Electrochemical Generation of Glycosyl Dioxalenium Ions and Their Application to the Synthesis of Cyclic β-Glucans

January 2024

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Contents

General introduction

Activation of organic molecules is a key issue in organic synthesis. We often use strong oxidants or reductants to activate substrates with low reactivities. Constant current electrolysis is a powerful alternative that demands electricity instead of oxidant or reductant. Electrochemical reactions can be started and stopped by switching on and off the power supply. Reaction rate can be controlled under the constant current conditions and constant potential electrolysis enables selective activation of organic compounds. Therefore, electrochemical method makes organic reactions controllable, repeatable, and reproducible. For example, 'Cation Pool Method' is a revolutionary method which enables generation and accumulation of carbocations by electrochemical oxidation at very low temperature (Figure 1).[1] Moreover, the method enables reaction with nucleophiles which have lower oxidation potentials than those of precursors of carbocations.

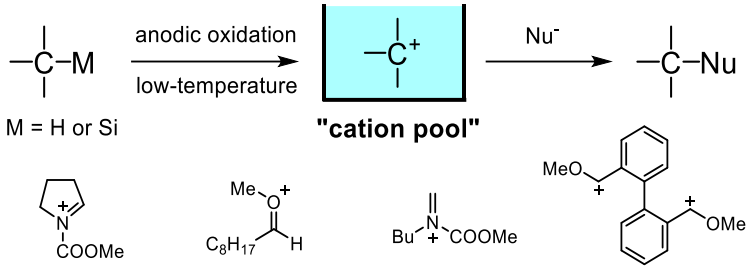


Figure 1. Examples of cations generated by the cation pool method.

Glycosyl cations have been proposed as a reactive intermediate for glycosylation; however, no one has been successful in detecting glycosyl cations by spectroscopy.[2] We expected that application of 'Cation Pool Method' to glycosylation would enable glycosyl cations to be spectroscopically observed. Although we tried to generate and accumulate a glycosyl cation by electrochemical oxidation of a thioglycoside using various electrolytes including tetrabutylammonium tetrakis(pentafluorophenyl) borate ($Bu_4NB(C_6F_5)_4$), we could not detect glycosyl cations by NMR even at low temperature.

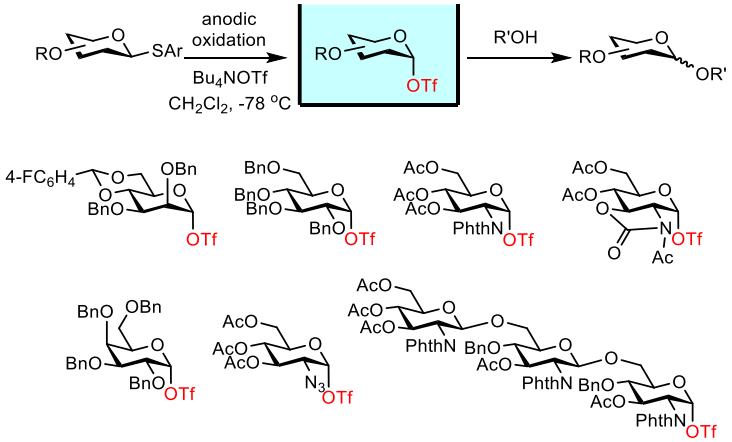


Figure 2. Structures of electrochemically generated glycosyl triflates.

Glycosyl triflates have been known as one of the most reactive intermediates for chemical glycosylation and observable by NMR under the low temperature conditions.[3] Thus, we expected that electrochemical activation of a thioglycoside in the presence of tetrabutylammonium triflate (Bu_4NOTf) might be useful

method to generate and accumulate of glycosyl triflates.[4] A variety of glycosyl triflates have been electrochemically generated and utilized in glycosylation with alcohols including hydroxyl groups of carbohydrates (Figure 2). Based on this result, we have developed 'automated electrochemical assembly' (AEA), which is an electrochemical glycosylation method controlled by a computer (Figure 3). In AEA experiments, glycosyl triflate intermediates, generated by electrochemical oxidation, are accumulated, and following addition of alcohols afford glycoside products.[5] In principle, reactive intermediates other than glycosyl triflate can be generated and accumulated.

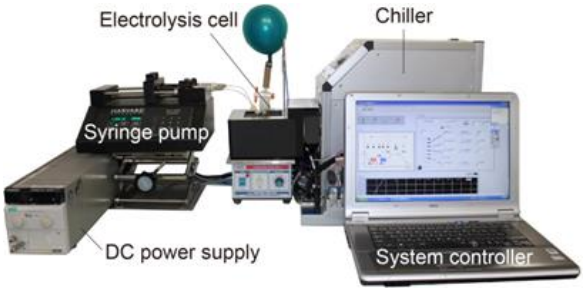


Figure 3. Equipments for AEA.

Cyclic oligosaccharides such as cyclodextrins (CDs) have hydrophilic outer region and hydrophobic inner region. Therefore, they can be used as host molecules that include hydrophobic guest molecules. To date, δ-CD (nonasaccharide) is the largest CD that has been chemically synthesized.[6] Thus, sizes and linkage types of synthesized cyclic oligosaccharides are still limited.

We then focused on a natural oligosaccharide shown in Figure 4. This compound is a cyclic (1,3;1,6)-β-glucan, which has a cyclic dodecasaccharide structure consisting of glucosidic β-(1,3)- and β-(1,6)-linkages,[7] produced by root-nodulating bacteria *Bradyrhizobium japonicum* MTCC 120. The glucan is related to osmotic regulation, nodulation, and suppression of plant defense response.[8] Due to its large-sized ring, the compound is expected to be applied to separation of chiral molecules, drug delivery system (DDS) and catalysts. We intended to efficiently synthesize the cyclic β-glucan with our originally developed AEA method.

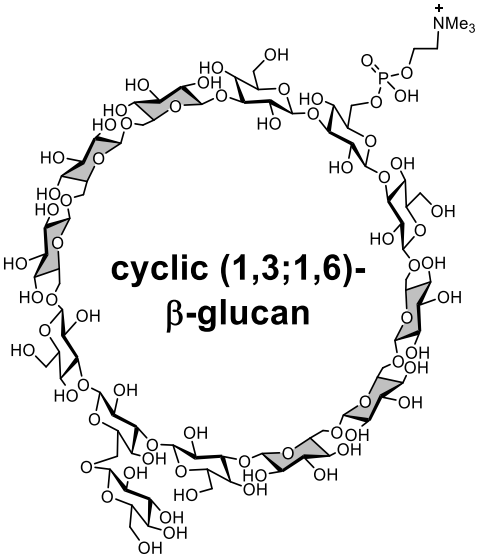


Figure 4. Cyclic (1,3;1,6)-β-glucan isolated from *Bradyrhizobium japonicum* MTCC 120.

References

[1] a) J. Yoshida, A. Shimizu, Y. Ashikari, T. Morofuji, R. Hayashi, T. Nokami, A. Nagaki, *Bull. Chem. Soc. Jpn.* **2015**, *88*, 763–775. b) J. Yoshida, A. Shimizu, R. Hayashi, *Chem. Rev.* **2018**, *118*, 4702–4730.

[2] S. Suzuki, K. Matsumoto, K. Kawamura, S. Suga, J. Yoshida, *Org. Lett.* **2004**, *6*, 3755–3758.

[3] D. Crich, S. Sun, *J. Am. Chem. Soc.* **1997**, *119*, 11217–11223.

[4] a) T. Nokami, A. Shibuya, H. Tsuyama, S. Suga, A. A. Bowers, D. Crich, J. Yoshida, *J. Am. Chem. Soc.* **2007**, *129*, 10922–10928. b) T. Nokami, A. Shibuya, S. Manabe, Y. Ito, J. Yoshida, *Chem. Eur. J.* **2009**, *15*, 2252–2255. c) T. Nokami, Y. Nozaki, Y. Saigusa, A. Shibuya, S. Manabe, Y. Ito, J. Yoshida, *Org. Lett.* **2011**, *13*, 1544–1547. d) T. Nokami, A. Shibuya, Y. Saigusa, S. Manabe, Y. Ito, J. Yoshida, *Beilstein J. Org. Chem.* **2012**, *8*, 456–460.

[5] a) T. Nokami, R. Hayashi, Y. Saigusa, A. Shimizu, C.-Y. Liu, K.-K. T. Mong, J. Yoshida, *Org. Lett.* **2013**, *15*, 4520–4523. b) T. Nokami, Y. Isoda, N. Sasaki, A. Takaiso, S. Hayase, T. Itoh, A. Shimizu, R. Hayashi, J. Yoshida, *Org. Lett.* **2015**, *17*, 1525–1528.

[6] M. Wakao, K. Fukase and S. Kusumoto, *J. Org. Chem.* **2002**, *67*, 8182-8190.

[7] a) M.W. Breedveld and K. J. Miller, *Microbiol. Rev.* **1994**, *58*, 145-161. b) A. V. Nair, S. N. Gummadi and M. Doble, *Biotechnol. Lett.* **2016**, *38*, 1519-1525. c) E. Cho, D. Jeong, Y. Choi and S. Jung, *J. Inclusion Phenom. Macrocyclic Chem.* **2016**, *85*, 175-185.

[8] V. A. Stanisich and B. A. Stone, *Chemistry, Biochemistry, and Biology of (1-3)-β-Glucans and Related Polysaccharides*, **2009**, 327-352.

Chapter 1.

Glycosyl Dioxalenium Ions as Reactive Intermediates of Automated Electrochemical Assembly

Introduction

Stereoselectivity in chemical glycosylation is a crucial issue for total synthesis of complex oligosaccharides.[1] One of the most reliable methods is using glycosyl donor with a stereo-controlling group as a protecting group of the hydroxyl group at C-2 position (2-OH). For example, acetyl (R = Me), benzoyl (R = Ph), pivaloyl (R = ^{t}Bu), and other acyl groups at 2-OH can work as neighboring groups which can form glycosyl dioxalenium ions (Figure 1-1).[2] Thus-generated glycosyl dioxalenium ions have been known as reactive glycosylation intermediates and important chemical species for stereoselective synthesis of 1,2-*trans* glycosidic linkages including β-glucosides and α-mannosides.

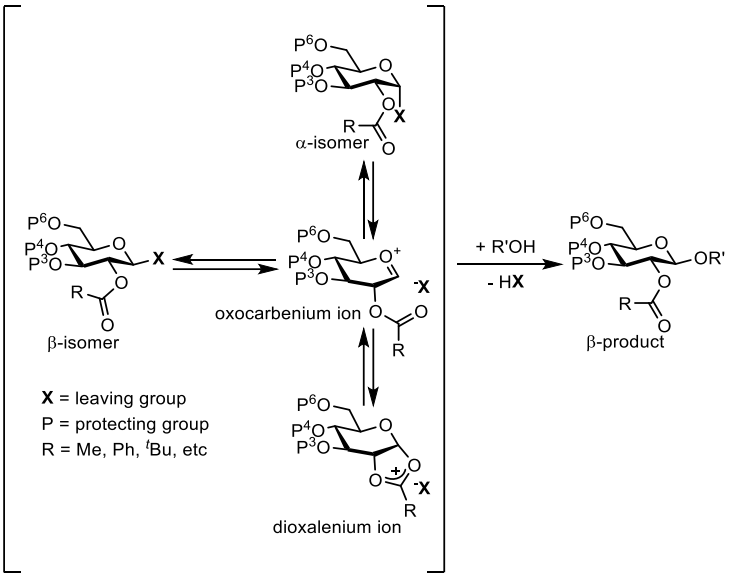


Figure 1-1. Possible glycosylation intermediates for β-selective glycosylation of glucoside.

We have been interested in synthesis of cyclic β-(1,3)-β-(1,6)-glucan[3] as a target oligosaccharide of automated electrochemical assembly (Figure 1-2).[4] Cyclic β-glucans including the cyclic β-(1,3)-β-(1,6)-glucan have potential applications for separation of chiral molecules, drug delivery, and catalyst.[3c] Although synthesis of hexasaccharide, which is a half structure of the cyclic oligosaccharide, has already been achieved, the yield was not high enough to complete the total synthesis.[5] Therefore, we decided to revise the synthetic route for the half structure and re-optimized the reaction conditions. Here, we report optimization of the synthesis of β-1,6-glucan trisaccharide and NMR study of electrochemically generated glycosylation intermediates.[6]

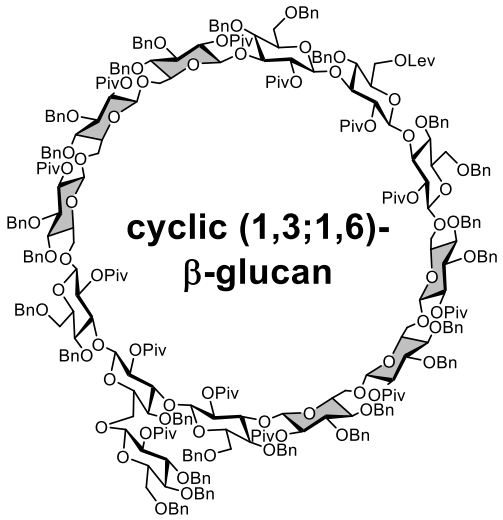
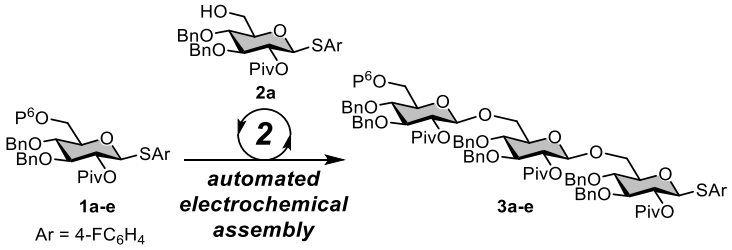


Figure 1-2. β-1,6-Glucan trisaccharide as a partial structure of the cyclic oligosaccharide.

Results and Discussion

We initiated the synthesis by using 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-thioglycoside **1a** (P^2 = Piv, P^6 = Bn) as a model compound and the desired trisaccharide **3a** was obtained in 61% yield (78% yield per cycle) (Table 1-1, entry 1). To prepare the trisaccharide unit for the total synthesis of the cyclic oligosaccharide, the reaction of thioglycoside **1b** (P^2 = Piv, P^6 = 9-fluorenylmethyloxycarbonyl (Fmoc)) with the Fmoc group as a temporary protecting group of the hydroxyl group at C-6 position (6-OH) was tested; however, the yield of trisaccharide **3b** (P^6 = H) was only 6% after one-pot deprotection of the Fmoc group (entry 2). Other thioglycoside **1c** (P^2 = Piv, P^6 = Piv), **1d** (P^2 = Piv, P^6 = Ac), and **1e** (P^2 = Piv, P^6 = TBDPS) also gave the desired trisaccharide **3c-e**; however, the yields of trisaccharide **3c-e** were moderate (entries 3-5).

Table 1-1. β-1,6-Glucan trisaccharide as a partial structure of the cyclic oligosaccharide.

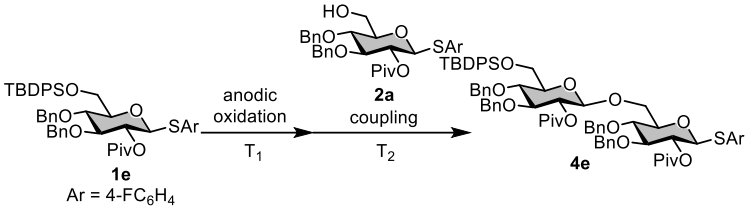


entry[a]	thioglycoside **1**	product **3** (yield)	selectivity (α:β)
1	**1a** (P^6 = Bn)	**3a** (61%, P^6 = Bn)	β only
2	**1b** (P^6 = Fmoc)	**3b** (6%, P^6 = H)[b]	β only
3	**1c** (P^6 = Ac)	**3c** (24%, P^6 = Ac)	β only
4	**1d** (P^6 = Piv)	**3d** (36%, P^6 = Piv)	β only
5	**1e** (P^6 = TBDPS)	**3e** (29%, P^6 = TBDPS)	β only

[a] Anodic oxidation was performed using a divided cell at -80 °C (T_1) under constant current (12 mA, 1.2 F/mol) in CH_2Cl_2 with 0.1 M Bu_4NOTf as electrolyte. The subsequent one-pot glycosylation was carried out at -50 °C (T_2) for 1 h. [b] Deprotection of Fmoc group was carried out in one pot.

Optimization of reaction temperature was performed using thioglycoside **1e** (P^2 = Piv, P^6 = TBDPS) because of its better yield among the thioglycosides with a temporary protecting group (Table 1-2). We tested reactions at different temperatures from -60 to 0 °C and performed reactions at same temperature for both anodic oxidation and glycosylation. Although the yield of disaccharide **4e** did not change at -80 and -60 °C (entries 1 and 2), the best yield was observed at -40 °C (entry 3). To our surprise, the desired disaccharide **4e** was obtained even at elevated temperature -20 and 0 °C (entries 4 and 5).

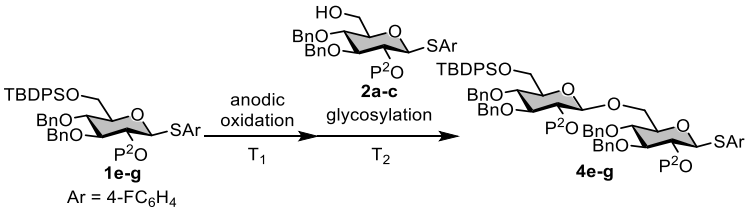
Table 1-2. Temperature effect on glycosylation.



entry	T_1 (°C)	T_2 (°C)	yield	selectivity (α:β)
1	-80	-50	67%	β only
2	-60	-60	67%	β only
3	-40	-40	72%	β only
4	-20	-20	53%	β only
5	0	0	45%	β only

Inspired by successful glycosylation at elevated temperature, further optimization of protecting group at 2-OH (P^2) was carried out (Table 1-3). Although both Ac group (entries 3 and 4) and benzoyl (Bz) group (entries 5 and 6) gave the product, their yields were lower than those of Piv group (entries 1 and 2). Therefore, thioglycoside **1e** (P^2 = Piv, P^6 = TBDPS) may provide the most stable intermediate which does not decompose during accumulation at elevated temperature. These results encouraged us to observe glycosylation intermediates by NMR, because reactive glycosyl triflates, which have been generated by anodic oxidation, seemed to be unstable at elevated temperatures.

Table 1-3. Effect of protecting group at 2-OH.

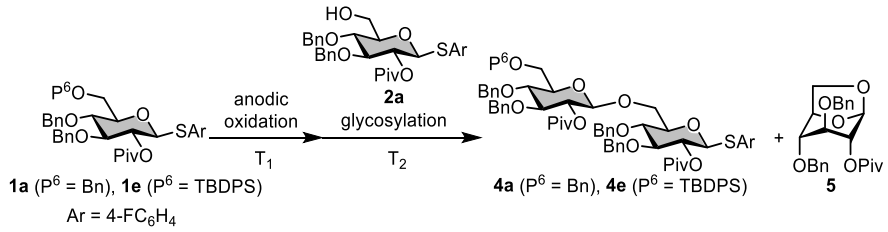


entry	thioglycoside **1**	thioglycoside **2**	T_1, T_2	product (yield)	selectivity (α:β)
1	**1e** (P_2 = Piv)	**2a** (P_2 = Piv)	-40 °C	**4e** (72%)	β only
2	**1e** (P_2 = Piv)	**2a** (P_2 = Piv)	0 °C	**4e** (45%)	β only
3	**1f** (P_2 = Bz)	**2b** (P_2 = Bz)	-40 °C	**4f** (65%)	β only
4	**1f** (P_2 = Bz)	**2b** (P_2 = Bz)	0 °C	**4f** (25%)[a]	β only
5	**1g** (P_2 = Ac)	**2c** (P_2 = Ac)	-40 °C	**4g** (56%)	β only
6	**1g** (P_2 = Ac)	**2c** (P_2 = Ac)	0 °C	**4g** (36%)	β only

[a]1,6-anhydrosugar **9** was obtained as a by-product in 7% yield.

Prior to the NMR analysis, we again investigated effect of protecting group at 6-OH (P^6) at elevated temperature (Table 1-4). Thioglycoside **1a** (P^2 = Piv, P^6 = Bn) gave the desired disaccharide **4a** in lower yield than that with TBDPS group (entries 1 and 2). Decrease of the yields of disaccharide **4a** and **4e** was significant at 0 °C and 1,6-anhydrosugar **5** was obtained in 33% yield together with disaccharide **4a** (entries 3 and 4). Therefore, TBDPS group at 6-OH must contribute to prevent intramolecular glycosylation at elevated temperature.

Table 1-4. Effect of protecting group at 6-OH under elevated temperature conditions.



entry	thioglycoside **1**	T_1, T_2	product (yield)	selectivity (α:β)
1	**1a** (P^6 = Bn)	-40 °C	**4a** (61%)	β only
2	**1e** (P^6 = TBDPS)	-40 °C	**4e** (72%)	β only
3	**1a** (P^6 = Bn)	0 °C	**4a** (12%), **5** (33%)	β only
4	**1e** (P^6 = TBDPS)	0 °C	**4e** (45%)	β only

Low temperature ^{1}H NMR, ^{13}C NMR, and VT-NMR measurements were performed using three thioglycosides **1a**, **1e**, and **1f** equipped with different protecting groups at 2-OH and 6-OH (Figures 1-3, 1-4 and 1-5).[7] At first, thioglycoside **1a** (P^2 = Piv, P^6 = Bn) was activated, and low temperature NMR spectra were measured at -80 °C. Downfield shift of the anomeric proton (δ 7.3) and the carbonyl carbon of Piv group (δ 197.1) suggested that the major accumulated species was glycosyl dioxalenium ion, not glycosyl

triflate. Then, temperature was gradually raised from -80 °C to 24 °C with 15 min interval. The peaks derived from glycosyl dioxalenium ion was detected up to -20 °C; however, the corresponding peaks of glycosyl dioxalenium ion **6** was disappeared and the new sets of peaks, which were derived from 1,6-anhydrosugar **5**, appeared at 0 °C. These VT-NMR experiments revealed that 1,6-anhydrosugar **5** derived from **1a** and 6-OH of **6** with benzyl protecting group was reactive enough at elevated temperature. This result was consistent with the lower yield of glycosylation using thioglycoside **1a** at 0 °C (Table 1-4, entry 3).

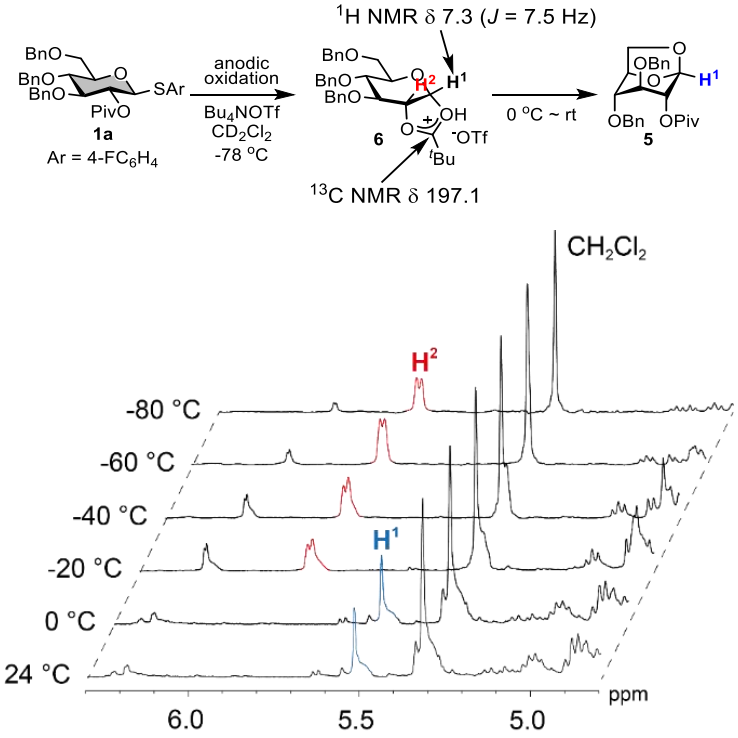


Figure 1-3. VT-NMR of glycosyl dioxalenium ion **6** (P^2 = Piv, P^6 = Bn)

By changing protecting group P^6 at 6-OH of thioglycoside **1** from Bn group to TBDPS group, glycosyl dioxalenium ion **7** (P^2 = Piv, P^6 = TBDPS) was again observed (Figure 1-4). Although the spectra became complex by raising temperature, the corresponding peaks of glycosyl dioxalenium ion **7** were still observed at 0 °C without peaks derived from 1,6-anhydrosugar **5**. This result clearly indicates that glycosyl dioxalenium ion was accumulated reactive intermediate at 0 °C (Table 1-2, entry 5) and the TBDPS group at 6-OH contributed higher stability of glycosyl dioxalenium ion **7**. We presume that the steric effect of TBDPS group may prevent the nucleophilic attack of 6-OH to the anomeric carbon because similar chemical shifts of the cationic carbons of glycosyl dioxalenium ions (197.1 ppm for **6** and 196.9 ppm for **7**) suggest the small electronic effect of protecting groups at 6-OH.

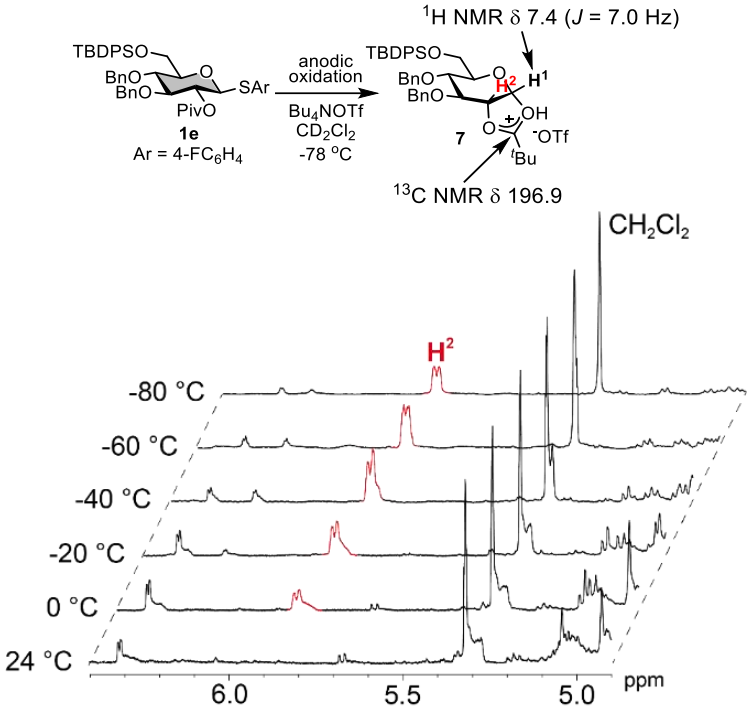


Figure 1-4. VT-NMR of glycoyl dioxalenium ion **7** (P^2 = Piv, P^6 = TBDPS)

Other thioglycoside **1f** with Bz group at 2-OH also afforded the corresponding glycosyl dioxalenium ion **8** (P^2 = Bz, P^6 = TBDPS); however, stability of glycosyl dioxalenium ion **8** was lower than that of **7** (Figure 1-5). Formation of 1,6-anhydrosuger **9** was observed at -20 °C and glycosyl dioxalenium ion **8** was completely disappeared at 0 °C. These results suggest that not only TBDPS group at 6-OH but Piv group at 2-OH also contribute to higher stability of glycosyl dioxalenium ion intermediate. Based on the formation of 1,6-anhydrosugar as a decomposition product of glycosyl dioxalenium ions, the order of stability of glycosyl dioxalenium ions **6-8** was as follows; **7** (P^2 = Piv, P^6 = TBDPS) > **6** (P^2 = Piv, P^6 = Bn) > **8** (P^2 = Bz, P^6 = TBDPS). We assume that bulky protecting groups such as Piv group at 2-OH and TBDPS group at 6-OH may kinetically stabilize the dioxalenium ion **7** by preventing the formation of 1,6-anhydrosugar **5** via intramolecular glycosylation. Although further NMR analysis is required to identify other chemical species than glycosyl dioxalenium ion observed at low temperature, α- and/or β-isomer of glycosyl triflate is the most plausible intermediate.[8]

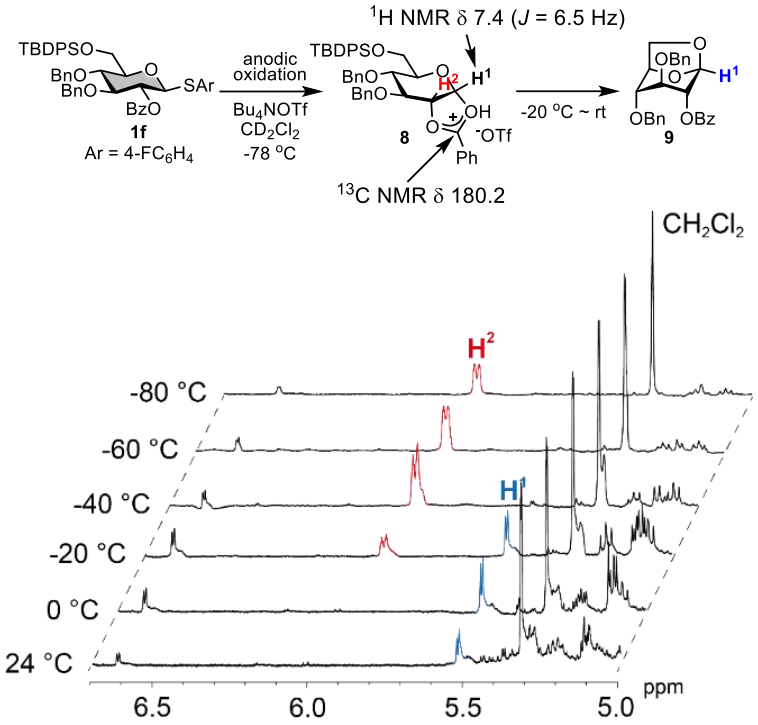
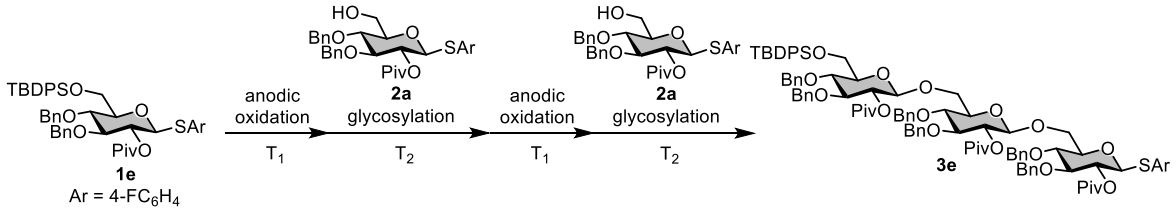


Figure 1-5. VT-NMR of glycosyl dioxalenium ion **8** (P^2 = Bz, P^6 = TBDPS)

Finally, we reinvestigated the trisaccharide synthesis at elevated temperature (Table 1-5). Based on optimization of disaccharide synthesis and VT-NMR study, both anodic oxidation and glycosylation were performed at -40 °C (entry 2). The desired trisaccharide **3e** was obtained in 46% yield, which is 1.5 times higher than the yield under conventional reaction conditions (entry 1). Although further optimization of reaction conditions and the temporary protecting group at 6-OH must be necessary, higher thermal stability of glycosyl dioxalenium ions enables both anodic oxidation and glycosylation at elevated temperature.

Table 1-5. Synthesis of trisaccharide **3e** at elevated temperature.



entry	T_1 (°C)	T_2 (°C)	yield	average yield per cycle	selectivity (α:β)
1	-80	-50	29%	54%	β only
2	-40	-40	46%	68%	β only

Conclusion

In conclusion, we improved the yield of synthesis β-1,6-glucan trisaccharide based on temperature optimization and VT-NMR experiment of glycosylation intermediate. Electrochemically generated glycosyl dioxalenium ions were more stable than glycosyl triflates which decompose at elevated

temperature such as 0 °C.[9] VT-NMR study clearly indicated that not only protecting groups at 2-OH but also protecting group at 6-OH influenced thermal stability of glycosyl dioxalenium ions. Based on these findings, further optimization of synthesis of β-1,3-glucan trisaccharide and synthesis of the linear precursor of cyclic dodecasaccharide are in progress in our laboratory.

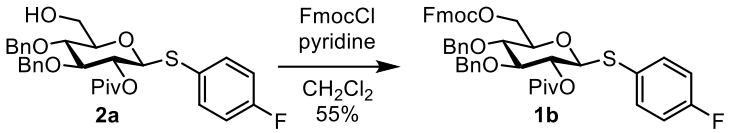
Experimental

1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE II 600 (^{1}H 600 MHz, ^{13}C 150 MHz) and JEOL JNM-ECZ500R (^{1}H 500 MHz, ^{13}C 125 MHz). Electro-spray ionization mass spectra (ESI-MS) were recorded on Thermo Scientific Exactive spectrometer. Preparative recycling gel permeation chromatography (PR-GPC) was performed on Japan Analytical Industry LC-5060. Kanto silica gel 60 N (spherical, neutral, 63-210 μm) was used for silica gel column chromatography. The automated synthesizer is consisting of the commercially available instruments such as the chiller with a cooling bath (UCR-150, Techno Sigma), the power supply 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 F254) was used for TLC analysis. Starting materials **S1**,[5] **1a**,[5] and **2a**[5] were prepared according to the reported procedures. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification.

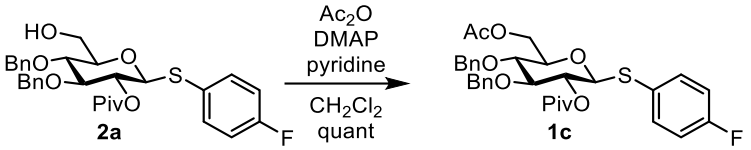
2. Preparation of building blocks

Preparation of 4-fluorophenyl 3,4-di-*O*-benzyl-6-*O*-(9-fluorenylmethyloxycarbonyl)-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**1b**)



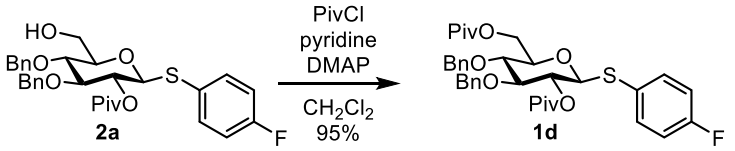
To the solution of **2a** (1.00 mmol, 555 mg) in CH_2Cl_2 (6.4 mL), pyridine (13.0 mmol, 1.0 mL) and FmocCl (2.00 mmol, 523 mg) were added at room temperature and the reaction mixture was stirred for another 2 days. After the completion of the reaction determined by TLC (hexane/EtOAc 4:1). The reaction 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 **1b** in 55% yield (0.553 mmol, 430 mg) as a pale-yellow solid. **4-Fluorophenyl 3,4-di-*O*-benzyl-6-*O*-(9-fluorenylmethyloxycarbonyl)-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (1b)**; TLC (Hexane/EtOAc 4:1): R_f 0.52; $[\alpha]_D$ = -6.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.76 (d, *J* = 7.2 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 2 H), 7.51–7.48 (m, 2 H), 7.40 (t, *J* = 7.2 Hz, 2 H), 7.32–7.22 (m, 12 H), 6.95 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.04 (*pseudo*-t, *J* = 9.6 Hz, 1 H, H-2), 4.79 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.75 (d, *J* = 10.8 Hz, 2 H, benzylic-H), 4.70 (d, *J* = 10.8 Hz, 1 H, benzylic-H), 4.56–4.52 (m, 2 H, H-1 and benzylic-H), 4.47–4.40 (m, 3 H, H-6' and Fmoc-2H), 4.28–4.23 (m, 2 H, H-6 and Fmoc-1H), 3.73 (*pseudo*-t, *J* = 9.0 Hz, 1 H, H-3), 3.60–3.58 (m, 2 H, H-4 and H-5), 1.25 (s, 9 H, Piv); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.7, 163.0 (d, *J* = 246.0 Hz, ArS), 155.0, 143.4, 143.3, 141.4, 137.8, 137.5, 135.7 (d, *J* = 7.5 Hz, ArS), 128.6, 128.5, 128.1, 128.0, 127.8, 127.4, 127.3, 125.2, 125.1, 120.2, 116.0 (d, *J* = 21.0 Hz, ArS), 86.3 (C-1), 84.7 (C-3), 77.2 (C-4 or C-5), 77.0 (C-4 or C-5), 75.4 (benzylic-C), 75.2 (benzylic-C), 71.4 (C-2), 70.0 (Fmoc-CH_2), 66.6 (C-6), 46.8 (Fmoc-CH), 38.9 (Piv-1C), 27.2 (Piv-3C); HRMS (ESI) *m/z* calculated for $C_{46}H_{45}FKO_8S$ $[M+K]^+$ 815.2456; found 815.2463.

Preparation of 4-fluorophenyl 6-*O*-acetyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**1c**)



To the solution of **2a** (0.533 mmol, 296 mg) in CH_2Cl_2 (3.00 mL), DMAP (0.066 mmol, 8.1 mg), pyridine (0.30 mL), and Ac_2O (1.8 mmol, 0.17 mL) 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. After filtration and removal of solvent under reduced pressure the crude product was purified with silica gel chromatography to obtain **1c** in quantitative yield (0.544 mmol, 324 mg) as a white solid. **4-Fluorophenyl 6-*O*-acetyl-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (1c)**; TLC (Hexane/EtOAc 4:1): R_f 0.50; $[\alpha]_D$ = -8.1 (*c* = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50–7.48 (m, 2 H), 7.33–7.22 (m, 10 H), 6.99 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.01 (*pseudo*-t, *J* = 9.6 Hz, 1 H, H-2), 4.78 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.77 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.70 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.55–4.51 (m, 2 H, H-1 and benzylic-H), 4.43 (d, *J* = 12.0 Hz, 1 H, H-6'), 4.17 (dd, *J* = 12.0, 1.2 Hz, 1 H, H-6), 3.75–3.71 (m, 1 H, H-3), 3.58–3.54 (m, 2 H, H-4 and H-5), 2.04 (s, 3 H, Ac), 1.25 (s, 9 H, Piv); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.7, 170.6, 163.1 (d, *J* = 245.7 Hz, ArS), 137.8, 137.5, 135.9 (d, *J* = 7.5 Hz, ArS), 128.6, 128.5, 128.1, 127.8, 127.4, 127.02, 127.0, 115.9 (d, *J* = 19.5 Hz, ArS), 86.0 (C-1), 84.7 (C-3), 75.4 (benzylic-C), 75.1 (benzylic-C), 71.4 (C-2), 77.1 (C-4 or C-5), 77.0 (C-4 or C-5), 62.9 (C-6), 38.8 (Piv-1C), 27.2 (Piv-3C), 20.9 (Ac); HRMS (ESI) *m/z* calculated for $C_{33}H_{37}FKO_7S$ $[M+K]^+$ 635.1881; found 635.1879.

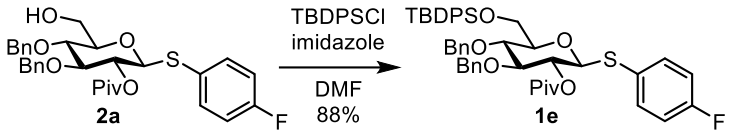
Preparation of 4-fluorophenyl 3,4-di-*O*-benzyl-2,6-di-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**1d**)



To the solution of **2a** (0.542 mmol, 301 mg) were added pyridine (0.30 mL) and DMAP (0.61 mmol, 74 mg) in CH_2Cl_2 (2.0 mL), and pivaloyl chloride (0.82 mmol, 0.10 mL) was added at room temperature. 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 aqueous hydrochloric acid solution. The reaction mixture was extracted with CH_2Cl_2 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 **1d** in 95% yield (0.516 mmol, 329 mg) as a white solid. **4-Fluorophenyl 3,4-di-*O*-benzyl-2,6-di-*O*-pivaloyl-1-thio-β-D-glucopyranoside (1d)** TLC (hexane/EtOAc 4:1): R_f 0.72; $[\alpha]_D$ = -15.1 (*c* = 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.49 (dd, *J* = 5.4, 4.4 Hz, 2 H), 7.34–7.27 (m, 6 H), 7.25–7.22 (m, 4 H), 6.98 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 4.99 (d, *J* = 9.4 Hz, 1 H, H-2), 4.78 (d, *J* = 10.7 Hz, 1 H, benzylic-H), 4.75 (d, *J* = 10.9 Hz, 1 H, benzylic-H), 4.68 (d, *J* = 10.9 Hz, 1 H, benzylic-H), 4.54 (d, *J* = 10.0 Hz, 1 H, H-1), 4.53 (d, *J* = 10.7 Hz, 1 H, benzylic-H), 4.47 (dd, *J* = 12.0, 1.7 Hz, 1 H, H-6'), 4.18 (dd, *J* = 12.0, 4.8 Hz, 1 H, H-6), 3.73 (*pseudo*-t, *J* = 8.8 Hz, 1 H, H-3), 3.58 (ddd, *J* = 9.8, 4.8, 1.8 Hz, 1 H, H-5), 3.55 (dd, *J* = 9.7, 8.5 Hz, 1H, H-4), 1.25 (s, 9 H, Piv), 1,21 (s, 9 H, Piv); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.1 (Piv-CO), 176.6 (Piv-CO), 163.0 (d, *J* = 246.9 Hz, ArS), 137.7, 137.5 (d, *J* = 8.5 Hz, ArS), 128.6,

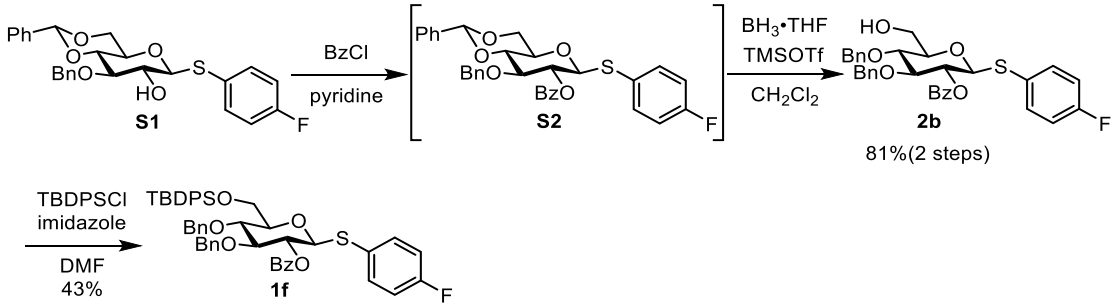
128.5, 128.1, 128.0, 127.8, 127.5, 126.88, 126.86, 115.9 (d, *J* =21.5 Hz, ArS), 86.0 (C-1), 84.7 (C-3), 77.49 (C-4 or C-5), 77.47 (C-4 or C-5), 75.5 (benzylic-C), 75.3 (benzylic-C), 71.4 (C-2), 62.9 (C-6), 38.9 (Piv-1C), 38.8 (Piv-1C), 27.24 (Piv-3C), 27.22 (Piv-3C); HRMS (ESI) *m/z* calculated for $C_{33}H_{37}FKO_7S$, $[M+K]^+$ 677.2345; found 677.2318.

Preparation of 4-Fluorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**1e**)



To the solution of **2a** (1.22 mmol, 700 mg) in DMF (4.0 mL), imidazole (2.44 mmol, 166 mg), and *tert*-butylchlorodiphenylsilane (1.83 mmol, 0.469 mL) were added at 0 ℃ 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 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 **1e** in 88% yield (1.10 mmol, 876 mg) as colorless oil. **4-Fluorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (1e)**; TLC (hexane/EtOAc 4:1): R_f 0.69; $[\alpha]_D$ = -18.9 (*c* = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.77 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.70 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.52 (dd, *J* = 7.2, 5.4 Hz, 2 H), 7.43–7.24 (m, 14 H), 7.10 (dd, *J* = 7.8, 4.2 Hz, 2 H), 6.89 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.09 (*pseudo*-t, *J* = 9.6 Hz, 1 H, H-2), 4.79 (d, *J* = 10.7 Hz, 1 H, benzylic-H), 4.78 (d, *J* = 10.9 Hz, 1 H, benzylic-H), 4.70 (d, *J* = 10.9 Hz, 1 H, benzylic-H), 4.62 (d, *J* = 10.7 Hz, 1 H, benzylic-H), 4.58 (d, *J* = 10.1 Hz, 1 H, H-1), 3.99 (dd, *J* = 11.4, 1.8 Hz, 1 H, H-6'), 3.93 (dd, *J* = 11.4, 4.2 Hz, 1 H, H-6), 3.81 (*pseudo*-t, *J* = 9.6 Hz, 1 H, H-4), 3.74 (*pseudo*-t, *J* = 9.0 Hz, 1 H, H-3), 3.44 (ddd, *J* = 15.6, 3.6, 1.2 Hz, 1 H, H-5), 1.26 (s, 9 H, pivaloyl-H), 1.08 (s, 9 H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 174.1, 162.9 (d, *J* = 246.5 Hz, ArS), 138.1, 138.0, 135.9, 135.7, 135.1 (d, *J* = 8.0 Hz, ArS), 133.4, 133.0, 129.8, 128.5, 128.03, 128.01, 127.9, 127.8, 127.5, 115.9 (d, *J* = 21.8 Hz, ArS), 86.6 (C-1), 84.9 (C-3), 80.3 (C-5), 77.3 (C-4), 75.5 (benzylic-C), 75.2 (benzylic-C), 71.6 (C-2), 62.7 (C-6), 38.9 (pivaloyl-1C), 27.3 (pivaloyl-3C), , 26.6 (^{t}Bu-3C), 19.4 (^{t}Bu-1C); HRMS (ESI) *m/z* calculated for $C_{47}H_{53}FNaO_6SSi$ $[M+Na]^+$ 815.3208; found 815.3206.

Preparation of 4-Fluorophenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-glucopyranoside (**1f**)

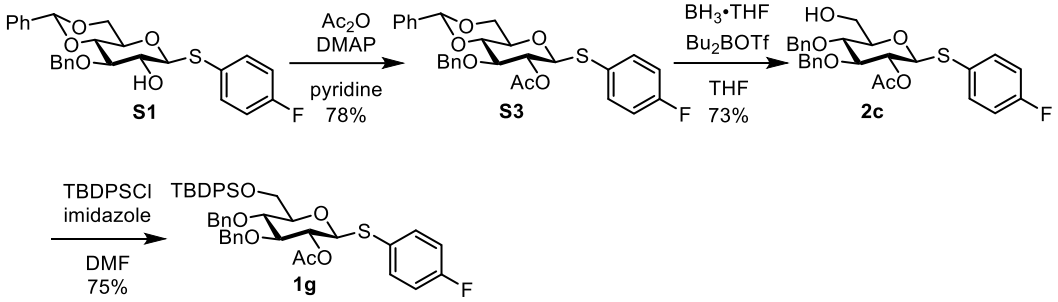


To the solution of **S1** (4.27 mmol, 2.00 g) in pyridine (15.0 mL), benzoyl chloride (4.27 mmol, 2.00 g) was added, and the reaction mixture was stirred at 50 ℃ overnight. After the completion of the reaction

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. Solid was removed by filtration and the reaction mixture was evaporated to obtain crude product of **S2**. To the solution of **S2** in CH_2Cl_2 (22.0 mL), tetrahydrofuran borane (23.5 mmol, 25.0 mL) was added at 0 ℃ and the reaction mixture was stirred at 0 ℃ for 10 min. And trimethylsilyl triflate (0.676 mmol, 0.125 mL) was added at 0 ℃ and the reaction mixture was stirred at room temperature for 6 h. After the completion of the reaction determined by TLC (eluent: 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 **2b** in 81% yield (3.44 mmol, 1.98 g) as a white solid. **4-Fluorophenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (2b)**; TLC (hexane/EtOAc 4:1): R_f 0.14; $[\alpha]_D = 37.6$ (*c* = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.05 (d, *J* = 7.2 Hz, 2 H), 7.59–7.55 (m, 1 H), 7.47–7.42 (m, 4 H), 7.33–7.27 (m, 5 H), 7.11 (bs, 5 H), 6.95 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.22 (*pseudo*-t, *J* = 9.6 Hz, 1 H, H-2), 4.84 (d, *J* = 11.0 Hz, 1 H, benzylic-H), 4.74 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.73 (d, *J* = 10.8 Hz, 1 H, benzylic-H), 4.64 (d, *J* = 11.0 Hz, 2 H, H-1 and benzylic-H), 3.92 (dd, *J* = 11.9, 2.2 Hz, 1 H, H-6'), 3.86 (*pseudo*-t, *J* = 9.1 Hz, 1 H, H-3), 3.74 (dd, *J* = 12.1, 4.7 Hz, 1 H, H-6), 3.67 (*pseudo*-t, *J* = 9.4 Hz, 1 H, H-4), 3.52–3.48 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 162.6 (d, *J* = 247.2 Hz, ArS), 137.7, 137.6, 135.7 (d, *J* = 8.1 Hz, ArS), 133.4, 130.2, 129.9, 128.6, 128.58, 128.54, 128.37, 128.30, 128.19, 128.13, 127.8, 127.0, 126.9, 116.1 (d, *J* = 21.8 Hz, ArS), 86.1 (C-1), 84.0 (C-3), 79.7 (C-5), 77.4 (C-4), 75.4 (benzylic-C), 75.2 (benzylic-C), 72.4 (C-2), 62.0 (C-6); HRMS (ESI) *m/z* calculated for $C_{33}H_{31}FKO_6S$ $[M+K]^+$ 597.1718; found 597.1714.

To the solution of **2b** (1.39 mmol, 800 mg) in DMF (4.3 mL), imidazole (2.78 mmol, 190 mg), and *tert*-butylchlorodiphenylsilane (2.09 mmol, 0.536 mL) were added at 0 ℃ 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 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 **1f** in 43% yield (0.602 mmol, 490 mg) as a white solid. **4-Fluorophenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-glucopyranoside (1f)**; TLC (Hexane/EtOAc 4:1): R_f 0.59; $[\alpha]_D = 13.1$ (*c* = 5.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.06 (d, *J* = 7.2 Hz, 2 H), 7.79 (d, *J* = 7.2 Hz, 2 H), 7.71 (d, *J* = 7.2 Hz, 2 H), 7.58 (t, *J* = 7.2 Hz, 1 H), 7.51–7.48 (m, 3 H), 7.47–7.41 (m, 4 H), 7.38 (t, *J* = 7.8 Hz, 2 H), 7.35 (*pseudo*-t, *J* = 7.8 Hz, 2 H), 7.26 (dd, *J* = 6.6, 3.6 Hz, 3 H), 7.15–7.13 (m, 2 H), 6.86 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.27 (*pseudo*-t, *J* = 9.0 Hz, 1 H, H-2), 4.86 (d, *J* = 10.7 Hz, 1 H, benzylic-H), 4.75 (d, *J* = 11.0 Hz, 1 H, benzylic-H), 4.71 (d, *J* = 10.0 Hz, 1 H, H-1), 4.67 (d, *J* = 10.7 Hz, 1 H, benzylic-H), 4.64 (d, *J* = 11.0 Hz, 1 H, benzylic-H), 4.02 (dd, *J* = 4.0, 1.6 Hz, 1 H, H-6'), 3.97 (dd, *J* = 11.4, 4.2 Hz, 1 H, H-6), 3.87 (dt, *J* = 14.4, 9.0 Hz, 2 H, H-4), 3.48 (ddd, *J* = 9.3, 3.6, 1.6 Hz, 1 H, H-5), 1.09 (s, 9 H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 162.9 (d, *J* = 264.4 Hz, ArS), 137.9, 137.6, 135.9, 135.7, 135.5 (d, *J* = 8.0 Hz, ArS), 133.38, 133.27, 132.9, 130.0, 129.9, 129.8, 128.5, 128.3, 128.2, 128.0, 127.9, 128.8, 127.78, 127.76, 127.4 (d, *J* = 3.1 Hz, ArS), 115.9 (d, *J* = 21.7 Hz, ArS), 86.2 (C-1), 84.4 (C-3), 80.3 (C-5), 77.4 (C-4), 75.5 (benzylic-C), 75.2 (benzylic-C), 72.4 (C-2), 62.6 (C-6), 26.7 (^{t}Bu), 19.3 (^{t}Bu); HRMS (ESI) *m/z* calculated for $C_{49}H_{49}FNaO_6SSi$ $[M+Na]^+$ 835.2895; found 835.2889.

Preparation of 4-Fluorophenyl 2-*O*-acetyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-glucopyranoside **(1g)**

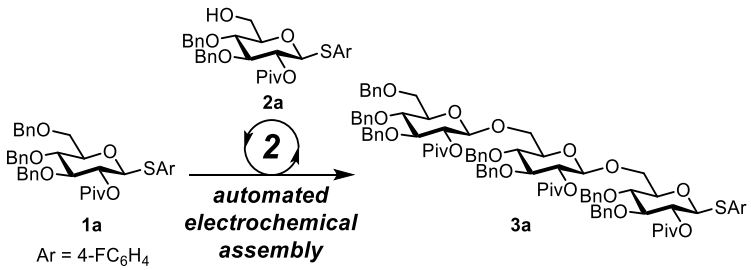


To the solution of **S1** (2.77 mmol, 1.31 g) in pyridine (12.0 mL), DMAP (0.83 mmol, 100 mg) and acetic anhydride (3.6 mmol, 0.34 mL) were added, and the reaction mixture was stirred at 25 ℃ overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 4:1), the reaction was quenched 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 of **S3**. Thus-obtained crude product was purified with silica gel chromatography to obtain **S3** in 78% yield (2.15 mmol, 1.10 g) as a white solid. **4-Fluorophenyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (S3)**; TLC (Hexane/EtOAc 4:1): R_f 0.30; $[\alpha]_D$ = -5.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.49–7.46 (m, 4 H), 7.41–7.37 (m, 3 H), 7.32–7.25 (m, 4 H), 7.01 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.56 (s, 1 H, benzylidene-H), 4.95 (dd, *J* = 10.2, 8.4 Hz, 1 H, H-2), 4.85 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.65 (d, *J* = 12.0 Hz, 1 H, benzylic-H), 4.58 (d, *J* = 11.4 Hz, 1 H, H-1), 4.38 (dd, *J* = 10.8, 4.8 Hz, 1 H, H-6'), 3.78 (*pseudo*-t, *J* = 10.8 Hz, 1 H, H-6), 3.74 (*pseudo*-t, *J* = 9.0 Hz, 1 H, H-3), 3.69 (*pseudo*-t, *J* = 9.0 Hz, 1 H, H-4), 3.48 (td, *J* = 10.2, 5.4 Hz, 1 H, H-5), 2.04 (s, 3 H, Ac); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.3 (Ac-CO), 163.1 (*J* = 247.5 Hz, ArS), 138.0, 137.1, 136.1 (d, *J* = 9.0 Hz, ArS), 129.1, 128.6, 128.34, 128.29, 128.1, 127.93, 127.85, 127.7, 126.3 (d, *J* = 3.0 Hz, ArS), 126.0, 116.0 (d, *J* = 21.0 Hz, ArS), 101.2 (benzylidene-C), 86.4 (C-1), 81.3 (C-4), 79.7 (C-3), 74.4 (benzylic-C), 71.2 (C-2), 70.5 (C-5), 68.5 (C-6), 21.0 (Ac); HRMS (ESI) *m/z* calculated for $C_{28}H_{27}FKO_6S$ $[M+K]^+$ 549.1144; found 549.1122.

To the solution of **S3** (2.15 mmol, 1.10 g) in THF (16.0 mL), BH_3-THF (14.0 mmol, 16.0 mL) was added at 0 ℃ and the reaction mixture was stirred at 0 ℃ for 15 min. And 1.0 M dibutyl boron triflate dichloromethane solution (3.0 mmol, 3.0 mL) was added dropwise at 0 ℃ and the reaction mixture was stirred at room temperature for 3 h. After the completion of the reaction determined by TLC (eluent: Hexane/EtOAc 7:3). 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 **2c** in 73% yield (1.56 mmol, 0.80 g) as a white solid. **4-Fluorophenyl 2-*O*-acetyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (2c)**; TLC (Hexane/EtOAc 7:3): R_f 0.15; $[\alpha]_D$ = 2.7 (*c* = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.46 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.35–7.25 (m, 9 H), 7.01 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 4.93 (dd, *J* = 9.6, 9.0 Hz, 1 H, H-2), 4.811 (d, *J* = 10.8 Hz, 1 H, benzylic-H), 4.807 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.67 (d, *J* = 11.4 Hz, 1 H, benzylic-H), 4.63 (d, *J* = 10.8 Hz, 1 H, benzylic-H), 4.54 (d, *J* = 10.2 Hz, 1 H, H-1), 3.87 (ddd, *J* = 12.0, 5.4, 2.4 Hz, 1 H, H-6'), 3.71–3.67 (m, 2 H, H-3 and H-6), 3.59 (*pseudo*-t, *J* = 9.0 Hz, 1 H, H-4), 3.40 (ddd, *J* = 9.6, 4.2, 2.4 Hz, 1 H, H-5), 2.01 (s, 1 H, Ac), 1.78 (t, *J* = 6.6 Hz, 1 H, OH); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.5 (Ac-CO), 163.0 (d, *J* = 247.5 Hz, ArS), 138.0, 137.7, 135.5 (d, *J* = 7.5 Hz, ArS), 128.6, 128.5, 128.43, 128.35, 128.12, 128.09, 128.0, 127.88, 126.9, 116.1 (d, *J* = 21.0 Hz, ArS), 85.9 (C-1), 84.1 (C-3), 79.6 (C-5), 77.4 (C-4), 75.3 (benzylic-C), 75.2 (benzylic-C), 71.8 (C-2), 61.9 (C-6), 21.0 (Ac); HRMS (ESI) *m/z* calculated for $C_{28}H_{29}FKO_6S$ $[M+K]^+$ 551.1300; found 551.1282.

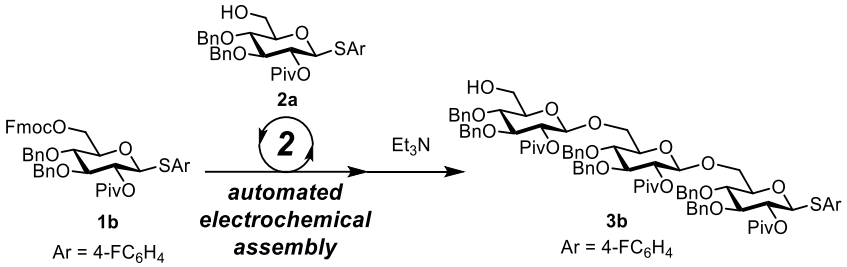
To the solution of **2c** (0.977 mmol, 501 mg) in DMF (3.0 mL), imidazole (1.95 mmol, 134 mg), and *tert*-butylchlorodiphenylsilane (1.5 mmol, 0.40 mL) were added at 0 °C and the reaction mixture was stirred at room temperature overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 9:1), the reaction was quenched with sat. aqueous $NaHCO_3$. The reaction mixture was diluted with EtOAc and 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 **1g** in 75% yield (0.732 mmol, 550 mg) as colorless oil. **4-Fluorophenyl 2-*O*-acetyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-glucopyranoside (1g)** TLC (Hexane/EtOAc 4:1): R_f 0.72; $[\alpha]_D$ = -15.1 (*c* = 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.75 (dd, *J* = 7.4, 1.3 Hz, 1 H), 7.69 (dd, *J* = 7.4, 1.1 Hz, 2 H), 7.52–7.49 (m, 2 H), 7.42 (td, *J* = 7.4, 1.5 Hz, 2 H), 7.37–7.31 (m, 6 H), 7.30–7.25 (m, 6 H), 7.13–7.11 (m, 2 H), 6.89 (*pseudo*-t, *J* = 8.7 Hz, 2 H), 4.98 (*pseudo*-t, *J* = 9.6 Hz, 1 H, H-2), 4.83 (d, *J* = 11.3 Hz, 1 H, benzylic-H), 4.82 (d, *J* = 10.6 Hz, 1 H, benzylic-H), 4.67 (d, *J* = 11.5 Hz, 1 H, benzylic-H), 4.65 (d, *J* = 10.7 Hz, 1 H, benzylic-H) 4.53 (d, *J* = 10.1 Hz, 1 H, H-1), 3.98 (dd, *J* = 11.4, 1.4 Hz, 1 H, H-6'), 3.92 (dd, *J* = 11.4, 3.8 Hz, 1 H, H-6), 3.81 (*pseudo*-t, *J* = 9.4 Hz, 1 H, H-4), 3.68 (*pseudo*-t, *J* = 9.2 Hz, 1 H, H-3), 3.40 (ddd, *J* = 9.8, 3.5, 1.3 Hz, 1 H, H-5), ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.6 (Ac-CO), 162.8 (d, *J* = 246.9 Hz, ArS), 135.9, 135.7, 135.3 (d, *J* = 8.5 Hz, ArS), 133.3, 132.9, 129.8, 128.54, 128.49, 127.98, 127.89, 127.82, 127.7, 127.5, 127.48, 115.9 (d, *J* = 21.5 Hz, ArS), 86.1 (C-1), 84.5 (C-3), 80.2 (C-5), 77.3 (C-4), 75.5 (benzylic-C), 75.2 (benzylic-C), 71.7 (C-2), 62.5 (C-6), 26.8 (^{t}Bu-3C), 21.1 (Ac), 17.3 (^{t}Bu-1C); HRMS (ESI) *m/z* calculated for $C_{44}H_{47}FKO_6SSi$, $[M+K]^+$ 789.2448; found 789.2477.

3. Synthesis of trisaccharides

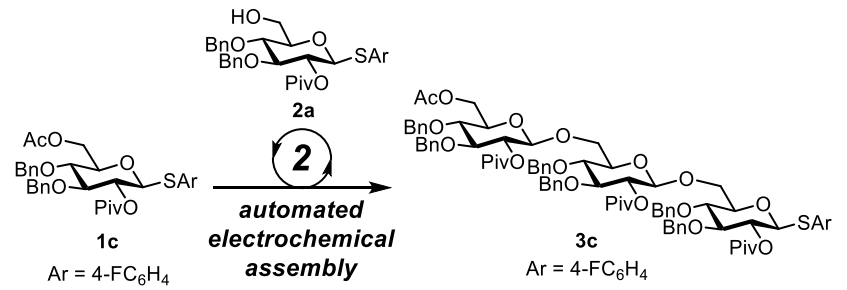


The automated synthesis of trisaccharide **3a** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm×20 mm). In the anodic chamber were placed terminal building block **1a** (0.300 mmol, 196 mg), Bu_4NOTf (1.55 mmol, 613 mg) and CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.63 mmol, 55 μL), Bu_4NOTf (1.55 mmol, 611 mg) and 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, building block **2a** (0.210 mmol, 353 mg) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump (1.0 mL (0.105 mmol) for one cycle) under an argon atmosphere at -50 °C and kept for 60 min. Then the second cycle started 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 the crude product was purified with silica gel chromatography and the mixture was purified by PR-GPC with $CHCl_3$ as an eluent and trisaccharide **3a** was obtained in 61% isolated yield (0.184 mmol, 276 mg) as a white solid. **4-Fluorophenyl 3,4,6-tri-*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-glucopyranoside (3a);** TLC

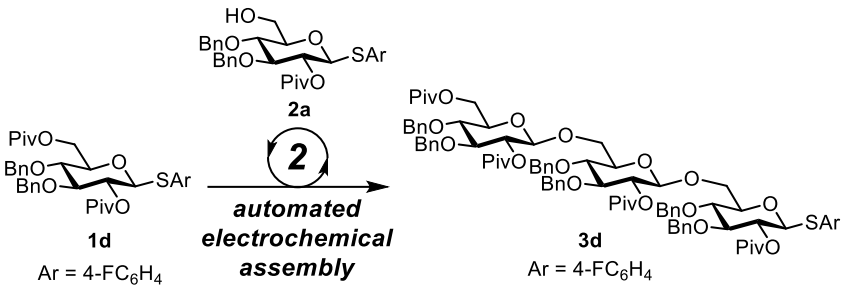
(Hexane/EtOAc 4:1): R_f = 0.66; $[\alpha]_D$ = -0.6 (*c* = 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.50–7.47 (m, 2 H), 7.32–7.21 (m, 3 H), 7.18 (d, *J* = 7.3 Hz, 2 H), 7.13–7.11 (m, 2 H), 7.03 (*pseud*o-t, *J* = 11.2 Hz, 2 H), 5.10–5.06 (m, 2 H), 4.99 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.76 (d, *J* = 11.0 Hz, 1 H), 4.74–4.54 (m, 13 H), 4.51 (d, *J* = 9.8 Hz, 2 H), 3.97 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.91 (dd, *J* = 11.4, 1.2 Hz, 1 H), 3.73–3.55 (m, 12 H), 3.48–3.45 (m, 1 H), 3.40 (*pseudo*-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, 176.73, 176.61, 162.8 (d, *J* = 246.5 Hz), 138.3, 138.28, 138.21, 138.13, 138.07, 137.9, 135.3 (d, *J* = 8.3 Hz), 128.6, 128.5, 128.45, 128.41, 128.39, 128.3, 128.1, 128.0, 127.9, 127.78, 127.75, 127.6, 127.4, 127.3, 116.1 (d, *J* = 21.7 Hz), 101.8, 101.1, 86.5, 84.7, 83.3, 83.27, 79.0, 78.1, 78.0, 75.3, 75.2, 75.09, 74.05, 74.9, 74.89, 74.85, 73.5, 73.2, 72.9, 72.0, 71.5, 69.0, 68.9, 68.3, 38.85, 38.83, 38.80, 27.27, 27.24, 27.22; HRMS (ESI) *m/z* calculated for $C_{88}H_{101}FKO_{18}S$, $[M+K]^+$ 1535.6324; found 1535.6309.



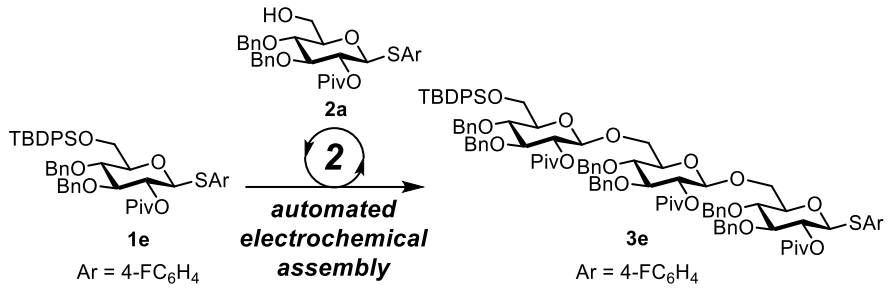
Automated electrochemical glycosylation of building blocks **1b** (0.308 mmol, 239 mg) and **2a** (0.629 mmol, 349 mg) afforded **3b** (0.0178 mmol, 25.0 mg) in 6% yield as a white solid, following the same procedure as that of compound **3a** except deprotection of Fmoc group by adding excess amount of Et_3N (3.0 mL). **4-Fluorophenyl 3,4-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-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (3b)**; TLC (Hexane/EtOAc 4;1): R_f 0.3; $[\alpha]_D$ = -6.7 (*c* = 1.0, $CHCl_3$) ^1H NMR ($CDCl_3$, 600 MHz) δ7.48 (dd, *J* = 8.4, 6.0 Hz, 2 H), 7.34–7.21 (m, 30 H), 7.01 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.04–4.99 (m, 3 H), 4.80–4.68 (m, 8 H), 4.65 (d, *J* = 11.5 Hz, 1 H), 4.62–4.56 (m, 3 H), 4.41 (d, *J* = 7.7 Hz, 1 H), 4.39 (d, *J* = 7.9 Hz, 1 H), 3.86 (d, *J* = 10.8 Hz, 1 H), 3.82–3.79 (m, 1 H), 3.80 (d, *J* = 10.8 Hz, 1 H), 3.75 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.70–3.60 (m, 7 H), 3.59 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 3.49 (dd, *J* = 9.0 Hz, 1 H), 3.44 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.36 (bs, 1 H), 2.50 (bs, 1 H), 1.23 (s, 9 H), 1.13 (s, 9 H), 1.13 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 176.6, 176.5, 161.9, 138.2, 138.04, 137.97 137.93, 137.7, 135.0 (d, *J* = 8.25 Hz), 128.48, 128.46, 128.43, 128.31, 128.30, 128.2, 128.1, 127.98, 127.96, 127.9, 127.64, 127.59, 127.55, 127.4, 127.32, 127.30, 116.0 (d, *J* = 21.6 Hz), 102.1, 101.4, 86.5, 84.6, 83.2, 83.0, 78.7, 77.8, 77.6, 75.8, 75.1, 74.93, 74.89, 74.86, 74.7, 73.2, 73.0, 71.4, 69.6, 68.9, 61.9, 38.79, 38.76 ,38.7, 27.2, 27.1; HRMS (ESI) *m/z* calculated for $C_{81}H_{95}FKO_{18}S$; $[M+K]^+$ 1445.5860; found 1445.5852.



Automated electrochemical glycosylation of building blocks **1c** (0.100 mmol, 59.7 mg) and **2a** (0.204 mmol, 113 mg) afforded **3c** (0.0239 mmol, 34.7 mg) in 24% yield as a white solid, following the same procedure as that of compound **3a**. **4-Fluorophenyl 6-*O*-acetyl-3,4-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-glucopyranoside (3c)**; TLC (Hexane/EtOAc 4:1): R_f 0.27; $[\alpha]_D$ = -9.2 (*c* = 2.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.49 (dd, *J* = 8.4, 5.4 Hz, 2 H), 7.32–7.23 (m, 26 H), 7.21 (d, *J* = 7.2 Hz, 2 H), 7.18 (d, *J* = 7.2 Hz, 2 H), 7.04 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.07 (dd, *J* = 9.0, 7.8 Hz, 1 H), 5.04 (dd, *J* = 9.6, 7.8 Hz, 1 H), 4.98 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 4.78 (d, *J* = 11.4 Hz, 1 H), 4.75–4.65 (m, 8 H), 4.58 (dd, *J* = 10.8, 5.4 Hz, 2 H), 4.53 (d, *J* = 10.2 Hz, 1 H), 4.44–4.42 (m, 3 H), 4.28 (dd, *J* = 11.8, 1.8 Hz, 1 H), 4.19 (dd, *J* = 12.0, 5.4 Hz, 1 H), 3.96 (d, *J* = 10.2 Hz, 1 H), 3.89 (d, *J* = 9.6 Hz, 1 H), 3.73 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 3.67–3.60 (m, 5 H), 3.55 (*pseudo*-t, *J* = 9.6 Hz, 2 H), 3.52–3.47 (m, 2 H), 3.40 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 1.96 (s, 3 H), 1.23 (s, 9 H), 1.15 (s, 9 H), 1.13 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.71, 176.67, 176.5, 170.7, 162.8 (d, *J* = 246.0 Hz), 138.04, 138.02, 137.95, 137.9, 137.8, 137.6, 135.3 (d, *J* = 9.0 Hz), 128.5, 128.4, 128.3, 128.2, 128.1, 128.05, 128.01, 127.68, 127.66, 127.6, 127.4, 127.4, 127.2, 116.0 (d, *J* = 22.5 Hz), 101.3, 101.0, 86.4, 84.7, 83.2, 83.2, 79.0, 78.1, 77.9, 77.5, 75.3, 74.9, 74.9, 74.8, 73.2, 72.9, 71.4, 68.6, 68.2, 63.2, 38.79, 38.78, 38.75, 27.18, 27.17, 27.15, 20.9; HRMS (ESI) *m/z* calculated for $C_{83}H_{97}FKO_{19}S$; $[M+K]^+$ 1487.5966; found 1487.5952.



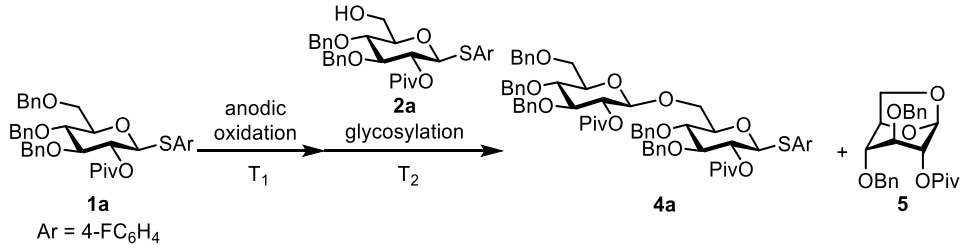
Automated electrochemical glycosylation of building blocks **1d** (0.106 mmol, 67.5 mg) and **2a** (0.211 mmol, 117 mg) afforded **3b** (0.0383 mmol, 57.1 mg) in 36% yield as a white solid, following the same procedure as that of compound **3a**. **4-Fluorophenyl 3,4-di-*O*-benzyl-2,6-di-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (3d)** TLC (Hexane/EtOAc 4:1): R_f 0.42; $[\alpha]_D$ = -11.0 (*c* = 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.48 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.33–7.16 (m, 30 H), 7.04 (*pseudo*-t, *J* = 8.4 Hz, 2 H), 5.07–5.02 (m, 4 H), 4.98 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.79–4.63 (m, 9 H), 4.57 (d, *J* = 12.0 Hz, 1 H), 4.47–4.43 (m, 3 H), 4.38 (dd, *J* = 12.0, 1.8 Hz, 1 H), 4.16 (dd, *J* = 12.4, 4.8 Hz, 1 H), 3.97 (d, *J* = 10.7 Hz, 1 H), 3.90 (dd, *J* = 11.3, 1.4 Hz, 1 H), 3.74 (*pseudo*-t, *J* = 9.0 Hz, 1H), 3.67–3.61 (m, 5 H), 3.57–3.54 (m, 2 H), 3.46–3.44 (m, 1 H), 3.41 (*pseudo*-t, *J* = 9.1 Hz, 1 H), 1.23 (s, 9 H), 1.17 (s, 9 H), 1.15 (s, 9 H), 1.12 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.1, 176.71, 176.66, 176.6, 162.8 (d, *J* = 246.3 Hz), 138.04, 137.93, 137.79, 137.69, 135.2 (d, *J* = 7.6 Hz), 128.6, 128.5, 128.48, 128.39. 128.35, 128.2, 127.98, 127.94, 127.91, 127.7, 127.64, 127.58, 127.45, 127.4, 127.21, 116.1 (d, *J* = 21.7 Hz), 101.27, 101.0, 86.4, 84.7, 83.2, 83.1, 79.0, 78.2, 77.9, 77.8, 77.3, 77.1, 76.9, 75.3, 75.1, 74.99, 74.96, 74.8, 73.5, 72.8, 38.79, 38.76, 27.3, 27.2, 27.18, 27.15; HRMS (ESI) *m/z* calculated for $C_{86}H_{103}FNaO_{19}S$; $[M+Na]^+$ 1513.6691; found 1513.6671.



Automated electrochemical glycosylation of building blocks **1e** (0.300 mmol, 238 mg) and **2a** (0.633 mmol, 351 mg) afforded **3e** (0.0875 mmol, 144 mg) in 29% yield as a white solid, following the same procedure as that of compound **3e**. **4-Fluorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-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-glucopyranoside (3e)**; TLC (Hexane/EtOAc 4:1); R_f 0.56; $[\alpha]_D$ = -13.3 (*c* = 1.0, $CHCl_3$) ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.71 (dd, *J* = 7.2, 3.6 Hz, 2 H), 7.67 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.49 (dd, *J* = 9.0, 5.4 Hz, 2 H), 7.38 (tt, *J* = 7.2, 1.8 Hz, 1 H), 7.36–7.15 (m, 33 H), 7.08 (dd, *J* = 7.2, 4.2 Hz, 2 H), 7.03 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.11–5.05 (m, 2 H), 4.97 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.77–4.46 (m, 16 H), 4.02 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 3.89–3.83 (m, 2 H), 3.75–3.60 (m, 7 H), 3.45 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.41 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.31–3.28 (m, 1 H), 1.22 (s, 9 H), 1.17 (s, 9 H), 1.13 (s, 9 H), 1.03 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.70, 176.68, 162.9 (d, *J* = 246.5 Hz), 138.2, 138.1, 137.9, 137.8, 135.8, 135.6, 135.3 (d, *J* = 8.25 Hz), 129.8, 129.7, 128.49, 128.45, 128.4, 128.3, 128.2, 128.1, 127.9, 127.84, 127.79, 127.76, 127.7, 127.65, 127.59, 127.5, 127.4, 127.2, 116.1 (d, *J* = 21.6 Hz), 101.3, 101.0, 86.4, 84.7, 83.30, 83.27, 79.1, 78.5, 77.9, 77.7, 77.3, 77.1, 76.9, 76.3, 75.33, 75.25, 75.0, 75.0, 74.9, 74.8, 73.1, 72.9, 71.4, 68.1, 67.9, 38.85, 38.82, 38.79, 27.3, 27.2, 26.9, 19.3; HRMS (ESI) *m/z* calculated for $C_{97}H_{113}FNaO_{18}SSi$; $[M+Na]^+$ 1667.7293; found 1667.7330.

4. Synthesis of disaccharides

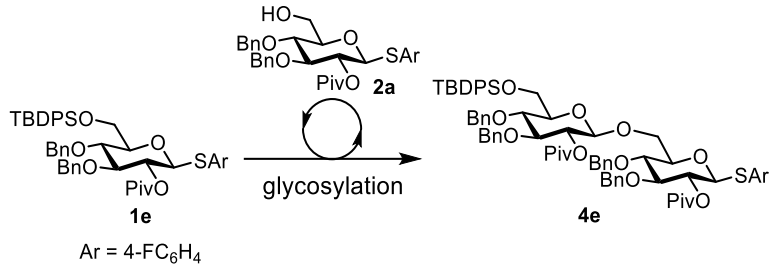
Preparation of 4-Fluorophenyl 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**4a**)



The automated synthesis of trisaccharide **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 (10 mm×20 mm). In the anodic chamber were placed terminal building block **1a** (0.300 mmol, 193 mg), Bu_4NOTf (1.48 mmol, 578 mg) and CH_2Cl_2 (15.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.296 mmol, 26 μL), Bu_4NOTf (1.51 mmol, 590 mg) and CH_2Cl_2 (15.0 mL). The constant current electrolysis (12.0 mA) was carried out at -40 °C with magnetic stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, building block **2a** (0.315 mmol, 176 mg) dissolved in CH_2Cl_2 (2.0 mL)

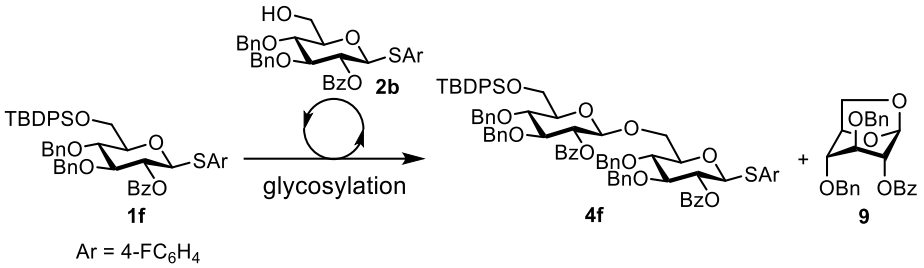
was subsequently added by the syringe pump under an argon atmosphere at -40 ℃, and kept for 60 min. After the cycle, Et_3N (0.5 mL) was added, and the mixture was filtered through a short column (4×3 cm) of silica gel to remove Bu_4NOTf. Removal of the solvent under reduced pressure and the crude product was purified with silica gel chromatography to obtain **4a** in 61% isolated yield (0.183 mmol, 196 mg) as a white solid. **4-Fluoropheny 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (4a)** TLC (hexane/EtOAc 4:1): R_f ; $[\alpha]_D$ = -12.6 (*c* = 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.48 (dd, *J* = 8.8, 5.3 Hz, 2 H), 7.40–7.24 (m, 22 H), 7.23–7.21 (m, 4 H), 7.15 (dd, *J* = 7.3, 2.4 Hz, 2 H), 7.04 (*pseudo*-t, *J* = 8.8 Hz, 2 H), 5.10 (dd, *J* = 9.2, 8.0 Hz, 1 H), 5.01 (dd, *J* = 9.8, 9.4 Hz, 1 H), 4.77–4.71 (m, 4 H), 4.69 (d, *J* = 11.1 Hz, 1 H), 4.66 (d, *J* = 11.0 Hz, 1 H), 4.58–4.52 (m, 3 H), 4.49–4.47 (m, 2 H), 4.46 (d, *J* = 7.9 Hz, 1 H), 4.00 (dd, *J* = 11.2, 1.5 Hz, 1 H), 3.75–3.70 (m, 2 H), 3.70–3.65 (m, 4 H), 3.61–3.57 (m, 1 H), 3.48 (ddd, *J* = 9.7, 4.4, 1.9 Hz, 1 H), 3.44 (*pseudo*-t, *J* = 9.3 Hz, 1 H), 1.23 (s, 9 H), 1.13 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.7, 162,8 (d, *J* = 246.7 Hz), 138.13, 138.09, 138.0, 137.8, 135.0 (d, *J* = 8.4 Hz), 128.45, 128.43, 128.40, 128.05, 128.01, 127.9, 127.83, 127.81, 127.67, 127.64, 127.5, 127.3, 116.2 (d, *J* = 21.7 Hz), 101.2, 86.7, 84.6, 83.4, 78.3, 77.8, 77.5, 75.23, 75.21, 75.0, 74.95, 73.5, 72.9, 71.4, 68.8, 68.1, 38.8, 38.77, 27.20, 27.15; HRMS (ESI) *m/z* calculated for $C_{63}H_{71}FKO_{12}S$, $[M+K]^+$ 1109.4283; found 1109.4279.

1,6-Anhydrosugar **5** was obtained as a major product (33% yield) when the reaction was performed at elevated temperature ($T_1 = T_2 = 0$ ℃). ^1H NMR and HRMS of **5** were compared with those reported in a literature to confirm its formation.[10] **1,6-Anhydro-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranose (5)** ^1H NMR ($CDCl_3$, 600 MHz) δ 7.33–7.25 (m, 10 H), 5.42 (s, 1 H), 4.78 (d, *J* = 12.0 Hz, 1 H), 4.71 (s, 1 H), 4.62 (d, *J* = 5.4 Hz, 1 H), 4.57 (d, *J* = 12.0 Hz, 1 H), 4.50 (d, *J* = 12.6 Hz, 1 H), 4.37 (d, *J* = 12.0 Hz, 1 H), 4.04 (d, *J* = 7.2 Hz, 1 H), 3.72 (*pseudo*-t, *J* = 6.0 Hz, 1 H), 3.50 (brs, 1 H), 3.33 (brs, 1 H), 1.22 (s, 9 H); HRMS (ESI) *m/z* calculated for $C_{25}H_{30}NaO_6$, $[M+Na]^+$ 465.1674; found 465.1669.



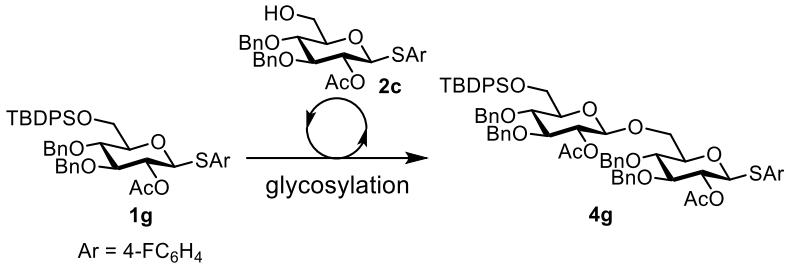
Automated electrochemical glycosylation of building blocks **1e** (0.299 mmol, 237 mg) and **2a** (0.315 mmol, 176 mg) afforded **3e** (0.216 mmol, 263 mg) in 72% yield as a white solid, following the same procedure as that of compound **4a**. **4-Fluorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (4e)**; TLC (Hexane/EtOAc 4:1); R_f 0.64; $[\alpha]_D$ = -11.7 (*c* = 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.72 (dd, *J* = 6.6, 3.6 Hz, 2 H), 7.67 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.49 (dd, *J* = 8.4, 4.8 Hz, 2 H), 7.39 (t, *J* = 7.8 Hz, 2 H), 7.33–7.23 (m, 18 H), 7.21 (d, *J* = 7.2 Hz, 2 H), 7.18 (dd, *J* = 6.0, 2.4 Hz, 2 H), 7.15 (dd, *J* = 6.0, 2.4 Hz, 2 H), 7.03 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 5.09 (dd, *J* = 9.6, 8.4 Hz, 1 H), 4.97 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.82 (d, *J* = 20.4 Hz, 1 H), 4.80 (d, *J* = 20.4 Hz, 1 H), 4.75–4.65 (m, 5 H), 4.53–4.48 (m, 3 H), 4.01 (d, *J* = 10.2 Hz, 1 H), 3.95–3.90 (m, 2 H), 3.87 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.72–3.61 (m, 4 H), 3.36 (ddd, *J* = 9.6, 3.0, 1.8 Hz, 1 H), 3.32 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 1.23 (s, 9 H), 1.16 (s, 9 H), 1.04 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 176.6, 162.1, 138.2, 138.1, 137.9, 137.7, 135.9, 135.6, 135.4 (d, *J* = 8.1 Hz), 133.6,

133.0, 129.69, 129.67, 128.43, 128.41, 128.39, 127.93, 127.88, 127.8, 127.7, 127.6, 127.5, 127.3, 116.2 (d, J = 21.8 Hz), 101.1, 86.3, 84.7, 83.4, 79.7, 78.0, 77.6, 76.2, 75.2, 75.2, 75.1, 74.9, 73.1, 71.4, 67.8, 62.7, 38.8, 29.7, 27.2, 26.9, 19.3; HRMS (ESI) *m/z* calculated for $C_{72}H_{83}FNaO_{12}SSi$; $[M+Na]^+$ 1241.5251; found 1241.5277.



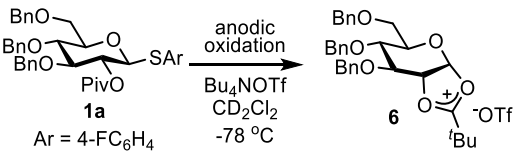
Automated electrochemical glycosylation of building blocks **1f** (0299 mmol, 243 mg) and **2b** (0.315 mmol, 182 mg) afforded **4f** (0.194 mmol, 245 mg) in 65% yield as a white solid, following the same procedure as that of compound **4a**. **4-Fluoropheny 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranosyl-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (4f).** TLC (Hexane/EtOAc 4:1): R_f = 0.39 ; $[\alpha]_D$ = 10.4 (c = 12.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.00 (d, J = 8.4 Hz, 2 H), 7.96 (d, J = 8.3 Hz, 2 H), 7.77 (dd, J = 7.8, 1.2 Hz, 2 H), 7.71 (dd, J = 7.9, 1.2 Hz, 2 H), 7.58 (*pseudo*-t, J = 7.4 Hz, 1 H), 7.46–7.34 (m, 11 H), 7.30–7.28 (m, 5 H), 7.25–7.21 (m, 5 H), 7.15–7.13 (m, 5 H), 7.10–7.06 (m, 5 H), 6.95 (*pseudo*-t, J = 8.7 Hz, 1 H), 5.37 (dd, J = 8.4, 8.1 Hz, 1 H), 5.06 (*pseudo*-t, J = 9.3 Hz, 1 H), 4.91 (d, J = 10.8 Hz, 1 H), 4.78 (d, J = 11.0 Hz, 1 H), 4.75 (d, J = 10.9 Hz, 1 H), 4.69 (d, J = 11.5 Hz, 1 H), 4.63 (d, J = 7.8 Hz, 1 H), 4.57 (d, J = 11.0 Hz, 1 H), 4.56 (d, J = 9.8 Hz, 1 H), 4.49 (d, J = 11.0 Hz, 1 H), 4.47 (d, J = 11.1 Hz, 1 H), 4.38 (d, J = 11.4 Hz, 1 H), 4.00–3.97 (m, 3 H), 3.84 (*pseudo*-t, J = 9.2 Hz, 1 H), 3.70 (*pseudo*-t, J = 8.9 Hz, 1 H), 3.65 (dd, J = 11.6 Hz, 6.0 Hz, 1 H), 3.58–3.56 (m, 1 H), 3.44 (d, J = 9.7 Hz, 1 H), 3.40 (*pseudo*-t, J = 9.2 Hz, 1 H), 1.06 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 165.0, 163.0 (d, J = 246.9 Hz), 138.1, 137.84, 137.83, 137.6, 136.0, 135.9 (d, J = 7.4 Hz), 135.6, 133.6, 123.7, 133.2, 132.99, 132.96, 130.0, 129.9, 129.7, 128.5, 128.48, 128.39, 128.36, 128.2, 128.16, 128.1, 127.99, 127.88, 127.83, 127.8, 127.74, 127.65, 126.65, 126.63, 116.0 (d, J = 21.7 Hz), 101.2, 85.6, 84.13, 83.0, 79.1, 77.8, 77.5, 77.3, 77.1, 76.9, 76.2, 75.3, 75.2, 75.1, 74.8, 73.9, 72.0, 67.7, 62.6, 26.9, 19.4; HRMS (ESI) *m/z* calculated for $C_{76}H_{75}FKO_{12}SSi$, $[M+K]^+$ 1297.4364; found 1297.4343.

1,6-Anhydrosugar **9** was obtained as a minor product (7%) when the reaction was performed at elevated temperature ($T_1 = T_2$ = 0 °C). ^{1}H NMR and HRMS of **9** were compared with those reported in a literature to confirm its formation.[11] **1,6-Anhydro-2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-glucopyranose (9)** ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.10–8.06 (m, 2 H), 7.60–7.55 (m, 1 H), 7.45–7.40 (m, 2 H), 7.35–7.23 (m, 10 H), 5.59 (s, 1 H), 5.01 (s, 1 H), 4.83 (d, J = 12.0 Hz, 1 H), 4.69 (d, J = 5.4 Hz, 1 H), 4.61 (d, J = 12.0 Hz, 1 H), 4.50 (d, J = 12.0 Hz, 1 H), 4.46 (d, J = 12.0 Hz, 1 H), 4.13 (d, J = 7.2 Hz, 1 H), 3.78 (*pseudo*-t, J = 6.6 Hz, 1 H), 3.70 (*pseudo*-t, J = 1.8 Hz, 1 H), 3.42 (s, 1 H); HRMS (ESI) *m/z* calculated for $C_{27}H_{26}NaO_6$, $[M+Na]^+$ 469.1622; found 469.1606.



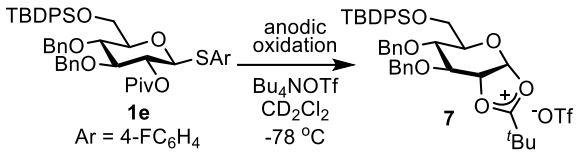
Automated electrochemical glycosylation of building blocks **1g** (0.305 mmol, 229 mg) and **2c** (0.315 mmol, 161 mg) afforded **4g** (0.172 mmol, 195 mg) in 56% yield as a white solid, following the same procedure as that of compound **4a**. **4-Fluoropheny 2-*O*-acetyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranosyl-(1→6)-2-*O*-acetyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (4g).** TLC (Hexane/EtOAc 4:1): R_f ; $[\alpha]_D$ = 0.3 (*c* = 4.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.74 (d, *J* = 7.3 Hz, 2 H), 7.68 (d, *J* = 7.7 Hz, 2 H), 7.47 (dd, *J* = 7.9, 5.4 Hz, 2 H), 7.41–7.25 (m, 22 H), 7.24–7.19 (m, 6 H), 5.28 (s, 1 H), 5.06 (*pseudo*-t, *J* = 8.6 Hz, 1 H), 4.89–4.87 (m, 2 H), 4.84 (d, *J* = 11.3 Hz, 1 H), 4.76 (d, *J* = 11.0 Hz, 1 H), 4.75 (d, *J* = 11.3 Hz, 1 H), 4.73 (d, *J* = 11.3 Hz, 1 H), 4.69 (d, *J* = 11.3 Hz, 1 H), 4.64 (d, *J* = 11.3 Hz, 1 H), 4.55 (d, *J* = 11.1 Hz, 1 H), 4.50 (d, *J* = 10.0 Hz, 1 H), 4.42 (d, *J* = 8.0 Hz, 1 H), 4.13 (d, *J* = 9.8 Hz, 1 H), 3.95–3.90 (m, 3 H), 3.68–3.64 (m, 2 H), 3.60–3.55 (m, 2 H), 3.39 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.34 (d, *J* = 9.6 Hz, 1 H), 1.99 (s, 3 H), 1.96 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.45. 169.42, 162.9 (d, *J* = 247.1 Hz), 137.9, 137.7, 135.9, 135.6, 135.3 (d, *J* = 8.5 Hz), 133.6, 132.9, 129.71, 129.70, 128.52, 128.49, 128.0, 127.97, 127.94, 127.87, 127.84, 127.8, 127.7, 127.1, 116.1 (d, *J* = 21.8 Hz), 85.8, 84.3, 83.1, 79.0, 77.8, 77.7, 76.0, 75.4, 75.3, 75.2, 75.0, 73.1, 71.5, 67.8, 62.4, 53.5, 26.8, 21.0, 19.3; HRMS (ESI) *m/z* calculated for $C_{66}H_{71}FNaO_{12}SSi$, $[M+Na]^+$ 1157.4312; found 1157.4324.

5. NMR analysis of glycosyl dioxalenium ions

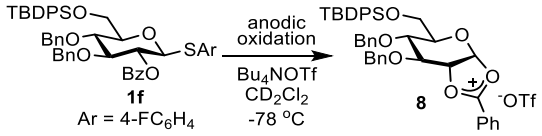


The anodic oxidation of thioglycoside **1a** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm×20 mm). In the anodic chamber were placed terminal building block **1a** (0.100 mmol, 64.7 mg), Bu_4NOTf (0.49 mmol, 191 mg) and CD_2Cl_2 (5.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.091 mmol, 8 μL), Bu_4NOTf (0.50 mmol, 195 mg) and CD_2Cl_2 (5.0 mL). The constant current electrolysis (4.0 mA) was carried out at -80 °C with magnetic stirring until 1.05 F/mol of electricity was consumed. After the electrolysis, the reaction mixture of anodic chamber was transferred to 5 mm ϕ NMR tubes with a septum cap under argon atmosphere at -78 °C. The NMR measurement was carried out at low temperature. Chemical shifts were reported using signals of CH_2Cl_2 at 5.32 ppm for ^{1}H NMR and CD_2Cl_2 at 53.8 ppm for ^{13}C NMR as standard. Selected data for **3,4,6-tri-*O*-benzyl-D-glucopyranosyl pivaloxonium triflate (6)**. ^{1}H NMR (CD_2Cl_2, 500 MHz, at -40 °C) δ 5.77 (d, *J* = 7.5 Hz, 1 H, H-2), 4.54 (d, *J* = 12.0 Hz, 1 H, benzylic-H), 4.47 (d, *J* = 11.5 Hz, 1 H, benzylic-H), 4.46 (d, *J* = 12.0 Hz, 1 H, benzylic-H), 4.43 (d, *J* = 11.5 Hz, 1 H, benzylic-H), 4.39 (d, *J* = 11.5 Hz, 1 H, benzylic-H), 4.32 (d, *J* = 11.5 Hz, 1 H, benzylic-H), 3.99 (brs, 1 H, H-3), 3.86 (dd, *J* = 10.0, 5.5 Hz, 1 H, H-5), 3.74 (brs, 1 H, H-4), 3.58 (dd, *J*

= 10.5, 5.5 Hz, 1 H, H-6), 3.49 (dd, *J* = 10.0, 5.0 Hz, 1 H, H-6); ^{13}C NMR (CD_2Cl_2, 125 MHz, at -80 °C) δ 197.1 (cationic-C), 111.5 (C-1), 77.5 (C-2), 74.1 (C-5), 72.6 (benzylic-C), 71.6 (benzylic-C), 71.5 (benzylic-C), 69.1 (C-4), 67.8 (C-3 and C-6).



3,4-Di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-D-glucopyranosyl pivaloxonium triflate (7). Anodic oxidation of thioglycoside **1e** (0.102 mmol, 81.0 mg) afforded **7**. Selected data for **7**. ^{1}H NMR (CD_2Cl_2, 500 MHz, at -40 °C) δ 5.79 (d, *J* = 7.0 Hz, 1 H, H-2), 4.60 (d, *J* = 12.0 Hz, 1 H, benzylic-H), 4.51 (d, *J* = 12.0 Hz, 1 H, benzylic-H), 4.46 (d, *J* = 11.0 Hz, 1 H, benzylic-H), 4.28 (d, *J* = 11.5 Hz, 1 H, benzylic-H), 4.00 (brs, 1 H, H-3), 3.87 (brs, 1 H, H-4), 3.76–3.71 (m, 1 H, H-6), 3.67–3.62 (m, 2 H, H-5 and H-6); ^{13}C NMR (CD_2Cl_2, 125 MHz, at -80 °C) δ 196.9 (cationic-C), 112.2 (C-1), 78.4 (C-2), 75.1 (C-5), 72.0 (benzylic-C), 71.6 (benzylic-C), 69.7 (C-4), 69.3 (C-3), 61.3 (C-6).



3,4-Di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-D-glucopyranosyl benzoxonium triflate (8). Anodic oxidation of thioglycoside **1f** (0.101 mmol, 82.2 mg) afforded **8**. Selected data for **8**. ^{1}H NMR (CD_2Cl_2, 500 MHz, at -80 °C) δ 5.89 (d, *J* = 7.0 Hz, 1 H, H-2), 4.70 (d, *J* = 11.5 Hz, 1 H, benzylic-H), 4.59 (d, *J* = 12.0 Hz, 1 H, benzylic-H), 4.36 (d, *J* = 10.5 Hz, 1 H, benzylic-H), 4.27 (d, *J* = 10.5 Hz, 1 H, benzylic-H), 4.26 (brs, 1 H, H-3), 4.07 (brs, 2 H, H-4 and H-5), 3.88–3.80 (m, 1 H, H-6), 3.76–3.68 (m, 1 H, H-6); ^{13}C NMR (CD_2Cl_2, 125 MHz, at -80 °C) δ 180.2 (cationic-C), 110.7 (C-1), 77.4 (C-2), 75.2 (C-5), 72.2 (benzylic-C), 71.8 (benzylic-C), 70.6 (C-4), 69.5 (C-3), 61.6 (C-6).

References

[1] a) Selective Glycosylations, C. S. Bennett, Ed. Wiley-VCH, Weinheim, Germany **2017**. b) W.-L. Leng, H. Yao, J.-X. He, X.-W. Liu, *Acc*. *Chem*. *Res*. **2018**, *51*, 628–639. c) M. Guberman, P. H. Seeberger, *J*. *Am*. *Chem*. *Soc*. **2019**, *141*, 5581–5592.

[2] a) D. Crich, Z. Dai, S. Gastaldi, *J*. *Org*. *Chem*. **1999**, *64*, 5224–5229. b) Y. Zeng, Z. Wang, D. Whitfield, X. Huang, *J*. *Org*. *Chem*. **2008**, *73*, 7952–7962. c) T. Hamsen, H. Elferink, J. M. A. van Hengst, K. J. Houthuijs, W. A. Remmerswaal, A. Kromm, G. Berden, S. van der Vorm, A. M. Rijs, H. S. Overkleeft, D. V. Filippov, F. P. J. T. Rutjes, G. A. van der Marel, J. Martens, J. Oomens, J. D. C. Codée, T. J. Boltje, *Nature*. *Commun*. **2020**, *11*:2664. d) A. A. Hettikankanamalage, R. Lassfolk, F. S. Ekholm, R. Leino, D. Crich, *Chem*. *Rev*. **2020**, *120*, 7104–7151.

[3] a) M. W. Breedveld, K. J. Miller, *Microbiol*. *Rev*. **1994**, *58*, 145–161. b) A. V. Nair, S. N. Gummadi, M. Doble, *Biotechnol*. *Lett*. **2016**, *38*, 1519–1525. c) E. Cho, D. Jeong, Y. Choi, S. Jung, *J*. *Incl*. *Phenom*. *Macrocycl*. *Chem*. **2016**, *85*, 175–185.

[4] a) S. Manmode, K. Matsumoto, T. Itoh, T. Nokami, *Asian J*. *Org*. *Chem*. **2018**, *7*, 1719–1729; b) A. Shibuya, T. Nokami, *Chem*. *Rec*. **2021**, *21*, 2389–2396. c) K. Yano, N. Sasaki, T. Itoh, T. Nokami, *J*. *Synth*. *Org*. *Chem*. *Jpn* **2021**, *79*, 839–848.

[5] S. Manmode, M. Kato, T. Ichiyanagi, T. Nokami, T. Itoh, *Asian J*. *Org*. *Chem*. **2018**, *7*, 1802–1805.

[6] a) J. Yoshida, S. Suga, *Chem*. *Eur*. *J*. **2002**, *8*, 2650–2658. b) J. Yoshida, Y. Ashikari, K. Matsumoto, T. Nokami, *J*. *Synth*. *Chem*. *Soc*. *Jpn* **2013**, *71*, 1136–1144. c) J. Yoshida, A. Shimizu, Y. Ashikari, T. Morofuji, R. Hayashi, T. Nokami, A. Nagaki, *Bull*. *Chem*. *Soc*. *Jpn* **2015**, *88*, 763–775.

[7] ^{1}H NMR spectra of the VT-NMR experiments is normalized by the peak height of CH_2Cl_2 at 5.32 ppm.

[8] a) D. Crich, S. Sun, *J*. *Am*. *Chem*. *Soc*. **1997**, *119*, 11217–11223. b) T. G. Frihed, M. Bols, C. M. Pedersen, *Chem*. *Rev*. **2015**, *115*, 4963–5013.

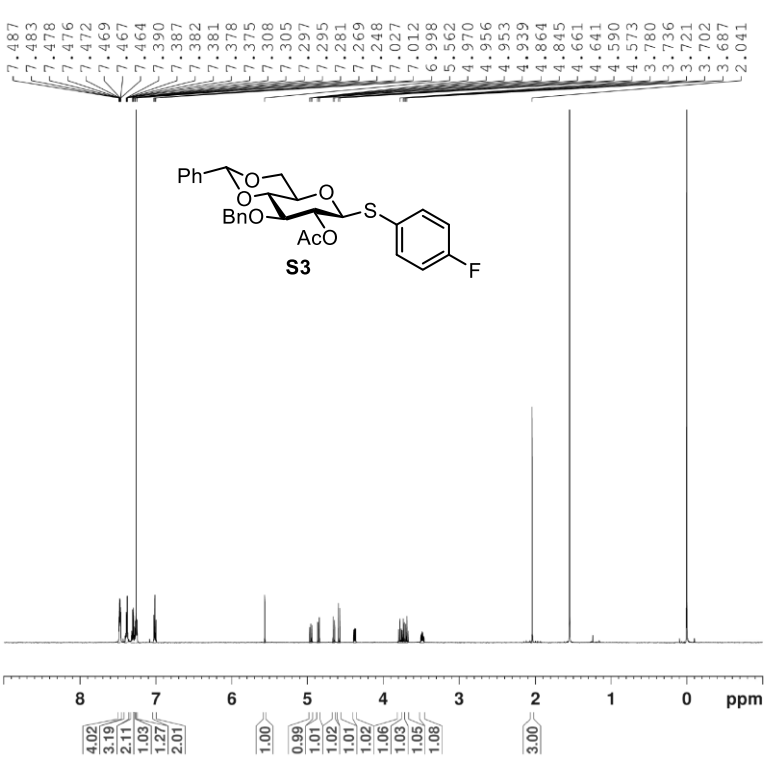
[9] a) T. Nokami, A. Shibuya, H. Tsuyama, S. Suga, A. A. Bowers, D. Crich, J. Yoshida, *J*. *Am*. *Chem*. *Soc*. **2007**, *129*, 10922–10928. b) T. Nokami, A. Shibuya, S. Manabe, Y. Ito, J. Yoshida, *Chem*. *Eur*. *J*. **2009**, *15*, 2252–2255. c) T. Nokami, Y. Nozaki, Y. Saigusa, A. Shibuya, S. Manabe, Y. Ito, J. Yoshida, *Org*. *Lett*. **2011**, *13*, 1544–1547. d) T. Nokami, A. Shibuya, Y. Saigusa, S. Manabe, Y. Ito, J. Yoshida, *Beilstein J*. *Org*. *Chem*. **2012**, *8*, 456–460.

[10] X. Zhu, R. T. Dere, J. Jiang, L. Zhang, X. Wang, *J*. *Org*. *Chem*. **2011**, *76*, 10187-10197.

[11] H. Hori, Y. Nishida, H. Ohrui, H. Meguro, *J*. *Org*. *Chem*. **1989**, *54*, 1346-1353.

^{1}H and ^{13}C NMR spectra of synthetic intermediate S3 and building blocks

^{1}H NMR



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TD                    65536
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FIDRES                0.188225 Hz
AQ                2.6564426 sec
RG                       203
DW                  40.533 usec
DE                   6.50 usec
TE                   297.6 K
D1               1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.00 usec
PL1                    -2.00 dB
PL1W            18.91009140 W
SFO1           600.1337060 MHz
SI                      32768
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PC                      1.00
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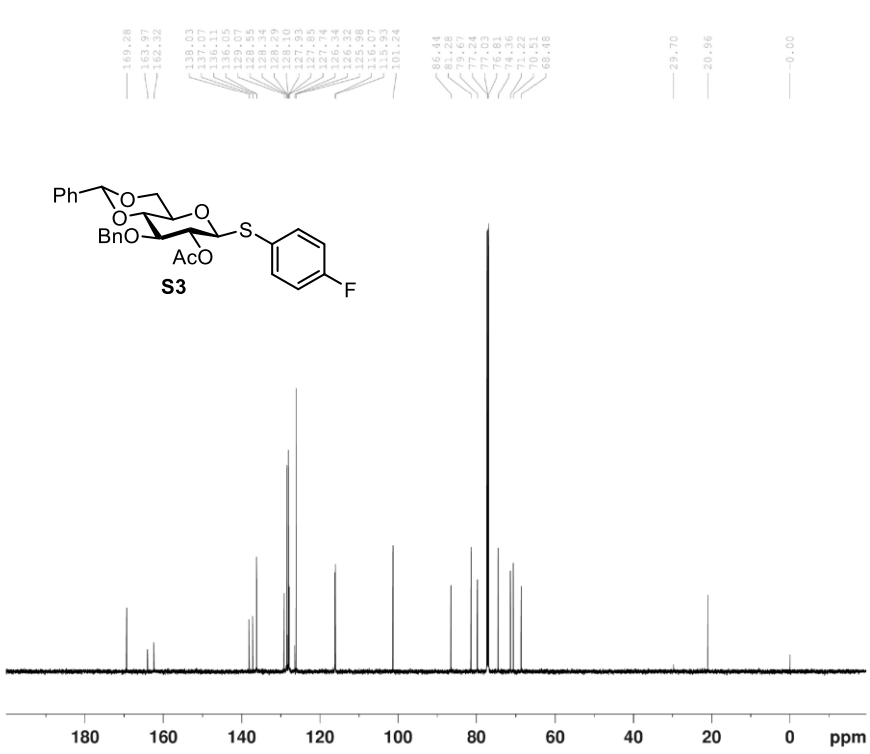
^{13}C NMR



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FIDRES                0.550197 Hz
AQ                0.9088159 sec
RG                       203
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DE                   6.50 use
TE                   298.5 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                        1

======== CHANNEL f1 =======
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P1                     10.00 use
PL1                    -1.00 dB
PL1W           125.22619629 W
SFO1           150.9178988 MHz

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CPDPRG2             waltz16
NUC2                      1H
PCPD2                  80.00 use
PL2                    -2.00 dB
PL12                   13.78 dB
PL13                   14.00 dB
PL2W            18.91009140 W
PL12W            0.49968192 W
PL13W            0.47499999 W
SFO2           600.1324005 MHz
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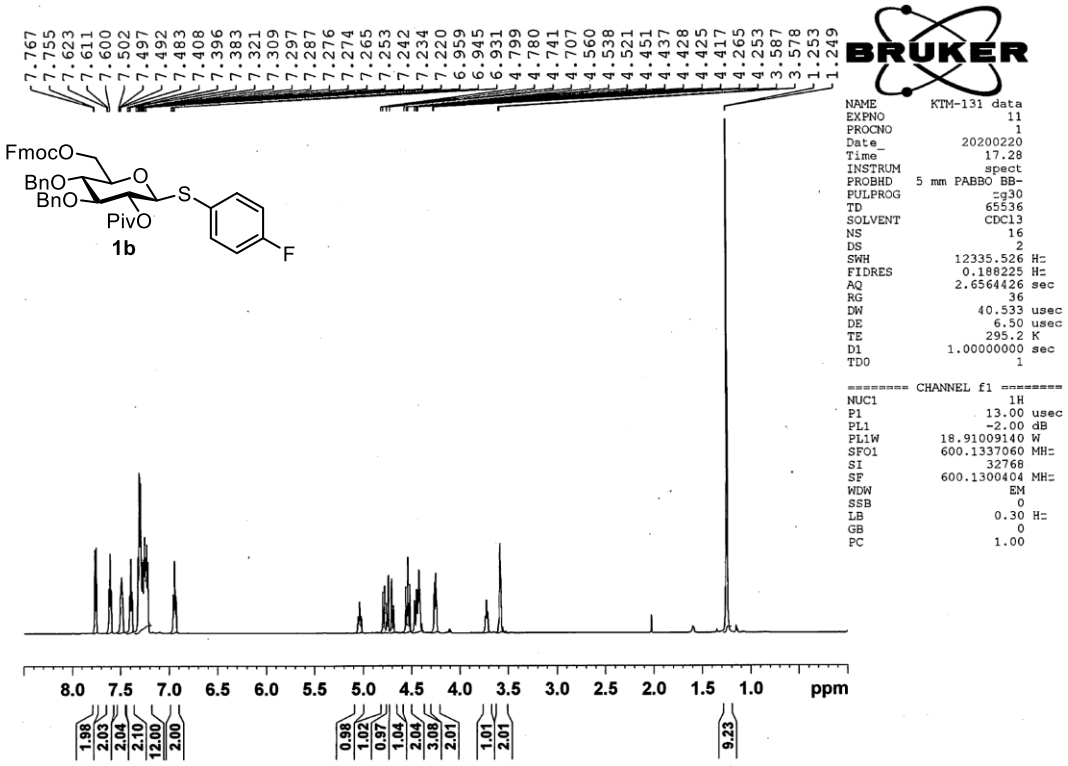
^{1}H NMR

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SOLVENT           CDCl3
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DS                    2
SWH           12335.526 Hz
FIDRES        0.188225 Hz
AQ            2.6564426 sec
RG                   36
DW               40.533 usec
DE                6.50 usec
TE                295.2 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                  1H
P1                13.00 usec
PL1               -2.00 dB
PL1W        18.91009140 W
SFO1       600.1337060 MHz
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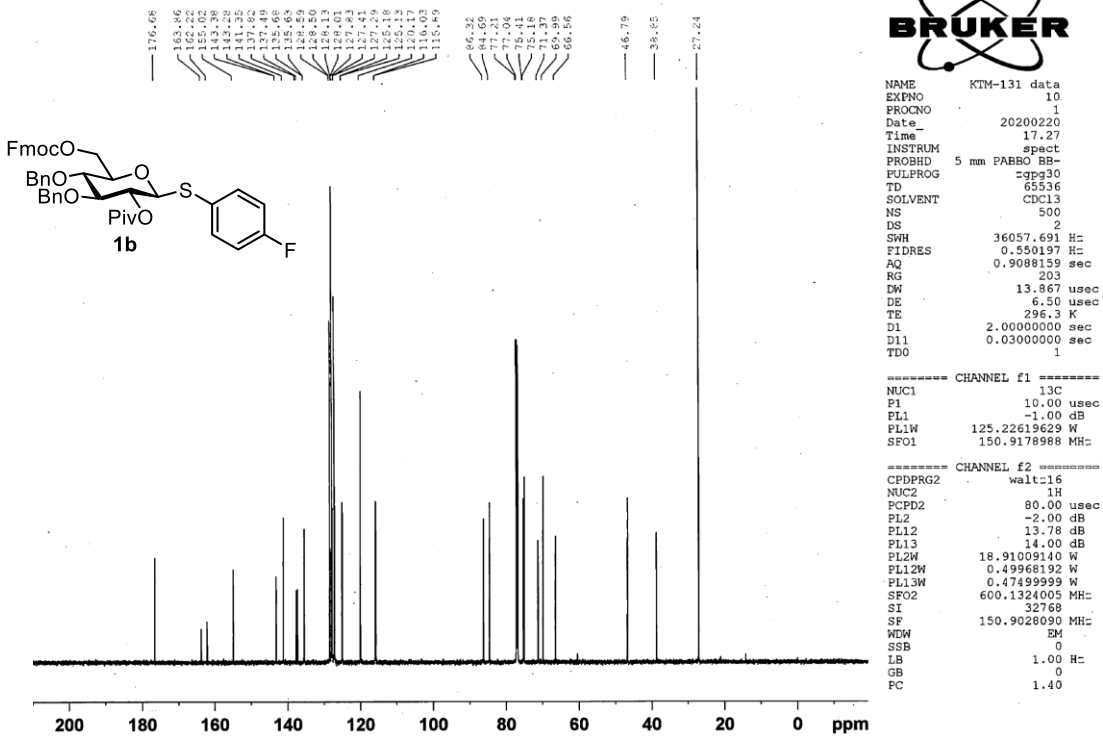
^{13}C NMR

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DS                    2
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FIDRES        0.550197 Hz
AQ            0.9088159 sec
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======== CHANNEL f1 ========
NUC1                 13C
P1                10.00 usec
PL1               -1.00 dB
PL1W       125.22619629 W
SFO1       150.9178988 MHz

======== CHANNEL f2 ========
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NUC2                  1H
PCPD2             80.00 usec
PL2               -2.00 dB
PL12              13.78 dB
PL13              14.00 dB
PL2W        18.91009140 W
PL12W        0.49968192 W
PL13W        0.47499999 W
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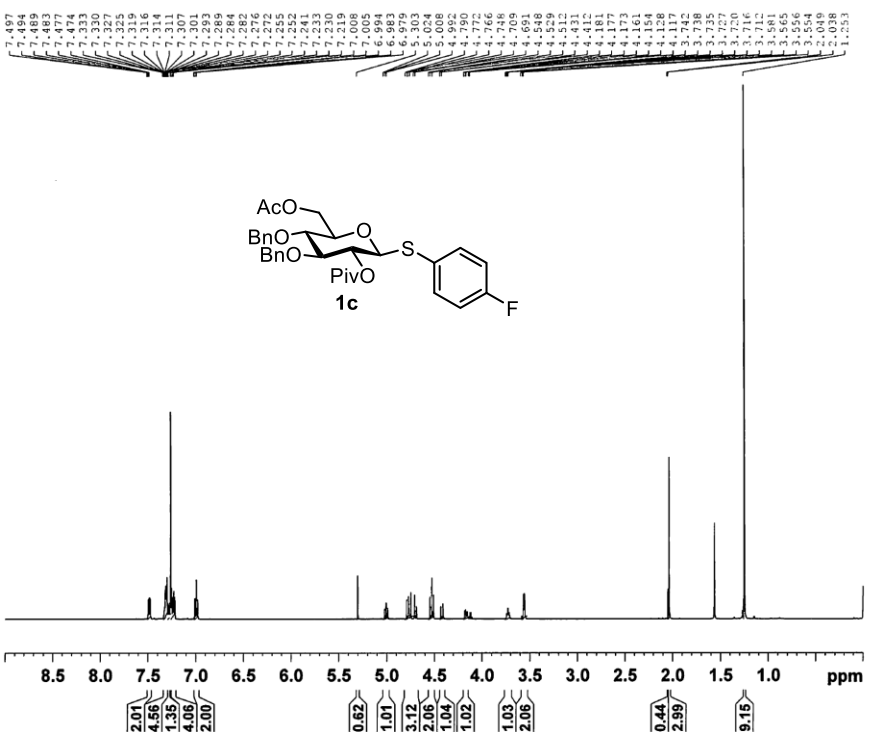
^{1}H NMR

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FIDRES          0.188225 Hz
AQ              2.6564426 sec
RG                    203
DW                 40.533 usec
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TE                 292.5 K
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TD0                     1

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PL1                 -2.00 dB
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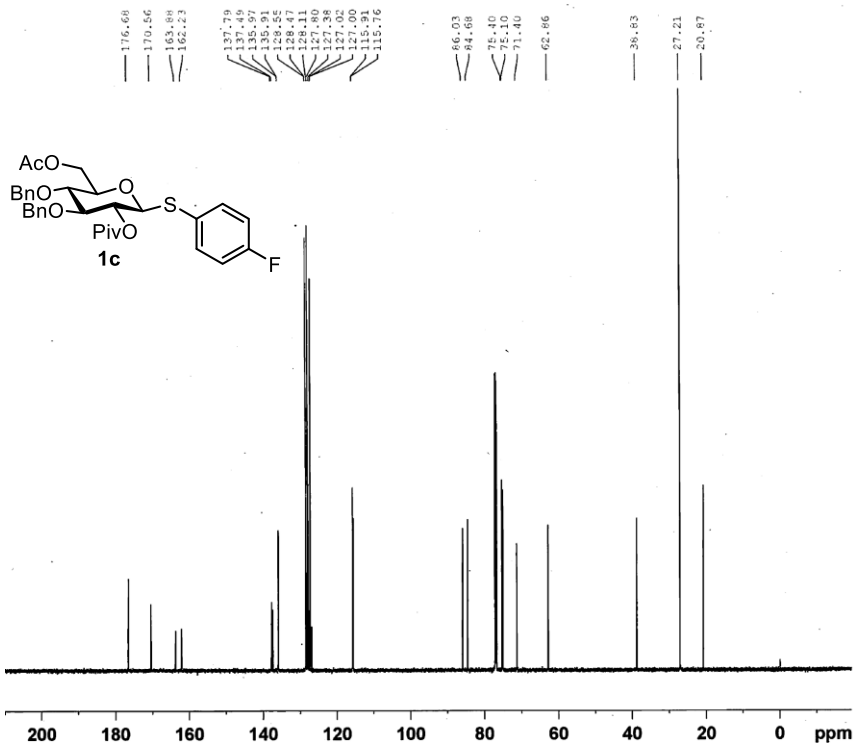
^{13}C NMR

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FIDRES          0.550197 Hz
AQ              0.9088159 sec
RG                    203
DW                 13.867 usec
DE                  6.50 usec
TE                 296.6 K
D1              2.00000000 sec
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TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.00 usec
PL1                 -1.00 dB
PL1W        125.22619629 W
SFO1         150.9178988 MHz

======== CHANNEL f2 ========
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NUC2                   1H
PCPD2               80.00 usec
PL2                 -2.00 dB
PL12                13.78 dB
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PL2W         18.91009140 W
PL12W         0.49968192 W
PL13W         0.47499999 W
SFO2        600.1324005 MHz
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PC                   1.40
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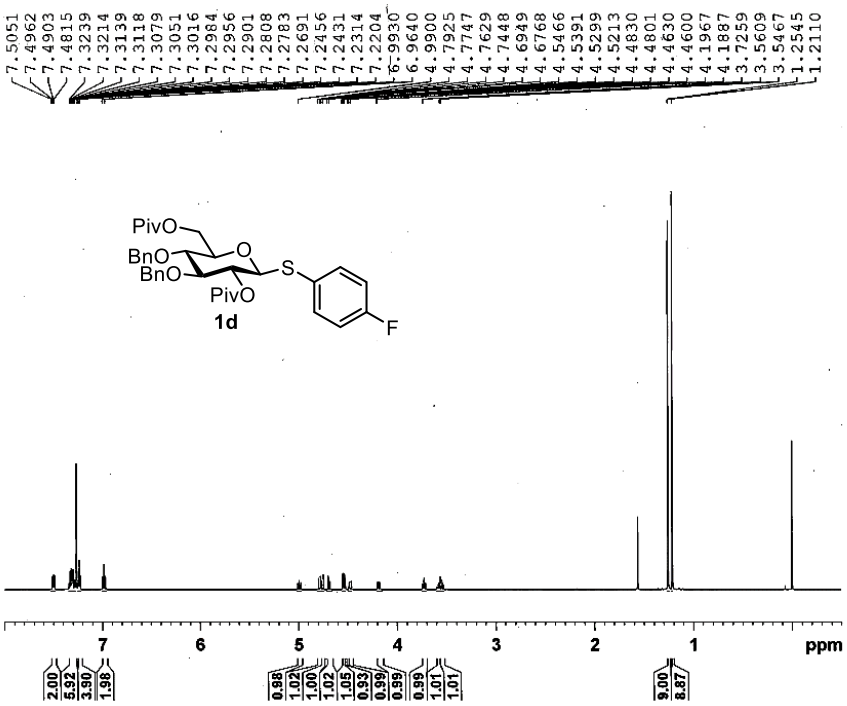
^{1}H NMR

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FIDRES             0.188225 Hz
AQ                 2.6564426 sec
RG                       203
DW                  40.533 usec
DE                   6.50 usec
TE                   294.0 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
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P1                   13.00 usec
PL1                  -2.00 dB
PL1W              18.91009140 W
SFO1              600.1337060 MHz
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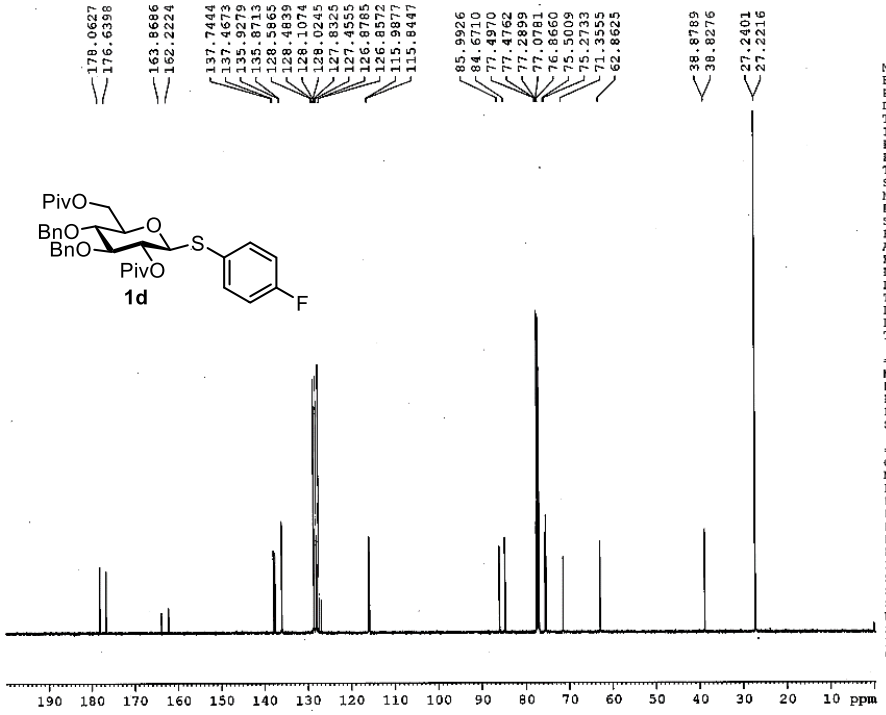
^{13}C NMR

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NS                       500
DS                         2
SWH                36057.691 Hz
FIDRES             0.550197 Hz
AQ                 0.9088159 sec
RG                       203
DW                  13.867 usec
DE                   6.50 usec
TE                   295.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                   10.00 usec
PL1                  -1.00 dB
PL1W             125.22619629 W
SFO1              150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                80.00 usec
PL2                  -2.00 dB
PL12                 13.78 dB
PL13                 14.00 dB
PL2W              18.91009140 W
PL12W              0.49968192 W
PL13W              0.47499999 W
SFO2              600.1324005 MHz
SI                       32768
SF                150.9028090 MHz
WDW                       EM
SSB                        0
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GB                         0
PC                      1.40
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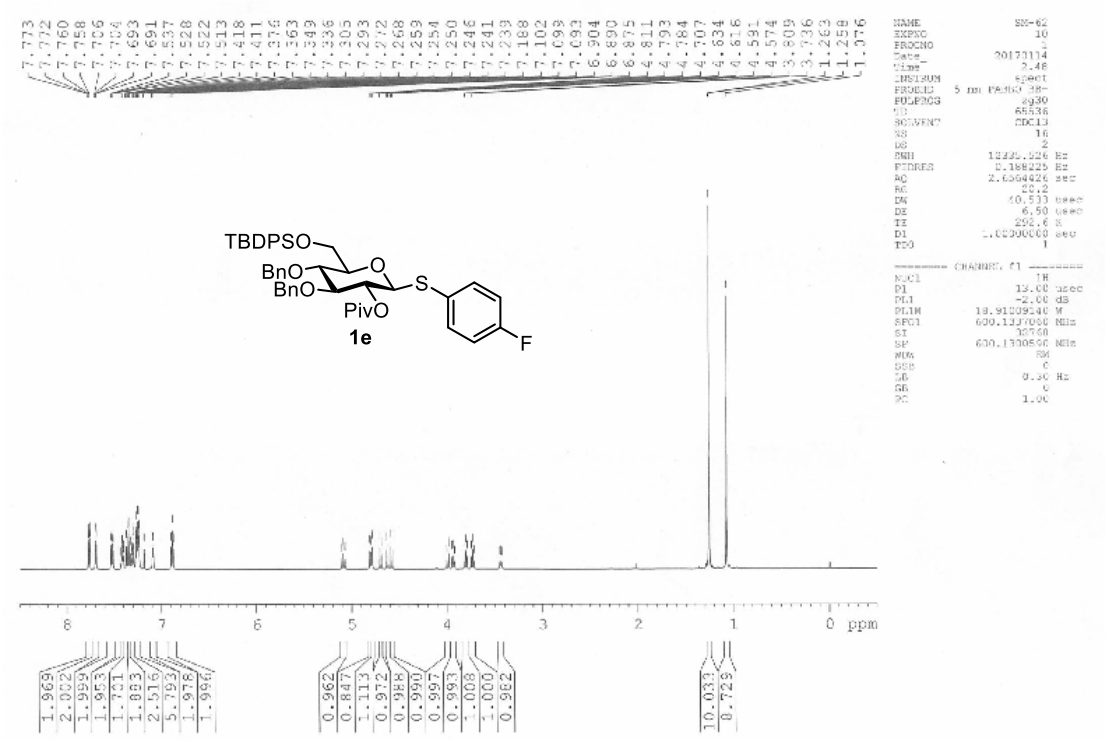
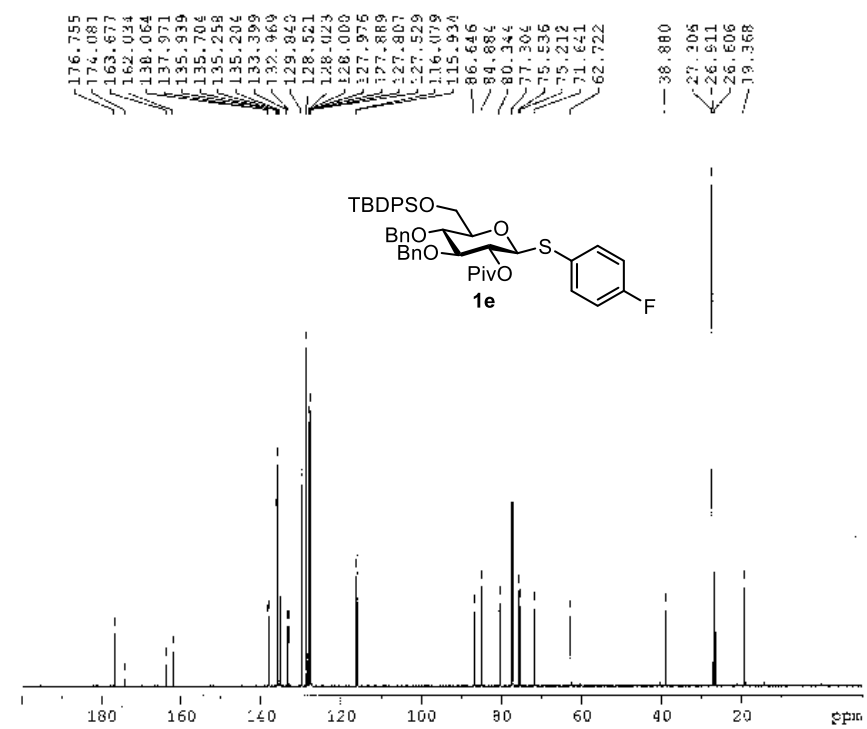
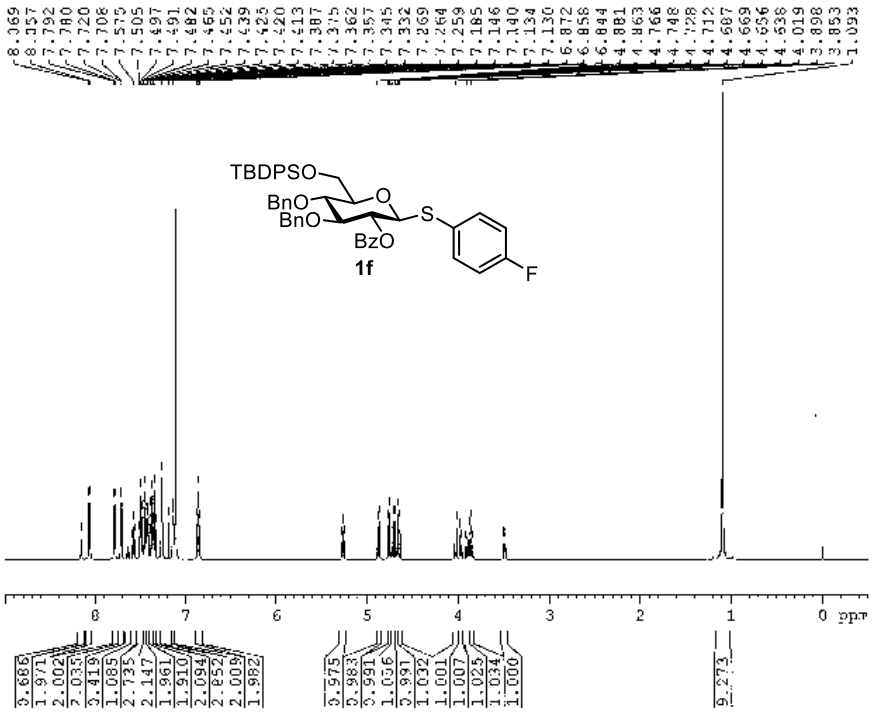
[1]H NMR



[13]C NMR



^{1}H NMR



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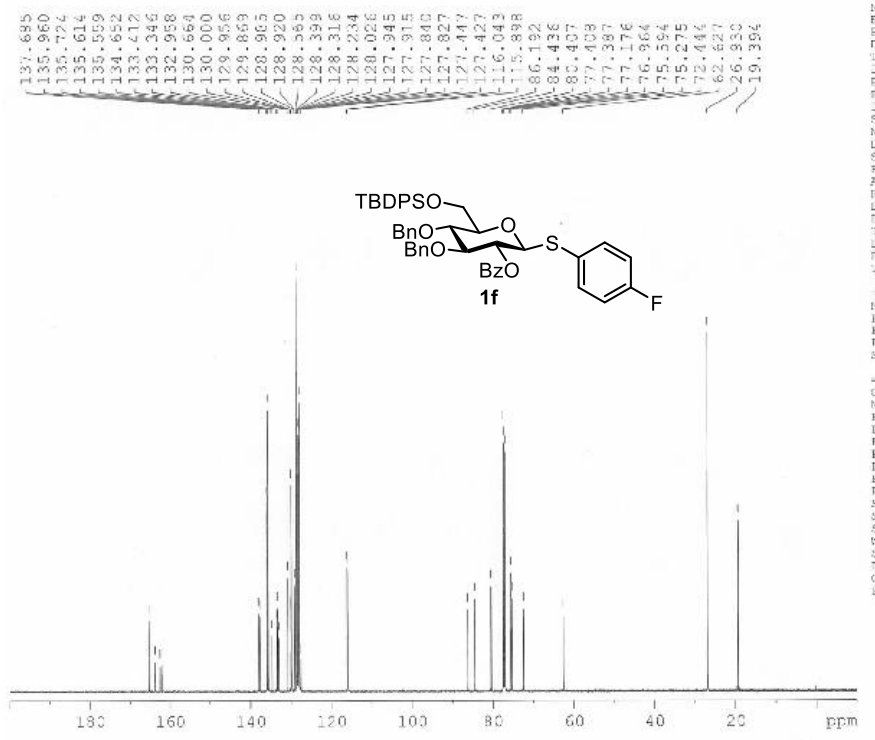
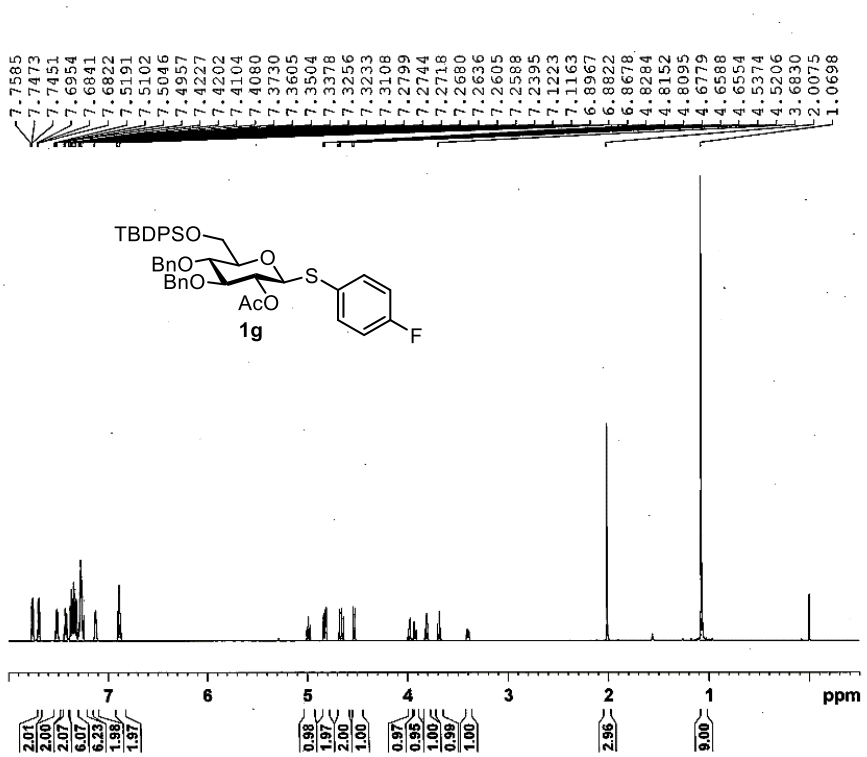


^{1}H NMR



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FIDRES	0.188225 Hz
AQ	2.6564426 sec
RG	114
DW	40.533 usec
DE	6.50 usec
TE	294.9 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	13.00 usec
PL1	-2.00 dB
PL1W	18.91009140 W
SFO1	600.1337060 MHz
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SF	600.1300284 MHz
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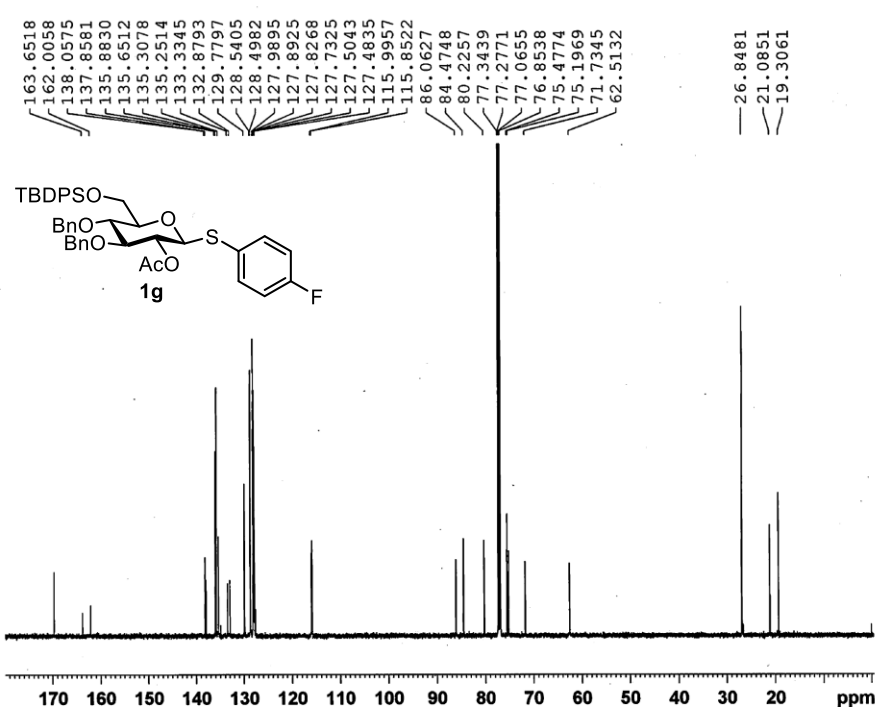
PC	1.00

^{13}C NMR



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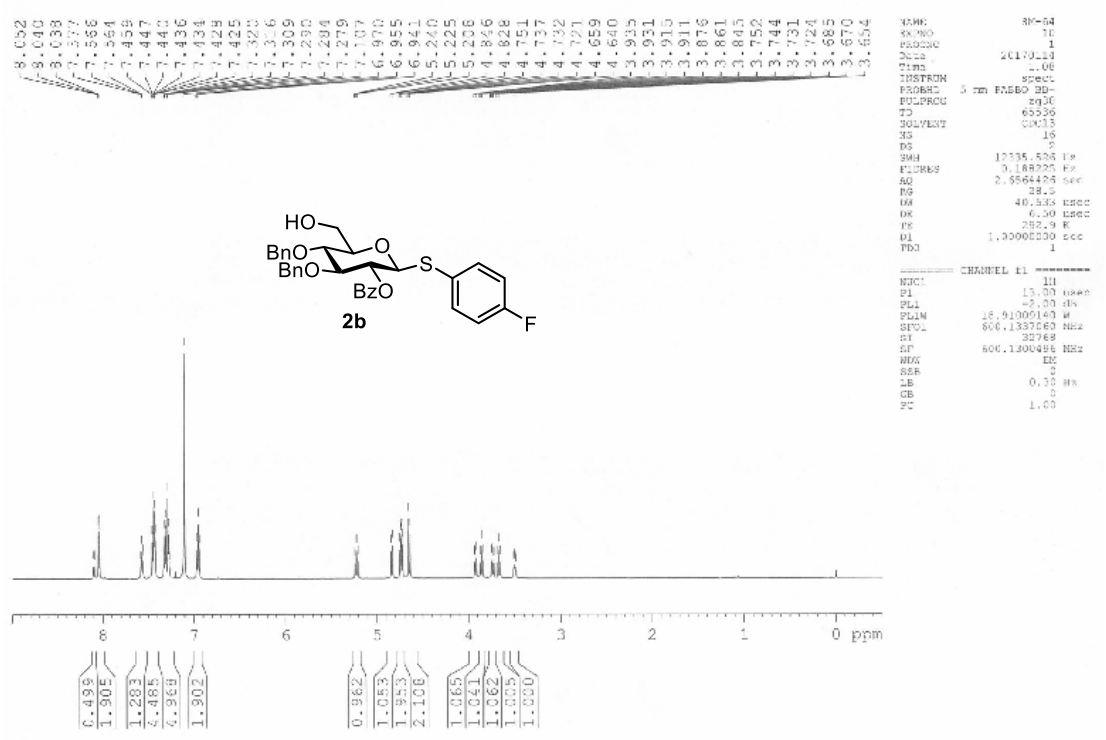
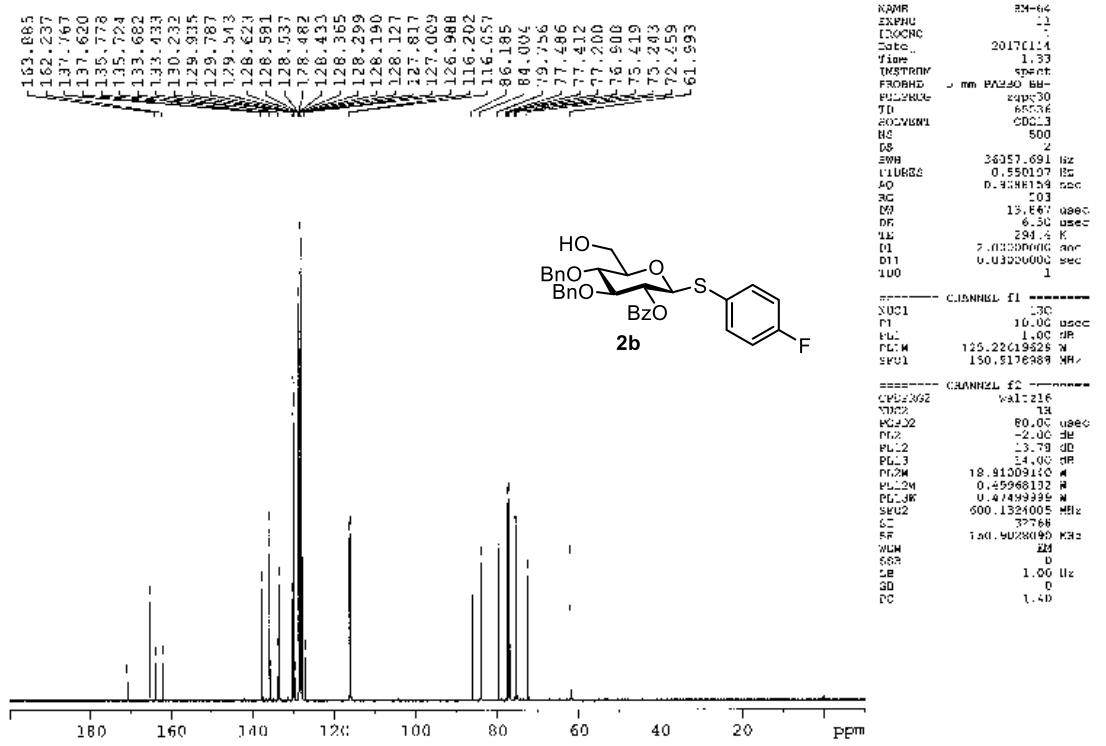
Time	9.25
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	500
DS	2
SWH	36057.691 Hz
FIDRES	0.550197 Hz
AQ	0.9088159 sec
RG	203
DW	13.867 usec
DE	6.50 usec
TE	295.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	10.00 usec
PL1	-1.00 dB
PL1W	125.22619629 W
SFO1	150.9178988 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	13.78 dB
PL13	14.00 dB
PL2W	18.91009140 W
PL12W	0.49968192 W
PL13W	0.47499999 W
SFO2	600.1324005 MHz
SI	32768
SF	150.9028090 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

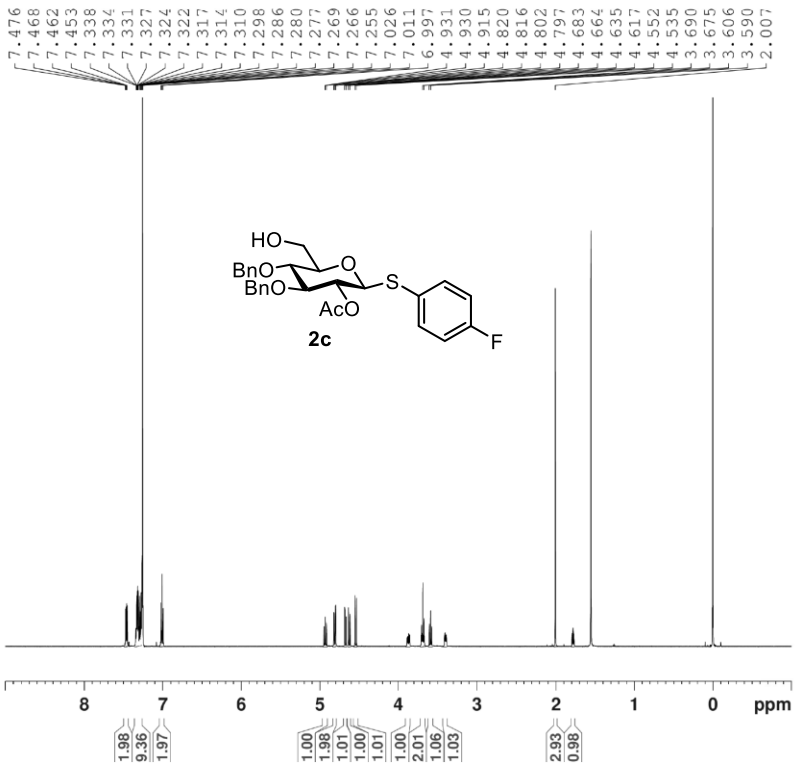
^{1}H NMR

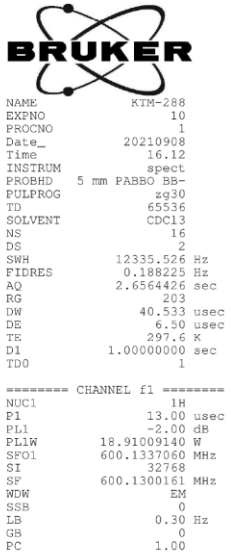


^{13}C NMR



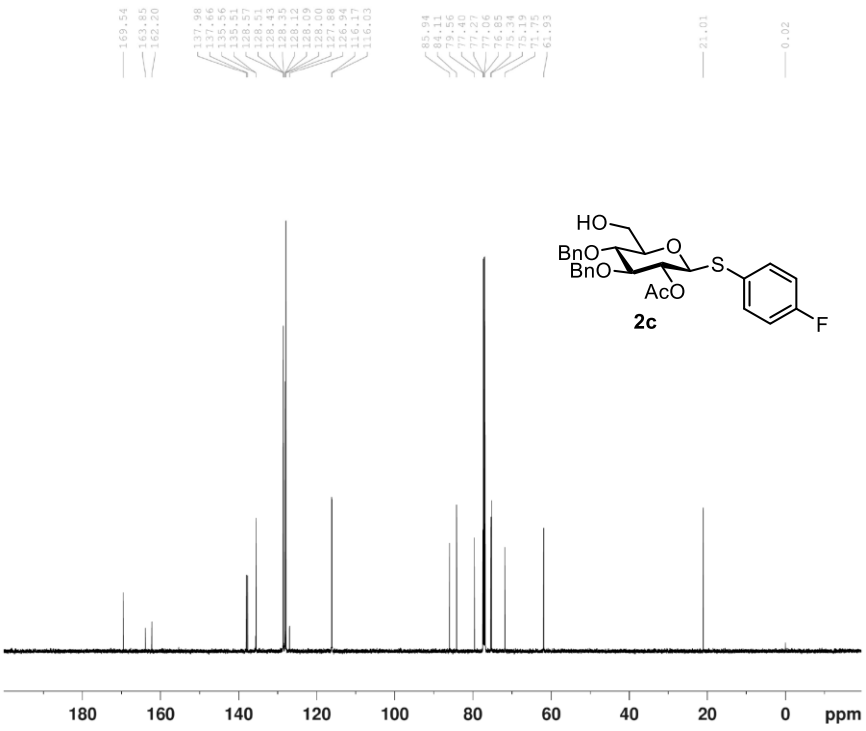
^{1}H NMR





```
NAME                 KTM-288
EXPNO                     10
PROCNO                     1
Date_               20210908
Time                   16.12
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               12335.526 Hz
FIDRES             0.188225 Hz
AQ                 2.6564426 sec
RG                      203
DW                   40.533 usec
DE                    6.50 usec
TE                   297.6 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.00 usec
PL1                    -2.00 dB
PL1W           18.91009140 W
SFO1           600.1337060 MHz
SI                     32768
SF             600.1300161 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

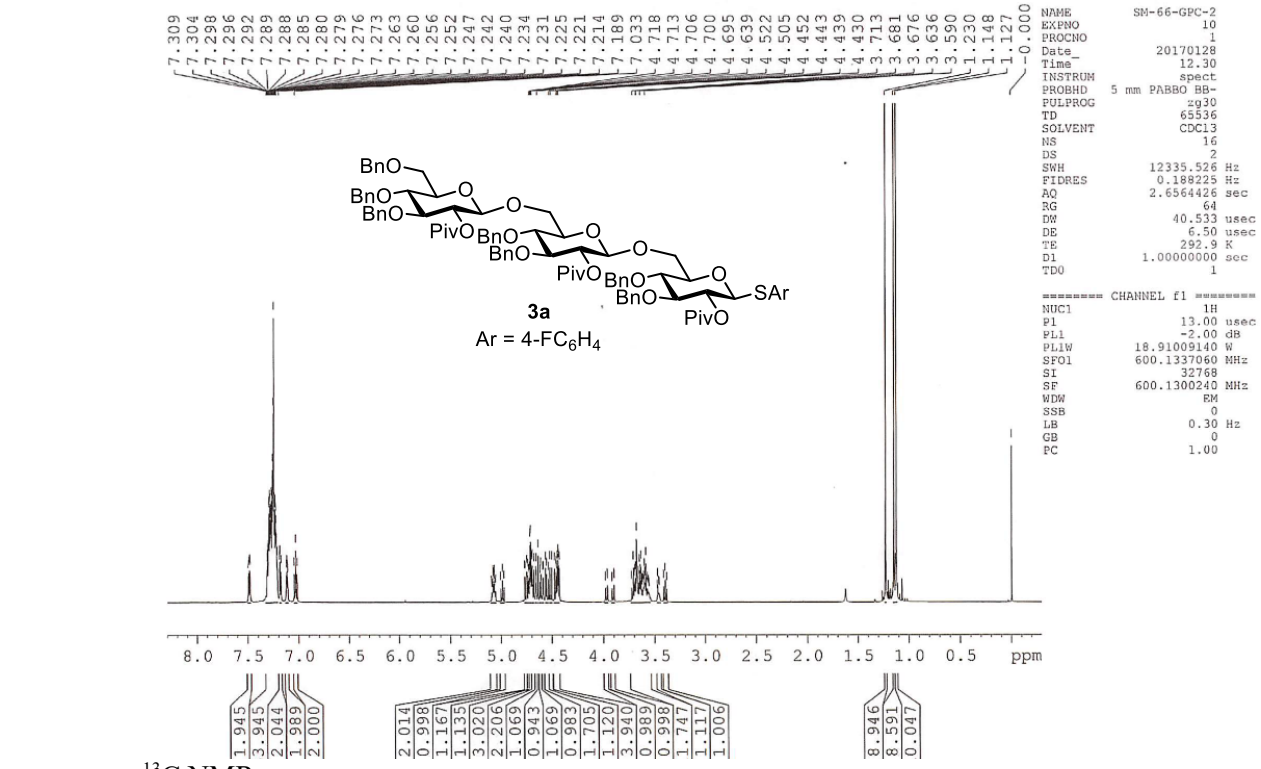
^{13}C NMR



```
NAME                 KTM-288
EXPNO                     20
PROCNO                     1
Date_               20210909
Time                   11.58
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      500
DS                        2
SWH               36057.691 Hz
FIDRES             0.550197 Hz
AQ                 0.9088159 sec
RG                      203
DW                   13.867 use
DE                    6.50 use
TE                   298.6 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                        1

======== CHANNEL f1 =======
NUC1                     13C
P1                    10.00 use
PL1                   -1.00 dB
PL1W          125.22619629 W
SFO1           150.9178988 MHz

======== CHANNEL f2 =======
CPDPRG2              waltz16
NUC2                      1H
PCPD2                 80.00 use
PL2                   -2.00 dB
PL12                  13.78 dB
PL13                  14.00 dB
PL2W           18.91009140 W
PL12W           0.49968192 W
PL13W           0.47499999 W
SFO2           600.1324005 MHz
SI                     32768
SF             150.9028090 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

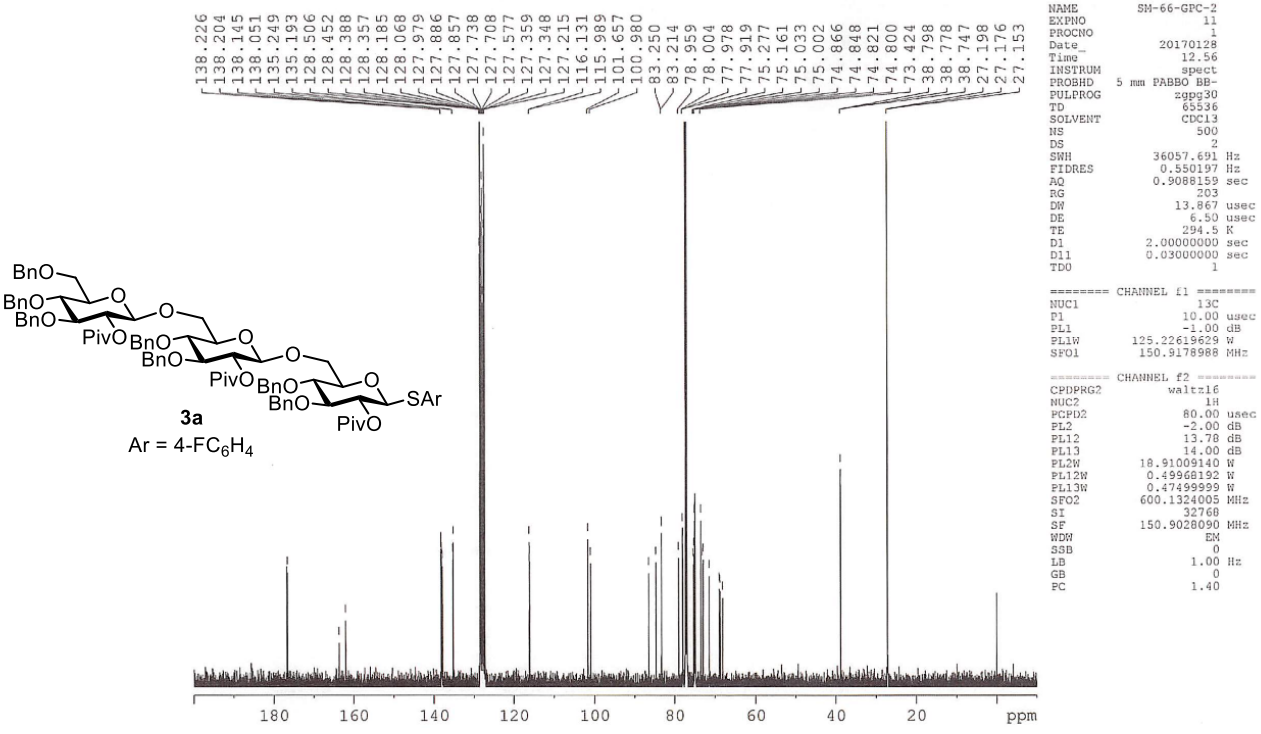
^{1}H, ^{13}C NMR, H-H COSY and HMQC spectra of trisaccharides

^{1}H NMR



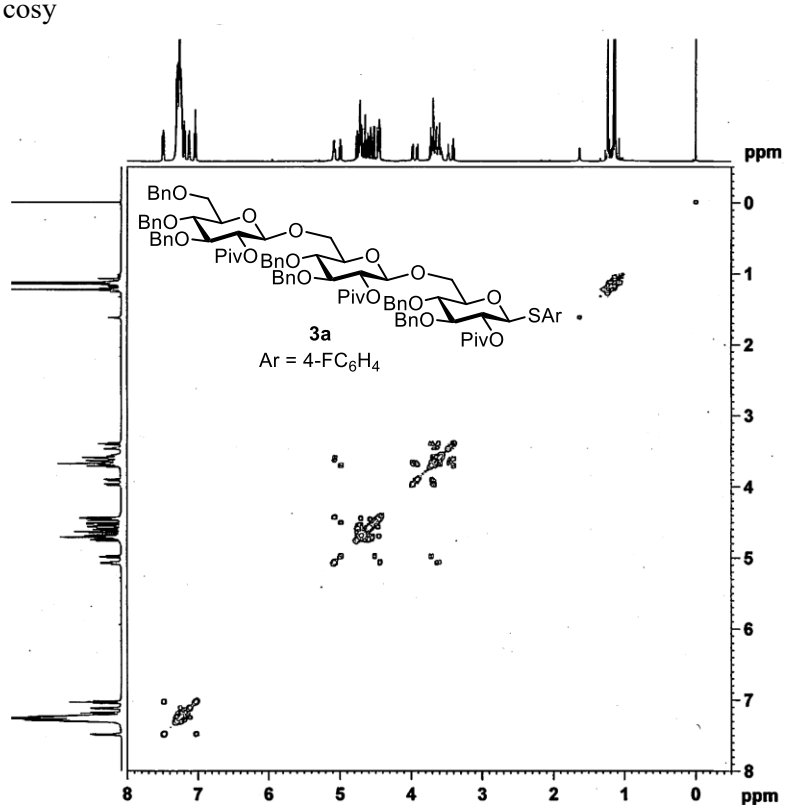

```
NAME            SM-66-GPC-2
EXPNO                    10
PROCNO                    1
Date_              20170128
Time                  12.30
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               12335.526 Hz
FIDRES            0.188225 Hz
AQ                2.6564426 sec
RG                       64
DW                  40.533 usec
DE                   6.50 usec
TE                  292.9 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    13.00 usec
PL1                   -2.00 dB
PL1W          18.91009140 W
SFO1          600.1337060 MHz
SI                    32768
SF            600.1300240 MHz
WDW                      EM
SSB                       0
LB                 0.30 Hz
GB                        0
PC                    1.00
```

^{13}C NMR



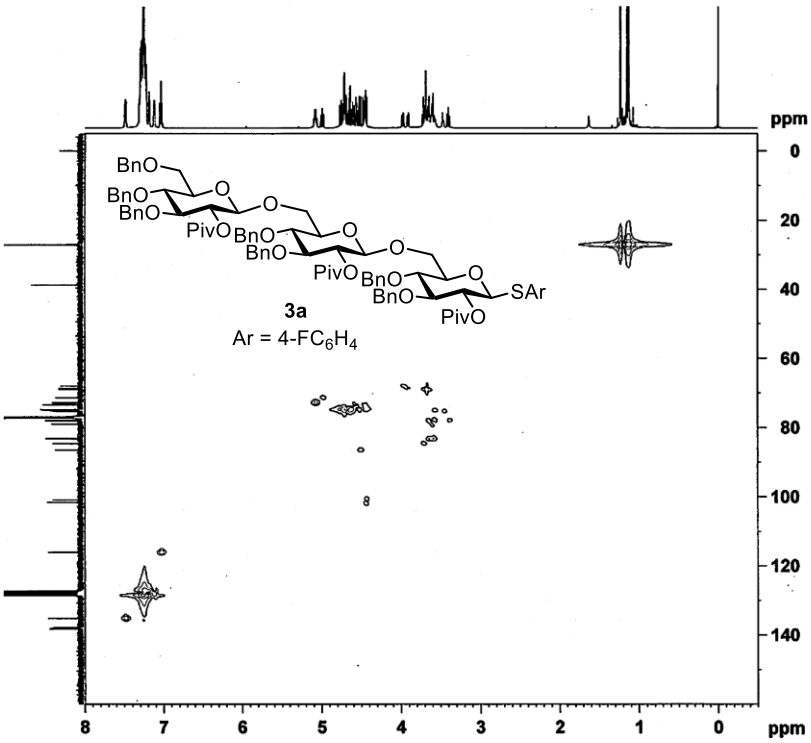

```
NAME            SM-66-GPC-2
EXPNO                    11
PROCNO                    1
Date_              20170128
Time                  12.56
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      500
DS                        2
SWH               36057.691 Hz
FIDRES            0.550197 Hz
AQ                0.9088159 sec
RG                      203
DW                  13.867 usec
DE                   6.50 usec
TE                  294.5 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.00 usec
PL1                  -1.00 dB
PL1W         125.22619629 W
SFO1         150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -2.00 dB
PL12                 13.78 dB
PL13                 14.00 dB
PL2W          18.91009140 W
PL12W          0.49968192 W
PL13W          0.47499999 W
SFO2          600.1324005 MHz
SI                    32768
SF            150.9028090 MHz
WDW                      EM
SSB                       0
LB                   1.00 Hz
GB                        0
PC                    1.40
```

H-H cosy



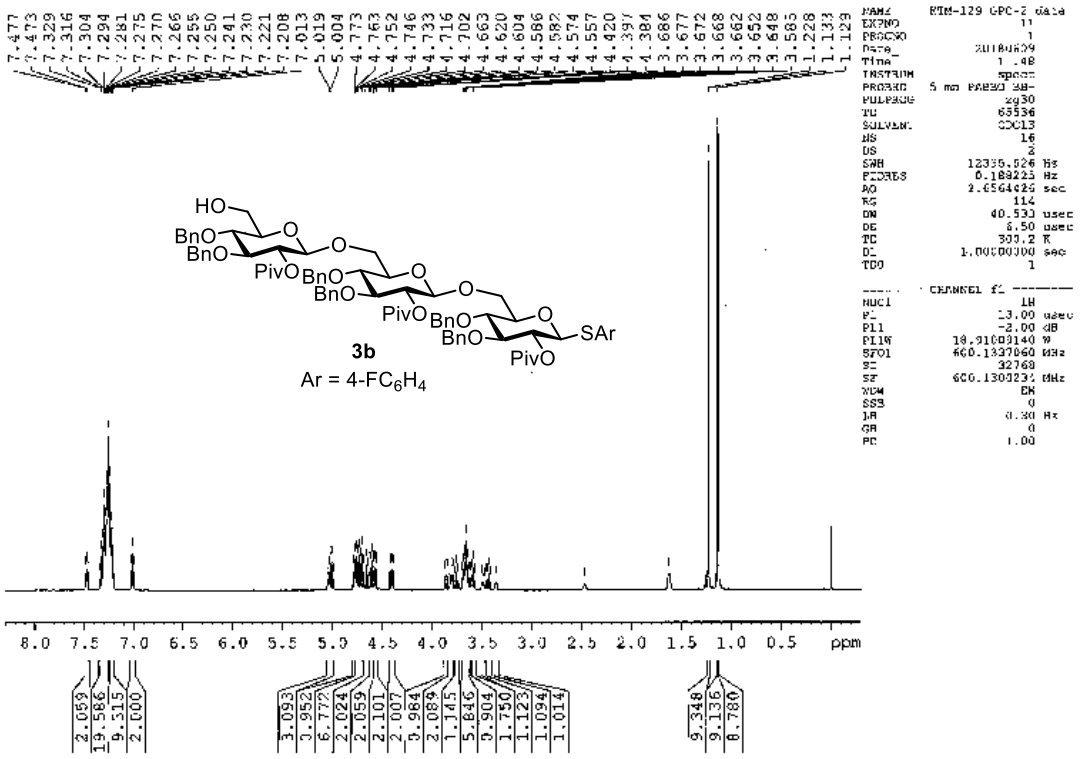

```
NAME            SM-66-GPC-2
EXPNO                    14
PROCNO                    1
Date_              20170128
Time                  13.12
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG           cosygpqf
TD                    2048
SOLVENT               CDCl3
NS                        1
DS                        8
SWH              5319.149 Hz
FIDRES           2.597241 Hz
AQ             0.1925620 sec
RG                     45.2
DW                94.000 usec
DE                 6.50 usec
TE                293.1 K
D0             0.00000300 sec
D1             1.42217505 sec
D13            0.00000400 sec
D16            0.00010000 sec
IN0            0.00018800 sec

======== CHANNEL f1 ========
NUC1                  1H
P0                 13.00 usec
P1                 13.00 usec
PL1                -2.00 dB
PL1W          18.91009140 W
SFO1         600.1323079 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPZ1               10.00 %
P16              1000.00 usec
NDO                   1
TD                  128
SFO1           600.1323 MHz
FIDRES         41.555851 Hz
SW                8.863 ppm
FnMODE               QF
SI                  1024
SF           600.1300241 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.40
SI                  1024
MC2                  QF
SF           600.1300241 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
```

HMQC

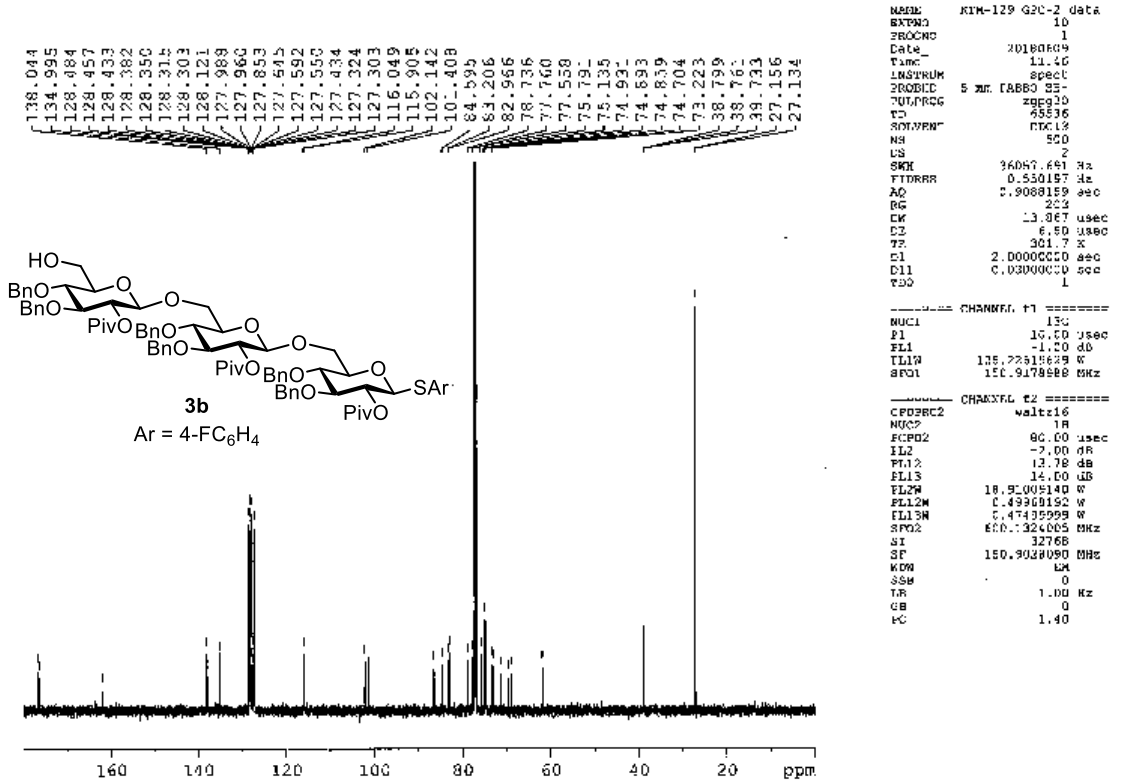



```
NAME            SM-66-GPC-2
EXPNO                    10
PROCNO                    1
Date_              20170128
Time                  12.30
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH             12335.526 Hz
FIDRES           0.188225 Hz
AQ               2.6564426 sec
RG                       64
DW                40.533 usec
DE                 6.50 usec
TE                292.9 K
D1             1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                  1H
P1                 13.00 usec
PL1                -2.00 dB
PL1W          18.91009140 W
SFO1         600.1337060 MHz
SI                   32768
SF           600.1300240 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

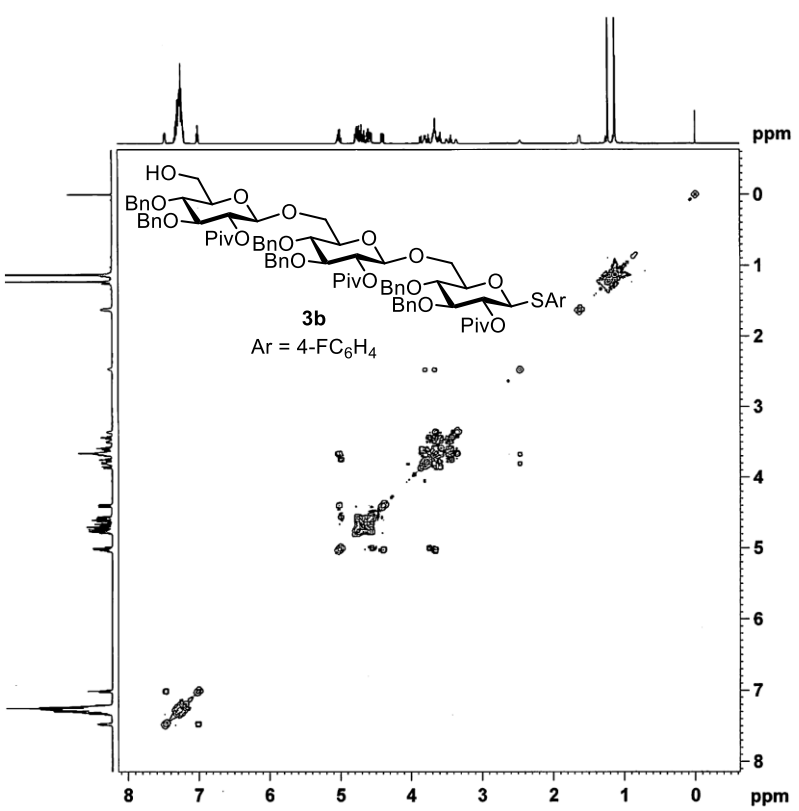
^{1}H NMR



^{13}C NMR

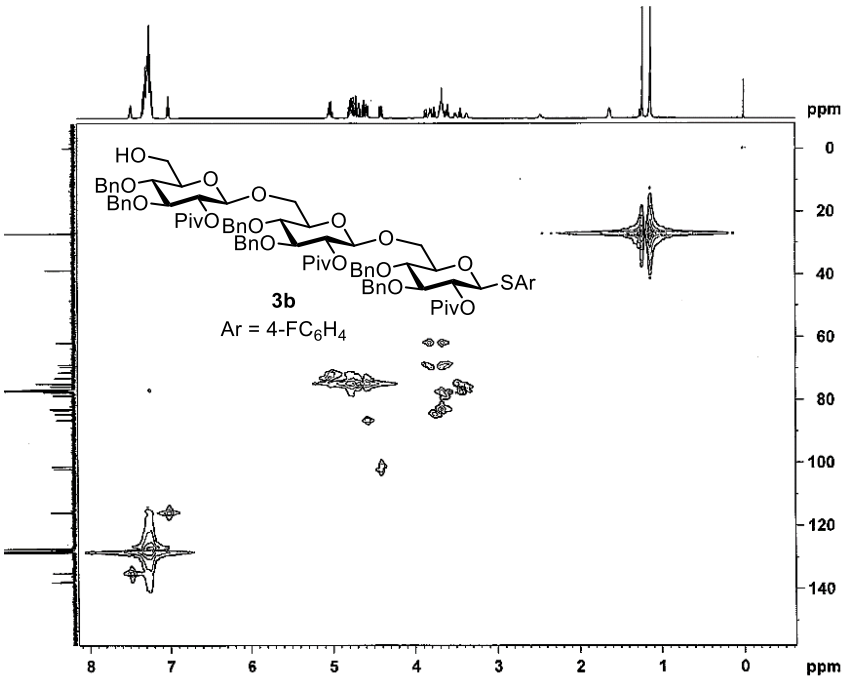


H-H cosy



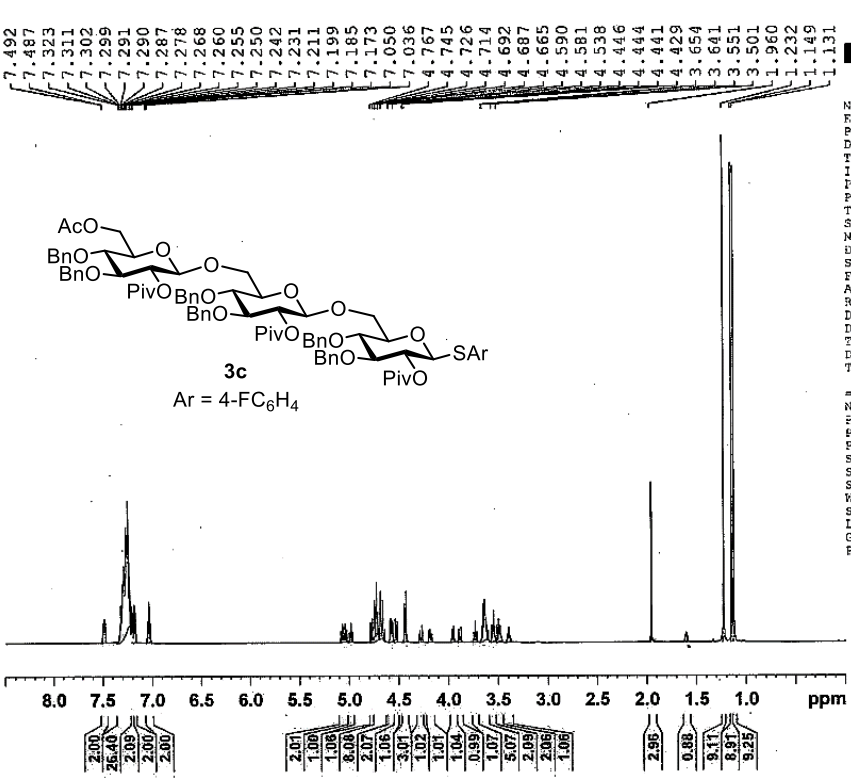

```
NAME        KTM-129 GPC-2 data
EXPNO                      12
PROCNO                      1
Date_                20180609
Time                    11.48
INSTRUM                 spect
PROBHD    5 mm PABBO BB-
PULPROG              cosygpqf
TD                       2048
SOLVENT                CDCl3
NS                          1
DS                          8
SWH                  5263.158 Hz
FIDRES               2.569901 Hz
AQ                  0.1946100 sec
RG                         64
DW                    95.000 usec
DE                     6.50 usec
TE                     300.0 K
D0                  0.00000300 sec
D1                  1.42012703 sec
D13                 0.00000400 sec
D16                 0.00010000 sec
IN0                 0.00019000 sec

======== CHANNEL f1 ========
NUC1                       1H
P0                      13.00 usec
P1                      13.00 usec
PL1                     -2.00 dB
PL1W               18.91009140 W
SFO1               600.1322776 MHz

====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPZ1                     10.00 %
P16                    1000.00 usec
ND0                         1
TD                        128
SFO1                 600.1323 MHz
FIDRES               41.118420 Hz
SW                       8.770 ppm
FnMODE                     QF
SI                       1024
SF                 600.1300234 MHz
WDW                      SINE
SSB                         0
LB                       0.00 Hz
GB                          0
PC                       1.40
SI                       1024
MC2                        QF
SF                 600.1300234 MHz
WDW                      SINE
SSB                         0
LB                       0.00 Hz
GB                          0
```

HMQC




```
NAME        KTM-129 GPC-2 data
EXPNO                      11
PROCNO                      1
Date_                20180609
Time                    11.48
INSTRUM                 spect
PROBHD    5 mm PABBO BB-
PULPROG                 zg30
TD                       65536
SOLVENT                CDCl3
NS                         16
DS                          2
SWH                12335.526 Hz
FIDRES              0.188225 Hz
AQ                  2.6564426 sec
RG                        114
DW                    40.533 usec
DE                     6.50 usec
TE                     300.2 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 =======
NUC1                       1H
P1                      13.00 usec
PL1                     -2.00 dB
PL1W               18.91009140 W
SFO1               600.1337060 MHz
SI                       32768
SF                 600.1300234 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

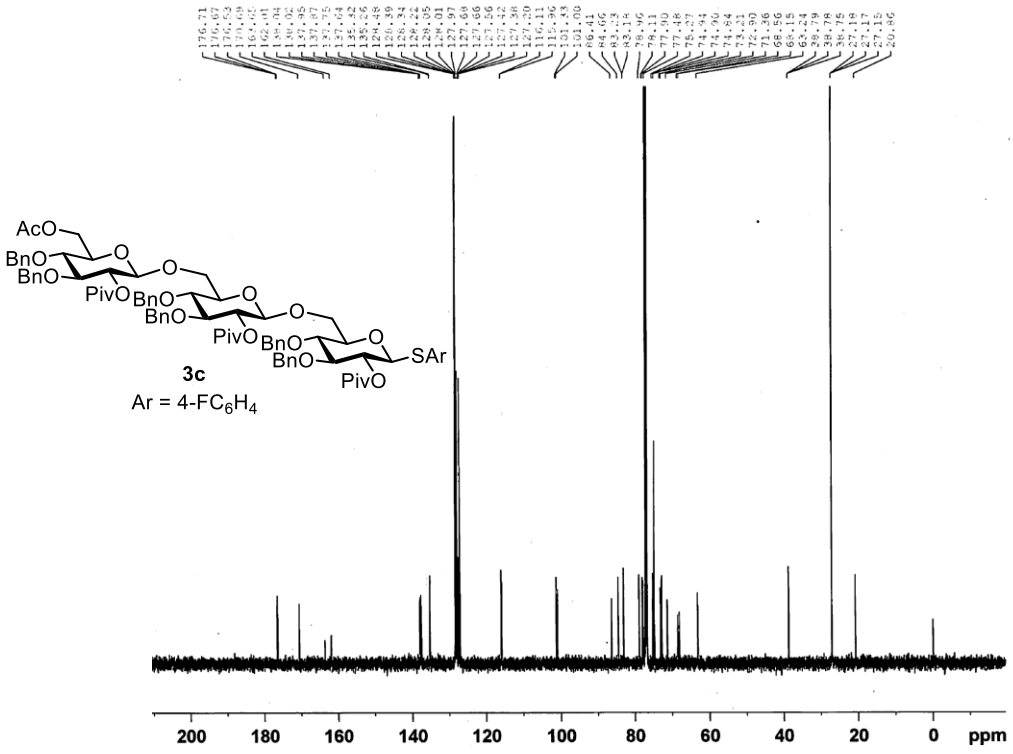
^{1}H NMR



BRUKER

```
NAME        KTM-232 GPC-1 data
EXPNO                      11
PROCNO                      1
Date_                20200218
Time                    21.10
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                12335.526 Hz
FIDRES             0.188225 Hz
AQ                 2.6564426 sec
RG                      90.5
DW                    40.533 usec
DE                      6.50 usec
TE                     295.6 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.00 usec
PL1                    -2.00 dB
PL1W              18.91009140 W
SFO1              600.1337060 MHz
SI                       32768
SF                600.1300221 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

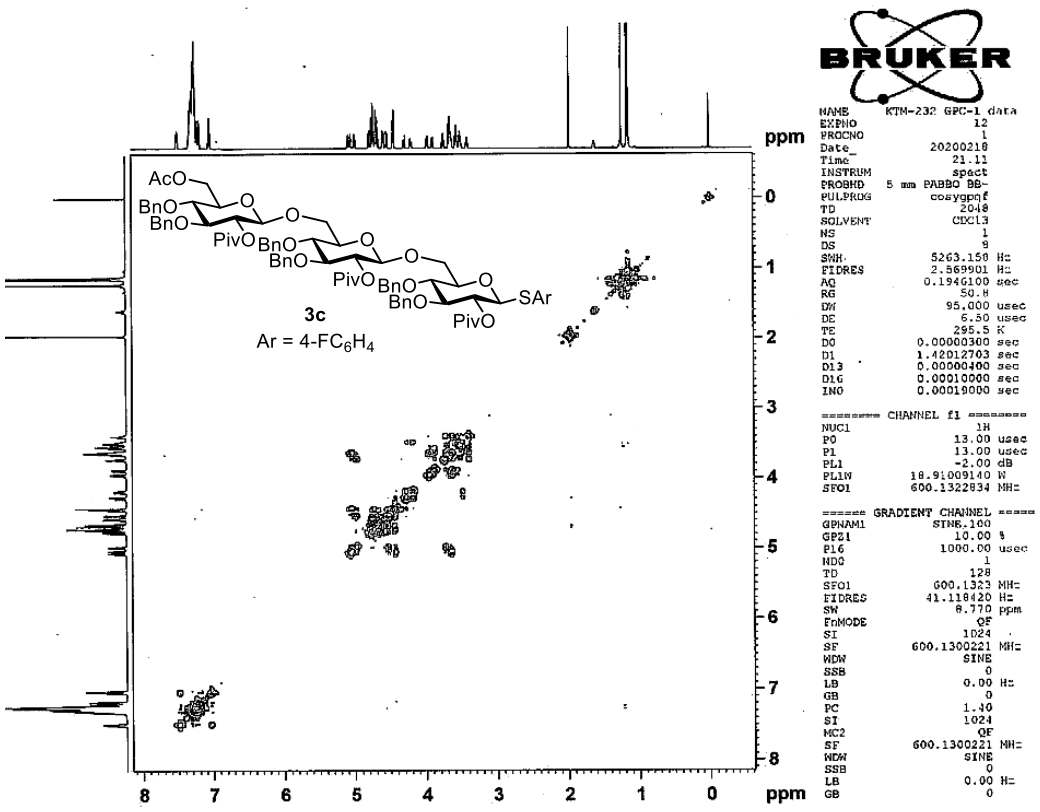
^{13}C NMR



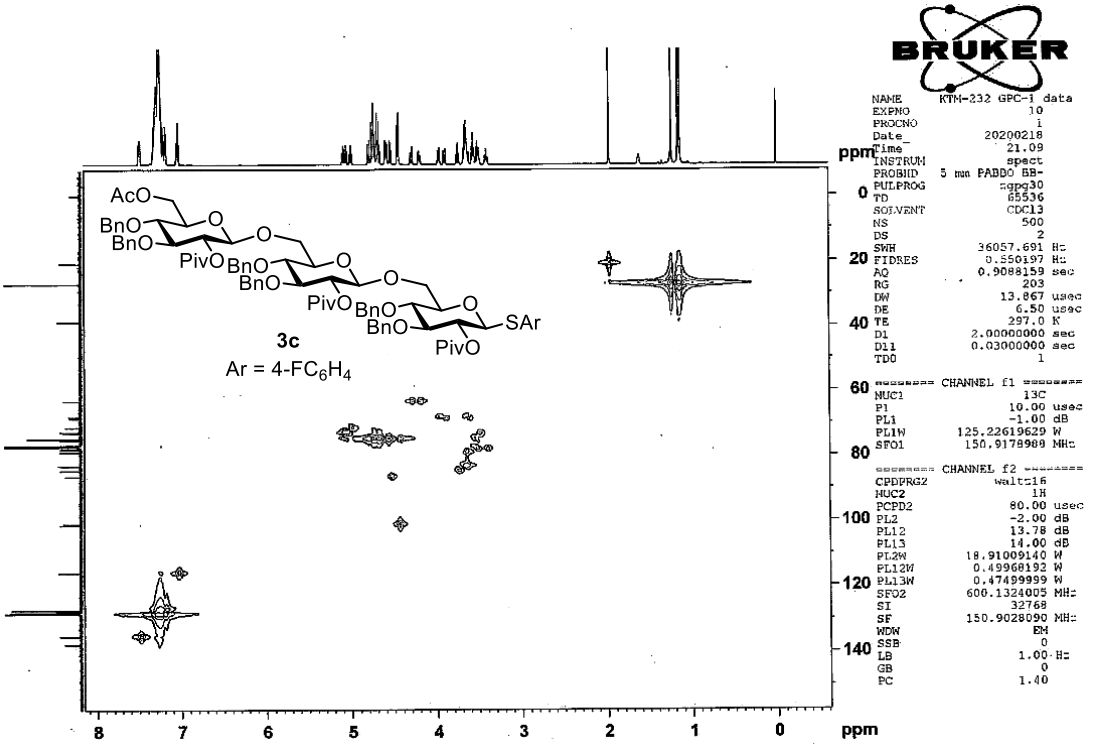
BRUKER

```
NAME        KTM-232 GPC-1 data
EXPNO                      10
PROCNO                      1
Date_                20200218
Time                    21.09
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG                 zgpg30
TD                     65536
SOLVENT                CDCl3
NS                        500
DS                         2
SWH                36057.691 Hz
FIDRES             0.550197 Hz
AQ                 0.9088159 sec
RG                       203
DW                    13.867 usec
DE                      6.50 usec
TE                     297.0 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.00 usec
PL1                    -1.00 dB
PL1W              125.22619629 W
SFO1              150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                  80.00 usec
PL2                    -2.00 dB
PL12                   13.78 dB
PL13                   14.00 dB
PL2W              18.91009140 W
PL12W              0.49968192 W
PL13W              0.47499999 W
SFO2              600.1324005 MHz
SI                       32768
SF                150.9028090 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

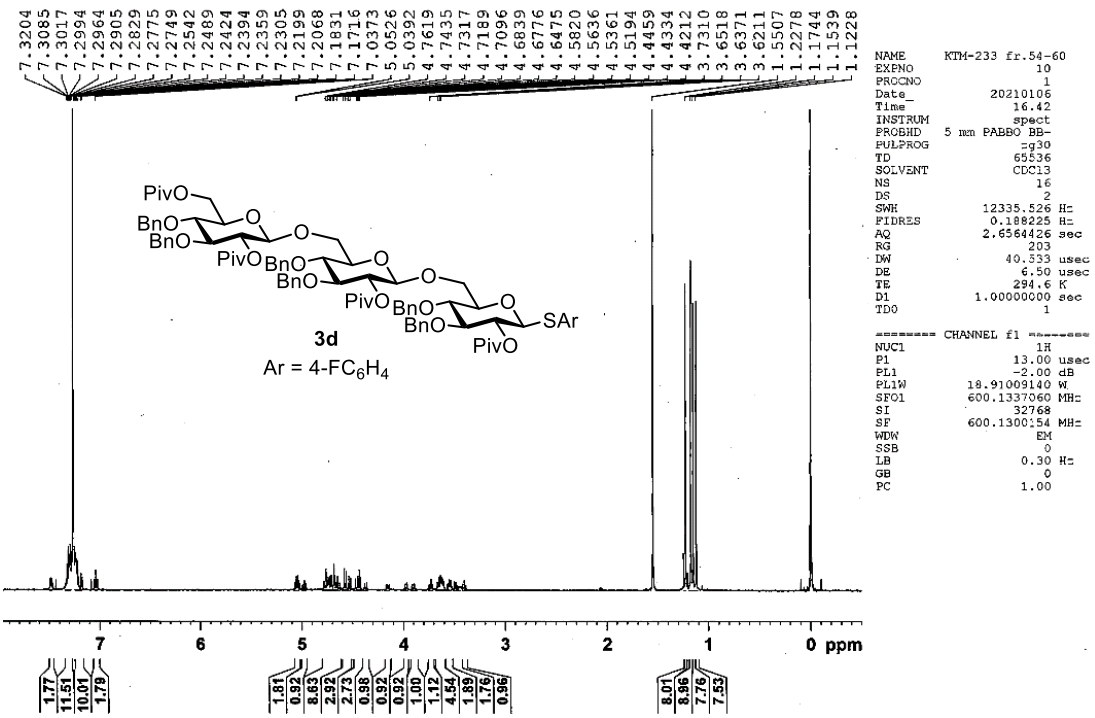
H-H cosy


AcO
BnO
BnO
PivO
BnO
BnO
PivO
BnO
BnO
PivO
BnO
BnO
SAr
PivO
3c
Ar = 4-FC6H4
ppm
0
1
2
3
4
5
6
7
8
ppm
8 7 6 5 4 3 2 1 0 ppm
BRUKER
NAME KTM-232 GPC-1 data
EXPNO 12
PROCNO 1
Date_ 20200218
Time 21.11
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 8
SWH 5263.158 Hz
FIDRES 2.569901 Hz
AQ 0.1946100 sec
RG 50.8
DW 95.000 usec
DE 6.50 usec
TE 295.5 K
D0 0.00000300 sec
D1 1.42012703 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00019000 sec
======== CHANNEL f1 ========
NUC1 1H
P0 13.00 usec
P1 13.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1322834 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPZ1 10.00 %
P16 1000.00 usec
NDC 1
TD 128
SFO1 600.1323 MHz
FIDRES 41.118420 Hz
SW 8.770 ppm
FnMODE QF
SI 1024
SF 600.1300221 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 600.1300221 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

HMQC

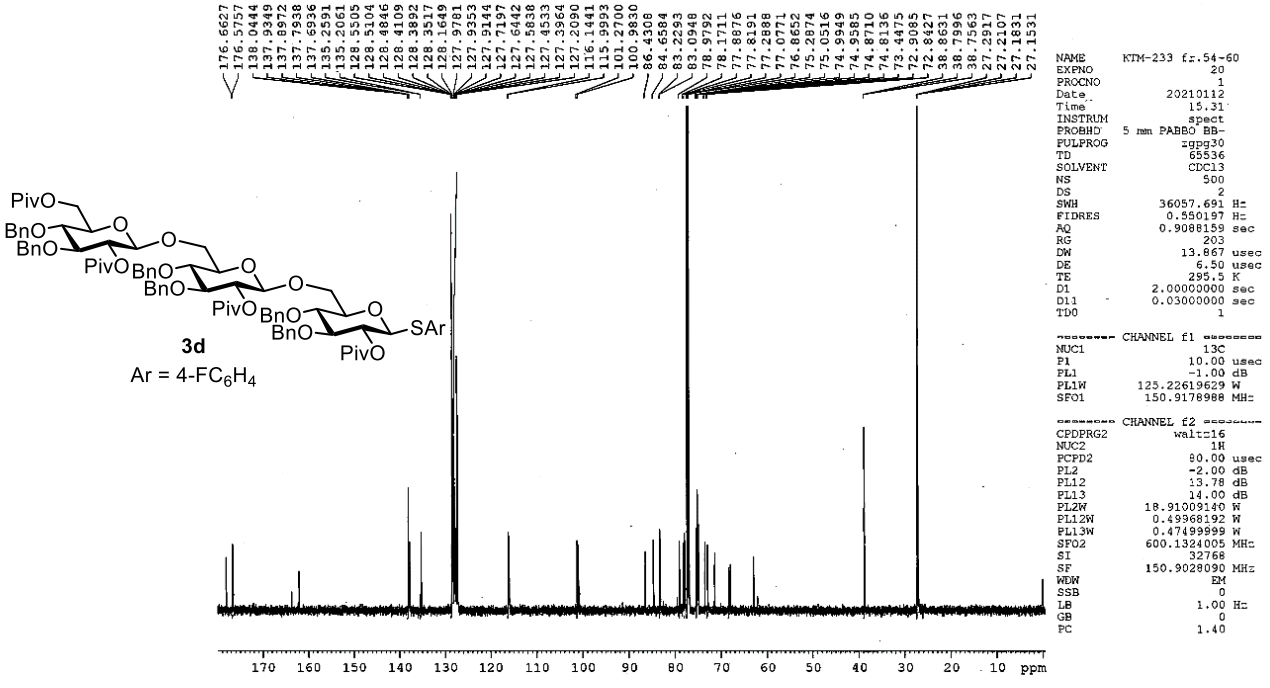

AcO
BnO
BnO
PivO
BnO
BnO
PivO
BnO
BnO
PivO
BnO
BnO
SAr
PivO
3c
Ar = 4-FC6H4
ppm
0
20
40
60
80
100
120
140
8 7 6 5 4 3 2 1 0 ppm
BRUKER
NAME KTM-232 GPC-1 data
EXPNO 10
PROCNO 1
Date_ 20200218
Time 21.09
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 500
DS 2
SWH 36057.691 Hz
FIDRES 0.550197 Hz
AQ 0.9088159 sec
RG 203
DW 13.867 usec
DE 6.50 usec
TE 297.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -1.00 dB
PL1W 125.22619629 W
SFO1 150.9178988 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 13.78 dB
PL13 14.00 dB
PL2W 18.91009140 W
PL12W 0.49968192 W
PL13W 0.47499999 W
SFO2 600.1324005 MHz
SI 32768
SF 150.9028090 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

^{1}H NMR



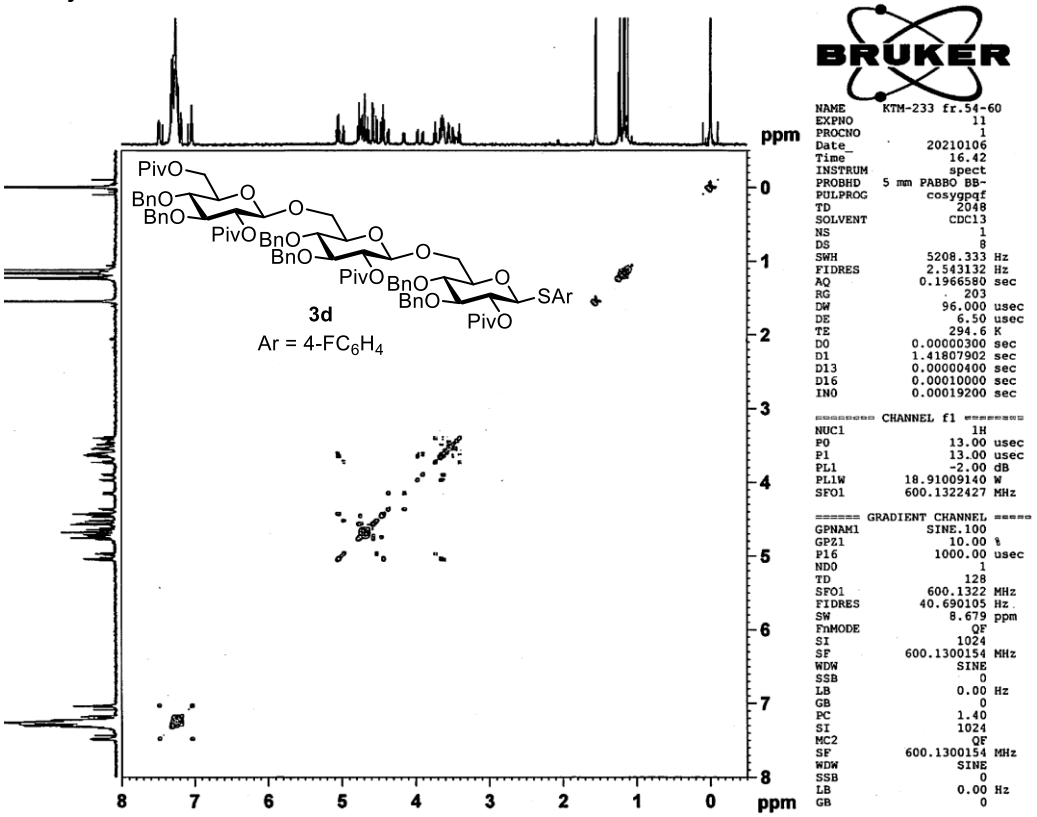
NAME	KTM-233 fr.54-60
EXPNO	10
PROCNO	1
Date_	20210106
Time	16.42
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12335.526 Hz
FIDRES	0.188225 Hz
AQ	2.6564426 sec
RG	203
DW	40.533 usec
DE	6.50 usec
TE	294.6 K
D1	1.00000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	1H
P1	13.00 usec
PL1	-2.00 dB
PL1W	18.91009140 W
SFO1	600.1337060 MHz
SI	32768
SF	600.1300154 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

^{13}C NMR



NAME	KTM-233 fr.54-60
EXPNO	20
PROCNO	1
Date_	20210112
Time	15.31
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	500
DS	2
SWH	36057.691 Hz
FIDRES	0.550197 Hz
AQ	0.9088159 sec
RG	203
DW	13.867 usec
DE	6.50 usec
TE	295.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	13C
P1	10.00 usec
PL1	-1.00 dB
PL1W	125.22619629 W
SFO1	150.9178988 MHz
========	CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	13.78 dB
PL13	14.00 dB
PL2W	18.91009140 W
PL12W	0.49968192 W
PL13W	0.47499999 W
SFO2	600.1324005 MHz
SI	32768
SF	150.9028090 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

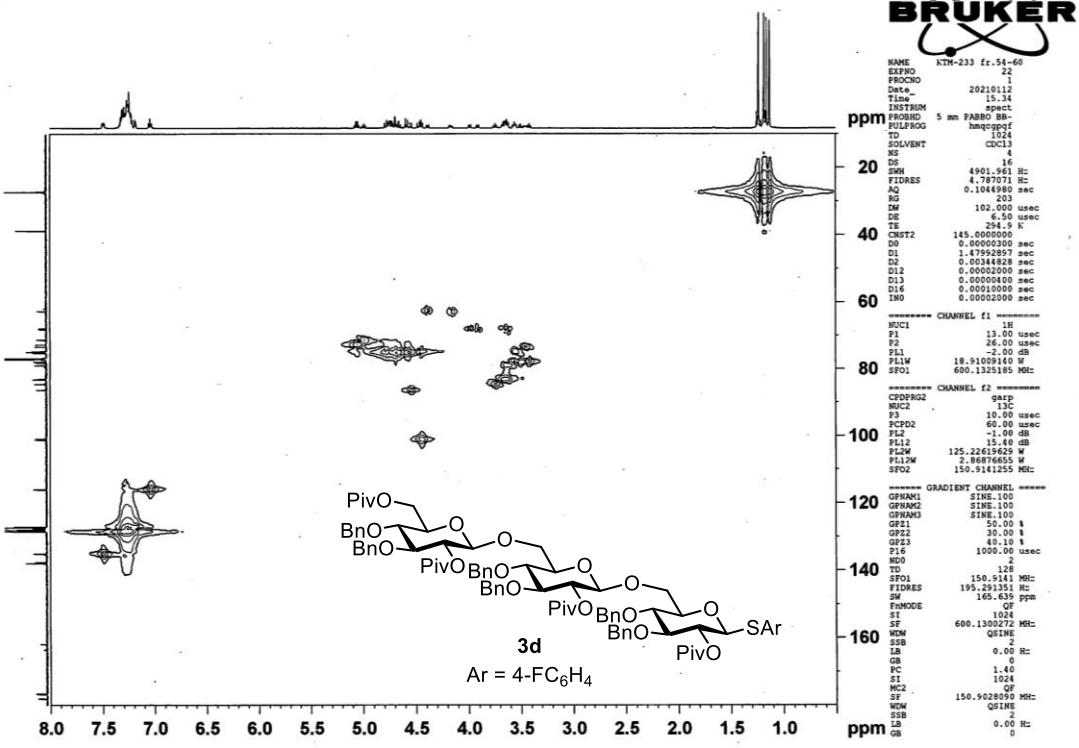
H-H cosy



BRUKER

NAME	KTM-233 fr.54-60
EXPNO	11
PROCNO	1
Date_	20210106
Time	16.42
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	cosygpqf
TD	2048
SOLVENT	CDCl3
NS	1
DS	8
SWH	5208.333 Hz
FIDRES	2.543132 Hz
AQ	0.1966580 sec
RG	203
DW	96.000 usec
DE	6.50 usec
TE	294.6 K
D0	0.00000300 sec
D1	1.41807902 sec
D13	0.00000400 sec
D16	0.00010000 sec
IN0	0.00019200 sec
======== CHANNEL f1 ========	
NUC1	1H
P0	13.00 usec
P1	13.00 usec
PL1	-2.00 dB
PL1W	18.91009140 W
SFO1	600.1322427 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPZ1	10.00 %
P16	1000.00 usec
ND0	1
TD	128
SFO1	600.1322 MHz
FIDRES	40.690105 Hz
SW	8.679 ppm
FnMODE	QF
SI	1024
SF	600.1300154 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.40
SI	1024
MC2	QF
SF	600.1300154 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

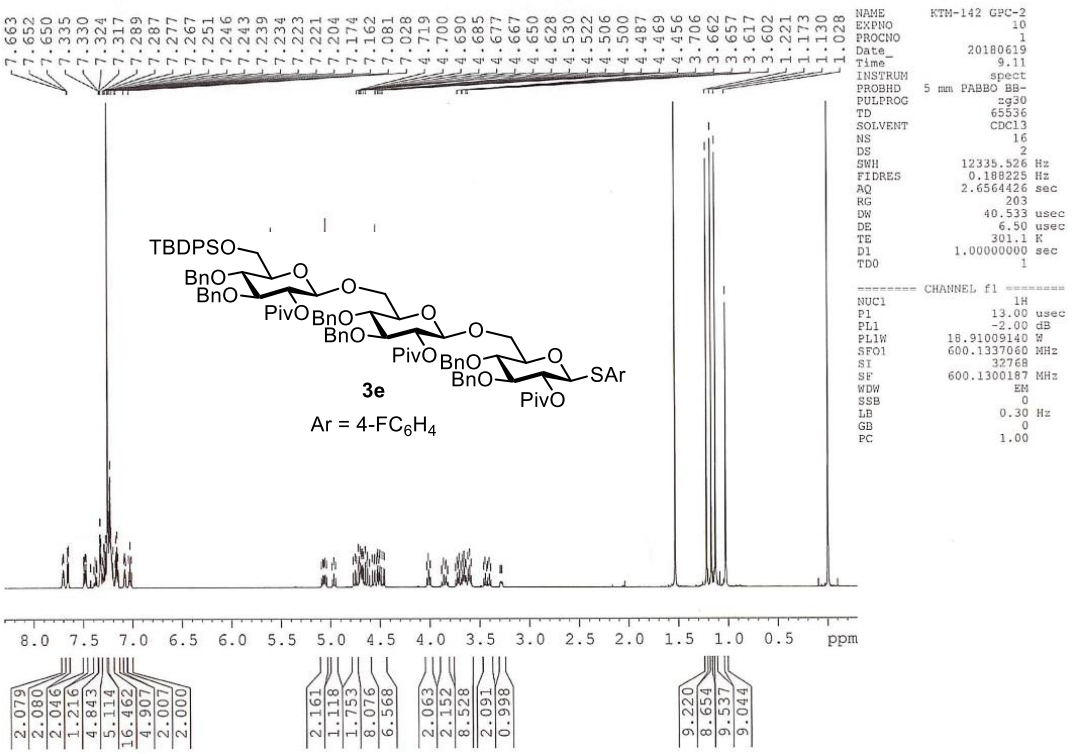
HMQC



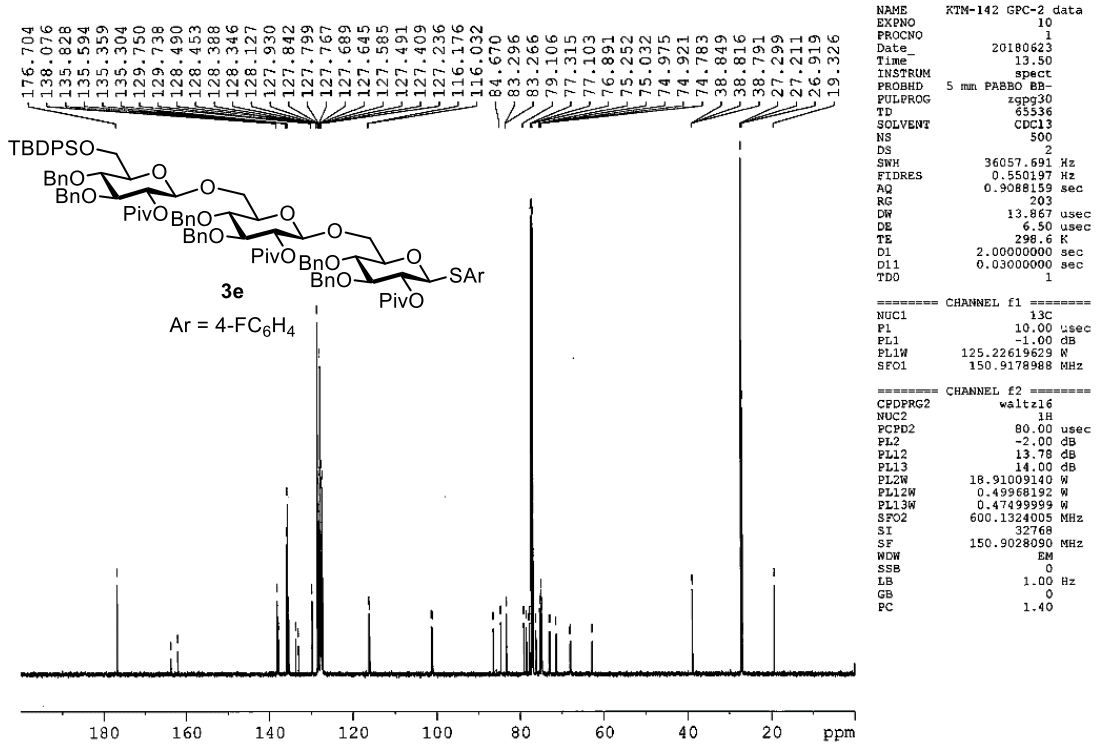
BRUKER

NAME	KTM-233 fr.54-60
EXPNO	22
PROCNO	1
Date_	20210112
Time	15.34
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	hmqcgpqf
TD	1024
SOLVENT	CDCl3
NS	4
DS	16
SWH	4901.961 Hz
FIDRES	4.787071 Hz
AQ	0.1044980 sec
RG	203
DW	102.000 usec
DE	6.50 usec
TE	294.9 K
CNST2	145.0000000
D0	0.00000300 sec
D1	1.47992897 sec
D2	0.00344828 sec
D12	0.00002000 sec
D13	0.00000400 sec
D16	0.00010000 sec
IN0	0.00002000 sec
======== CHANNEL f1 ========	
NUC1	1H
P1	13.00 usec
P2	26.00 usec
PL1	-2.00 dB
PL1W	18.91009140 W
SFO1	600.1325185 MHz
======== CHANNEL f2 ========	
CPDPRG2	garp
NUC2	13C
P3	10.00 usec
PCPD2	60.00 usec
PL2	-1.00 dB
PL12	15.40 dB
PL2W	125.22619629 W
PL12W	2.86876655 W
SFO2	150.9141255 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPNAM2	SINE.100
GPNAM3	SINE.100
GPZ1	50.00 %
GPZ2	30.00 %
GPZ3	40.10 %
P16	1000.00 usec
ND0	2
TD	128
SFO1	150.9141 MHz
FIDRES	195.291351 Hz
SW	165.639 ppm
FnMODE	QF
SI	1024
SF	600.1300272 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.40
SI	1024
MC2	QF
SF	150.9028090 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0

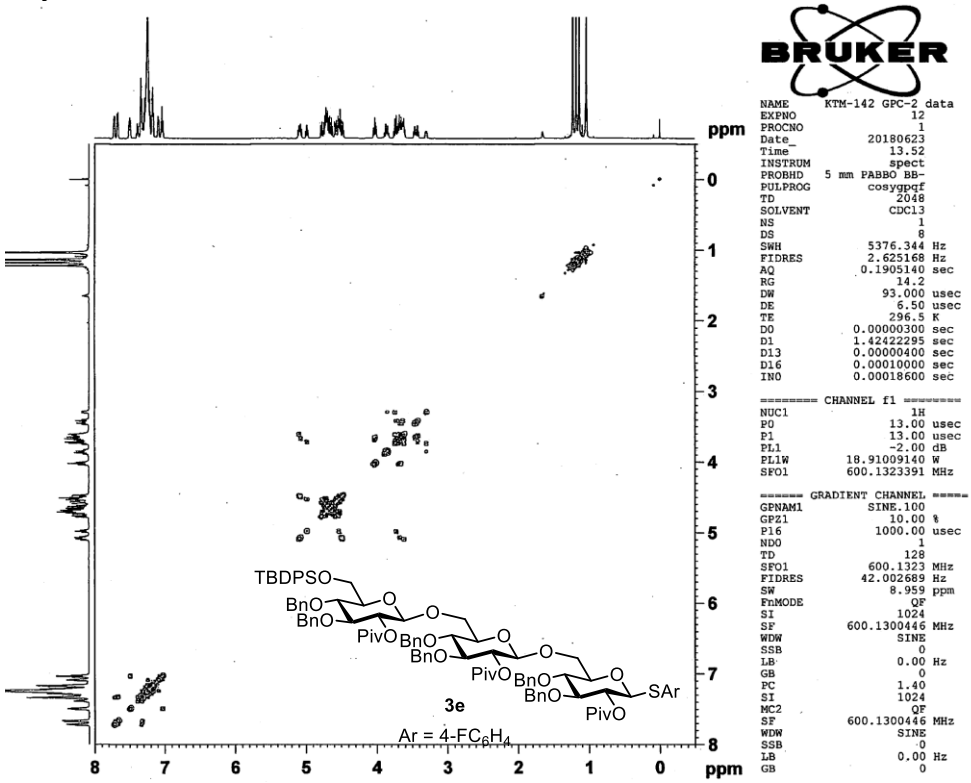
^{1}H NMR



^{13}C NMR



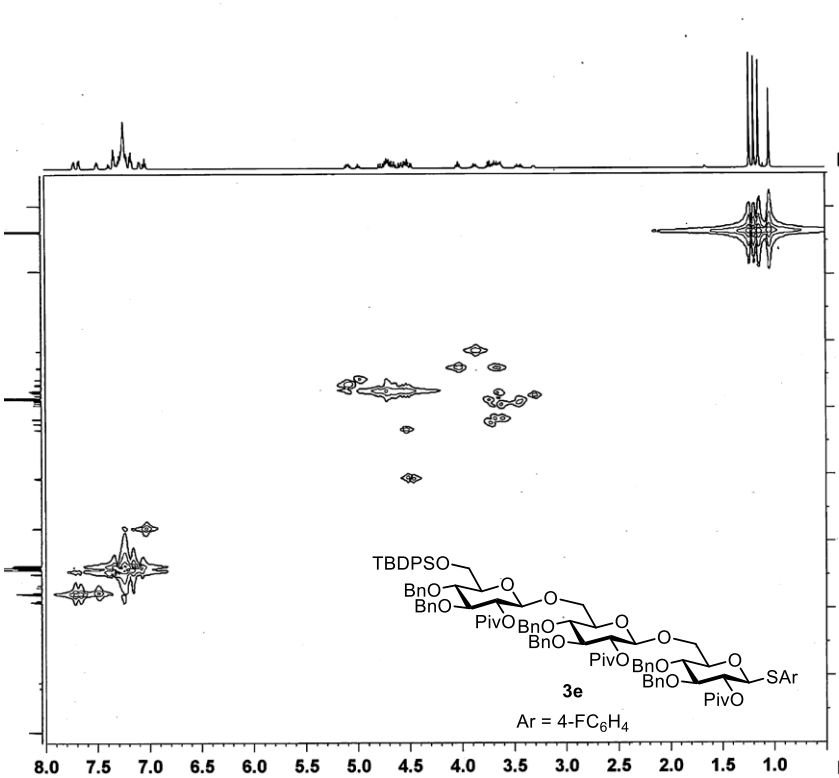
H-H cosy



BRUKER

```
NAME          KTM-142 GPC-2 data
EXPNO                        12
PROCNO                        1
Date_                  20180623
Time                      13.52
INSTRUM                   spect
PROBHD     5 mm PABBO BB-
PULPROG                cosygpqf
TD                         2048
SOLVENT                  CDCl3
NS                            1
DS                            8
SWH                5376.344 Hz
FIDRES             2.625168 Hz
AQ                 0.1905140 sec
RG                        14.2
DW                   93.000 usec
DE                    6.50 usec
TE                    296.5 K
D0                 0.00000300 sec
D1                 1.42422295 sec
D13                0.00000400 sec
D16                0.00010000 sec
IN0                0.00018600 sec

======== CHANNEL f1 ========
NUC1                         1H
P0                    13.00 usec
P1                    13.00 usec
PL1                   -2.00 dB
PL1W              18.91009140 W
SFO1             600.1323391 MHz

======= GRADIENT CHANNEL =====
GPNAM1               SINE.100
GPZ1                    10.00 %
P16                   1000.00 usec
NDO                           1
TD                          128
SFO1                600.1323 MHz
FIDRES             42.002689 Hz
SW                      8.959 ppm
FnMODE                     QF
SI                        1024
SF               600.1300446 MHz
WDW                      SINE
SSB                         0
LB                       0.00 Hz
GB                          0
PC                       1.40
SI                        1024
MC2                        QF
SF               600.1300446 MHz
WDW                      SINE
SSB                         0
LB                       0.00 Hz
GB                          0
```

HMQC

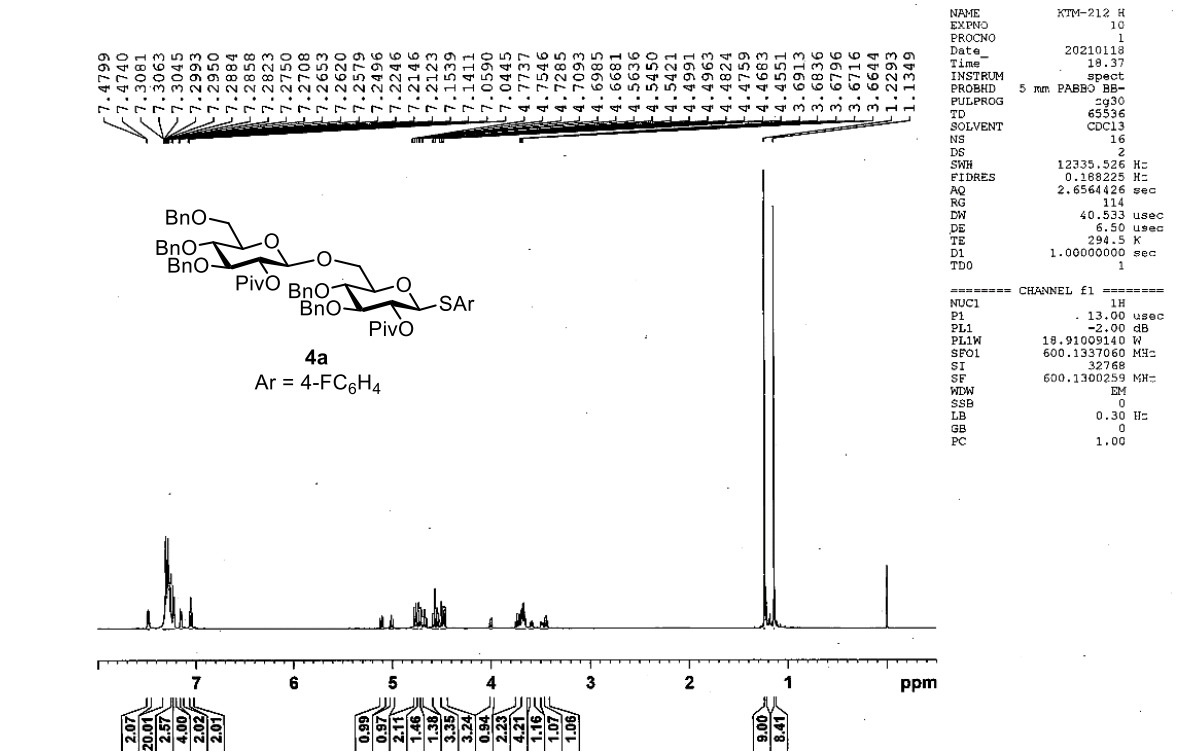


BRUKER

```
NAME          KTM-142 GPC-2 data
EXPNO                        13
PROCNO                        1
Date_                  20180623
Time                      13.56
INSTRUM                   spect
PROBHD     5 mm PABBO BB-
PULPROG                hmqcgpqf
TD                         1024
SOLVENT                  CDCl3
NS                            4
DS                           16
SWH                5376.344 Hz
FIDRES             5.250336 Hz
AQ                 0.09528820 sec
RG                          203
DW                   93.000 usec
DE                    6.50 usec
TE                    296.2 K
CNST2             145.0000000
D0                 0.00000300 sec
D1                 1.48914599 sec
D2                 0.00344828 sec
D12                0.00002000 sec
D13                0.00000400 sec
D16                0.00010000 sec
IN0                0.00002000 sec

======== CHANNEL f1 ========
NUC1                         1H
P1                    13.00 usec
P2                    26.00 usec
PL1                   -2.00 dB
PL1W              18.91009140 W
SFO1             600.1323391 MHz

======== CHANNEL f2 ========
CPDPRG2                   garp
NUC2                       13C
P3                    10.00 usec
PCPD2                 60.00 usec
PL2                   -1.00 dB
PL12                  15.40 dB
PL2W             125.22619629 W
PL12W              2.86876655 W
SFO2             150.9141255 MHz

======= GRADIENT CHANNEL =====
GPNAM1               SINE.100
GPNAM2               SINE.100
GPNAM3               SINE.100
GPZ1                    50.00 %
GPZ2                    30.00 %
GPZ3                    40.10 %
P16                   1000.00 usec
NDO                           2
TD                          128
SFO1               150.9141 MHz
FIDRES             195.291351 Hz
SW                     165.639 ppm
FnMODE                     QF
SI                        1024
SF               600.1300446 MHz
WDW                     QSINE
SSB                         2
LB                       0.00 Hz
GB                          0
PC                       1.40
SI                        1024
MC2                        QF
SF               150.9028090 MHz
WDW                     QSINE
SSB                         2
LB                       0.00 Hz
GB                          0
```

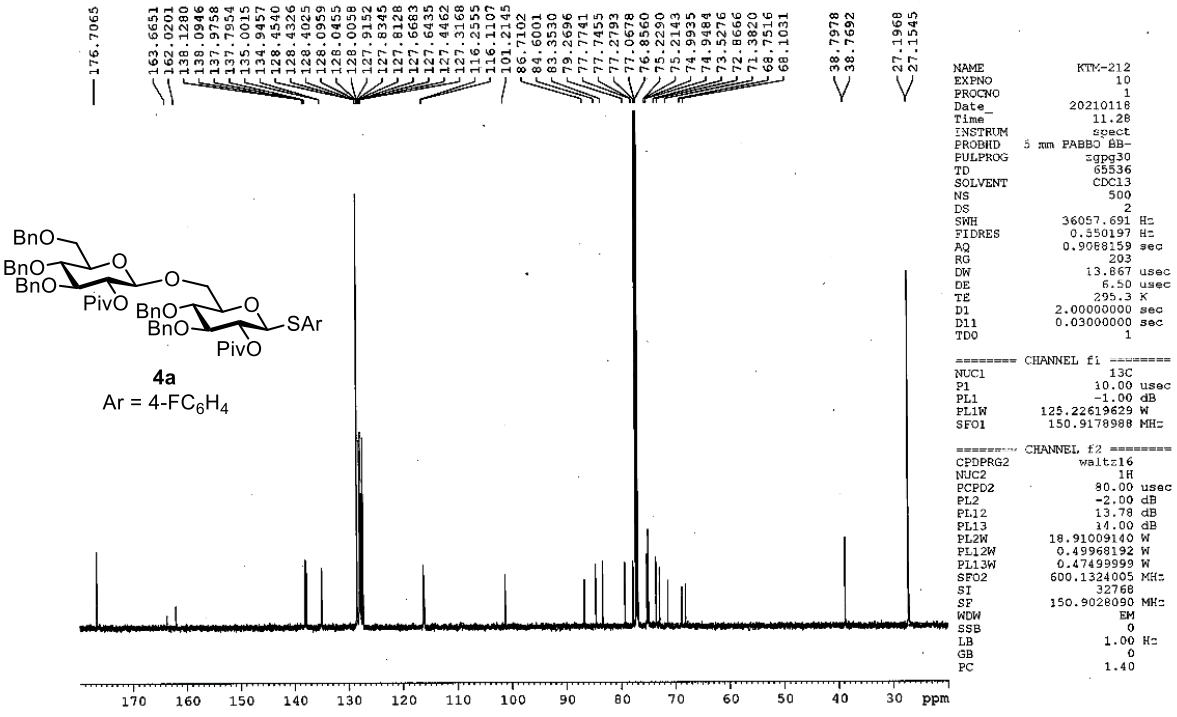
9. ^{1}H, ^{13}C NMR, H-H COSY and HMQC spectra of disaccharides

^{1}H NMR



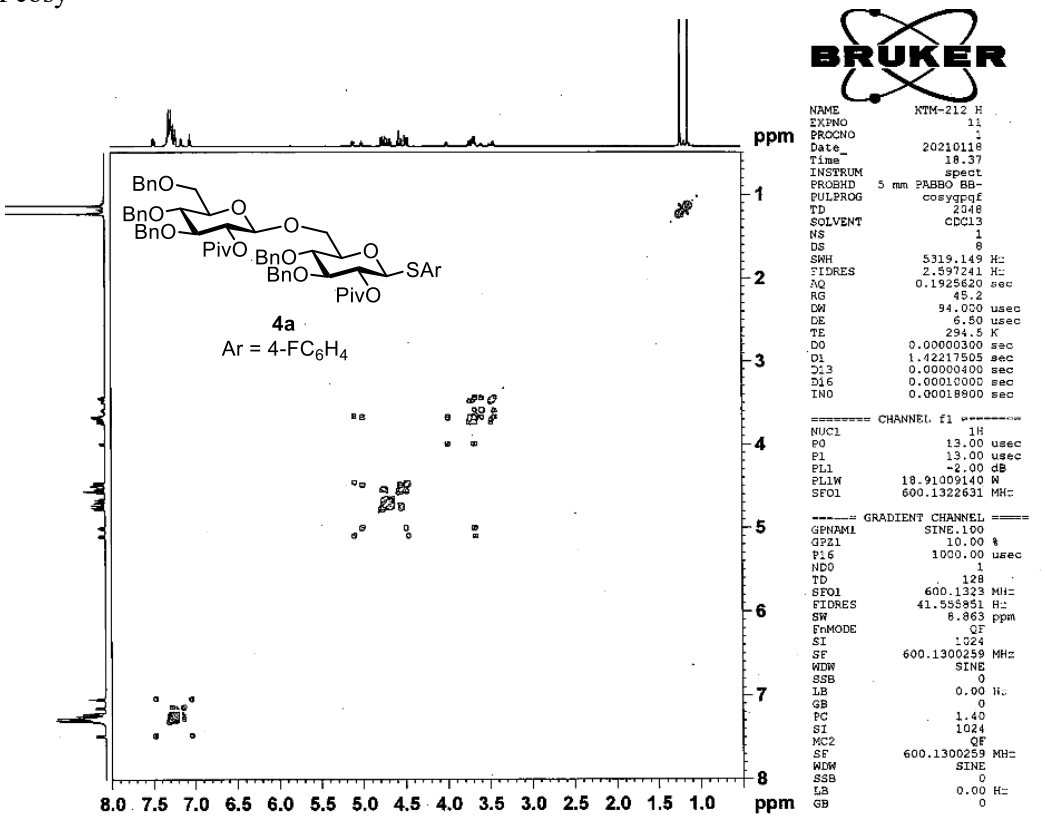

```
NAME                KTM-212 H
EXPNO                      10
PROCNO                      1
Date_                20210118
Time                    18.37
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                         16
DS                          2
SWH                12335.526 Hz
FIDRES             0.188225 Hz
AQ                 2.6564426 sec
RG                        114
DW                    40.533 usec
DE                      6.50 usec
TE                     294.5 K
D1                 1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      13.00 usec
PL1                     -2.00 dB
PL1W               18.91009140 W
SFO1              600.1337060 MHz
SI                       32768
SF                600.1300259 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

^{13}C NMR

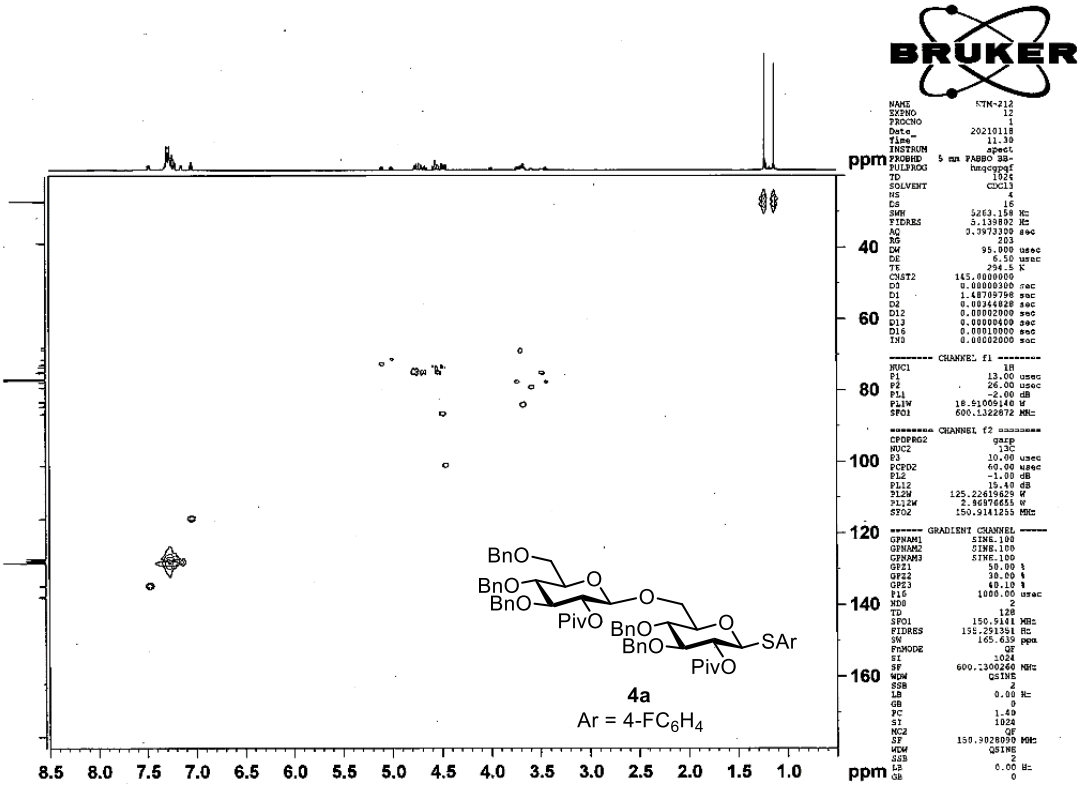



```
NAME                  KTM-212
EXPNO                      10
PROCNO                      1
Date_                20210118
Time                    11.28
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG                 zgpg30
TD                     65536
SOLVENT                CDCl3
NS                        500
DS                          2
SWH                36057.691 Hz
FIDRES             0.550197 Hz
AQ                 0.9088159 sec
RG                        203
DW                    13.867 usec
DE                      6.50 usec
TE                     295.3 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                      10.00 usec
PL1                     -1.00 dB
PL1W              125.22619629 W
SFO1              150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   80.00 usec
PL2                     -2.00 dB
PL12                    13.78 dB
PL13                    14.00 dB
PL2W               18.91009140 W
PL12W               0.49968192 W
PL13W               0.47499999 W
SFO2              600.1324005 MHz
SI                       32768
SF                150.9028090 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```

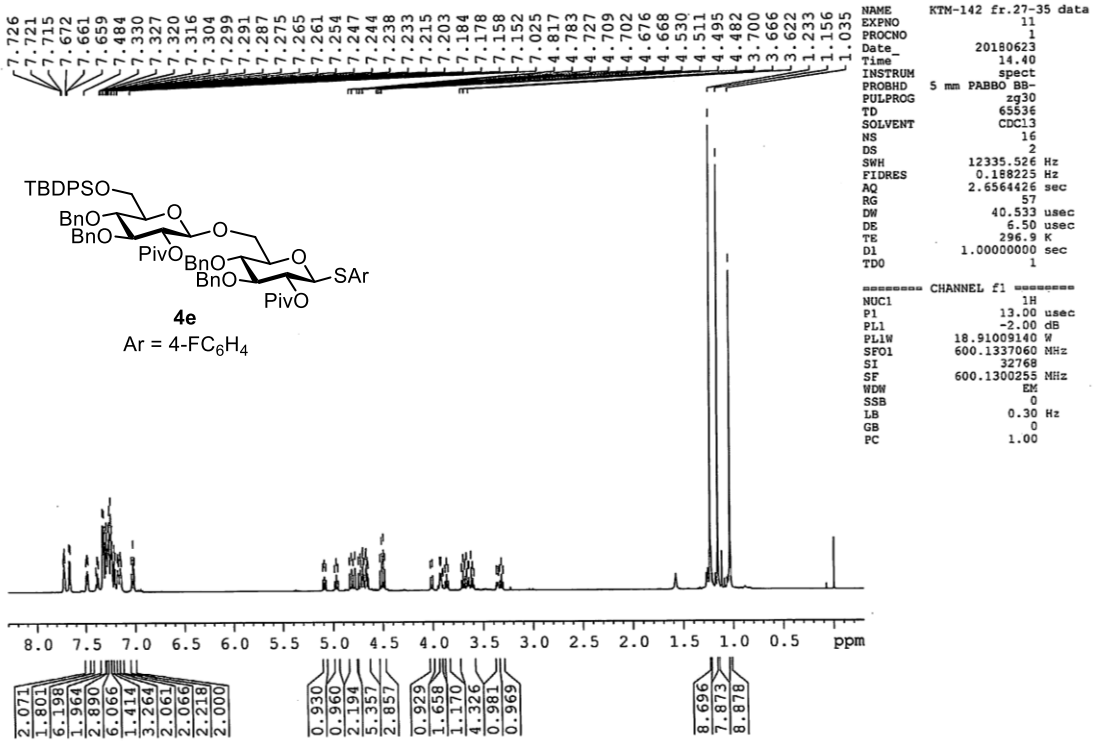
H-H cosy


BnO
BnO
BnO
PivO
BnO
BnO
PivO
SAr
4a
Ar = 4-FC6H4
ppm
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
BRUKER
NAME KTM-212 H
EXPNO 11
PROCNO 1
Date_ 20210118
Time 18.37
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 8
SWH 5319.149 Hz
FIDRES 2.597241 Hz
AQ 0.1925620 sec
RG 45.2
DW 94.000 usec
DE 6.50 usec
TE 294.5 K
D0 0.00000300 sec
D1 1.42217505 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00018800 sec
======== CHANNEL f1 ========
NUC1 1H
P0 13.00 usec
P1 13.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1322631 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPZ1 10.00 %
P16 1000.00 usec
ND0 1
TD 128
SFO1 600.1323 MHz
FIDRES 41.555851 Hz
SW 8.863 ppm
FnMODE QF
SI 1024
SF 600.1300259 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 600.1300259 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

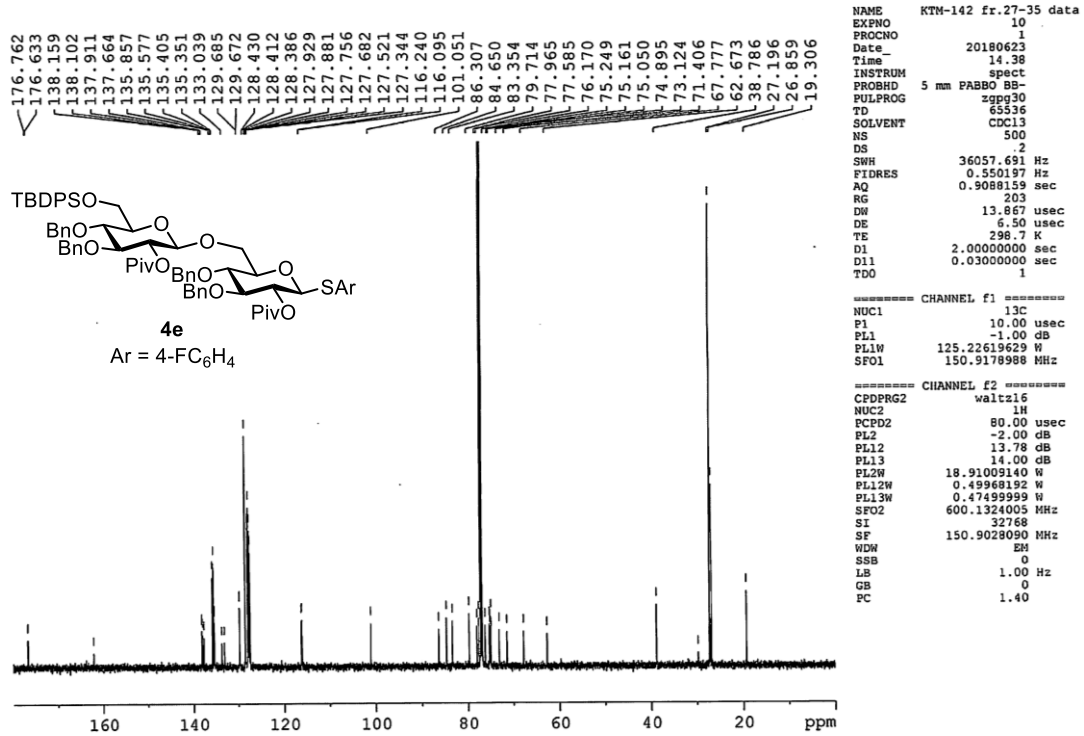
HMQC


BnO
BnO
BnO
PivO
BnO
BnO
PivO
SAr
4a
Ar = 4-FC6H4
ppm
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
BRUKER
NAME KTM-212
EXPNO 12
PROCNO 1
Date_ 20210118
Time 11.30
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG hmqcgpqf
TD 1024
SOLVENT CDCl3
NS 4
DS 16
SWH 5263.158 Hz
FIDRES 5.139802 Hz
AQ 0.3973309 sec
RG 203
DW 95.000 usec
DE 6.50 usec
TE 294.5 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.48705798 sec
D2 0.00344828 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00002000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
P2 26.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1322872 MHz
======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 10.00 usec
PCPD2 60.00 usec
PL2 -1.00 dB
PL12 15.40 dB
PL2W 125.22619829 W
PL12W 2.96976655 W
SFO2 150.9141255 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec
ND0 2
TD 128
SFO1 150.9141 MHz
FIDRES 151.291391 Hz
SW 165.639 ppm
FnMODE QF
SI 1024
SF 600.1300260 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 150.9028090 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

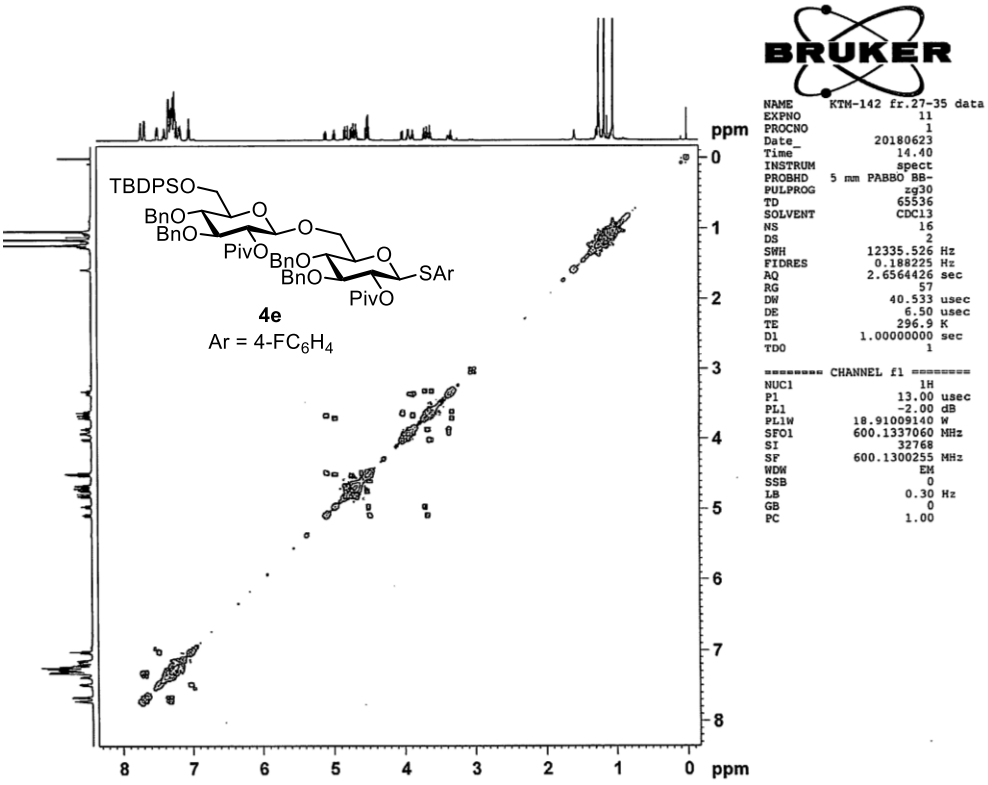
^{1}H NMR



^{13}C NMR

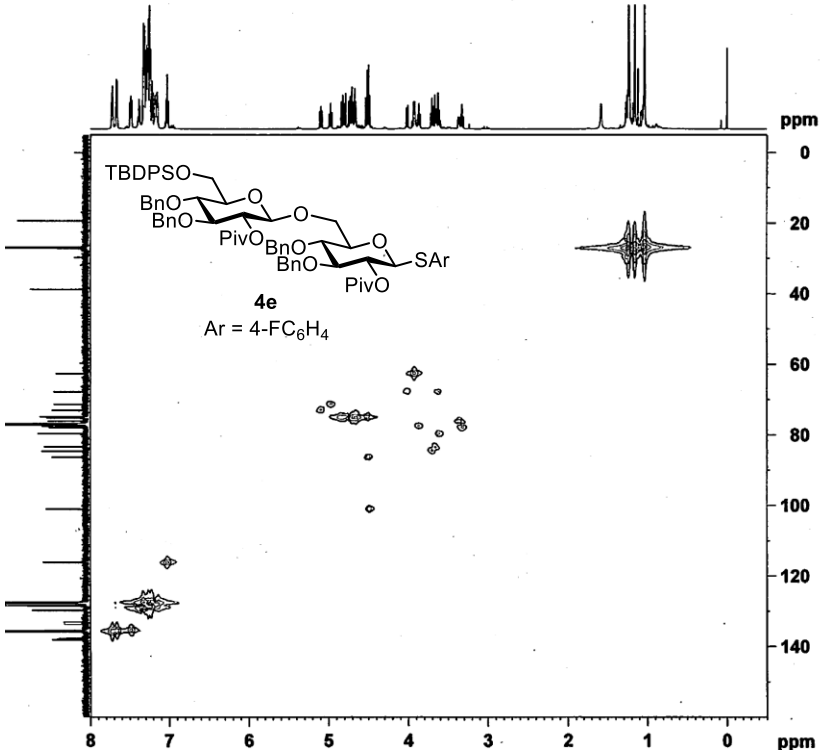


H-H cosy



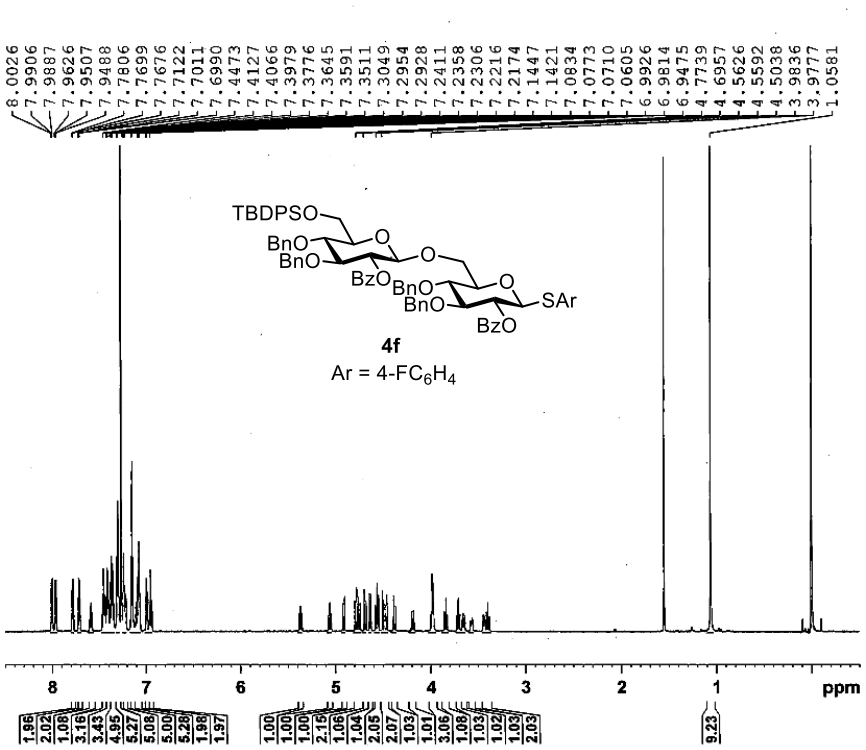

```
NAME        KTM-142 fr.27-35 data
EXPNO                 11
PROCNO                 1
Date_           20180623
Time               14.40
INSTRUM            spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES         0.188225 Hz
AQ             2.6564426 sec
RG                    57
DW                40.533 usec
DE                 6.50 usec
TE                296.9 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                13.00 usec
PL1               -2.00 dB
PL1W         18.91009140 W
SFO1        600.1337060 MHz
SI                 32768
SF          600.1300255 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.00
```

HMQC



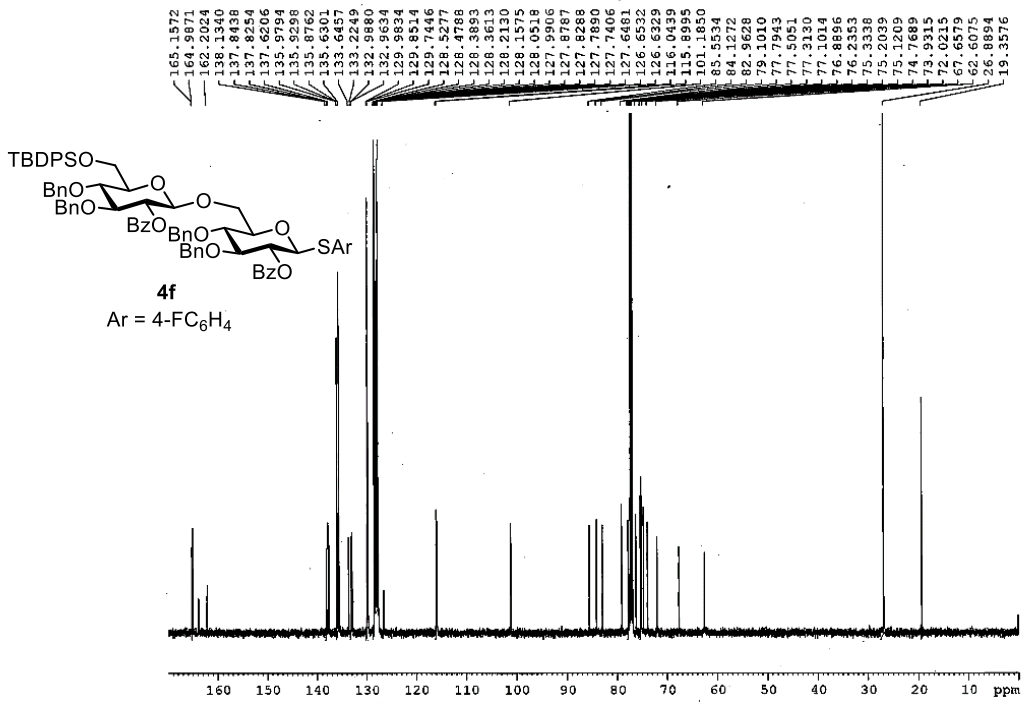

```
NAME        KTM-142 fr.27-35 data
EXPNO                 11
PROCNO                 1
Date_           20180623
Time               14.40
INSTRUM            spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES         0.188225 Hz
AQ             2.6564426 sec
RG                    57
DW                40.533 usec
DE                 6.50 usec
TE                296.9 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                13.00 usec
PL1               -2.00 dB
PL1W         18.91009140 W
SFO1        600.1337060 MHz
SI                 32768
SF          600.1300255 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.00
```

^{1}H NMR



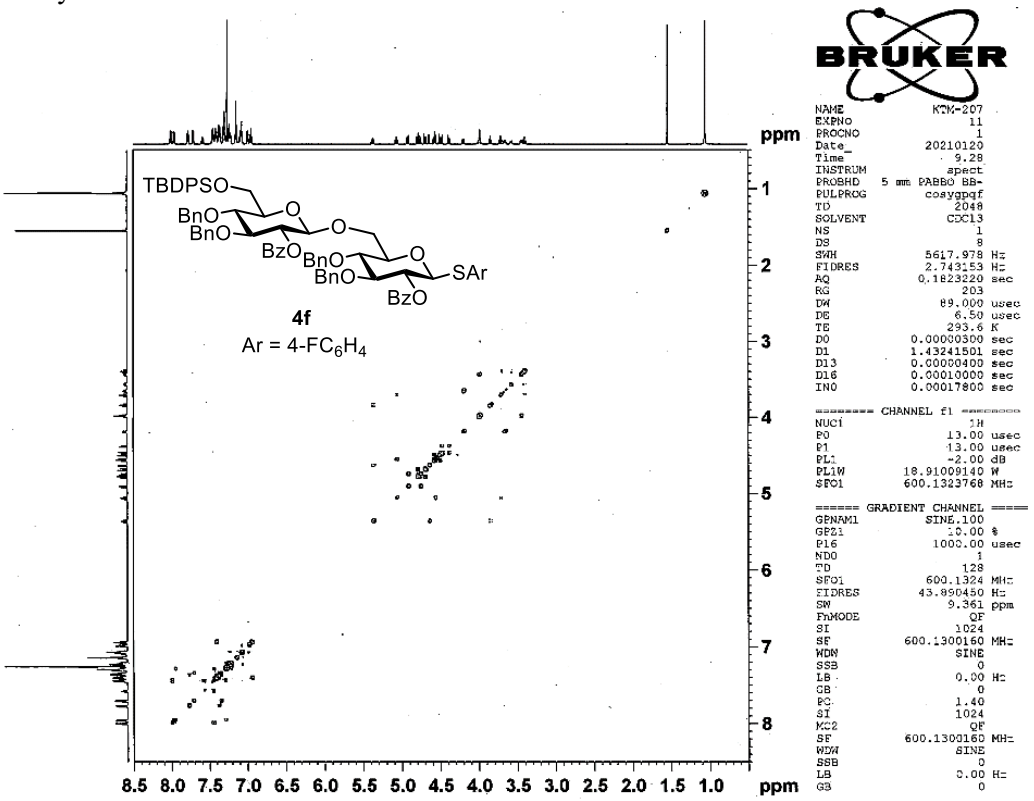
NAME	KTM-207
EXPNO	10
PROCNO	1
Date_	20210120
Time	9.28
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12335.526 Hz
FIDRES	0.188225 Hz
AQ	2.6564426 sec
RG	203
DW	40.533 usec
DE	6.50 usec
TE	293.6 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	13.00 usec
PL1	-2.00 dB
PL1W	18.91009140 W
SFO1	600.1337060 MHz
SI	32768
SF	600.1300160 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

^{13}C NMR

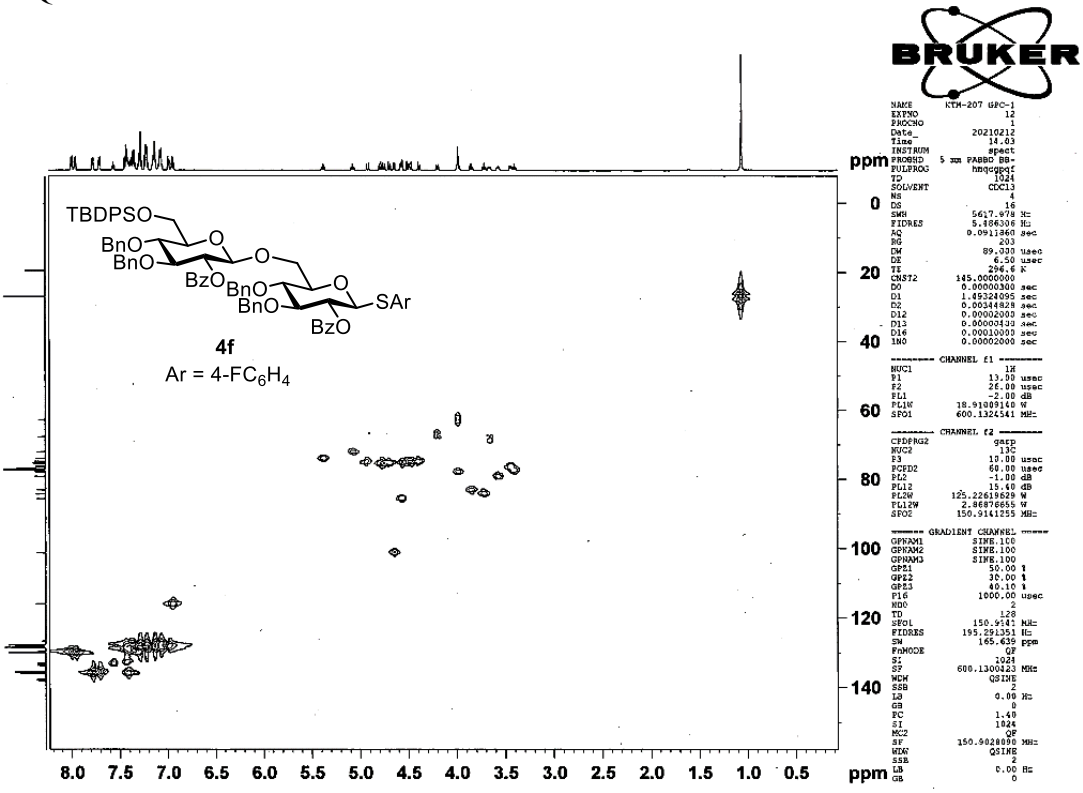


NAME	KTM-207 GPC-1
EXPNO	10
PROCNO	1
Date_	20210212
Time	14.00
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	500
DS	2
SWH	36057.691 Hz
FIDRES	0.550197 Hz
AQ	0.9088159 sec
RG	203
DW	13.867 usec
DE	6.50 usec
TE	297.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	10.00 usec
PL1	-1.00 dB
PL1W	125.22619629 W
SFO1	150.9178988 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	13.78 dB
PL13	14.00 dB
PL2W	18.91009140 W
PL12W	0.49968192 W
PL13W	0.47499999 W
SFO2	600.1324005 MHz
SI	32768
SF	150.9028090 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

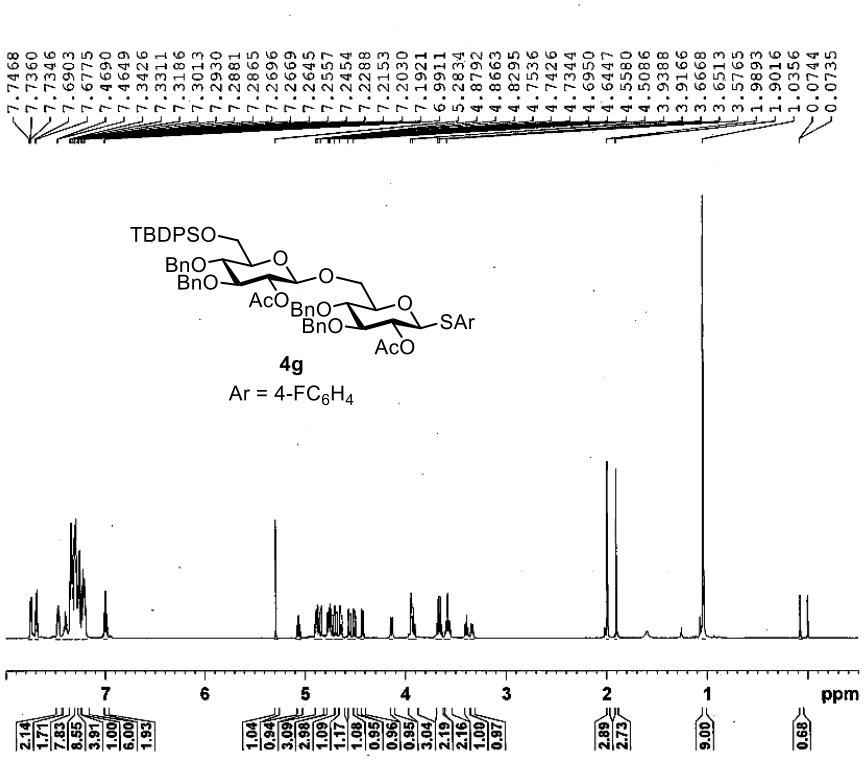
H-H cosy


TBDPSO
BnO
BnO
BzO
BnO
BnO
BzO
SAr
4f
Ar = 4-FC6H4
ppm
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
BRUKER
NAME KTM-207
EXPNO 11
PROCNO 1
Date_ 20210120
Time 9.28
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 8
SWH 5617.978 Hz
FIDRES 2.743153 Hz
AQ 0.1823220 sec
RG 203
DW 89.000 usec
DE 6.50 usec
TE 293.6 K
D0 0.00000300 sec
D1 1.43241501 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00017800 sec
CHANNEL f1
NUC1 1H
P0 13.00 usec
P1 13.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1323768 MHz
GRADIENT CHANNEL
GPNAM1 SINE.100
GPZ1 10.00 %
P16 1000.00 usec
ND0 1
TD 128
SFO1 600.1324 MHz
FIDRES 43.890450 Hz
SW 9.361 ppm
FnMODE QF
SI 1024
SF 600.1300160 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 600.1300160 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

HMQC

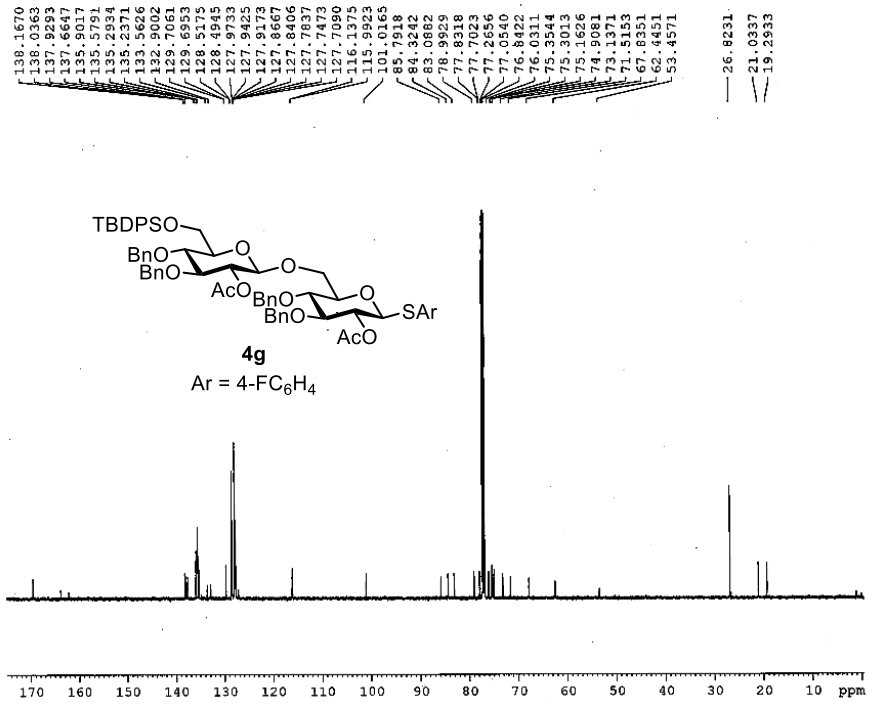

TBDPSO
BnO
BnO
BzO
BnO
BnO
BzO
SAr
4f
Ar = 4-FC6H4
ppm
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
BRUKER
NAME KTM-207 GPC-1
EXPNO 12
PROCNO 1
Date_ 20210212
Time 14.03
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG hmqcgpqf
TD 1024
SOLVENT CDCl3
NS 4
DS 16
SWH 5617.978 Hz
FIDRES 5.486306 Hz
AQ 0.0911860 sec
RG 203
DW 89.000 usec
DE 6.50 usec
TE 296.6 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.49324095 sec
D2 0.00344828 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00002000 sec
CHANNEL f1
NUC1 1H
P1 13.00 usec
P2 26.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1324541 MHz
CHANNEL f2
CPDPRG2 garp
NUC2 13C
P3 10.00 usec
PCPD2 60.00 usec
PL2 -1.00 dB
PL12 15.40 dB
PL2W 125.22619629 W
PL12W 2.86876655 W
SFO2 150.9141255 MHz
GRADIENT CHANNEL
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec
ND0 2
TD 128
SFO1 150.9141 MHz
FIDRES 195.291351 Hz
SW 165.639 ppm
FnMODE QF
SI 1024
SF 600.1300323 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 150.9028090 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

^{1}H NMR



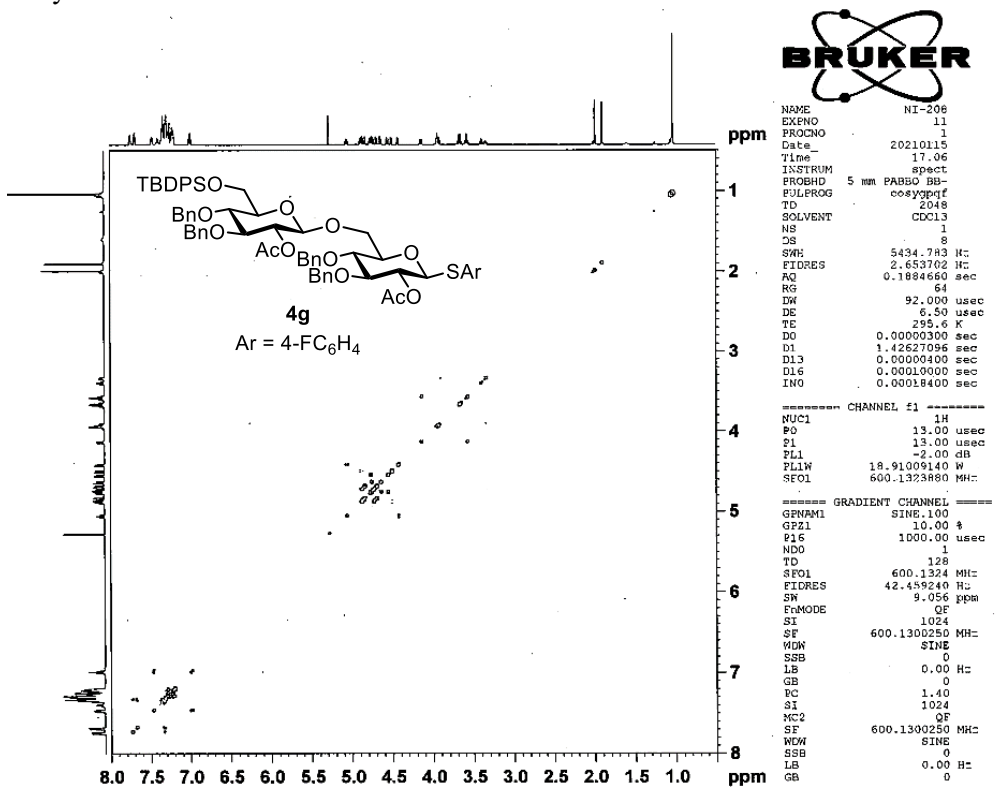

```
NAME                NI-208
EXPNO                   10
PROCNO                   1
Date_             20210115
Time_                17.05
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               12335.526 Hz
FIDRES            0.188225 Hz
AQ                2.6564426 sec
RG                      128
DW                   40.533 usec
DE                     6.50 usec
TE                    295.6 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.00 usec
PL1                  -2.00 dB
PL1W          18.91009140 W
SFO1         600.1337060 MHz
SI                    32768
SF           600.1300250 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

^{13}C NMR

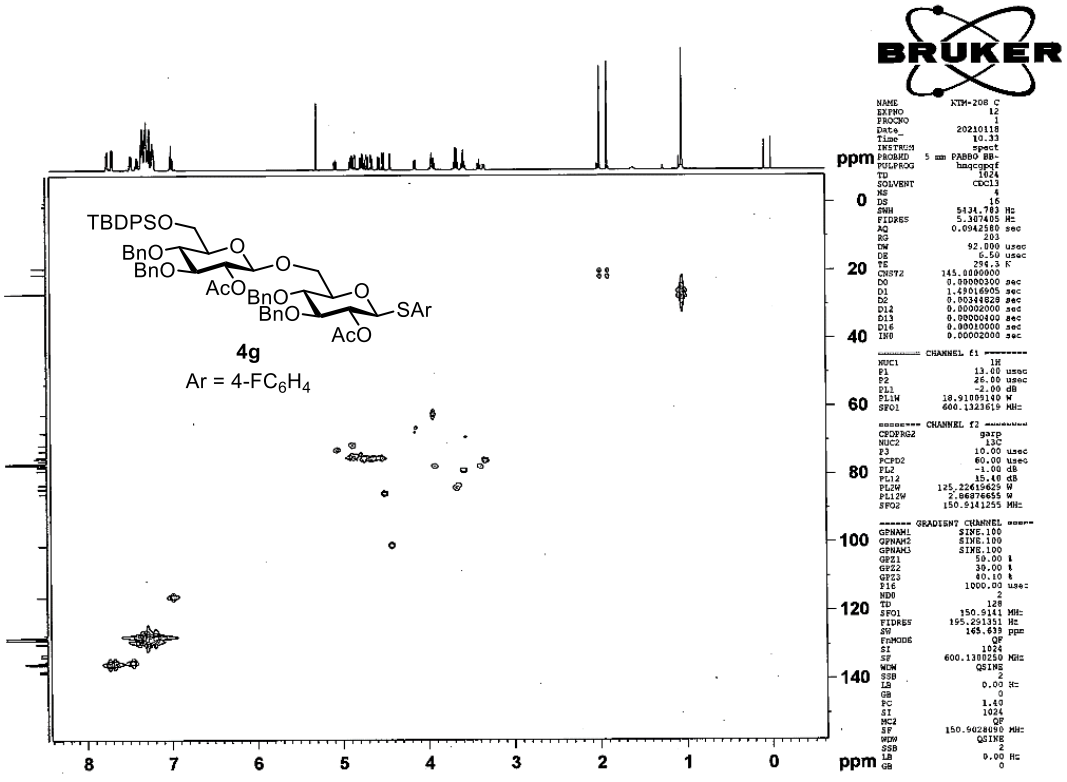



```
NAME                NI-208
EXPNO                   12
PROCNO                   1
Date_             20210115
Time                 17.35
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      500
DS                        2
SWH               36057.691 Hz
FIDRES            0.550197 Hz
AQ                0.9088159 sec
RG                      203
DW                   13.867 usec
DE                     6.50 usec
TE                    297.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.00 usec
PL1                  -1.00 dB
PL1W         125.22619629 W
SFO1          150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                  -2.00 dB
PL12                 13.78 dB
PL13                 14.00 dB
PL2W          18.91009140 W
PL12W          0.49968192 W
PL13W          0.47499999 W
SFO2         600.1324005 MHz
SI                    32768
SF           150.9028090 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

H-H cosy

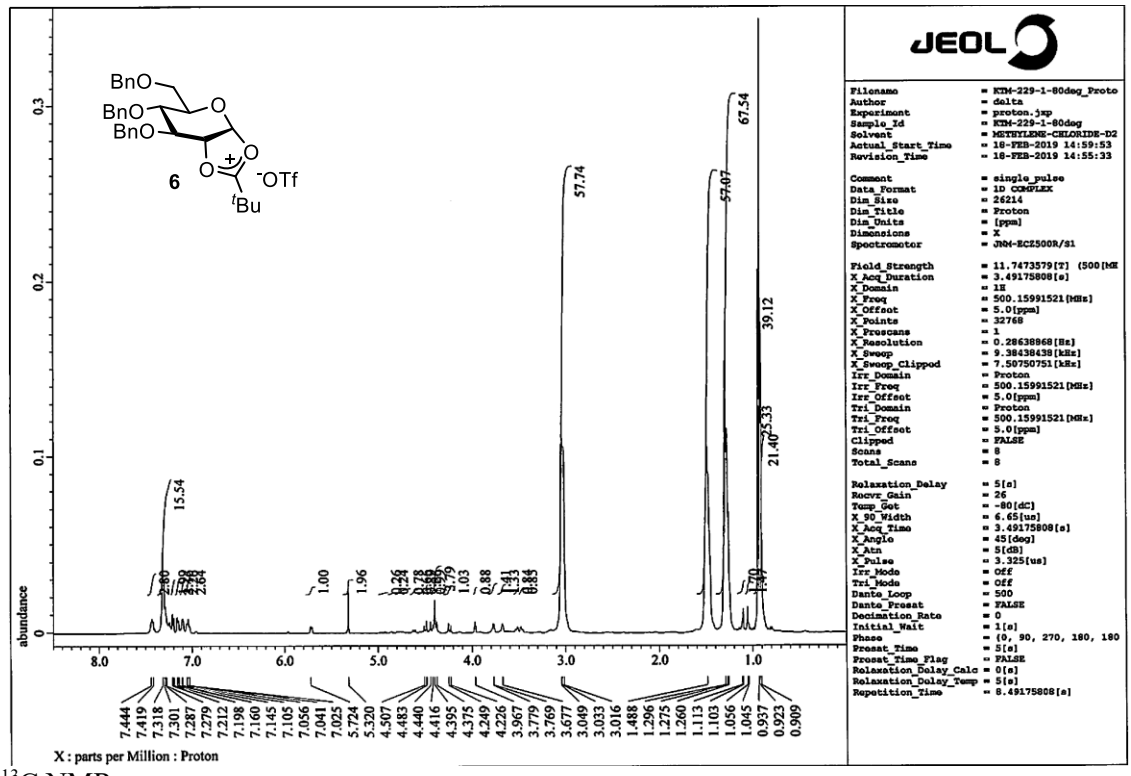

TBDPSO
BnO
BnO
AcO
BnO
BnO
AcO
SAr
4g
Ar = 4-FC6H4
ppm
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
BRUKER
NAME NI-206
EXPNO 11
PROCNO 1
Date_ 20210115
Time 17.06
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 8
SWH 5434.783 Hz
FIDRES 2.653702 Hz
AQ 0.1884660 sec
RG 64
DW 92.000 usec
DE 6.50 usec
TE 295.6 K
D0 0.00000300 sec
D1 1.42627096 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00018400 sec
======== CHANNEL f1 ========
NUC1 1H
P0 13.00 usec
P1 13.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1323880 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPZ1 10.00 %
P16 1000.00 usec
ND0 1
TD 128
SFO1 600.1324 MHz
FIDRES 42.459240 Hz
SW 9.056 ppm
FnMODE QF
SI 1024
SF 600.1300250 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 600.1300250 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

HMQC

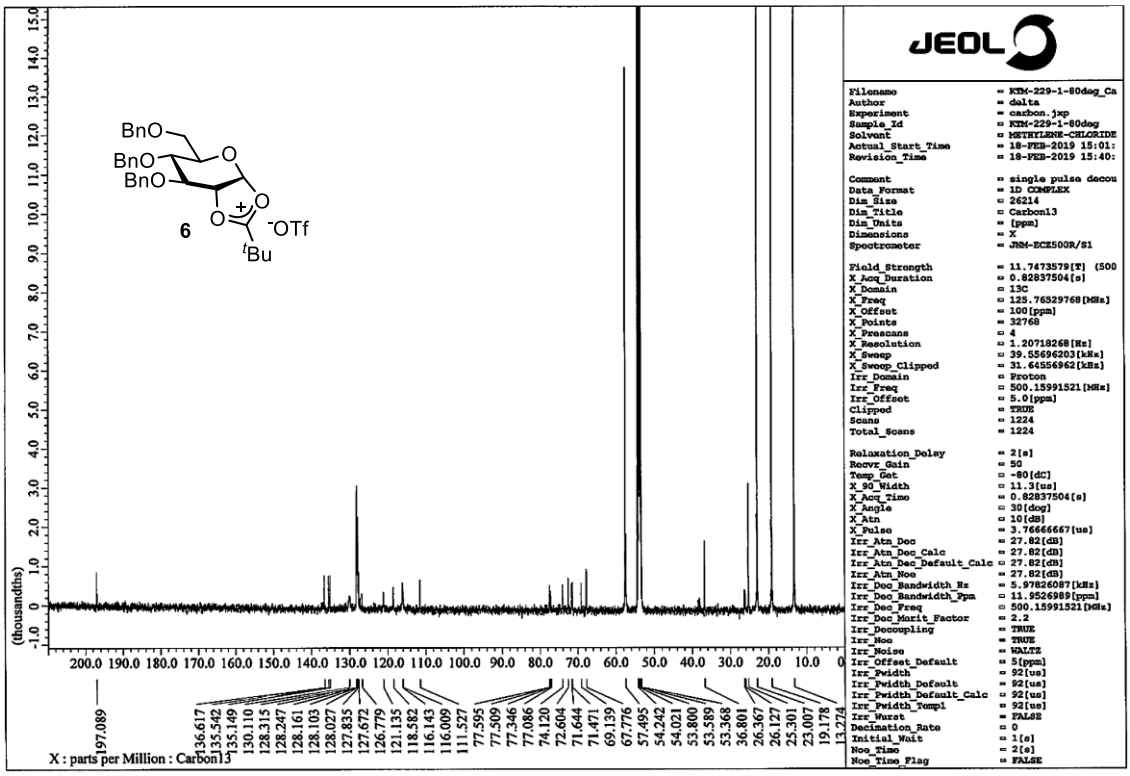

TBDPSO
BnO
BnO
AcO
BnO
BnO
AcO
SAr
4g
Ar = 4-FC6H4
ppm
8 7 6 5 4 3 2 1 0 ppm
BRUKER
NAME NTM-208 C
EXPNO 12
PROCNO 1
Date_ 20210118
Time 10.33
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG hmqcgpsf
TD 1024
SOLVENT CDCl3
NS 4
DS 16
SWH 5434.783 Hz
FIDRES 5.307405 Hz
AQ 0.0942580 sec
RG 203
DW 92.000 usec
DE 6.50 usec
TE 294.3 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.49016905 sec
D2 0.00344828 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00002000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
P2 26.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1323619 MHz
======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 10.00 usec
PCPD2 60.00 usec
PL2 -1.00 dB
PL12 15.40 dB
PL2W 125.22615625 W
PL12W 2.86876655 W
SFO2 150.9141255 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec
ND0 2
TD 128
SFO1 150.9141 MHz
FIDRES 195.291351 Hz
SW 165.639 ppm
FnMODE QF
SI 1024
SF 600.1300250 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 150.9028090 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

^{1}H, ^{13}C NMR, H-H COSY and HMQC spectra of glycosyl dioxalenium ions

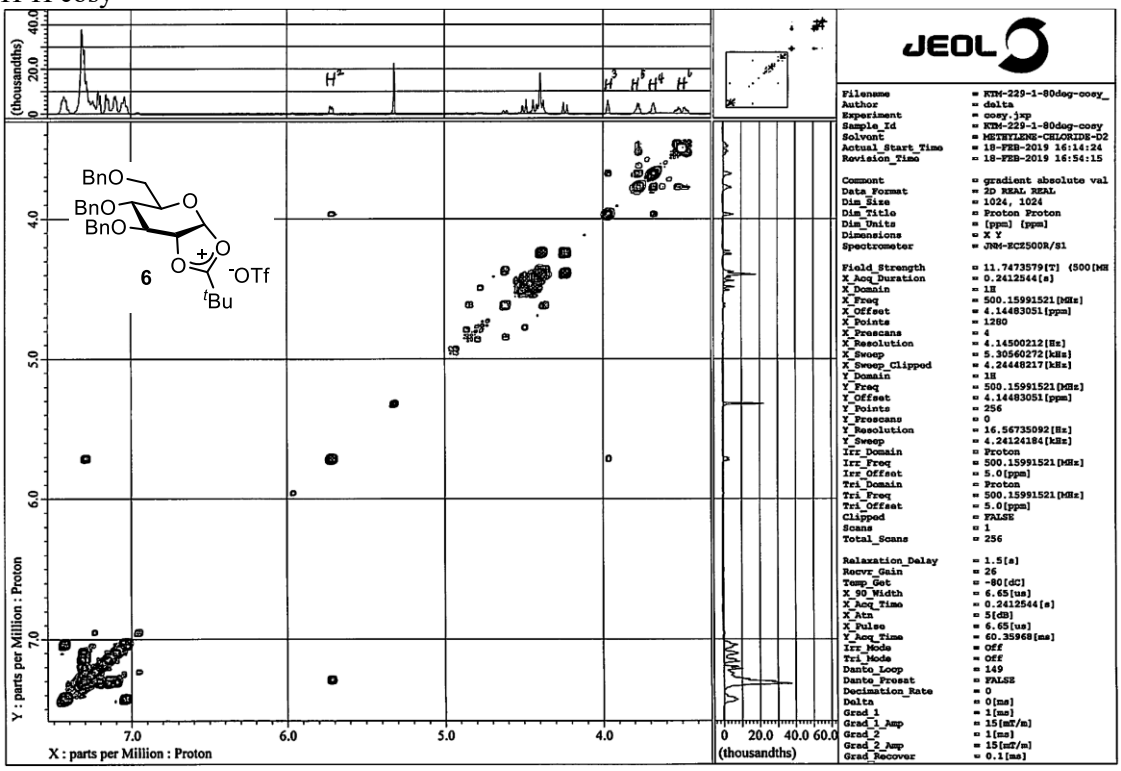
^{1}H NMR



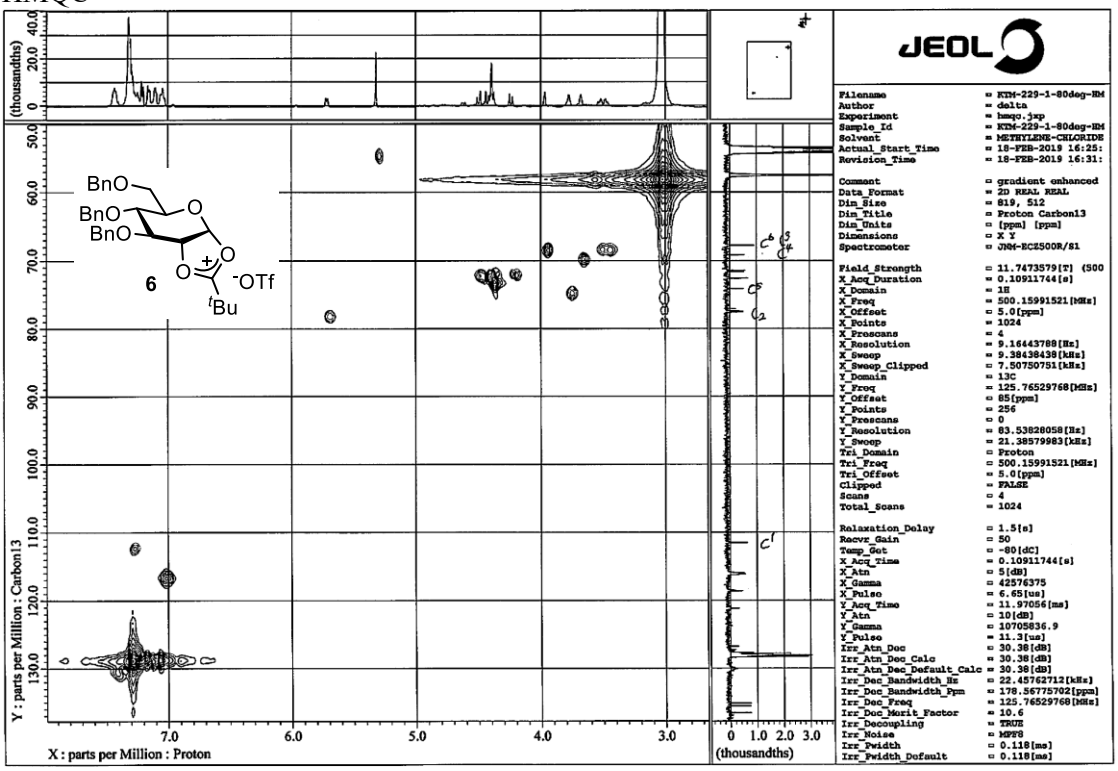
^{13}C NMR



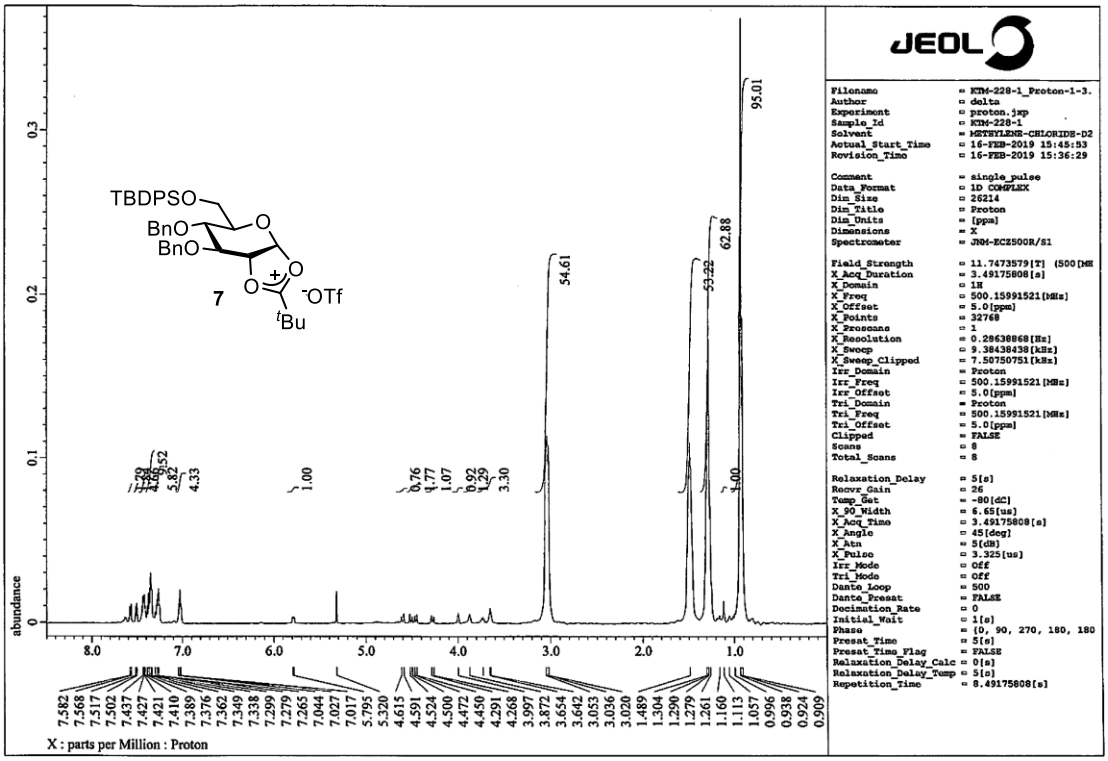
H-H cosy


BnO
BnO
BnO
O
O
O
6
-OTf
tBu
X : parts per Million : Proton
Y : parts per Million : Proton
(thousandths)
JEOL

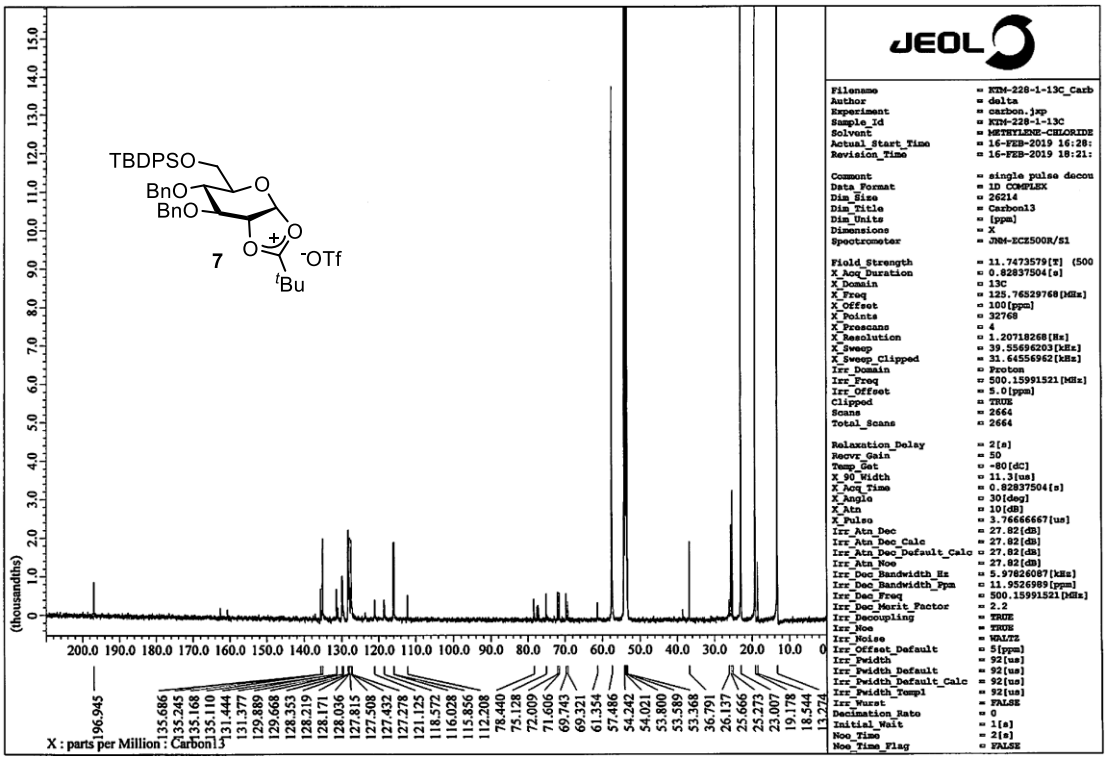
HMQC


BnO
BnO
BnO
O
O
O
6
-OTf
tBu
X : parts per Million : Proton
Y : parts per Million : Carbon13
(thousandths)
JEOL

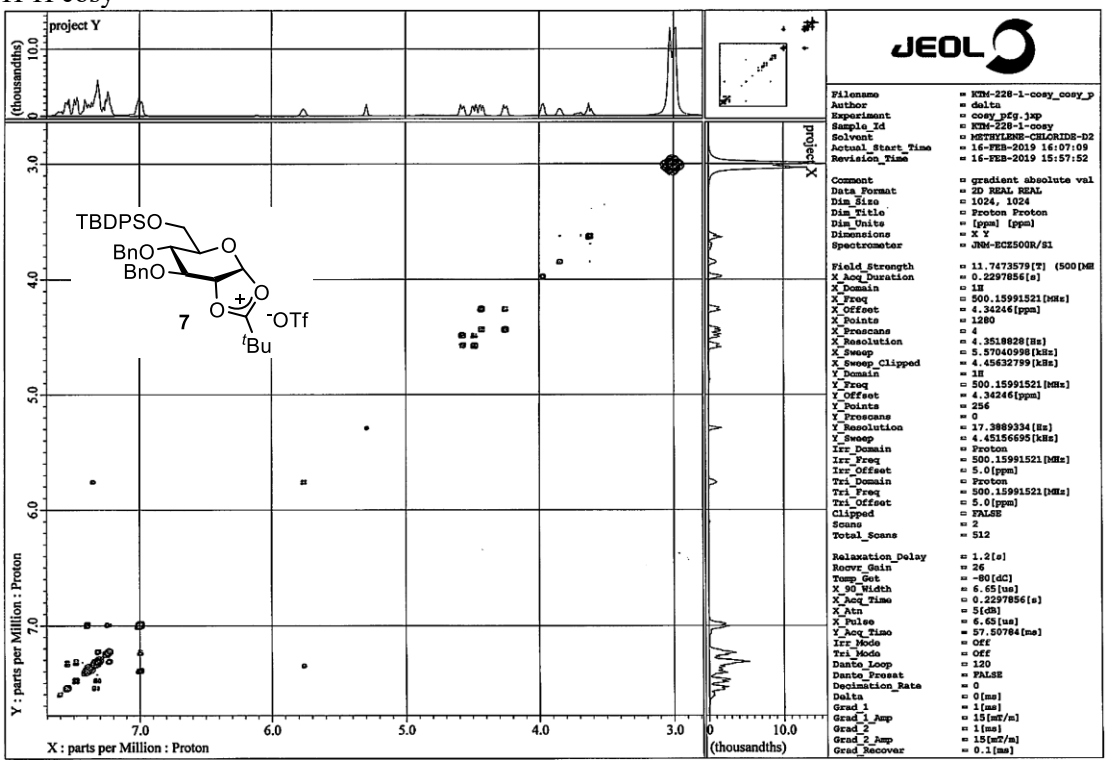
^{1}H NMR



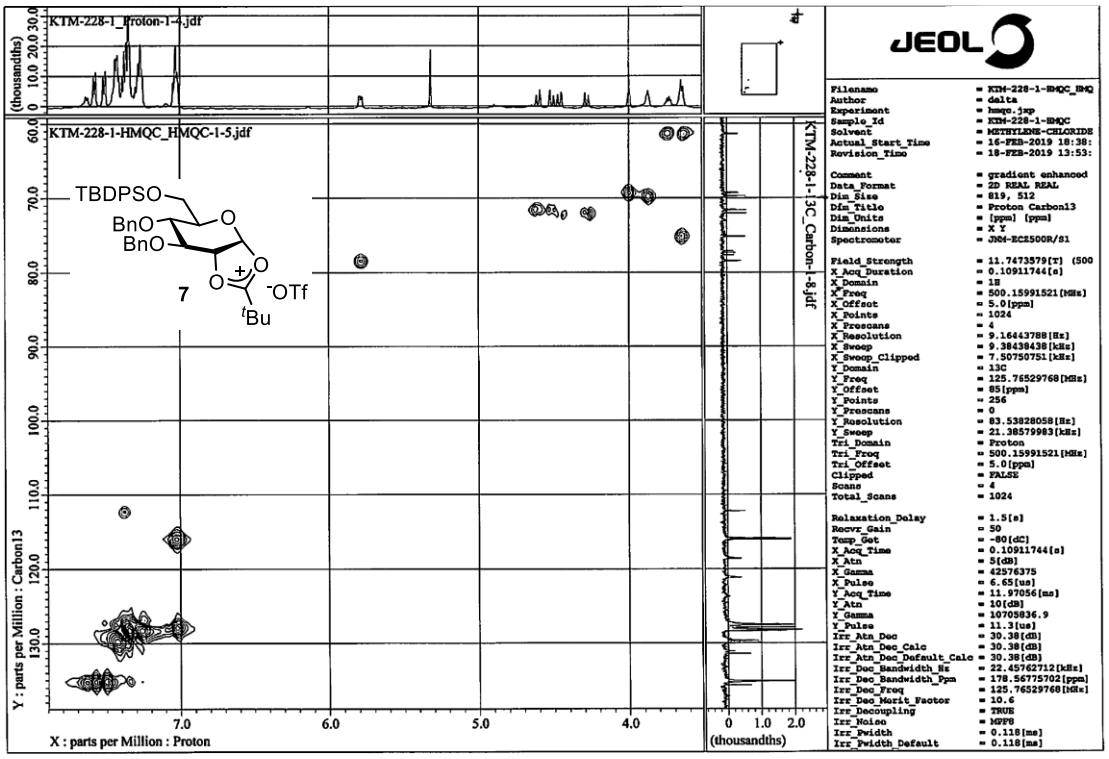
^{13}C NMR



H-H cosy


project Y
project X
TBDPSO
BnO
BnO
O
O
O
7
-OTf
tBu
Y : parts per Million : Proton
X : parts per Million : Proton
(thousandths)
(thousandths)
JEOL
Filename = KTM-228-1-cosy_cosy_p
Author = delta
Experiment = cosy_pfg.jxp
Sample_Id = KTM-228-1-cosy
Solvent = METHYLENE-CHLORIDE-D2
Actual_Start_Time = 16-FEB-2019 16:07:09
Revision_Time = 16-FEB-2019 15:57:52
Comment = gradient absolute val
Data_Format = 2D REAL REAL
Dim_Size = 1024, 1024
Dim_Title = Proton Proton
Dim_Units = [ppm] [ppm]
Dimensions = X Y
Spectrometer = JNM-ECZ500R/S1
Field_Strength = 11.7473579[T] (500[MH
X_Acq_Duration = 0.2297856[s]
X_Domain = 1H
X_Freq = 500.15991521[MHz]
X_Offset = 4.34246[ppm]
X_Points = 1280
X_Prescans = 4
X_Resolution = 4.3518828[Hz]
X_Sweep = 5.57040998[kHz]
X_Sweep_Clipped = 4.45632799[kHz]
Y_Domain = 1H
Y_Freq = 500.15991521[MHz]
Y_Offset = 4.34246[ppm]
Y_Points = 256
Y_Prescans = 0
Y_Resolution = 17.3889334[Hz]
Y_Sweep = 4.45156695[kHz]
Irr_Domain = Proton
Irr_Freq = 500.15991521[MHz]
Irr_Offset = 5.0[ppm]
Tri_Domain = Proton
Tri_Freq = 500.15991521[MHz]
Tri_Offset = 5.0[ppm]
Clipped = FALSE
Scans = 2
Total_Scans = 512
Relaxation_Delay = 1.2[s]
Recvr_Gain = 26
Temp_Set = -80[dC]
X_90_Width = 6.65[us]
X_Acq_Time = 0.2297856[s]
X_Atn = 5[dB]
X_Pulse = 6.65[us]
Y_Acq_Time = 57.50784[ms]
Irr_Mode = Off
Tri_Mode = Off
Dante_Loop = 120
Dante_Presat = FALSE
Decimation_Rate = 0
Delta = 0[ms]
Grad_1 = 1[ms]
Grad_1_Amp = 15[mT/m]
Grad_2 = 1[ms]
Grad_2_Amp = 15[mT/m]
Grad_Recover = 0.1[ms]

HMQC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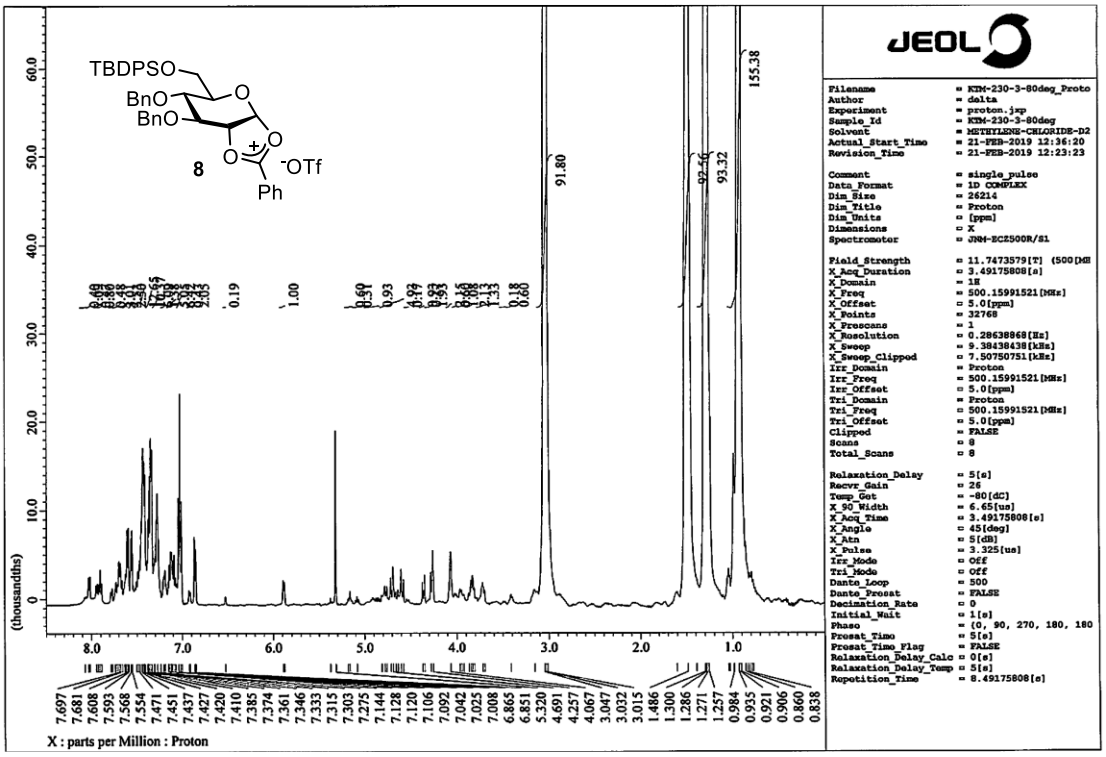
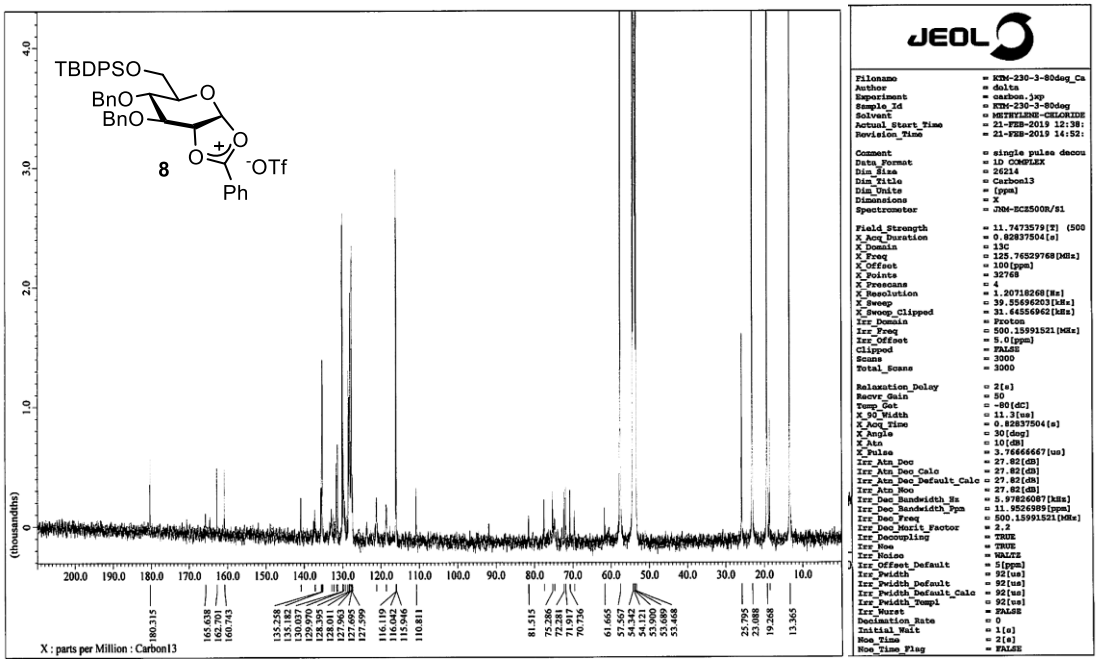
KTM-228-1-HMQC_HMQC-1-5.jdf
KTM-228-1-13C_Carbon-1-8.jdf
TBDPSO
BnO
BnO
O
O
O
7
-OTf
tBu
Y : parts per Million : Carbon13
X : parts per Million : Proton
(thousandths)
(thousandths)
JEOL
Filename = KTM-228-1-HMQC_HMQ
Author = delta
Experiment = hmqc.jxp
Sample_Id = KTM-228-1-HMQC
Solvent = METHYLENE-CHLORIDE
Actual_Start_Time = 16-FEB-2019 18:38:
Revision_Time = 18-FEB-2019 13:53:
Comment = gradient enhanced
Data_Format = 2D REAL REAL
Dim_Size = 819, 512
Dim_Title = Proton Carbon13
Dim_Units = [ppm] [ppm]
Dimensions = X Y
Spectrometer = JNM-ECZ500R/S1
Field_Strength = 11.7473579[T] (500
X_Acq_Duration = 0.10911744[s]
X_Domain = 1H
X_Freq = 500.15991521[MHz]
X_Offset = 5.0[ppm]
X_Points = 1024
X_Prescans = 4
X_Resolution = 9.16443788[Hz]
X_Sweep = 9.38438438[kHz]
X_Sweep_Clipped = 7.50750751[kHz]
Y_Domain = 13C
Y_Freq = 125.76529768[MHz]
Y_Offset = 85[ppm]
Y_Points = 256
Y_Prescans = 0
Y_Resolution = 83.53828058[Hz]
Y_Sweep = 21.38579983[kHz]
Tri_Domain = Proton
Tri_Freq = 500.15991521[MHz]
Tri_Offset = 5.0[ppm]
Clipped = FALSE
Scans = 4
Total_Scans = 1024
Relaxation_Delay = 1.5[s]
Recvr_Gain = 50
Temp_Set = -80[dC]
X_Acq_Time = 0.10911744[s]
X_Atn = 5[dB]
X_Gamma = 42576375
X_Pulse = 6.65[us]
Y_Acq_Time = 11.97056[ms]
Y_Atn = 10[dB]
Y_Gamma = 10705836.9
Y_Pulse = 11.3[us]
Irr_Atn_Dec = 30.38[dB]
Irr_Atn_Dec_Calc = 30.38[dB]
Irr_Atn_Dec_Default_Calc = 30.38[dB]
Irr_Dec_Bandwidth_Hz = 22.45762712[kHz]
Irr_Dec_Bandwidth_Ppm = 178.56775702[ppm]
Irr_Dec_Freq = 125.76529768[MHz]
Irr_Dec_Merit_Factor = 10.6
Irr_Decoupling = TRUE
Irr_Noise = MPFH
Irr_Pwidth = 0.118[ms]
Irr_Pwidth_Default = 0.118[ms]

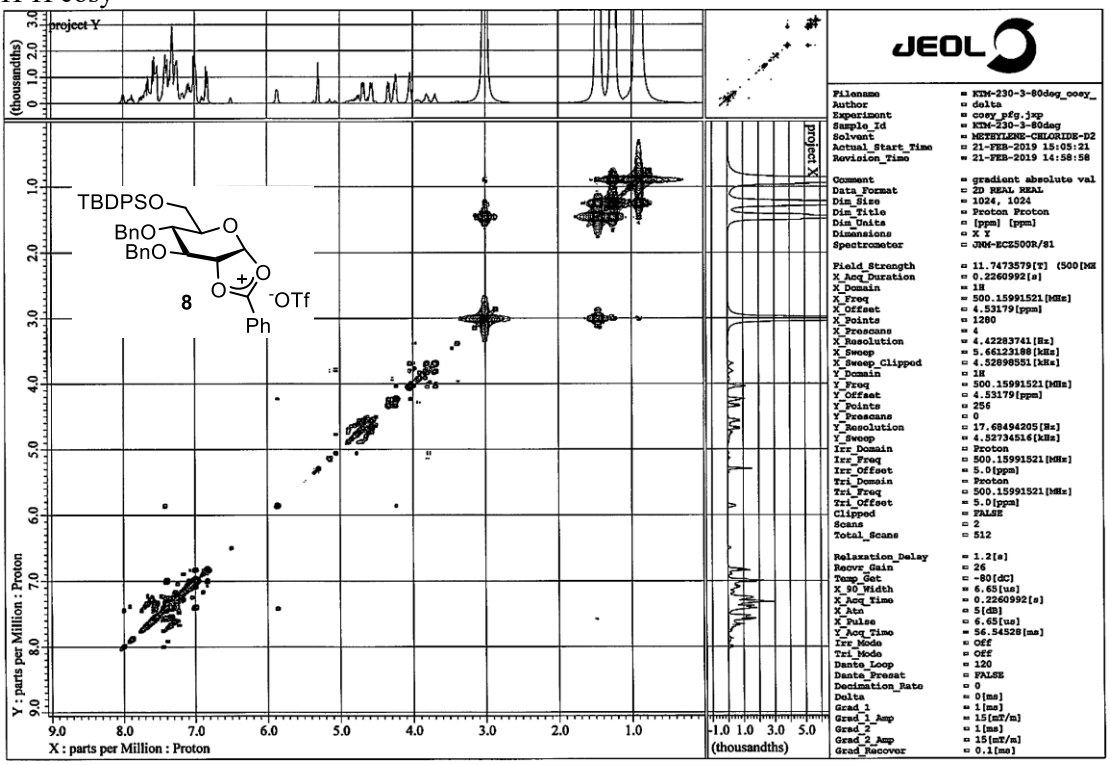
^{1}H NMR



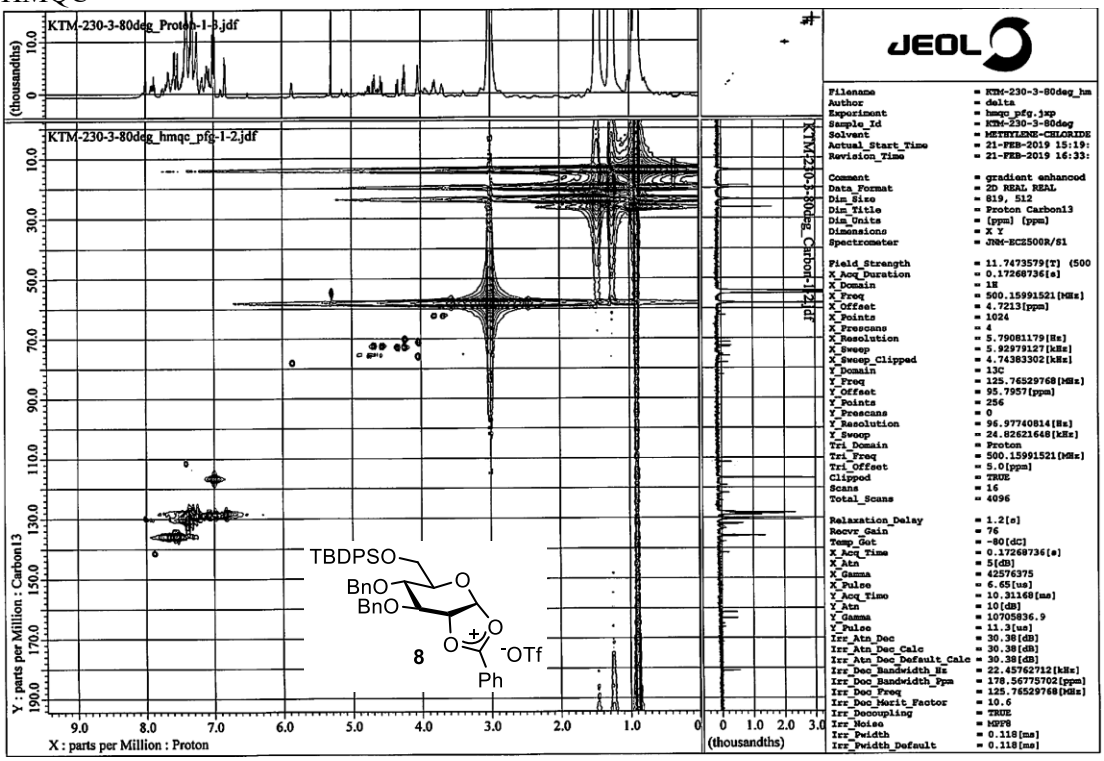
^{13}C NMR



H-H cosy


project Y
project X
TBDPSO
BnO
BnO
O
O
O
8
-OTf
Ph
Y : parts per Million : Proton
X : parts per Million : Proton
(thousandths)
JEOL
Filename = KTM-230-3-80deg_cosy_
Author = delta
Experiment = cosy_pfg.jxp
Sample_Id = KTM-230-3-80deg
Solvent = METHYLENE-CHLORIDE-D2
Actual_Start_Time = 21-FEB-2019 15:05:21
Revision_Time = 21-FEB-2019 14:58:58
Comment = gradient absolute val
Data_Format = 2D REAL REAL
Dim_Size = 1024, 1024
Dim_Title = Proton Proton
Dim_Units = [ppm] [ppm]
Dimensions = X Y
Spectrometer = JNM-EC2500R/S1
Field_Strength = 11.7473579[T] (500[MH
X_Acq_Duration = 0.2260992[s]
X_Domain = 1H
X_Freq = 500.15991521[MHz]
X_Offset = 4.53179[ppm]
X_Points = 1280
X_Prescans = 4
X_Resolution = 4.42283741[Hz]
X_Sweep = 5.66123188[kHz]
X_Sweep_Clipped = 4.52898551[kHz]
Y_Domain = 1H
Y_Freq = 500.15991521[MHz]
Y_Offset = 4.53179[ppm]
Y_Points = 256
Y_Prescans = 0
Y_Resolution = 17.68494205[Hz]
Y_Sweep = 4.52734516[kHz]
Irr_Domain = Proton
Irr_Freq = 500.15991521[MHz]
Irr_Offset = 5.0[ppm]
Tri_Domain = Proton
Tri_Freq = 500.15991521[MHz]
Tri_Offset = 5.0[ppm]
Clipped = FALSE
Scans = 2
Total_Scans = 512
Relaxation_Delay = 1.2[s]
Recvr_Gain = 26
Temp_Set = -80[dC]
X_90_Width = 6.65[us]
X_Acq_Time = 0.2260992[s]
X_Atn = 5[dB]
X_Pulse = 6.65[us]
Y_Acq_Time = 56.54528[ms]
Irr_Mode = Off
Tri_Mode = Off
Dante_Loop = 120
Dante_Preset = FALSE
Decimation_Rate = 0
Delta = 0[ms]
Grad_1 = 1[ms]
Grad_1_Amp = 15[mT/m]
Grad_2 = 1[ms]
Grad_2_Amp = 15[mT/m]
Grad_Recover = 0.1[ms]

HMQC


KTM-230-3-80deg_Proton-1-3.jdf
KTM-230-3-80deg_hmqc_pfg-1-2.jdf
KTM-230-3-80deg_Carbon-1-2.jdf
TBDPSO
BnO
BnO
O
O
O
8
-OTf
Ph
Y : parts per Million : Carbon13
X : parts per Million : Proton
(thousandths)
JEOL
Filename = KTM-230-3-80deg_hm
Author = delta
Experiment = hmqc_pfg.jxp
Sample_Id = KTM-230-3-80deg
Solvent = METHYLENE-CHLORIDE
Actual_Start_Time = 21-FEB-2019 15:19:
Revision_Time = 21-FEB-2019 16:33:
Comment = gradient enhancod
Data_Format = 2D REAL REAL
Dim_Size = 819, 512
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Dim_Units = [ppm] [ppm]
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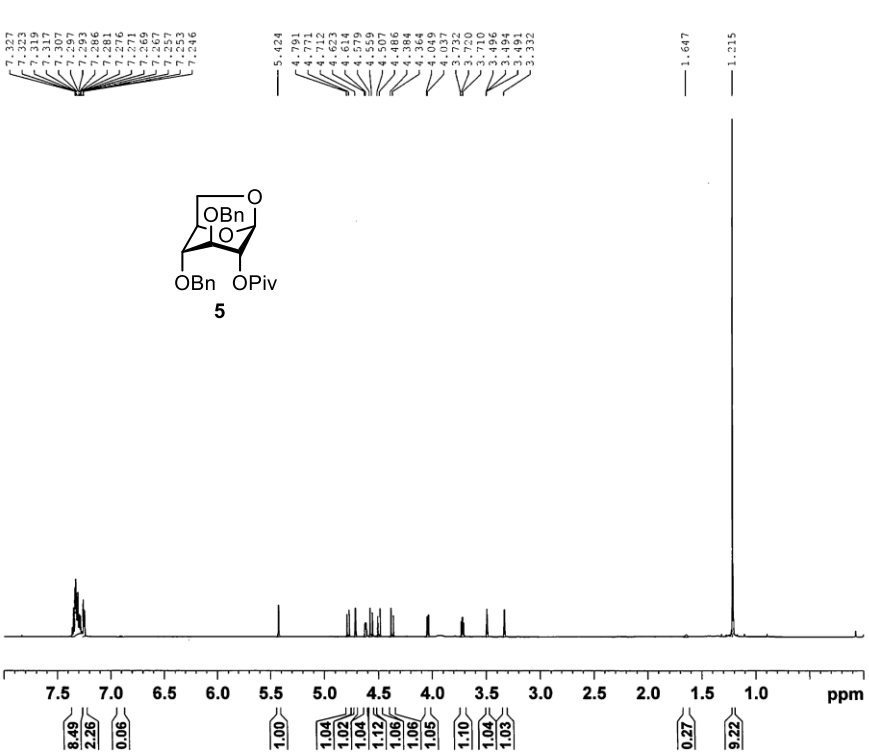
[1]H NMR spectra of 1,6-anhydrosugars

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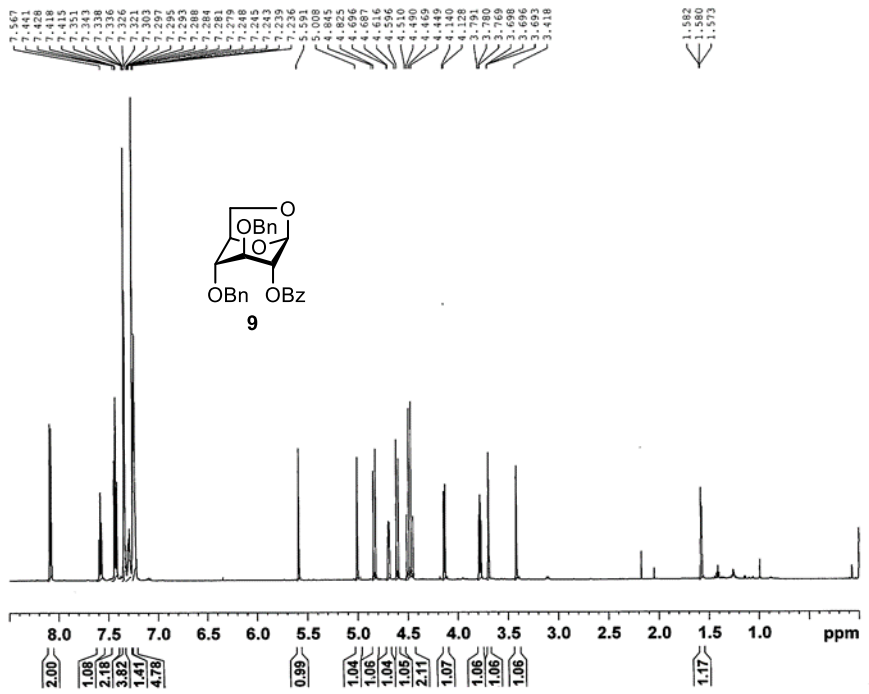


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Chapter 2.

Electrochemical Synthesis of the Protected Cyclic (1,3;1,6)-β-Glucan Dodecasaccharide

Introduction

Electrochemical transformations of small molecules have been used as a powerful set of tools in organic synthesis for many decades.[1] Recent progress in this area has enabled the synthesis of complex molecules such as natural products,[2] peptides,[3] and oligosaccharides.[4] We have been interested in the automated synthesis of oligosaccharides using electrochemical methods and have developed a method named 'automated electrochemical assembly' (AEA), which is based on electrochemical generation of a glycosylation intermediate and its subsequent coupling with alcohols, including oligosaccharides.[5]

Cyclic oligosaccharides such as cyclodextrins (CDs), which contain 1,4-α-linked D-glucopyranose, have attracted the interest of researchers for more than a century because of their unique structures and properties.[6] To our knowledge, δ-CD (nonasaccharide) is the largest CD that has been chemically synthesized to date.[7] With regard to cyclic oligosaccharides containing other glycosidic linkages and monosaccharides, cyclic oligo-1,6-β-D-glucosamines up to the heptasaccharide were synthesized by the Nifantiev group[8] and our group.[9] More recently, our group reported the synthesis of cyclic oligo-1,4-α-*N*-acetylglucosamine 'cyclokasaodorin' through an electrochemical polyglycosylation-isomerization-cyclization process.[10] In this case, however, only hexasaccharide and heptasaccharide were obtained. Therefore, the chemical synthesis of large cyclic oligosaccharides remains challenging.

We then focused on a natural oligosaccharide isolated from *Bradyrhizobium japonicum* MTCC120.[11] The oligosaccharide has a cyclic dodecasaccharide structure that consists of two types of glucose trisaccharides with β-(1,3)- and β-(1,6)-glycosidic linkages. Here, we report the electrochemical synthesis of the protected cyclic (1,3;1,6)-β-glucan dodecasaccharide as a potential precursor of the natural cyclic dodecasaccharide.

Results and Discussion

Protected cyclic dodecasaccharide **1** has a symmetric structure that consists of β-(1,3)- and β-(1,6)-glycosidic linkages (Figure 2-1). Thus, we envisioned that an ideal approach to synthesize protected cyclic dodecasaccharide **1** would be through dimerization of the semi-circular hexasaccharide building block **2** followed by cyclization in the same pot. These semi-circular hexasaccharides **2a** and **2b** were considered suitable building blocks because they both have a protecting-group-free hydroxy group (**2a**: 3-OH, **2b**: 6-OH) and thioaryl (SAr, **2a**: Ar = 4-FC_6H_4, **2b**: Ar = 4-ClC_6H_4) leaving group at the anomeric position (C-1). To examine the hypothesis, we synthesized the semi-circular hexasaccharide building block **2a**, bearing two β-(1,3)-glycosidic linkages and three β-(1,6)-glycosidic linkages.[12] Although **2a** was prepared under the electrochemical conditions, its total yield was very low. Moreover, **2a** had a protecting-group-free 3-OH which must be less reactive than the 6-OH group. Therefore, we designed semi-circular hexasaccharide **2b** as a building block equipped with a protecting-group-free 6-OH. Semi-circular hexasaccharide **2b** could be disconnected to disaccharide building block **3** and tetrasaccharide building block **4b** with β-(1,6)-glycosidic and β-(1,3)-glycosidic linkages, respectively (Figure 2-2). Tetrasaccharide **4a**, as the precursor of **4b** derived from disaccharide building block **5**, with a β-(1,3)-glycosidic linkage, and two equivalents of monosaccharide building block **6**, equipped with the protecting-group-free 3-OH.

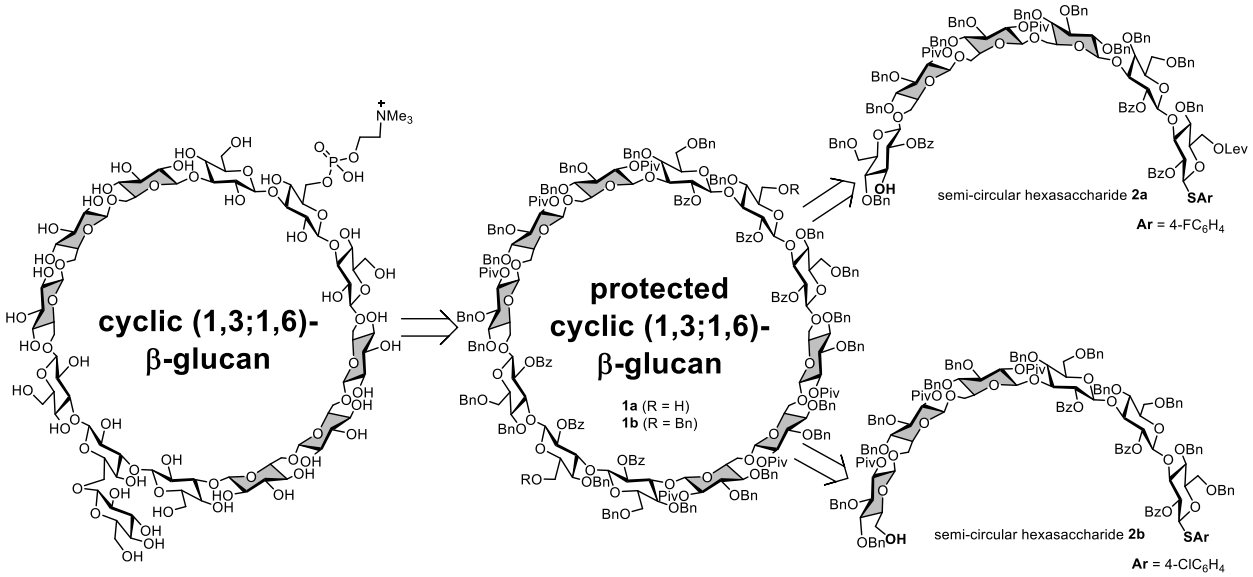


Figure 2-1. Semi-circular hexasaccharide building blocks for the protected cyclic (1,3; 1,6)-β-glucan.

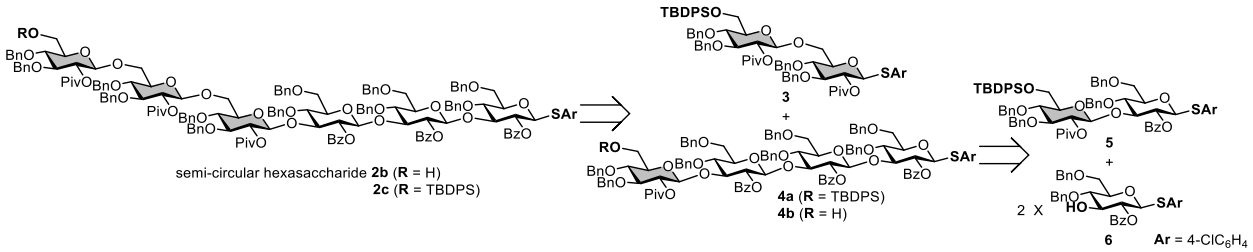


Figure 2-2. Retrosynthesis of semi-circular hexasaccharide **2b** and its building blocks **3-6**.

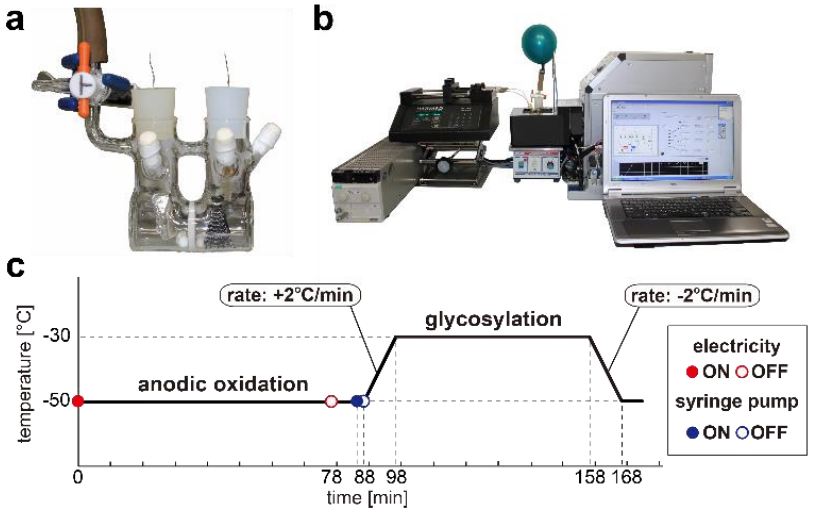


Figure 2-3. Devises for automated electrochemical assembly. a) Divided electrolysis cell equipped with platinum plate cathode and carbon fiber anode. b) The 1st generation automated electrochemical synthesizer. c) Schedule of synthesizer for a single cycle.

Automated electrochemical assembly was performed using a middle-size divided electrolysis cell (15 mL for anode and cathode) equipped with carbon fiber anode and platinum plate cathode under argon

atmosphere (Figure 2-3a). The electrolysis was placed in the cooling bath of the 1st generation automated electrochemical synthesizer (Figure 2-3b). The synthesizer was composed of chiller with a cooling bath, stable direct current (DC) power supply, syringe pump, magnetic stirrer, and personal computer (PC), and these devices were controlled by LabVIEW installed in the notebook PC. The schedule of a single cycle was shown in Figure 2-3c. The DC power supply applied a constant current (13 mA, 1.05 F/mol) during the anodic oxidation and the electrolysis time (4677 sec = ca 78 min) depended on both reaction scale (0.60 mmol) and current value (13 mA). The chiller kept two temperatures -50 °C and -30 °C during anodic oxidation and glycosylation, respectively. In some cases, we switched off the chiller before quenching of the reaction and raised the temperature up to 0 °C to complete the glycosylation. Two gastight syringes were filled with solution of a building block and solvent for anodic chamber and cathodic chamber, respectively. They were set to the syringe pump and solutions were added at rate 1.0 mL/min after electrolysis.

Monosaccharide building blocks **6**, **7a** and **7b** were prepared from D-glucose pentaacetate according to the reported procedures (Figure 2-4). Disaccharide building block **3**, with a β-(1,6)-glycosidic linkage, was prepared using AEA between **7a** and **7b** in the presence of tetrabutylammonium triflate (Bu_4NOTf) as an electrolyte. Glycosyl dioxalenium ion intermediate **8** was generated by anodic oxidation of **7a** under constant current conditions at -50 °C. Subsequent coupling of **8** and building block **7b** (1.2 equiv.) afforded disaccharide **3** in 81% yield. This is a standard AEA protocol, and the details of reaction conditions and structures of possible intermediates have been omitted from the following figures (see the ESI for details of reaction conditions). Although disaccharide building block **5**, with a β-(1,3)-glycosidic linkage, was also prepared using AEA of **7a** and **6** (1.2 equiv.) in 85% yield, the one-pot synthesis of tetrasaccharide **4a** from monosaccharide building block **7a** using AEA with three cycles was sluggish.

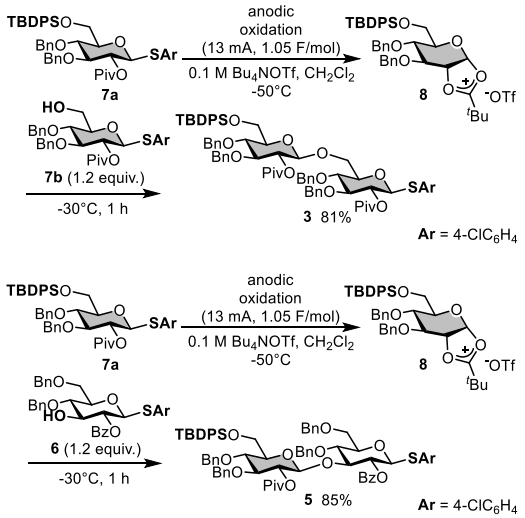
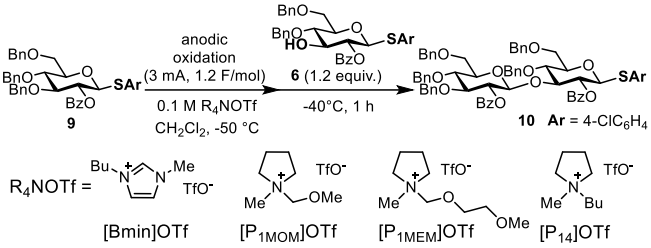


Figure 2-4. Synthesis of disaccharide building blocks **3** and **5**.

The electrolyte for AEA was optimized using the electrochemical formation of β-(1,3)-glycosidic linkages using monosaccharides **9** and **6** (1.2 equiv.) as model building blocks (Table 2-1). Whereas the use of tetraethylammonium triflate (Et_4NOTf) afforded disaccharide **10** in moderate yield (entry 1), Bu_4NOTf, which has been used as a standard electrolyte for AEA, gave the product **10** in good yield (entry 2). We also examined the use of ionic liquids (entries 3−6). The initial voltage of anodic oxidation was significantly influenced by the electrolyte; however, there was no clear relationship between the initial voltage and the

product yield. Amongst these ionic liquids, 1-butyl-1-methylpyrrolidinium triflate ([P_{14}]OTf) afforded the desired disaccharide **10** in the highest yield (entry 6). Therefore, we used ionic liquid [P_{14}]OTf as an electrolyte in the following glycosylation reactions. It has not been clarified why [P_{14}]OTf gave the best yield; however, oxidation potential (Eox) of monosaccharide building block **9** measured with [P_{14}]OTf (Eox = 1.67 V vs. SCE) was slightly lower than that measured with Bu_4NOTf (Eox = 1.70 V vs. SCE). We assume that electrolytes may influence the structure of electrical double layer and the process of single electron transfer.

Table 2-1. Optimization of electrolyte of AEA



entry	electrolyte	initial	yield[b]
1	Et_4NOTf	26 V	61%
2[a]	Bu_4NOTf	14 V	79%
3[a]	[Bmim]OTf	59 V	70%
4	[P_{1MOM}]OTf	93 V	81%
5	[P_{1MEM}]OTf	26 V	89%
6	[P_{14}]OTf	51 V	97%

[a]Inter-electrode voltage. [b]Determined by NMR.

The synthesis of tetrasaccharide **4a**, with three β-(1,3)-glycosidic linkages, from disaccharide **5** was carried out using AEA with two consecutive glycosylation cycles with monosaccharide building block **6** (1.0 equiv). The process was still challenging; however, performing the reaction sequence in the presence of [P_{14}]OTf gave a slightly better yield than with Bu_4NOTf (Figure 2-5). Deprotection of the tert-butyldiphenylsilyl (TBDPS) group of 4a was achieved successfully in the presence of hydrogen fluoride pyridine complex (HF•pyridine) to obtain tetrasaccharide building block **4b**, equipped with a protecting-group-free 6-OH, in 83% yield.

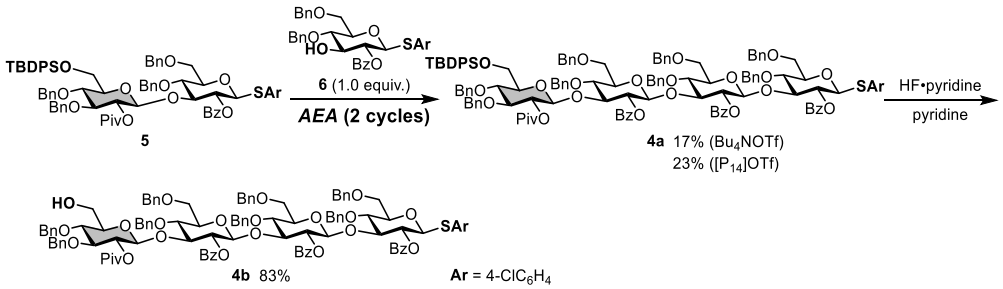


Figure 2-5. Synthesis of tetrasaccharide building block **4b**.

Semi-circular hexasaccharide building block **2b** was prepared using AEA and subsequent TBDPS deprotection (Figure 2-6). Disaccharide **3** and tetrasaccharide **4b** (1.2 equiv.) were assembled to prepare TBDPS-protected semi-circular hexasaccharide **2c** in the presence of [P_{14}]OTf as an electrolyte.

Deprotection of the TBDPS group at 6-OH was carried out under the standard reaction conditions with HF•pyridine, and the desired semi-circular hexasaccharide **2b** was obtained in 86% yield. Thus-obtained **2b**, equipped with a protecting-group-free 6-OH, was used as a building block in the one-pot dimerization−cyclization process to synthesize protected cyclic dodecasaccharide **1b** (Scheme 2-1). Although the yield of **1b** was very low (3%), protected cyclic (1,3;1,6)-β-glucan dodecasaccharide was obtained, together with by-products such as cyclic hexasaccharide and larger cyclic oligosaccharides, which were detected by MALDI-TOF-MS (see the experimental section for details).

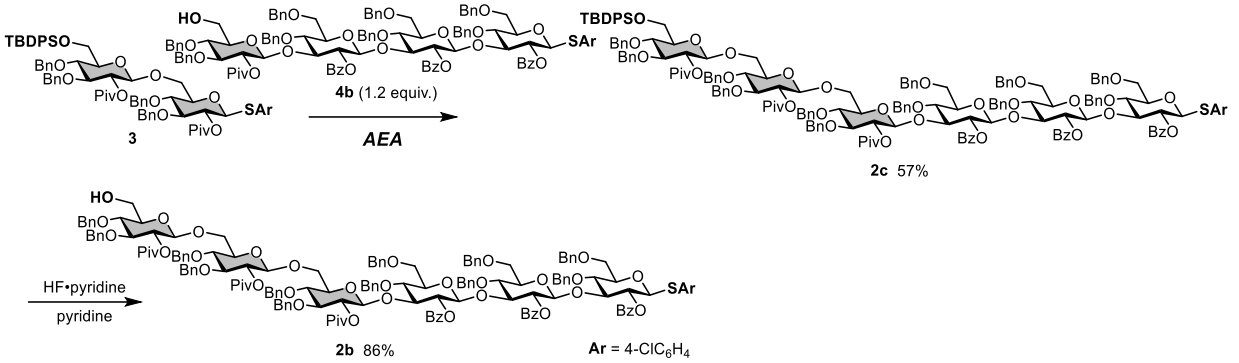
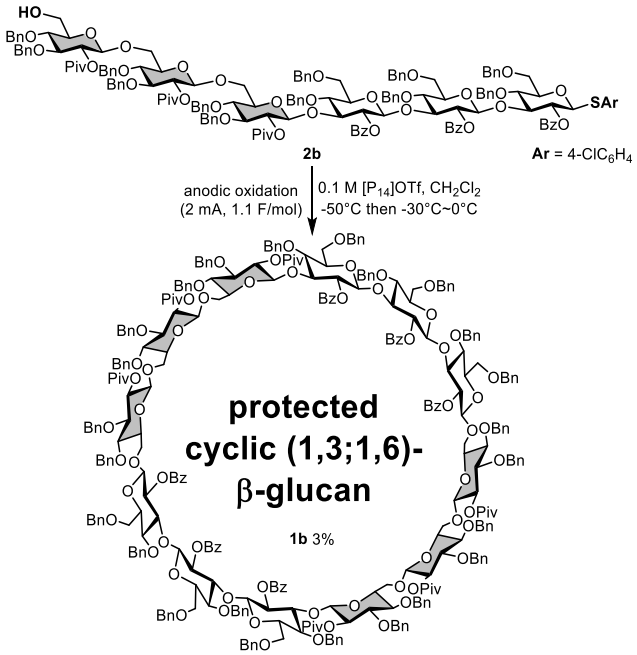


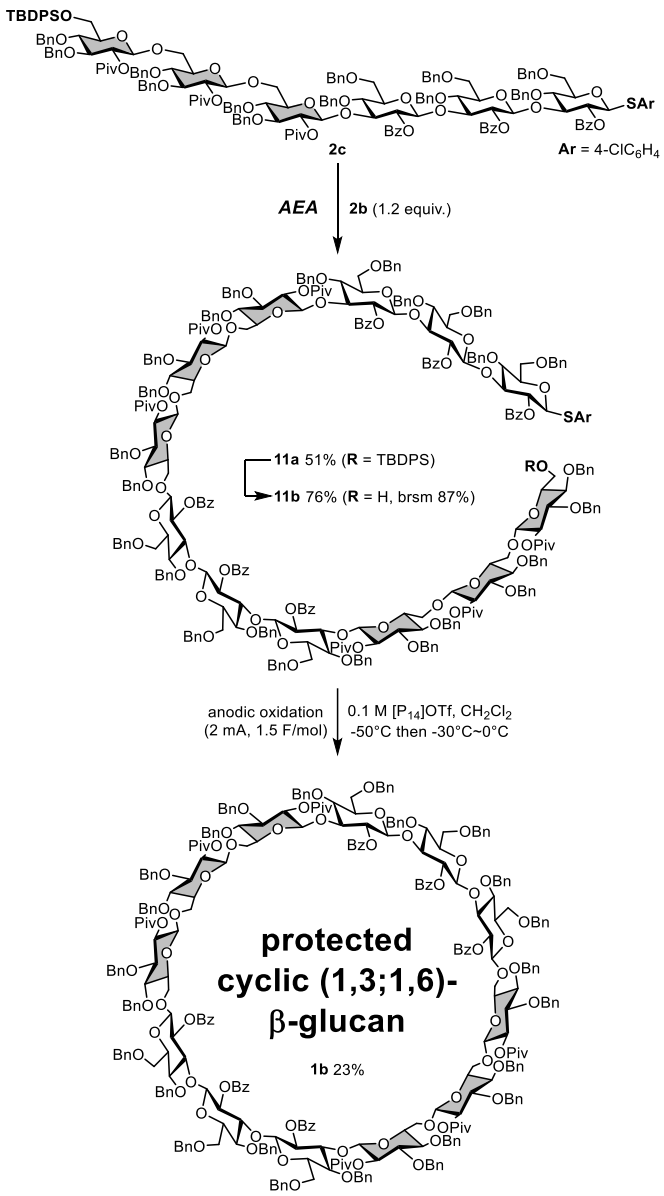
Figure 2-6. Synthesis of semi-circular hexasaccharide **2b**.



Scheme 2-1. One-pot dimerization-cyclization process for the preparation of protected cyclic dodecasaccharide **1b**.

The results of the one-pot dimerization−cyclization process encouraged us to synthesize protected cyclic dodecasaccharide **1b** using AEA (Scheme 2-2). Two semi-circular hexasaccharide building blocks, **2b** and **2c** (1.2 equiv.), were assembled using AEA to prepare linear dodecasaccharide **11a** in 51% yield. The major by-product of the reaction was hydroxy sugar of **2c**, which was detected by MALDI-TOF-MS. The TBDPS group on the 6-OH of **11a** was then deprotected to obtain **11b** as a precursor of protected cyclic dodecasaccharide **1b**. Finally, the intramolecular electrochemical glycosylation of **11b** was performed at a

low concentration (5 mM) to synthesize **1b** in 23% yield. The three-step yield of **1b** was ca. 10%, which was three times higher than that of the one-pot process shown in Scheme 2-1.



Scheme 2-2. Synthesis of protected cyclic dodecasaccharide **1b**.

Conclusion

We have synthesized the protected precursor of cyclic (1,3;1,6)-β-glucan dodecasaccharide, which is the core structure of the natural oligosaccharide isolated from *Bradyrhizobium japonicum* MTCC120. We designed a semi-circular hexasaccharide and its reactivity was confirmed by the electrochemical one-pot dimerization−cyclization process. Finally, the linear precursor of cyclic dodecasaccharide was prepared using AEA of linear hexasaccharides and subsequent electrochemical intramolecular glycosylation afforded the protected cyclic dodecasaccharide in a higher yield. Further optimization of the electrochemical intramolecular glycosylation and global deprotection to obtain cyclic dodecasaccharide are in progress in our laboratory.

Experimental

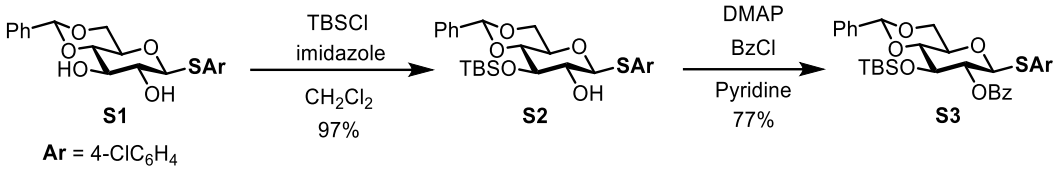
1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE II 600 (^{1}H 600 MHz, ^{13}C 150 MHz). ESI-MS and MALDI-TOF-MS were recorded on Thermo Scientific Exactive spectrometer and Bruker ultrafleXtreme, respectively. Measurements of oxidation potentials of monosaccharides (conc. 4.0 mM) were carried out in 0.1 M of electrolyte in 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 2000 rpm. Preparative recycling gel permeation chromatography (PR-GPC) was performed on Japan Analytical Industry LC-5060. Kanto silica gel 60 N (spherical, neutral, 63-210 μm) was used for silica gel column chromatography. The automated synthesizer is consisting of the commercially available instruments such as the chiller with a cooling bath (UCR-150, Techno Sigma), the power supply 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). Merck TLC (silica gel 60 F254) was used for TLC analysis. Starting material **S1** was prepared by the conventional method and characterized according to the reported method.[13] Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification.

2. Preparation of building blocks

2-1. Preparation of 4-Chlorophenyl 2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside (**6**)

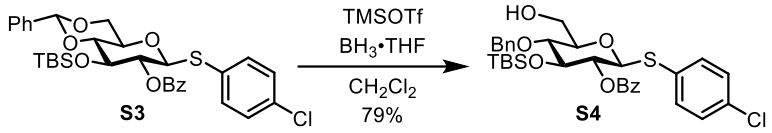
2-1-1. 4-Chlorophenyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (**S3**)



To the solution of **S1** (25.05 mmol, 9.89 g) in CH_2Cl_2 (48 mL), *tert*-butyldimethylsilyl chloride (30.1 mmol, 4.53 g) and imidazole (35.1 mmol, 2.39 g) were sequentially added at 0 ℃ and the reaction mixture was stirred at room temperature overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 1:1), the reaction mixture was quenched with MeOH. The mixture was washed with sat. aqueous $NaHCO_3$ for three times and H_2O and extracted with EtOAc. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified with silica gel chromatography to obtain **S2** in 97% yield (24.3 mmol, 12.4 g). To the solution of **S2** (8.02 mmol, 3.89 g) and DMAP (0.802 mmol, 99.2 mg) in pyridine (64 mL), benzoyl chloride (16.04 mmol, 1.85 mL) was added, and the reaction mixture was stirred at 55 ℃ overnight. The reaction was quenched by 1 N aqueous solution of hydrochloric acid and washed with deionized water three times. The organic layer was dried over Na_2SO_4 and concentrated under the reduced pressure. Thus-obtained crude product was purified by silica gel chromatography (eluent: Hexane/EtOAc 7:3) to afford **S3** (6.15 mmol, 3.62 g) in 77% yield. TLC (Hexane/EtOAc 5:1) $R_f = 0.70$; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.06 (dd, J = 8.4, 1.2 Hz, 2 H), 7.58 (td, J = 7.2, 1.2 Hz, 1 H), 7.46 (td, J = 7.8, 1.8 Hz, 4 H), 7.39−7.34 (m, 5 H), 7.25 (td, J = 8.4, 2.4 Hz, 2 H), 5.53 (s, 1 H), 5.21 (*pseudo*-t, J = 9.6 Hz, 1 H), 4.80 (d, J = 10.2 Hz, 1 H), 4.39 (dd, J = 10.8, 4.8 Hz, 1 H), 4.03 (*pseudo*-t, J = 9.0 Hz, 1 H), 3.79 (*pseudo*-t, J = 9.0 Hz, 1 H), 3.61−3.55 (m, 2 H), 0.67 (s, 9 H), -0.07 (s, 3

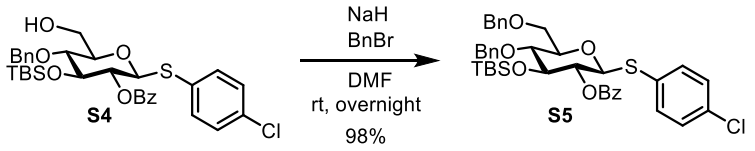
H), -0.15 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.1, 136.9, 134.5, 133.2, 130.5, 129.9, 129.8, 129.1, 129.0, 128.4, 128.1, 126.3, 101.9, 86.7, 81.1, 74.3, 73.4, 70.8, 68.5, 25.5, 17.9, -4.2, -4.9; HRMS (ESI) *m/z* calculated for $C_{32}H_{37}ClKO_6SSi$; $[M+K]^+$ 651.1400; found 651.1402.

2-1-2. 4-Chlorophenyl 2-*O*-benzoyl-4-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (**S4**)



To the mixture of **S3** (2.60 mmol, 1.60 g) and MS4A (855 mg) in CH_2Cl_2 (13 mL), BH_3-THF (1 M) (13 mmol, 13 mL) was added, and the reaction mixture was stirred at 0 ℃ for 10 min. Then TMSOTf (0.39 mmol, 0.07 mL) was added, and the reaction mixture was stirred at room temperature overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 5:1), the reaction mixture was diluted with CH_2Cl_2 and quenched with sat. aqueous $NaHCO_3$. The 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 **S4** in 79% yield (2.06 mmol, 1.27 g). TLC (Hexane/EtOAc 5:1) R_f = 0.34; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.06−8.03 (m, 2 H), 7.59 (*pseudo*-t, *J* = 6.0 Hz, 1 H), 7.47 (*pseudo*-t, *J* = 6.0 Hz, 2 H), 7.36−7.29 (m, 7 H), 7.24−7.23 (m, 2 H), 5.16 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.85 (d, *J* = 11.4 Hz, 1 H), 4.74 (d, *J* = 10.2 Hz, 1 H), 4.63 (d, *J* = 12.0 Hz, 1 H), 3.95 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.86 (ddd, *J* = 12.0, 6.0, 2.4 Hz, 1 H), 3.69−3.64 (m, 1 H), 3.55 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.47 (ddd, *J* = 9.6, 4.8, 2.4 Hz, 1 H), 1.80 (dd, *J* = 7.8, 6.0 Hz, 1 H), 0.77 (s, 9 H), 0.004 (s, 3 H), -0.17 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.4, 137.8, 134.3, 133.9, 133.3, 133.1, 130.04, 129.93, 129.1, 128.5, 127.8, 127.6, 86.3, 79.7, 78.1, 76.5, 75.1, 73.1, 62.0, 25.6, 17.8, -4.0, -4.3; HRMS (ESI) *m/z* calculated for $C_{32}H_{39}ClKO_6SSi$; $[M+K]^+$,653.1557; found 653.1556.

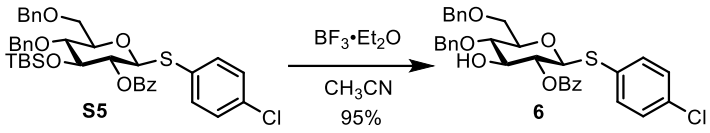
2-1-3. 4-Chlorophenyl 2-*O*-benzoyl-4,6-di-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (**S5**)



To the mixture of **S4** (2.06 mmol, 1.27 g) and DMF (10 mL), benzyl bromide (7.4 mmol, 0.18 g) was added at 0 ℃. NaH 60% in mineral oil (7.42 mmol, 298 mg) was dissolved in DMF (10 mL) and added to the reaction mixture in five portions (2.0 mL). After the completion of the reaction confirmed by TLC (Hexane/EtOAc 5:1), the reaction mixture was quenched with MeOH. The 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 **S5** in 98% yield (2.01 mmol, 1.42 g). TLC (Hexane/EtOAc 5:1) R_f = 0.67; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04 (d, *J* = 7.2 Hz, 2 H), 7.58 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 7.46 (*pseudo*-t, *J* = 7.8 Hz, 2 H), 7.40 (d, *J* = 8.4 Hz, 2 H), 7.41−7.34 (m, 8 H), 7.33−7.27 (m, 2 H), 7.14 (td, *J* = 9.0, 2.4 Hz, 2 H), 5.16 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.81 (d, *J* = 11.4 Hz, 1 H), 4.69 (d, *J* = 10.2 Hz, 1 H), 4.59 (d, *J* = 11.4 Hz, 1 H), 4.55 (d, *J* = 12.0 Hz, 1 H), 4.52 (d, *J* = 12.0 Hz, 1 H),

3.95−3.91 (m, 1 H), 3.75 (d, *J* = 10.2 Hz, 1 H), 3.68 (dd, *J* = 10.8, 3.6 Hz, 1 H), 3.58 (d, *J* = 6.0 Hz, 2 H), 0.76 (s, 9 H), -0.02 (s, 3 H), -0.18 (s, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 138.1, 138.0, 134.0, 133.2, 131.3, 130.1, 129.9, 128.9, 128.8, 128.41, 128.35, 127.7, 127.6, 127.5, 86.0, 79.4, 78.6, 76.8, 75.0, 73.4, 73.0, 69.0, 25.6, 17.7, -4.0, -4.3; HRMS (ESI) *m/z* calculated for $C_{39}H_{45}ClNaO_6SSi$; $[M+Na]^+$,727.2287; found 727.2271.

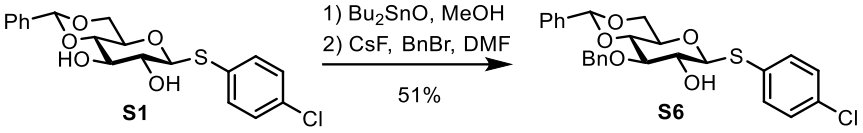
2-1-4. 4-Chlorophenyl 2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside (**6**)



To the solution of **S5** (3.88 mmol, 2.74 g) in CH_3CN (50 mL), BF_3-Et_2O (5.82 mmol, 0.736 mL) was added, and the reaction mixture was stirred at 0 ℃ for 30 min. After the completion of the reaction determined by TLC (hexane/EtOAc 9:1), the reaction mixture was quenched with 1 N HCl. The 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 **6** in 96% yield (3.71 mmol, 2.19 g). TLC (Hexane/EtOAc 9:1) R_f 0.086; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.06 (d, *J* = 7.2 Hz, 2 H), 7.56 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 7.45−7.23 (m, 14 H), 7.13 (d, *J* = 8.4 Hz, 2 H), 5.01 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 4.78 (d, *J* = 11.4 Hz, 1 H), 4.72 (d, *J* = 9.6 Hz, 1 H), 4.62 (d, *J* = 11.4 Hz, 1 H), 4.59 (d, *J* = 11.4 Hz, 1 H), 4.44 (d, *J* = 12.0 Hz, 1 H), 3.91−3.88 (m, 1 H), 3.80 (d, *J* = 10.8 Hz, 1 H), 3.72 (dd, *J* = 10.8, 4.2 Hz, 1 H), 3.59−3.56 (m, 2 H), 2.73 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.2, 138.14, 138.05, 134.4, 133.6, 130.7, 130.1, 129.5, 129.1, 128.62, 128.56, 128.51, 128.12, 128.06, 127.82, 127.79, 85.3, 79.2, 77.9, 77.2, 75.0, 73.5, 73.2, 69.0; HRMS (ESI) *m/z* calculated for $C_{33}H_{31}ClKO_6S$; $[M+K]^+$,629.1161; found 629.1168.

2-2. Preparation of 4-Chlorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**7a**)

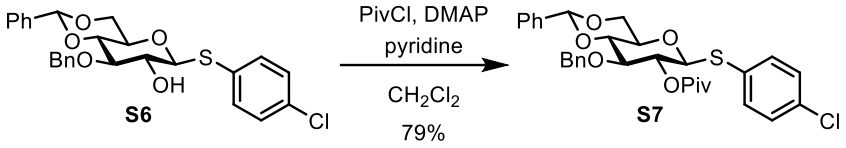
2-2-1. 4-Chlorophenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**S6**)



To the solution of **S1** (8.17 mmol, 3.23 g) in MeOH (33 mL), and dibutyltin oxide (10.2 mmol, 2.54 g) was added at room temperature and the reaction mixture was stirred at 80 ℃ for 6 h. After removal of solvent under reduced pressure, DMF (63 mL), CsF (10.22 mmol, 1.55 g) and BnBr (10.2 mmol, 1.22 mL) were added, and the reaction mixture was stirred at room temperature for 16 h. After the completion of the reaction determined by TLC (Hexane/EtOAc 1:1). 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 **S6** in 51% yield (4.15 mmol, 2.01 mg). TLC (Hexane/EtOAc 1:1) R_f = 0.89; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48-7.46 (m, 4 H), 7.39−7.28 (m, 10 H), 5.56 (s, 1 H), 4.95 (d, *J* = 12.0 Hz, 1 H), 4.77 (d, *J* = 12.0 Hz, 1 H), 4.59 (d, *J* = 9.6 Hz, 1 H), 4.36 (dd, *J* = 10.2, 4.8 Hz, 1 H), 3.78 (*pseudo*-t, *J* = 10.8 Hz, 1 H), 3.68 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.64 (*pseudo*-t, *J* =

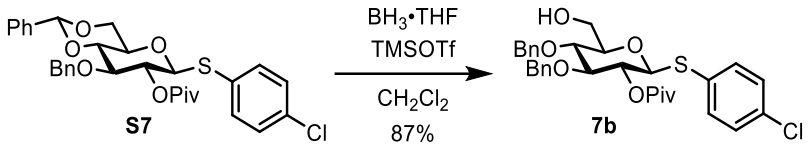
9.0 Hz, 1 H), 3.51 (dd, *J* = 9.6, 4.8 Hz, 1 H), 3.47 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 2.56 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.1, 137.2, 134.8, 134.7, 129.2, 129.1, 128.5, 128.3, 128.1, 128.0, 126.0, 101.3, 88.1, 81.6, 81.1, 74.8, 72.1, 70.8, 68.6, 29.7.

2-2-2. 4-Chlorophenyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**S7**)



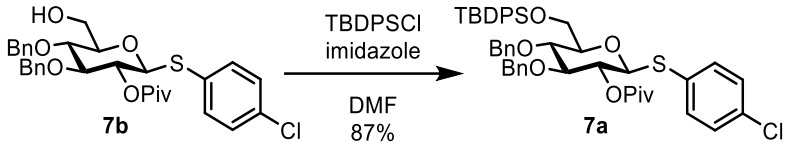
To the solution of **S6** (2.13 mmol, 1.00 g) in CH_2Cl_2 (6.81 mL), DMAP (3.20 mmol, 391 mg), pyridine (10.7 mmol, 0.860 mL) and pivaloyl chloride (3.20 mmol, 0.395 mL) were added and the reaction mixture was stirred at 50 ℃ overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 4:1), the reaction mixture was quenched with 1 N HCl. The 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 **S7** in 79% yield (1.68 mmol, 928 mg). TLC (Hexane/EtOAc 4:1) Rf = 0.68; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.47−7.46 (m, 2 H), 7.41 (dt, *J* = 9.0, 2.4 Hz, 2 H), 7.39−7.36 (m, 3 H), 7.29−7.24 (m, 7 H), 5.56 (s, 1 H), 5.08−5.00 (m, 1 H), 4.86 (dd, *J* = 11.4, 3.0 Hz, 1 H), 4.68 (d, *J* = 11.4 Hz, 1 H), 4.64 (d, *J* = 11.4 Hz, 1 H), 4.38 (dd, *J* = 10.8, 4.8 Hz, 1 H), 3.82−3.77 (m, 2 H), 3.73 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.52 (td, *J* = 9.6, 5.4 Hz, 1 H), 1.23 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.5, 138.0, 137.1, 134.7, 134.5, 130.4, 129.13, 129.07, 128.3, 127.6, 127.5, 126.0, 101.3, 86.7, 81.2, 80.4, 74.6, 70.9, 70.6, 68.5, 38.8, 27.2; HRMS (ESI) *m/z* calculated for $C_{31}H_{33}ClKO_6S$ $[M+K]^+$ 607.1318; found 607.1328.

2-2-3. 4-Chlorophenyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**7b**)



To the solution of **S7** in CH_2Cl_2 (8.12 mL), BH_3-THF (8.16 mmol, 9.06 mL) was added at 0 ℃ and the reaction mixture was stirred at 0 ℃ for 10 min. Then trimethylsilyl triflate (0.245 mmol, 0.0451 mL) was added at 0 ℃ and the reaction mixture was stirred at room temperature for 2.5 h. After the completion of the reaction determined by TLC (eluent: Hexane/EtOAc 4:1), the reaction mixture was quenched with sat. aqueous $NaHCO_3$. The 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 **7b** in 87% yield (1.43 mmol, 815 mg). TLC (Hexane/EtOAc 4:1) R_f = 0.36; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.39 (dt, *J* = 8.4, 1.8 Hz, 2 H), 7.33−7.24 (m, 12 H), 5.04 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.79 (d, *J* = 11.4 Hz, 1 H), 4.78 (d, *J* = 10.8 Hz, 1 H), 4.70 (d, *J* = 11.4 Hz, 1 H), 4.62 (dd, *J* = 13.2, 10.8 Hz, 2 H), 3.88 (ddd, *J* = 12.0, 6.0, 2.4 Hz, 1 H), 3.74 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.73−3.68 (m, 1 H), 3.63 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.44 (ddd, *J* = 9.6, 4.8, 3.0 Hz, 1 H), 2.47 (s, 1 H), 1.23 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 138.11, 138.07, 138.05, 137.94, 137.89, 134.3, 133.7, 131.5, 129.3, 128.6, 128.5, 128.1, 128.0, 127.8, 127.4, 86.4, 84.5, 79.90, 79.85, 75.3, 75.2, 71.6, 61.9, 38.9, 27.3; HRMS (ESI) *m/z* calculated for $C_{31}H_{35}ClKO_6S$ $[M+K]^+$ 609.1474; found 609.1480.

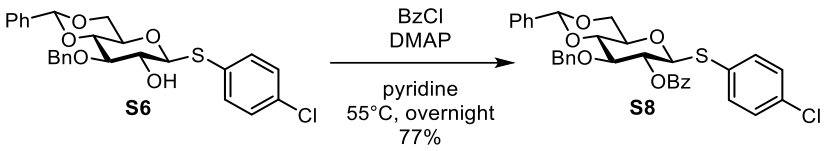
2-2-4. 4-Chlorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**7a**)



To the solution of **7b** (2.71 mmol, 1.55 g) in DMF (8.41 mL), imidazole (5.43 mmol, 370 mg) and *tert*-butylchlorodiphenylsilane (4.07 mmol, 1.05 mL) 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 mixture was quenched with sat. aqueous $NaHCO_3$. The 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 **7a** in 67% yield (1.83 mmol, 1.48 g). TLC (Hexane/EtOAc 4:1) R_f = 0.67; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.75 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.69 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.45 (d, *J* = 9.0 Hz, 2 H), 7.42 (td, *J* = 7.2, 1.2 Hz, 2 H), 7.36−7.24 (m, 12 H), 7.15 (dt, *J* = 9.0, 2.4 Hz, 2 H), 7.09 (dd, *J* = 7.8, 3.6 Hz, 2 H), 5.09 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.79 (d, *J* = 10.8 Hz, 1 H), 4.78 (d, *J* = 10.8 Hz, 1 H), 4.69 (d, *J* = 10.8 Hz, 1 H), 4.61 (dd, *J* = 7.8 Hz, 2 H), 3.98 (dd, *J* = 11.4, 1.2 Hz, 1 H), 3.92 (dd, *J* = 11.4, 4.2 Hz, 1 H), 3.80 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.73 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.44 (ddd, *J* = 9.6, 3.6, 1.2 Hz, 1 H), 1.24 (s, 9 H), 1.07 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.7, 138.1, 138.0, 136.0, 135.7, 134.1, 133.8, 133.4, 133.0, 131.8, 129.9, 129.1, 128.5, 128.0, 127.9, 127.8, 127.5, 86.4, 84.9, 80.4, 75.5, 75.2, 71.7, 62.8, 38.9, 27.3, 27.0, 19.4; HRMS (ESI) *m/z* calculated for $C_{47}H_{53}ClKO_6SSi$ $[M+K]^+$ 847.2652; found 847.2664.

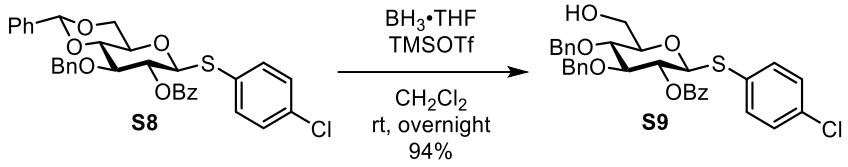
2-3. Preparation of 4-Chlorophenyl 2-*O*-benzoyl-3,4,6-*O*-tribenzyl-1-thio-β-D-glucopyranoside (**9**)

2-3-1. 4-Chlorophenyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**S8**)



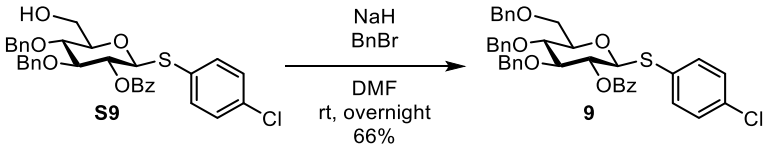
To the mixture of **S6** (8.02 mmol, 3.89 g) and DMAP (0.802 mmol, 97.98 mg) in pyridine (64 mL), benzoyl chloride (16.0 mmol, 1.86 mL) was added, and the reaction mixture was stirred at 55 °C overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 7:3), the reaction mixture was quenched with 1 N HCl. The mixture was diluted with CH_2Cl_2, 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 **S8** in 77% yield (6.15 mmol, 3.62 g). TLC (Hexane/EtOAc 4:1) R_f = 0.67; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02−8.00 (m, 2 H), 7.62 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 7.51−7.46 (m, 4 H), 7.42−7.38 (m, 5 H), 7.25 (s, 2 H), 7.14−7.04 (m, 5 H), 5.61 (s, 1 H), 5.24 (dd, *J* = 10.2, 9.0 Hz, 1 H), 4.80 (d, *J* = 12.0 Hz, 1 H), 4.78 (d, *J* = 9.6 Hz, 1 H), 4.66 (d, *J* = 12.0 Hz, 1 H), 4.42 (dd, *J* = 10.2, 5.4 Hz, 1 H), 3.88 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.83 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 3.79 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 3.56 (td, *J* = 9.6, 4.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.9, 137.5, 137.0, 134.7, 133.3, 130.0, 129.0, 128.4, 128.2, 128.1, 128.0, 127.5, 125.9, 101.2, 86.4, 81.3, 79.1, 74.2, 71.8, 70.5, 68.4; HRMS (ESI) *m/z* calculated for $C_{33}H_{29}ClKO_6S$ $[M+K]^+$ 627.1005; found 627.1010.

2-3-2. 4-Chlorophenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (**S9**)



To the mixture of **S8** (4.70 mmol, 2.77 g) and MS4A (1.5 g) in CH_2Cl_2 (24 mL), BH_3-THF (1.0 M, 24 mmol, 24 mL) and TMSOTf (0.703 mmol, 127 μL) were added at 0 ℃ and the reaction mixture was stirred at room temperature overnight. After the completion of the reaction determined by TLC (Hexane/EtOAc 7:3), the reaction mixture was diluted with CH_2Cl_2 and quenched with sat. aqueous $NaHCO_3$. The 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 **S9** in 81% yield (3.81 mmol, 2.25 g). TLC (Hexane/EtOAc 5:1) R_f = 0.20; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04−8.01 (m, 2 H), 7.62−7.59 (*m*, 1 H), 7.46 (*pseudo*-t, *J* = 7.8 Hz, 2 H), 7.38−7.29 (m, 8 H), 7.24 (s, 1 H), 7.14−7.09 (m, 5 H), 5.22 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.84 (d, *J* = 10.8 Hz, 1 H), 4.76 (d, *J* = 9.6 Hz, 1 H), 4.74 (d, *J* = 11.4 Hz, 1 H), 4.66 (d, *J* = 10.8 Hz, 1 H), 4.65 (d, *J* = 10.8 Hz, 1 H), 4.62 (d, *J* = 10.8 Hz, 1 H), 3.91 (ddd, *J* = 12.0, 6.0, 3.0 Hz, 1 H), 3.86 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.75−3.71 (m, 1 H), 3.68 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.44 (ddd, *J* = 9.6, 4.8, 3.0 Hz, 1 H), 1.82 (dd, *J* = 7.8, 6.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.20, 137.83, 137.72, 137.57, 134.48, 134.14, 133.98, 133.40, 133.25, 130.74, 129.89, 129.69, 129.24, 129.15, 128.59, 128.54, 128.33, 128.21, 128.14, 128.10, 128.07, 127.78, 86.53, 85.95, 83.97, 79.77, 79.47, 77.42, 75.86, 75.61, 75.40, 75.22, 72.43, 62.00; HRMS (ESI) *m/z* calculated for $C_{33}H_{31}ClKO_6S$ $[M+K]^+$ 629.1161; found 629.1163.

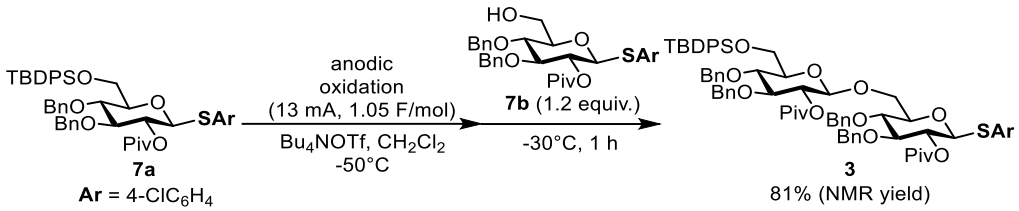
2-3-3. 4-Chlorophenyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (**9**)



To the mixture of **S9** (3.81 mmol, 2.25 g) and DMF (30 mL), BnBr (13.7 mmol, 1.63 mL) was added at 0 ℃. NaH 60% in mineral oil (13.7 mmol, 548 mg) was dissolved in DMF (10 mL) and added to the reaction mixture in five portions (2.0 mL×5). After the completion of the reaction determined by TLC (Hexane/EtOAc 4:1), the reaction mixture was quenched with MeOH, diluted with EtOAc. The 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 60% yield (2.30 mmol, 1.57 g). TLC (Hexane/EtOAc 5:1) R_f = 0.25; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.03 (d, *J* = 7.8 Hz, 2 H), 7.58 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 7.45 (*pseudo*-t, *J* = 7.8 Hz, 2 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 7.38−7.28 (m, 8 H), 7.21 (d, *J* = 7.2 Hz, 2 H), 7.15−7.07 (m, 7 H), 5.23 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.80 (d, *J* = 10.8 Hz, 1 H), 4.72 (d, *J* = 10.2 Hz, 2 H), 4.63 (d, *J* = 10.8 Hz, 1 H), 4.60−4.53 (m, 3 H), 3.84 (d, *J* = 9.0 Hz, 1 H), 3.83−3.79 (m, 1 H), 3.75−3.69 (m, 2 H), 3.62−3.58 (m, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.18, 138.15, 137.89, 137.64, 134.33, 134.26, 133.34, 130.85, 129.90, 129.81, 128.97, 128.62, 128.52, 128.48, 128.33, 128.07, 127.97, 127.77, 127.72, 85.67, 84.25, 79.45, 77.75, 75.43, 75.19, 73.52, 72.36, 68.95; HRMS (ESI) *m/z* calculated for $C_{40}H_{37}ClKO_6S$ $[M+K]^+$ 719.1631; found 719.1630.

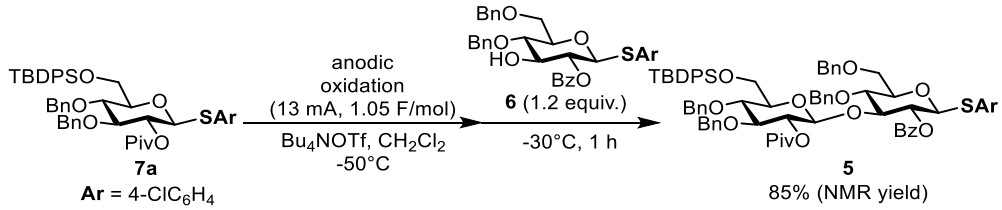
3. Synthesis of disaccharide building blocks

3-1. Preparation of 4-Chlorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**3**)



The automated synthesis of **3** 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 **7a** (0.601 mmol, 486 mg), Bu_4NOTf (1.50 mmol, 588 mg) and CH_2Cl_2 (15 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.65 mmol, 57 μL), Bu_4NOTf (1.50 mmol, 588 mg) and CH_2Cl_2 (15 mL). The constant current electrolysis (13.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.05 F/mol of electricity was consumed. After the electrolysis, building block **7b** (0.72 mmol, 418 mg) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump under an argon atmosphere at -30 ℃, and kept for 60 min. After the cycle, Et_3N (0.50 mL) was added, and the mixture was filtered through a short column (4×3 cm) of silica gel to remove Bu_4NOTf. After removal of the solvent under reduced pressure, the crude product was purified with silica gel chromatography to obtain **3** (241 mg). NMR yield was determined using tetrachloroethane as internal standard (0.487 mmol, 81% yield). TLC (Hexane/EtOAc 4:1) R_f 0.66; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.74−7.70 (*m*, 2 H), 7.67 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 7.38 (d, *J* = 7.2 Hz, 1 H), 7.34−7.22 (m, 21 H), 7.21 (d, *J* = 6.6 Hz, 2 H), 7.18 (ddd, *J* = 5.4, 2.4, 1.2 Hz, 2 H), 7.15 (dd, *J* = 6.0, 2.4 Hz, 2 H), 5.09 (dd, *J* = 9.6, 8.4 Hz, 1 H), 4.99 (*pseudo*-t, *J* = 10.2 Hz, 1 H), 4.84−4.66 (m, 7 H), 4.54 (*pseudo*-t, *J* = 9.6 Hz, 2 H), 4.48 (d, *J* = 7.8 Hz, 1 H), 4.01 (d, *J* = 9.6 Hz, 1 H), 3.86 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.71 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.67−3.61 (m, 3 H), 3.36−3.32 (m, 2 H), 1.22 (s, 9 H), 1.15 (s, 9 H), 1.04 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.8, 176.7, 138.23, 138.16, 137.95, 137.69, 135.9, 135.6, 134.3, 134.1, 133.6, 133.1, 131.4, 129.8, 129.3, 128.5, 128.1, 128.0, 127.84, 127.77, 127.73, 127.6, 127.4, 101.1, 86.3, 84.7, 83,4, 79.8, 78.0, 77.7, 76.2, 75.34, 75.27, 75.1, 75.0, 73.2, 71.5, 67.8, 62.7, 38.9, 38.8, 27.3, 19.4; HRMS (ESI) *m/z* calculated for $C_{72}H_{83}ClKO_{12}SSi$ $[M+K]^+$ 1273.4695; found 1273.4636.

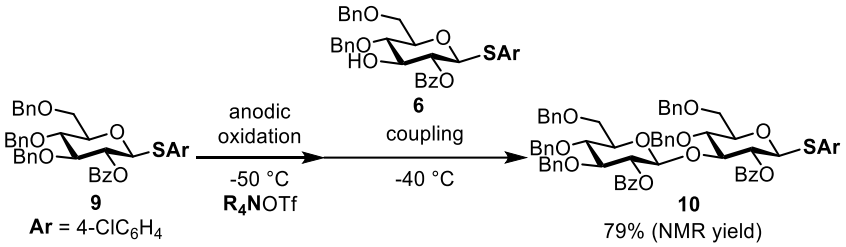
3-2. Preparation of 4-Chlorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside (**5**)



The automated synthesis of **5** 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 **7a** (0.603 mmol, 489 mg), Bu_4NOTf (1.50 mmol, 595 mg) and CH_2Cl_2 (15 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.67 mmol, 59

μL), Bu_4NOTf (1.50 mmol, 595 mg) and CH_2Cl_2 (15 mL). The constant current electrolysis (13.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.05 F/mol of electricity was consumed. After the electrolysis, building block **6** (0.741 mmol, 438 mg) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump under an argon atmosphere at -30 ℃, and kept for 60 min. After the cycle, Et_3N (0.50 mL) was added, and the mixture was filtered through a short column (4×3 cm) of silica gel to remove Bu_4NOTf. After removal of the solvent under reduced pressure, the crude product was purified with silica gel chromatography to obtain **5** (276 mg). NMR yield was determined using tetrachloroethane as internal standard (0.513 mmol, 85% yield). TLC (Hexane/EtOAc 4:1) R_f 0.63; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.02 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.74 (dd, *J* = 5.4, 2.4 Hz, 2 H), 7.68 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.60 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 7.45−7.20 (m, 28 H), 7.10 (dt, *J* = 9.0, 2.4 Hz, 2 H), 7.05 (dd, *J* = 7.2, 1.2 Hz, 2 H), 5.21 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 5.05 (dd, *J* = 9.6, 7.8 Hz, 1 H), 4.96 (d, *J* = 12.0 Hz, 1 H), 4.72 (d, *J* = 10.8 Hz, 1 H), 4.68−4.56 (m, 6 H), 4.52 (d, *J* = 10.8 Hz, 1 H), 4.50 (d, *J* = 10.8 Hz, 1 H), 4.48 (d, *J* = 12.0 Hz, 1 H), 3.92 (dd, *J* = 10.8, 1.2 Hz, 1 H), 3.77 (dt, *J* = 11.4, 1.8 Hz, 2 H), 3.69 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.60 (ddd, *J* = 9.6, 6.6, 1.8 Hz, 1 H), 3.52−3.48 (m, 2 H), 3.44 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.19 (dd, *J* = 9.6, 3.6 Hz, 1 H), 1.21 (s, 9 H), 1.02 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.3, 164.9, 138.3, 138.1, 137.8, 136.0, 135.7, 134.1, 133.8, 133.2, 133.1, 131.8, 129.8, 129.6, 129.0, 128.9, 128.8, 128.6, 128.5, 128.3, 128.2, 127.99, 127.95, 127.8, 127.63, 127.56, 98.8, 86.3, 83.2, 79.4, 78.2, 77.8, 76.7, 75.31, 75.25, 74.8, 74.0, 73.5, 69.6, 62.6, 39.0, 27.3, 26.9, 19.3; HRMS (ESI) *m/z* calculated for $C_{74}H_{79}ClKO_{12}SSi$ $[M+K]^+$1293.4382; found 1293.4398.

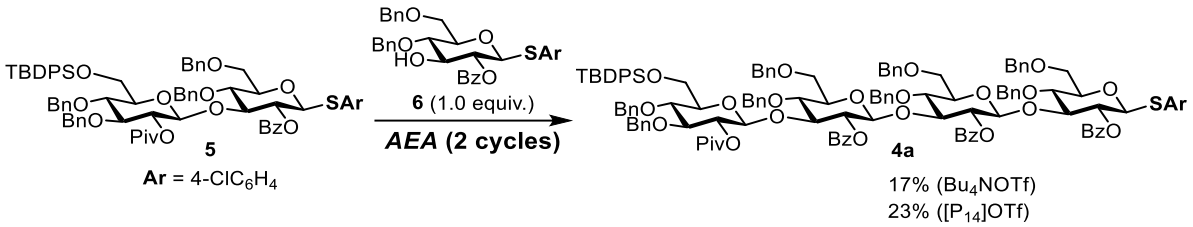
4. Optimization of electrolyte



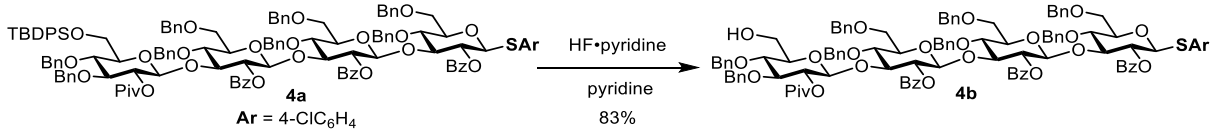
The automated synthesis of disaccharide **10** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm×20 mm). In the anodic chamber were placed terminal building block **9** (0.101 mmol, 68.9 mg), Bu_4NOTf (0.5 mmol, 196 mg) and CH_2Cl_2 (5.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.09 mmol, 8.0 μL), Bu_4NOTf (0.5 mmol, 196 mg) and CH_2Cl_2 (5.0 mL). The constant current electrolysis (3.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, building block **6** (0.120 mmol, 71.2 mg) dissolved in CH_2Cl_2 (0.60 mL) was subsequently added by the syringe pump under an argon atmosphere at -40 ℃, and kept for 60 min. After the cycle, Et_3N (0.20 mL) was added, and the mixture was filtered through a short column (4×3 cm) of silica gel to remove Bu_4NOTf. After removal of the solvent under reduced pressure, NMR yield was determined using tetrachloroethane as internal standard (0.079 mmol, 79% yield). **4-Chlorophenyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside** (**10**). TLC (Hexane/EtOAc 7:3) R_f = 0.53; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.2, 1.2 Hz, 2 H), 7.80 (d, *J* = 7.2 Hz, 2 H), 7.66 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 7.59 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 7.52 (*pseudo*-t, *J* = 7.8 Hz, 2 H), 7.43−7.41 (m, 2 H), 7.35−7.33 (m, 2 H), 7.30−7.27 (m, 13 H), 7.22-7.21 (m, 4 H), 7.14−7.08 (m, 8 H), 7.00 (d, *J* = 6.6 Hz, 2 H), 5.24 (dd, *J* = 9.6, 7.8 Hz, 1 H), 5.16 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 5.06 (d, *J* = 11.4 Hz, 1 H), 4.80 (d, *J* = 7.8 Hz, 1 H), 4.73 (d, *J* = 10.8 Hz, 1 H), 4.65 (d, *J* = 5.4 Hz, 1 H), 4.55 (d, *J* =

12.0 Hz, 2 H), 4.53−4.48 (m, 4 H), 4.44 (*pseudo*-t, *J* = 11.4 Hz, 2 H), 4.28 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.82 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.75 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.62−3.57 (m, 5 H), 3.52 (ddd, *J* = 10.2, 6.0, 3.6 Hz, 1 H), 3.44 (ddd, *J* = 10.8, 5.4, 1.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.45, 164.60, 138.45, 138.42, 138.20, 137.71, 137.58, 133.73, 133.61, 133.18, 133.07, 132.16, 129.96, 129.90, 129.77, 129.56, 129.36, 128.93, 128.71, 128.60, 128.53, 128.45, 128.42, 128.41, 128.40, 128.27, 128.24, 128.16, 128.01, 128.00, 127.91, 127.84, 127.76, 127.69, 127.59, 127.54, 127.48, 127.31, 100.27, 86.23, 83.00, 80.41, 79.22, 78.14, 75.81, 75.69, 75.25, 75.15, 75.04, 74.00, 73.57, 73.50, 73.44, 73.01, 69.32, 69.12, 29.76; HRMS (ESI) *m/z* calculated for $C_{67}H_{63}ClKO_{12}S$ $[M+K]^+$ 1165.3360; found 1165.3311.

5. Synthesis of tetrasaccharide building block



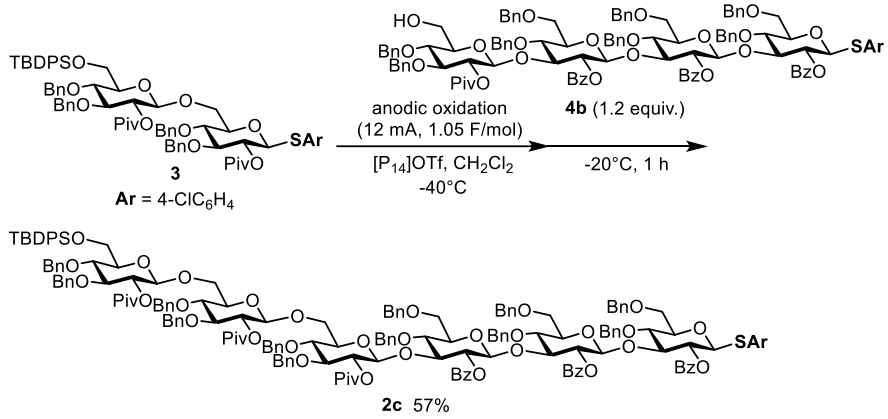
The automated synthesis of tetrasaccharide **4a** was carried out in an H-type divided cell equipped with a carbon felt anode and a platinum plate cathode (10 mm×10 mm). In the anodic chamber were placed disaccharide building block **5** (0.10 mmol, 126 mg), $[P_{14}]OTf$ (0.50 mmol, 0.12 mL) and CH_2Cl_2 (5 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.1 mmol, 9 μL), $[P_{14}]OTf$ (0.50 mmol, 0.12 mL) and CH_2Cl_2 (5 mL). The constant current electrolysis (3.0 mA) was carried out at -50 °C with stirring until 1.2 F/mol of electricity was consumed. After the electrolysis, building block **6** (0.10 mmol, 59 mg) dissolved in CH_2Cl_2 (0.6 mL) was subsequently added by the syringe pump under an argon atmosphere at -50 °C and then -30°C kept for 60 min. This process was repeated two cycles. After the second cycle, Et_3N (0.2 mL) was added, and the reaction mixture was filtered through a short column (4×3 cm) of silica gel to remove electrolyte. Removal of the solvent under reduced pressure and the crude product was purified with silica gel chromatography (eluent: Hexane/EtOAc 4:1) and preparative recycling GPC (eluent: $CHCl_3$). Target tetrasaccharide **4a** was obtained in 23% isolated yield (0.023 mmol, 49 mg). Thus-obtained **4a** was used as a starting material for the next step without detailed structural characterization.



Tetrasaccharide **4a** (0.46 mmol, 0.98 g) was dissolved in pyridine (3.5 mL) and the solution was cooled to 0 °C. 70% HF•pyridine (0.35 mL) was added to the solution and the reaction mixture was stirred at 0 °C to room temperature for overnight. Conversion of **4a** was confirmed by TLC (Hexane/EtOAc 3:1) and aqueous sodium bicarbonate solution was added to quench the reaction. The aqueous solution was extracted with chloroform and the combined organic layer was washed with aqueous sodium bicarbonate solution and 1 N aqueous hydrochloric acid. The reaction mixture was dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product (1.45 g). Thus-obtained crude product was purified by silica gel chromatography (eluent: Hexane/EtOAc 4:1) and tetrasaccharide **4b** (0.38 mmol, 723 mg) in 83% yield. **4-Chlorophenyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-**

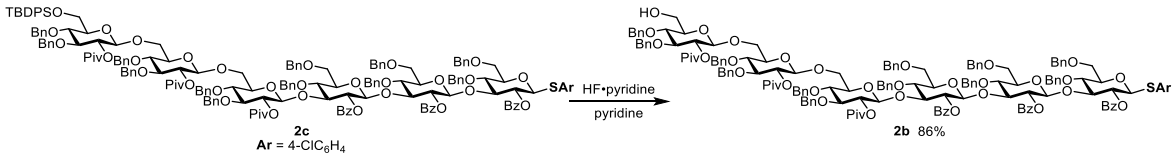
benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside (**4b**). TLC (Hexane/EtOAc 3:1) R_f = 0.19; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.4, 1.8 Hz, 2 H), 7.73 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.67−7.62 (m, 3 H), 7.61−7.57(m, 1 H), 7.55−7.51 (m, 1 H), 7.46−7.43 (m, 2 H), 7.38−7.35 (m, 4 H), 7.34−7.18 (m, 40 H), 7.16−7.14 (m, 2 H), 7.07−7.04 (m, 2 H), 5.05 (dd, *J* = 9.0, 7.8 Hz, 1 H), 4.98−4.90 (m, 4 H), 4.89 (dd, *J* = 9.6, 7.8 Hz, 1 H), 4.81 (d, *J* = 10.8 Hz, 1 H), 4.71 (d, *J* = 7.8 Hz, 1 H), 4.67 (d, *J* = 10.8 Hz, 1 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.57 (d, *J* = 7.8 Hz, 1 H), 4.55 (d, *J* = 9.6 Hz, 1 H), 4.51 (d, *J* = 10.2 Hz, 1 H), 4.47−4.38 (m, 10 H), 4.33 (d, *J* = 12.0 Hz, 1 H), 4.11 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.90 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 3.88 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.73−3.62 (m, 4 H), 3.55−3.36 (m, 10 H), 3.30 (ddd, *J* = 9.6, 4.8, 1.8 Hz, 1 H), 3.27 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.00 (ddd, *J* = 9.6, 4.8, 1.8 Hz, 1 H), 1.03 (s, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 164.5, 164.4, 164.3, 138.49, 138.46, 138.31, 138.14, 137.8, 137.6, 133.6, 133.4, 133.2, 133.1, 132.1, 129.88, 123.83, 129.79, 129.76, 129.53, 129.37, 129.35, 128.79, 128.46, 128.38, 128.31, 128.25, 128.13, 128.05, 127.81, 127.65, 127.62, 127.45, 127.16, 100.3, 100.2, 99.5, 86.1, 82.7, 80.7, 79.6, 79.1, 78.1, 77.6, 76.1, 76.0, 75.8, 75.4, 75.3, 75.2, 75.0, 74.9, 74.8, 74.6, 74.2, 74.0, 73.39, 73.38, 73.31, 73.0, 72.9, 69.6, 69.2, 68.9, 61.4, 38.7, 27.0; HRMS (ESI) *m/z* calculated for $C_{112}H_{113}ClKO_{24}S$ $[M+K]^+$ 1947.6663; found 1947.6721.

6. Synthesis of semi-circular hexasaccharide



The automated synthesis of semi-circular hexasaccharide **2c** was carried out in an H-type divided cell equipped with a carbon felt anode and a platinum plate cathode (20 mm×20 mm). In the anodic chamber were placed disaccharide building block **3** (0.75 mmol, 930 mg), $[P_{14}]OTf$ (1.6 mmol, 0.63 g) and CH_2Cl_2 (15 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.79 mmol, 70 μL), $[P_{14}]OTf$ (0.50 mmol, 0.12 mL) and CH_2Cl_2 (15 mL). The constant current electrolysis (12 mA) was carried out at -40 °C with stirring until 1.05 F/mol of electricity was consumed. After the electrolysis, tetrasaccharide building block **4b** (0.90 mmol, 1.71 g) dissolved in CH_2Cl_2 (3.5 mL) was subsequently added by the syringe pump under an argon atmosphere at -40 °C and then -20 °C kept for 60 min. Then Et_3N (0.75 mL) was added, and solvent was removed under reduced pressure. The crude product was purified with silica gel chromatography (eluent: Hexane/EtOAc 5:1). Target semi-circular hexasaccharide **2c** was obtained in 57% isolated yield (0.423 mmol, 1.27 g). **4-Chlorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-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-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside** (**2c**); (Hexane/EtOAc 3:1) R_f = 0.50; ^{1}H NMR (600 MHz, $CDCl_3$)

δ 7.82 (d, *J* = 7.2 Hz, 2 H), 7.78 (d, *J* = 7.2 Hz, 2 H), 7.70−7.69 (m, 2 H), 7.63 (d, *J* = 7.2 Hz, 2 H), 7.55−7.48 (m, 4 H), 7.37−7.08 (m, 75 H), 7.06 (d, *J* = 8.4 Hz, 2 H), 5.09−5.04 (m, 3 H), 4.94−4.85 (m, 5 H), 4.83 (d, *J* = 10.8 Hz, 1 H), 4.76−4.66 (m, 8 H), 4.64−4.51 (m, 10 H), 4.49−4.44 (m, 4 H), 4.41 (d, *J* = 12.6 Hz, 1 H), 4.38 (d, *J* = 11.4 Hz, 1 H), 4.34−4.29 (m, 3 H), 4.26 (d, *J* = 12.0 Hz, 1 H), 4.20 (d, *J* = 12.4 Hz, 1 H), 4.10 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.07 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 3.99 (d, *J* = 10.8 Hz, 1 H), 3.95−3.90 (m, 3 H), 3.85−3.79 (m, 2 H), 3.75 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.71 (dd, *J* = 12.0, 5.4 Hz, 1 H), 3.67−3.64 (m, 4 H), 3.59 (d, *J* = 10.8 Hz, 1 H), 3.35−3.26 (m, 13 H), 3.21 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.13 (ddd, *J* = 9.6, 3.6, 1.8 Hz, 1 H), 1.14 (s, 9 H), 1.13 (s, 9 H), 1.06 (s, 9 H), 1.00 (s, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 176.64, 176.59, 164.51, 164.47, 164.45, 138.5, 138.4, 138.3, 138.2, 138.1, 138.0, 137.98, 137.91, 137.66, 135.8, 135.7, 135.5, 135.4, 133.54, 133.45, 133.26, 133.0, 132.9, 132.1, 129.77, 129.72, 129.64, 129.60, 129.45, 129.24, 129.16, 128.75, 128.42, 128.35, 128.27, 128.20, 128.13, 128.01, 127.91, 127.84, 127.62, 127.57, 127.51, 127.46, 127.41, 127.35, 127.30, 127.26, 126.9, 100.9, 100.3, 99.80, 99.77, 99.5, 86.0, 83.13, 83.11, 82.5, 80.3, 79.04, 78.98, 78.6, 78.2, 77.8, 77.4, 76.2, 76.1, 76.0, 75.8, 75.7, 75.14, 75.05, 74.89, 74.85, 74.79, 74.76, 74.73, 74.65, 74.55, 74.52, 74.46, 74.35, 74.03, 73.8, 73.3, 73.2, 73.1, 72.7, 72.6, 69.8, 69.2, 69.1, 67.5, 66.4, 62.5, 38.7, 38.6, 27.23, 27.18, 27.0, 26.7, 19.2; HRMS (ESI) *m/z* calculated for $C_{178}H_{191}ClKO_{36}SSi$ $[M+K]^+$ 3038.1925; found 3038.2100.

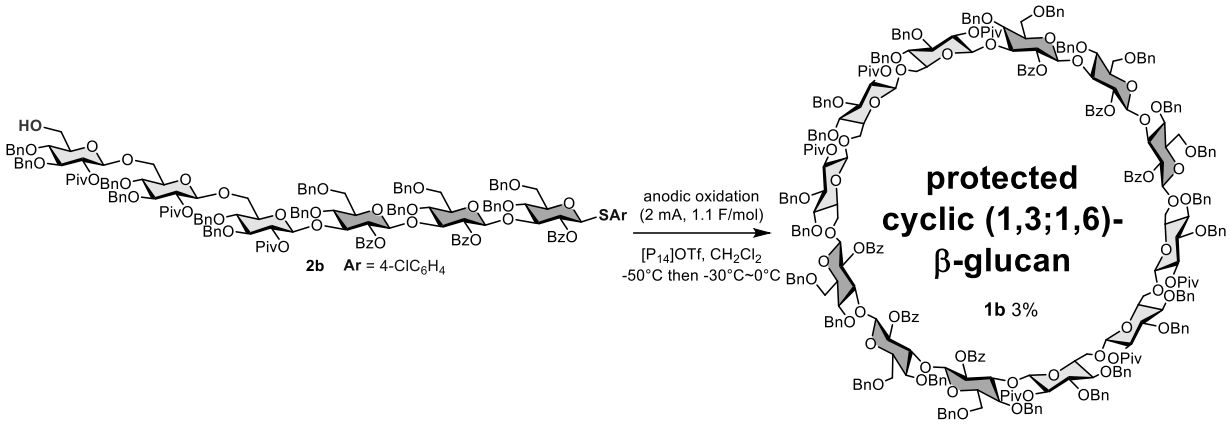


Semi-circular hexasaccharide **2c** (0.26 mmol, 790 mg) was dissolved in pyridine (2.0 mL) and the solution was cooled to 0 °C. 70% HF•pyridine (0.35 mL) was added to the solution and the reaction mixture was stirred at 0 °C to room temperature for 4 h. Conversion of **2c** was confirmed by TLC (Hexane/EtOAc 7:3) and aqueous sodium bicarbonate solution was added to quench the reaction. The aqueous solution was extracted with chloroform and the combined organic layer was washed with aqueous sodium bicarbonate solution and 1 N aqueous hydrochloric acid. The reaction mixture was dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Thus-obtained crude product was purified by silica gel chromatography (eluent: Hexane/EtOAc 3:1) and semi-circular hexasaccharide **2b** (0.227 mmol, 628 mg) in 86% yield. **4-Chlorophenyl 3,4-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-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside** (**2b**); TLC (Hexane/EtOAc 7:3) R_f = 0.50; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.2, 4.2 Hz, 4 H), 7.55 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 7.49 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 7.45 (d, *J* = 7.8 Hz, 2 H), 7.38−7.14 (m, 63 H), 7.12−7.07 (m, 8 H), 5.12 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 5.01−4.89 (m, 3 H), 4.88−4.70 (m, 7 H), 4.69−4.58 (m, 6 H), 4.58−4.44 (m, 11 H), 4.42 (d, *J* = 12.0 Hz, 1 H), 4.37 (d, *J* = 12.0 Hz, 1 H), 4.32 (d, *J* = 12.0 Hz, 1 H), 4.29−4.27 (m, 2 H), 4.24 (d, *J* = 12.0 Hz, 1 H), 4.21 (d, *J* = 12.0 Hz, 1 H), 4.12 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 4.09 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 3.93 (*pseudo*-t, *J* = 7.2 Hz, 1 H), 3.88 (d, *J* = 10.2 Hz, 1 H), 3.74−3.42 (m, 20 H), 3.37−331 (m, 5 H), 3.26 (ddd, *J* = 10.2, 4.8, 2.4 Hz, 1 H), 3.11 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 2.15 (*pseudo*-t, 1 H), 1.18 (s, 9 H), 1.11 (s, 9 H), 1.09 (m, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.2, 176.6, 176.5, 164.53, 164.49, 138.52, 138.47, 138.26, 138.23, 138.20, 138.15, 138.09, 138.07, 138.02, 137.9, 137.8, 133.7, 133.6, 133.56, 133.32, 133.25, 133.0, 132.9, 132.1, 129.8, 129.7, 129.6, 129.5, 129.2, 129.1, 128.77, 128.65, 128.49, 128.36, 128.29, 128.24, 128.21, 128.19, 128.13, 128.08, 128.01, 127.95, 127.92, 127.78, 127.74, 127.64, 127.57, 127.47, 127.41, 127.38, 127.33, 127.28, 127.25, 127.22, 127.14, 127.04,

126.99, 101.4, 100.6, 99.71, 99.68, 99.63, 86.0, 83.0, 82.8, 82.4, 80.3, 79.1, 78.8, 78.7, 77.8, 77.7, 77.4, 76.2, 76.0, 75.7, 75.5, 75.1, 74.90, 74.78, 74.76, 74.62, 74.58, 74.55, 74.49, 74.37, 74.29, 73.8, 73.7, 73.3, 73.2, 73.1, 72.84, 72.79, 72.57, 70.0, 69.2, 68.5, 67.3, 61.8, 38.73, 38.69, 38.66, 27.25, 27.08, 27.00. 26.9; HRMS (ESI) *m/z* calculated for $C_{162}H_{173}ClKO_{36}S$ $[M+K]^+$ 2800.0753; found 2800.0688.

7. Synthesis of protected cyclic dodecasaccharide

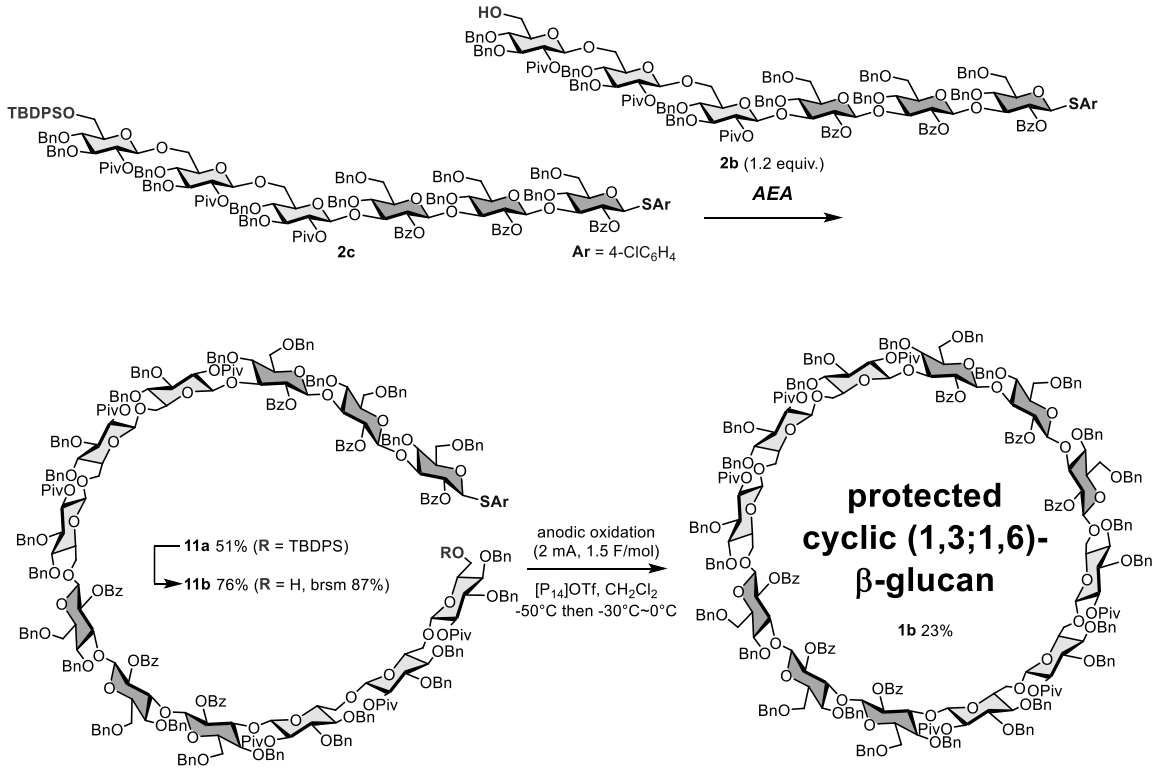
7-1. One-pot dimerization-cyclization process



The dimerization and cyclization of linear dodecasaccharide **2b** was carried out in an H-type divided cell equipped with a carbon felt anode and a platinum plate cathode (10 mm×10 mm). In the anodic chamber were placed protected linear dodecasaccharide **2b** (0.135 mmol, 374 mg), $[P_{14}]OTf$ (0.63 mmol, 0.15 mL) and CH_2Cl_2 (5.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.15 mmol, 13 μL), $[P_{14}]OTf$ (0.50 mmol, 0.12 mL) and CH_2Cl_2 (4.2 mL). The constant current electrolysis (2.0 mA) was carried out at -50 °C with stirring until 1.1 F/mol of electricity was consumed and then -30 °C kept for 60 min. After elevation of the reaction temperature to 0 °C, Et_3N (0.2 mL) was added to both chambers, and the reaction mixture was dissolved in $CHCl_3$ and washed with water to remove electrolyte $[P_{14}]OTf$. Thus-obtained organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to obtain the crude product (479 mg). Silica gel chromatography (eluent: Hexane/EtOAc 4:1) and preparative recycling GPC (eluent: $CHCl_3$) afforded target protected cyclic dodecasaccharide **1b** in 3% yield (2.3 μmol, 12 mg). **Cyclobis-(1→6)-(3,4-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-β-D-glucopyranosyl)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl)** (**1b**); TLC (Hexane/EtOAc 3:1) Rf = 0.30; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (*pseudo*-t, *J* = 6.6 Hz, 4 H), 7.67−7.62 (m, 4 H), 7.59 (d, *J* = 7.2 Hz, 4 H), 7.46−7.43 (m, 6 H), 7.36−7.14 (m, 126 H), 7.05 (d, *J* = 6.0 Hz, 2 H), 5.09−5.00 (m, 12 H), 4.96−4.88 (m, 6 H), 4.74 (d, *J* = 7.8 Hz, 2 H), 4.70 (dd, *J* = 10.8, 3.0 Hz, 2 H), 4.66−4.61 (m, 6 H), 4.56−4.42 (m, 26 H), 4.38−4.25 (m, 12 H), 4.15 (d, *J* = 7.8 Hz, 2 H), 4.09 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 4.02 (*pseudo*-t, *J* = 9.0 Hz, 2 H), 4.00−3.96 (m, 4 H), 3.79−3.74 (m, 4 H), 3.67−3.27 (m, 48 H), 3.21−3.15 (m, 4 H), 1.11 (s, 36 H), 1.08 (s, 18 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.0, 176.5, 176.4, 164.7, 164.4, 163.8, 138.7, 138.6, 138.43, 138.38, 138.2, 138.1, 138.04, 137.95, 137.91, 133.30, 133.24, 133.20, 129.82, 129.75, 129.5, 129.4, 129.3, 128.8, 128.61, 128.56, 128.43, 128.35, 128.25, 128.20, 128.15, 128.10, 128.05, 128.01, 127.96, 127.7, 127.6, 127.45, 127.39, 127.35, 127.31, 127.26, 127.21, 127.13, 127.0, 126.9, 126.8, 100.7, 100.5, 100.43, 100.35, 100.14, 99.3, 83.0, 82.9, 82.8, 82.7, 79.75, 79.66, 78.3,

78.2, 78.1, 77.6, 77.5, 76.3, 76.1, 75.6, 75.3, 75.2, 75.1, 74.85, 74.80, 74.72, 74.59, 74.54, 74.48, 74.33, 74.21, 73.84, 73.76, 73.3, 73.2, 73.1, 72.9, 72.2, 69.7, 69.15, 69.07, 67.7, 66.9, 38.65, 38.63, 38.59, 27.3, 27.1, 26.9; MS (MALDI) *m/z* calculated for $C_{312}H_{336}KO_{72}$ $[M+K]^+$ 5273.22; found 5273.04.

7-2. Stepwise process via AEA



The automated synthesis of linear dodecasaccharide **11a** was carried out in an H-type divided cell equipped with a carbon felt anode and a platinum plate cathode (20 mm×20 mm). In the anodic chamber were placed hexasaccharide building block **2c** (0.135 mmol, 405 mg), $[P_{14}]OTf$ (0.76 mmol, 0.175 mL) and CH_2Cl_2 (3.9 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.20 mmol, 18 μL), $[P_{14}]OTf$ (0.50 mmol, 0.12 mL) and CH_2Cl_2 (4.9 mL). The constant current electrolysis (2.0 mA) was carried out at -50 °C with stirring until 1.1 F/mol of electricity was consumed. After the electrolysis, hexasaccharide building block **2b** (0.162 mmol, 450 mg) dissolved in CH_2Cl_2 (0.9 mL) was subsequently added by the syringe pump under an argon atmosphere at -50 °C and then -30 °C kept for 60 min. After elevation of the reaction temperature to 0 °C, Et_3N (0.4 mL) was added, and the reaction mixture was filtered through a short column (4×3 cm) of silica gel to remove electrolyte Bu_4NOTf. Removal of the solvent under reduced pressure and the crude product was purified with silica gel chromatography (eluent: Hexane/EtOAc 3:1) and preparative recycling GPC (eluent: $CHCl_3$). Target linear dodecasaccharide **11a** was obtained in 51% isolated yield (0.069 mmol, 389 mg). Thus-obtained **11a** was used as a starting material for the next step without detailed structural characterization.

Linear dodecasaccharide **11a** (0.069 mmol, 389 mg) was dissolved in pyridine (0.53 mL) and the solution was cooled to 0 °C. 70% HF•pyridine (0.10 mL) was added to the solution and the reaction mixture was stirred at 0 °C to room temperature for 2 h. Conversion of **11a** was confirmed by TLC (Hexane/EtOAc 7:3) and aqueous sodium bicarbonate solution was added to quench the reaction. The aqueous solution was

extracted with chloroform and the combined organic layer was washed with aqueous sodium bicarbonate solution and 1 N aqueous hydrochloric acid. The reaction mixture was dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product (430 mg). Thus-obtained crude product was purified by silica gel chromatography (eluent: Hexane/EtOAc 7:3) and **11b** (0.053 mmol, 284 mg) in 76% yield (87% conversion). **4-Chlorophenyl 3,4-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-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-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-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside** (**11b**); TLC (Hexane/EtOAc 7:3) Rf = 0.20; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.2 Hz, 2 H), 7.76−7.73 (m, 5 H), 7.52−7.48 (m, 2 H), 7.45 (d, J = 7.2 Hz, 1 H), 7.41−7.39 (m, 2 H), 7.36−6.99 (m, 141 H), 6.89−6.86 (m, 1 H), 5.08−5.05 (m, 2 H), 4.99−4.80 (m, 16 H), 4.74−4.14 (m, 55 H), 4.10−4.00 (m, 6 H), 3.90−3.82 (m, 5 H), 3.71−3.62 (m, 6 H), 3.60−3.16 (m, 41 H), 3.04−3.00 (m, 1 H), 2.17 (*pseudo*-t, *J* = 6.0 Hz, 1 H), 1.10 (s, 18 H), 1.08 (s, 9 H), 1.06 (s, 9 H), 1.05 (s, 9 H), 1.04 (s, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.3, 177.2, 177.1, 176.7, 176.6, 176.5, 176.4, 164.52, 164.47, 163.9, 138.58, 138.54, 138.51, 138.45, 138.35, 138.31, 138.28, 138.21, 138.18, 138.15, 138.11, 138.07, 138.01, 137.96, 137.87, 137.8, 137.7, 133.6, 133.28, 133.25, 133.22, 133.14, 133.0, 132.93, 132.90, 132.1, 129.78, 129.72, 129.65, 129.55, 129.48, 129.45, 129.38, 129.32, 129.25, 129.18, 129.15, 128.8, 128.7, 128.6, 128.53, 128.46, 128.35, 128.29, 128.24, 128.21, 128.18, 128.14, 128.03, 127.97, 127.94, 127.92, 127.91, 127.76, 127.73, 127.69, 127.63, 127.60, 127.56, 127.43, 127.41, 127.37, 127.35, 127.31, 127.26, 127.22, 127.21, 127.1, 127.0, 126.9, 101.5, 100.8, 100.7, 100.6, 100.5, 100.2, 99.8, 99.6, 99.5, 86.0, 83.1, 82.99, 82.95, 82.93, 82.85, 82.5, 82.4, 80.4, 79.1, 79.0, 78.78, 78.60, 77.73, 77.65, 77.63, 77.43, 76.4, 76.3, 75.98, 75.93, 75.89, 75.87, 75.72, 75.59, 75.56, 75.44, 75.15, 75.11, 75.03, 74.85, 74.77, 74.65, 74.61, 74.51, 74.37, 74.34, 74.27, 74.15, 74.12, 74.02, 73.96, 73.87, 73.79, 73.30, 73.25, 73.17, 73.11, 73.09, 72.82, 72.80, 72.52, 72.44, 72.22, 69.9, 69.21, 69.17, 69.10, 67.6, 61.8, 38.68, 38.62, 38.58, 27.24, 27.19, 27.13, 27.09, 26.99, 26.80, 26.76; MS (MALDI) *m/z* calculated for $C_{318}H_{341}ClKO_{72}S$ $[M+K]^+$ 5417.21; found 5417.67.

The intramolecular glycosylation of linear dodecasaccharide **11b** was carried out in an H-type divided cell equipped with a carbon felt anode and a platinum plate cathode (10 mm×10 mm). In the anodic chamber were placed protected linear dodecasaccharide **11b** (0.028 mmol, 151 mg), $[P_{14}]$OTf (0.74 mmol, 0.17 mL) and CH_2Cl_2 (5.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.14 mmol, 12 μL), $[P_{14}]$OTf (0.50 mmol, 0.12 mL) and CH_2Cl_2 (5.1 mL). The constant current electrolysis (2.0 mA) was carried out at -50 °C with stirring until 1.5 F/mol of electricity was consumed and then -30 °C kept for 60 min. After elevation of the reaction temperature to 0 °C, Et_3N (0.1 mL) was added to both chambers, and the reaction mixture was dissolved in $CHCl_3$ and washed with water to remove electrolyte $[P_{14}]$OTf. Thus-obtained organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to obtain the crude product (160 mg). Silica gel chromatography (eluent: Hexane/EtOAc 3:1) and preparative recycling GPC (eluent: $CHCl_3$) afforded target protected cyclic dodecasaccharide **1b** in 23% yield (6.9 μmol, 36 mg).

References

[1] (a) J. Yoshida, K. Kataoka, R. Horcajada and A. Nagaki, *Chem. Rev.*, **2008**, *108*, 2265; (b) J. Yoshida, Y. Ashikari, K. Matsumoto and T. Nokami, *J. Synth. Org. Chem. Jpn.*, **2013**, *71*, 1136; (c) J. Yoshida, A. Shimizu, Y. Ashikari, T. Morofuji, R. Hayashi, T. Nokami and A. Nagaki, *Bull. Chem. Soc. Jpn.*, **2015**, *88*, 763; (d) M. Yan, Y. Kawamata and P. S. Baran, *Chem. Rev.*, **2017**, *117*, 13230; (e) J. Yoshida, A. Shimizu and R. Hayashi, *Chem. Rev.*, **2018**, *118*, 4702; (f) K. D. Moeller, *Chem. Rev.*, **2018**, *118*, 4817; (g) C. Zhu, N. W. J. Ang, T. H. Meyer, Y. Qiu and L. Ackermann, *ACS Cent. Sci.*, **2021**, *7*, 415.

[2] (a) P. Hu, B. K. Peters, C. A. Malapit, J. C. Vantourout, P. Wang, J. Li, L. Mele, P.-G. Echeverria, S. D. Minteer and P. S. Baran, *J. Am. Chem. Soc.*, **2020**, *142*, 20979; (b) Y. Gao, D. E. Hill, W. Hao, B. J. McNicholas, J. C. Vantourout, R. G. Hadt, S. E. Reisman, D. G. Blackmond and P. S. Baran, *J. Am. Chem. Soc.*, **2021**, *143*, 9478; (d) K. Hayashi, J. Griffin, K. C. Harper, Y. Kawamata and P. S. Baran, *J. Am. Chem. Soc.*, **2022**, *144*, 5762; (e) S. J. Harwood, M. D. Palkowitz, C. N. Gannett, P. Perez, Z. Yao, L. Sun, H. D. Abruña, S. L. Anderson and P. S. Baran, *Science*, **2022**, *375*, 745.

[3] S. Nagahara, Y. Okada, Y. Kitano and K. Chiba, *Chem. Sci.*, **2021**, *12*, 12911.

[4] (a) S. Manmode, K. Matsumoto, T. Itoh and T. Nokami, *Asian J. Org. Chem.*, **2018**, *7*, 1719; (b) A. Shibuya and T. Nokami, *Chem. Rec.*, **2021**, *21*, 2389; (c) K. Yano, N. Sasaki, T. Itoh and T. Nokami, *J. Synth. Org. Chem. Jpn*, **2021**, *79*, 839.

[5] (a) T. Nokami, R. Hayashi, Y. Saigusa, A. Shimizu, C.-Y. Liu, K.-K. Mong and J. Yoshida, *Org. Lett.*, **2013**, *15*, 4520; (b) T. Nokami, Y. Isoda, N. Sasaki, A. Takaiso, S. Hayase, T. Itoh, R. Hayashi, A. Shimizu and J. Yoshida, *Org. Lett.*, **2015**, *17*, 1525.

[6] (a) M. Davis and M. Brewster, *Nat. Rev. Drug Discov.*, **2004**, *3*, 1023; (b) G. Crini, *Chem. Rev.*, **2014**, *114*, 10940.

[7] M. Wakao, K. Fukase and S. Kusumoto, *J. Org. Chem.*, **2002**, *67*, 8182.

[8] (a) M. L. Gening, D. V. Titov, A. A. Grachev, A. G. Gerbst, O. N. Yudina, A. S. Shashkov, A. O. Chizhov, Y. E. Tsvetkov and N. E. Nifantiev, *Eur. J. Org. Chem.*, **2010**, 2465; (b) D. V. Titov, M. L. Gening, A. G. Gerbst, A. O. Chizhov, Y. E. Tsvetkov and N. E. Nifantiev, *Carbohydr. Res.*, **2013**, *381*, 161; (c) M. L. Gening, Y. E. Tsvetkov, D. V. Titov, A. G. Gerbst, O. N. Yudina, A. A. Grachev, A. S. Shashkov, S. Vidal, A. Imberty, T. Saha, D. Kand, P. Talukdar, G. B. Pier and N. E. Nifantiev, *Pure Appl. Chem.*, **2013**, *85*, 1879.

[9] S. Manmode, S. Tanabe, T. Yamamoto, N. Sasaki, T. Nokami and T. Itoh, *ChemistryOpen*, **2019**, *8*, 869.

[10] H. Endo, M. Ochi, M. A. Rahman, T. Hamada, T. Kawano and T. Nokami, *Chem. Commun.*, **2022**, *58*, 7948.

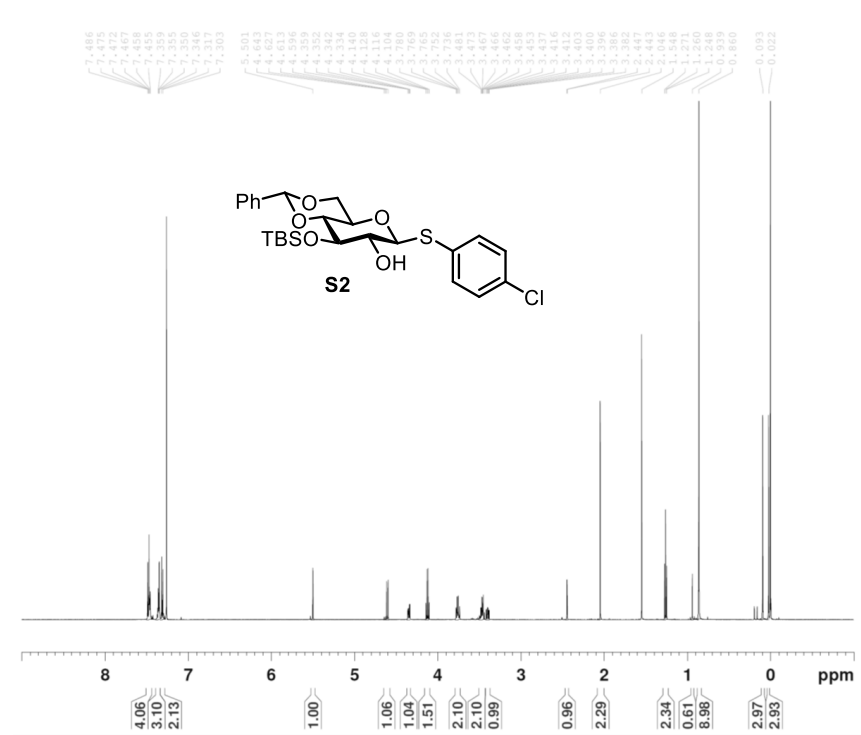
[11] (a) M. W. Breedveld and K. J. Miller, *Microbiol. Rev.*, **1994**, *58*, 145; (b) A. V. Nair, S. N. Gummadi and M. Doble, *Biotechnol. Lett.*, **2016**, *38*, 1519; (c) E. Cho, D. Jeong, Y. Choi and S. Jung, *J. Incl. Phenom. Macrocycl. Chem.*, **2016**, *85*, 175.

[12] (a) S. Manmode, M. Kato, T. Ichiyanagi, T. Nokami and T. Itoh, *Asian J. Org. Chem.*, **2018**, *7*, 1802; (b) A. Shibuya, M. Kato, A. Saito, S. Manmode, N. Nishikori, T. Itoh, A. Nagaki and T. Nokami, *Eur. J. Org. Chem.*, **2022**, *19*, e202200135.

[13] N. Basu, S. K. Maity, S. Roy, S. Singha and R. Ghosh, *Carbohydr. Res.*, 2011, 346, 534.

^{1}H and ^{13}C NMR spectra of synthetic intermediates and monosaccharide building blocks

^{1}H NMR

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FIDRES           0.188225 Hz
AQ               2.6564426 sec
RG                     203
DW                40.533 use
DE                 6.50 use
TE                297.0 K
D1             1.00000000 sec
TD0                      1

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PL1                  -2.00 dB
PL1W          18.91009140 W
SFO1          600.1337060 MHz
SI                   32768
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SSB                      0
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GB                       0
PC                    1.00
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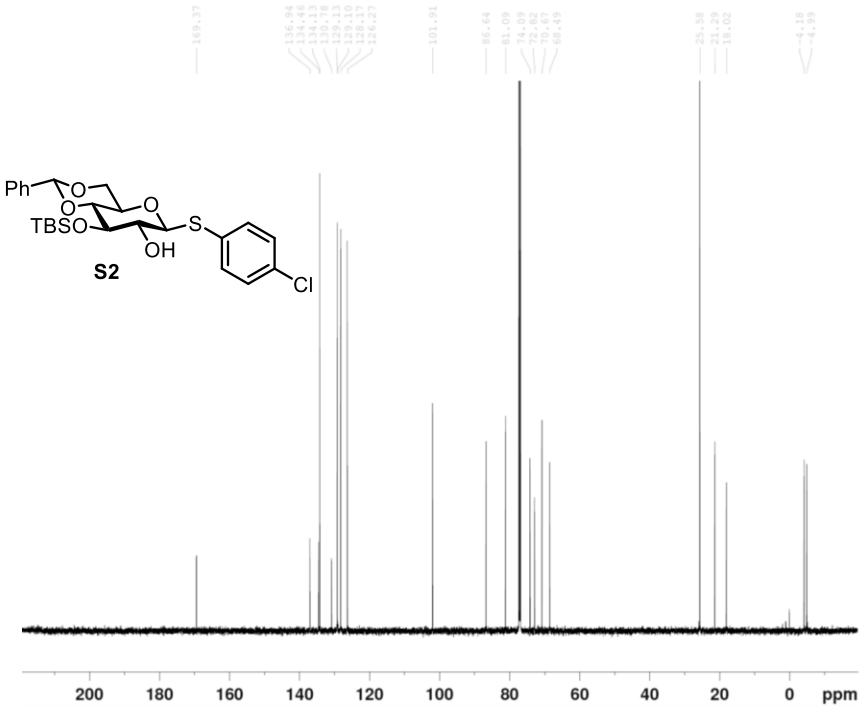
^{13}C NMR

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PROCNO                   1
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PULPROG             zgpg30
TD                   65536
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DS                       2
SWH              36057.691 Hz
FIDRES           0.550197 Hz
AQ               0.9088159 sec
RG                     203
DW                13.867 usec
DE                 6.50 usec
TE                296.6 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 =======
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P1                   10.00 usec
PL1                  -1.00 dB
PL1W         125.22619629 W
SFO1          150.9178988 MHz

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NUC2                    1H
PCPD2                80.00 usec
PL2                  -2.00 dB
PL12                 13.78 dB
PL13                 14.00 dB
PL2W          18.91009140 W
PL12W          0.49968192 W
PL13W          0.47499999 W
SFO2          600.1324005 MHz
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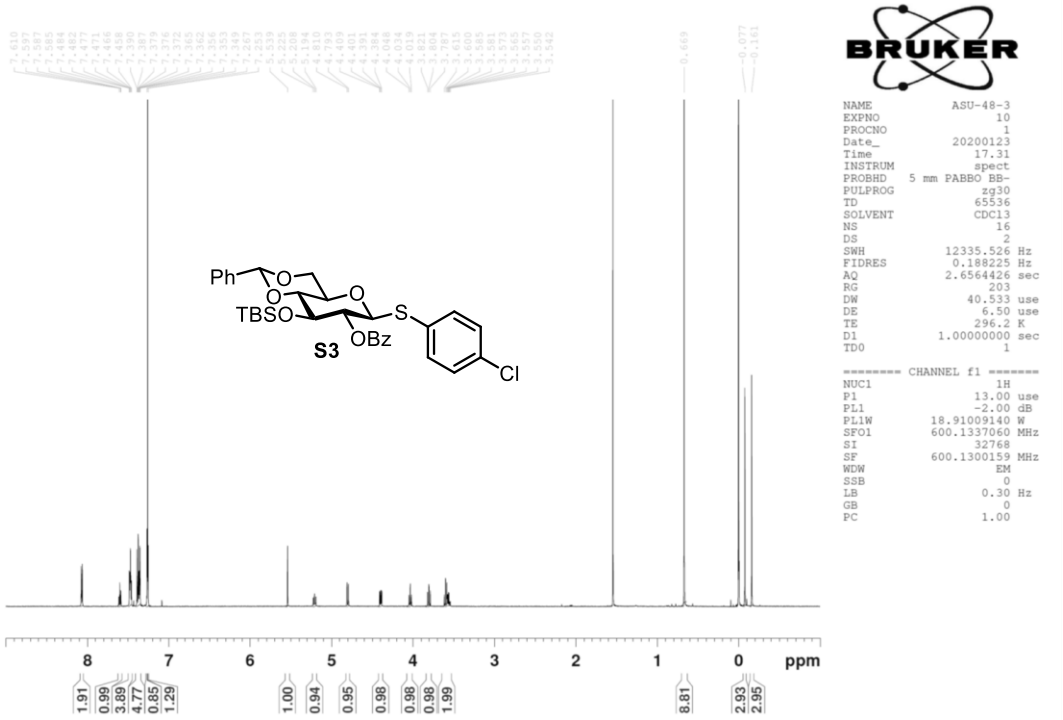

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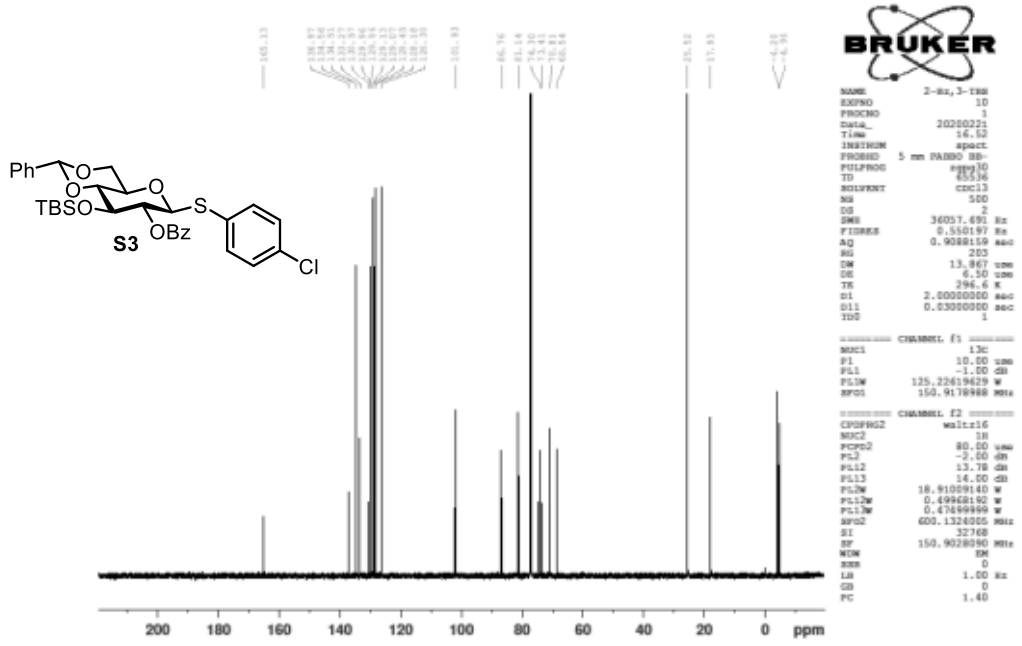

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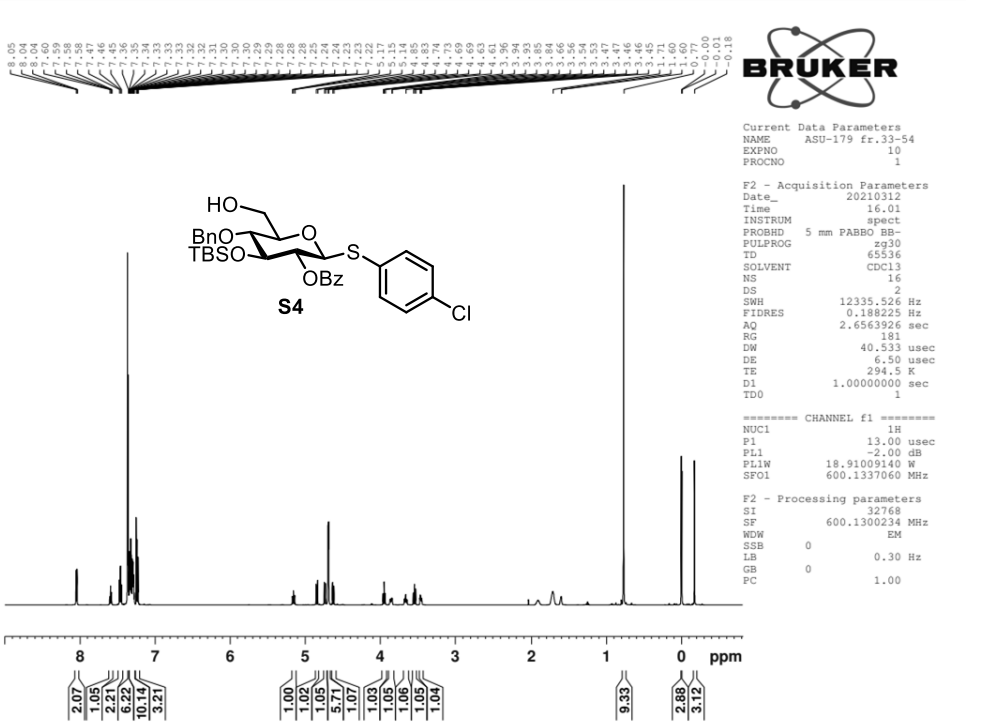

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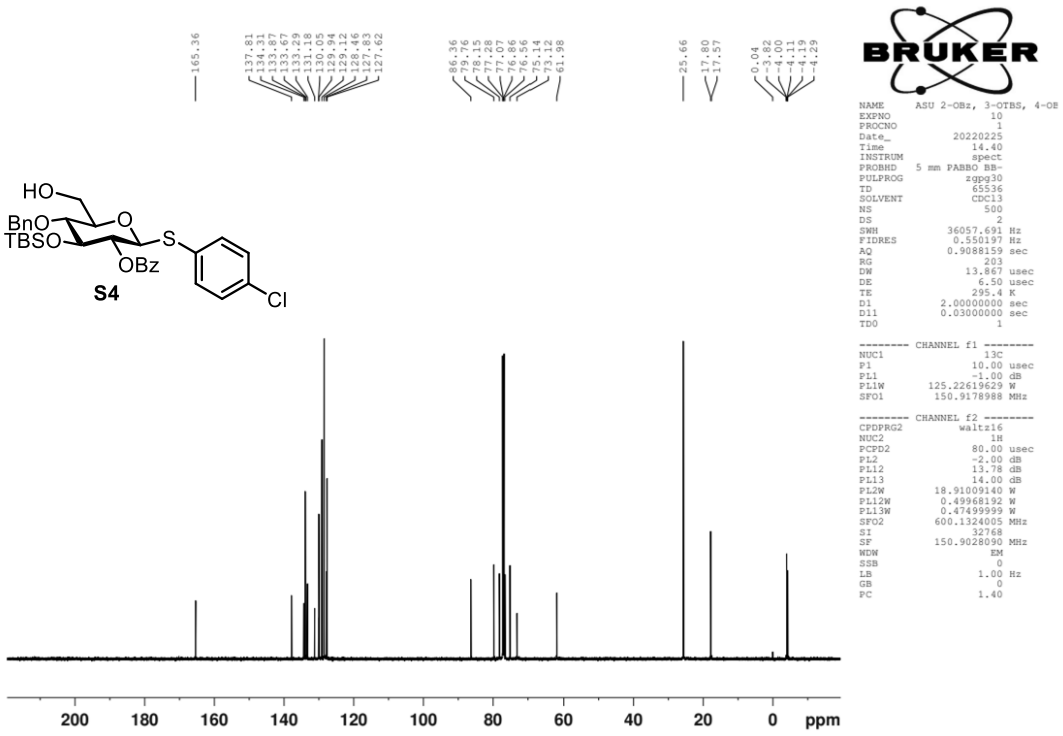

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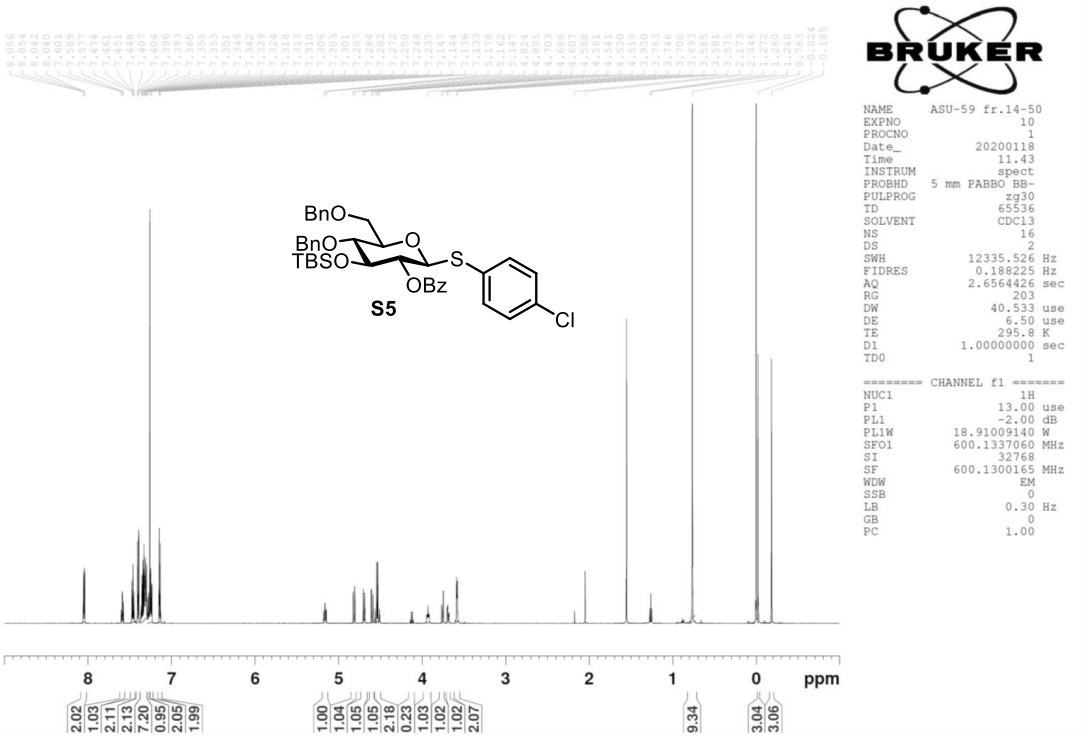

BRUKER

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TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES             0.188225 Hz
AQ             2.6564426 sec
RG                   203
DW                40.533 use
DE                 6.50 use
TE                295.8 K
D1            1.00000000 sec
TD0                    1

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NUC1                  1H
P1                 13.00 use
PL1                -2.00 dB
PL1W          18.91009140 W
SFO1         600.1337060 MHz
SI                 32768
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SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
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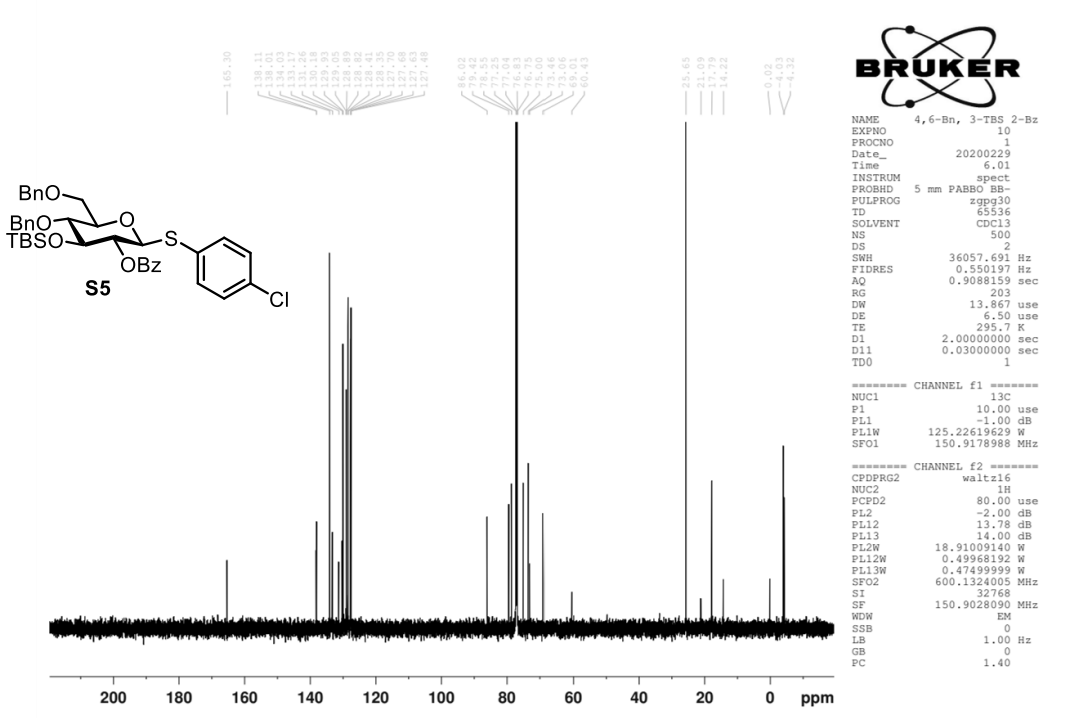
^{13}C NMR



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TD                 65536
SOLVENT            CDCl3
NS                   500
DS                     2
SWH            36057.691 Hz
FIDRES             0.550197 Hz
AQ             0.9088159 sec
RG                   203
DW                13.867 use
DE                 6.50 use
TE                295.7 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 =======
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P1                 10.00 use
PL1                -1.00 dB
PL1W         125.22619629 W
SFO1          150.9178988 MHz

======== CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 use
PL2                -2.00 dB
PL12               13.78 dB
PL13               14.00 dB
PL2W          18.91009140 W
PL12W          0.49968192 W
PL13W          0.47499999 W
SFO2         600.1324005 MHz
SI                 32768
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WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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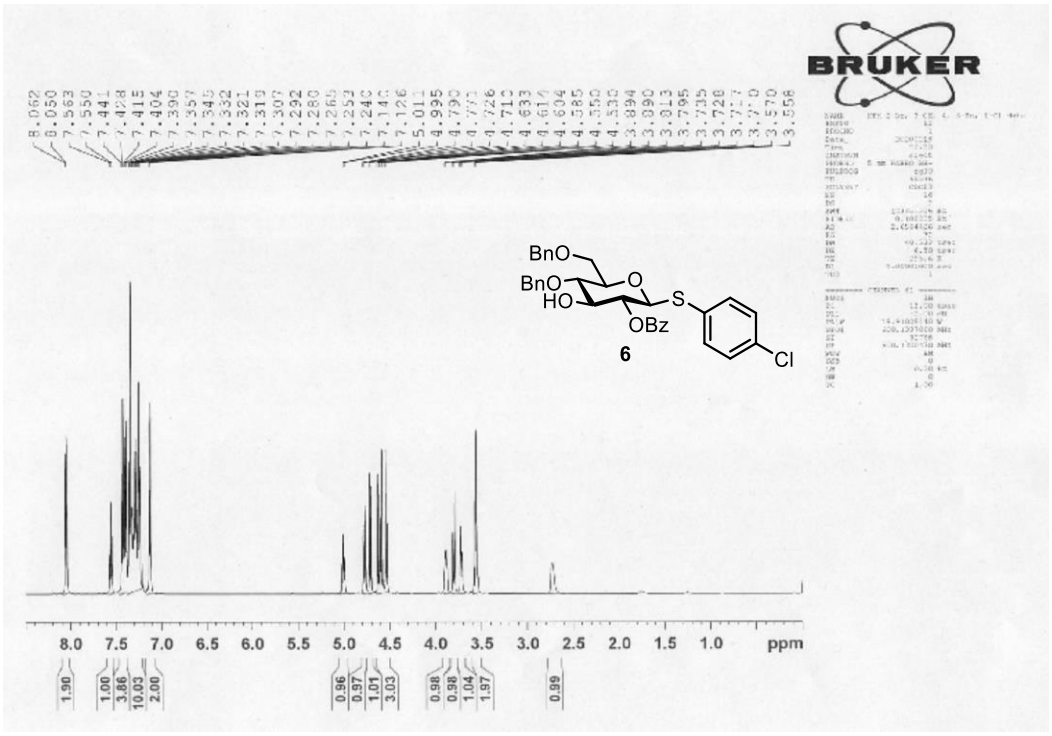
^{1}H NMR



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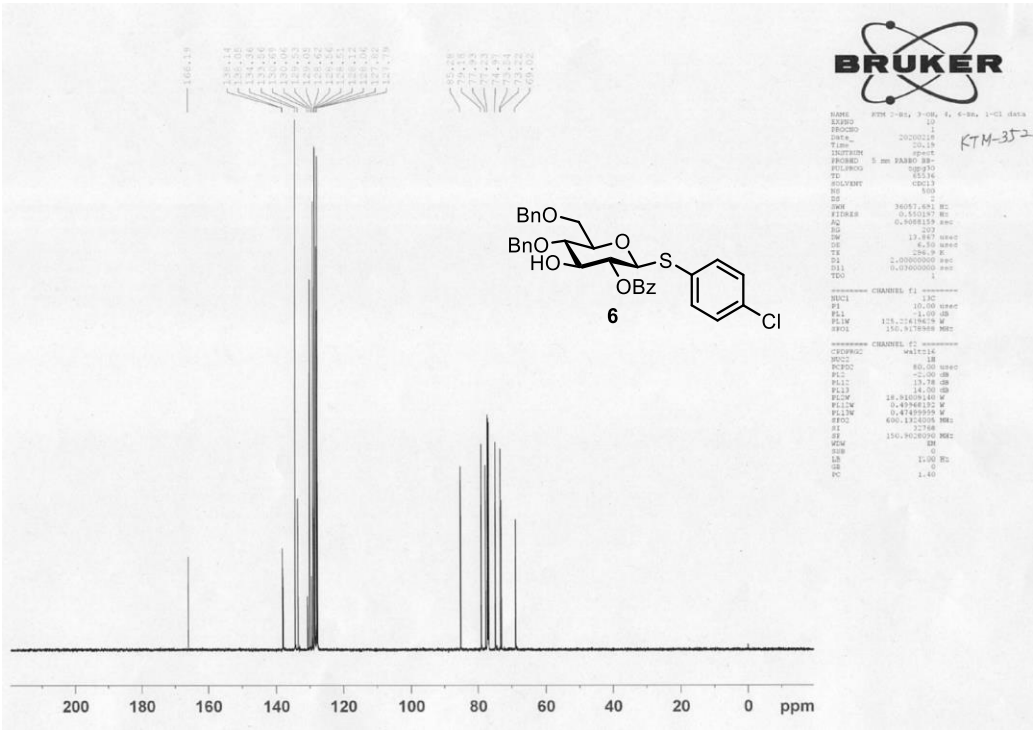

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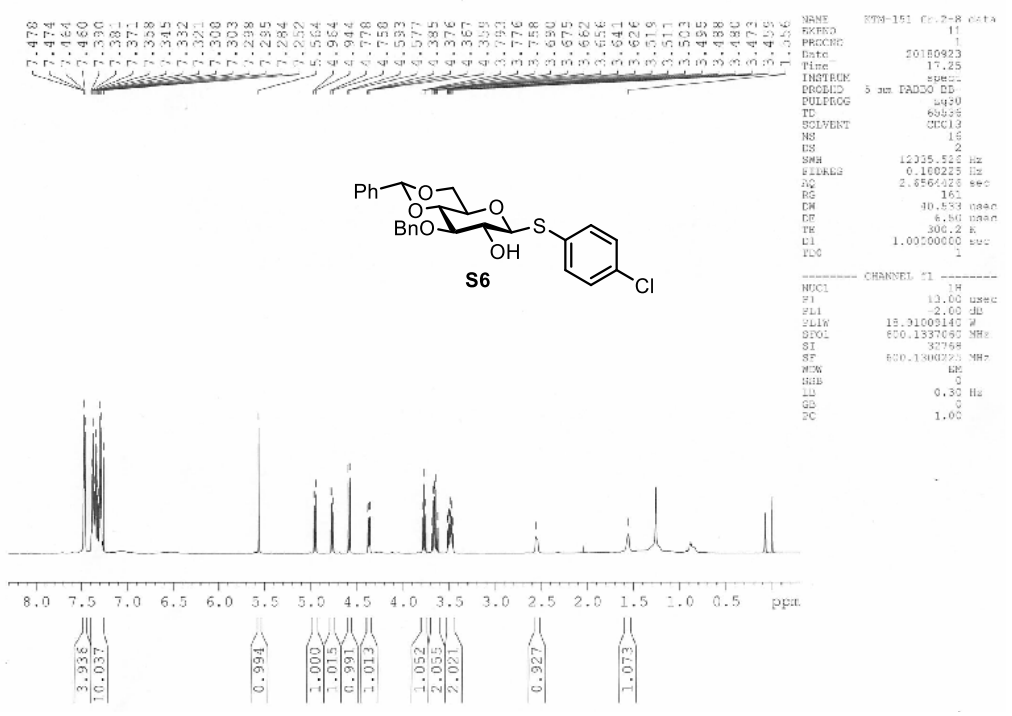

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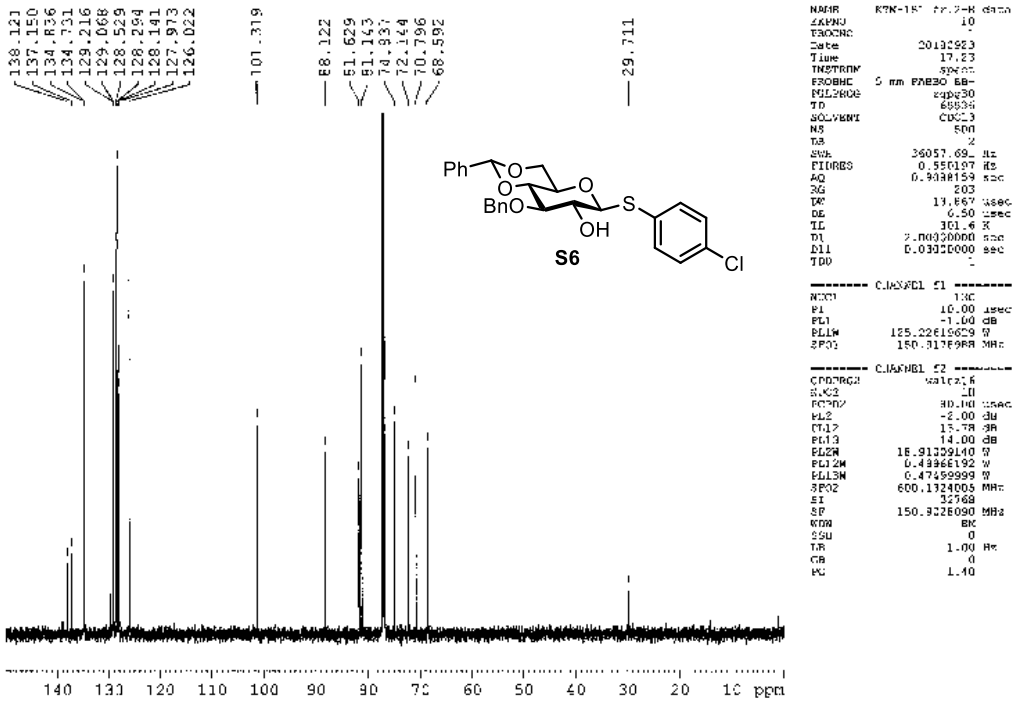

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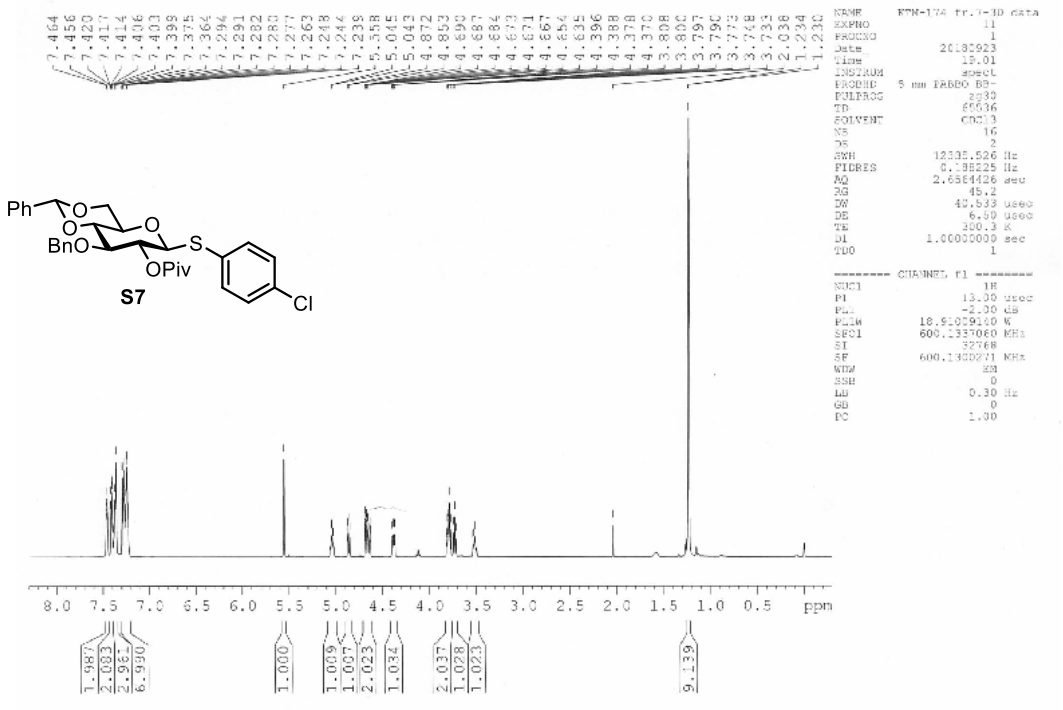

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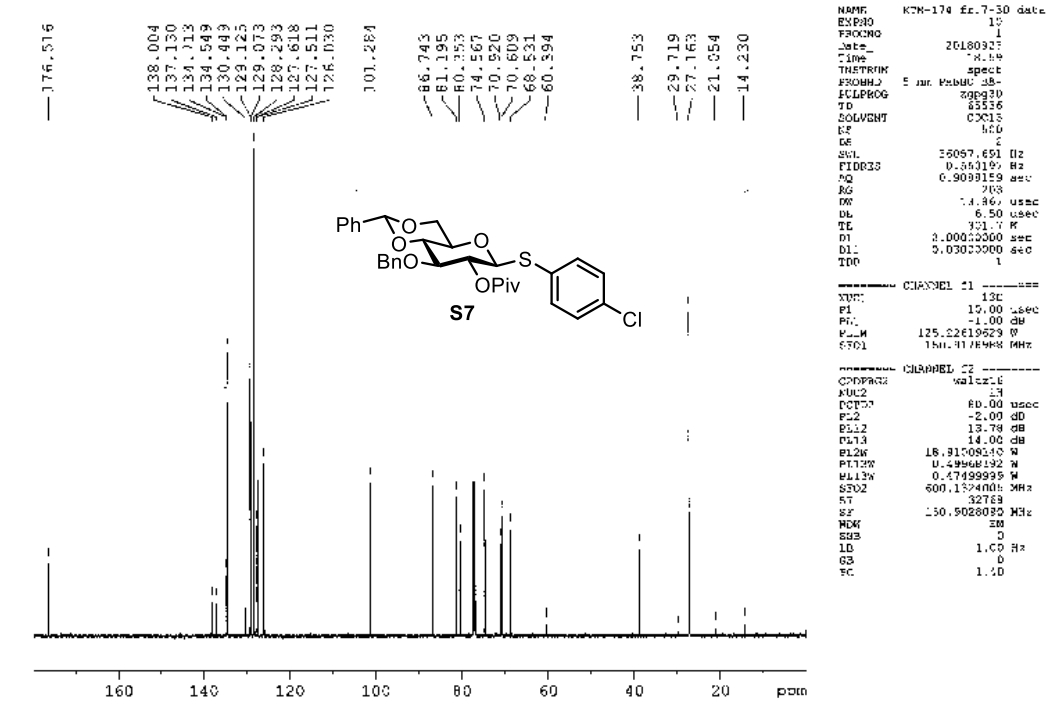

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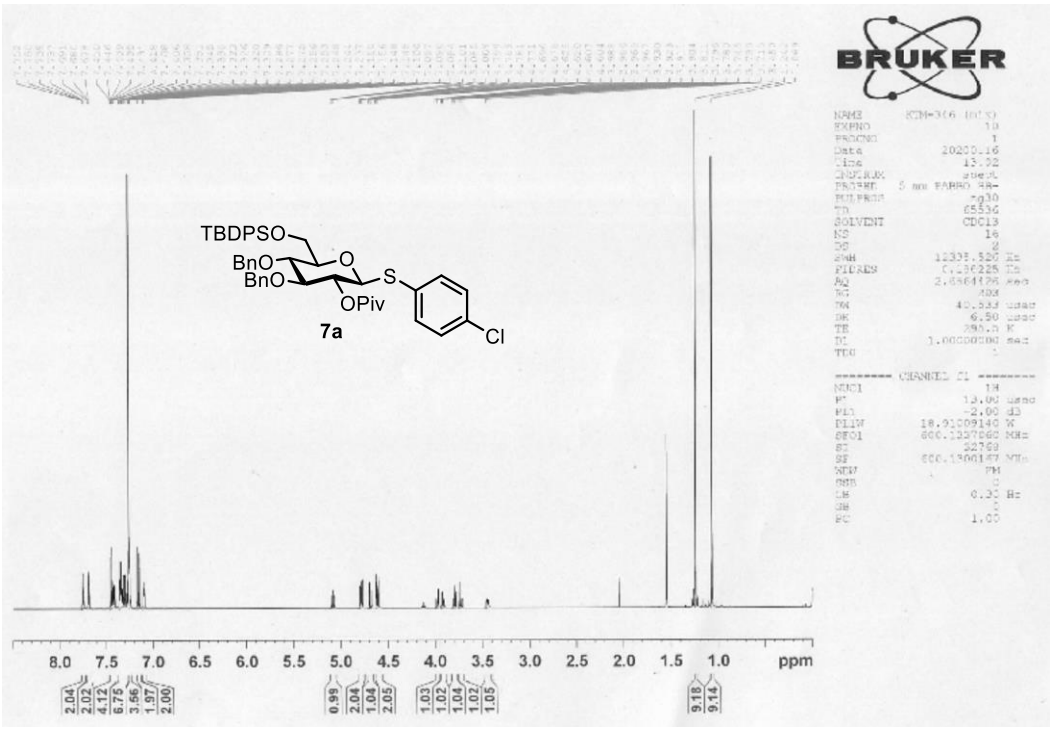
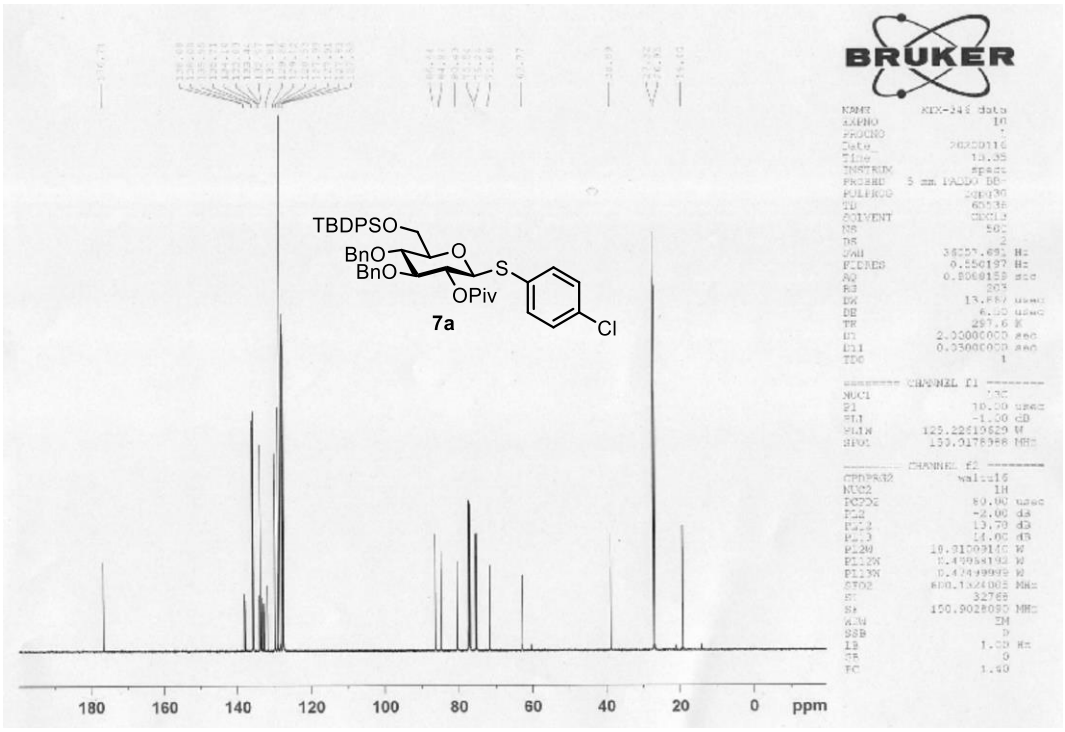


^{13}C NMR



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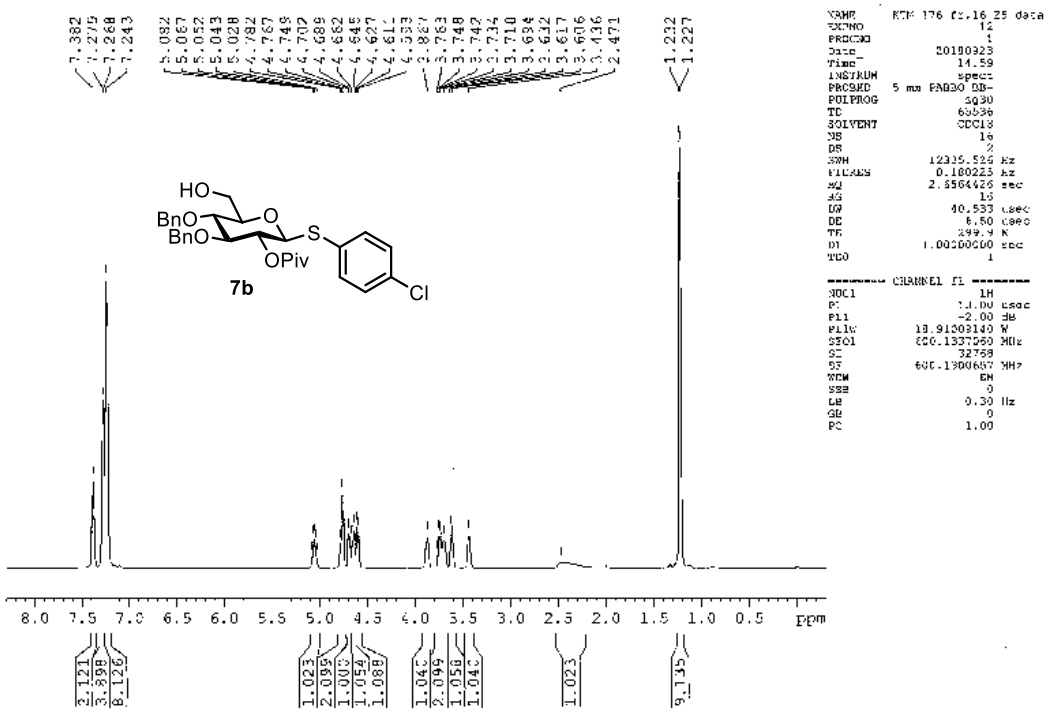

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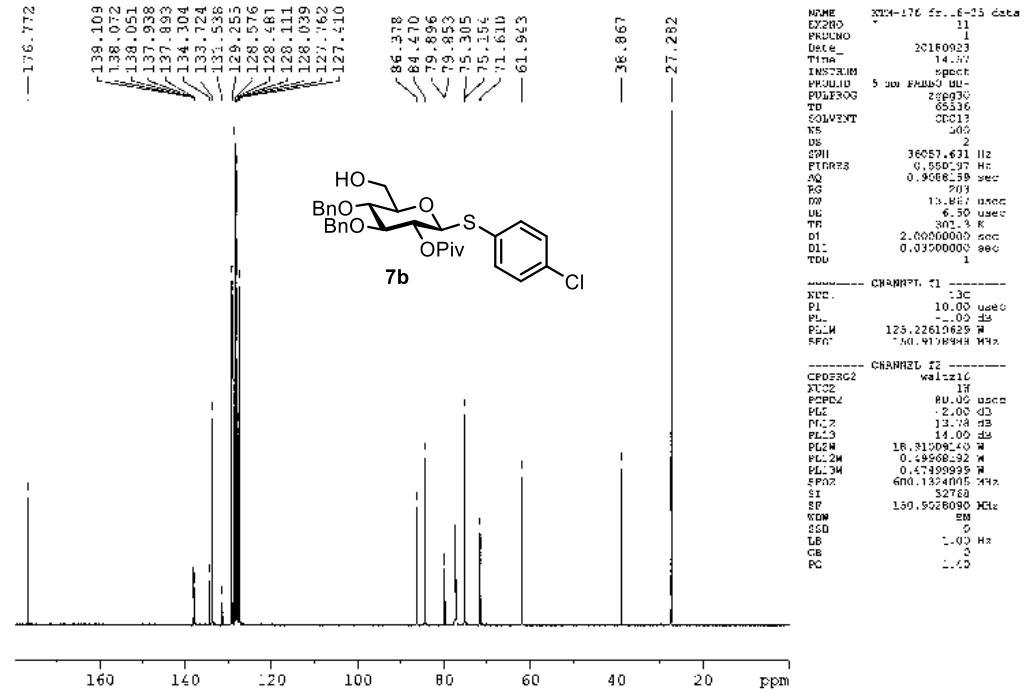

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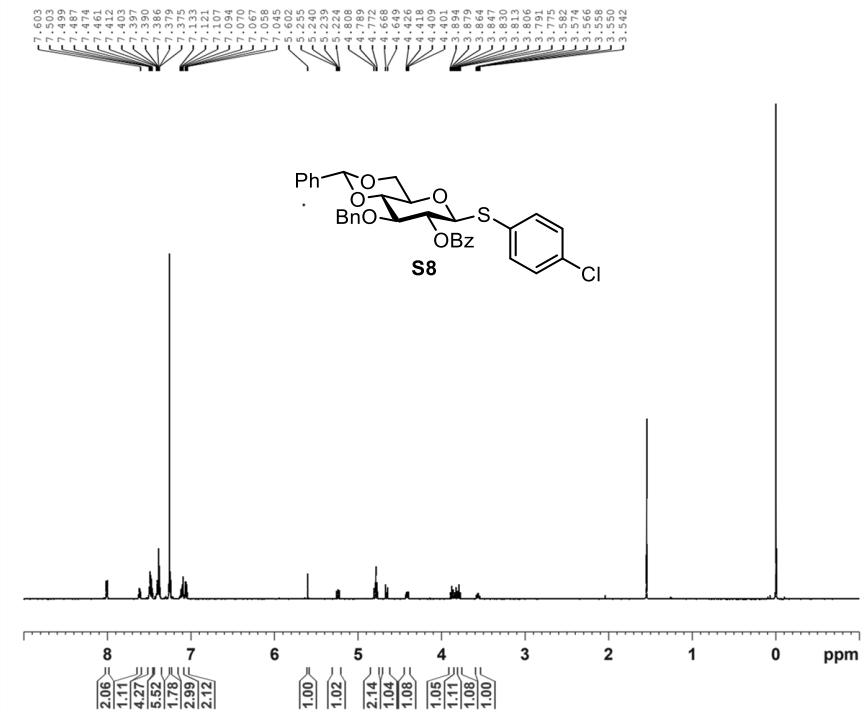


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DS                   2
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FIDRES        0.188225 Hz
AQ            2.6563926 sec
RG                 203
DW              40.533 usec
DE               6.50 usec
TE              293.8 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        600.1337060 MHz
NUC1               1H
P1              14.00 usec
PLW1       13.50000000 W

F2 - Processing parameters
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SSB       0
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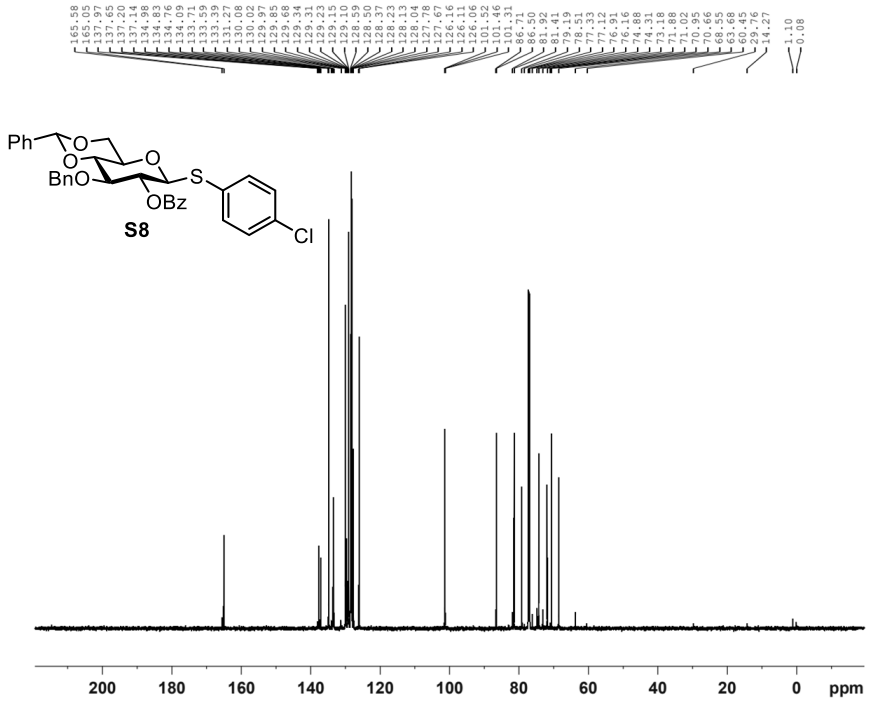


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SWH          36057.691 Hz
FIDRES        0.550197 Hz
AQ            0.9087659 sec
RG                 203
DW              13.867 usec
DE               6.50 usec
TE              294.5 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
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NUC1               13C
P1              12.00 usec
PLW1       79.40000153 W

======== CHANNEL f2 ========
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NUC2               1H
CPDPRG[2         waltz16
PCPD2           70.00 usec
PLW2       13.50000000 W
PLW12       0.54000002 W
PLW13       0.26460001 W

F2 - Processing parameters
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SSB       0
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GB        0
PC              1.40
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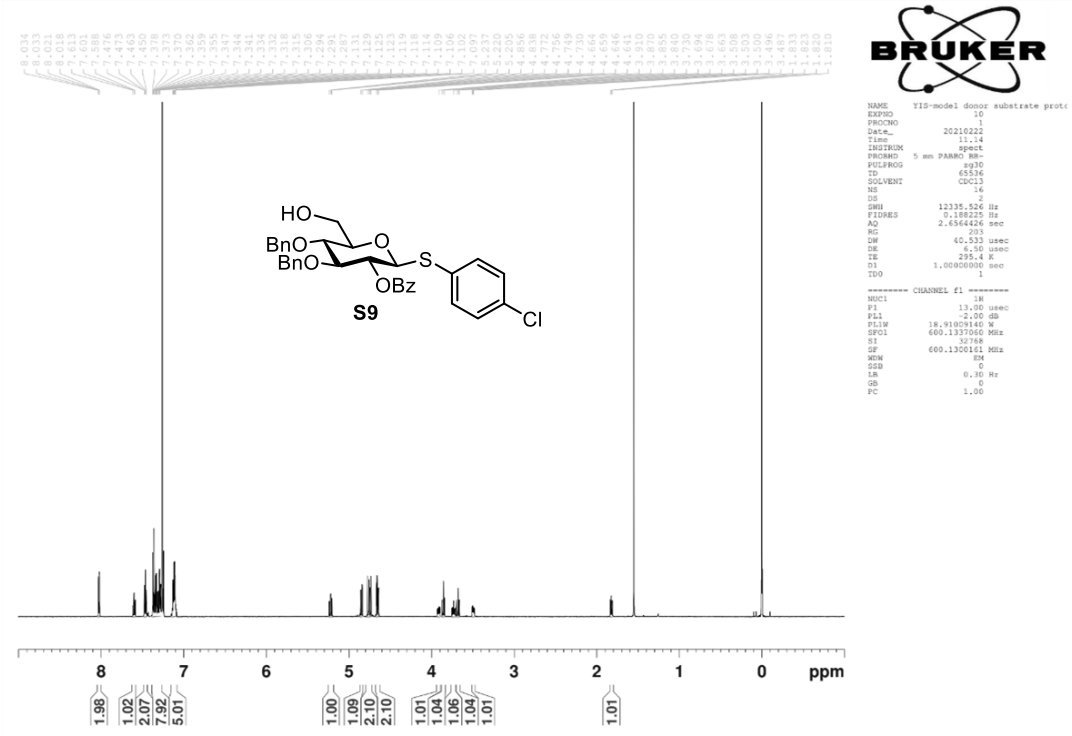
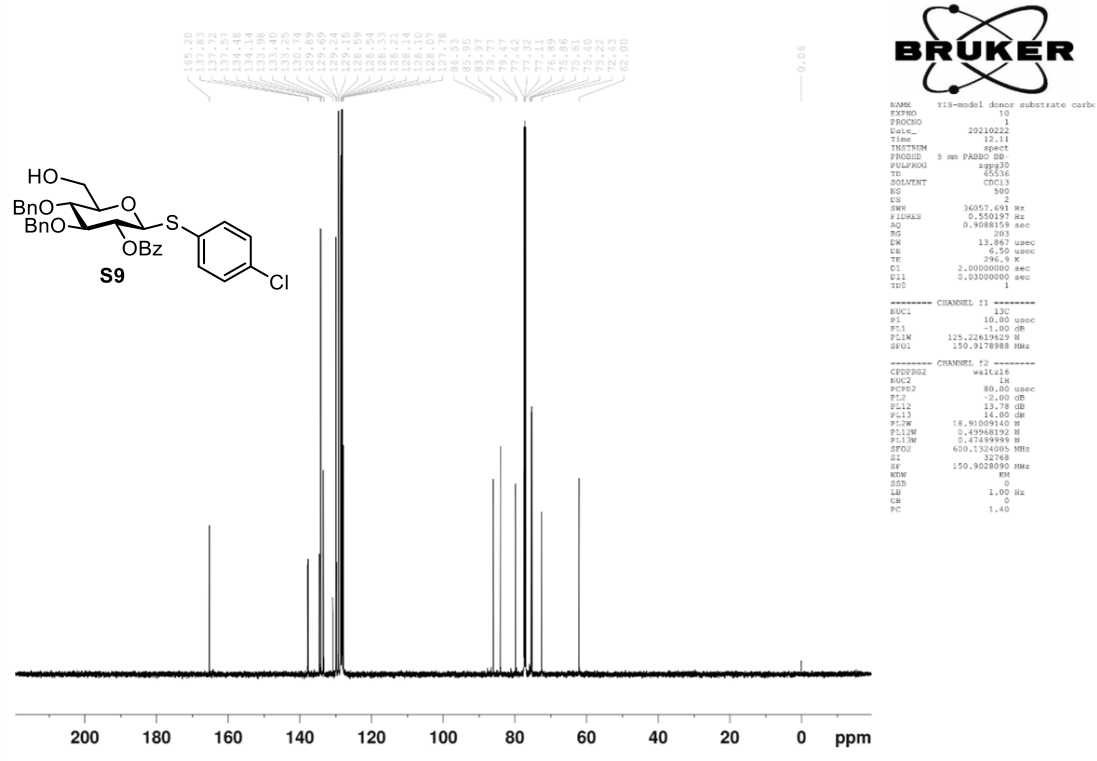
^{1}H NMR



^{13}C NMR



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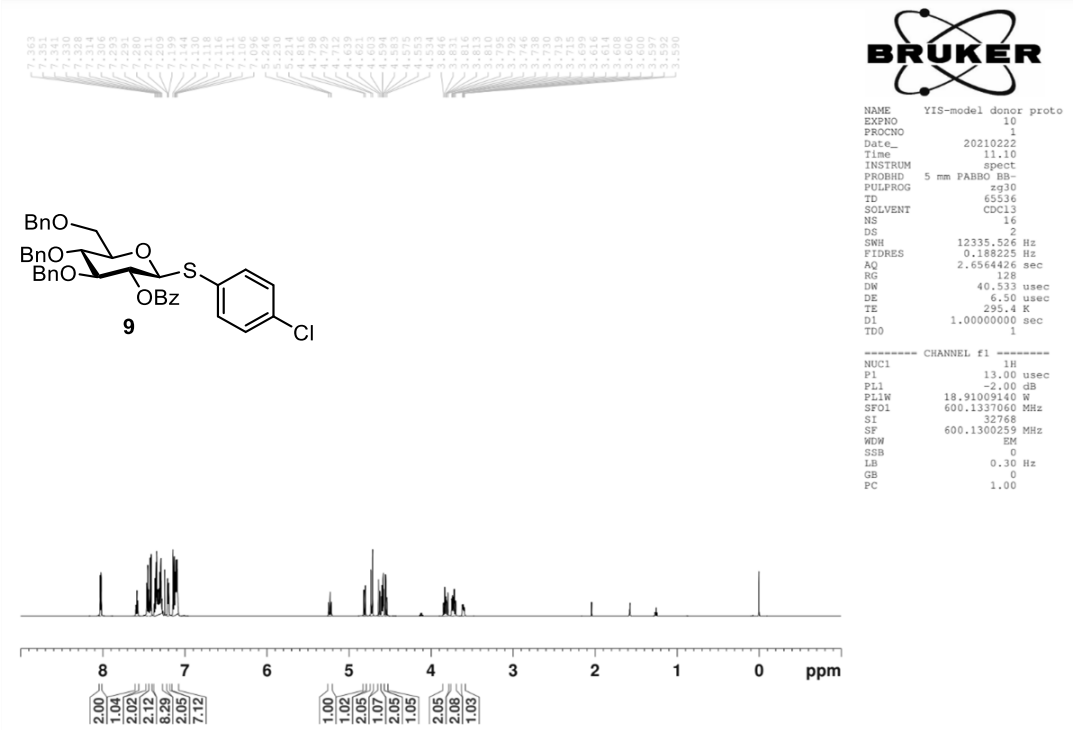


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TD                         65536
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NS                            16
DS                             2
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FIDRES                 0.188225 Hz
AQ                     2.6564426 sec
RG                           128
DW                        40.533 usec
DE                         6.50 usec
TE                        295.4 K
D1                   1.00000000 sec
TD0                            1

======== CHANNEL f1 ========
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P1                        13.00 usec
PL1                       -2.00 dB
PL1W                18.91009140 W
SFO1               600.1337060 MHz
SI                         32768
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WDW                           EM
SSB                            0
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GB                             0
PC                         1.00
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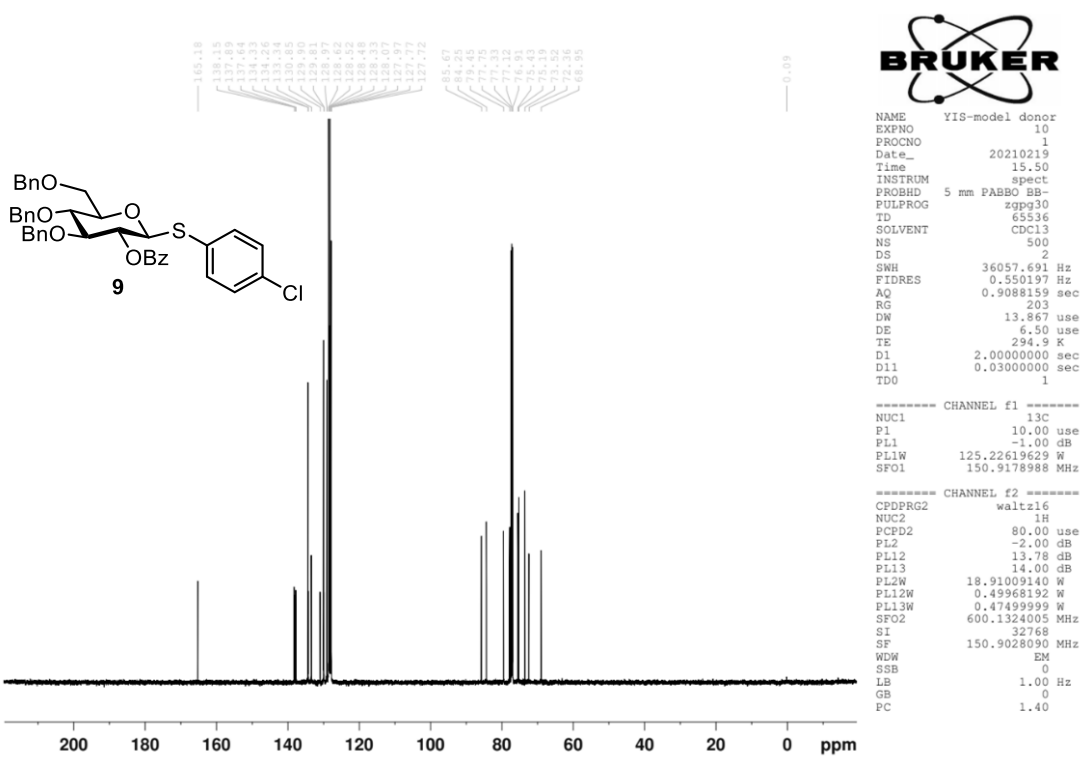
^{13}C NMR

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SWH                    36057.691 Hz
FIDRES                 0.550197 Hz
AQ                     0.9088159 sec
RG                           203
DW                        13.867 use
DE                         6.50 use
TE                        294.9 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                        13C
P1                        10.00 use
PL1                       -1.00 dB
PL1W               125.22619629 W
SFO1               150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                     80.00 use
PL2                       -2.00 dB
PL12                      13.78 dB
PL13                      14.00 dB
PL2W                18.91009140 W
PL12W                0.49968192 W
PL13W                0.47499999 W
SFO2               600.1324005 MHz
SI                         32768
SF                 150.9028090 MHz
WDW                           EM
SSB                            0
LB                         1.00 Hz
GB                             0
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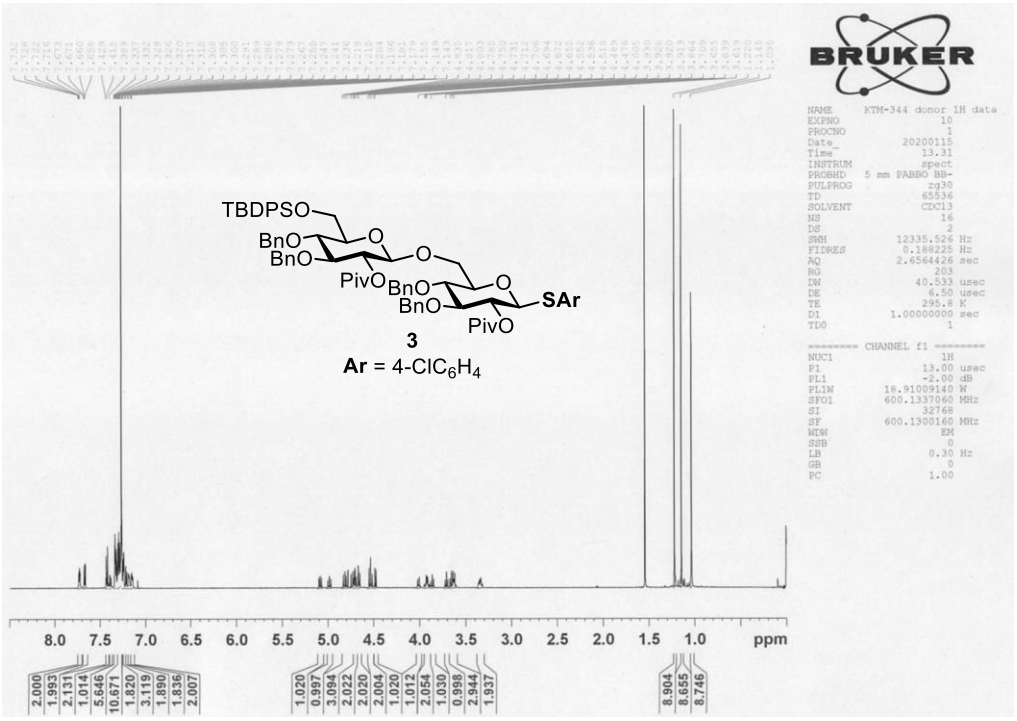
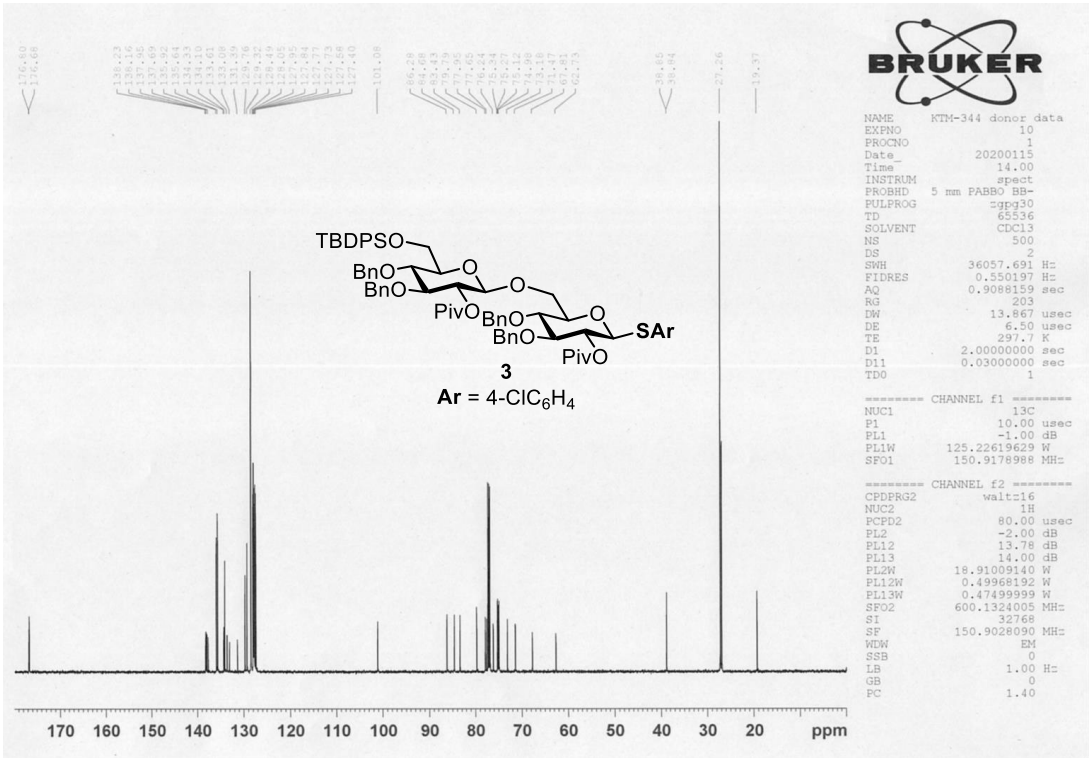
^{1}H, ^{13}C NMR, H-H COSY and HMQC spectra of disaccharides.

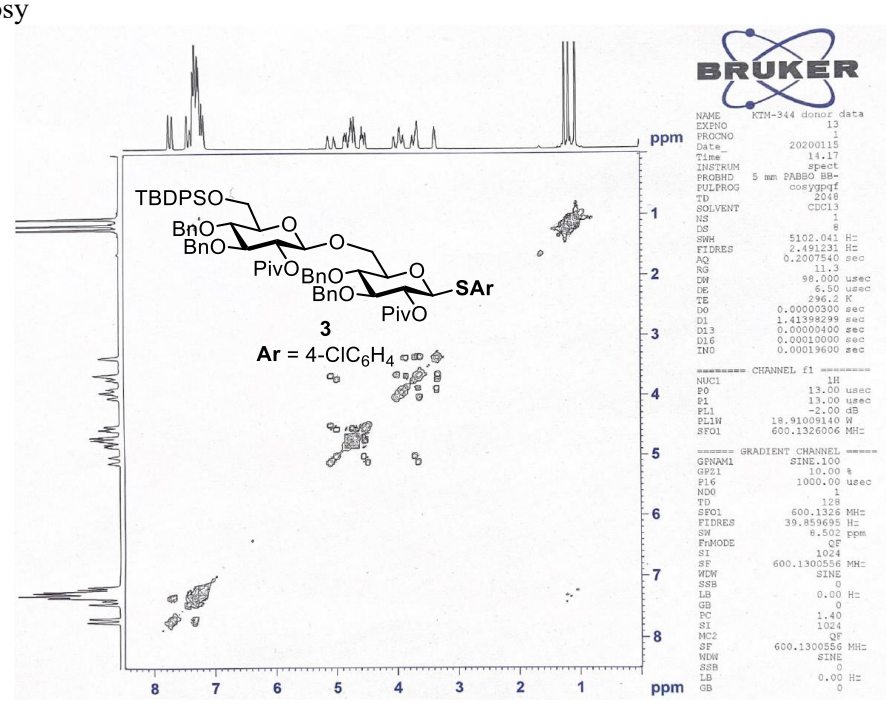
^{1}H NMR



^{13}C NMR



H-H cosy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ppm
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2
3
4
5
6
7
8
8 7 6 5 4 3 2 1 ppm
BRUKER
NAME KTM-344 donor data
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PROCNO 1
Date_ 20200115
Time 14.17
INSTRUM spect
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PULPROG cosygpqf
TD 2048
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DS 8
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FIDRES 2.491231 Hz
AQ 0.2007540 sec
RG 11.3
DW 98.000 usec
DE 6.50 usec
TE 296.2 K
D0 0.00000300 sec
D1 1.41398299 sec
D13 0.00000400 sec
D16 0.00010000 sec
IN0 0.00019600 sec
======== CHANNEL f1 ========
NUC1 1H
P0 13.00 usec
P1 13.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1326006 MHz
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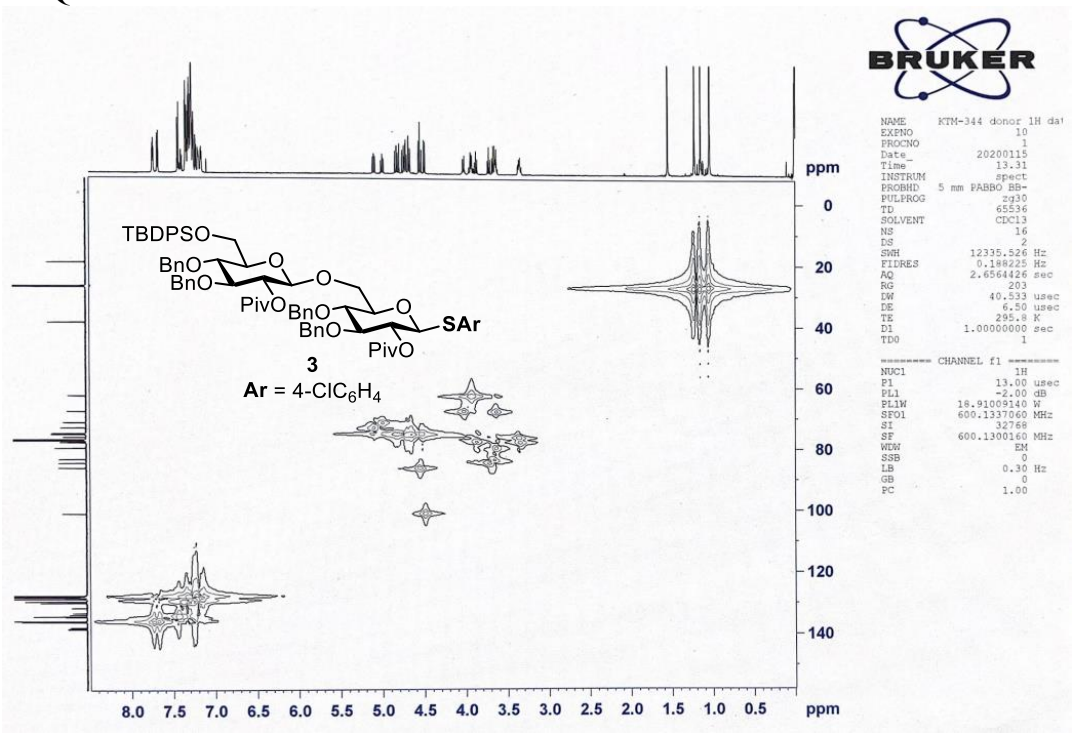
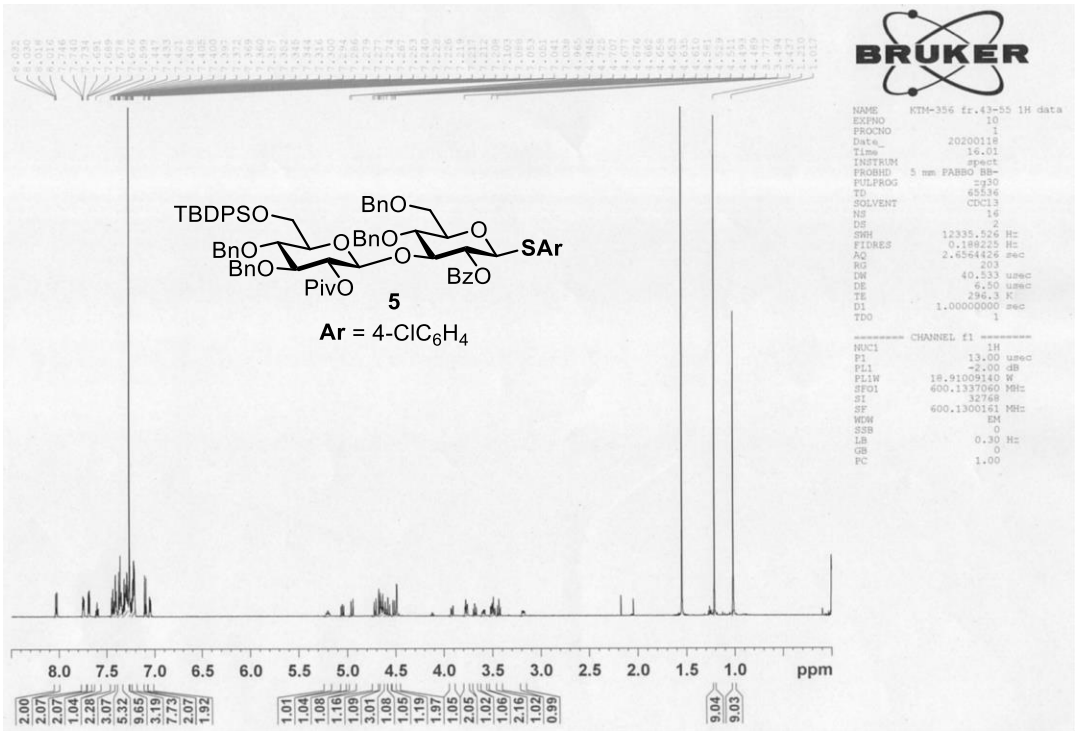
GPNAM1 SINE.100
GPZ1 10.00 %
P16 1000.00 usec
ND0 1
TD 128
SFO1 600.1326 MHz
FIDRES 39.859695 Hz
SW 8.502 ppm
FnMODE QF
SI 1024
SF 600.1300556 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 QF
SF 600.1300556 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

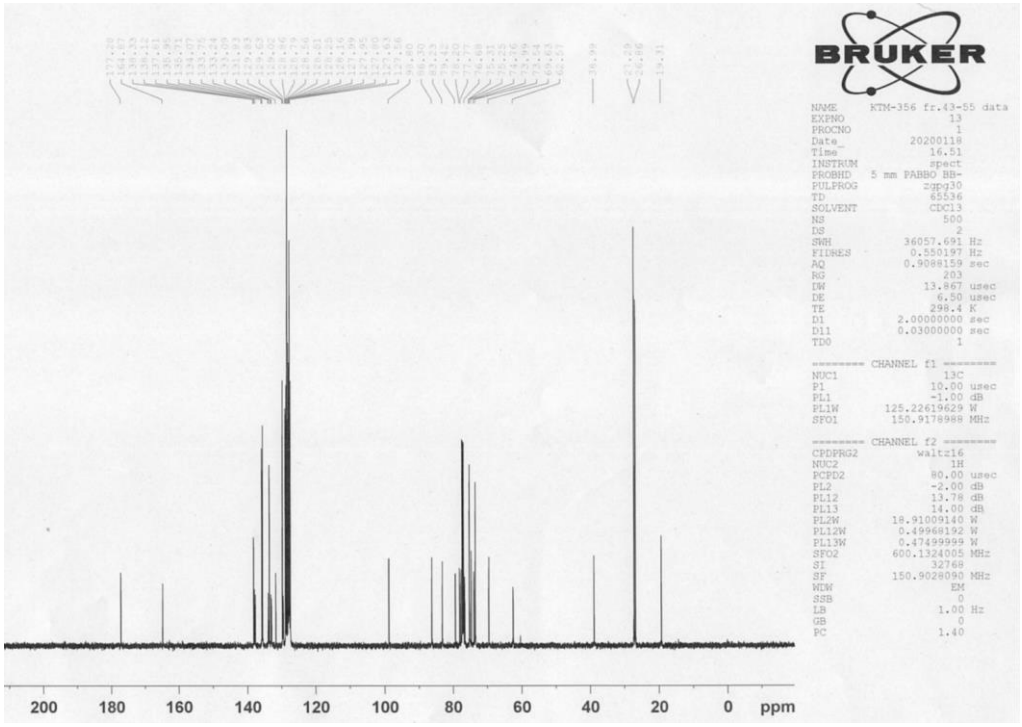
HMQC


TBDPSO
BnO
BnO
PivO
BnO
BnO
PivO
SAr
3
Ar = 4-ClC6H4
ppm
0
20
40
60
80
100
120
140
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
BRUKER
NAME KTM-344 donor 1H da
EXPNO 10
PROCNO 1
Date_ 20200115
Time 13.31
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 12335.526 Hz
FIDRES 0.188225 Hz
AQ 2.6564426 sec
RG 203
DW 40.533 usec
DE 6.50 usec
TE 295.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
PL1 -2.00 dB
PL1W 18.91009140 W
SFO1 600.1337060 MHz
SI 32768
SF 600.1300160 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

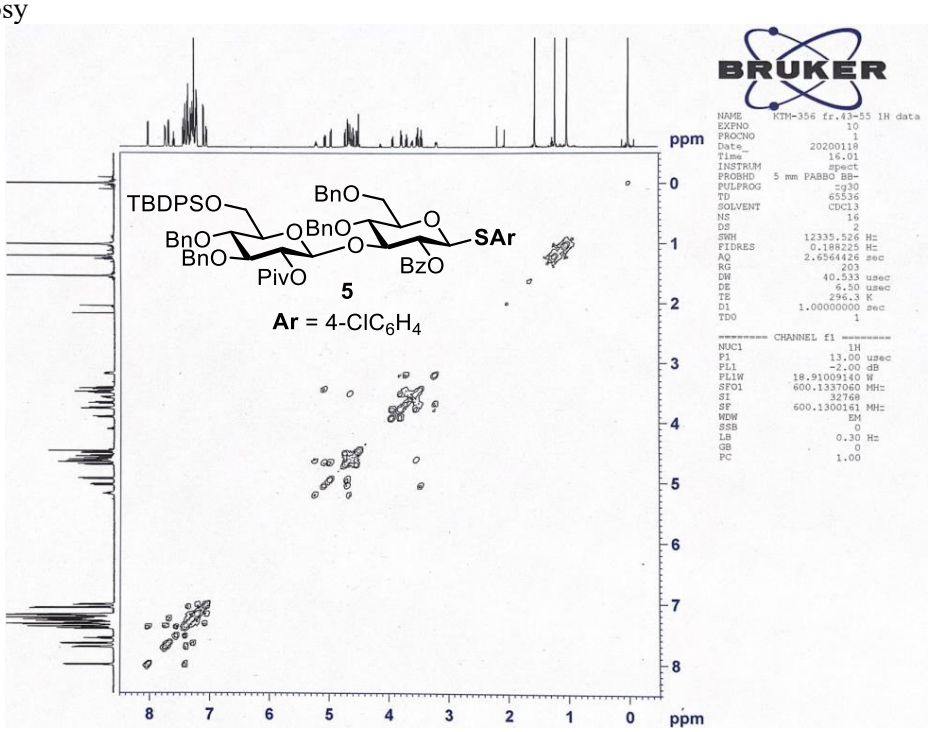
^{1}H NMR



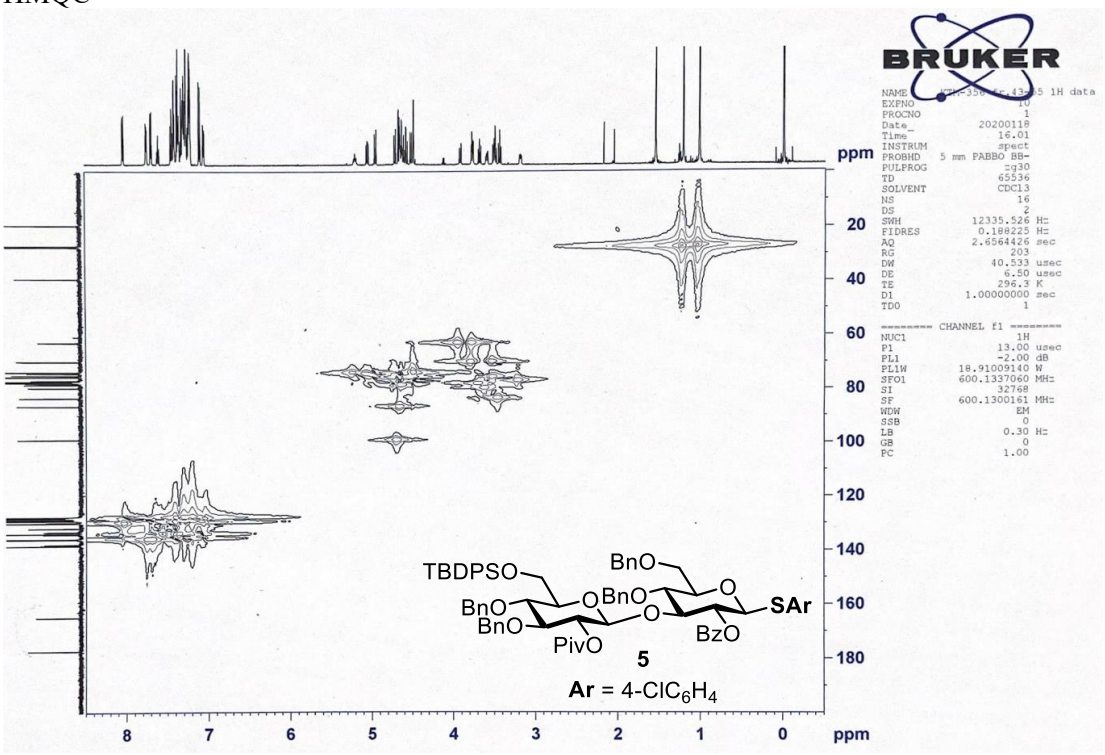
^{13}C NMR



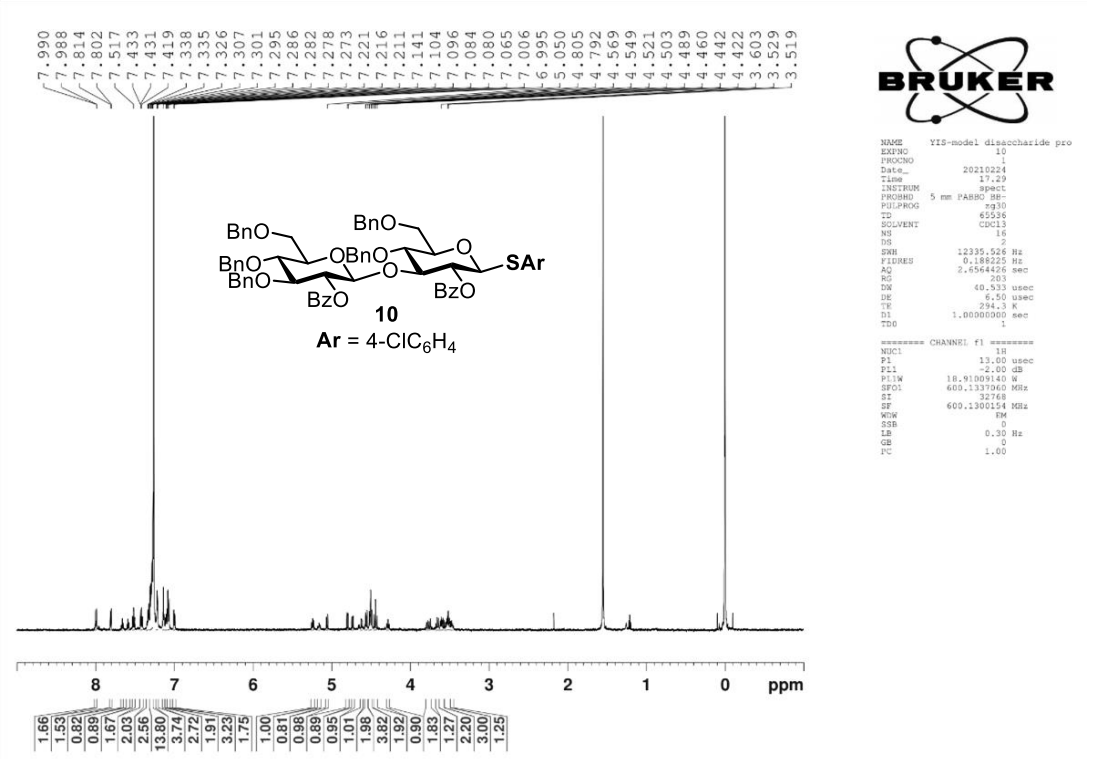
H-H cosy


BRUKER
TBDPSO
BnO
BnO
BnO
BnO
PivO
BzO
SAr
5
Ar = 4-ClC6H4
ppm

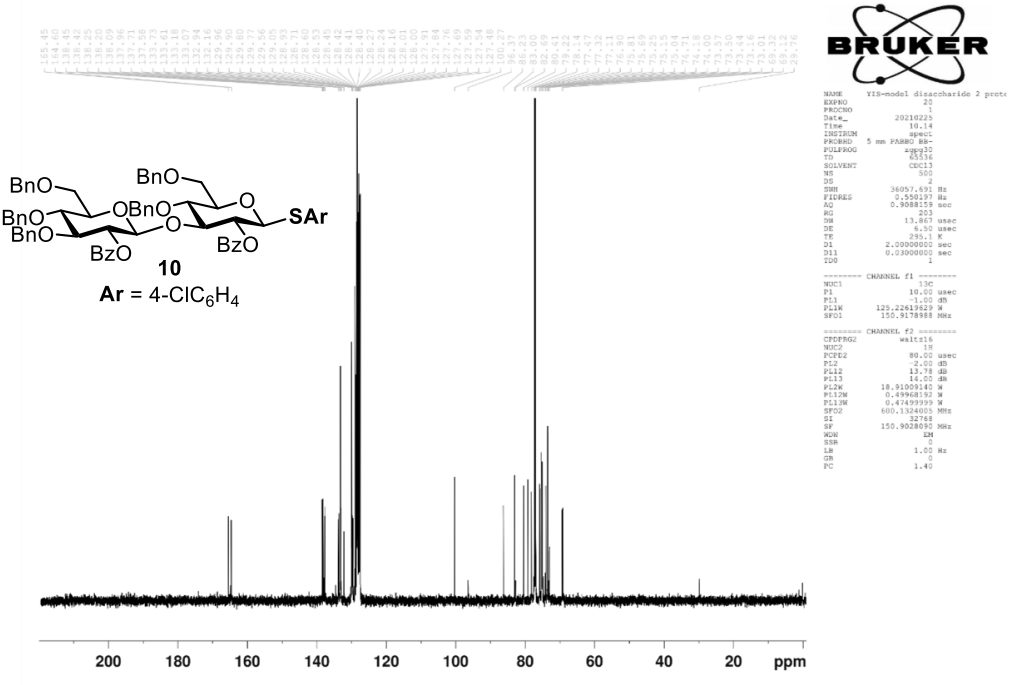
HMQC


BRUKER
TBDPSO
BnO
BnO
BnO
BnO
PivO
BzO
SAr
5
Ar = 4-ClC6H4
ppm

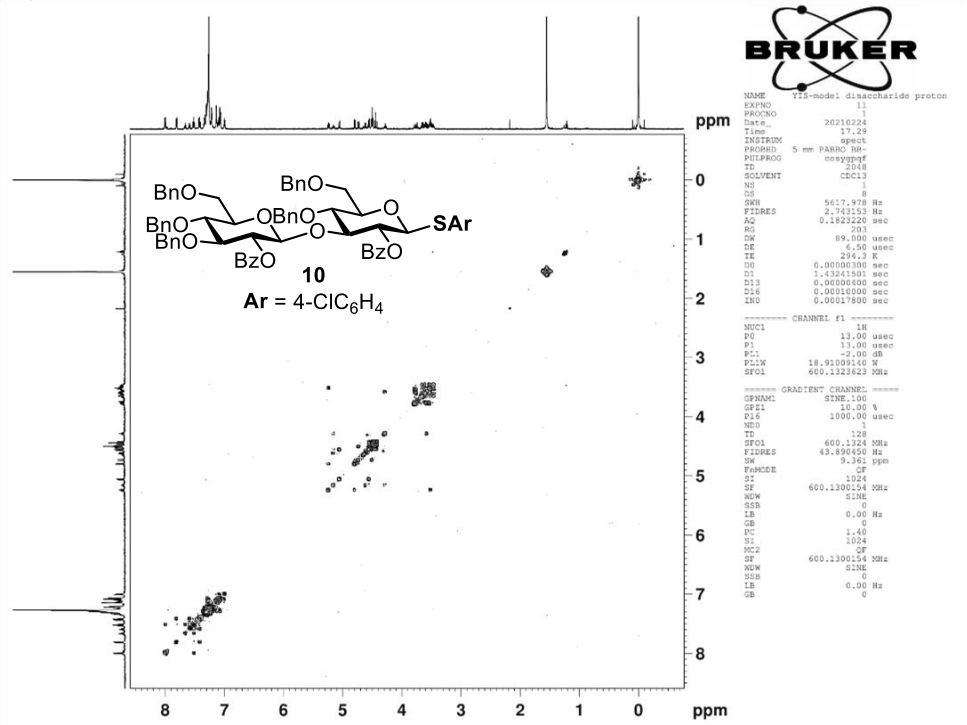
^{1}H NMR



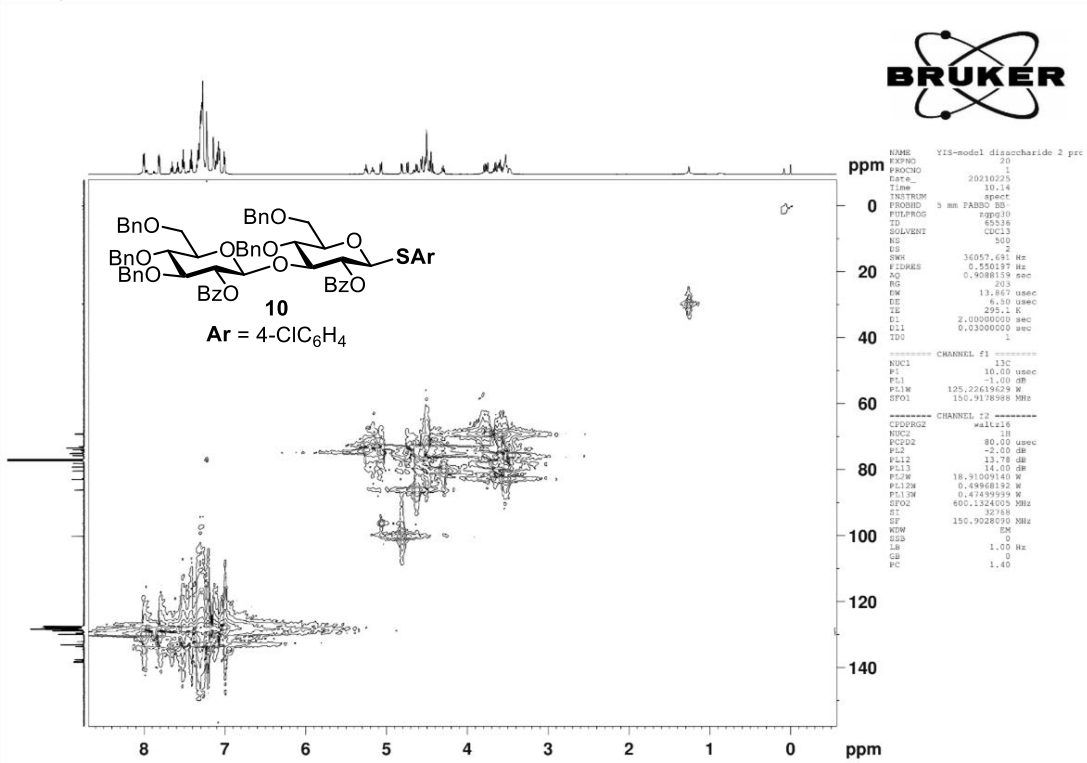
^{13}C NMR



H-H cosy

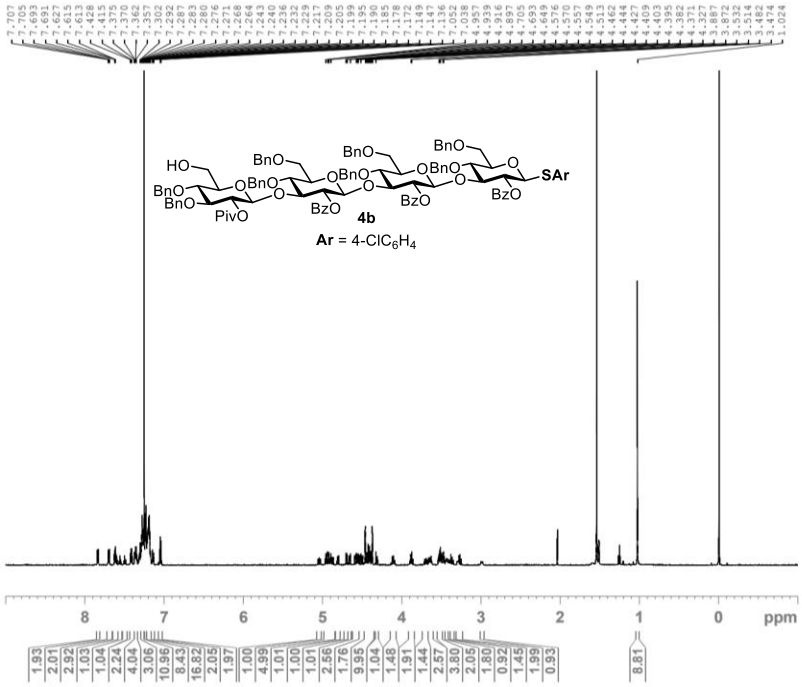

BRUKER
BnO
BnO
BnO
OBnO
O
BnO
O
SAr
BzO
BzO
10
Ar = 4-ClC6H4
ppm
8 7 6 5 4 3 2 1 0 ppm

HMQC


BRUKER
BnO
BnO
BnO
OBnO
O
BnO
O
SAr
BzO
BzO
10
Ar = 4-ClC6H4
ppm
0 20 40 60 80 100 120 140
8 7 6 5 4 3 2 1 0 ppm

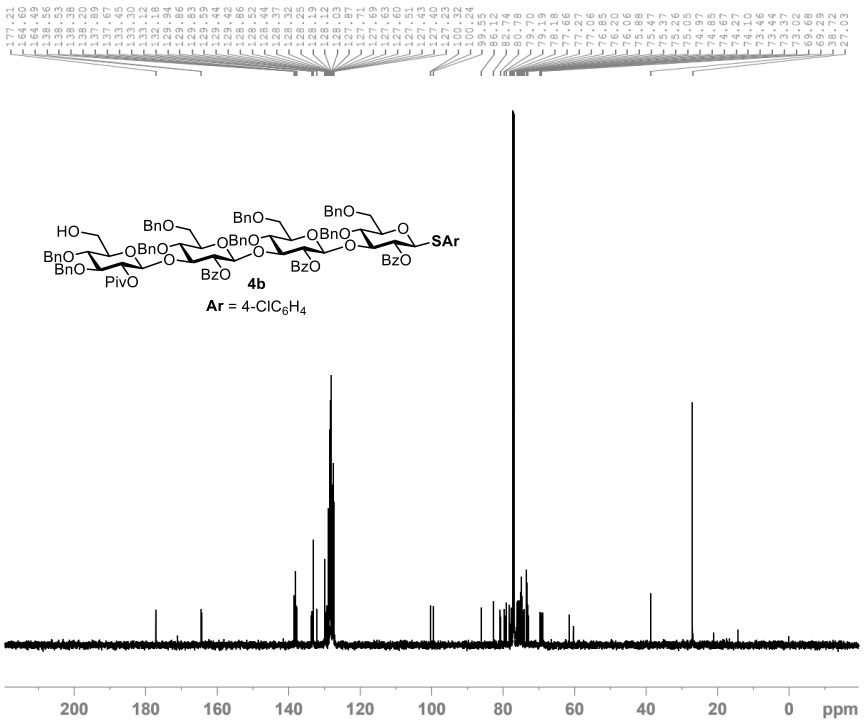
^{1}H, ^{13}C NMR, H-H COSY and HMQC spectra of tetrasaccharide building block

^{1}H NMR



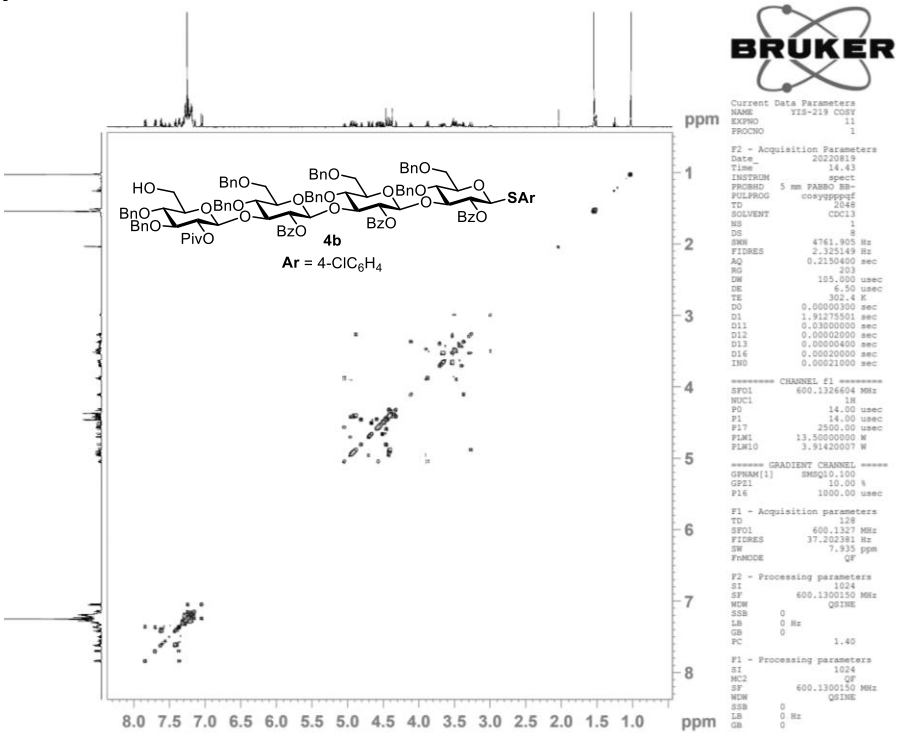

```
Current Data Parameters
NAME        YIS-219 COSY
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220819
Time_              14.43
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES         0.188225 Hz
AQ             2.6563926 sec
RG                   203
DW                40.533 usec
DE                 6.50 usec
TE                302.4 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          600.1337060 MHz
NUC1                  1H
P1                 14.00 usec
PLW1          13.50000000 W

F2 - Processing parameters
SI                 32768
SF            600.1300184 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

^{13}C NMR

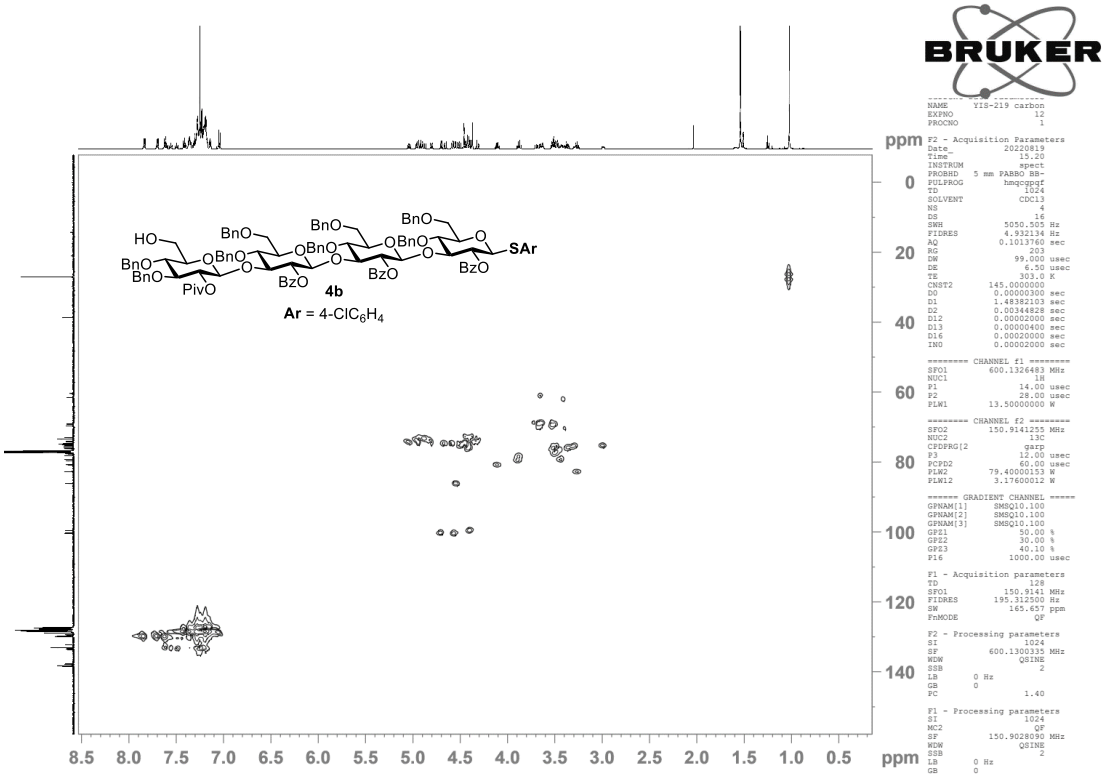



```
Current Data Parameters
NAME      YIS-219 carbon
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220819
Time_              15.17
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   500
DS                     2
SWH            36057.691 Hz
FIDRES         0.550197 Hz
AQ             0.9087659 sec
RG                   203
DW                13.867 usec
DE                 6.50 usec
TE                303.3 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          150.9178988 MHz
NUC1                  13C
P1                 12.00 usec
PLW1          79.40000153 W

======== CHANNEL f2 ========
SFO2          600.1324005 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2              70.00 usec
PLW2          13.50000000 W
PLW12          0.54000002 W
PLW13          0.26460001 W

F2 - Processing parameters
SI                 32768
SF            150.9028090 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

H-H cosy

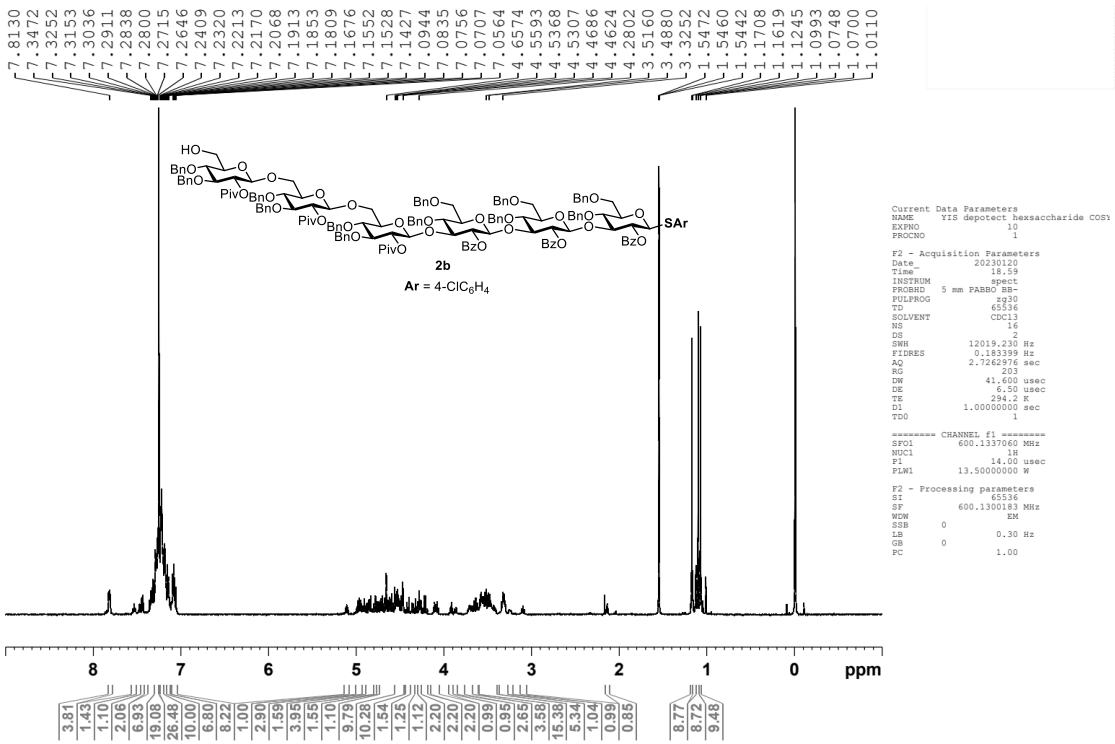

BRUKER
HO
BnO
PivO
BzO
SAr
4b
Ar = 4-ClC6H4
ppm
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
1 2 3 4 5 6 7 8

HMQC

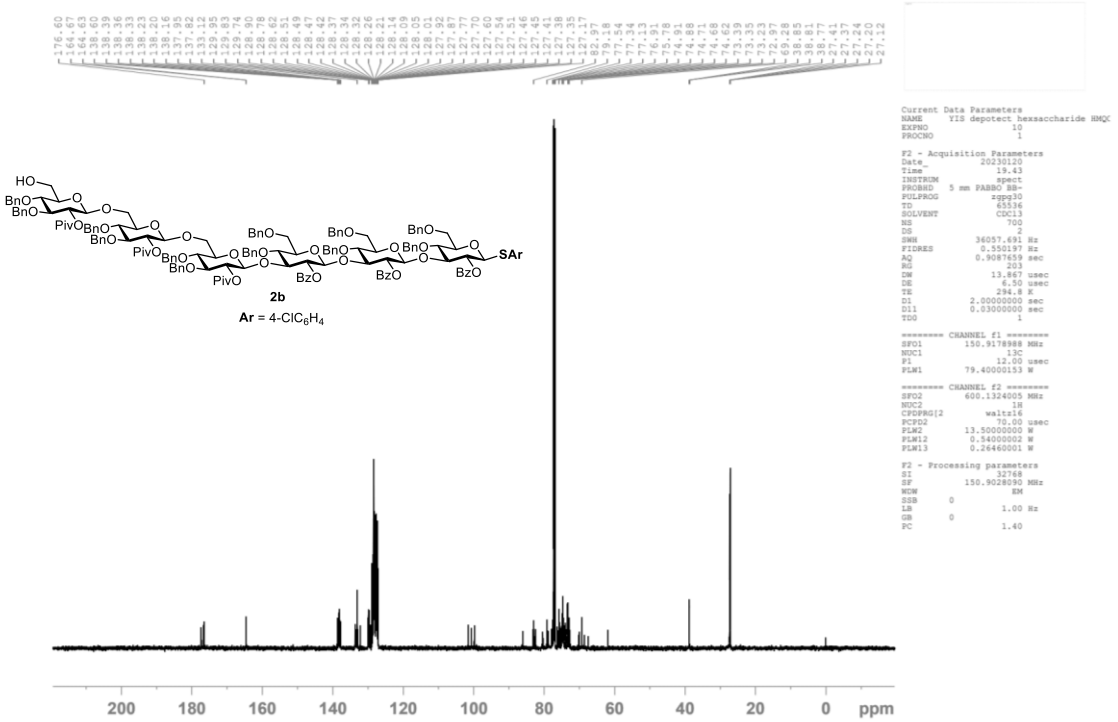

BRUKER
HO
BnO
PivO
BzO
SAr
4b
Ar = 4-ClC6H4
ppm
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
0 20 40 60 80 100 120 140

^{1}H, ^{13}C NMR, H-H COSY and HMQC spectra of semi-circular hexasaccharide

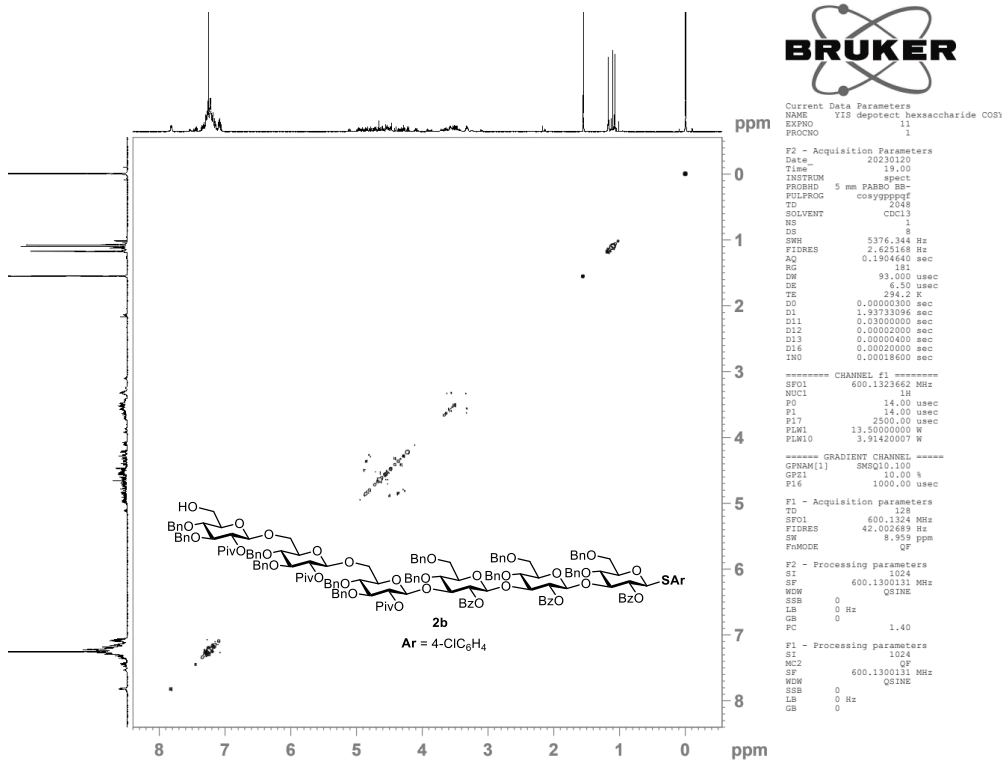
^{1}H NMR



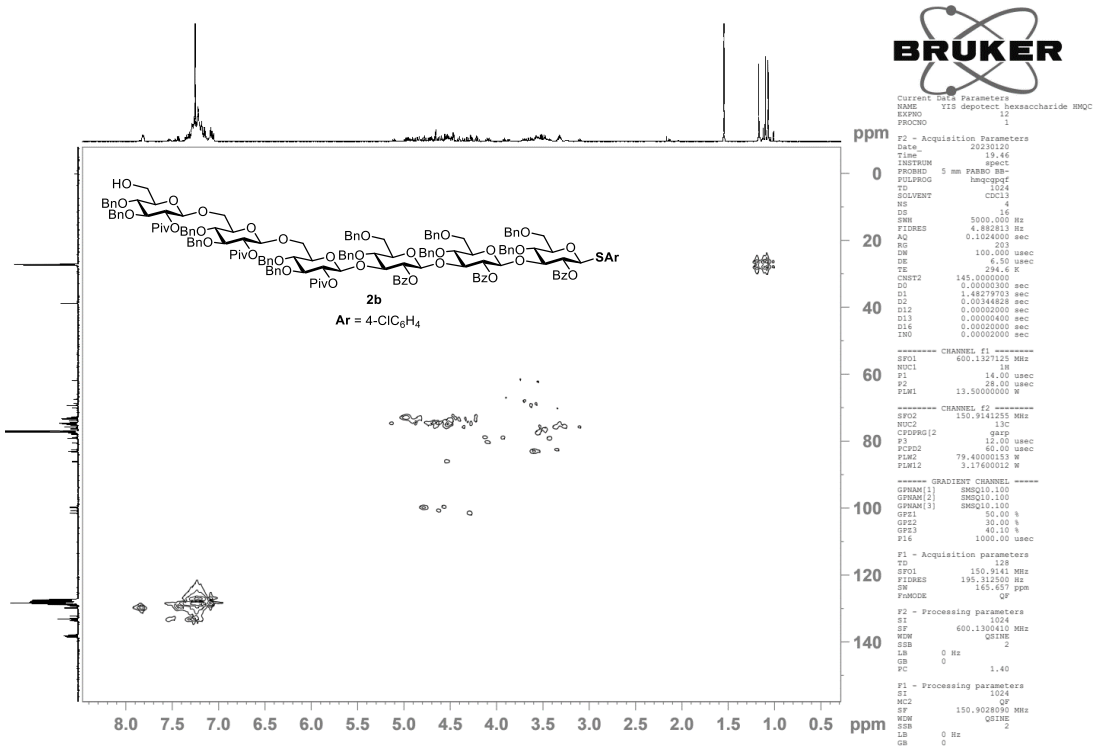
^{13}C NMR



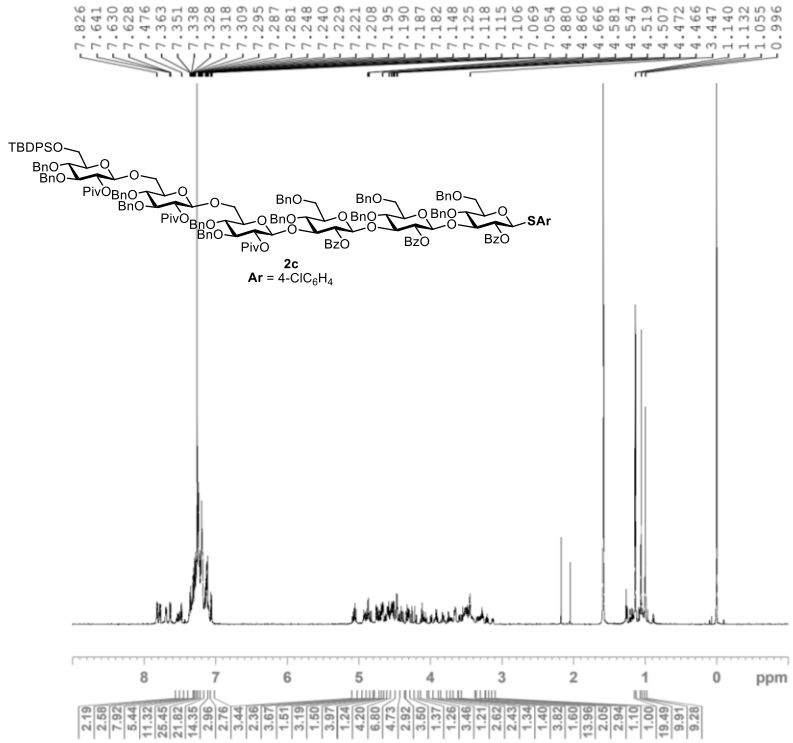
H-H cosy


BRUKER
Current Data Parameters
NAME YIS depotect hexsaccharide COSY
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20230120
Time 19.00
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpppqf
TD 2048
SOLVENT CDCl3
NS 1
DS 8
SWH 5376.344 Hz
FIDRES 2.625168 Hz
AQ 0.1904640 sec
RG 181
DW 93.000 usec
DE 6.50 usec
TE 294.2 K
D0 0.00000300 sec
D1 1.93733096 sec
D11 0.03000000 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00018600 sec
======== CHANNEL f1 ========
SFO1 600.1323662 MHz
NUC1 1H
P0 14.00 usec
P1 14.00 usec
P17 2500.00 usec
PLW1 13.50000000 W
PLW10 3.91420007 W
====== GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 128
SFO1 600.1324 MHz
FIDRES 42.002689 Hz
SW 8.959 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 600.1300131 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 600.1300131 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0
ppm
0
1
2
3
4
5
6
7
8
HO
BnO
PivO
BzO
SAr
2b
Ar = 4-ClC6H4

HMQC


BRUKER
Current Data Parameters
NAME YIS depotect hexsaccharide HMQC
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20230120
Time 19.46
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG hmqcgpqf
TD 1024
SOLVENT CDCl3
NS 4
DS 16
SWH 5000.000 Hz
FIDRES 4.882813 Hz
AQ 0.1024000 sec
RG 203
DW 100.000 usec
DE 6.50 usec
TE 294.6 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.48279703 sec
D2 0.00344828 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00002000 sec
======== CHANNEL f1 ========
SFO1 600.1327125 MHz
NUC1 1H
P1 14.00 usec
P2 28.00 usec
PLW1 13.50000000 W
======== CHANNEL f2 ========
SFO2 150.9141255 MHz
NUC2 13C
CPDPRG[2 garp
P3 12.00 usec
PCPD2 60.00 usec
PLW2 79.40000153 W
PLW12 3.17600012 W
====== GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPNAM[2] SMSQ10.100
GPNAM[3] SMSQ10.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 128
SFO1 150.9141 MHz
FIDRES 195.312500 Hz
SW 165.657 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 600.1300410 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 150.9028090 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
ppm
0
20
40
60
80
100
120
140
HO
BnO
PivO
BzO
SAr
2b
Ar = 4-ClC6H4

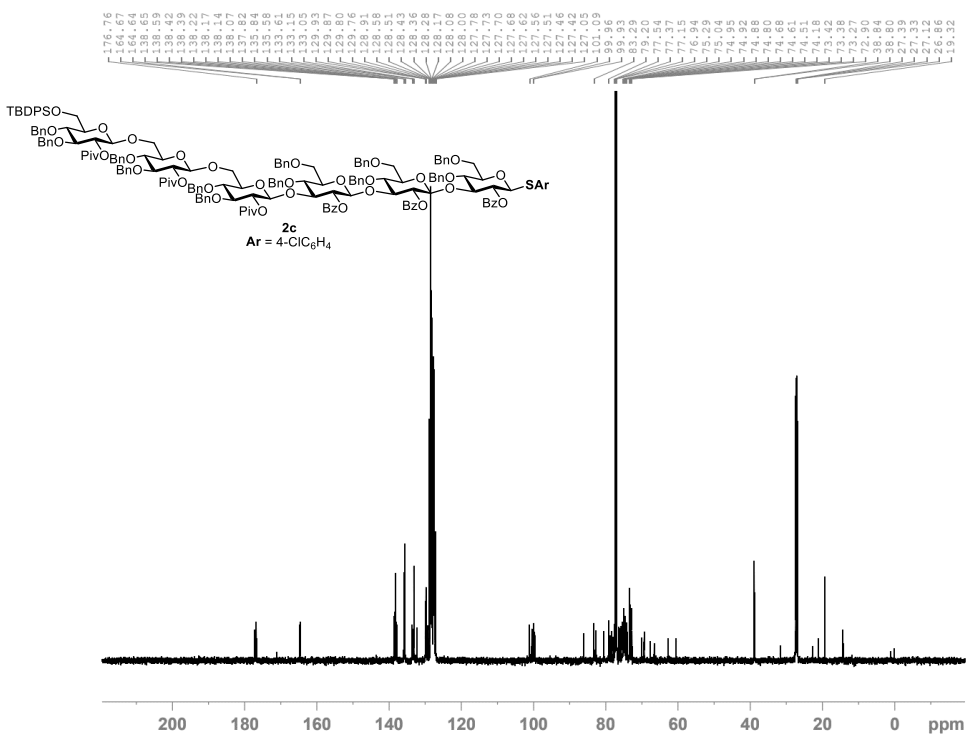
^{1}H NMR



BRUKER

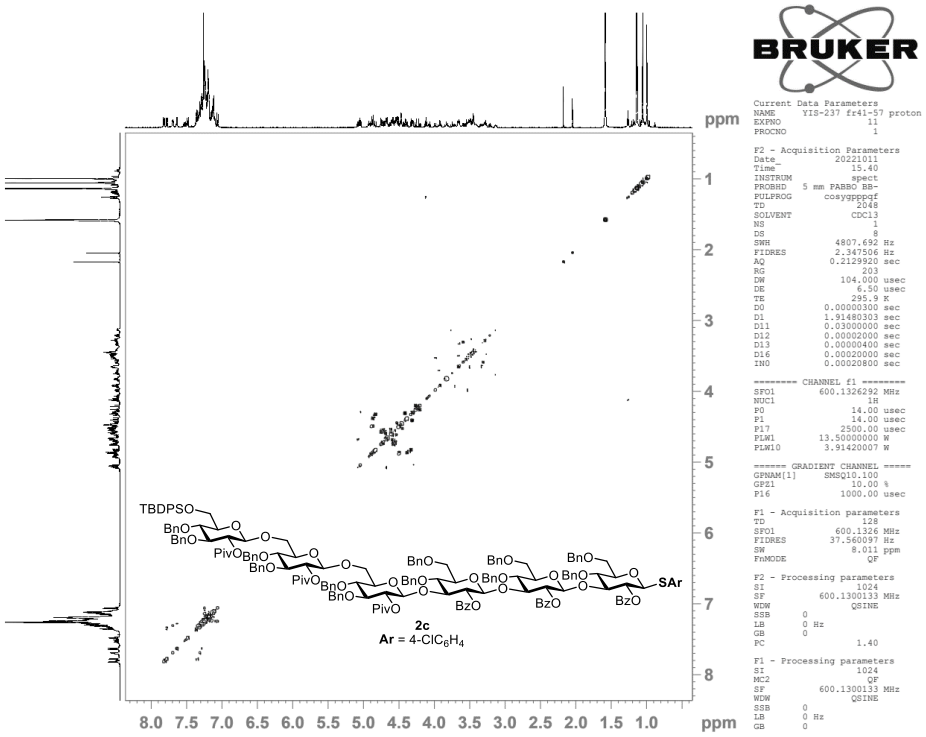
```
Current Data Parameters
NAME      YIS-237 fr41-57 proton
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20221011
Time               15.40
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           12019.230 Hz
FIDRES         0.183399 Hz
AQ             2.7262976 sec
RG                  203
DW               41.600 usec
DE                6.50 usec
TE               295.9 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         600.1337060 MHz
NUC1                 1H
P1                14.00 usec
PLW1         13.50000000 W

F2 - Processing parameters
SI                 65536
SF           600.1300133 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

^{13}C NMR




```
Current Data Parameters
NAME      YIS-237 fr41-57 carbon
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20221011
Time               16.14
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  500
DS                    2
SWH           36057.691 Hz
FIDRES         0.550197 Hz
AQ             0.9087659 sec
RG                  203
DW               13.867 usec
DE                6.50 usec
TE               296.8 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        150.9178988 MHz
NUC1                13C
P1               12.00 usec
PLW1         79.40000153 W

======== CHANNEL f2 ========
SFO2         600.1324005 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2              70.00 usec
PLW2         13.50000000 W
PLW12         0.54000002 W
PLW13         0.26460001 W

F2 - Processing parameters
SI                 32768
SF           150.9028090 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

H-H cosy



BRUKER

Current Data Parameters
NAME YIS-237 fr41-57 proton
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
Date_ 20221011
Time 15.40
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpppqf
TD 2048
SOLVENT CDCl3
NS 1
DS 8
SWH 4807.692 Hz
FIDRES 2.347506 Hz
AQ 0.21299920 sec
RG 203
DW 104.000 usec
DE 6.50 usec
TE 295.9 K
D0 0.00000300 sec
D1 1.91480303 sec
D11 0.03000000 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00020800 sec

======== CHANNEL f1 ========
SFO1 600.1326292 MHz
NUC1 1H
P0 14.00 usec
P1 14.00 usec
P17 2500.00 usec
PLW1 13.50000000 W
PLW10 3.91420007 W

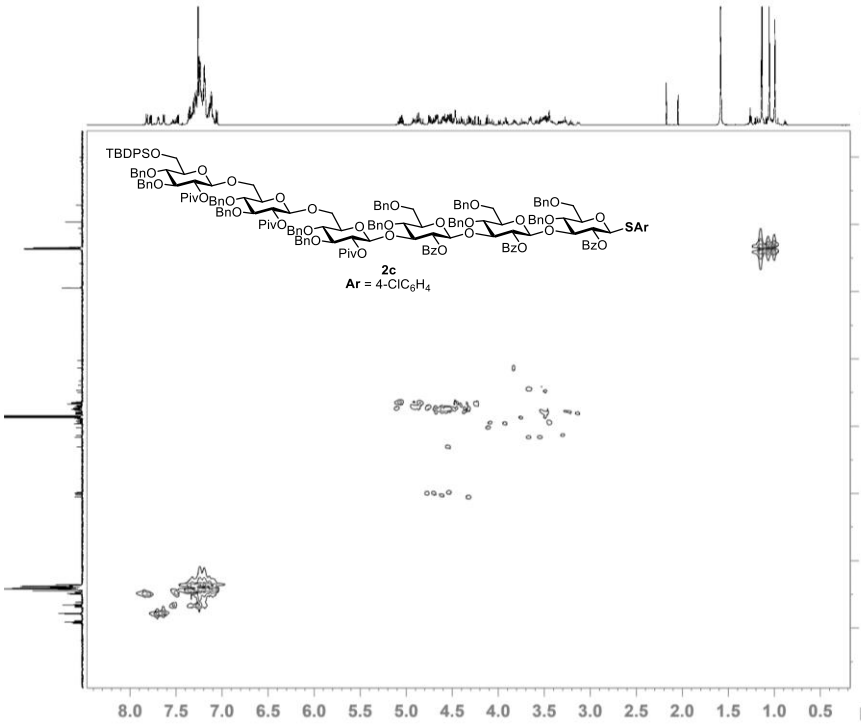
====== GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 128
SFO1 600.1326 MHz
FIDRES 37.560097 Hz
SW 8.011 ppm
FnMODE QF

F2 - Processing parameters
SI 1024
SF 600.1300133 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 1024
MC2 QF
SF 600.1300133 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0

HMQC



BRUKER

Current Data Parameters
NAME YIS-237 fr41-57 carbon
EXPNO 12
PROCNO 1

F2 - Acquisition Parameters
Date_ 20221011
Time 16.16
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG hmqcgpqf
TD 1024
SOLVENT CDCl3
NS 4
DS 16
SWH 5050.505 Hz
FIDRES 4.932134 Hz
AQ 0.1013760 sec
RG 203
DW 99.000 usec
DE 6.50 usec
TE 294.4 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.48382103 sec
D2 0.00344828 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00002000 sec

======== CHANNEL f1 ========
SFO1 600.1326828 MHz
NUC1 1H
P1 14.00 usec
P2 28.00 usec
PLW1 13.50000000 W

======== CHANNEL f2 ========
SFO2 150.9141255 MHz
NUC2 13C
CPDPRG[2 garp
P3 12.00 usec
PCPD2 60.00 usec
PLW2 79.40000153 W
PLW12 3.17600012 W

====== GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPNAM[2] SMSQ10.100
GPNAM[3] SMSQ10.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec

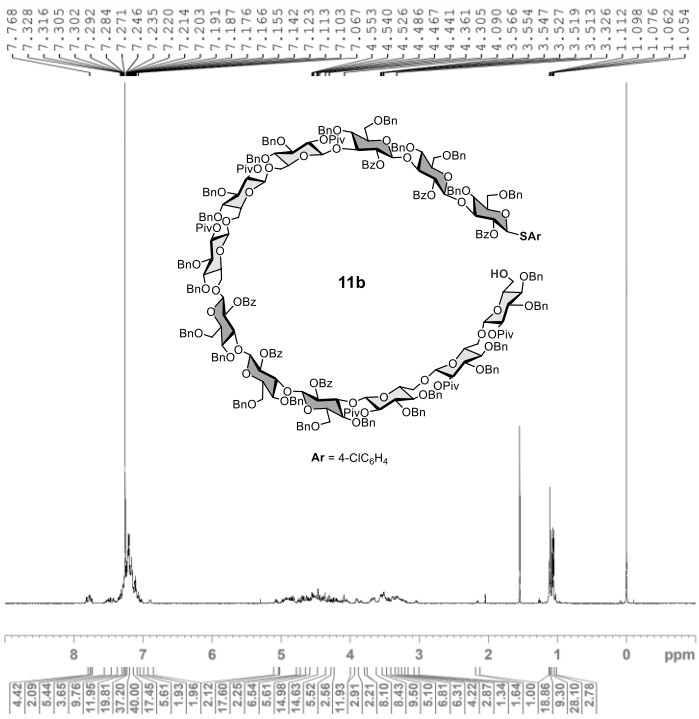
F1 - Acquisition parameters
TD 128
SFO1 150.9141 MHz
FIDRES 195.312500 Hz
SW 165.657 ppm
FnMODE QF

F2 - Processing parameters
SI 1024
SF 600.1300520 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 1024
MC2 QF
SF 150.9028090 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0

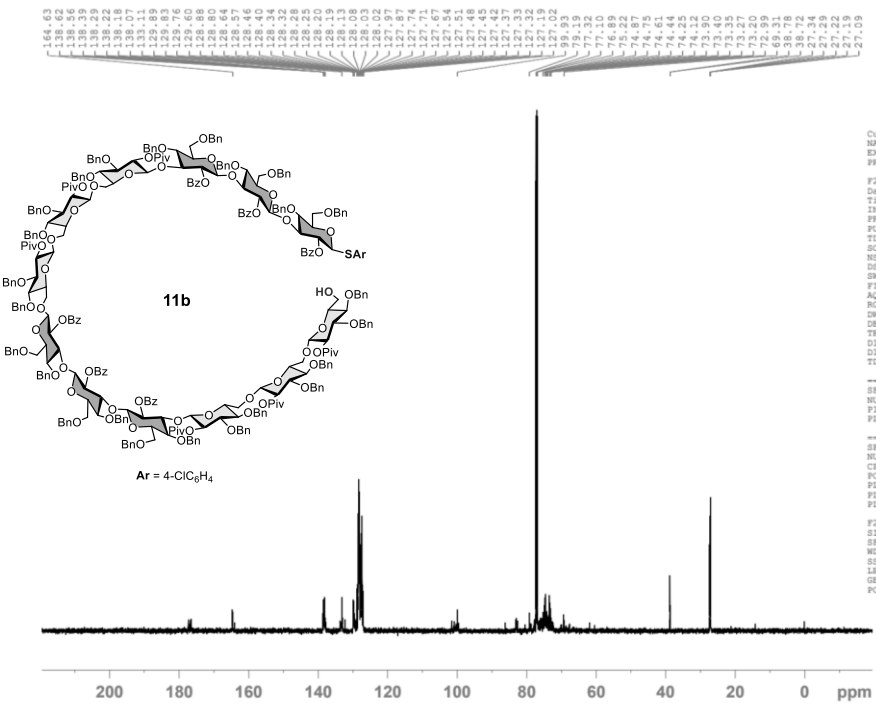
^{1}H, ^{13}C NMR, H-H COSY and HMQC spectra of linear and cyclic dodecasaccharides

^{1}H NMR



```
Current Data Parameters
NAME      YIS-281 fr33-48 proton, cosy
EXPNO             10
PROCNO             1

F2 - Acquisition Parameters
Date_         20230126
Time              12.01
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           12019.230 Hz
FIDRES        0.183399 Hz
AQ            2.7262976 sec
RG                 203
DW               41.600 usec
DE                6.50 usec
TE               297.1 K
D1            1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        600.1337060 MHz
NUC1               1H
P1               14.00 usec
PLW1        13.50000000 W

F2 - Processing parameters
SI                65536
SF          600.1300142 MHz
WDW                EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

^{13}C NMR




```
Current Data Parameters
NAME      YIS-281 fr33-48 carbon HMQC
EXPNO             10
PROCNO             1

F2 - Acquisition Parameters
Date_         20230126
Time              12.45
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
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SOLVENT          CDCl3
NS                 700
DS                   2
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FIDRES        0.550197 Hz
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RG                 203
DW               13.867 usec
DE                6.50 usec
TE               297.9 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                  1

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NUC1               13C
P1               12.00 usec
PLW1        79.40000153 W

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NUC2               1H
CPDPRG[2        waltz16
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PLW13        0.26460001 W

F2 - Processing parameters
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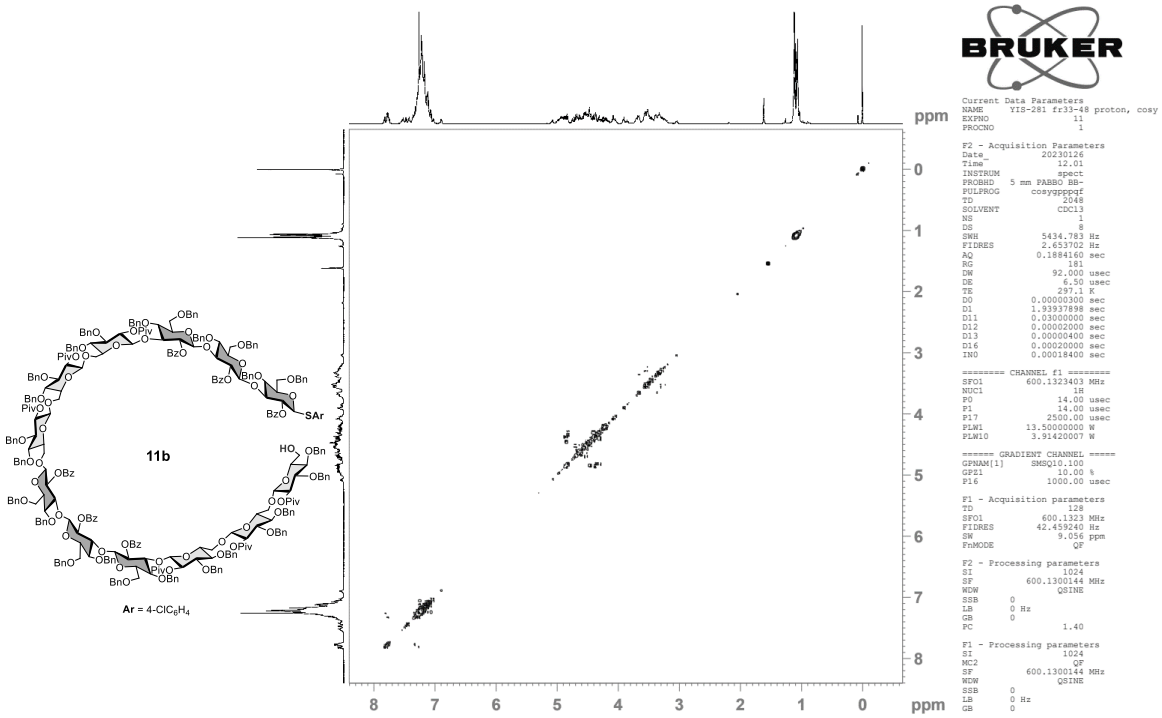
H-H cosy

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PROCNO                 1

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TD                 2048
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DS                    8
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TE                297.1 K
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D11            0.03000000 sec
D12            0.00002000 sec
D13            0.00000400 sec
D16            0.00020000 sec
IN0            0.00018400 sec

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NUC1               1H
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P1                14.00 usec
P17             2500.00 usec
PLW1         13.50000000 W
PLW10         3.91420007 W

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P16              1000.00 usec

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FIDRES       42.459240 Hz
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FnMODE              QF

F2 - Processing parameters
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SSB                0
LB                 0 Hz
GB                 0
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F1 - Processing parameters
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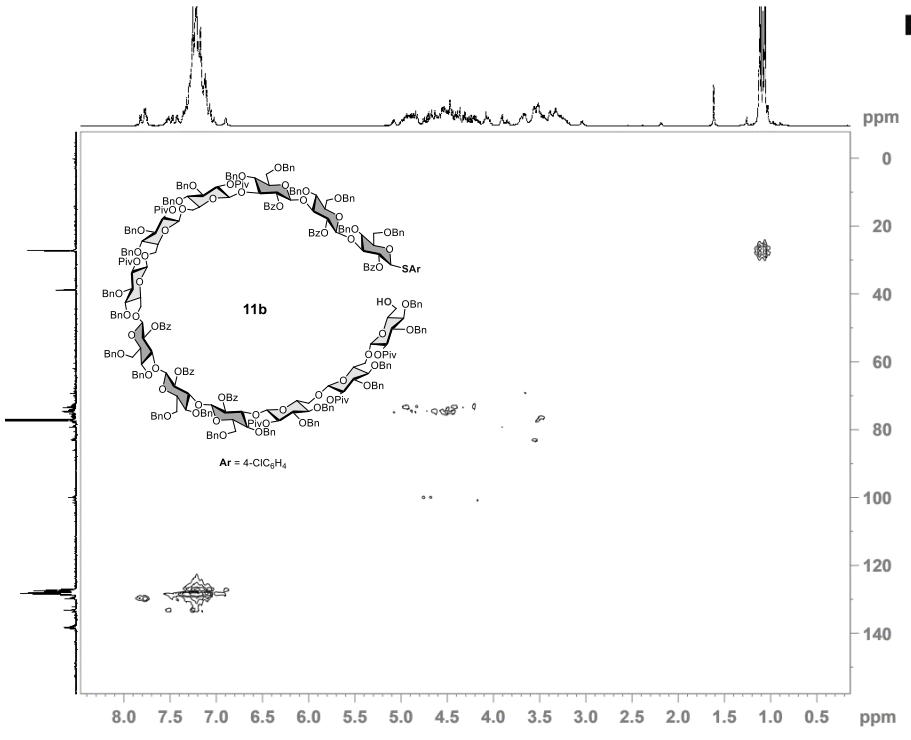
HMQC

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PROCNO                 1

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SOLVENT            CDCl3
NS                    4
DS                   16
SWH             5000.000 Hz
FIDRES          4.882813 Hz
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DW                100.000 usec
DE                 6.50 usec
TE                297.7 K
CNST2          145.0000000
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D1             1.48279703 sec
D2             0.00344828 sec
D12            0.00002000 sec
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D16            0.00020000 sec
IN0            0.00002000 sec

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SFO1         600.1326225 MHz
NUC1               1H
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PLW1         13.50000000 W

======== CHANNEL f2 ========
SFO2         150.9141255 MHz
NUC2               13C
CPDPRG[2           garp
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PCPD2             60.00 usec
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PLW12         3.17600012 W

====== GRADIENT CHANNEL =====
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GPNAM[2]       SMSQ10.100
GPNAM[3]       SMSQ10.100
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GPZ2               30.00 %
GPZ3               40.10 %
P16              1000.00 usec

F1 - Acquisition parameters
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SFO1          150.9141 MHz
FIDRES       195.312500 Hz
SW                165.657 ppm
FnMODE              QF

F2 - Processing parameters
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WDW                QSINE
SSB                2
LB                 0 Hz
GB                 0
PC                 1.40

F1 - Processing parameters
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SF          150.9028090 MHz
WDW                QSINE
SSB                2
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GB                 0
```
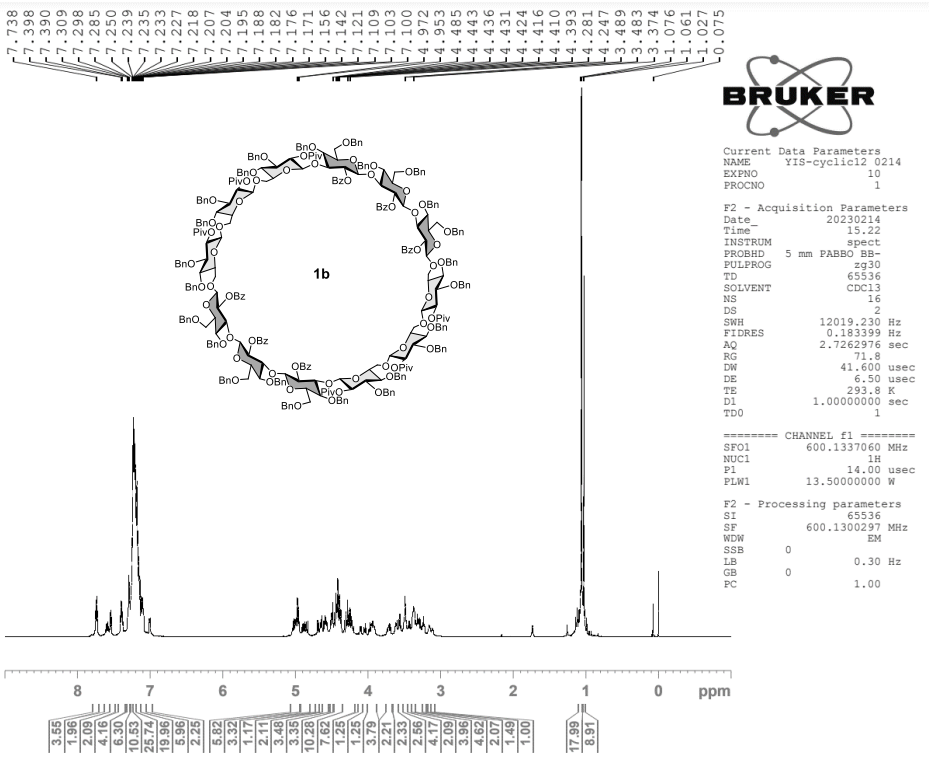

^{1}H NMR



BRUKER

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PROCNO                   1

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PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              12019.230 Hz
FIDRES            0.183399 Hz
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RG                     71.8
DW                  41.600 usec
DE                   6.50 usec
TE                  293.8 K
D1                1.00000000 sec
TD0                      1

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P1                   14.00 usec
PLW1            13.50000000 W

F2 - Processing parameters
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PC                    1.00
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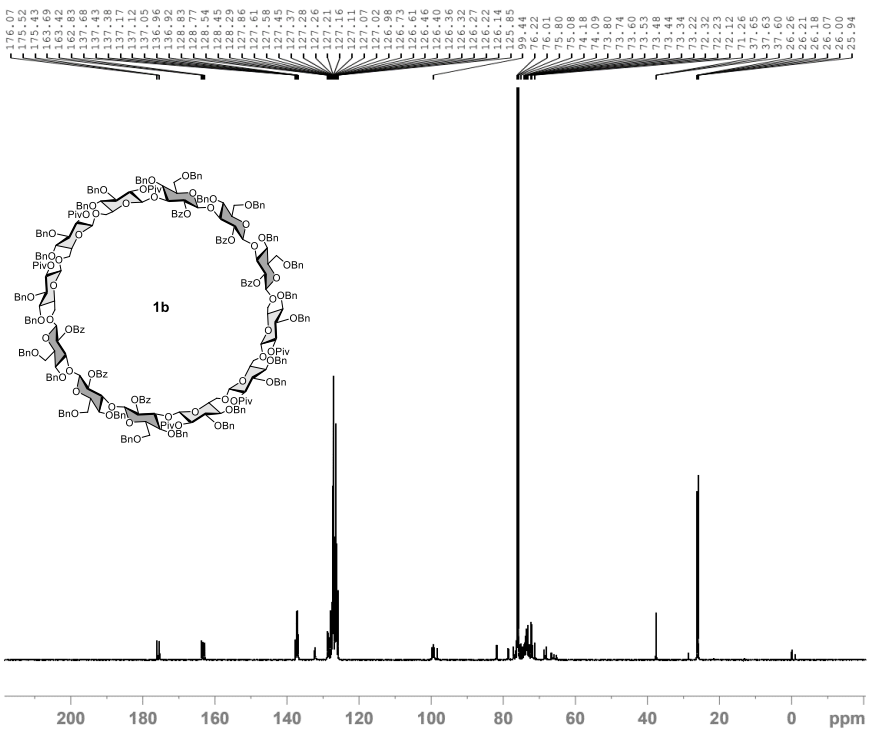
^{13}C NMR

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PROCNO                   1

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INSTRUM               spect
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PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                   17000
DS                       2
SWH              36057.691 Hz
FIDRES            0.550197 Hz
AQ                0.9087659 sec
RG                     203
DW                  13.867 usec
DE                   6.50 usec
TE                  295.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1            150.9178988 MHz
NUC1                   13C
P1                   12.00 usec
PLW1            79.40000153 W

======== CHANNEL f2 ========
SFO2            600.1324005 MHz
NUC2                    1H
CPDPRG[2             waltz16
PCPD2                70.00 usec
PLW2            13.50000000 W
PLW12            0.54000002 W
PLW13            0.26460001 W

F2 - Processing parameters
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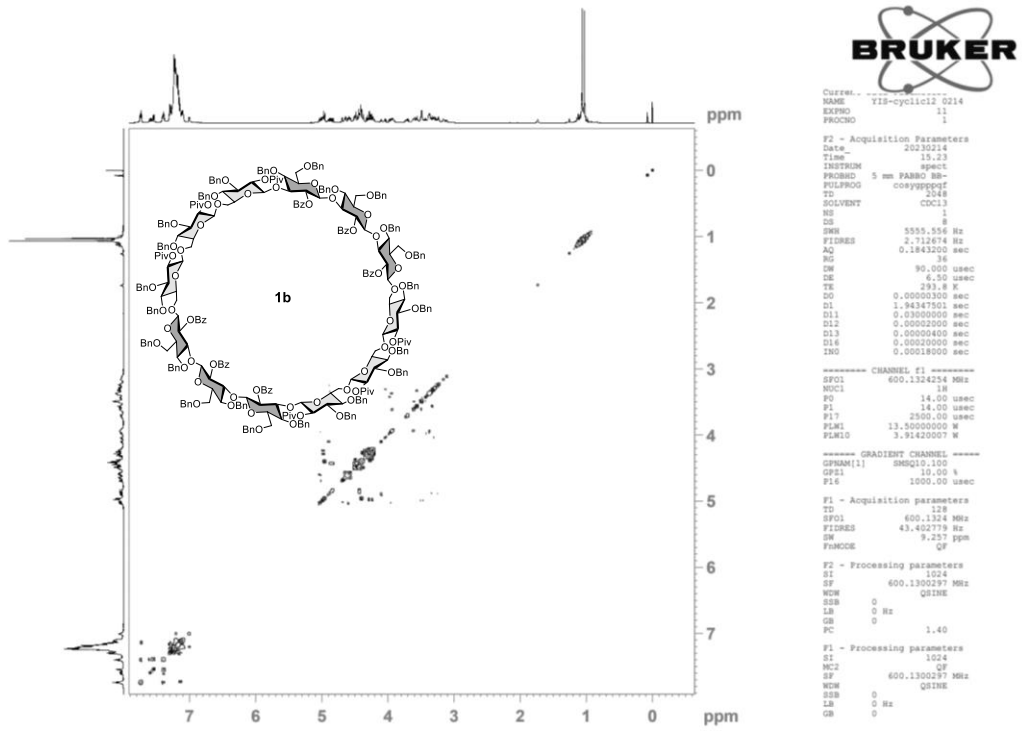
H-H cosy



BRUKER

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EXPNO 11
PROCNO 1

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Time 15.23
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpppqf
TD 2048
SOLVENT CDCl3
NS 1
DS 0
SWH 5555.556 Hz
FIDRES 2.712674 Hz
AQ 0.1843200 sec
RG 36
DW 90.000 usec
DE 6.50 usec
TE 293.8 K
D0 0.00000300 sec
D1 1.94347501 sec
D11 0.03000000 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00018000 sec

======== CHANNEL f1 ========
SFO1 600.1324254 MHz
NUC1 1H
P0 14.00 usec
P1 14.00 usec
P17 2500.00 usec
PLW1 13.50000000 W
PLW10 3.91420007 W

====== GRADIENT CHANNEL =====
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GPZ1 10.00 %
P16 1000.00 usec

F1 - Acquisition parameters
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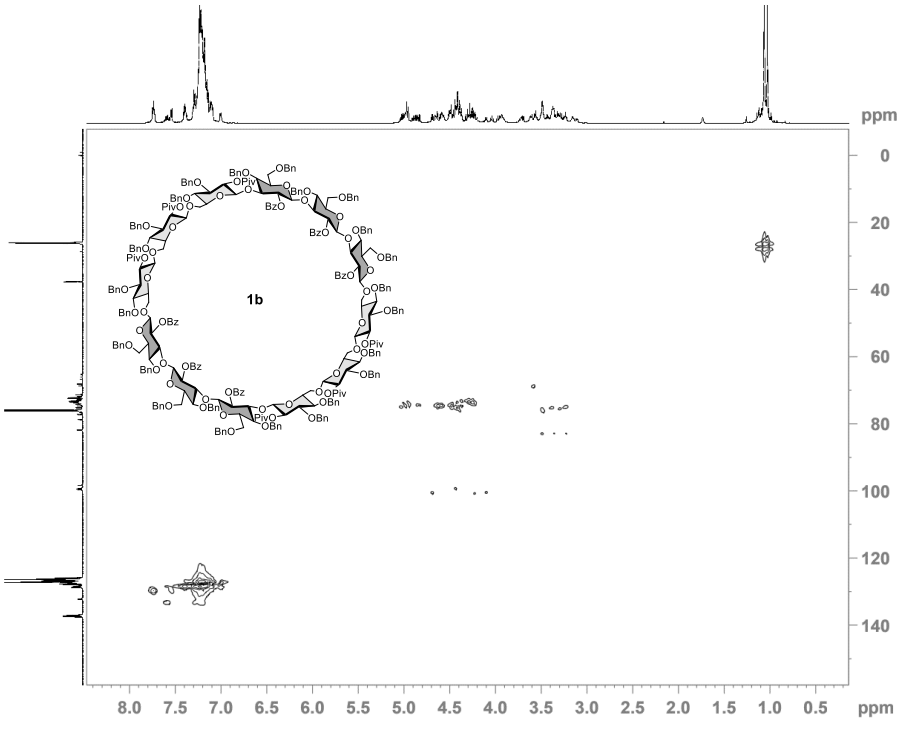
SFO1 600.1324 MHz
FIDRES 43.402779 Hz
SW 9.257 ppm
FnMODE QF

F2 - Processing parameters
SI 1024
SF 600.1300297 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 1024
MC2 QF
SF 600.1300297 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0

HMQC



BRUKER

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EXPNO 22
PROCNO 1

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INSTRUM spect
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PULPROG hmqcgpqf
TD 1024
SOLVENT CDCl3
NS 4
DS 16
SWH 5494.505 Hz
FIDRES 5.365728 Hz
AQ 0.0931840 sec
RG 203
DW 91.000 usec
DE 6.50 usec
TE 294.2 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.49201298 sec
D2 0.00344828 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00002000 sec

======== CHANNEL f1 ========
SFO1 600.1324043 MHz
NUC1 1H
P1 14.00 usec
P2 28.00 usec
PLW1 13.50000000 W

======== CHANNEL f2 ========
SFO2 150.9141255 MHz
NUC2 13C
CPDPRG[2 garp
P3 12.00 usec
PCPD2 60.00 usec
PLW2 79.40000153 W
PLW12 3.17600012 W

====== GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPNAM[2] SMSQ10.100
GPNAM[3] SMSQ10.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 128
SFO1 150.9141 MHz
FIDRES 195.312500 Hz
SW 165.657 ppm
FnMODE QF

F2 - Processing parameters
SI 1024
SF 600.1300298 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 1024
MC2 QF
SF 150.9028090 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0

Chapter 3.

Towards Rational Design of Oligosaccharide Building Blocks of Cyclic β-Glucans

Introduction

As described in chapter 2, protected cyclic dodecasaccharide **1** was successfully synthesized from semi-circular hexasaccharide **2a** (Figure 3-1). To explore the possibility of further improvement of the yield, we planned to synthesize the cyclic dodecasaccharide **1** from other hexasaccharide precursors **2b** and **2c** (Figure 3-2). Among potential precursors, semi-circular hexasaccharide **2c** was synthesized because it also has protecting-group free 6-OH as a reaction site and can be synthesized by automated electrochemical assembly of building blocks in hand.

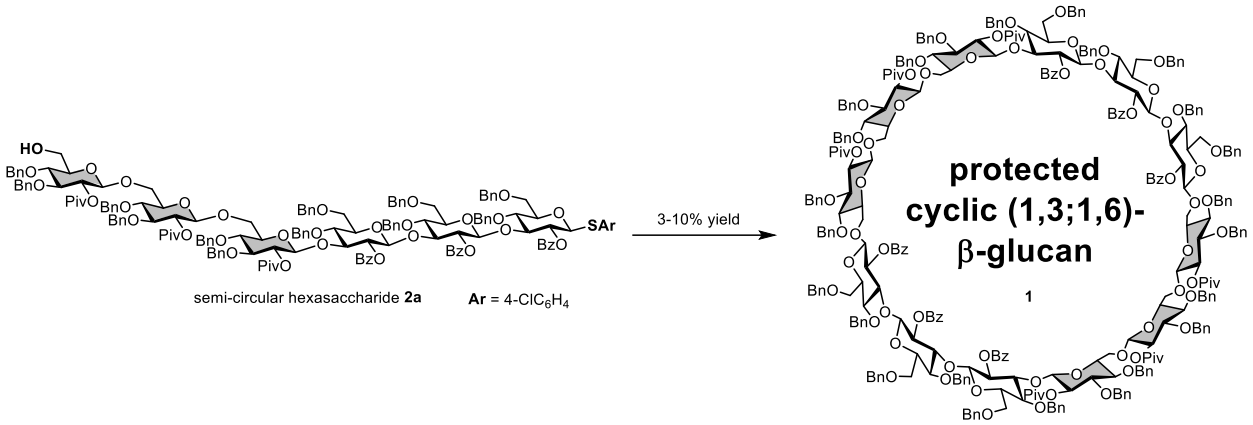


Figure 3-1. Dimerization-cyclization of semi-circular hexasaccharide precursor **2a**.

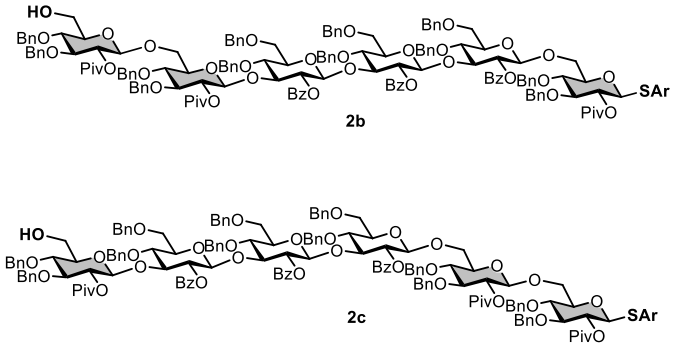
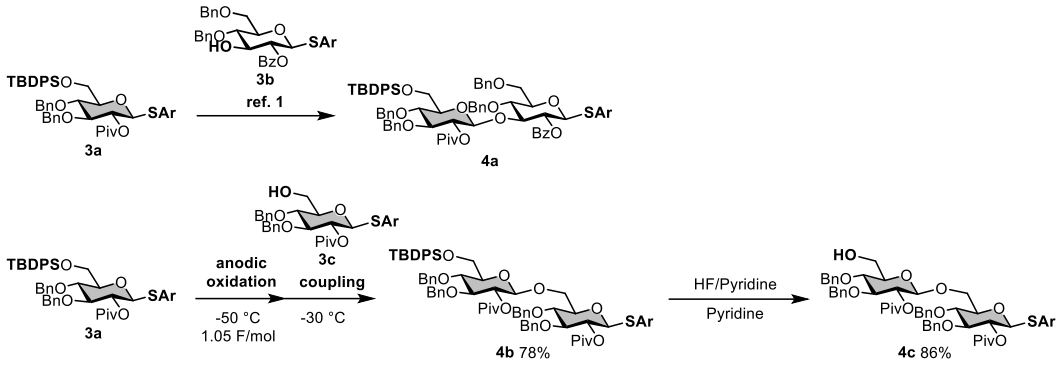


Figure 3-2. Potential hexasaccharide precursors of cyclic dodecasaccharide **1**.

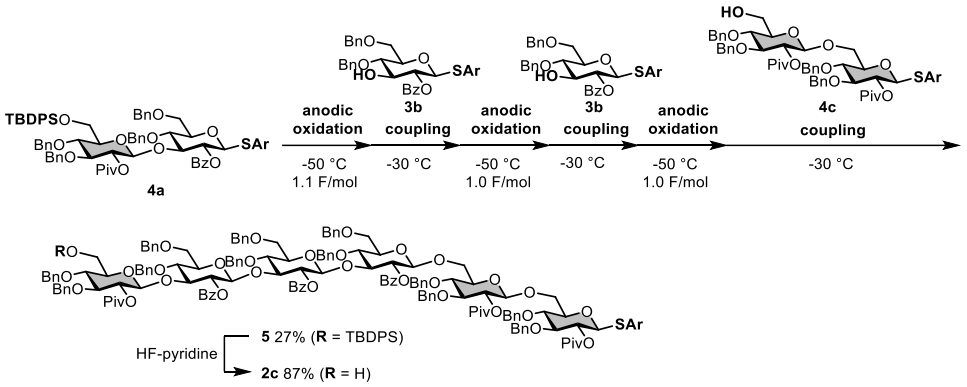
Results and Discussion

First, disaccharide building blocks **4a** and **4c** were synthesized (Scheme 3-1). Disaccharide **4a** and monosaccharides **3a-c** were prepared according to the reported procedures.[1] Glycosylation reaction of **3a** and **3c** and following deprotection of TBDPS group afforded disaccharide building block **4c**. Then, hexasaccharide **5** was synthesized by three steps of AEA using disaccharides **4a** and **4c** and two equivalents

of monosaccharide **3b**. Hexasaccharide **5** was converted to hexasaccharide precursor **2c** by deprotection of TBDPS group (Scheme 3-2).



Scheme 3-1. Synthesis of disaccharide building blocks **4a** and **4c**.



Scheme 3-2. Synthesis of semi-circular hexasaccharide precursor **2c**.

Contrary to our expectation, electrochemical oxidation of precursor **2c** afforded neither cyclic dodecasaccharide nor linear dodecasaccharide. Then we carefully checked by-products of the reaction and found formation of hydroxysugars of hexasaccharide **6** and pentasaccharide **7** (Figure 3-2). MALDI-TOF-MS showed two major molecular ion peaks $[M+K]^+$ which are derived from hydroxysugars **6** and **7** (Figure 3-3). Although hydroxysugars are typical by-products of glycosylation, the formation of shorter oligosaccharide **7** is rare. By comparison of the structures of precursors **2a** and **2c**, glycosidic linkage of the disaccharide unit of the reducing end was supposed to be a key factor for the side reactions. For better understanding of the relationship between the disaccharide structure and its reactivity, we planned to investigate using model disaccharides **4d-e** (Scheme 3-3). β-1,3-Disaccharide **4d** is a model compound of hexasaccharide **2a** and β-1,6-disaccharide **4e** is a model compound of hexasaccharide **2c**, respectively. Disaccharide **4d** was synthesized according to the reported procedure.[1] Disaccharide **4e** was synthesized by glycosylation reaction of monosaccharides **3c** and **3e**.

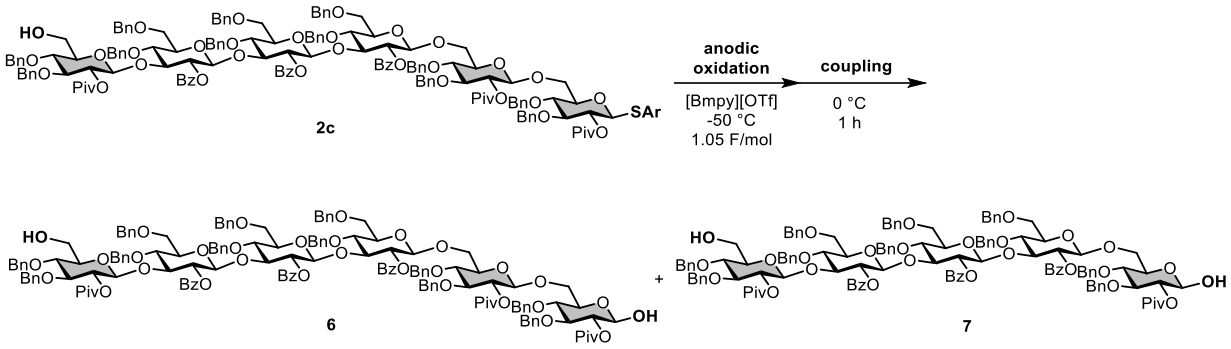


Figure 3-2. By-products of electrochemical oxidation of hexasaccharide **2c**.

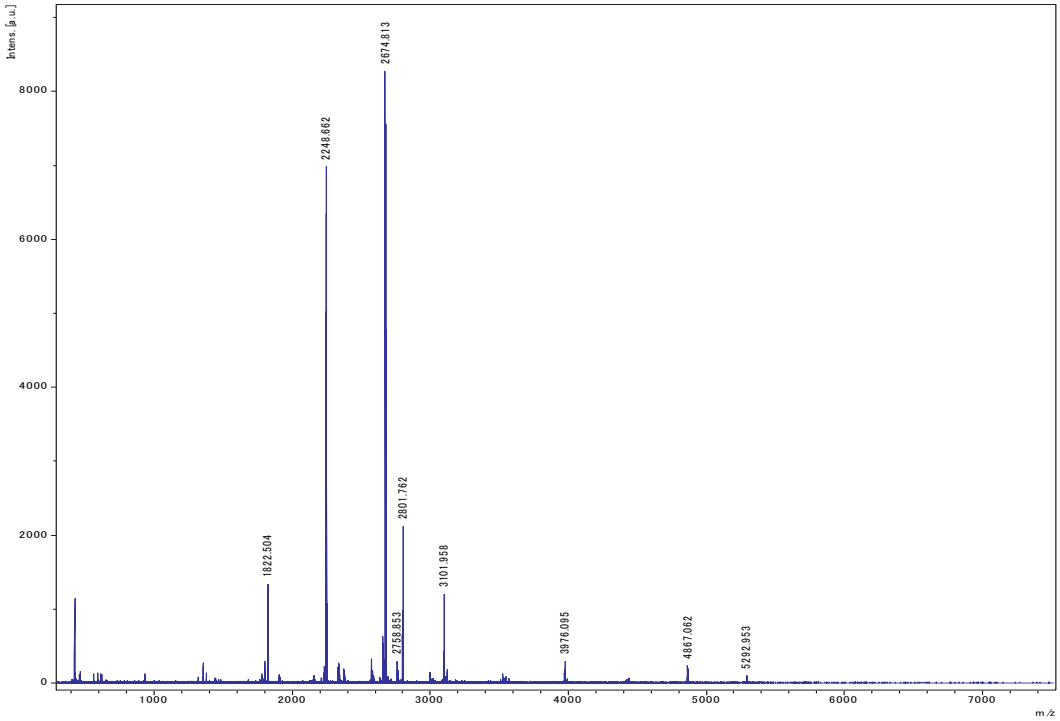
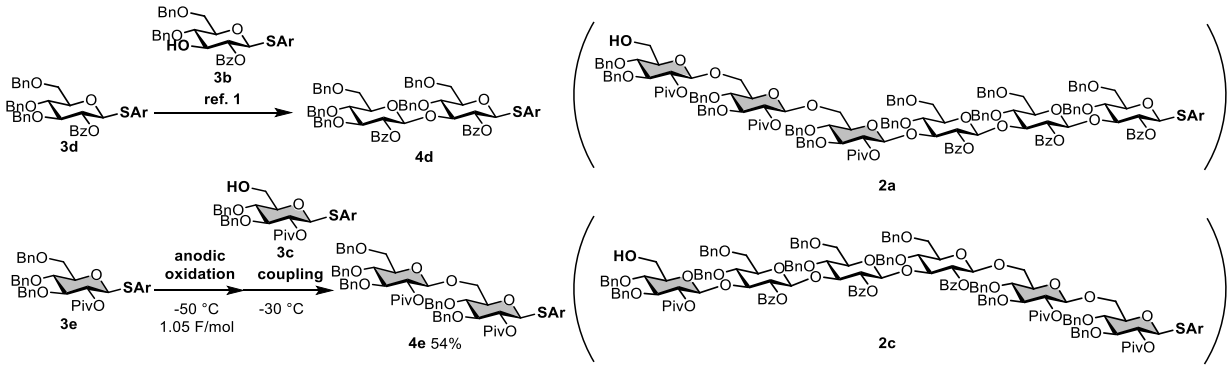


Figure 3-3. MALDI-TOF MS of crude products of electrochemical oxidation of **2c**.



Scheme 3-3. Synthesis of model disaccharides of the hexasaccharide precursors.

To explore information which can reveal the relationship, we focused on RRV (Relative Reactivity Value). RRV, developed by C.-H. Wong and co-workers, is an index of reactivity of glycosyl donors.[2] RRV is calculated based on ratio of reaction rate between a target thioglycoside and a standard thioglycoside (Figure 3-4). Competitive reaction of them with methanol gives relative reactivity of the target thioglycoside. Reactivities of multiple thioglycosides can be compared by comparing RRVs of them. We examined RRVs of model disaccharides **4d** and **4e**. RRV values of **4d** and **4e** are 108.9 and 57.7, respectively (Figure 3-5). Although RRV of **4d** was larger than that of **4e** as we expected, the difference was not enough to explain the relationship between the structure and the reactivity.

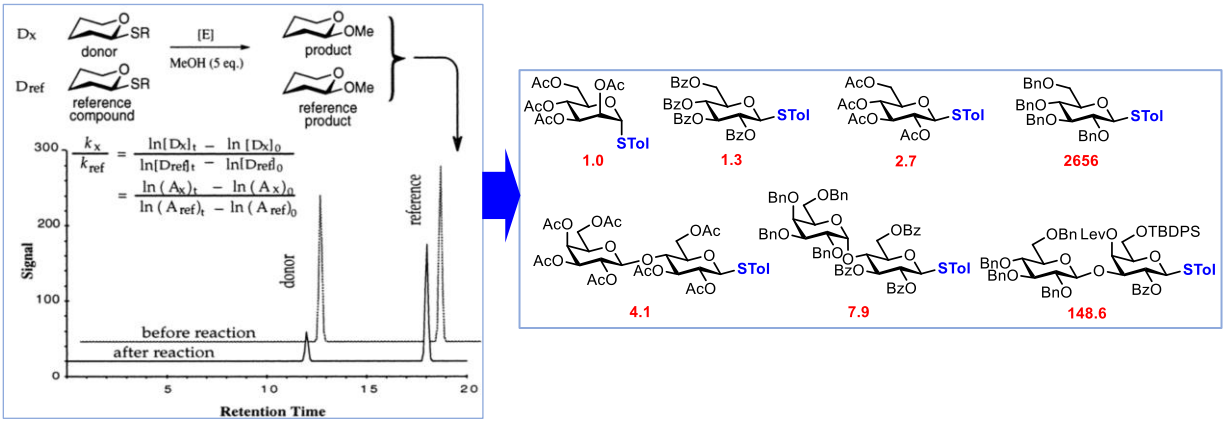


Figure 3-4. Principle of RRV.

Figure 3-5. RRV values of model disaccharides **4d** and **4e**.

We turned our attention to mechanism of formation of pentasaccharide hydroxysugar **7**. Because 1,6-anhydrosugar **10** was often observed as a by-product in glycosylation reaction, we presumed that leaving of 1,6-anhydrosugar **10** caused the fragmentation. Our plausible mechanism is depicted in Figure 3-6. Electrochemical oxidation of **2c** afford the corresponding dioxalenium ion **8**. The 6-position oxygen in the reducing end attacks the anomer carbon of **8**. The following attack of 2-pivaloyl oxygen on the anomer carbon leads to leaving of 1,6-anhydrosugar **10**. Thus-obtained pentasaccharide dioxalenium ion **11** was finally hydrolysed to form pentasaccharide hydroxysugar **7**. Although 1,6-anhydrosugar **10** was not isolated from the reaction mixture, we regarded it as a potential by-product.

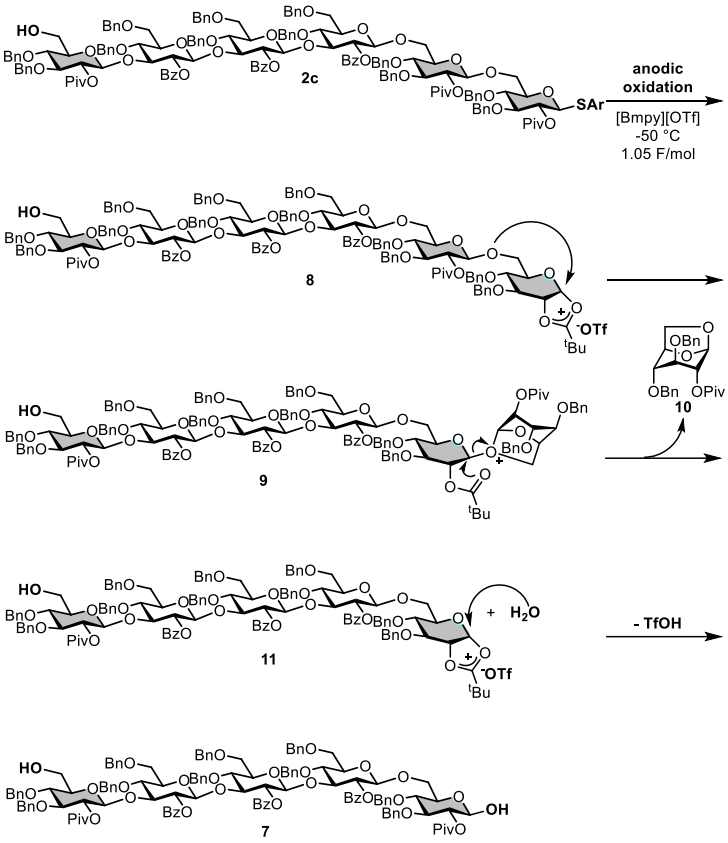


Figure 3-6. Plausible mechanism of the shortening reaction.

Next, β-1,6-disaccharide **4e** was electrochemically oxidized, followed by addition of methanol. Not only 1-methylglycoside disaccharide **4f** but also 1-methylglycoside monosaccharide **3f** was observed (Figure 3-7). In other words, the fragmentation also occurred in the reaction using disaccharide **4e**. We presumed that monosaccharide **3f** was produced by the mechanism shown in Figure 3-8 via leaving of 1,6-anhydrosugar **10**. Although 1,6-anhydrosugar **10** was not isolated, it was detected by mass analysis of the reaction mixture.

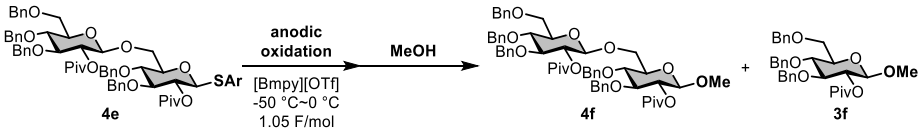


Figure 3-7. Model reaction using β-1,6-disaccharide **4e** as a glycosyl donor.

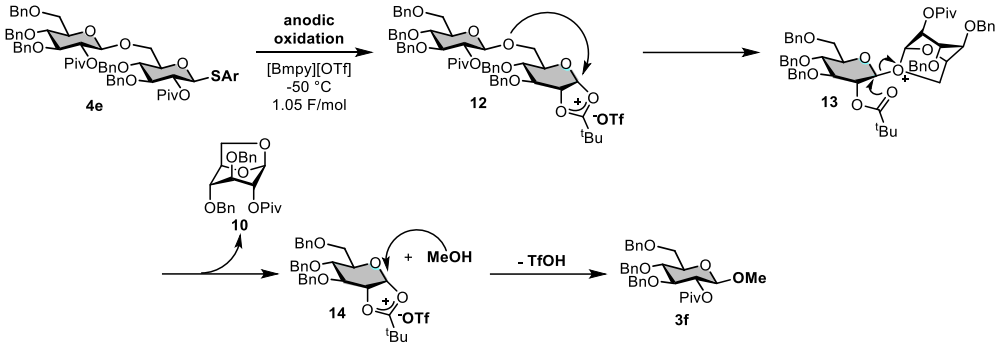


Figure 3-8. Plausible mechanism of formation of 1-methylglycoside monosaccharide **3f**.

We have focused on the reducing end of the hexasaccharide precursors. However, there is still room for investigation in other moieties. For example, glycosidic linkage of the disaccharide unit of the non-reducing end could affect the dimerization-cyclization and the side reactions. Deeper understanding of glycosylation of semi-circular hexasaccharides is expected to lead to rational design of oligosaccharide building blocks for the cyclic dodecasaccharide.

Conclusion

In the course of synthetic study of protected cyclic dodecasaccharide **1**, two hexasaccharide precursors **2a** and **2c** exhibited different reactivity. Dimerization-cyclization of hexasaccharide **2c** was failed. In this reaction, hydroxysugars of hexasaccharide **6** and pentasaccharide **7** were obtained. By comparison of the structures of the precursors, glycosidic linkage of the disaccharide unit of the reducing end was supposed to be a key factor for the side reactions. In the reaction using disaccharide **4e**, which is a model compound of hexasaccharide **2c**, fragmentation was also observed. Monosaccharide **3f** and 1,6-anhydrosugar **10** were detected by mass analysis. The result was consistent with our plausible mechanism. More detailed knowledge regarding structure-reactivity relationship is expected to lead to rational design of oligosaccharide building blocks in future.

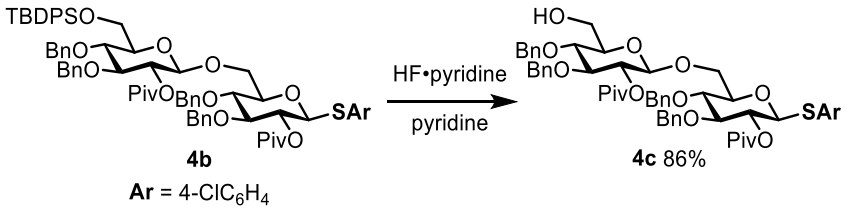
Experimental

1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE II 600 (^{1}H 600 MHz, ^{13}C 150 MHz). ESI-MS and MALDI-TOF-MS were recorded on Thermo Scientific Exactive spectrometer and Bruker ultrafleXtreme, respectively. Preparative recycling gel permeation chromatography (PR-GPC) was performed on Japan Analytical Industry LC-5060. Kanto silica gel 60 N (spherical, neutral, 63-210 μm) was used for silica gel column chromatography. The automated synthesizer is consisting of the commercially available instruments such as the chiller with a cooling bath (UCR-150, Techno Sigma), the power supply 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). Merck TLC (silica gel 60 F254) was used for TLC analysis. Monosaccharide **S1**, monosaccharides **3a-d** and disaccharides **4a**, **4b**, and **4d** were prepared according to the reported procedures.[1] Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification.

2. Preparation of building blocks

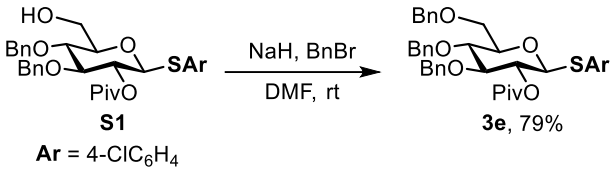
2-1. 4-Chlorophenyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**4c**)



Disaccharide **4b** (0.880 mmol, 1.09 g) was dissolved in pyridine (8.8 mL) and the solution was cooled to 0 °C. 70% HF•pyridine (0.70 mL) was added to the solution and the reaction mixture was stirred at 0 °C to room temperature for 5 h. Conversion of **4b** was confirmed by TLC (Hexane/EtOAc 7:3) and aqueous sodium bicarbonate solution was added to quench the reaction. The aqueous solution was extracted with chloroform and the combined organic layer was washed with aqueous sodium bicarbonate solution and 1 N aqueous hydrochloric acid. The reaction mixture was dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Thus-obtained crude product was purified by silica gel chromatography to obtain **4c** (0.761 mmol, 759 mg) in 86% yield. TLC (Hexane/EtOAc 4:1) R_f 0.21; $[\alpha]^{22}_{D}$ = 28.181 (*c* = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.41 (d, *J* = 8.4 Hz, 2 H), 7.34-7.27 (m, 16 H), 7.24 (d, *J* = 7.2 Hz, 4 H), 5.06 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 5.02 (*pseudo*-t, *J* = 9.6 Hz, 1 H), 4.81 (d, *J* = 9.6 Hz, 1 H), 4.77 (d, *J* = 10.4 Hz, 2 H), 4.74 (d, *J* = 9.6 Hz, 1 H), 4.70 (d, *J* = 10.4 Hz, 1 H), 4.68 (d, *J* = 10.4 Hz, 1 H), 3.91 (dd, *J* = 10.2, 1.6 Hz, 1 H), 3.82 (ddd, *J* = 16.0, 8.8, 4.0 Hz, 1 H), 3.72-3.64 (m, 5 H), 3.56-3.53 (m, 1 H), 3.47 (*Pseudo*-t, *J* = 9.6 Hz, 1 H), 3.40-3.37 (m, 1 H), 1.22 (s, 9 H), 1.12 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.71, 138.06, 137.89, 137.82, 137.74, 134.19, 133.58, 131.83, 129.31, 128.54, 128.43, 128.13, 128.06, 128.01, 127.74, 127.69, 127.45, 127.36, 101.20, 86.73, 84.58, 83.11, 79.37, 77.58, 77.51, 75.56, 75.30, 75.05, 75.01, 74.99, 72.84, 71.36, 68.30, 62.02.

2-2. 4-Chlorophenyl 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**4e**)

2-2-1. 4-Chlorophenyl 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**3e**)



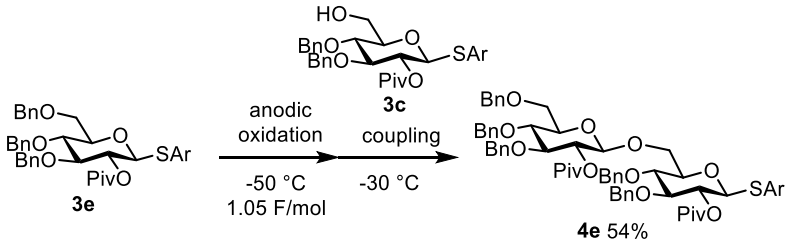
S1

Ar = 4-ClC$_6$H$_4$

3e, 79%

4-Chlorophenyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside **S1** (4.90 mmol, 2.80 g) was dissolved in DMF (35 mL) and the solution was cooled to 0 °C. BnBr (17.6 mmol, 2.10 g) was added to the solution, followed by addition of a solution of NaH (17.9 mmol, 0.430 g) in DMF (15 mL). The reaction mixture was stirred at 0 °C to room temperature for 5 h. Conversion of **S1** was confirmed by TLC (Hexane/EtOAc 4:1) and methanol was added to quench the reaction. The solution was diluted with hexane/EtOAc (4:1), washed with water, dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Thus-obtained crude product was purified by silica gel chromatography to obtain **3e** (3.90 mmol, 2.58 g) in 79% yield. TLC (Hexane/EtOAc 4:1) R_f 0.56; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.44 (d, *J* = 8.4 Hz, 2 H), 7.37-7.28 (m, 11 H), 7.23 (d, *J* = 7.2 Hz, 2 H), 7.17 (d, *J* = 8.4 Hz, 4 H), 5.05 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.76 (d, *J* = 4.8 Hz, 1 H), 4.75 (d, *J* = 4.8 Hz, 1 H), 4.68 (d, *J* = 10.8 Hz, 1 H), 4.59 (*pseudo*-t, *J* = 6.6 Hz, 1 H), 4.56 (d, *J* = 7.8 Hz, 1 H), 4.53 (d, *J* = 12.0 Hz, 2 H), 3.78 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.73-3.70 (m, 2 H), 3.66 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 1.23 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.74, 138.21, 138.07, 137.98, 134.23, 134.13, 133.94, 133.77, 133.52, 132.15, 131.49, 131.33, 129.26, 129.23, 128.55, 128.53, 128.51, 128.07, 127.81, 127.79, 127.77, 127.20, 86.05, 84.74, 80.75, 77.07, 75.59, 75.16, 74.89, 73.52, 71.55, 69.01, 38.87, 38.82, 27.29, 27.17; HRMS (ESI) *m/z* calculated for $C_{87}H_{83}ClKO_{18}S$; $[M+K]^+$ 699.1944; found 699.1951.

2-2-2. 4-Chlorophenyl 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**4e**)



4e 54%

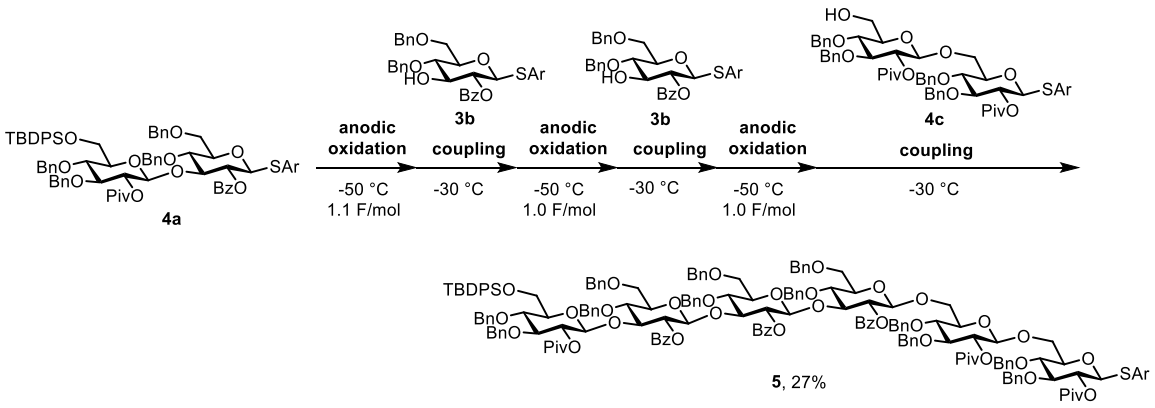
The automated synthesis of **4e** was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7) and a platinum plate cathode (10 mm×20 mm). In the anodic chamber were placed terminal building block **3e** (0.60 mmol, 497 mg), Bu_4NOTf (1.50 mmol, 587 mg) and CH_2Cl_2 (15 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.63 mmol, 56 μL), Bu_4NOTf (1.50 mmol, 587 mL) and CH_2Cl_2 (15 mL). The constant current electrolysis (13.0 mA) was carried out at -50 °C with magnetic stirring until 1.05 F/mol of electricity was consumed. After the electrolysis, building block **3c** (0.72 mmol, 411 mg) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump under an argon atmosphere at -30 °C, and kept for 60 min. After the cycle, Et_3N (0.50 mL) was added to quench the mixture. After removal of the solvent under reduced pressure, the crude

product was purified with silica gel chromatography to obtain **4e** (0.52 mmol, 570 mg) in 54% yield. TLC (Hexane/EtOAc 4:1) R_f 0.56; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.41 (d, *J* = 8.4 Hz, 2 H), 7.33-7.27 (m, 20 H), 7.22 (d, *J* = 7.2 Hz, 5 H), 7.15-7.13 (m, 2 H), 5.10 (*pseudo*-t, *J* = 8.4 Hz, 1 H), 5.02 (*pseudo*-t, *J* = 9.0 Hz, 1 H), 4.76 (t, *J* = 14.4 Hz, 3 H), 4.70 (*pseudo*-t, *J* = 10.8 Hz, 1 H), 4.66 (d, *J* = 10.8 Hz, 1 H), 4.49-4.57 (m, 5 H), 4.46 (*pseudo*-t, *J* = 7.8 Hz, 1 H), 4.00 (dd, *J* = 10.4, 1.8 Hz, 1 H), 3.75-3.66 (m, 6 H), 3.60 (td, *J* = 7.2, 1.8 Hz, 1 H), 3.50-3.43 (m, 2 H), 1.21 (s, 9 H), 1.12 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.69, 176.65, 138.15, 138.11, 137.98, 137.98, 137,78, 134.09, 133.64, 131.86, 129.28, 128.48, 128.45, 128.42, 128.09, 128.02, 127.85, 127.83, 127.70, 127.65, 127.46, 127.32, 101.22, 86.55, 84.57, 83.36, 79.28, 77.77, 77.10, 76.89, 75.27, 75.21, 75.02, 74.99, 73.52, 72.86, 71.39, 68.76, 68.08, 38.81, 38.77, 27.20, 27.16; HRMS (ESI) *m/z* calculated for $C_{87}H_{83}ClKO_{18}S$; $[M+K]^+$ 1125.3986; found 1125.3959.

3. Synthesis of hexasaccharide precursor 2c by AEA

3-1. 4-Chlorophenyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-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-glucopyranoside (**2c**)

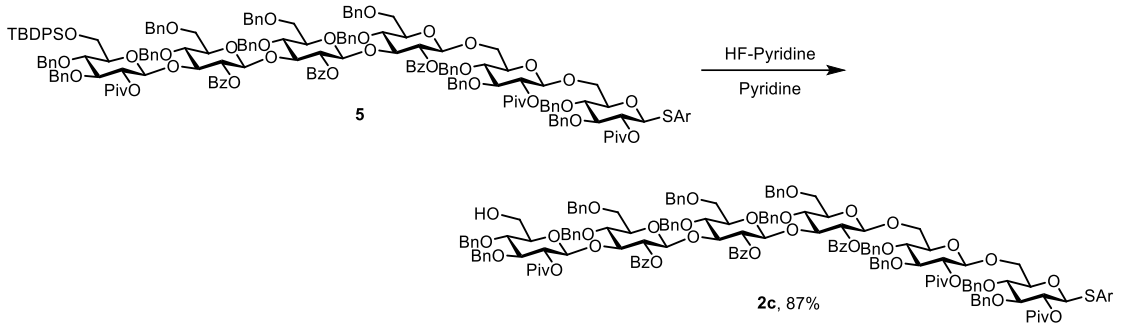
3-1-1. 4-Chlorophenyl 3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**5**)



The automated synthesis of **5** 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 **4a** (0.30 mmol, 377 mg), [Bmpy][OTf] (1.50 mmol, 0.35 mL) and CH_2Cl_2 (15 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.32 mmol, 28 μL), [Bmpy][OTf] (1.50 mmol, 0.35 mL) and CH_2Cl_2 (15 mL). The constant current electrolysis (12.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.1 F/mol of electricity was consumed. After the electrolysis, building block **3b** (0.30 mmol, 178 mg) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump under an argon atmosphere at -30 ℃, and kept for 60 min. After cooling to -50 ℃, The constant current electrolysis (12.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.1 F/mol of electricity was consumed. After the electrolysis, building block **3b** (0.30 mmol, 178 mg) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump under an argon atmosphere at -30 ℃, and kept for 60 min. After cooling to -50 ℃, The constant current electrolysis (12.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.1 F/mol of electricity was consumed. After the electrolysis, building

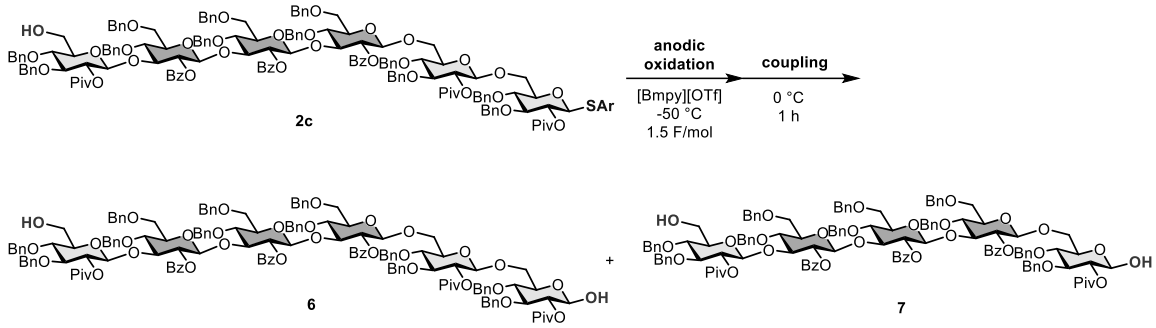
block **4c** (0.30 mmol, 300 mg) dissolved in CH_2Cl_2 (2.0 mL) was subsequently added by the syringe pump under an argon atmosphere at -30 ℃, and kept for 60 min. After the cycle, Et_3N (0.50 mL) was added, and the mixture was filtered through a short column (4×3 cm) of silica gel to remove [Bmpy][OTf]. After removal of the solvent under reduced pressure, the crude product was purified with silica gel chromatography to obtain 486 mg of a mixture containing **5**. The mixture was purified by PR-GPC to obtain **5** (0.0822 mmol, 247 mg) in 27% yield.

3-1-2. 4-Chlorophenyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-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-glucopyranoside (**2c**)



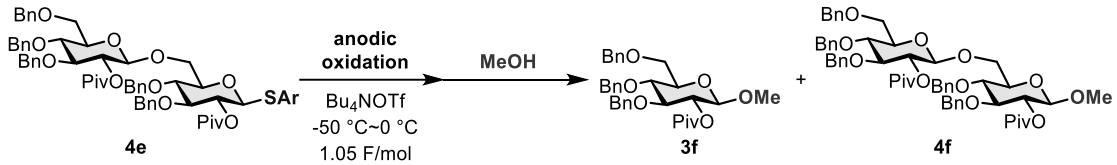
Hexasaccharide **5** (0.121 mmol, 365 mg) was dissolved in pyridine (1.0 mL) and the solution was cooled to 0 °C. 70% HF-pyridine (0.10 mL) was added to the solution and the reaction mixture was stirred at 0 °C to room temperature for 5 h. Conversion of **5** was confirmed by TLC (Hexane/EtOAc 7:3) and aqueous sodium bicarbonate solution was added to quench the reaction. The aqueous solution was extracted with chloroform and the combined organic layer was washed with aqueous sodium bicarbonate solution and 1 N aqueous hydrochloric acid. The reaction mixture was dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Thus-obtained crude product was purified by silica gel chromatography to obtain **2c** (0.105 mmol, 289 mg) in 87% yield. TLC (Hexane/EtOAc 7:3) Rf. 0.65; $[\alpha]^{22}_D$ = -16.363 (*c* = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.78 (d, *J* = 7.2 Hz, 2 H), 7.66 (d, *J* = 7.2 Hz, 2 H), 7.58-7.55 (m, 4 H), 7.31-7.27 (m, 7 H), 7.25-7.13 (m, 46 H), 7.09-6.94 (m, 2 H), 5.00 (dd, *J* = 19.5, 19.5, 9.0 Hz, 4 H), 4.95-4.92 (m, 3 H), 4.87 (dd, *J* = 9.0, 7.8 Hz, 1 H), 4.80 (d, *J* = 10.8 Hz, 1H), 4.68 (ddd, *J* = 8.7, 8.7, 2.4 Hz, 3 H), 4.61 (dd, *J* = 10.8, 4.8 Hz, 3 H), 4.58 (d, *J* = 13.8 Hz, 2 H), 4.52 (dd, *J* = 10.2, 6.0 Hz, 3 H), 4.45-4.35 (m, 12 H), 4.31 (*pseudo*-t, *J* = 12.0 Hz, 2 H), 4.26 (d, *J* = 7.8 Hz, 1 H), 4.21 (dd, *J* = 23.4, 10.8 Hz, 2 H), 4.07 (*pseudo*-t, 18 Hz, 1 H), 4.00 (d, *J* = 9.6 Hz, 1 H), 3.88 (*pseudo*-t, *J* = 16.8 Hz, 1 H), 3.81 (dd, *J* = 18.0, 9.0 Hz, 2 H), 3.72 (d, *J* = 10.2 Hz, 1 H), 3.63-3.57 (m, 4 H), 3.54-3.47 (m, 7 H), 3.45-3.38 (m, 6 H), 3.36 (m, 1 H), 3.32 (*pseudo*-t, *J* = 18.0 Hz, 1 H), 3.28-3.23 (m, 4 H), 2.95 (m, 1 H), 1.21 (s, 9 H), 1.06 (s, 9 H), 1.01 (s, 9 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.18, 176.57, 176.48, 164.52, 138.61, 138.38, 138.35, 138.24, 138.15, 138.00, 137.89, 137.80, 137.72, 137.57, 133.79, 129.83, 129.75, 129.64, 129.18, 128.48, 128.41, 128.39, 128.31, 128.28, 128.26, 128.19, 128.17, 128.13, 128.12, 128.09, 128.03, 127.99, 127.86, 127.80, 127.73, 127.68, 127.63, 127.53, 127.50, 127.47, 127.38, 127.29, 127.19, 127.16, 100.37, 84.41, 82.64, 77.51, 77.49, 75.23, 75.06, 75.01, 74.96, 74.80, 74.78, 74.74, 73.37, 73.34, 73.33, 38.71, 38.64, 38.60, 27.13, 27.05, 26.94.

4. Electrochemical oxidation of hexasaccharide precursor 2c



The one-pot synthesis of **2c** 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×10 mm). In the anodic chamber were placed hexasaccharide building block **2c** (0.10 mmol, 277 mg), [Bmpy][OTf] (0.50 mmol, 117 μL) and CH_2Cl_2 (5.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.10 mmol, 8 μL), [Bmpy][OTf] (0.50 mmol, 117 μL) and CH_2Cl_2 (5.0 mL). The constant current electrolysis (3.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.5 F/mol of electricity was consumed. After the electrolysis, the reaction temperature was raised to 0 ℃, and kept for 60 min. Then, Et_3N (0.20 mL) was added to quench the reaction. After removal of the solvent under reduced pressure, electrolyte was removed by silica gel short pad (eluent: hexane/EtOAc 1:1). Crude product (333 mg) was analyzed by MALDI-TOF- MS and formation of hydroxy sugars **6** and **7** was confirmed.

5. Electrochemical glycosylation of model disaccharide 4e with methanol



Electrochemical activation of **4e** 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×10 mm). In the anodic chamber were placed disaccharide building block **4e** (0.10 mmol, 109 mg), Bu_4NOTf (0.50 mmol, 210 mg) and CH_2Cl_2 (5.0 mL). In the cathodic chamber were placed trifluoromethanesulfonic acid (0.11 mmol, 10 μL), Bu_4NOTf (0.50 mmol, 203 mL) and CH_2Cl_2 (5.0 mL). The constant current electrolysis (4.0 mA) was carried out at -50 ℃ with magnetic stirring until 1.05 F/mol of electricity was consumed. Then the reaction temperature was raised to 0 ℃ and kept for 1 h. Methanol (1.0 mmol, 40μL) was added at 0 ℃ and kept for another 1 h. After the cycle, Et_3N (0.10 mL) was added to quench the mixture. After removal of the solvent under reduced pressure, the crude product was purified with silica gel chromatography to obtain methyl glycoside **3f**[3] and disaccharide **4f** have been detected by MALDI-TOF-MS.

References

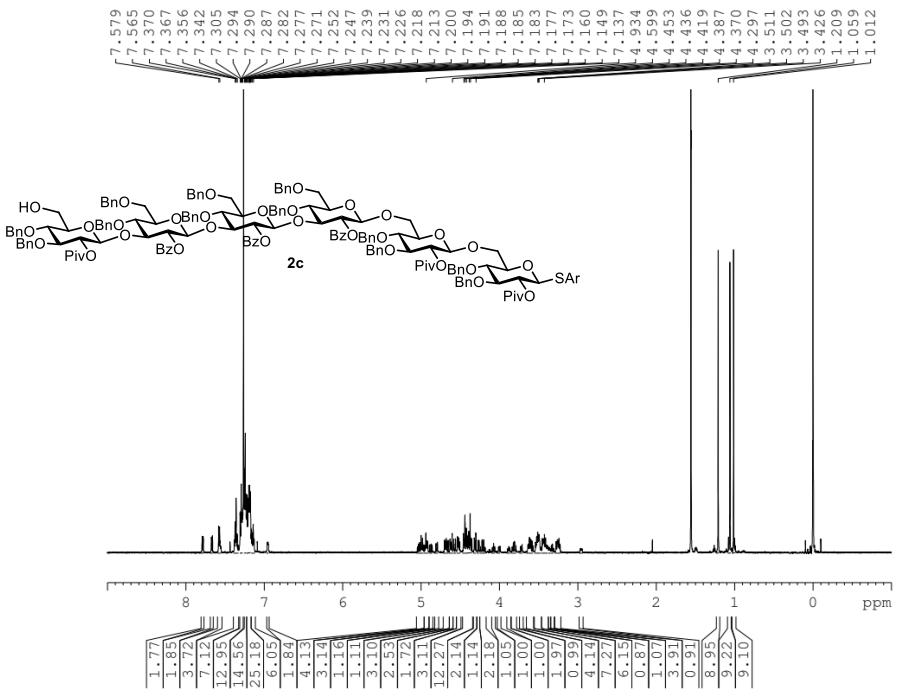
[1] A. Shibuya, Y. Ishisaka, A. Saito, M. Kato, S. Manmode, H. Komatsu, M. A. Rahman, N. Sasaki, T. Itoh, T. Nokami, *Faraday Discuss.*, **2023**, *247*, 59-69.

[2] Z. Zhang, I. R. Ollmann, X.-S. Ye, R. Wischnat, T. Baasov, C.-H. Wong, *J. Am. Chem. Soc.*, **1999**, *121*, 734-753.

[3] J. A. Turner, N. Rosano, D. J. Gorelik, M. S. Taylor, *ACS Catal.* **2021**, *11*, 11171-11179.

^{1}H,^{13}C NMR, H-H cosy and HMQC spectra

^{1}H NMR



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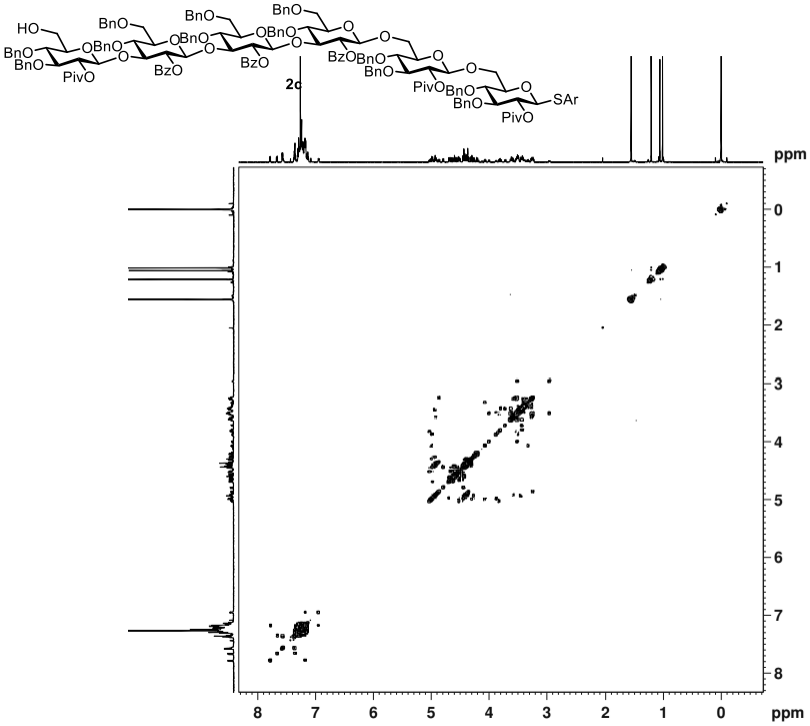
H-H cosy



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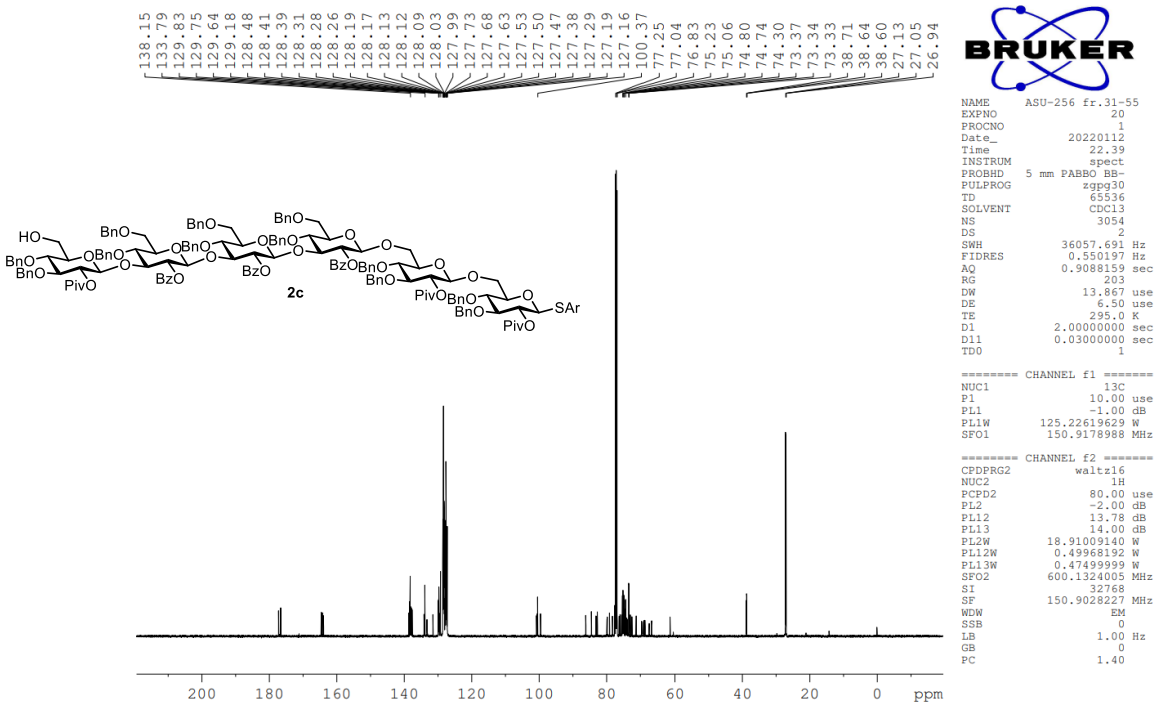
^{13}C NMR



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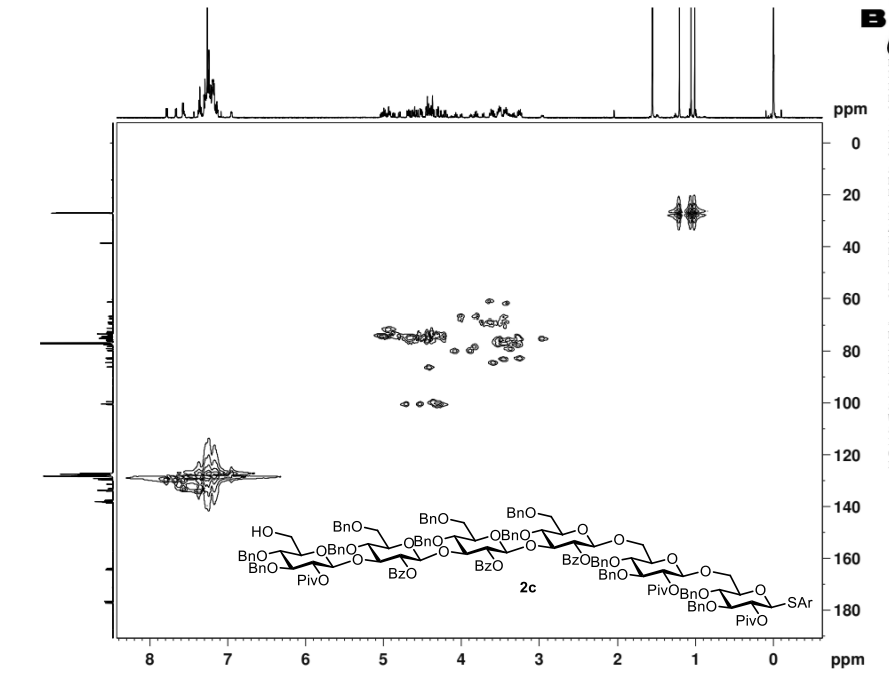
PL2 -2.00 dB
PL12 13.78 dB
PL13 14.00 dB
PL2W 18.91009140 W
PL12W 0.49968192 W
PL13W 0.47499999 W
SFO2 600.1324005 MHz
SI 32768
SF 150.9028227 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

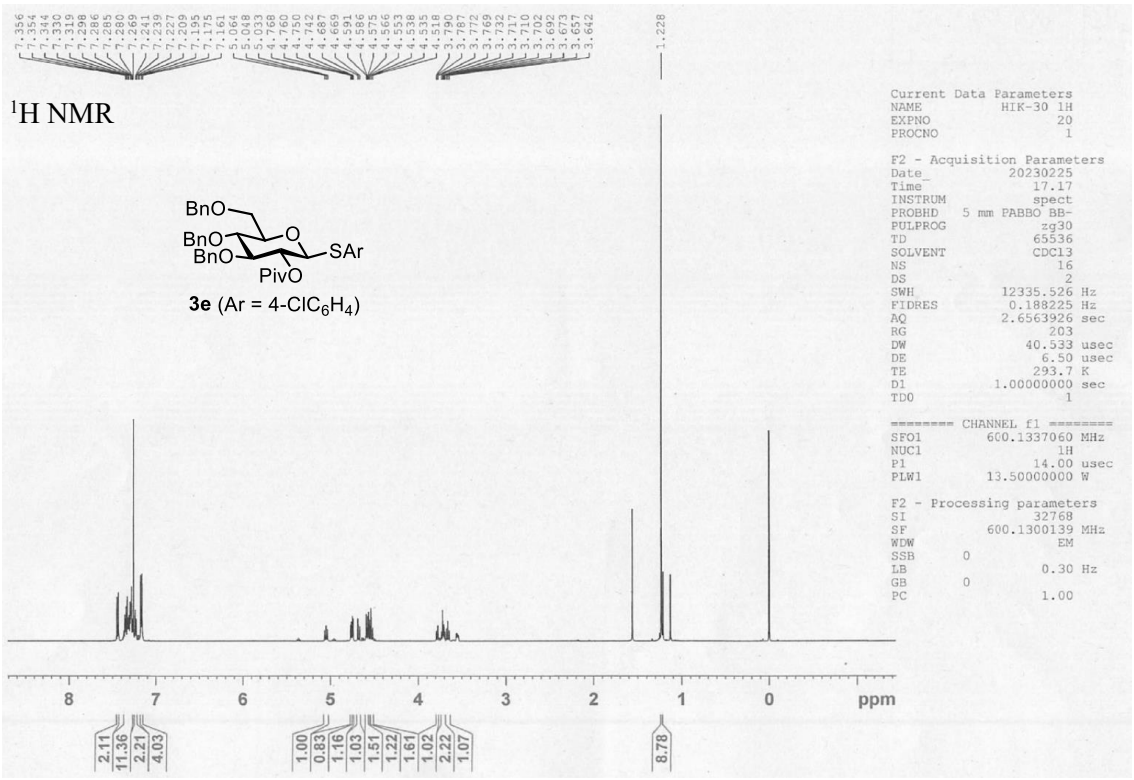
HMQC



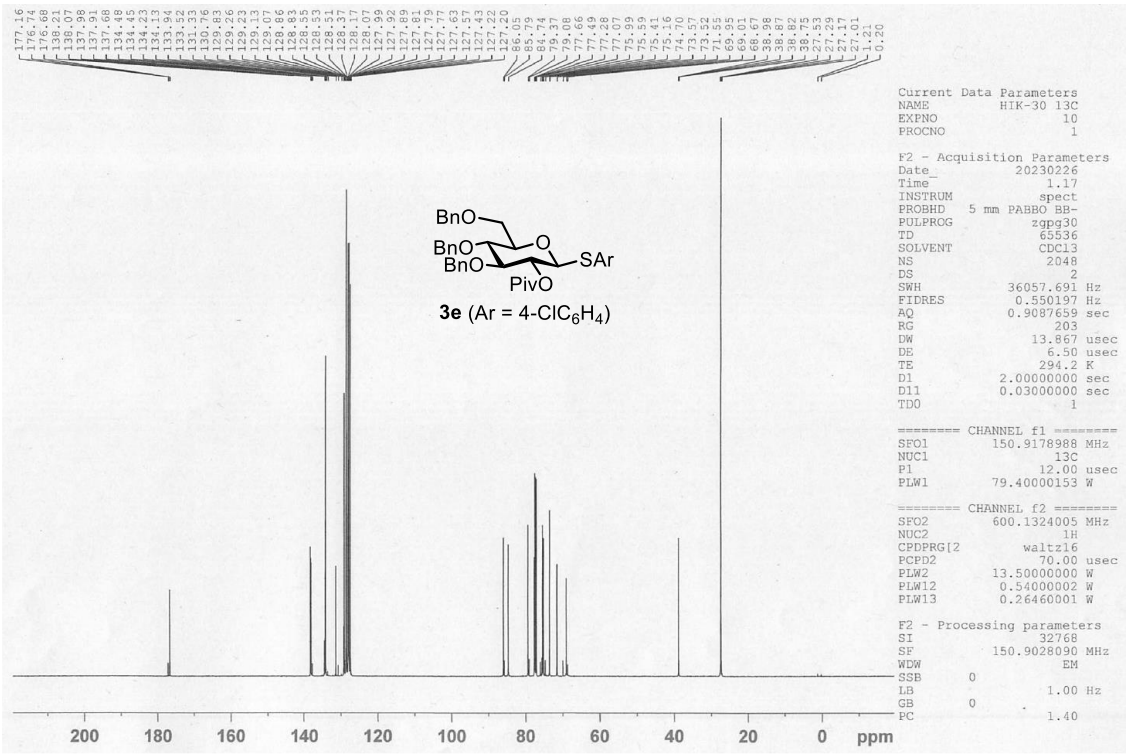
NAME ASU-256 fr.31-
EXPNO 10
PROCNO 1
Date_ 20220112
Time 18.38
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 12335.526
FIDRES 0.188225
AQ 2.6564426
RG 203
DW 40.533
DE 6.50
TE 294.0
D1 1.00000000
TD0 1

======== CHANNEL f1 ===
NUC1 1H
P1 13.00
PL1 -2.00
PL1W 18.91009140
SFO1 600.1337060
SI 32768
SF 600.1300155
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

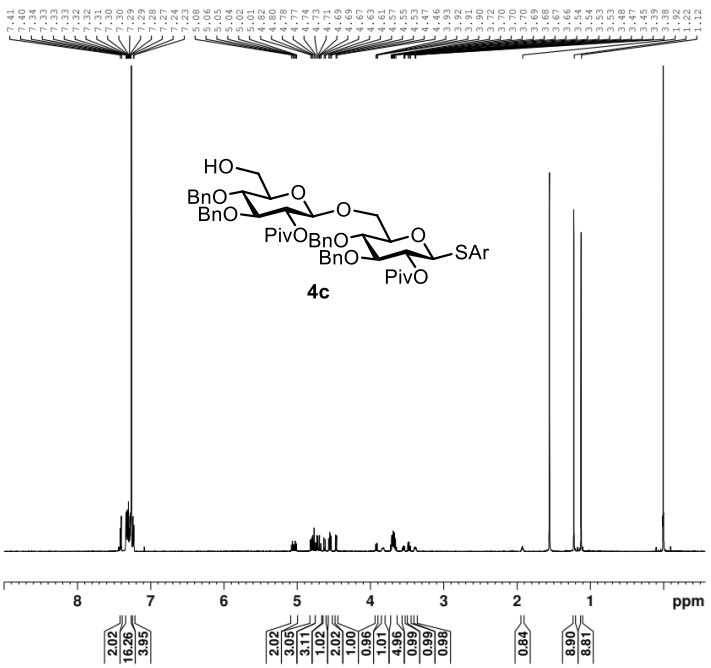
^{1}H NMR



^{13}C NMR

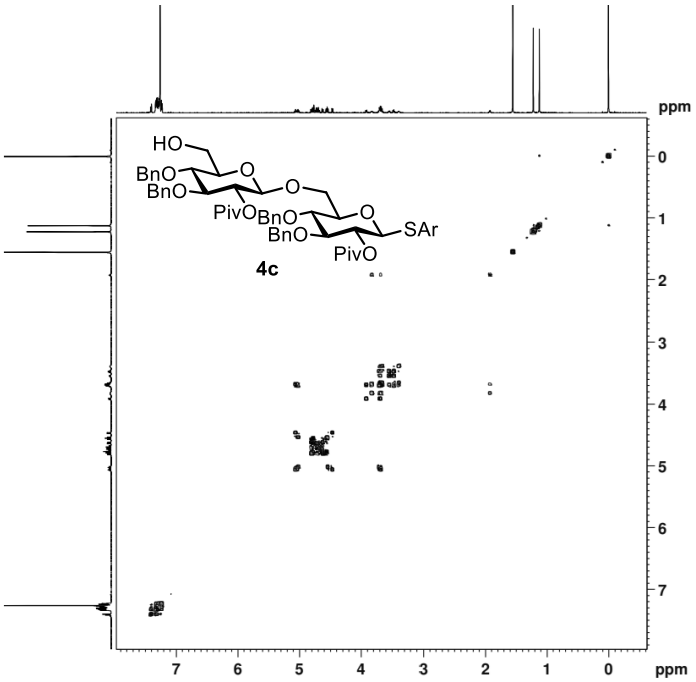


^{1}H NMR



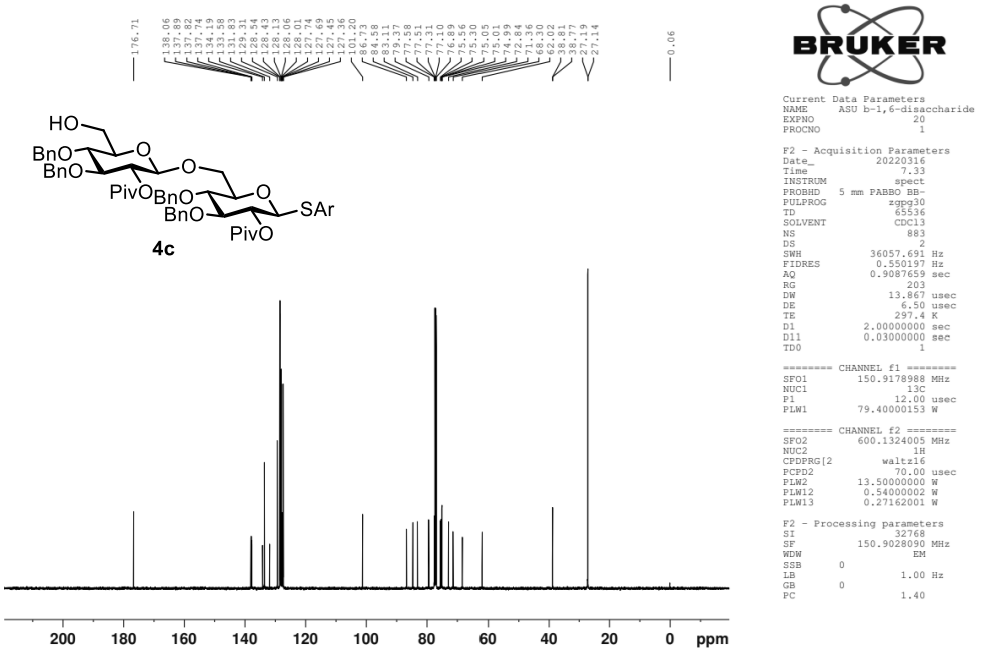

```
Current Data Parameters
NAME      ASU b-1,6-disaccharide
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220316
Time               6.40
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH          12335.526 Hz
FIDRES        0.188225 Hz
AQ            2.6563926 sec
RG                 203
DW              40.533 usec
DE               6.50 usec
TE              296.4 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1       600.1337060 MHz
NUC1               1H
P1               14.00 usec
PLW1       13.50000000 W

F2 - Processing parameters
SI               32768
SF         600.1300133 MHz
WDW                EM
SSB       0
LB               0.30 Hz
GB        0
PC               1.00
```

H-H cosy



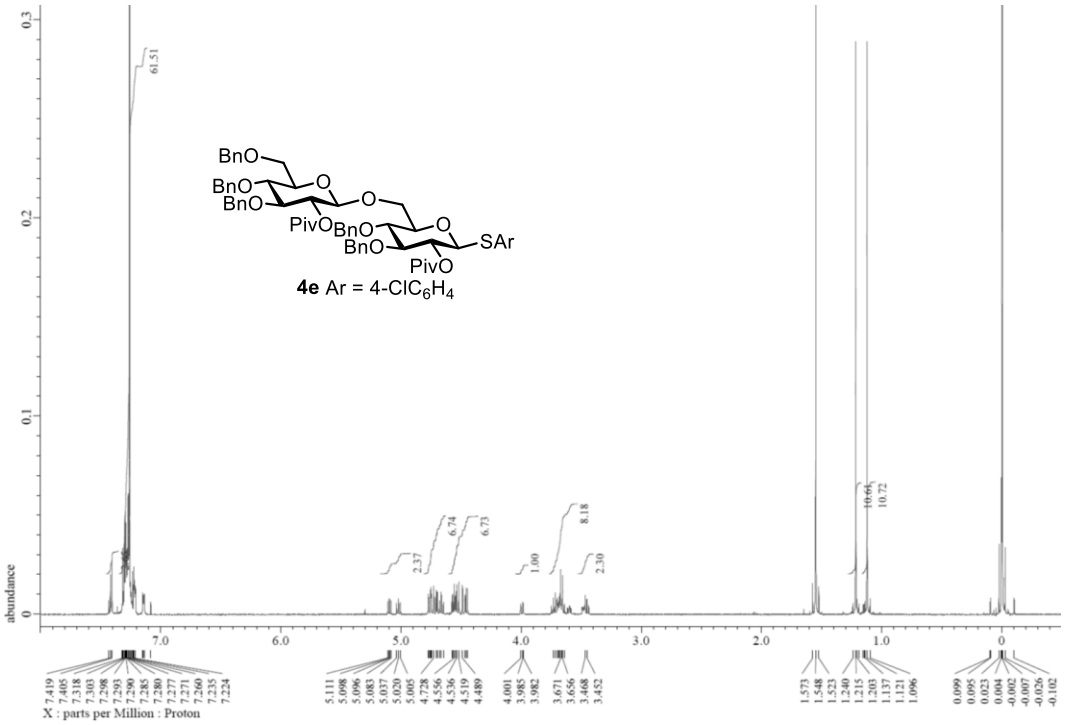

```
Current Data Parameters
NAME      ASU b-1,6-disaccharide
EXPNO                 31
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220316
Time               7.58
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG       cosygpppqf
TD                 2048
SOLVENT          CDCl3
NS                    1
DS                    8
SWH           5154.639 Hz
FIDRES        2.516914 Hz
AQ            0.1986560 sec
RG                  203
DW               97.000 usec
DE               6.50 usec
TE              296.6 K
D0           0.00000300 sec
D1           1.92913902 sec
D11          0.03000000 sec
D12          0.00002000 sec
D13          0.00000400 sec
D16          0.00020000 sec
IN0          0.00019400 sec

======== CHANNEL f1 ========
SFO1       600.1322198 MHz
NUC1               1H
P0               14.00 usec
P1               14.00 usec
P17            2500.00 usec
PLW1       13.50000000 W
PLW10       4.23360014 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPZ1             10.00 %
P16            1000.00 usec

F1 - Acquisition parameters
TD                  128
SFO1          600.1322 MHz
FIDRES        40.270618 Hz
SW                8.589 ppm
FnMODE               QF

F2 - Processing parameters
SI                 1024
SF          600.1300135 MHz
WDW                QSINE
SSB       0
LB        0 Hz
GB        0
PC                 1.40

F1 - Processing parameters
SI                 1024
MC2                QF
SF          600.1300135 MHz
WDW                QSINE
SSB       0
LB        0 Hz
GB        0
```

^{13}C NMR

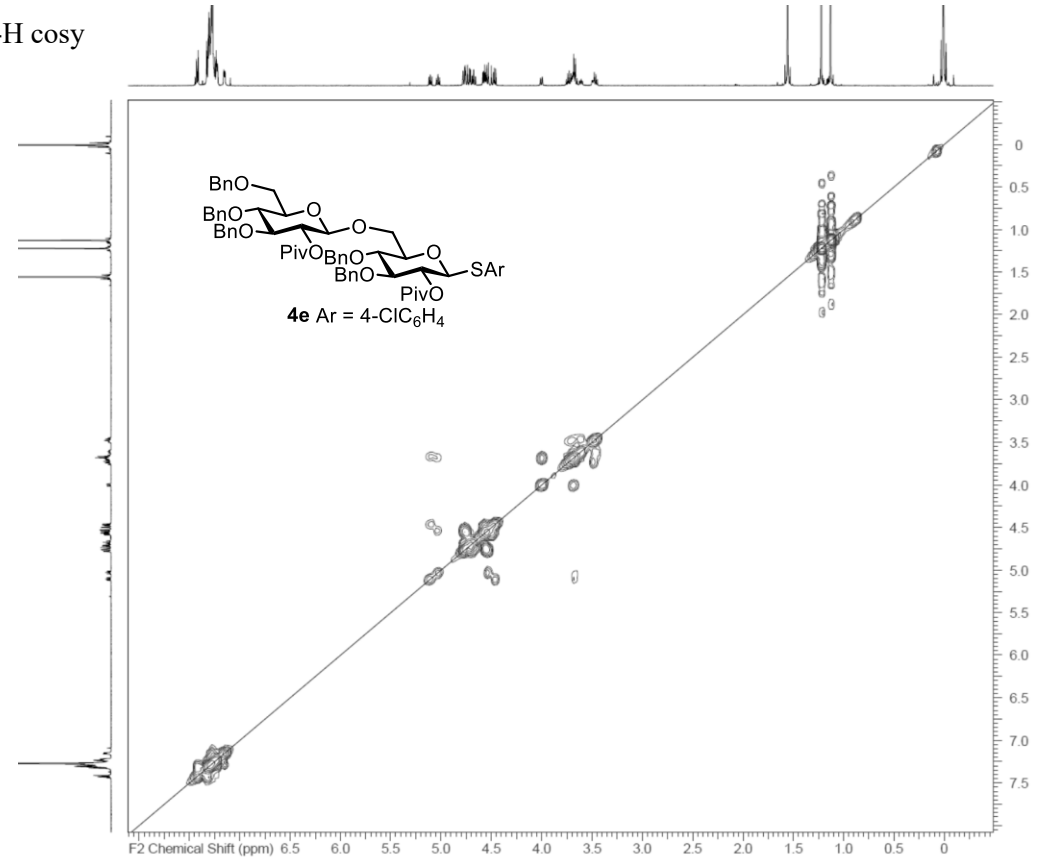



```
Current Data Parameters
NAME      ASU b-1,6-disaccharide
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220316
Time                7.33
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT             CDCl3
NS                    883
DS                      2
SWH             36057.691 Hz
FIDRES              0.550197 Hz
AQ                0.9087659 sec
RG                    203
DW                 13.867 usec
DE                  6.50 usec
TE                297.4 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          150.9178988 MHz
NUC1                 13C
P1                 12.00 usec
PLW1          79.40000153 W

======== CHANNEL f2 ========
SFO2          600.1324005 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2              70.00 usec
PLW2          13.50000000 W
PLW12          0.54000002 W
PLW13          0.27162001 W

F2 - Processing parameters
SI                  32768
SF            150.9028090 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

^{1}H NMR

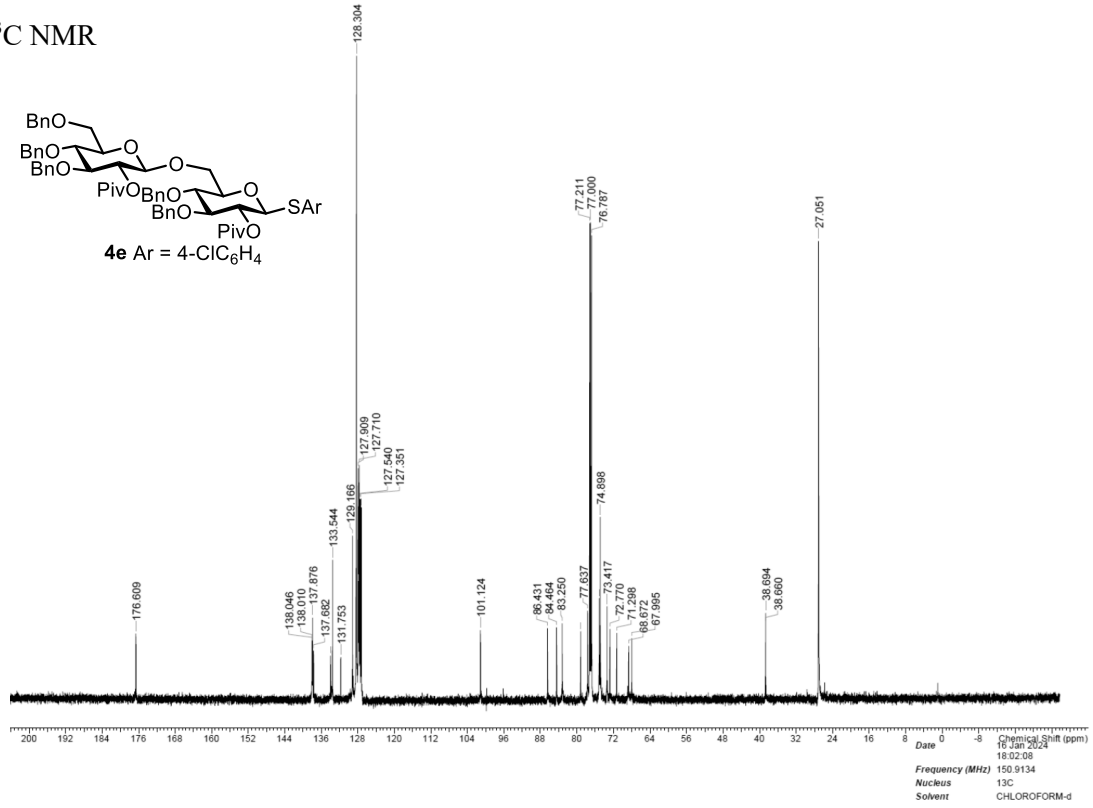


H-H cosy



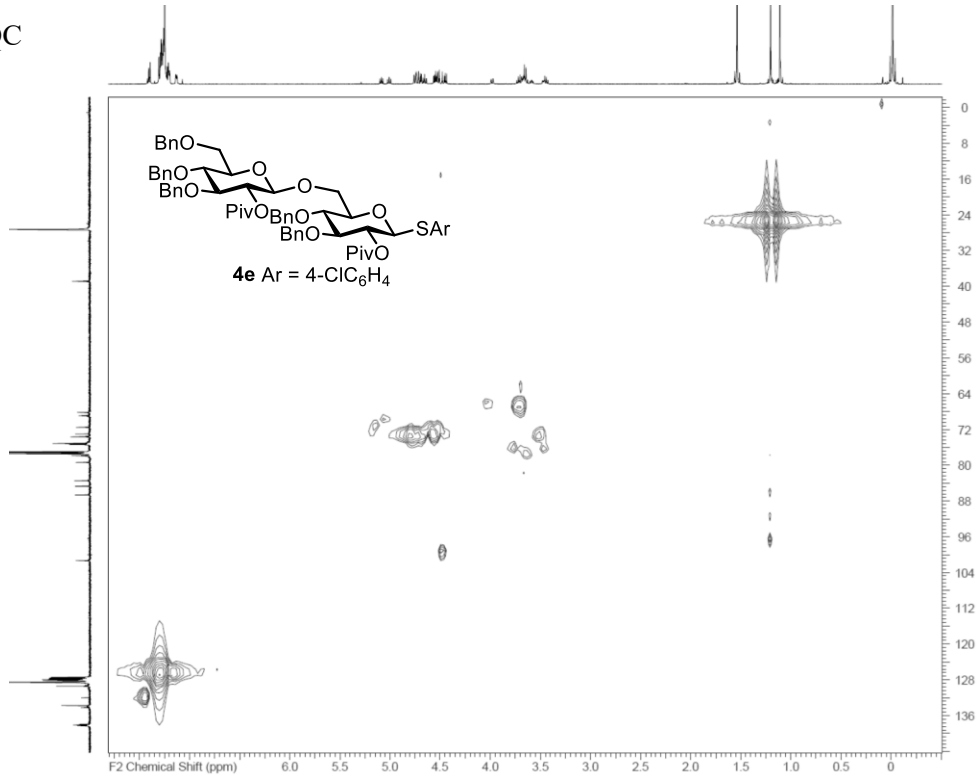
4e Ar = 4-ClC$_6$H$_4$

^{13}C NMR



4e Ar = 4-ClC$_6$H$_4$

HMQC


BnO
BnO
BnO
PivO
BnO
BnO
PivO
SAr
4e Ar = 4-ClC6H4
F2 Chemical Shift (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136

Summary

We have been interested in electrochemical glycosylation, which can computationally control activation of thioglycosides, and developed 'automated electrochemical assembly' (AEA). A variety of oligosaccharides have been synthesized with AEA method. In this study, we then focused on a cyclic (1,3;1,6)-β-glucan, which is produced by root-nodulating bacteria *Bradyrhizobium japonicum* MTCC 120.

In Chapter 1, for efficient glycosylation, we analyzed the reactive intermediates by VT-NMR. As a result, the glycosyl dioxalenium ion intermediates were identified and their thermal stability was evaluated. Based on the thus-obtained knowledge, reaction conditions were optimized and a β-(1,6)-glucan trisaccharide was synthesized in good yield.

In Chapter 2, our target compound had a symmetric dodecasaccharide structure that consists of β-(1,3)- and β-(1,6)-glycosidic linkages. As a result of our investigation, it was found that one of the semi-circular hexasaccharide precursors can be dimerized and cyclized in one-pot manner to form the cyclic dodecasaccharide. Moreover, the yield can be increased by separation of dimerization and cyclization.

In Chapter 3, in the course of synthetic study of the cyclic dodecasaccharide, it was found that side reactions vary depending on monosaccharide sequences of the hexasaccharide precursors. In particular, the glycosidic linkage of the disaccharide unit of the reducing end has great effect on reactivity. Therefore, we prepared model disaccharides of the hexasaccharides. One of the hexasaccharides and its model disaccharide caused similar fragmentation reaction. More detailed knowledge regarding structure-reactivity relationship is expected to lead to rational design of oligosaccharide building blocks in future.

Acknowledgement

The studies presented in this thesis have been carried out under the direction of Professor Toshiki Nokami at Graduate School of Tottori University.

The author would like to express my sincerest gratitude to Professor Nokami for his kind guidance and fruitful discussions throughout this work. Professor Nokami not only directed the research in doctoral course at Tottori University but also led my training as a chemist in master's course at Kyoto University. Since the author ordinarily works at the company far from the university, the author has received a lot of special support from Professor Nokami.

The author wishes to thank Dr. Sasaki for his support. Dr. Sasaki checked his papers and led students who experimented and collected the data. The author also wishes to thank to Ms. Moeko Kato, Ms. Asuka Saito, Ms. Yui Ishisaka, Mr. Hiroto Komatsu and Ms. Yu-Cong Sun. The great data in this thesis was collected by their hard work. As the author ordinarily works as a corporate researcher, it is valuable to talk with younger students and enjoy the academic atmosphere. Communication with younger researchers motivates an older researcher.

The author must make special mention of Yoshida Laboratory at Kyoto University. The author learned the knowledge and the techniques of electrochemical glycosylation and low-temperature NMR analysis under the direction of the late Professor Jun-ichi Yoshida, Professor Seiji Suga (Okayama University), Professor Toshiki Nokami and Professor Aiichiro Nagaki (Hokkaido University). The VT-NMR experiment shown in this thesis was carried out at Kyoto University with cooperation with Professor Nagaki.

The author heartily thanks to his colleagues in Yoshida Laboratory at Kyoto University. The author learned a lot of things by spending time with Dr. Yutaka Tomida, Mr. Koji Ueoka, Mr. Ikuo Shimizu, Mr. Hirotsugu Usutani, Mr. Kazuya Soga, Mr. Hiroaki Tsuyama, Mr. Kosuke Ohata, Mr. Masafumi Inoue and all other members of Yoshida Laboratory.

The author is thankful to Cardurion Pharmaceuticals Inc. for financial support. All members of the company understanded his situation and kindly allowed him to spend his time for the activities of the university.

Finally, the author would like to express deep appreciation to his wife Miho Shibuya and his parents Noriaki Shibuya and Hiromi Shibuya for their constant assistance and encouragement.

List of publications

Title: Electrochemical synthesis of the protected cyclic (1,3;1,6)-β-glucan dodecasaccharide
Author name: Akito Shibuya, Yui Ishisaka, Asuka Saito, Moeko Kato, Sujit Manmode, Hiroto Komatsu, Md Azadur Rahman, Norihiko Sasaki, Toshiyuki Itoh and Toshiki Nokami
Journal name: Faraday Discussions (volume 247, issue 01 November 2023, page 59-69)
Publication date: 2023/05/16

Title: Glycosyl Dioxalenium Ions as Reactive Intermediates of Automate Electrochemical Assembly
Author name: Akito Shibuya, Moeko Kato, Asuka Saito, Sujit Manmode, Naoto Nishikori, Toshiyuki Itoh, Aiichiro Nagaki and Toshiki Nokami
Journal name: European Journal of Organic Chemistry (volume 2022, issue 19, page e202200135)
Publication date: 2022/05/18

Title: Electrochemical Assembly for Synthesis of Middle-Sized Organic Molecules
Author name: Akito Shibuya and Toshiki Nokami
Journal name: The Chemical Record (volume 21, issue 9, page 2389-2396)
Publication date: 2021/06/08

List of publications before 2019

Title: Electrochemical Generation of Glycosyl Triflate Pools
Author name: T. Nokami, A. Shibuya, H. Tsuyama, S. Suga, A. A. Bowers, D. Crich and J. Yoshida
Journal name: Journal of American Chemical Society (volume 129, issue 35, page 10922-10928)
Publication date: 2007/08/17

Title: Iterative Molecular Assembly Based on the Cation-Pool Method. Convergent Synthesis of Dendritic Molecules
Author name: T. Nokami, K. Ohata, M. Inoue, H. Tsuyama, A. Shibuya, K. Soga, M. Okajima, S. Suga and J. Yoshida
Journal name: Journal of American Chemical Society (volume 130, issue 33, page 10864–10865)
Publication date: 2008/07/29

Title: Oligosaccharide Synthesis Based on a One-pot Electrochemical Glycosylation–Fmoc Deprotection Sequence
Author name: T. Nokami, H. Tsuyama, A. Shibuya, T. Nakatsutsumi and J. Yoshida
Journal name: Chemistry Letters (volume 39, issue 9, 942-943)
Publication date: 2008/08/02

Title: Electrochemical Conversion of Thioglycosides to Glycosyl Triflates
Author name: T. Nokami, A. Shibuya, and J. Yoshida
Journal name: Trends in Glycoscience and Glycotechnology (volume 20, issue 114, 175-185)
Publication date: 2008/09/01

Title: α- and β-Glycosyl Sulfonium Ions: Generation and Reactivity
Author name: T. Nokami, A. Shibuya, S. Manabe, Y. Ito and J. Yoshida
Journal name: Chemistry A European Journal (volume 15, issue 10, page 2252 – 2255)
Publication date: 2009/02/12

Title: Glycosyl Sulfonium Ions as Storable Intermediates for Glycosylations
Author name: T. Nokami, Y. Nozaki, Y. Saigusa, A. Shibuya, S. Manabe, Y. Ito and J. Yoshida
Journal name: Organic Letters (volume 13, issue 6, page 1544–1547)
Publication date: 2011/02/16

Title: Electrochemical generation of 2,3-oxazolidinone glycosyl triflates as an intermediate for stereoselective glycosylation
Author name: T. Nokami, A. Shibuya, Y. Saigusa, S. Manabe, Y. Ito and J. Yoshida
Journal name: Beilstein Journal of Organic Chemistry (volume 8, page 456–460)
Publication date: 2012/03/28