), 70.6(C-3), 68.8(C-

4), 68.4(C-6), 63.5(C-6), 54.4(C-2), 53.8(C-2), 40.7(O=C-$\underline{C}H_2Cl$), 20.6(O=C-CH_3), 20.4(-tO=C-CH_3), 20.4(O=C-CH_3); HRMS (ESI) m/z calcd for $C_{44}H_{36}FNO_9S$ $[M+K]^+$, 1041.1716; found, 1041.1688.



4c

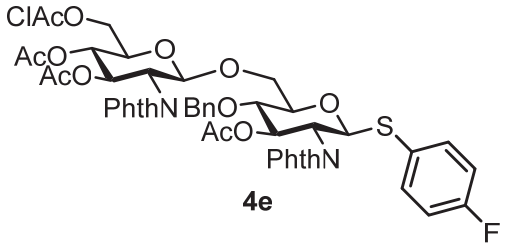
Preparation of glycosyl triflate **2c** from thioglycoside **1c** (0.251 g, 0.40 mmol) and its reaction with 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** (0.231 g, 0.42 mmol) afforded disaccharide **4b** as white foam in 45% isolated yield after silica gel chromatography (0.190 g, 0.180 mmol). **4-Fluorophenyl-6-*O*-chloroacetyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4c).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.42. $[\alpha]_D$ = 20.99 (c = 1.03 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.65 (s, 3H, O=C-C$\underline{H}_3$), 1.85 (s, 3H, O=C-C$\underline{H}_3$), 3.45 (t, *J* = 9.6 Hz, 1H, H-4), 3.68 (dd, *J* = 8.4, 3.6 Hz, 1H, H-5), 3.74 – 3.78 (m, 3H, H-4, H-6 & H-6), 3.98 (d, *J* = 15.0 Hz, 1H, , O=C-C$\underline{H}_2$Cl), 4.04 (d, *J* = 15.6 Hz, 1H, O=C-C$\underline{H}_2$Cl), 4.05 (d, *J* = 9.6 Hz, 1H, H-2), 4.09 (d, *J* = 10.2 Hz, 1H, H-5), 4.29 - 4.35 (m, 4H, H-2, H-6, 2 X Ph-C$\underline{H}_2$-O), 4.55 (d, *J* = 11.4 Hz, 1H, H-6), 4.62 (d, *J* = 11.4 Hz, 1H, Ph-C$\underline{H}_2$-O), 4.69 (d, *J* = 11.4 Hz, 1H, Ph-C$\underline{H}_2$-O), 5.52 (d, *J* = 10.8 Hz, 1H, H-1), 5.55 (d, *J* = 8.4 Hz, 1H, H-1), 5.65 (t, *J* = 9.6 Hz, 1H, H-3), 5.80 (td, *J* = 9.0, 4.2 Hz, 1H, H-3), 7.01 (*pseudo*-t, *J* = 9.0 Hz, 4H, aromatic C$\underline{H}$), 7.21-7.36 (m, 11H, aromatic C$\underline{H}$), 7.62 (dd, *J* = 5.4, 3.0 Hz, 2H, aromatic C$\underline{H}$), 7.72 (bs, 2H, aromatic C$\underline{H}$), 7.76 (pseudo-t, *J* = 4.2 Hz, 2H, aromatic C$\underline{H}$), 7.81 (*pseudo*-t, *J* = 5.4 Hz, 2H, aromatic C$\underline{H}$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.0(O=$\underline{C}$-CH_3), 169.9(O=$\underline{C}$-CH_3), 167.7(O=$\underline{C}$-; phthalimido), 167.2(O=$\underline{C}$-; phthalimido), 167.0(O=$\underline{C}$-CH_2Cl), 163.1 (d, *J* = 247.2Hz) (aromatic-C), 137.4(aromatic-C), 137.2(aromatic-C), 135.9 (d, *J* = 8.4 Hz) (aromatic-C), 134.4(aromatic-C), 134.1(aromatic-C), 131.6(aromatic-C), 131.1(aromatic-C), 128.4(aromatic-C), 128.1(aromatic-C), 128.0(aromatic-C), 128.0(aromatic-C), 127.8(aromatic-C), 127.4(aromatic-C), 125.8 (d, *J* = 2.85 Hz) (aromatic-C), 123.6(aromatic-C), 123.6(aromatic-C), 116.0 (d, *J* = 21.6 Hz) (aromatic-C), 98.1(C-1), 82.3(C-1), 78.2(C-5), 76.6(C-5), 76.0(C-4), 74.6(Ph-C$\underline{H}_2$-O), 74.5(Ph-C$\underline{H}_2$-O), 73.8(C-4), 73.4(C-3), 72.7(C-3), 68.3(C-6), 64.1(C-6), 54.9(C-2), 53.7(C-2), 40.7(O=C-$\underline{C}H_2Cl$), 20.6(O=C-$\underline{C}H_3$), 20.4(O=C-$\underline{C}H_3$); HRMS (ESI) m/z calcd for $C_{44}H_{36}FNO_9S$ $[M+K]^+$, 1089.2080; found, 1089.2042.



4d

To a stirred solution of 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acety-l-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **4e** (1.0 g, 1.03 mmol) in dimethoxyethane (5.7 mL) was added NaI (0.61 g, 4.12 mmol), chloromethyl methyl ether (0.4 mL, 5.15 mmol), *N*,*N*-Diisopropylethylamine (1.00 mL, 5.67 mmol) and allowed the reaction to reflux at 90 ^{0}C for 4h. after which TLC analysis shows completion of reaction. The reaction is then diluted with CH_2Cl_2 (25 mL) and washed successively with 10% $NaHCO_3$ (3 X 25 mL) and brine. The product is then dried over Na_2SO_4 and filtered. After evaporation of filtrate under reduced pressure the product was

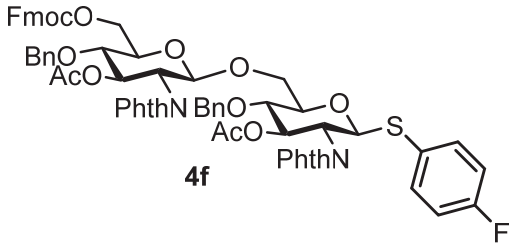
purified using silica gel chromatography to furnished desired product 1d (0.61 g, 0.62 mmol) in 61 % yield. **4-Fluorophenyl-6-*O*-methoxymethyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4d).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.42, $[\alpha]_D$ = 6.19 (c = 1.0 %, $CHCl_3$). 1H NMR ($CDCl_3$, 600 MHz) δ 1.64 (s, 3H, O=C-C<u>H</u>$_3$), 1.80 (s, 3H, O=C-C<u>H</u>$_3$), 3.51 (s, 3H, O-C<u>H</u>$_3$), 3.52 (*pseudo*-t, *J* = 9.0 Hz, 1H, H-4), 3.67 (m, 1H, H-5), 3.73 (m, 1H, H-5), 3.78 (dd, *J* = 11.4, 4.8 Hz, 1H, H-6), 3.85 (dd, *J* = 6.6, 2.4 Hz, 1H, H-6), 3.87 (d, *J* = 4.2 Hz, 1H, H-4), 3.93 (dd, *J* = 10.8, 9.0 Hz, 1H, H-6), 4.05 (t, *J* = 10.2 Hz, 1H, H-2), 4.14 (dd, *J* = 10.8, 1.2 Hz, 1H, H-6), 4.31 (d, *J* = 8.4 Hz, 1H, Ph-C<u>H</u>$_2$-O), 4.33 (dd, *J* = 9.0, 5.4 Hz, 1H, H-2), 4.37 (d, *J* = 11.4 Hz, 1H, Ph-C<u>H</u>$_2$-O), 4.70 (m, 4H, 2 X Ph-C<u>H</u>$_2$-O & 2 X O-C<u>H</u>$_2$-O-CH$_3$), 5.52 (d, *J* = 10.2 Hz, 1H, H-1), 5.55 (d, *J* = 8.4 Hz, 1H, H-1), 5.65 (dd, *J* = 10.2, 9.6 Hz, 1H, H-3), 5.80 (dd, *J* = 10.8, 9.0 Hz, 1H, H-3), 7.02 (m, 4H, aromatic C<u>H</u>), 7.22 (m, 3H, aromatic C<u>H</u>), 7.28 (m, 3H, aromatic C<u>H</u>), 7.35 (m, 4H, aromatic C<u>H</u>), 7.60 (dd, *J* = 5.4, 2.4 Hz, 2H, aromatic C<u>H</u>), 7.72 (m, 4H, aromatic C<u>H</u>), 7.82 (bs, 2H, aromatic C<u>H</u>); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.2(O=<u>C</u>-CH$_3$), 169.9(O=<u>C</u>-CH$_3$), 167.7(O=<u>C</u>-; phthalimido), 167.2(O=<u>C</u>-; phthalimido), 163.1 (d, *J* = 246.0 Hz) (aromatic-C), 137.8(aromatic-C), 137.5(aromatic-C), 136.0 (d, *J* = 7.5 Hz) (aromatic-C), 134.4(aromatic-C), 134.1(aromatic-C), 131.7(aromatic-C), 131.5(aromatic-C), 131.1(aromatic-C), 128.5(aromatic-C), 128.5(aromatic-C), 128.3(aromati-c-C), 128.3(aromatic-C), 128.0(aromatic-C), 127.9(aromatic-C), 127.8(aromatic-C), 127.7(aromatic-C), 127.6(aromatic-C), 127.4(aromatic-C), 125.8 (d, *J* = 3.0 Hz) (aromatic-C), 123.6(aromatic-C), 123.4(aromatic-C), 116.0 (d, *J* = 21.0 Hz)(aromatic-C), 98.1(C-1), 96.9(-O-<u>C</u>H$_2$-O-CH$_3$), 82.2(C-1), 78.3(C-5), 76.7(C-4), 76.5(C-4), 74.7(Ph-<u>C</u>H$_2$-O), 74.7(C-5), 74.5(Ph-<u>C</u>H$_2$-O), 73.8(C-3), 73.4(C-3), 68.2(C-6), 66.0(C-6), 55.4(-O-<u>C</u>H$_3$), 55.1(C-2), 53.8(C-2), 20.6, 20.4; HRMS (ESI) m/z calcd for $C_{54}H_{51}FN_2O_{15}S$ $[M+K]^+$, 1057.2626; found, 1057.2600.



4e

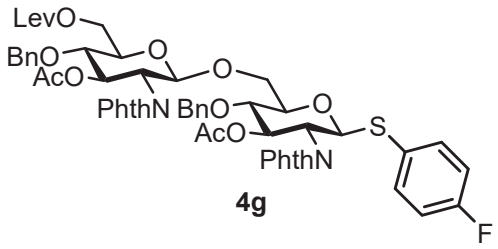
Preparation of glycosyl triflate **2e** from thioglycoside **1e** (0.310 g, 0.40 mmol) and its reaction with 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** (0.232 g, 0.42 mmol) afforded disaccharide **4e** as white foam in 59% isolated yield after silica gel chromatography (0.230 g, 0.235 mmol). **4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-p-hthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acety-l-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4e).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.41. $[\alpha]_D$ = 20.79 (c = 1.02 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.65 (s, 3H, -O=C-C<u>H</u>$_3$), 1.89 (s, 3H, -O=C-C<u>H</u>$_3$), 2.06 (s, 3H, -O=C-C<u>H</u>$_3$), 3.48 (t, *J* = 9.6 Hz, 1H, H-4), 3.70 (dd, *J* = 9.0, 5.6 Hz, 1H, H-5), 3.80 (dd, *J* = 10.8, 4.8 Hz, 1H, H-5 & H-6), 4.05 (t, *J* = 10.2 Hz, 1H, H-2), 4.08 (d, *J* = 10.8 Hz, 1H, H-6), 4.13 (s, 2H, -O=C-C<u>H</u>$_2$Cl), 4.33 (dd, *J* = 7.8, 7.2 Hz, 2H, H-6, Ph-C<u>H</u>$_2$-O-), 4.39 (m, 3H, H-2, H-6 & Ph-C<u>H</u>$_2$-O-), 5.18 (t, *J* = 9.6 Hz, 1H, H-4), 5.55 (t, *J* = 10.2, 2H, H-1 & H-1), 5.67 (t, *J* = 9.6 Hz, 1H), H-3, 5.78 (t, *J* = 9.6 Hz, 1H, H-3), 7.03 (m, 4H, aromatic C<u>H</u>), 7.23 (m, 3H, aromatic C<u>H</u>), 7.36 (t, *J* = 7.2 Hz, 2H, aromatic C<u>H</u>), 7.65 (bs, 2H, aromatic C<u>H</u>), 7.78 (bs, 2H, aromatic C<u>H</u>), 7.78 (bs ,2H, aromatic C<u>H</u>), 7.83 (bs, 2H, aromatic C<u>H</u>); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.1(O=C-CH3), 169.9(O=C-CH3), 169.5(O=C-CH3), 167.7(O=C-; phthalimido), 167.2; H(-O=<u>C</u>-CH$_2$Cl), 163.1(aromatic-C), 137.4(aromatic-C), 135.9(aromatic-C), 135.8(aromatic-C), 134.4(aromatic-

C), 134.3(aromatic-C), 134.1(aromatic-C), 131.6(aromatic-C), 131.2(aromatic-C), 131.1(aromatic-C), 128.4(aromatic-C), 127.8(aromatic-C), 127.4(aromatic-C), 125.7(aromatic-C), 125.6(aromatic-C), 123.7(aromatic-C), 123.5(aromatic-C), 116.1(aromatic-C), 116.0(aromatic-C), 98.1(C-1), 82.1(C-1), 78.4(C-5), 76.5(C-4), 74.5(Ph-$\underline{C}H_2$-O), 73.8(C-3), 71.8(C-5), 70.6(C-3), 68.8(C-4), 68.4(C-6), 63.5(C-5), 54.5(C-2), 53.8(C-2), 40.7(-O=C-$\underline{C}H_2$Cl), 20.6(-O=C-$\underline{C}H_3$), 20.4(-O=C-$\underline{C}H_3$), 20.4(-O=C-$\underline{C}H_3$); HRMS (ESI) m/z calcd for $C_{44}H_{36}FNO_9S$ $[M+Na]^+$, 1041.1716; found, 1041.1688.



4f

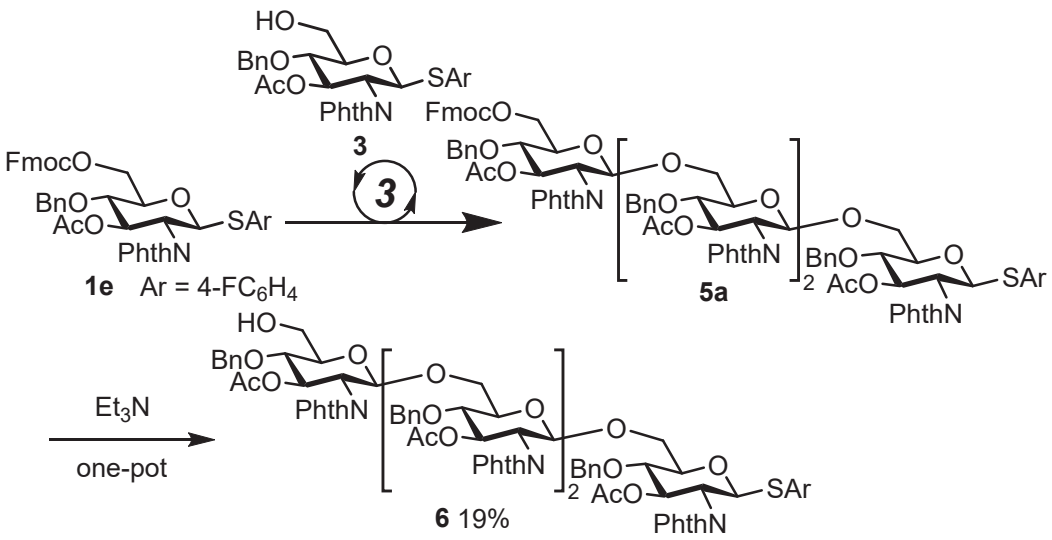
The compound **4b** (1.58 g, 1.62 mmol) is dissolved in the mixture of pyridine (2.0 mL) and CH_2Cl_2 (10.0 mL) and allowed the reaction to stir at 0 ^{0}C for 30 min, after which Fluorenylmethyloxycarbonyl chloride (0.83 g, 3.24 mmol) was added portion wise to the reaction mixture. After stirring the reaction at room temperature for next 24h, TLC analysis shows completion of reaction. Reaction is then diluted with CH_2Cl_2 (25 mL) and washed successively with 1N HCL for three times (3 X 20 mL) and then with brine. The crude product is then dried over Na_2SO_4 and filtered. Filtrate was evaporated under reduced pressure to furnished desired product. Finally, the crude product is purified using silica gel chromatography to get desired product **4f**. **4-Fluorophenyl-6-*O*-(9-fluorenylmethoxycarbonyl)-3-acetyl-4-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4f).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.81. $[\alpha]_D$ = 4.39 (c = 1.0 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.60 (s, 3H, -O=C-C$\underline{H}_3$), 1.83 (s, 3H, -O=C-C$\underline{H}_3$), 3.41 (t, *J* = 9.0 Hz, 1H, H-4), 3.61 (dd, *J* = 9.6, 3.0 Hz, 1H, H-5), 3.74 (dd, *J* = 10.8, 4.8 Hz, 1H, H-6), 3.83 (m, 1H, H-4), 3.86 (dd, *J* = 18.0, 9.6 Hz, 1H, H-5), 4.01 (t, *J* = 10.2 Hz, 1H, H-2), 4.11 (d, *J* = 10.2 Hz, 1H, H-6), 4.21 (d, *J* = 11.4 Hz, 1H, Ph-C$\underline{H}_2$-O) 4.26 (t, *J* = 7.2 Hz, 1H, Fmoc; -O-CH$_2$-C$\underline{H}$(Ar)), 4.30 (d, *J* = 12.6 Hz, 1H, Ph-C$\underline{H}_2$-O), 4.36 (m, 2H, H-2 & Ph-C$\underline{H}_2$-O), 4.42 (m, 2H, H-6 & Ph-C$\underline{H}_2$-O), 4.61 (d, *J* = 10.8 Hz, 1H, H-6), 4.68 (s, 2H, Fmoc; -O-C$\underline{H}_2$-CH(Ar)), 5.49 (d, *J* = 10.2 Hz, 1H, H-1), 5.57 (d, *J* = 8.4 Hz, 1H, H-1), 5.63 (t, *J* = 9.6 Hz, 1H, H-3), 5.82 (dd, *J* = 10.2, 8.4 Hz, 1H, H-3), 6.96 (m, 2H, aromatic C$\underline{H}$), 7.01 (t, *J* = 8.4 Hz, 2H, aromatic C$\underline{H}$), 7.18 (m, 3H, aromatic C$\underline{H}$), 7.33 (m, 10H, aromatic C$\underline{H}$), 7.38 (m, 2H, aromatic C$\underline{H}$), 7.59 (m, 3H, aromatic C$\underline{H}$), 7.65 (d, *J* = 7.2 Hz, 1H, aromatic C$\underline{H}$), 7.74 (m, 6H, aromatic C$\underline{H}$), 7.80 (t, *J* = 4.8 Hz, 2H, aromatic C$\underline{H}$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.1(O=$\underline{C}$-CH$_3$), 169.9(O=$\underline{C}$-CH$_3$), 167.7(O=C-; phthalimido), 167.2(O=C-; phthalimido), 163.1 (d, *J* = 247.05 Hz), 155.0(O=C-; Fmoc), 143.5(aromatic-C), 143.2(aromatic-C), 141.2(aromatic-C), 137.4(aromatic-C), 137.4(aromatic-C), 136.2 (d, *J* = 8.1 Hz) (aromatic-C), 134.4(-aromatic-C), 134.1(aromatic-C), 131.7(aromatic-C), 131.1(aromatic-C), 128.6(aromatic-C), 128.3(aromatic-C), 128.1(aromatic-C), 127.9(aromatic-C), 127.7(aromatic-C), 127.4(aromatic-C), 127.2(aromatic-C), 127.2(aromatic-C), 125.5(aromatic-C), 125.5(aromatic-C), 125.2 (d, *J* = 27.0 Hz) (aromatic-C), 123.6(aromatic-C), 123.4(aromatic-C), 120.0(aromatic-C), 116.0 (d, *J* = 21.45 Hz) (aromatic-C), 97.9(C-1), 81.9(C-1), 78.1(C-), 76.5(C-5), 76.5(C-4), 74.8(Fmoc; -O-$\underline{C}$H$_2$-CH(Ar)), 74.5(Ph-$\underline{C}$H$_2$-O), 73.8(C-3), 73.3(C-4), 73.1(C-3), 70.1(Ph-$\underline{C}$H$_2$-O), 68.0(C-6), 66.1(C-6), 54.9(C-2), 53.7(C-2), 46.6(Fmoc; -O-CH$_2$-$\underline{C}$H(Ar)), 20.6(O=C-$\underline{C}$H$_3$), 20.3; (O=C-$\underline{C}$H$_3$) HRMS (ESI) m/z calcd for $C_{44}H_{36}FNO_9S$ $[M+Na]^+$, 1219.3305; found, 1219.3307.



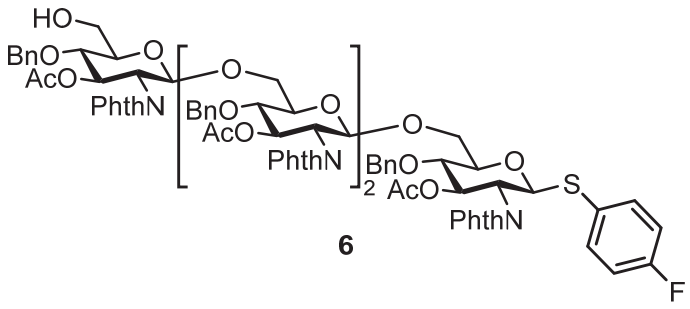
4g

The compound **4b** (1.00 g, 1.03 mmol), LevOH (0.17 mL, 1.65 mmol) and N,N′-Diisopropyl carbodiimide (0.24 mL, 1.55 mmol) was dissolved in the CH_2Cl_2 (10.0 mL) and allowed the reaction to stir at 0 ^{0}C for 30 min, after which DMAP (0.18 g, 1.55 mmol) was added to the reaction mixture. After stirring the reaction at room temperature for next 4h, TLC analysis shows completion of reaction. Reaction is then diluted with CH_2Cl_2 (25 mL) and washed successively with 1N HCL for three times (3 X 20 mL) and then with brine. The crude product is then dried over Na_2SO_4 and filtered. Filtrate was evaporated under reduced pressure to furnished desired product. Finally, the crude product is purified using silica gel chromatography to get desired product **4g** in 62% yield (0.684 g, 0.638 mmol). **4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-6-*O*-levulinoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-g-lucopyranoside (4g).** T-LC (hexane/ethyl acetate = 1:1) R_f = 0.74. $[\alpha]_D$ = 12.99 (c = 0.96 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.64 (s, 3H, -O=C-C<u>H</u>$_3$), 1.82 (s, 3H, -O=C-C<u>H</u>$_3$), 2.18 (s, 3H, -O=C-C<u>H</u>$_3$), 2.60 (m, 2H, Lev; -O-CO-C<u>H</u>$_2$-CH$_2$-CO-CH$_3$), 2.75 (m, 2H, Lev; -O-CO-C<u>H</u>$_2$-CH$_2$-CO-CH$_3$), 3.44 (t, *J* = 9.0 Hz, 1H, H-4), 3.69 (dd, *J* = 9.0, 4.2 Hz, 1H, H-5), 3.77 (m, 3H, H-4, H-5, H-6), 4.02 (t, *J* = 10.8 Hz, 1H, H-2), 4.13 (d, *J* = 10.8 Hz, 1H, H-6), 4.27 (d, *J* = 10.8 Hz, 1H, Ph-C<u>H</u>$_2$-O), 4.30 (d, *J* = 10.2 Hz, 1H, H-2), 4.33 (d, *J* = 10.8 Hz, 1H, H-6), 4.37 (d, *J* = 10.2 Hz, 1H, Ph-C<u>H</u>$_2$-O), 4.45 (d, *J* = 11.4 Hz, 1H, H-6), 4.66 (s, 2H, Ph-C<u>H</u>$_2$-O), 5.53 (*pseudo*-t, *J* = 10.2 Hz, 2H, H-1 & H-1), 5.65 (t, *J* = 9.6 Hz, 1H, H-3), 5.80 (t, *J* = 9,6 Hz, 1H, H-3), 7.01 (*pseudo*-t, *J* = 7.8 Hz, 4H, aromatic C<u>H</u>), 7.21-7.33 (m, 10H, aromatic C<u>H</u>), 7.60 (bs, 2H, aromatic C<u>H</u>), 7.72 (bs, 2H, aromatic C<u>H</u>), 7.74 (bs, 2H, aromatic C<u>H</u>), 7.82 (bs, 2H, aromatic C<u>H</u>); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 206.4(Lev; O=<u>C</u>-CH$_3$), 172.4(O=<u>C</u>-CH$_3$), 170.1(O=C-CH3), 169.9(O=C-CH3), 167.7(O=C-; phthalimido), 167.2(O=C-; phthalimido), 163.1 (d, *J* = 247.05 Hz) (aromatic-C), 137.5 (d, *J* = 10.8 Hz) (aromatic-C), 136.0 (d, *J* = 8.25 Hz) (aromatic-C), 134.4(aromatic-C), 134.1(aromatic-C), 131.7(aromatic-C), 131.1(aromatic-C), 128.5(aromatic-C), 128.3(aromatic-C), 128.0(aromatic-C), 127.8(aromatic-C), 127.8(aromatic-C), 127.4(aromatic-C), 125.7 (d, *J* = 3.0 Hz) (aromatic-C), 123.6(aromatic-C), 123.5(aromatic-C), 123.4(aromatic-C), 116.0 (d, *J* = 21.7 Hz) (aromatic-C), 97.9(C-1), 82.1(C-1), 78.2(C-5), 76.6(C-5), 76.5(C-4), 74.8(Ph-<u>C</u>H$_2$-O), 74.5(Ph-CH2-O), 73.8(C-3), 73.3(C-3), 73.1(C-4), 68.1(C-6), 62.7(C-6), 55.0(C-2), 53.7(C-2), 37.9(Lev; O-CO-<u>C</u>H$_2$-CH$_2$-CO-CH$_3$), 29.8(Lev; O-CO-CH$_2$-CH$_2$-CO-<u>C</u>H$_3$), 27.8(Lev; O-CO-<u>C</u>H$_2$-CH$_2$-CO-CH$_3$), 20.6(-O=C-<u>C</u>H$_3$), 20.4(-O=C-<u>C</u>H$_3$); HRMS (ESI) m/z calcd for $C_{57}H_{53}FN_2O_{16}S$ $[M+Na]^+$, 1095.2992; found, 1095.3453.

Synthesis of oligosaccharides

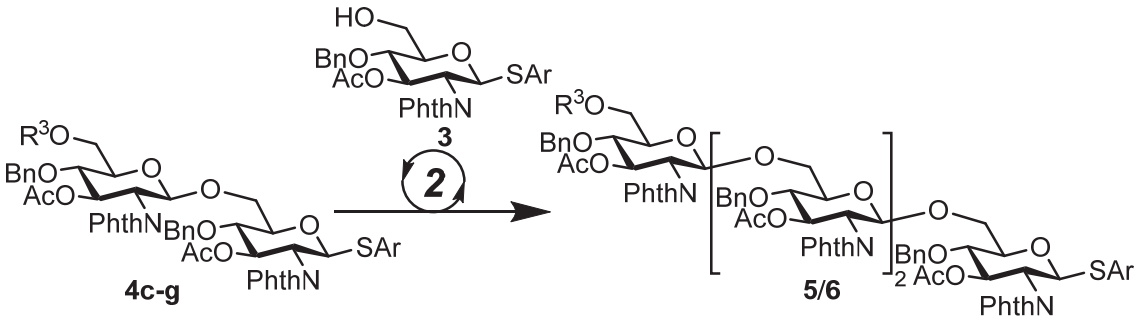


Scheme S4

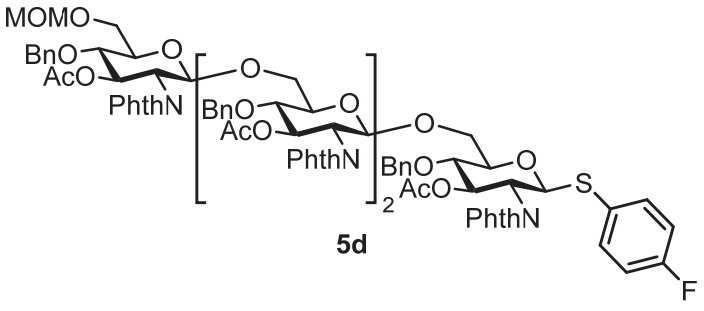


The automated synthesis of tetrasaccharide **6** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm×20 mm). In the anodic chamber were placed 4-Fluorophenyl-6-*O*-(9-fluorenylmethoxycarbonyl)-3-acetyl-4-benzyl-2-deoxy-2-phthalimi-do-1-thio-β-D-glucopyranoside **1e** (0.308 g, 0.400 mmol), Bu4NOTf (0.587 g, 1.50 mmol) and CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (133 μL, 1.5 mmol), Bu4NOTf (0.587 g, 1.50 mmol) and CH2Cl2 (15.0 mL). The constant current electrolysis (8.0 mA) was carried out at -80 ^{0}C with magnetic stirring until 1.05 F/mol of electricity was consumed. After the electrolysis, 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** (0.7943 g, 1.28 mmol) dissolved in CH_2Cl_2 (3.0 mL) was subsequently added by the syringe pump (1.0 mL (0.400 mmol) for one cycle) under an argon atmosphere at -80 ^{0}C, and then the temperature was raised to -50 ^{0}C and kept for 60 min. The reaction temperature was cooled down to -80 ^{0}C and the second and third cycle performed sequentially one after another automatically with preprogramed software. After the third cycle, Et_3N (3.3 mL) was added and the mixture was stirred at room temperature for 6h and then filtered through a short column (4×3 cm) of silica gel to remove Bu_4NOTf. Removal of the solvent under reduced pressure and short column (silica gel, hexane/EtOAc 1:1 as an eluent) afforded a mixture of oligosaccharides. The crude product was purified by PR-GPC with $CHCl_3$ as an eluent and tetrasaccharide **6** was obtained in 19% isolated yield (0.057 g, 0.077 mmol). **4-Fluorophenyl 3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyrano-syl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phtha-**

limido-1-thio-β-D-glucopyranoside (6). TLC (hexane/ethyl acetate = 2:5) R_f = 0.57 $[\alpha]_D$ = -4.21 ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.57 (s, 3H), 1.66 (s, 3H), 1.71 (s, 3H), 1.76 (s, 3H), 1.96 (s, 1H), 3.37 (t, *J* = 9.0 Hz, 1H), 3.54-3.58 (m, 4H), 3.64 (bs, 2H), 3.71 (bd, *J* = 7.8 Hz, 1H), 3.79-3.87 (m, 4H), 3.97 (dd, *J* = 19.8, 10.2 Hz, 2H), 4.04 (d, *J* = 10.8 Hz, 1H), 4.10 (t, *J* = 6.0 Hz, 2H), 4.16-4.25 (m, 4H), 4.30 (s, 1H), 4.36 (s, 1H), 4.43 (d, *J* = 11.4 Hz, 1H), 4.64 (d, *J* = 11.4 Hz, 1H), 4.70 (d, *J* = 11.4 Hz, 1H), 5.46 (d, *J* = 8.4 Hz, 1H), 5.49 (d, *J* = 10.2 Hz, 1H), 5.50 (d, *J* = 11.4 Hz, 1H), 5.54 (d, *J* = 7.8 Hz, 1H), 5.59 (t, *J* = 9.0 Hz, 1H), 5.64 (dd, *J* = 18.6, 10.2 Hz, 2H), 5.82 (t, *J* = 9.0 Hz, 1H), 6.96-7.03 (m, 6H), 7.08 (d, *J* = 6.6 Hz, 2H), 7.17 (bs, 6H), 7.24-7.34 (m, 10H), 7.59-7.62 (m, 6H), 7.72-7.81 (m, 10H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.1, 170.0, 170.0, 169.9, 168.1, 167.7, 167.1, 164.0, 163.1 (d, *J* = 246.9 Hz), 137.9, 137.7, 137.6, 136.3 (d, *J* = 8.4 Hz), 134.3, 134.0, 131.7, 131.3, 131.1, 128.4, 128.3, 127.8, 127.8, 127.7, 127.6, 127.4, 125.2 (d, *J* = 2.85 Hz), 123.6, 123.4, 116.0 (d, *J* = 21.6 Hz), 98.2, 98.0, 97.5, 81.6, 78.2, 76.7, 76.6, 76.3, 75.4, 74.7, 74.6, 74.5, 74.5, 74.5, 74.4, 73.9, 73.2, 73.1, 73.1, 68.1, 67.8, 67.4, 55.3, 55.0, 55.0, 53.7, 20.5, 20.5, 20.4, 20.3; HRMS (ESI) m/z calcd for $C_{98}H_{89}FN_4O_{28}S$ $[M+K]^+$, 1859.5000; found, 1859.5029.

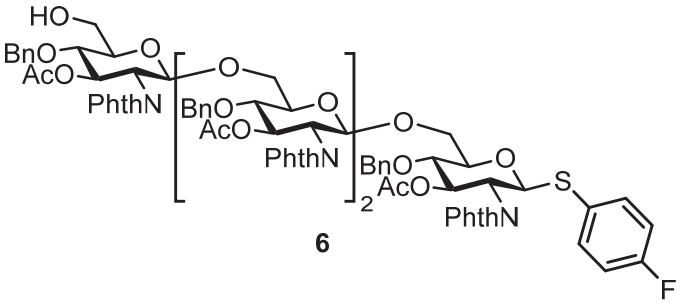


Scheme S5



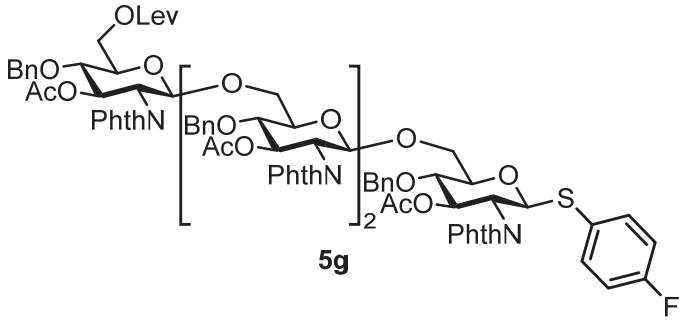
The automated synthesis of tetrasaccharide **5d** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm×20 mm). In the anodic chamber were placed 4-Fluorophenyl-6-*O*-methoxymethyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **4d** (0.407 g, 0.400 mmol), Bu_4NOTf (0.587 g, 1.50 mmol) and CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (71.0 μL), Bu_4NOTf (0.587 g, 1.50 mmol) and CH_2Cl_2 (15.0 mL). The constant current electrolysis (8.0 mA) was carried out at -80 ^{0}C with magnetic stirring until 1.05 F/mol of electricity was consumed. After the electrolysis, building block **3** (0.441 g, 0.800 mmol) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump (1.0 mL (0.400 mmol) for one cycle) under an argon atmosphere at -80 ^{0}C, and then the temperature was raised to -50 ^{0}C and kept for 60 min. The reaction temperature was cooled down to -80 ^{0}C and the second cycle starts automatically. After the 2nd cycle, Et_3N (0.5 mL) was added and

the mixture was filtered through a short column (4×3 cm) of silica gel to remove Bu_4NOTf. Removal of the solvent under reduced pressure and short column (silica gel, hexane/EtOAc 1:1 as an eluent) afforded a mixture of oligosaccharides. The crude product was purified by PR-GPC with $CHCl_3$ as an eluent and trisaccharide (**5d)** was obtained in 7% isolated yield (0.053 g, 0.028 mmol). **4-Fluorophenyl-6-*O*-methoxy methyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deo-xy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthali-mido-β-D-glucopy-ranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyrano-side (5d).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.55. $[\alpha]_D$ = -3.33 (c = 0.88 %, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) δ 1.55 (s, 3H), 1.68 (s, 3H), 1.68 (s, 3H), 1.76 (s, 3H), 3.33 (*pseudo*-t, *J* = 9.6 Hz, 1H), 3.40 (s, 3H), 3.46-3.53 (m, 4H), 3.63-3.73 (m, 4H), 3.80-3.87 (m, 3H), 3.90 (d, *J* = 10.8 Hz, 1H), 3.92 (t, *J* = 10.2 Hz, 1H), 4.04 (d, *J* = 10.8 Hz, 1H), 4.06 (td, *J* = 11.4, 1.2 Hz, 2H), 4.13 (d, *J* = 11.4 Hz, 1H), 4.18 (ddd, *J* = 16.2, 10.2, 8.4 Hz, 2H), 4.30 (d. *J* = 2.4 Hz, 1H), 4.31 (d, *J* = 3.6 Hz, 1H), 4.32 (s, 1H), 4.33 (d, *J* = 2.4 Hz, 1H), 4.40 (d, *J* = 11.4 Hz, 1H), 4.44 (d, *J* = 11.4 Hz, 1H), 4.64 (d, *J* = 11.4 Hz, 1H), 4.69 (d, *J* = 11.4 Hz, 1H), 4.69 (d. *J* = 7.2 Hz, 1H), 4.73 (d, *J* = 6.6 Hz, 1H), 5.40 (d, *J* = 7.6 Hz, 1H), 5.44 (d, *J* = 8.4 Hz, 1H), 5.46 (d, *J* = 8.4 Hz, 1H), 5.52 (d, *J* = 8.4 Hz, 1H), 5.57 (dd, *J* = 10.2, 9.6 Hz, 1H), 6.81 (dd, *J* = 7.8, 2.4 Hz, 2H), 7.01-7.09 (m, 6H), 7.15-7.38 (m, 16H), 7.53-7.88 (m, 16H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.1, 170.0, 170.0, 169.9, 167.7, 167.5, 167.1, 164.0, 163.2 (d, *J* = 246.7 Hz), 137.9, 137.7, 137.7, 137.6, 136.5 (d, *J* = 8.1 Hz), 134.3, `134.3, 134.0, 131.7, 131.5, 131.1, 128.5, 128.4, 128.3, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 127.3, 116.0 (d, *J* = 21.6 Hz), 98.1, 97.5, 97.3, 96.9, 81.4, 78.1, 77.2, 77.1, 77.0, 76.8, 76.7, 76.5, 74.6, 74.6, 74.6, 74.5, 74.5, 74.5, 74.4, 73.9, 73.3, 73.1, 73.0, 68.0, 67.2, 67.0, 66.0, 55.8, 55.4, 55.2, 55.0, 55.0, 53.6, 20.5, 20.4, 20.3; HRMS (ESI) m/z calcd for $C_{100}H_{93}FN_4O_{29}S$ $[M+K]^+$, 1903.5262; found, 1904.5372.



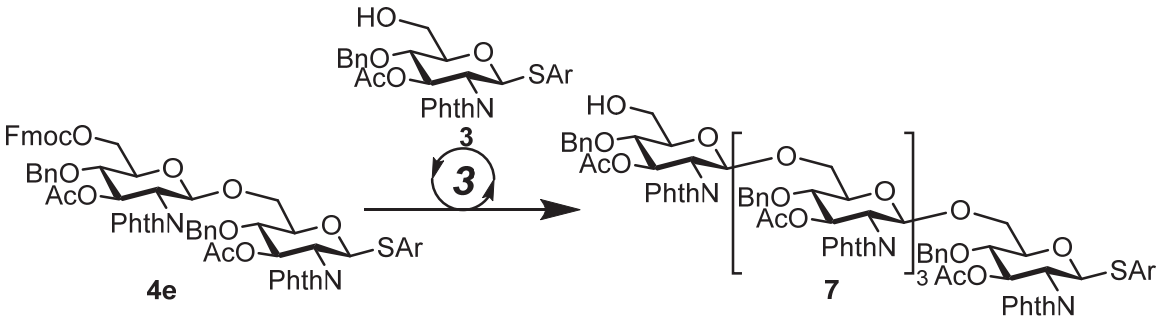
6

Automated electrochemical synthesis of **4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside 6** using terminal building blocks 4-Fluorophenyl-6-*O*-(9-fluorenylmethoxycarbonyl)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **4f** (0.299 g, 0.250 mmol) with glycosyl acceptor 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** (0.275 g, 0.500 mmol) afforded **(6)** (0.215 g, 0.118 mmol) in 47% yield, following the same procedure as that of compound **(5d).**



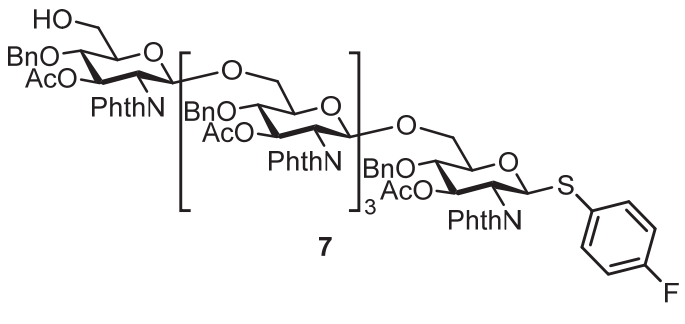
5g

Automated electrochemical synthesis of **4-Fluorophenyl-6-*O*-levulinoyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deo-xy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deox-y-2-phthali-mido-β-D-glucopyrano-syl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside 5g** using terminal building blocks 4-Fluorophenyl-6-*O*-levulinoyl-3-*O*-acetyl-4-*O*-benzyl-6-*O*-levulinoyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deo-pxy-2-phthalimido-1-thio-β-D-g-lucopyranoside **4g** (0.429 g, 0.400 mmol) with glycosyl acceptor 4-Fluoro-phenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucop-yranoside **3** (0.4413 g, 0.800 mmol) afforded **5g** (0.088 g, 0.046 mmol) in 12% yield, following the same procedure as that of compound **(5d).** TLC (hexane/ethyl acetate = 1:1) R_f = 0.45. $[\alpha]_D$ = -2.99 (c = 0.99 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ ^{13}C NMR ($CDCl_3$, 150 MHz) δ 1.55 (s, 3H), 1.67 (s, 3H), 1.68 (s, 3H), 1.78 (s, 3H), 2.18 (s, 3H), 2.56- 2.65 (m, 2H), 2.68-2.78 (m, 2H), 3.32 (*pseudo*-t, *J* = 9.6 Hz, 1H), 3.42-3.45 (m, 2H), 3.51 (m, 2H), 3.63 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.67 (ddd, *J* = 9.6, 4.8, 1.2 Hz, 1H), 3.71 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.75 (d, *J* = 5.4 Hz, 2H), 3.79 (dd, *J* = 11.4, 5.4 Hz, 1H), 3.91 (*pseudo*-t, *J* = 10.2 Hz, 1H), 4.04 (m, 2H), 4.09 (dd, *J* = 11.4, 1.8 Hz, 1H), 4.13 (d, *J* = 11.4 Hz, 1H), 4.17 (m, 2H), 4.31 (m, 4H), 4.37 (m, 1H), 4.39 (m, 1H), 4.45 (d, *J* = 11.4 Hz, 1H), 4.62 (m, 2H), 5.38 (d, *J* = 8.4 Hz, 1H), 5.44 (m, 2H), 5.51 (d, *J* = 8.4 Hz, 1H), 5.56 (dd, *J* = 9.6, 9.0 Hz, 1H), 5.66 (m, 2H), 5.81 (m, 1H), 6.98 (m, 2H), 7.02-7.08 (m, 5H), 7.16-7.27 (m, 14H), 7.30-7.34 (m, 4H), 7.57-7.84 (m, 16H); HRMS (ESI) m/z calcd for $C_{103}H_{95}FN_4O_{30}S$ $[M+Na]^+$, 1942.5662; found, 1942.5640.



4e **3** **7**

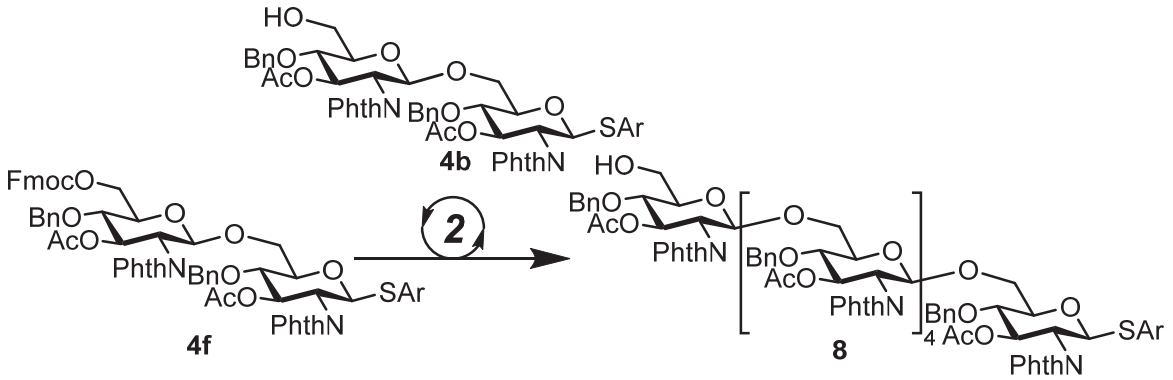
Scheme S6



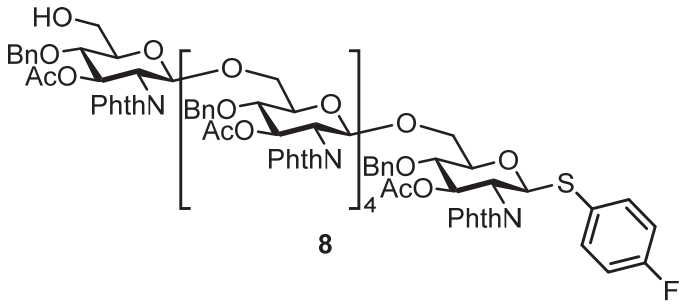
7

Automated electrochemical synthesis of **4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-b-enzyl-2-deoxy-2-phthalimido-β-D-g-lucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-**

acetyl-4-*O*-benzyl-2-deoxy-2-phthalimi-do-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside 7 using terminal building blocks 4-Fluorophenyl-6-*O*-(9-fluorenylmethoxycarbonyl)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **4f** (0.429 g, 0.400 mmol) with glycosyl acceptor 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** (0.4413 g, 0.800 mmol) afforded **7** (0.125 g, 0.055 mmol) in 14% yield, following the same procedure as that of compound **(6).** TLC (hexane/ethyl acetate = 2:3) R_f = 0.42, $[\alpha]_D$ = -11.17 (c = 1.79 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.54 (s, 3H), 1.64 (s, 3H), 1.65 (s, 3H), 1.77 (s, 3H), 2.91 (dd, *J* = 7.2, 6.6 Hz, 1H), 3.33 (t, *J* = 9.6 Hz, 1H), 3.46-3.52 (m, 2H), 3.55-3.58 (m, 3H), 3.60-3.66 (m, 3H), 3.70 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.75 (dd, *J* = 11.4, 4.8 Hz, 1H), 3.81-3.84 (m, 2H), 3.85 (d, *J* = 9.0 Hz, 1H), 3.87 (d, *J* = 9.6 Hz, 1H), 3.92 (t, *J* = 12.6 Hz, 1H), 3.96 (dd, *J* = 9.6 Hz, 1H), 4.00 (d, *J* = 12.6 Hz, 1H), 4.08-4.14 (m, 4H), 4.17-4.22 (m, 4H), 4.28 (d, *J* = 6.0 Hz, 1H), 4.31 (s, 1H), 4.31 (d, *J* = 7.8 Hz, 1H), 4.33 (s, 1H), 4.35 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.37 (d, *J* = 11.4 Hz, 1H), 4.50 (d, *J* = 11.4 Hz, 1H), 4.61 (d, *J* = 11.4 Hz, 1H), 4.68 (d, *J* = 11.4 Hz, 1H), 5.43 (d, *J* = 1.8 Hz, 1H), 5.44 (s, 1H), 5.45 (d, *J* = 13.2, 1H), 5.51 (d, *J* = 6.0 Hz, 1H), 5.53 (d, *J* = 6.0 Hz, 1H), 5.57 (dd, *J* = 10.2, 9.0 Hz, 1H), 5.63 (d, *J* = 8.4 Hz, 1H), 5.64 (d, *J* = 6.6 Hz, 1H), 5.65 (d, *J* = 8.4 Hz, 1H), 5.82 (dd, *J* = 10.2, 9.0 Hz, 1H), 6.95-6.96 (m, 3H), 7.01-7.06 (m, 6H), 7.13-7.15 (m, 3H), 7.18-7.25 (m, 12H), 7.28-7.31 (m, 2H), 7.32-7.35 (m, 2H), 7.53-7.67 (m, 9H), 7.70-7.76 (m, 10H), 7.80-7.84 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.2, 170.1, 170.1, 170.0, 170.0, 168.0, 167.8, 167.6, 167.2, 166.9, 164.0 (d, *J*= 247.0 Hz), 138.0, 137.8, 137.6, 137.6, 136.5 (d, *J* = 8.5 Hz), 134.4, 134.2, 134.1, 131.8, 131.3, 131.2, 128.4, 128.4, 128.4, 128.3, 127.8, 127.7, 127.7, 127.6, 127.6, 127.4, 127.4, 125.1, 123.5, 123.5, 123.4, 116.0 (d, *J* = 21.6 Hz), 98.3, 98.2, 97.6, 97.3, 81.4, 78.1, 77.3, 77.1, 76.9, 76.6, 76.5, 76.4, 75.6, 75.0, 74.7, 74.6, 74.5, 74.3, 74.2, 73.9, 73.2, 73.1, 68.0, 67.4, 67.2, 61.3, 55.4, 55.1, 55.1, 55.0, 53.7, 20.6, 20.4, 20.3; HRMS (ESI) m/z calcd for $C_{121}H_{110}FN_5O_{35}S$ $[M+K]^+$, 2283.6351; found, 2283.6243.



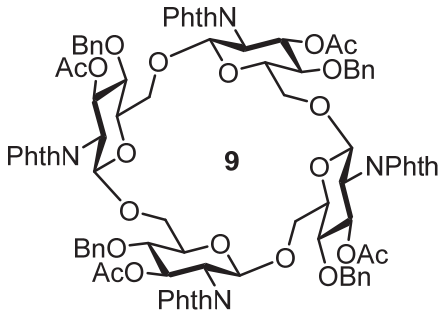
Scheme S7



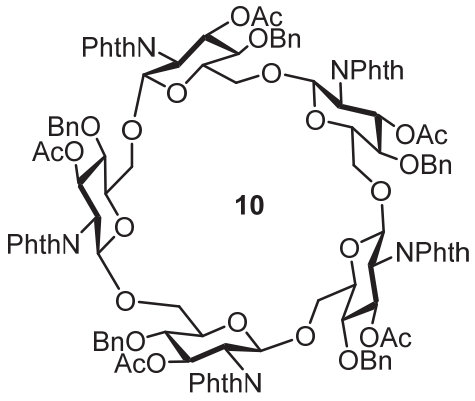
8

Automated electrochemical synthesis of **4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimi-do-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimi-do-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside 8** using terminal building blocks 4-Fluorophenyl-6-*O*-(9-fluorenylmethoxycarbonyl)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β–D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **4f** (0.478 g, 0.400 mmol) with building block 4-Fluorophenyl 6-*O*-chloroacetyl-3,4-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **4b** (0.780 g, 0.800 mmol) afforded **7** (0.150 g, 0.056 mmol) in 14% yield, following the same procedure as that of compound **(6).** TLC (hexane/ethyl acetate = 1:2) R_f = 0.42, $[\alpha]_D$ = -11.30 (c = 0.92 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.53 (s, 3H), 1.61 (s, 3H), 1.62 (s, 3H), 1.65 (s, 3H), 1.68 (s, 3H), 1.77 (s, 3H), 2.86 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.29 (*pseudo*-t, *J* = 9.6 Hz, 1H), 3.41 (m, 1H), 3.45 (*pseudo*-t, *J* = 9.0 Hz, 1H), 3.55 (m, 4H), 3.57 (m, 2H), 3.62 (t, *J* = 9.0 Hz, 1H), 3.64 (m, 1H), 3.70 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.76 - 3.85 (m, 4H), 3.87 (t, *J* = 10.2 Hz, 1H), 3.90 (d, *J* = 10.8 Hz, 1H), 3.98 (m, 2H), 4.00 (m, 2H), 4.10 (m, 3H), 4.13 (bs, 1H), 4.16 (*pseudo*-t, *J* = 2.4 Hz, 1H), 4.17 (t, *J* = 1.8 Hz, 1H), 4.19 (s, 1H), 4.22 (dd, *J* = 9.0, 1.8 Hz, 1H), 4.24 (d, *J* = 3.0 Hz, 1H), 4.27 (d, *J* = 4.8 Hz, 1H), 4.31 (*pseudo*-t, *J* = 9.6 Hz, 4H), 4.37 (dd, *J* = 10.8, 8.4 Hz, 1H), 4.39 (s, 1H), 4.45 (d, *J* = 11.4 Hz, 1H), 4.50 (d, *J* = 11.4 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.68 (d, *J* = 11.4 Hz, 1H), 5.54 (d, *J* = 8.4 Hz, 1H), 5.62 – 5.69 (m, 4H), 5.82 (dd, *J* = 10.8, 9.0 Hz, 1H), 5.37 (d, *J* = 8.4 Hz, 1H), 5.44 (d, *J* = 9.6 Hz, 1H), 5.44 (s, 1H), 5.46 (d, *J* = 9.0 Hz, 1H), 6.96 - 6.98 (m, 4H), 7.07 – 7.08 (m, 8H), 7.16 -7.23 (m, 15H), 7.27 – 7.35 (m, 4H), 7.55 (bs, 1H), 7.56 – 7.67 (m, 10 H), 7.68 – 7.73 (m, 4H), 7.73 -7.85 (m, 10H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.2, 170.1, 170.0, 170.0, 170.0, 169.9, 168.0, 167.8, 167.5, 167.1, 164.0, 163.2 (d = 246.9 Hz), 138.0, 137.9, 137.7, 137.7, 137.6, 137.6, 137.6, 136.6, 136.5, 134.4, 134.1, 131.7, 131.2, 131.1, 128.4, 128.3, 128.3, 128.3, 128.3, 127.8, 127.7, 127.6, 127.6, 127.5, 127.3, 127.3, 124.9, 123.5, 123.5, 123.4, 116.9 (d, *J* = 22.0 Hz), 98.3, 98.1, 97.6, 97.4, 97.4, 81.3, 77.9, 77.2, 72.0, 76.6, 76.4, 76.3, 75.5, 74.8, 74.7, 74.6, 74.5, 74.5, 74.5, 74.4, 74.4, 74.3, 73.8, 73.1, 73.0, 73.0, 68.2, 68.0, 67.2, 67.1, 61.3, 55.3, 55.0, 55.0, 53.5, 20.5, 20.4, 20.4, 20.4, 20. 3; HRMS (ESI) m/z calcd for $C_{144}H_{131}FN_6O_{42}S$ $[M+K]^+$, 2706.7669; found, 2706.7544.

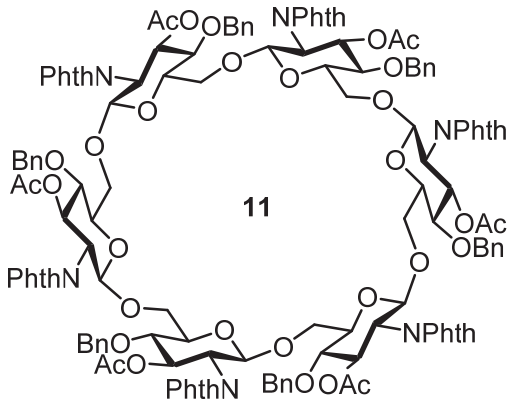
Synthesis of cyclic oligoglucosamine



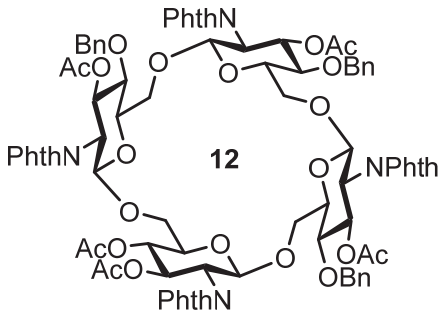
The automated synthesis of **Cyclotetrakis-(1→6)-(3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl) 9** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm×20 mm). In the anodic chamber were placed 4-Fluorophenyl-3-*O*-acetyl-4-*O*-b-enzyl-2-deoxy-2-phthalimido-β-D-g-lucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acet-yl-4-*O*-benzyl-2-deoxy-2-phthalimi-do-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **6** (0.0.072 g, 0.0.039 mmol), Bu_4NOTf (0.195 g, 0.50 mmol) and CH_2Cl_2 (5.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (3.5 µL), Bu_4NOTf (0.195 g, 0.50 mmol) and CH_2Cl_2 (5.0 mL). The constant current electrolysis (8.0 mA) was carried out at -80 ^{0}C with magnetic stirring until 1.6 F/mol of electricity was consumed. After the electrolysis, the temperature was raised to 0 ^{0}C and Et_3N (0.5 mL) was added and the mixture was evaporated under reduced pressure and extracted five times with ethyl acetate. Extract is then evaporated under reduced pressure and kept under strong vacuum for extreme dryness to furnish desired cyclic oligosaccharide **(9)** in 81% isolated yield (0.054 g, 0.031 mmol). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.61 (s, 3H), 3.66 (d, *J* = 8.4 Hz, 1H), 3.79 (pseudo-t, *J* = 9.6 Hz, 1H), 4.02-4.05 (m, 2H), 4.25 (d, *J* = 10.2 Hz, 1H), 4.38 (dd, *J* = 10.8, 8.4 Hz, 1H), 5.54-5.59 (m, 2H), 6.74 (d, *J* = 6.0 Hz, 2H), 7.09-7.12 (m, 2H), 7.43-7.67 (m, 4H);



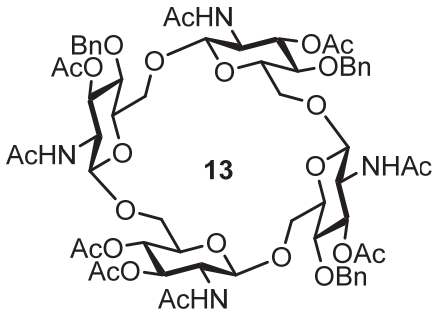
Automated electrochemical synthesis of **Cyclopentaakis-(1→6)-(3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-Dglucopyranosyl) 10** using 4-Fluorophenyl-3-*O*-acetyl-4-*O*-b-enzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-b-enzyl-2-deoxy-2-phthalimido-β-D-g-lucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimi-do-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **7** (0.089 g, 0.039 mmol) afforded **10** (0.083 g, 0.039 mmol) in 93% yield, following the same procedure as that of compound **(9).** $[\alpha]_D$ = 5.31 (c = 0.94 %, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.65 (s, 3H), 3.63 (s, 3H), 3.69 (m, 1H), 3.90 (dd, *J* = 10.8, 4.8 Hz, 1H), 4.16 (d, *J* = 9.6 Hz, 1H), 4.34 (m, 2H), 4.43 (d, *J* = 11.4 Hz, 1H), 5.50 (d, *J* = 8.4 Hz, 1H), 5.71 (dd, *J* = 10.8, 9.0 Hz, 1H), 7.03 (*pseudo*-t, *J* = 6.0 Hz, 2H), 7.23 (m, 3H), 7.61 (m, 2H), 7.71 (*pseudo*-t, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.1, 167.8, 166.7, 137.8, 134.1, 131.5, 128.3, 128.3, 128.2, 127.6, 127.6, 127.3, 123.4, 97.7, 77.4, 77.3, 77.1, 76.9, 74.3, 73.0, 67.6, 55.0, 29.7, 20.5; HRMS (ESI) m/z calcd for $C_{115}H_{105}N_2O_{35}$ $[M+K]^+$, 2155.6256; found, 2155.6106.



Automated electrochemical synthesis of **Cyclohexakis-(1→6)-(3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-Dglucopyranosyl) 11** using 4-Fluorophenyl-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-g-lucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-g-lucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-g-lucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimi-do-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **8** (0.088 g, 0.033 mmol) afforded **11** (0.067 g, 0.026 mmol) in 78% yield, following the same procedure as that of compound **(9).** $[\alpha]_D$ = 20.79. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.65 (s, 3 H), 3.56 (d, *J* = 4.2 Hz, 2 H), 3.95 (d, *J* = 10.8 Hz, 1 H), 4.20 (d, *J* = 2 H), 4.26 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.37 (d, *J* = 10.8 Hz, 1 H), 5.58 (d, *J* = 8.4 Hz, 1 H), 5.65 (m, 1H), 7.00 (d, *J* = 7.2 Hz, 2 H), 7.78 (dd, *J* = 4.8, 3.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.0, 167.8, 137.6, 134.1, 131.5, 128.5, 128.3, 127.7, 127.5, 123.5, 97.3, 77.3, 77.1, 77.0, 76.9, 74.6, 74.6, 73.2, 66.8, 55.1, 29.7, 23.9, 20.5; HRMS (ESI) *m/z* calcd for $C_{138}H_{126}N_6O_{42}$ $[M+K]^+$, 2578.7573; found, 2578.7454.



To a solution of **5a** (0.077 g, 0.042 mmol) in methanol (0.2 mL) was added 2M HCl/Et_2O (0.085 mL, 0.170 mmol) at 0 °C and allow reaction to stir at rt for 6h. Reaction is quenched with Et_3N (0.2 mL) afetr the dissapperance of statrting material on TLC analysis. The Crude product **5b** is then used for next reaction without further purification. Automated intramolecular electrochemical glycosylation of aformentioned product **5b** (0.104 g, 0.042mmol) is then carried out using same procedure as that of **9**, to get cyclic oligosaccharide. The above obtained cyclic oligosaccharide is then dissolved in the mixture of CH_2Cl_2 (0.1 mL) and pyridine (0.1 mL) and allowed to stir at 0 °C for 15 min under Ar atmosphere. Acetic anhydride (0.1 mL, 0.255 mmol) and DMAP (0.6 mg, 0.005 mmol) was then added sequencially to the reaction and allowed it to stir at rt for overnight. The crude product was then evaporated under reduced pressure. Crude product was then washed with EtOAc (3 x 20 mL) to furnish analytically pure cyclic oligoglucosamine **(12)** (42.1 mg) in 60% overall yield over three steps. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.48 (s, 3 H), 1.61 (s, 3H), 1.63 (s, 3 H), 1.64 (s, 3 H), 1.74 (s, 3 H), 3.64-3.66 (m, 3H), 3.73-3.81 (m, 5 H), 3.99-4.07 (m, 5 H), 4.12-4.26 (m, 8 H), 4.31 (t, *J* = 9.6 Hz, 1 H), 4.36 (t, *J* = 9.6 Hz, 1 H), 4.41 (t, *J* = 9.6 Hz, 1 H), 4.44 (t, *J* = 10.2 Hz, 1 H), 5.17 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 5.50-5.63 (m, 8 H), 6.77 (bs, 6 H), 7.11 (bs, 9 H), 7.50 (m, 6 H), 7.66-7.69 (m, 8 H), 7.80-7.85 (m, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.3, 170.1, 168.2, 167.4, 137.5, 137.4, 134.1, 133.8, 131.1, 128.2, 128.1, 127.6, 127.5, 127.3, 127.2, 123.4, 98.1, 97.9, 76.5, 74.8, 74.6, 74.5, 74.5, 74.4, 73.5, 73.4, 73.4, 71.2, 68.8, 68.5, 68.3, 68.1, 54.8, 54.7, 54.4, 20.4, 20.3, 19.8; HRMS (ESI) *m/z* calcd for $C_{87}H_{80}N_4O_{29}$ $[M+K]^+$, 1684.4573; found, 1684.4535.



To a solution of **12** (0.230 g, 0.136 mmol) in ethanol (6.6 mL) was added Ethylenediamine (1.35 mL, 20.2 mmol) and refluxed under Ar atmosphere at 100 ºC for overnight. Disappearance of starting material on TLC analysis suggested compleation of reactipon. Volatiles was then eveporated under reduced pressure and the crude product was used for next reaction without purification. The above obtained crude product was then dissolved in pyridine (6.4 mL) and allowed it to stir at 0 ºC for 15 min. To the reaction was then sequencially added acetic anhydride (2.21 mL, 23.4 mmol) and DMAP (0.033 g, 0.272 mmol) and allowed reaction to stir at rt for overnight. TLC analysis shows compleation of reaction. The crude product was then dissoved in CH_2Cl_2 and washed successively with 1N HCl (3 X 50 mL)and 10% NaHCO3 (2 X 50 mL) and finally with brine. The crude product was then dried over Na_2SO_4 and filter. Filtrate was then evaporated under reduced pressure to give desired product **13** (0.087 g, 0.064 mmol) in 48% overall yield over two steps. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.44 (s, 3 H), 1.44 (s, 3 H), 1.45 (s, 3 H), 1.71 (s, 3 H), 1.90 (s, 3 H), 1.93 (s, 3 H), 1.94 (s, 6 H), 1.94 (s, 3 H), 3.40-3.52 (m, 4 H), 3.60 (*pseudo*-t, *J* = 9.6 Hz, 2 H), 3.64-3.75 (m, 6 H), 3.82 (d, *J* = 3.6 Hz, 1 H), 3.84 (d, *J* = 3.6 Hz, 1 H), 3.90 (*pseudo*-t, *J* = 10.2 Hz, 2 H), 3.98 (d, *J* = 10.2 Hz, 1 H), 4.03 (s, 1 H), 4.05 (s, 1 H), 4.36 (d, J = 2.4 Hz, 1 H), 4.37 (d, J = 1.8 Hz, 1 H), 4.39 (d, *J* = 10.8 Hz, 1 H), 4.55-4.59 (m, 4 H), 4.63 (d, *J* = 9.0 Hz, 1 H), 4.67 (d, *J* = 9.0 Hz, 1 H), 4.73 (d, *J* = 8.4 Hz, 1 H), 4.92 (t, *J* = 9.6 Hz, 1 H), 4.95 (t, *J* = 10.2 Hz, 1 H), 5.01 (t, *J* = 10.2 Hz, 1 H), 5.03 (t, *J* = 9.6 Hz, 1 H), 5.09 (t, *J* = 10.2 Hz, 1 H), 7.26-7.30 (m, 9 H), 7.32-7.34 (m, 6 H); ^{13}C NMR (CDCl3, 150 MHz) δ 169.8, 169.7, 169.6, 168.9, 168.8, 168.2, 138.2, 128.1, 128.1, 128.1, 128.0, 127.6, 127.5, 99.9, 99.8, 99.7, 99.5, 75.2, 75.1, 75.0, 73.8, 73.3, 73.1, 73.1, 71.3, 67.9, 67.8, 67.1, 53.4, 53.3, 22.6, 22.6, 22.6, 22.5, 21.0, 20.5, 20.3, 20.3; HRMS (ESI) *m/z* calcd for $C_{63}H_{80}N_4O_{25}$ $[M+K]^+$, 1331.4743; found, 1331.4697.

References for experimental section

S1 T. Nokami, R. Hayashi, Y. Saigusa, A. Shimizu, C. Liu, K. K. T. Mong, J. Yoshida, *Org. Lett.* **2013**, *15*, 4520.

List of Other Publications

1) Propargyl 1,2-Orthoesters for a Catalytic and Stereoselective Synthesis of Pyrimidine Nucleosides;
B. V. Rao, S. Manmode, S. Hotha, *J. Org. Chem.* **2015**, *80*, 1499.

2) Propargyl 1,2-Orthoesters for stereoselective synthesis of thioglycosides and 1-thiotrehaloses.
B. V. Rao, S. Manmode, S. Hotha, *Carbohydr. Res.* **2015**, *417*, 103.

3) [Au]/[Ag]-catalyzed expedient synthesis of branched heneicosafuranosyl arabinogalactan motif of Mycobacterium tuberculosis cell wall.
S. A. Thadke, B. Mishra, M. Islam, S. Pasari, S. Manmode, B. V. Rao, M. Neralkar, G. P. Shinde, G. Walke, S. Hotha, *Nature Communications* **2018**, *8,* 14019.

4) Total Synthesis of TMG-chitotriomycin Based on Automated Electrochemical Assembly of a Disaccharide Building Block.
Y. Isoda, N. Sasaki, K. Kitamura, S. Takahashi, S. Manmode, N. Takeda-Okuda, J. Tamura, T. Nokami, T. Itoh, *Beilstein J. Org. Chem.* **2017**, *13*, 919.

5) Expedient Synthesis of a Linear Nonadecaarabinofuranoside of the Mycobacterium Tuberculosis Cellular Envelope.
B. Mishra, S. Manmode, R. R. Adhikari Panda, S. Hotha, *Eur. J. Org. Chem.* **2017**, *32*, 4794.

6) A Versatile Synthesis of Pentacosafuranoside Subunit Reminiscent of Mycobacterial Arabinogalactan Employing One Strategic Glycosidation Protocol.
S. Pasari, S. Manmode, G. Walke, S. Hotha, *Chem. Eur. J.* **2017**, *23*, 1128.