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Exploring Native Chemical Ligation Concept for Highly Stereospecific Glycosylation Reactions

*Kim Le Mai Hoang, Yaguang Bai, Xin Ge and Xue-Wei Liu**

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences,

Nanyang Technological University, 21 Nanyang Link, Singapore 637371

xuewei@ntu.edu.sg

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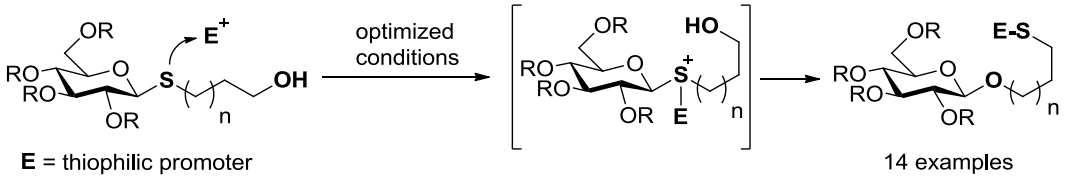
Table of Contents (TOC) graphic



ABSTRACT: Various O-alkyl glycosides were obtained in a highly stereospecific manner with retention of configuration at the anomeric center. Our method has customized native chemical ligation concept for glycoconjugates synthesis, utilizing a meticulously controlled activating system. To explain the origin of stereoselective preference, an S_Ni mechanism was proposed and corroborated by computational calculation.

KEYWORDS: native chemical ligation • stereospecific • glycosylation • S_Ni mechanism

INTRODUCTION

Ubiquitously decked on the surfaces of all cell types in nature, complex glycoconjugates play central roles in the development, cooperation and vitality of an organism[1-5]. Recent technical advances have allowed scientists to obtain the precise structure of these macromolecules, henceforth ushering in the need to synthesize such important glycans. Multitudinous approaches to make glycosidic bonds in a highly stereoselective manner, have steadily emerged for the last two decades[6-8], including those of intramolecular aglycon delivery concept[9]. Nonetheless, an efficient and universal method to confidently prepare various glycoconjugates have yet been established, especially one that is applicable for large scale and combinatorial chemistry.

There are many reasons for the current state of carbohydrate researches, including the formation of new stereogenic center following every glycosylation step, the arduous characterization and purification thereafter, as well as the common expression of carbohydrate chains in a nonlinear, branched fashion. Efforts are ongoing in our research group to overcome these challenges.

Native chemical ligation (NCL) is by far the most used form of chemical ligation, a technique for building a polypeptide from two unprotected peptides[10, 11]. A classical NCL involved a reaction between a C-terminal thioester peptide with another peptide bearing an N-terminal cysteine residue. Transthioesterification occurred reversibly to yield a thioester-bridged intermediate; this intermediate rearranged irreversibly to form the desired peptide bond, replacing the temporal thio-linkage. This

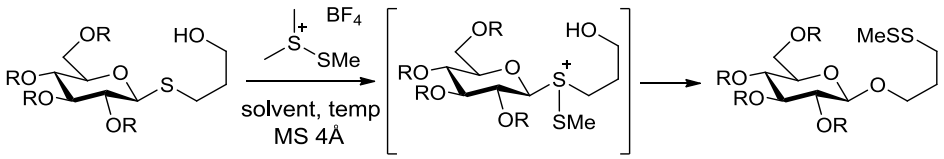
method lies at the heart of modern chemical protein synthesis[12, 13], and has been our routine method to prepare various proteins and enzymes[14-16]. In addition, there were previous reports by Ley and coworkers demonstrating the use of 2-benzenesulfonyl derivatives as viable leaving groups for various C-nucleophiles[17-18] and O-nuceophiles[19] substitution using organozinc reagents. A successful adaptation of NCL philosophy would be of great value to our glycosylation studies.

RESULTS AND DISCUSSION

Motivated by this notion, we studied glycosylation reaction bearing an analogous pattern to NCL. 2,3,4,6-tetra-O-acetyl glucose was firstly attached to a sulfide tether to give **1a**. Initial experiments scrutinizing over various thiophilic activators were conducted in the search for a suitable candidate to break the thio-linkage and stereoselectively form the O-glycoside product. This prompted us to DMTSF (dimethyl(methylthio)sulfonium tetrafluoroborate) as the best reagent.

Reaction under dry condition in dichloromethane at room temperature proceeded smoothly to give very good yield and stereoselectivity (Table 1, entry 1). Reactions at lower temperatures showed less yields (Table 1, entries 2-3) and below -40℃ essentially no conversion was observed (Table 1, entry 3). Assessments on solvents indicated DCM to be the most suitable medium, amidst Et_2O, MeCN, THF (Table 1, entries 4-6). We found that 3 equivalents of DMTSF in DCM at room temperature was sufficient for the reaction. On the complete stereoretention of product, it was ambiguous whether contiguous acetyl protecting groups were responsible for blocking α-face of intermediate **4a** through the formation of a transient bridging cation[20-22] or this was an intrinsic character of the sulfide tether.

Table 1. Optimization studies with DMTSF[a].



1a, R = OAc
1b, R = OBn

4a, R = OAc
4b, R = OBn

5a, R = OAc
5b, R = OBn

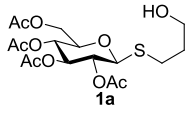
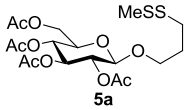
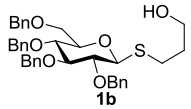
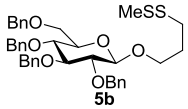
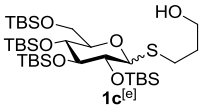
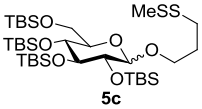
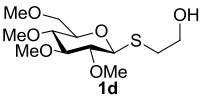
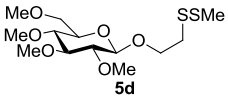
Entry	1	5	R	Temp.	Solvent	Yields[b]	α:β[c]
1	**1a**	**5a**	**Ac**	**r.t.**[d]	**CH_2Cl_2**	**90**	**β**
2	1a	5a	Ac	-20℃	CH_2Cl_2	51	β
3	1a	5a	Ac	-40℃	CH_2Cl_2	trace	β
4	1a	5a	Ac	r.t.[d]	Et_2O	72	β
5	1a	5a	Ac	r.t.[d]	MeCN	49	β
6	1a	5a	Ac	r.t.[d]	THF	66	β
7	1b	5b	Bn	r.t.[d]	CH_2Cl_2	70	1:1.4
8	1b	5b	Bn	r.t.[d]	MeCN	53	1:3.6
9	1b	5b	Bn	r.t.[d]	Et_2O	62	1:2.9
10	1b	5b	Bn	r.t.[d]	Dioxane	17	1:2.5
11	1b	5b	Bn	r.t.[d]	THF	31	1:2.1
12	1b	5b	Bn	-40℃	MeCN	33	1:5
13	1b	5b	Bn	-60℃	EtCN	29	1:7
14	**1b**	**5b**	**Bn**	**-78℃**	**EtCN**	**60[e]**	**β**
15	1n	5n	Bn	r.t.[d]	CH_2Cl_2	68	2.2:1
16	1n	5n	Bn	r.t.[d]	Et_2O	66	2.5:1
17	**1n**	**5n**	**Bn**	**-78℃**	**Et_2O**	**62[e]**	**α**

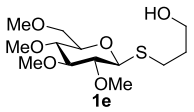
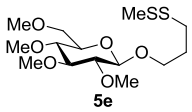
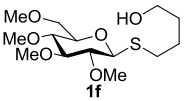
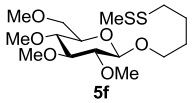
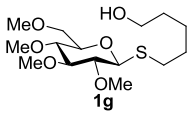
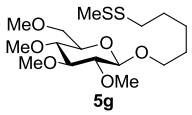
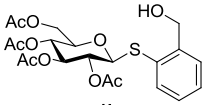
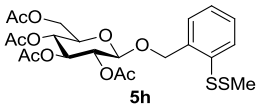
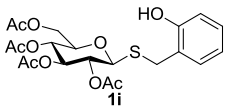
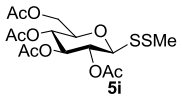
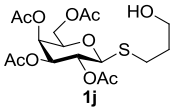
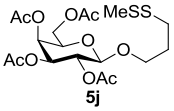
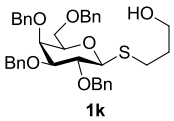
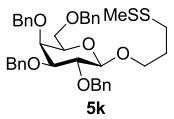
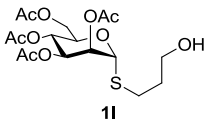
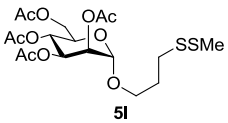
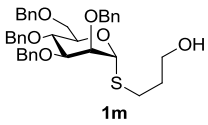
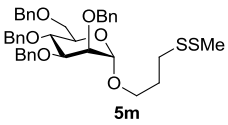
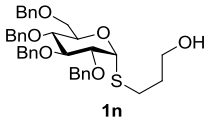
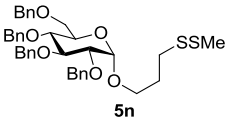
[a] Unless otherwise specified, all of the reactions were carried out with 1 equivalent of **1a** or **1b**, 3 equivalents of DMTSF, activated molecular sieves 4Å and 5 mL of solvent in 12 hours. [b] isolated yield. [c] determined by ^1H-NMR integration. [d] room temperature. [e] reaction time was 48 hours.

To answer this question, we conducted the reaction with 2,3,4,6-tetra-O-benzyl-β-thioglucoside **1b**, which was protected by non-participating groups. Under identical condition, we obtained an anomeric mixture of products in 70% yield, with α:β ratio at 1:1.4 (Table 1, entry 7). Mixture of anomers suggested existence of glucosyl oxocarbenium ion during reaction course[23], of which the hydroxyl acceptor on sulfide tether can approach from either faces of the carbocation, resulting in both diastereoisomers. Such implication suggested that variance in solvents and temperatures can greatly influence the outcome of reaction[24-25]. As a general "rule of thumb"[26], nitrile solvents[27] favored more β-anomer whereas ethereal solvents[28] favored more α-anomer. In addition, α-anomer was often found in larger percentage due to its stronger anomeric effect[29]. Surprisingly, the results contradicted our initial speculation that the reaction was a competition between S_N1 and S_N2 pathway: even though reaction in

acetonitrile indeed showed a higher ratio of β-isomer (Table 1, entry 8), ethereal solvents similarly exhibited inclinations towards retention of β-stereoconfiguration in the product (Table 1, entries 9-11). This inherent preference for hydroxyl acceptor to target oxocarbenium ion from β-face insinuated the mechanism being internal nucleophilic substitution (S_Ni) rather than a pure S_N1/S_N2 contention[30]. With this empirical guide, we geared reaction conditions towards generating exclusively the retention product (Table 1, entries 12-14). To our delight, reaction conducted at -78℃ in propionitrile medium afforded β-anomer as the only stereoisomer in 60% yield after 48 hours (Table 1, entry 14). Interestingly, a reversal of stereoselectivity was observed when the α-anomer of **1b**, compound **1n**, was subjected to glycosylation condition: an excess of α-isomer **5n** was observed (Table 1, entries 15-17). Longer reaction time was necessary in order to achieve a reasonable conversion rate. It was noteworthy that meticulous maneuvers were crucial in obtaining the stereochemically pure isomer. Based on these optimization results, we established that three equivalents of DMTSF in propionitrile or diethyl ether at -78℃ is the best condition to obtain β-retention or α-retention products, respectively. With the protocol delineated, evaluation on the versatility of this reaction was carried out by studying a diversified substrate scope.

Table 2. Exploration of substrate scope[a]

Entry	Sugar	Product	Yield[b] (%)	α:β[c]
1	 **1a**	 **5a**	90[d]	β
2	 **1b**	 **5b**	60	β
3	 **1c**[e]	 **5c**	55	1:1.1
4	 **1d**	 **5d**	49	β

5	 **1e**	 **5e**	51	β
6	 **1f**	 **5f**	49	β
7	 **1g**	 **5g**	50	β
8	 **1h**	 **5h**	81[d]	β
9	 **1i**	 **5i**	91[d]	β
10	 **1j**	 **5j**	89[d]	β
11	 **1k**	 **5k**	59	β
12	 **1l**	 **5l**	93[d]	α
13	 **1m**	 **5m**	63	α
14	 **1n**	 **5n**	62[f]	α

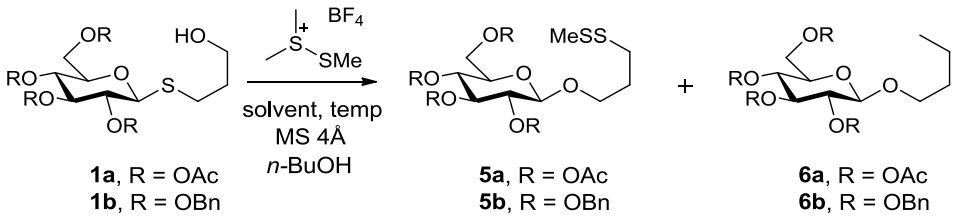
[a] Unless otherwise specified, all of the reactions were carried out with 3 equivalents of DMTSF, activated molecular sieves 4Å in EtCN at -78℃ in 48 hours. [b] isolated yield. [c] determined by ^{1}H-NMR integration. [d] CH_2Cl_2, room temperature. [e] mixture of 1α:14β. [f] Et_2O, -78℃.

As seen from Table 2, reaction of various β-glycosyl sulfides having different protecting groups, including acetate **1a**, benzyl ether **1b**, methyl ether **1e** proceeded smoothly to afford the ligated

O-glycosides in good to excellent yields (51-90%) with β-exclusivity. However, TBS-protected ether **1c**, gave 1α:1.1β mixture. Such discrepancy could be attributed to the suppression of S_Ni pathway: the steric bulk of silyl ethers could destabilize the transient species. In this cases, reaction was likely to follow S_N1/S_N2 mechanism, resulting in mixed anomers. Nevertheless, extension of reaction to 2,3,4,6-tetra-O-methyl-1-β-D-thioglucoside **1d-1g** bearing aliphatic tethers of different lengths proved to be successful. It was noteworthy that under this reaction condition even the longest carbon chain between hydroxyl acceptor and the sulfide tether can afford the *lipid-like* O-glycoside **5g** stereospecifically. Interestingly, aromatic tethers showed mixed results: O-benzyl glucoside **5h** starting from benzyl alcohol **1h** was obtained as expected, whereas phenol **1i**, prepared from the reaction between 2,3,4,6-tetra-O-acetyl-β-D-thioglucoside and 2-bromomethyl phenol, afforded methyldisulfanyl-1-β-D-glucoside **5i** in 91% yield. Upon closer examination, we reasoned that the thiobenzyl S-CH_2Ph bond was weaker than thioglycoside S-C_{sugar} bond, hence it was preferable for sulfonium intermediate **4i** to dispatch the aromatic moiety rather than the glycosyl donor. There were no significant differences in reaction yields and stereochemical outcomes when reactions were conducted with other epimeric sugars (galactosyl **1j-1k** and mannosyl **1l-1m**). In addition, we were able to obtain optically pure O-α-glucoside **5n** from the corresponding α-thioglucoside **1n**. The glycosylated products β-**5b** obtained from β-**1b** as well as α-**5n** from α-**1n** validated the capability of our method in making glycosides with preservation of stereochemical information.

Cross-over experiments were further conducted to study the extent of intramolecular against intermolecular impacts. 1.3 equivalents of *n*-butanol, which acted as a competitive nucleophile, were transferred to the reaction mixture before DMTSF was added. As seen from Table 3, the intramolecular products were obtained as the major product in all cases. Although the armed thioglucoside **1b** showed less preference for **5b** at room temperature compared to the disarmed **1a** under same condition (Table 3, entries 1-2), reaction of **1b** under optimized condition yielded the desired **5b** seven times more than butyl glucoside **6b** (Table 3, entry 3), with complete stereocontrol.

Table 3. Cross-over experiments[a].

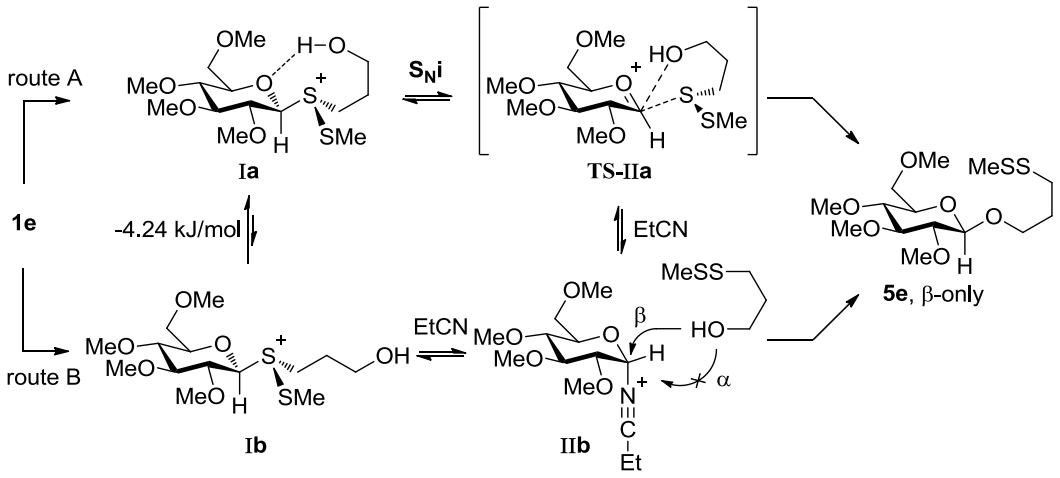


Entry	1	R	Temp.	Solvent	Yield of 5 (%, α:β)[b]	Yield of 6 (%, α:β)[b]
1	1a	Ac	r.t.[c]	CH_2Cl_2	5a (76%, β only)	6a (15%, β only)
2	1b	Bn	r.t.[c]	CH_2Cl_2	5a (58%, 1:1.6)	6a (22%, 1:1)
3	1b	Bn	-78℃	EtCN	5b (55%, β only)[d]	6b (8%, β only)[d]

[a] Unless otherwise specified, all of the reactions were carried out with 1 equivalent of **1a** or **1b**, 3 equivalents of DMTSF, 1.3 equivalents of n-BuOH, activated molecular sieves 4Å and 5 mL of solvent in 12 hours. [b] isolated yield, α:β ratio determined by ^1H-NMR integration. [c] room temperature. [d] reaction time was 48 hours.

Next, theoretical calculations on conformations of **1e** along the reaction pathway to understand the retentive anomeric outcome was carried out[31]. A plausible mechanism was depicted in Scheme 1. The compound could go through either an internal nucleophilic substitution pathway (route A) or a typical S_N1/S_N2 competition by intermolecular route B.

Scheme 1. Proposed mechanism for the retention of stereoconfiguration.



In route A, with the possbile presence of an internal H-bonding between hydroxyl acceptor and the ring oxygen, conformation **Ia** is more energetically favored than the unrestrictive conformation **Ib**, by a difference of 4.24 kJ/mol (Scheme 1, DFT, B3LYP/6-31+G(d) level). This conformational preference

for **Ia** facilitates anchoring of hydroxyl group to the β-face of the molecule during transitional state **IIa**. Being brought closer to reaction center, the glycosyl acceptor can readily target the anomeric position to give the retention product, especially at very low temperature, where thermal energy causing the sulfonium tether to freely dissociate from the carbohydrate species, was minimal. Counter-wise, if the two intermediates were to be separated in route B, reattachment of them would result in a mixture of anomers, of which the α:β ratio was dependent on solvent choice as well as temperature. As the temperature was lowered, more β-product of β-thioglucoside **1e** was obtained. Only β-anomer was observed at -78℃ when propionitrile was used as the medium because α-coordination of this nitrile solvent to anomeric carbon would ensure that only β-face of intermediate **IIb** was accessible to the glycosyl acceptor. Calculation for compound **1b** showed a similar profile, whereas in the case of α-substituted **1n**, it was energetically favorable for hydroxyl group to remain on the α-face throughout the reaction coordinates, leading to exclusive α-isomer.

Based on cross-over experiments as well as calculation results, we inferred that intramolecular pathway to be the prevalent factor in determining stereocontrol, while other factors including temperature, solvents and competing nucleophiles showing complement effects.

CONCLUSION

In conclusion, we have developed a simple yet effective method for highly stereospecific O-glycosylation based on the philosophy of native chemical ligation concept. The many subtle variables affecting stereochemical outcome were duly controlled to give good to excellent yields and stereoselectivity. Future work on mechanistic study as well as refining of this reaction for the synthesis of various glycoconjugates, especially glycolipids are in progress.

EXPERIMENTAL SECTION

All reactions were conducted under an atmosphere of nitrogen, unless otherwise indicated. Anhydrous solvents were transferred via oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. All reagents and solvents were obtained from commercial suppliers and used without further

purification unless otherwise stated. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm or by staining using a basic solution of potassium permanganate. Evaporation of organic solutions was achieved by rotary evaporation with a water bath temperature below 40℃. Product purification by flash column chromatography was accomplished using silica gel 60 (0.010-0.063 mm). Technical grade solvents were used for chromatography and distilled prior to use. Optical rotations were measured in $CHCl_3$ with a 1 cm cell (c given in g/100 mL). Melting points were obtained in open capillary tubes in melting point apparatus. IR spectra were recorded using FTIR and reported in cm^{-1}. High resolution mass spectra (HRMS) were recorded on Q-TOF mass spectrometer. Accurate masses are reported for the molecular ion $[M+H]^+$ or a suitable fragment ion. NMR spectra were recorded at room temperature on a 400 MHz and 500 MHz NMR spectrometer. The residual solvent signals were taken as the reference (7.26 ppm for ^{1}H-NMR spectroscopy and 77.23 ppm for ^{13}C-NMR spectroscopy). Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane (TMS). Chemical shift (δ) is referred in terms of ppm, coupling constants (J) are given in Hz. Following abbreviations classify the multiplicity: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q =quartet, m = multiplet, br = broad or unresolved. Assignments were based on analysis of coupling constants and COSY, HMQC spectra. Compound numbers used in the experimental section correspond to those employed in the main paper.

Synthesis of compound 1a

To a magnetically stirred solution of 2,3,4,6-tetra-O-acetyl-β-D-thioglucoside[31] (2.7g, 7.5 mmol) in DCM (5 mL) and triethylamine (Et_3N, 2 mL, 0.015 mol) was added dropwise 3-bromopropanol-1 (0.9 mL, 9.75 mmol) at 0℃. Reaction was allowed to reach room temperature and complete consumption of starting materials was observed after 3 hours. Reaction mixture was dissolved in DCM (30 mL), washed with water (50 mL), brine (50 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 1:2) afforded compound **1a** (2.85g, 90% yield) as a white solid. $[\alpha]_D^{20}$ -20.5 (*c* 2.79, $CHCl_3$); **m.p.** 86-88 °C; **IR** (KBr): 3429, 2943, 1747, 1371, 1230, 1037 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.22 (t, 1H, J = 9.6

Hz, H-3), 5.07 (t, 1H, *J* = 9.8 Hz, H-4), 5.05 (t, 1H, *J* = 9.6 Hz, H-2), 4.48 (d, 1H, *J* = 10.1 Hz, H-1), 4.23 (dd, 1H, *J* = 13.2 Hz, *J* = 3.3 Hz, H-6'), 4.16 (dd, 1H, *J* = 13.1 Hz, *J* = 2.3 Hz, H-6), 3.73-3.69 (m, 3H, H-5, C$\underline{H}_2$OH), 2.88-2.72 (m, 2H, SC$\underline{H}_2$), 2.08, 2.06, 2.02, 2.00 (s, 12H, 4xCOC$\underline{H}_3$), 1.87-1.64 (m, 2H, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 170.9, 170.4, 169.8, 169.6 (C$\underline{O}$CH$_3$ x4), 83.7 (C-1), 76.2 (C-5), 73.9 (C-2), 69.9 (C-3), 68.4 (C-4), 62.2 (C-6), 60.7 (-C$\underline{H}_2$OH), 32.2 (-C$\underline{H}_2$-), 26.3 (SC$\underline{H}_2$), 20.9, 20.8, 20.7 (CO$\underline{C}$H$_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{17}H_{26}O_{10}S$ $[M+Na]^+$, 445.1144, found: 445.1136.

Synthesis of compound 1b

To a magnetically stirred solution of 2,3,4,6-tetra-O-benzyl-β-D-(4-monomethoxytrityl) thioglucoside[32] (1.85g, 2.31 mmol) in DCM (10 mL) was added trifluoroacetic acid (TFA, 5 mL-per-mmol substrate). Complete consumption of starting materials was observed after 1 hour. Reaction mixture was dissolved in DCM (30 mL) and washed with ice-water (30 mL), aq. $NaHCO_3$ (30 mL), brine (30 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was dissolved in a solution of DCM (5 mL) and triethylamine (Et_3N, 0.65 mL, 4.63 mmol), followed by dropwise addition of 3-bromopropanol-1 (0.27 mL, 3.01 mmol) at 0℃. Reaction was allowed to reach room temperature and complete consumption of starting materials was observed after 3 hours. Reaction mixture was dissolved in DCM (30 mL), washed with water (50 mL), brine (50 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 2:1) afforded compound **1b** (1.27g, 89% yield) as a white solid. $[\alpha]_D^{20}$ +17.4 (*c* 1.36, $CHCl_3$); **m.p.** 65-68 °C; **IR** (KBr): 3414, 2866, 1653, 1454, 1066 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 7.38-7.12 (m, 20H, aromatic), 4.93-4.49 (m, 8H, 4xOC$\underline{H}_2$Ph), 4.44 (d, 1H, *J* = 9.8 Hz, H-1), 3.84-3.69 (m, 2H, C$\underline{H}_2$OH), 3.69-3.56 (m, 2H, H-6), 3.64 (t, 1H, *J* = 8.7 Hz, H-3), 3.52 (t, 1H, *J* = 8.7 Hz, H-4), 3.65-3.54 (m, 1H, H-5), 3.43 (t, 1H, *J* = 9.7 Hz, H-2), 2.96-2.75 (m, 2H, SC$\underline{H}_2$), 2.3 (t, 1H, *J* = 5.5 Hz, O$\underline{H}$), 1.91-1.79 (m, 2H, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 138.1, 128.6, 128.5, 128.2, 128.1, 127.9 (m, aromatic), 86.7 (C-1), 85.9 (C-3), 81.7 (C-2), 78.9 (C-4), 78.1 (C-5), 75.9, 75.7, 75.3, 73.6 (-O$\underline{C}$H$_2$Ph x4), 69.2 (C-6), 60.2 (C$\underline{H}_2$OH), 32.8

(-$\underline{C}H_2$-), 27.6 (S$\underline{C}H_2$-) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{37}H_{42}O_6S$ $[M+Na]^+$, 637.2601, found: 637.2587.

Synthesis of compound 1c

To a magnetically stirred solution of 1-thio-β-D-Glucose[34] (0.27g, 1.42 mmol) in anhydrous DMF (10 mL) and Et_3N (0.4 mL, 2.84 mmol) was added dropwise a solution of 3-bromopropyl acetate (0.33g, 1.85 mmol) in 10 mL of anhydrous DMF. Complete consumption of starting materials was observed after 3 hours, after which 2,6-lutidine (0.37 mL, 3.26 mmol) was added, followed by dropwise addition of *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf, 0.47 mL, 2.04 mmol) at 0 ℃. Reaction was allowed to reach room temperature, after which complete consumption of starting materials was observed after 4 hours. Reaction mixture was quenched by addition of ice-water (30 mL), followed by dissolution in ethyl ether (Et_2O, 30 mL) and washed with aq. $NaHCO_3$ (2x30 mL), brine (2x30 mL). The crude product was dissolved in MeOH (10 mL), followed by addition of catalytic amount of K_2CO_3 (2.85mg, 0.02 mmol). Complete consumption of starting materials was observed after 3 hours. Reaction mixture was dissolved in DCM (30 mL), washed with water (50 mL), brine (50 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 2:1) afforded compound **1c** (0.21g, 72% yield over 2 steps) as a colorless oil being a mixture of anomers (α:β = 1:14). **IR** (KBr): 3413, 1616, 1249, 1091, 781 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.23 (d, 1H, J = 4 Hz, H-1α), 4.67 (d, 1H, J = 7.7 Hz, H-1β), 3.9-3.89 (m, 1H), 3.81-3.71 (m, 6H), 3.65-3.63 (m, 1H), 2.87-2.68 (m, 2H, SC$\underline{H}_2$), 1.96 (t, 1H, J = 5.84 Hz, O$\underline{H}$), 1.89-1.80 (m, 2H, -C$\underline{H}_2$-), 0.89-0.88 (m, 36H, 4xSiC(C$\underline{H}_3$)$_3$), 0.13-0.05 (m, 24H, 4xSi(C$\underline{H}_3$)$_2$) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 84.5 (C-1), 83.6 (C-5), 78.1 (C-3), 76.7 (C-2), 70.4 (C-4), 64.6 (C-6), 60.9 ($\underline{C}H_2OH$), 32.5 (-$\underline{C}H_2$-), 27.6, 26.2, 26.1, 26.0 ($\underline{C}(CH_3)_3$ x4), 18.6, 18.3, 18.1, 18.0 (C($\underline{C}H_3$)$_3$ x4), -3.8, -3.9, -4.0, -4.1 (Si($\underline{C}H_3$)$_2$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{33}H_{75}O_6SSi_4$ $[M+H]^+$, 711.4362, found: 711.4362.

Synthesis of compound 1d

To a magnetically stirred solution of 2,3,4,6-tetra-O-methyl-β-D-thioglucose[31] in DCM (5 mL) and

triethylamine (Et_3N, 0.13 mL, 0.9 mmol), followed by dropwise addition of 2-bromoethanol (0.04 mL, 0.58 mmol) at 0℃. Reaction was allowed to reach room temperature and complete consumption of starting materials was observed after 3 hours. Reaction mixture was dissolved in DCM (30 mL), washed with water (50 mL), brine (50 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 2:1) afforded compound **1d** (0.25g, 89% yield) as a white solid. $[\alpha]_D^{20}$ +24.1 (*c* 0.46, $CHCl_3$); **m.p.** 41-42 °C; **IR** (KBr): 3419, 1635, 1458, 1093, 665 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 4.28 (d, 1H, *J* = 9.92 Hz, H-1), 3.81-3.75 (m, 2H, OC$\underline{H}_2$), 3.63-3.37 (m, 11H, 3xOC$\underline{H}_3$, H-6), 3.37 (s, 3H, OC$\underline{H}_3$), 3.34-3.33 (m, 1H, H-5), 3.18 (t, 1H, *J* = 8.8 Hz, H-4), 3.09 (t, 1H, *J* = 9.5 Hz, H-3), 2.96 (t, 1H, *J* = 9.9 Hz, H-2), 2.95-2.75 (m, 2H, SC$\underline{H}_2$) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 88.6 (C-1), 86.4 (C-3), 83.3 (C-2), 79.6 (C-4), 78.6 (C-5), 71.6 (C-6), 63.3 ($\underline{C}H_2OH$), 61.2, 61.1, 60.0, 59.4 (O$\underline{C}H_3$ x4), 36.7 (S$\underline{C}H_2$-) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{12}H_{24}O_6S$ $[M+Na]^+$, 319.1191, found: 319.1190.

Synthesis of compound 1e

Folowing the synthesis of compound **1d** using 3-bromopropanol-1 afforded **1e** (0.23g, 80% yield) as a white solid. $[\alpha]_D^{20}$ +1.5 (*c* 0.65, $CHCl_3$); **m.p.** 48-49 °C; **IR** (KBr): 3419, 2933, 1627, 1448, 1095 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 4.27 (d, 1H, *J* = 9.8 Hz, H-1), 3.85-3.69 (m, 2H, OC$\underline{H}_2$), 3.64-3.50 (m, 11H, 3xOC$\underline{H}_3$, H-6), 3.38 (s, 3H, OC$\underline{H}_3$), 3.33-3.28 (m, 1H, H-5), 3.18 (t, 1H, *J* = 8.8 Hz, H-4), 3.05 (t, 1H, *J* = 9.5 Hz, H-3), 2.96 (t, 1H, *J* = 9.8 Hz, H-2), 2.95-2.74 (m, 2H, SC$\underline{H}_2$), 2.57 (t, 1H, *J* = 5.8 Hz, O$\underline{H}$), 1.86-1.66 (m, 2H, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 88.6 (C-1), 85.8 (C-3), 83.5 (C-2), 79.9 (C-4), 78.6 (C-5), 71.9 (C-6), 63.2 ($\underline{C}H_2OH$), 61.1, 60.7, 59.9, 59.3 (O$\underline{C}H_3$ x4), 32.7 (-$\underline{C}H_2$-), 27.7 (S$\underline{C}H_2$-) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{13}H_{26}O_6S$ $[M+Na]^+$, 333.1348, found: 333.1351.

Synthesis of compound 1f

Folowing the synthesis of compound **1d** using 4-bromobutanol-1 afforded **1f** (0.18g, 83% yield) as a white solid. $[\alpha]_D^{20}$ +29.1 (*c* 0.32, $CHCl_3$); **m.p.** 54-55 °C; **IR** (KBr): 3419, 2933, 1627, 1458, 1095 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 4.24 (d, 1H, *J* = 9.8 Hz, H-1), 3.63-3.48 (m, 13H, 3xOC$\underline{H}_3$, OC$\underline{H}_2$,

H-6), 3.35 (s, 3H, OC$\underline{H}_3$), 3.27-3.23 (m, 1H, H-5), 3.15 (t, 1H, *J* = 8.7 Hz, H-4), 3.06 (t, 1H, *J* = 9.4 Hz, H-3), 2.93 (t, 1H, *J* = 9.8 Hz, H-2), 2.74-2.65 (m, 2H, SC$\underline{H}_2$), 1.74-1.22 (m, 4H, -C$\underline{H}_2$C$\underline{H}_2$-), 2.00 (s, 1H, O$\underline{H}$) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 88.6 (C-1), 85.3 (C-3), 83.5 (C-2), 79.7 (C-4), 78.8 (C-5), 71.8 (C-6), 62.2 (O$\underline{C}$H$_2$OH), 61.1, 60.9, 60.6, 59.4 (O$\underline{C}$H$_3$ x4), 31.7 (SCH$_2$CH$_2\underline{C}$H$_2$), 31.0 (S$\underline{C}$H$_2$-), 26.2 (SCH$_2\underline{C}$H$_2$-) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{14}H_{28}O_6S$ $[M+Na]^+$, 347.1504, found: 347.1508.

Synthesis of compound 1g

Folowing the synthesis of compound **1d** using 5-bromopentanol-1 afforded **1g** (0.22g, 86% yield) as a white solid. $[\alpha]_D^{20}$ +0.5 (*c* 0.31, $CHCl_3$); **m.p.** 63-65 °C; **IR** (KBr): 3419, 2933, 1627, 1095 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 4.25 (d, 1H, *J* = 9.8 Hz, H-1), 3.66-3.51 (m, 13H, 3xOC$\underline{H}_3$, OC$\underline{H}_2$, H-6), 3.38 (s, 3H, OC$\underline{H}_3$), 3.26-3.24 (m, 1H, H-5), 3.18 (t, 1H, *J* = 8.8 Hz, H-4), 3.10 (t, 1H, *J* = 9.4 Hz, H-3), 2.96 (t, 1H, *J* = 9.8 Hz, H-2), 2.93-2.67 (m, 2H, SC$\underline{H}_2$), 2.04-1.43 (m, 7H, -C$\underline{H}_2$C$\underline{H}_2$C$\underline{H}_2$-, O$\underline{H}$) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 88.7 (C-1), 85.4 (C-3), 83.6 (C-2), 79.7 (C-4), 71.8 (C-5), 62.8 (C-6), 61.1 ($\underline{C}$H$_2$OH), 61.0, 60.7, 59.5 (O$\underline{C}$H$_3$ x4), 32.3 ($\underline{C}$H$_2$CH$_2$OH), 31.1 (SCH$_2\underline{C}$H$_2$), 29.8 (S$\underline{C}$H$_2$), 25.1 (SCH$_2$CH$_2\underline{C}$H$_2$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{15}H_{30}O_6S$ $[M+Na]^+$, 361.1661, found: 361.1664.

Synthesis of compound 1h

To a magnetically stirred solution of 2,3,4,6-tetra-O-acetyl-α-D-glucosyl bromide[33] (0.41g, 1 mmol) in anhydrous acetonitrile (10 mL) was added Et_3N (0.28 mL, 2 mmol), followed by potionwise addition of 2-mercaptobenzyl alcohol (0.18g, 1.3 mmol). Complete consumption of starting materials was observed after 4 hours. Reaction mixture was dissolved in DCM (30 mL), washed with water (2x50 mL), brine (30 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 1:1) afforded compound **1h** (0.36g, 77% yield) as a white solid. $[\alpha]_D^{20}$ +28.8 (*c* 0.35, $CHCl_3$); **m.p.** 80-83 °C; **IR** (KBr): 3439, 1635, 1369, 1228, 1037 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 7.59-7.28 (m, 4H, aromatic), 5.21 (t, 1H, *J* = 9.4 Hz, H-3), 5.03 (t, 2H, *J* = 9.8 Hz, H-2, H-4), 4.88 (dd, 1H, *J* = 12.7 Hz, *J* = 5.7 Hz, OC$\underline{H}_2$Ph), 4.67 (dd, 1H, *J* = 12.6 Hz, *J* = 7.8 Hz, OCH$_2$Ph), 4.64 (d, 1H, *J* = 10.1 Hz, H-1), 4.19-4.09 (m, 2H, H-6), 3.66-3.62 (m, 1H, H-5), 2.76-2.73 (m, 1H, O$\underline{H}$), 2.14, 2.04, 2.01, 2.00 (s, 12H, 4xCOC$\underline{H}_3$) ppm; **^{13}C NMR (100**

MHz, $CDCl_3$): δ 170.8, 170.4, 169.6, 169.5 ($\underline{C}OCH_3$ x4), 145.5, 136.4, 130.2, 129.7, 128.9 (m, aromatic), 87.1 (C-1), 76.1 (C-5), 74.0 (C-3), 70.4 (C-2), 68.1 (C-4), 63.8 ($\underline{C}H_2O$), 61.9 (C-6), 21.0, 20.8, 20.7 ($CO\underline{C}H_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{21}H_{26}O_{10}S$ $[M+Na]^+$, 493.1144, found: 493.1140.

Synthesis of compound 1i

To a magnetically stirred solution of 2,3,4,6-tetra-O-acetyl-β-D-thioglucoside[31] (0.36g, 1 mmol) in anhydrous DCM (10 mL) and Et_3N (0.28 mL, 2 mmol) was added dropwise a solution of 2-bromomethyl phenol (0.24g, 1.3 mmol) in 10 mL of anhydrous DCM. Complete consumption of starting materials was observed after 3 hours. Reaction mixture was dissolved in DCM (30 mL), washed with water (30 mL), brine (30 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 1:1) afforded compound **1i** (0.38g, 81% yield) as a white solid. $[\alpha]_D^{20}$ +131.6 (*c* 0.06, $CHCl_3$); **m.p.** 54-55 °C; **IR** (KBr): 3415, 1629, 1230, 1037 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.26-7.11 (m, 2H, aromatic), 6.88-6.83 (m, 1H, aromatic), 6.13 (br, 1H, O$\underline{H}$), 5.19 (t, 1H, *J* = 9.2 Hz, H-3), 5.13-5.06 (m, 2H, H-2, H-4), 4.43 (d, 1H, *J* = 9.9 Hz, H-1) 4.24 (dd, 1H, *J* = 12.4 Hz, *J* = 4.8 Hz, H-6'), 4.14 (dd, 1H, *J* = 12.4 Hz, *J* = 2.5 Hz, H-6), 4.00 (d, 1H, *J* = 13.1 Hz, SC$\underline{H}_2$Ph), 3.85 (d, 1H, *J* = 13.1 Hz, SC$\underline{H}_2$Ph), 3.70-3.66 (m, 1H, H-5), 2.11, 2.05, 2.02, 2.01 (s, 12H, 4xCOC$\underline{H}_3$) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 171.0, 170.3, 170.0, 169.6 ($\underline{C}OCH_3$ x4), 154.9, 130.8, 129.7, 122.3, 120.8, 117.1 (m, aromatic), 82.3 (C-1), 76.1 (C-5), 73.7 (C-2), 69.8 (C-3), 68.5 (C-4), 62.3 (C-6), 29.1 (S$\underline{C}H_2$), 21.0, 20.9, 20.8, 20.7 ($CO\underline{C}H_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{21}H_{26}O_{10}S$ $[M+Na]^+$, 493.1144, found: 493.1143.

Synthesis of compound 1j

Folowing the synthesis of compound **1a** starting from D-galactose afforded **1j** (0.12g, 65% yield) as a colorless oil. $[\alpha]_D^{20}$ +1.9 (*c* 1.06, $CHCl_3$); **IR** (KBr): 3421, 1747, 1635, 1369, 1228, 1047 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.41 (dd, 1H, *J* = 3.4 Hz, *J* = 0.7 Hz, H-4), 5.23 (t, 1H, *J* = 9.9 Hz, H-2), 5.02 (dd, 1H, *J* = 10.0 Hz, *J* = 3.3 Hz, H-3), 4.46 (d, 1H, *J* = 9.9 Hz, H-1), 4.16-4.05 (m, 2H, H-6), 3.92 (m, 1H, H-5), 3.71 (m, 2H, C$\underline{H}_2$OH), 2.89-2.73 (m, 2H, SC$\underline{H}_2$), 2.13, 2.05, 2.03, 1.96 (s, 12H,

4xCOCH$_3$), 1.91-1.87 (m, 2H, -CH$_2$-) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 170.6, 170.4, 170.2, 169.9 (COCH$_3$ x4), 84.2 (C-1), 74.7 (C-5), 71.9 (C-2), 67.5 (C-3), 67.2 (C-4), 61.7 (C-6), 60.8 (CH$_2$OH), 32.2 (SCH$_2$CH$_2$), 26.5 (SCH$_2$), 21.2, 20.9, 20.7 (COCH$_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{17}H_{26}O_{10}S$ $[M+Na]^+$, 445.1144, found: 445.1151.

Synthesis of compound 1k

Folowing the synthesis of compound **1b** starting from D-galactose afforded **1k** (0.13g, 80% yield) as a colorless oil. $[\alpha]_D^{20}$ +118.7 (*c* 0.1, $CHCl_3$); **IR** (KBr): 3419, 1647, 1095, 790 cm^{-1}; **^{1}H NMR (500 MHz, CDCl$_3$)**: δ 7.45-7.32 (m, 20H, aromatic), 5.01-4.46 (m, 8H, 4xOCH$_2$Ph), 4.45 (d, 1H, *J* = 11.8 Hz, H-1), 3.96 (d, 1H, *J* = 2.45 Hz, H-4), 3.90 (t, 1H, *J* = 11.8 Hz, H-2), 3.79-3.73 (m, 2H, OCH$_2$), 3.72-3.60 (m, 3H, H-3, H-5, H-6), 3.55-3.31 (m, 1H, H-6), 2.97-2.77 (m, 2H, SCH$_2$), 2.41 (br, 1H, OH), 1.91-1.84 (m, 2H, -CH$_2$-) ppm; **^{13}C NMR (125 MHz, CDCl$_3$)**: δ 138.8, 138.6, 138.4, 138.3, 137.9, 137.8, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6 (m, aromatic), 85.9 (C-1), 84.1 (C-3), 75.8 (C-2), 74.5 (C-4), 73.6 (C-5), 72.9, 69.1 (OCH$_2$Ph x4), 60.5 (C-6), 32.6 (SCH$_2$CH$_2$), 27.3 (SCH$_2$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{37}H_{42}O_6S$ $[M+Na]^+$, 637.2601, found: 637.2596.

Synthesis of compound 1l

Folowing the synthesis of compound **1a** starting from D-mannose afforded **1l** (0.14g, 72% yield) as a white solid. $[\alpha]_D^{20}$ +67.2 (*c* 2.32, $CHCl_3$); **m.p.** 76-77 °C; **IR** (KBr): 3485, 2939, 1747, 1371, 1228, 1051 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 5.34-5.24 (m, 4H, H-1, H-2, H-3, H-4), 4.39-4.36 (m, 1H, H-5), 4.30 (dd, 1H, *J* = 9.7 Hz, *J* = 4.3 Hz, H-6'), 4.10 (dd, 1H, *J* = 9.7 Hz, *J* = 1.6 Hz, H-6), 3.75-3.74 (m, 2H, CH$_2$OH), 2.82-2.70 (m, 2H, SCH$_2$), 2.16, 2.09, 2.05, 2.99 (s, 12H, 4xCOCH$_3$), 1.91-1.86 (m, 2H, -CH$_2$-) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 170.9, 170.2, 170.0, 169.9 (COCH$_3$ x4) , 83.0 (C-1), 71.4 (C-5), 69.6 (C-3), 69.3 (C-2), 66.6 (C-4), 62.7 (OCH$_2$), 61.1 (C-6), 32.2 (SCH$_2$CH$_2$), 28.2 (SCH$_2$), 21.1, 20.9, 20.9, 20.8 (COCH$_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{17}H_{26}O_{10}S$ $[M+Na]^+$, 445.1144, found: 445.1138.

Synthesis of compound 1m

Folowing the synthesis of compound **1b** starting from D-galactose afforded **1m** (0.11g, 82% yield) as

a colorless oil. $[\alpha]_D^{20}$ +78.7 (*c* 0.53, $CHCl_3$); **IR** (KBr): 3439, 1635, 1093, 1026, 786 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.42-7.19 (m, 20H, aromatic), 5.43 (d, 1H, *J* = 0.6 Hz, H-1), 4.96-4.55 (m, 8H, 4xOC$\underline{H}_2$Ph), 4.23-4.20 (m, 1H, H-5), 3.97 (t, 1H, *J* = 7.32 Hz, H-4), 3.91-3.84 (m, 2H, H-2, H-3), 3.83-3.78 (m, 2H, H-6), 3.77-3.69 (m, 2H, OC$\underline{H}_2$), 2.81-2.67 (m, 2H, SC$\underline{H}_2$), 2.07 (br, 1H, O$\underline{H}$), 1.92-1.74 (m, 2H, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 138.5, 138.3, 138.2, 128.5, 128.1, 127.8, 127.7 (m, aromatic), 82.9 (C-1), 80.4 (C-3), 76.5 (C-2), 75.3 (C-4), 73.5, 72.3, 72.2 (O$\underline{C}H_2$Ph x4), 69.4 (C-5), 60.8 (C-6), 32.3 (SCH$_2\underline{C}$H$_2$), 28.3 (S$\underline{C}$H$_2$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{37}H_{42}O_6S$ $[M+Na]^+$, 637.2601, found: 637.2599.

Synthesis of compound 1n

To a magnetically stirred solution of 2,3,4,6-tetra-O-benzyl-α-D-thioglucose[35] was dissolved in DCM (10 mL), to which was added Et_3N (0.24 mL, 1.7 mmol), followed by dropwise addition of 3-bromopropanol-1 (0.1 mL, 1.1 mmol) at 0℃. Reaction was allowed to reach room temperature and complete consumption of starting materials was observed after 3 hours. Reaction mixture was dissolved in DCM (30 mL), washed with water (30 mL), brine (30 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 1:1) afforded compound **1n** (0.34g, 66% yield over 2 steps) as a white solid. $[\alpha]_D^{20}$ +47.4 (*c* 1.35, $CHCl_3$); **m.p.** 65-67 °C; **IR** (KBr): 3414, 2866, 1653, 1454, 1066 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.34-7.21 (m, 18H, aromatic), 7.09-7.07 (m, 2H, aromatic), 5.32 (d, 1H, *J* = 4.7 Hz, H-1), 4.91-4.39 (m, 8H, 4xOC$\underline{H}_2$Ph), 4.16-4.13 (m, 1H, H-5), 3.81-3.78 (m, 2H, H-2, H-3), 3.69-3.58 (m, 4H, H-6, C$\underline{H}_2$OH), 3.52 (t, 1H, *J* = 9.7 Hz, H-4), 2.66-2.58 (m, 2H, SC$\underline{H}_2$), 1.83-1.80 (m, 2H, -C$\underline{H}_2$-), 1.67 (t, 1H, *J* = 5.5 Hz, O$\underline{H}$) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 138.8, 138.3, 137.9, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 83.8 (C-1), 82.7 (C-3), 79.7 (C-2), 77.7 (C-4), 75.3, 73.6, 72.7, 70.8 (O$\underline{C}H_2$Ph x4), 68.9 (C-5), 61.5 (C-6), 32.2 (SCH$_2\underline{C}$H$_2$), 26.5 (S$\underline{C}$H$_2$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{37}H_{43}O_6S$ $[M+H]^+$, 615.2780, found: 615.2780.

Synthesis of compound 5a

To a magnetically stirred solution of compound **1a** (0.1g, 0.24 mmol) in anhydrous DCM (5 mL) was charged with pre-activated molecular sieves 4Å (100mg-per- mmol substrate), after which DMTSF (0.14g, 72 mmol) was added in one portion. After complete consumption of starting materials was observed, reaction mixture was quenched with aq. $NaHCO_3$ (5 mL), followed by dissolution in DCM (10 mL), washed with water (30 mL), brine (30 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 1.3:1) afforded compound **5a** (0.1g, 90% yield) as a colorless oil. $[\alpha]_D^{20}$ +31.7 (*c* 0.13, $CHCl_3$); **IR** (KBr): 3018, 1755, 1215, 1039, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.2 (t, 1H, *J* = 7.6 Hz), 5.08 (t, 1H, *J* = 7.8 Hz), 4.98 (t, 1H, *J* = 8.4 Hz), 4.51 (d, 1H, *J* = 6.4 Hz, H-1), 4.26 (dd, 1H, *J* = 9.8 Hz, *J* = 3.8 Hz, H-6'), 4.14 (dd, 1H, *J* = 9.6 Hz, *J* = 1.9 Hz, H-6), 3.97-3.95 (m, 1H, OC$\underline{H}_2$), 3.71-3.68 (m, 1H, H-5), 3.65-3.63 (m, 1H, OC$\underline{H}_2$), 2.76-2.72 (m, 2H, SC$\underline{H}_2$), 2.39 (s, 3H, $SSCH_3$), 2.09-1.95 (m, 14H, 4x$COCH_3$, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170.9, 170.5, 169.6, 169.5 ($\underline{C}OCH_3$), 101.1 (C-1), 73.0 (C-5), 72.0 (C-3), 71.5 (C-2), 68.6 (C-4), 68.1 (O$\underline{C}H_2$), 62.1 (C-6), 34.1 (S$\underline{C}H_2$), 28.8 ($SCH_2\underline{C}H_2$), 23.3 ($SS\underline{C}H_3$), 21.0, 20.9, 20.8 ($CO\underline{C}H_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{18}H_{28}O_{10}S_2$ $[M+Na]^+$, 491.1022, found: 491.1022.

Synthesis of compound 5b

To a magnetically stirred solution of compound **1b** (0.1g, 0.16 mmol) in anhydrous propionitrile (5 mL) was charged with pre-activated molecular sieves 4Å (100mg-per- mmol substrate). Reaction was cooled to -78℃ for 15 minutes, after which DMTSF (0.95g, 0.49 mmol) was added in one portion. Reaction was maintained at this temperature till complete consumption of starting materials was observed, after which reaction mixture was directly quenched with aq. $NaHCO_3$ (5 mL) at -78℃. The suspension was allowed to reach room temperature, followed by dissolution in DCM (20 mL), washed with water (30 mL), brine (30 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 6:1) afforded compound **5b** (63mg, 60% yield) as a colorless oil. $[\alpha]_D^{20}$ +25.1 (*c* 0.37, $CHCl_3$); **IR** (KBr): 2916, 1496, 1454, 1070, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.52-7.27 (m, 18H, aromatic), 7.16-7.14 (m, 2H,

aromatic), 4.93-4.51 (m, 8H, 4xOC$\underline{H}_2$Ph), 4.39 (d, 1H, *J* = 7.7Hz, H-1), 4.06-4.01 (m, 1H), 3.75-3.56 (m, 5H), 3.46-3.42 (m, 2H), 2.81 (t, 2H, *J* = 7.7 Hz, SC$\underline{H}_2$), 2.37 (s, 3H, SSC$\underline{H}_3$), 2.09-2.04 (m, 2H, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 138.6, 138.3, 130.9, 128.6, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8 (m, aromatic), 103.8 (C-1), 84.9 (C-3), 82.5 (C-2), 75.2 (C-4), 75.1 (m, O$\underline{C}$H$_2$Ph), 73.7 (C-5), 68.3 (C-6), 29.9 (d, SCH$_2\underline{C}$H$_2$, S$\underline{C}$H$_2$), 29.5 (SS$\underline{C}$H$_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{38}H_{44}O_6S_2$ $[M+Na]^+$, 683.2477, found: 683.2476.

Synthesis of compound 5c

Folowing the synthesis of compound **5b** starting from compound **1c** (α:β = 1:14) afforded **5c** (58mg, 55% yield) as a colorless oil being a mixture of anomers (α:β = 1:1.14). **IR** (KBr): 3419, 1635, 1095, 1056 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 5.25 (2, 1H, H-1α), 4.67 (d, 1H, *J* = 6.8 Hz, H-1β), 3.96-3.38 (m, 16H, H-2α,β, H-3α,β, H-4α,β, H-5α,β, H-6α,β, OC$\underline{H}_2$α,β), 2.81-2.73 (m, 4H, SC$\underline{H}_2$α, SC$\underline{H}_2$β), 2.40 (m, 6H, SSC$\underline{H}_3$α, SSC$\underline{H}_3$β), 2.07-1.99 (m, 2H, -C$\underline{H}_2$β-), 1.94-1.87 (m, 2H, -C$\underline{H}_2$α-), 0.92-0.87 (m, 72H, 4xSiC(C$\underline{H}_3$)$_3$α, 4xSiC(C$\underline{H}_3$)$_3$β), 0.14-0.01 (m, 48H, 4xSi(C$\underline{H}_3$)$_2$α, 4xSi(C$\underline{H}_3$)$_2$β) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{34}H_{76}O_6S_2Si_4$ $[M+H]^+$, 779.4058, found: 779.4055.

Synthesis of compound 5d

Folowing the synthesis of compound **5b** starting from compound **1d** afforded **5d** (56mg, 49% yield) as a colorless oil. $[\alpha]_D^{20}$ +19.8 (*c* 0.68, $CHCl_3$); **IR** (KBr): 3419, 2918, 1635, 1095 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 4.26 (d, 1H, *J* = 7.6 Hz, H-1), 4.14-4.1 (m, 1H, OC$\underline{H}_2$); 3.81-3.78 (m, 1H, OC$\underline{H}_2$), 3.63-3.52 (m, 11H, 3xOC$\underline{H}_3$, H-5, H-6), 3.40 (s, 3H, OC$\underline{H}_3$), 3.28-3.25 (m, 1H, H-4), 3.25-3.13 (m, 2H, H-3, H-6), 3.01-2.98 (m, 1H, H-2), 2.94 (t, 2H, *J* = 6.7 Hz, SC$\underline{H}_2$), 2.40 (s, 3H, SSC$\underline{H}_3$) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 103.7 (C-1), 86.6 (C-3), 83.8 (C-2), 79.5 (C-4), 74.8 (C-5), 71.5 (C-6), 68.3 (O$\underline{C}$H$_2$), 61.1, 60.8, 60.6, 59.6 (O$\underline{C}$H$_3$ x4), 37.8 (S$\underline{C}$H$_2$), 23.6 (SS$\underline{C}$H$_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{13}H_{26}O_6S_2$ $[M+Na]^+$, 365.1069, found: 365.1066.

Synthesis of compound 5e

Folowing the synthesis of compound **5b** starting from compound **1e** afforded **5e** (58g, 51% yield) as a colorless oil. $[\alpha]_D^{20}$ +22.1 (*c* 0.37, $CHCl_3$); **IR** (KBr): 3419, 2918, 1627, 1095 cm^{-1}; **^{1}H NMR (400**

MHz, $CDCl_3$): δ 4.22 (d, 1H, J = 7.7 Hz, H-1), 4.01-3.96 (m, 1H, OCH_2); 3.64-3.53 (m, 12H, 3xOCH_3, OCH_2, H-5, H-6), 3.40 (s, 3H, OCH_3), 3.28-3.24 (m, 1H, H-4), 3.17-3.11 (m, 2H, H-3, H-6), 3.00-2.96 (m, 1H, H-2), 2.80 (t, 2H, J = 7.4 Hz, SCH_2), 2.40 (s, 3H, $SSCH_3$); 2.05-1.98 (m, 2H, -CH_2-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 103.6 (C-1), 86.6 (C-3), 83.9 (C-2), 79.5 (C-4), 74.8 (C-5), 71.5 (C-6), 68.1 (OCH_2), 61.0, 60.7, 60.6, 59.6 (OCH_3 x4), 34.7 (SCH_2), 29.5 (SCH_2CH_2), 23.4 ($SSCH_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{14}H_{28}O_6S_2$ $[M+Na]^+$, 379.1225, found: 379.1225.

Synthesis of compound 5f

Folowing the synthesis of compound **5b** starting from compound **1f** afforded **5f** (55mg, 49% yield) as a colorless oil. $[\alpha]_D^{20}$ +1.24 (*c* 1.7, $CHCl_3$); **IR** (KBr): 3419, 2918, 1635, 1446, 1095 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 4.21 (d, 1H, J = 7.8 Hz, H-1), 3.95-3.91 (m, 1H, OCH_2); 3.63-3.51 (m, 12H, 3xOCH_3, OCH_2, H-5, H-6), 3.40 (s, 3H, OCH_3), 3.27-3.24 (m, 1H, H-4), 3.15-3.10 (m, 2H, H-3, H-6), 2.98-2.75 (m, 1H, H-2), 2.73-2.46 (m, 2H, SCH_2), 2.40 (s, 3H, $SSCH_3$); 1.83-1.71 (m, 4H, -CH_2CH_2-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 103.5 (C-1), 86.6 (C-3), 83.9 (C-2), 79.6 (C-4), 74.7 (C-5), 71.6 (C-6), 69.4 (OCH_2), 62.6, 61.0, 60.7, 59.6 (OCH_3 x4), 38.1 (SCH_2), 31.6 (OCH_2CH_2), 28.6 (SCH_2CH_2), 23.5 ($SSCH_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{15}H_{30}O_6S_2$ $[M+Na]^+$, 393.1382, found: 393.1396.

Synthesis of compound 5g

Folowing the synthesis of compound **5b** starting from compound **1g** afforded **5g** (57mg, 50% yield) as a colorless oil. $[\alpha]_D^{20}$ +6.8 (*c* 0.93, $CHCl_3$); **IR** (KBr): 3421, 1627, 1074, 794 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 4.21 (d, 1H, J = 7.8 Hz, H-1), 3.94-3.88 (m, 1H, OCH_2); 3.63-3.45 (m, 12H, 3xOCH_3, OCH_2, H-5, H-6), 3.40 (s, 3H, OCH_3), 3.26-3.24 (m, 1H, H-4), 3.17-3.09 (m, 2H, H-3, H-6), 2.99-2.96 (m, 1H, H-2), 2.70 (t, 2H, J = 7.4 Hz, SCH_2), 2.40 (s, 3H, $SSCH_3$); 1.76-1.25 (m, 6H, -$CH_2CH_2CH_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 103.6 (C-1), 86.6 (C-3), 83.9 (C-2), 79.6 (C-4), 74.7 (C-5), 71.6 (C-6), 69.8 (OCH_2), 62.9, 61.0, 60.6 (OCH_3 x4), 29.5 (SCH_2), 29.1 (OCH_2CH_2), 25.2 (SCH_2CH_2), 24.8 ($SCH_2CH_2CH_2$), 23.5 ($SSCH_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{16}H_{32}O_6S_2$ $[M+Na]^+$, 407.1538, found: 407.1535.

Synthesis of compound 5h

Folowing the synthesis of compound **5a** starting from compound **1h** afforded **5h** (0.088g, 81% yield) as a colorless oil. $[\alpha]_D^{20}$ -1.19 (*c* 0.57, $CHCl_3$); **IR** (KBr): 3421, 1749, 1629, 1226, 1039 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.78-7.76 (m, 1H, aromatic), 7.37-7.28 (m, 3H, aromatic), 5.18 (t, 1H, *J* = 9.4 Hz, H-3), 5.13-5.04 (m, 2H, H-4, H-2), 4.98 (d, 1H, *J* = 12.5 Hz, OC$\underline{H}_2$Ph), 4.81 (d, 1H, *J* = 12.5 Hz, OC$\underline{H}_2$Ph), 4.55 (d, 1H, *J* = 7.8 Hz, H-1), 4.29 (dd, 1H, *J* = 12.3 Hz, *J* = 4.8 Hz, H-6'), 4.18 (dd, 1H, *J* = 12.2 Hz, *J* = 2.4 Hz, H-6), 3.72-3.68 (m, 1H, H-5), 2.42 (s, 3H, SSC$\underline{H}_3$), 2.11, 2.02, 2.02, 1.99 (s, 12H, 4xCOC$\underline{H}_3$) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170.9, 170.5, 169.6 (C$\underline{O}$CH_3 x4), 136.1, 129.4, 129.3, 129.0, 127.6 (m, aromatic), 99.5 (C-1), 73.0 (C-5), 72.1 (C-3), 71.4 (C-2), 68.7 (C-4), 68.6 (O$\underline{C}H_2$), 62.1 (C-6), 22.9 (SS$\underline{C}H_3$), 21.0, 20.8 (CO$\underline{C}H_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{22}H_{28}O_{10}S_2$ $[M+Na]^+$, 539.1022, found: 539.1021.

Synthesis of compound 5i

Folowing the synthesis of compound **5a** starting from compound **1i** afforded **5i** (0.1g, 91% yield) as a colorless oil. $[\alpha]_D^{20}$ -51.0 (*c* 1.1, $CHCl_3$); **IR** (KBr): 3419, 1747, 1635, 1224, 1041 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.48-5.23 (m, 2H, H-3, H-4), 5.11 (t, 1H, *J* = 9.4 Hz, H-2), 4.57 (d, 1H, *J* = 9.4 Hz, H-1), 4.21-4.14 (m, 2H, H-6), 3.76-3.72 (m, 1H, H-5), 2.47 (s, 3H, SSC$\underline{H}_3$), 2.07, 2.06, 2.03, 2.01 (s, 12H, 4xCOC$\underline{H}_3$) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170.7, 170.4, 169.6, 169.4 (C$\underline{O}$CH_3 x4), 88.1 (C-1), 76.2 (C-5), 74.0 (C-3), 69.2 (C-2), 68.2 (C-4), 62.2 (d, O$\underline{C}H_2$, C-6), 24.8 (SS$\underline{C}H_3$), 20.9, 20.8, 20.7 (CO$\underline{C}H_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{15}H_{22}O_9S_2$ $[M+Na]^+$, 433.0603, found: 433.0606.

Synthesis of compound 5j

Folowing the synthesis of compound **5a** starting from compound **1j** afforded **5j** (0.99g, 89% yield) as a colorless oil. $[\alpha]_D^{20}$ +26.9 (*c* 0.33, $CHCl_3$); **IR** (KBr): 3018, 1755, 1218, 1037, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.38 (dd, 1H, *J* = 3.4 Hz, *J* = 0.9 Hz), 5.19 (dd, 1H, *J* = 10.5 Hz, *J* = 7.9 Hz), 5.01 (dd, 1H, *J* = 10.5 Hz, *J* = 3.4 Hz), 4.46 (d, 1H, *J* = 7.9 Hz, H-1), 4.17-4.09 (m, 2H), 3.98-3.96 (m, 1H), 3.92-3.90 (m, 1H), 3.65-3.63 (m, 1H), 2.77-2.71 (m, 2H, SC$\underline{H}_2$), 2.39 (s, 3H, SSC$\underline{H}_3$), 2.14-1.95 (m, 14H, 4xCOC$\underline{H}_3$, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170.6, 170.5, 170.4, 169.6 (C$\underline{O}$CH_3 x4),

101.6 (C-1), 71.1 (C-5), 70.8 (C-3), 69.0 (C-2), 68.1 (C-4), 67.2 (O<u>C</u>H$_2$), 61.5 (C-6), 34.1 (S<u>C</u>H$_2$), 28.8 (SCH$_2$<u>C</u>H$_2$), 23.2 (SS<u>C</u>H$_3$), 21.0, 20.9, 20.8 (CO<u>C</u>H$_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{18}H_{28}O_{10}S_2$ $[M+Na]^+$, 491.1022, found: 491.1023.

Synthesis of compound 5k

Folowing the synthesis of compound **5b** starting from compound **1k** afforded **5k** (62mg, 59% yield) as a colorless oil. $[\alpha]_D^{20}$ +112.7 (*c* 0.1, $CHCl_3$); **IR** (KBr): 2916, 1497, 1455, 1070, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.36-7.27 (m, 20H, aromatic), 4.95-4.39 (m, 8H, 4xOC<u>H</u>$_2$Ph), 4.35 (d, 1H, *J* = 7.7Hz, H-1), 4.01-3.98 (m, 2H, OC<u>H</u>$_2$), 3.89 (t, 1H, *J* = 2.6 Hz, H-4), 3.80 (dd, *J* = 9.7 Hz, *J* = 7.7 Hz, H-6), 3.64-3.50 (m, 5H, OC<u>H</u>$_2$, H-2, H-3, H-5, H-6), 2.79 (t, 2H, *J* = 7.32 Hz, SC<u>H</u>$_2$), 2.36 (s, 3H, SSC<u>H</u>$_3$), 2.05-2.01 (m, 2H, -C<u>H</u>$_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 128.6, 128.5, 128.3, 128.1, 128.0, 127.8, 127.7, 104.1 (C-1), 82.5 (C-3), 79.7 (C-2), 77.5 (C-4), 75.5, 74.7, 73.6 (O<u>C</u>H$_2$Ph x4), 73.0 (C-5), 69.0 (C-6), 68.2 (O<u>C</u>H$_2$), 34.9 (S<u>C</u>H$_2$), 29.6 (SCH$_2$<u>C</u>H$_2$), 23.5 (SS<u>C</u>H$_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{38}H_{44}O_6S_2$ $[M+Na]^+$, 683.2477, found: 683.2467.

Synthesis of compound 5l

Folowing the synthesis of compound **5a** starting from compound **1l** afforded **5l** (0.104g, 93% yield) as a colorless oil. $[\alpha]_D^{20}$ -72.8 (*c* 0.15, $CHCl_3$); **IR** (KBr): 3019, 1756, 1215, 1039, 755 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.33-5.22 (m, 3H, H-2, H-3, H-4), 4.81 (d, 1H, *J* = 1.6 Hz, H-1), 4.27 (dd, 1H, *J* = 12.2 Hz, *J* = 5.4 Hz, H-6'), 4.11 (dd, 1H, *J* = 9.2 Hz, *J* = 2.4 Hz, H-6), 3.99-3.95 (m, 1H, H-5), 3.85-3.80 (m, 1H, OC<u>H</u>$_2$), 3.57-3.52 (m, 1H, OC<u>H</u>$_2$), 2.78 (t, 2H, *J* = 7 Hz, SC<u>H</u>$_2$), 2.40 (s, 3H, SSC<u>H</u>$_3$), 2.15-1.98 (m, 14H, 4xCOC<u>H</u>$_3$, -C<u>H</u>$_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170.8, 170.3, 170.1, 169.9 (<u>C</u>OCH$_3$ x4), 97.8 (C-1), 69.7 (C-5), 69.3 (C-3), 68.8 (C-2), 66.4 (C-4), 66.3 (O<u>C</u>H$_2$), 62.6 (C-6), 34.3 (S<u>C</u>H$_2$), 28.6 (SCH$_2$<u>C</u>H$_2$), 23.2 (SS<u>C</u>H$_3$), 21.0, 20.9 (CO<u>C</u>H$_3$ x4) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{18}H_{28}O_{10}S_2$ $[M+Na]^+$, 491.1022, found: 491.1025.

Synthesis of compound 5m

Folowing the synthesis of compound **5b** starting from compound **1m** afforded **5m** (66mg, 63% yield)

as a colorless oil. $[\alpha]_D^{20}$ +23.6 (*c* 0.05, $CHCl_3$); **IR** (KBr): 2926, 1496, 1454, 1070, 744 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.39-7.24 (m, 18H, aromatic), 7.17-7.1(m, 2H, aromatic), 4.86 (d, 1H, *J* = 1.7Hz, H-1), 4.88-4.49 (m, 8H, 4xOC$\underline{H}_2$Ph), 3.95 (t, 1H, *J* = 9.2 Hz, H-4), 3.87 (dd, *J* = 9.6 Hz, *J* = 2.9 Hz, H-3), 3.78-3.71 (m, 5H, OC$\underline{H}_2$, H-2, H-5, H-6), 3.47-3.44 (m, 1H, OC$\underline{H}_2$), 2.69 (t, 2H, *J* = 7.0 Hz, SC$\underline{H}_2$), 2.37 (s, 3H, SSC$\underline{H}_3$), 1.95-1.91 (m, 2H, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 138.7, 138.6, 128.6, 128.5, 128.3, 128.0, 127.9, 127.8 (m, aromatic), 104.7 (C-1), 98.2 (C-3), 80.3 (C-2), 77.5 (C-4), 75.4, 75.1, 74.9, 73.6 (O$\underline{C}H_2$Ph x4), 72.2 (C-5), 69.5 (C-6), 65.8 (O$\underline{C}H_2$), 34.8 (S$\underline{C}H_2$), 29.1 (SCH$_2\underline{C}$H$_2$), 23.4 (SS$\underline{C}H_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{38}H_{44}O_6S_2$ $[M+Na]^+$, 683.2477, found: 683.2476.

Synthesis of compound 5n

To a magnetically stirred solution of compound **1n** (0.1g, 0.16 mmol) in anhydrous Et_2O (5 mL) was charged with pre-activated molecular sieves 4Å (100mg-per- mmol substrate). Reaction was cooled to -78℃ for 15 minutes, after which DMTSF (0.95g, 0.49 mmol) was added in one portion. Reaction was maintained at this temperature till complete consumption of starting materials was observed, after which reaction mixture was directly quenched with aq. $NaHCO_3$ (5 mL) at -78℃. The suspension was allowed to reach room temperature, followed by dissolution in Et_2O (20 mL), washed with water (30 mL), brine (30 mL). Organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, after which flash chromatography on silica gel (hexane/EtOAc = 6:1) afforded compound **5n** (65mg, 62% yield) as a colorless oil. $[\alpha]_D^{20}$ +50.1 (*c* 0.03, $CHCl_3$); **IR** (KBr): 2912, 1495, 1453, 1068, 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.52-7.28 (m, 18H, aromatic), 7.14-7.11 (m, 2H, aromatic), 4.99-4.45 (m, 8H, 4xOC$\underline{H}_2$Ph), 4.48 (d, 1H, *J* = 2.7 Hz, H-1), 3.96 (t, 1H, *J* = 9.3 Hz, H-4); 3.78-3.70 (m, 3H, OC$\underline{H}_2$, H-6), 3.65-3.61 (m, 2H, H-3, H-5), 3.57-3.48 (m, 2H, OC$\underline{H}_2$, H-2), 2.82-2.77 (m, 2H, SC$\underline{H}_2$), 2.38 (s, 3H, SSC$\underline{H}_3$), 2.07-1.99 (m, 2H, -C$\underline{H}_2$-) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 128.7, 128.6, 128.2, 128.1, 127.9, 97.4 (C-1), 82.3 (C-3), 80.3 (C-2), 77.5 (C-4), 75.9, 75.3, 73.7 (O$\underline{C}H_2$Ph x4), 73.5 (C-5), 70.5 (C-6), 66.4 (O$\underline{C}H_2$), 34.7 (S$\underline{C}H_2$), 30.1 (SCH$_2\underline{C}$H$_2$) 23.4 (SS$\underline{C}H_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{38}H_{44}O_6S_2$ $[M+Na]^+$, 683.2477, found: 683.2476.

Compound 6a: $[\alpha]_D^{20}$ -15.0 (*c* 1.15, $CHCl_3$); **m.p.** 47-48 °C; **IR** (KBr): 3435, 3299, 2959, 2875, 1750, 1372, 1227 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 5.18 (t, 1H, *J* = 9.6 Hz, H-3), 5.06 (t, 1H, *J* = 9.6 Hz, H-4), 4.96 (t, 1H, *J* = 9.6 Hz, H-2), 4.50 (d, 1H, *J* = 8.0 Hz, H-1), 4.27 (dd, 1H, *J* = 12.3 Hz, *J* = 4.8 Hz, H-6a), 4.14 (dd, 1H, *J* = 12.3 Hz, *J* = 2.4 Hz, H-6b), 3.88 (dt, 1H, *J* = 9.7 Hz, *J* = 6.3 Hz, OC$\underline{H}_2$), 3.70 (ddd, 1H, *J* = 9.6 Hz, *J* = 4.8 Hz, *J* = 2.4 Hz, H-5), 3.49 (dt, 1H, *J* = 9.7 Hz, *J* = 6.8 Hz, OC$\underline{H}_2$), 2.06-1.98 (m, 12H, 4xCOC$\underline{H}_3$), 1.56 (m, 2H, $OCH_2C\underline{H}_2$), 1.35 (m, 2H, $OCH_2CH_2C\underline{H}_2$), 0.91 (t, 3H, *J* = 7.4 Hz, C$\underline{H}_3$) ppm; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 170.9, 170.5, 169.6, 169.5 ($\underline{C}OCH_3$ x4), 101.0 (C-1), 73.1 (C-3), 71.9 (C-5), 71.5 (C-2), 70.1 (O$\underline{C}H_2$), 68.7 (C-4), 62.2 (C-6), 31.5 ($\underline{C}H_2$), 20.9, 20.8, 20.7, 19.1 (CH_2), 13.9 ($\underline{C}H_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{18}H_{28}O_{10}Na$ $[M+Na]^+$, 427.1580, found: 427.1584.

Compound 6b: $[\alpha]_D^{20}$ +16.5 (*c* 1.3, $CHCl_3$); **m.p.** 69-71 °C; **IR** (KBr): 2912, 1495, 1453, 1068, 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.36-7.25 (m, 18H, aromatic), 7.17-7.14 (m, 2H, aromatic), 4.94-4.51 (m, 8H, 4xOC$\underline{H}_2$Ph), 4.39 (d, 1H, *J* = 7.8 Hz, H-1), 3.96 (dt, 1H, *J* = 12.5 Hz, *J* = 5.9 Hz, OC$\underline{H}_2$); 3.73 (dd, 1H, *J* = 10.5 Hz, *J* = 1.9 Hz, H-6a), 3.69-3.54 (m, 5H), 3.46-3.44 (m, 2H, OC$\underline{H}_2$, H-2), 1.65-1.25 (m, 4H, OC$\underline{H}_2$C$\underline{H}_2$), 0.93 (s, 3H, *J* = 7.26 Hz, C$\underline{H}_3$) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 138.8, 138.7, 138.4, 138.3, 128.6-127.7 (aromatic), 103.8 (C-1), 84.9 (C-3), 82.5 (C-4), 78.2 (C-5), 77.5, 75.9, 75.2 75.0 (O$\underline{C}H_2$Ph x4), 70.0 (C-6), 69.2 (O$\underline{C}H_2$), 32.1 ($OCH_2\underline{C}H_2$), 19.5 ($OCH_2CH_2\underline{C}H_2$), 14.1 ($\underline{C}H_3$) ppm; **HRMS (ESI)**: *m/z* calcd for $C_{38}H_{45}O_6$ $[M+H]^+$, 597.3211, found: 597.3213.

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Supporting Information Available: Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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