Protective group strategies in carbohydrate and peptide chemistry

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CHAPTER

2

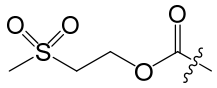
The methylsulfonylethoxycarbonyl (Msc) as hydroxyl protecting group in carbohydrate chemistry[1]

Introduction:

The synthesis of (complex) oligosaccharides is a multi-step process, in which protective group manipulations play a central role.[2] Protecting groups in the donor and acceptor molecules, the reaction partners in a glycosylation event, not only control the regioselectivity but also determine the productivity and stereochemistry of glycosylation reactions.[3] Additionally, elongation of oligosaccharides generally requires the selective removal of one of the protecting groups in the growing chain. Therefore, progress in the assembly of oligosaccharides can be realized by the development of new protecting groups with improved properties, such as ease of introduction and removal and orthogonality toward other protective groups.[4] This chapter describes the use of the

methylsulfonylethoxycarbonyl group (Msc, **1**, Figure 1) as hydroxyl protecting group in carbohydrate chemistry.

Figure 1: The Msc protecting group.



1, Msc

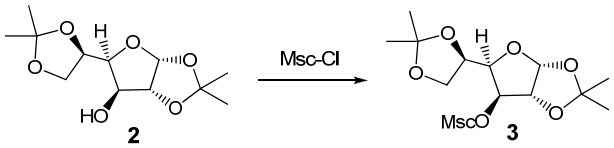
The methylsulfonylethoxycarbonyl (Msc) group, developed by Tesser and coworkers,[5] is well known in peptide chemistry for the protection of amino functions. The Msc-group is removed by base-mediated β-elimination while it resists catalytic hydrogenation and is highly stable in acidic media. The Msc group has also proven to be suitable for the protection of the guanidino function in the side chain of arginine during solid phase peptide synthesis.[6] In addition, methylsulfonylethyl esters have been employed to mask carboxylic acids[7] and used as protective groups en route to phosphate mono- and diesters.[8,9] Conversely, the sulfonylethoxycarbonyl groups, related to the Msc group, have only scarcely been applied to protect alcohol functions.[10,11] In the meantime, the 9-fluorenylmethyl carbonate (Fmoc) is becoming increasingly popular in carbohydrate chemistry for the protection of alcohol functions.[12,13] It was envisaged that the Msc group could be a promising hydroxyl protecting group as it would be equally stable but sterically less demanding and less lipophilic than the Fmoc carbonate.

Results and discussion:

As a first research objective, the optimal conditions for the introduction of the Msc group were investigated using glucofuranose **2** as a model compound (Table 1). In the first attempt a DCM solution of compound **2** was treated with methylsulfonylethoxycarbonyl chloride (Msc-Cl) and 3 equivalents of triethylamine (TEA) (Table 1, Entry 1). The reaction did not proceed and the starting material could be recovered. Employment of the same solvent and 2,6-lutidine (3 eq.) as a base led to the isolation of 1,2:5,6-di-*O*-isopropylidene-3-*O*-methylsulfonylethoxycarbonyl-α-D-glucofuranose **3** in moderate yield (41%, Table 1, Entry 2). Using pyridine (3 eq.) as base in dioxane (Table 1, Entry 3) the

reaction proceeded equally sluggishly, but the yield of **3** was improved to 55%. Returning to the use of DCM as a solvent not only reduced the reaction time to 4 hours, but also increased the yield of **3** to 99% (Table 1, Entry 4).

Table 1: Installation of the Msc group on carbohydrate hydroxyls.

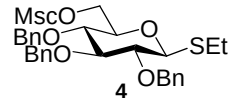
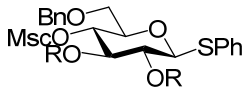
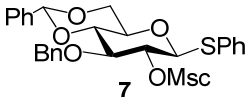
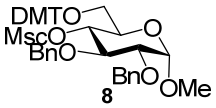
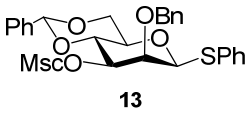
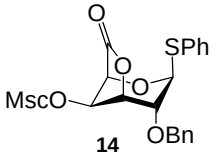
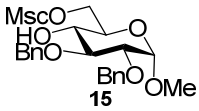


2 **3**

Entry	Conditions	Time	Yield
(1)	DCM, Et_3N (3 eq.), 0 ^oC-rt	90h	No Conversion
(2)	DCM, Lutidine (3 eq.), 0 ^oC-rt	90h	41%
(3)	Dioxane, Pyridine (3 eq.), 0 ^oC-rt	90h	55%
(4)	DCM, Pyridine (3 eq.), 0 ^oC-rt	4h	99%

The applicability of the DCM/pyridine conditions was further evaluated by the introduction of the Msc group onto a range of partially protected pyranose building blocks. The Msc group was readily introduced on the primary hydroxyl function of ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside to give **4** in 98% yield (Table 2, Entry 1). The protection of a variety of secondary hydroxyl functions with the Msc group proceeded uneventfully, leading to high yields of the expected products (Table 2, Entry 2-6).[14] It is of interest to note that migration of the benzoyl group in the starting compound (Table 2, entry 2) was not observed and that the labile galacturonic acid lactone endured the mild conditions (Table 2, Entry 6). Moreover, subjection of ethyl 2,3-di-*O*-benzyl-α-D-glucopyranoside to these conditions, albeit at a lower temperature (-20 ^oC), led to the regioselective introduction of the Msc group at the primary position of the diol starting compound (Table 2, Entry 7).

Table 2: Installation of the Msc on carbohydrate hydroxyls.[a]

Entry	Product	Temperature	Time	Yield
1	 **4**	0 ºC-RT	3 h	98%
2	 **5** R = Bn **6** R = Bz	0 ºC-RT	5 h	**5** (R = Bn): 78% **6** (R =Bz): 76%
3	 **7**	0 ºC-RT	4 h	79%
4	 **8**	0 ºC-RT	4 h	79%
5	 **13**	0 ºC-RT	4 h	93%
6	 **14**	0 ºC-RT	3 h	88%
7	 **15**	-20 ºC-RT	5 h	90%

[a] Msc-Cl (2 eq.), pyridine (3 eq.), DCM (0.2 M).

Next, the most favorable conditions for cleavage of the Msc group were examined using 1,2:5,6-di-*O*-isopropylidene-3-*O*-methylsulfonylethoxycarbonyl-α-D-glucofuranose **3**. As summarized in Table 3, the use of a catalytic amount of sodium methoxide (NaOMe, 0.1 eq.) in methanol required 18 hours to completely remove the Msc group (Table 3, Entry

1). The deblocking of the Msc on **3** *via* a β-elimination with the aid of 30 equivalents of triethylamine reached completion after 20 hours (Table 3, Entry 2). On the other hand, tetrabutylammonium fluoride (TBAF, 0.1 eq.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.1 eq.) eliminated the Msc group within 30 minutes (Table 3, Entries 3 and 4). The removal of the Msc group from **6** went smoothly and left all the benzoyl groups intact, thereby illustrating the mildness of the cleavage conditions (Table 3, Entry 5). Analogously, cleavage of the Msc group from galacturonic acid lactone **14**[15] was accomplished without compromising the integrity of the labile lactone ring to afford the expected alcohol in 97% yield (Table 3, Entry 6).

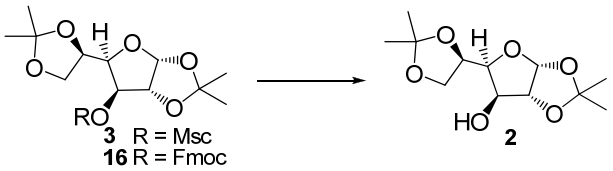
Table 3: Cleavage of the Msc group.

Entry	Substrate	Conditions	Quantity	Time	Yield
1	**3**	NaOMe, MeOH	0.1 eq	18 h	100%
2	**3**	Et_3N, DCM	30 eq	20 h	100%
3	**3**	TBAF, THF	0.1 eq	30 min.	100%
4	**3**	DBU, DMF	0.1 eq	25 min.	100%
5	**6**	DBU, DMF	0.1 eq	30 min	98%
6	**14**	DBU, DMF	0.1 eq	1 min.	97%

Having established the conditions for both installation and cleavage of the Msc group, the stabilities of the Msc group and the 9-fluorenylmethoxycarbonyl (Fmoc) group were compared. With 0.1 equivalents DBU the Fmoc group was cleaved from glucofuranose **16** within 5 minutes while the removal of the Msc group in the corresponding glucofuranose **3** needed 25 minutes (Table 4, Entry 1 and 2). The removal of the Fmoc group in **16** required 2 hours when triethylamine (TEA, 30 eq.) was used in DCM (Table 4, Entry 3) while cleavage of the Msc group in **3** under identical conditions took 20

hours (Table 4, Entry 4). The outcome of these experiments indicates that the Msc group is slightly more stable than the Fmoc group.

Table 4: Comparison of the stability of the Msc group and the Fmoc group.

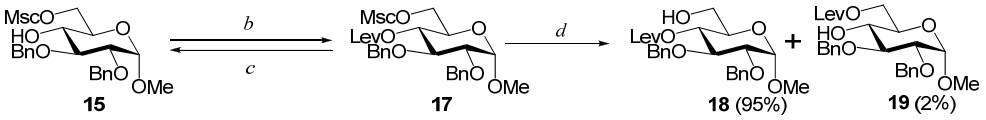


Entry	Conditions	R	Quantity	Time	Yield
1	DBU, DMF	Fmoc	0.1 eq	5 min	87%
2		Msc	0.1 eq	25 min.	92%
3	Et_3N, DCM	Fmoc	30 eq	2 h	89%
4		Msc	30 eq	20 h	93%

Protecting groups that can be selectively cleaved en route to a target oligosaccharide are of prime importance in synthetic carbohydrate chemistry. As the Msc group could be selectively cleaved in the presence of benzoyl esters (*vide supra*), the orthogonality of the Msc group and the levulinoyl (Lev) ester was explored. To this end alcohol **15** was levulinoylated to provide fully protected glucopyranoside **17** (Scheme 1).

The levulinoyl group of **17** could be cleaved without affecting the Msc carbonate at the primary C6-OH position by standard treatment with hydrazine hydrate in a mixture of

Scheme 1: Orthogonality of the Msc and the Lev.

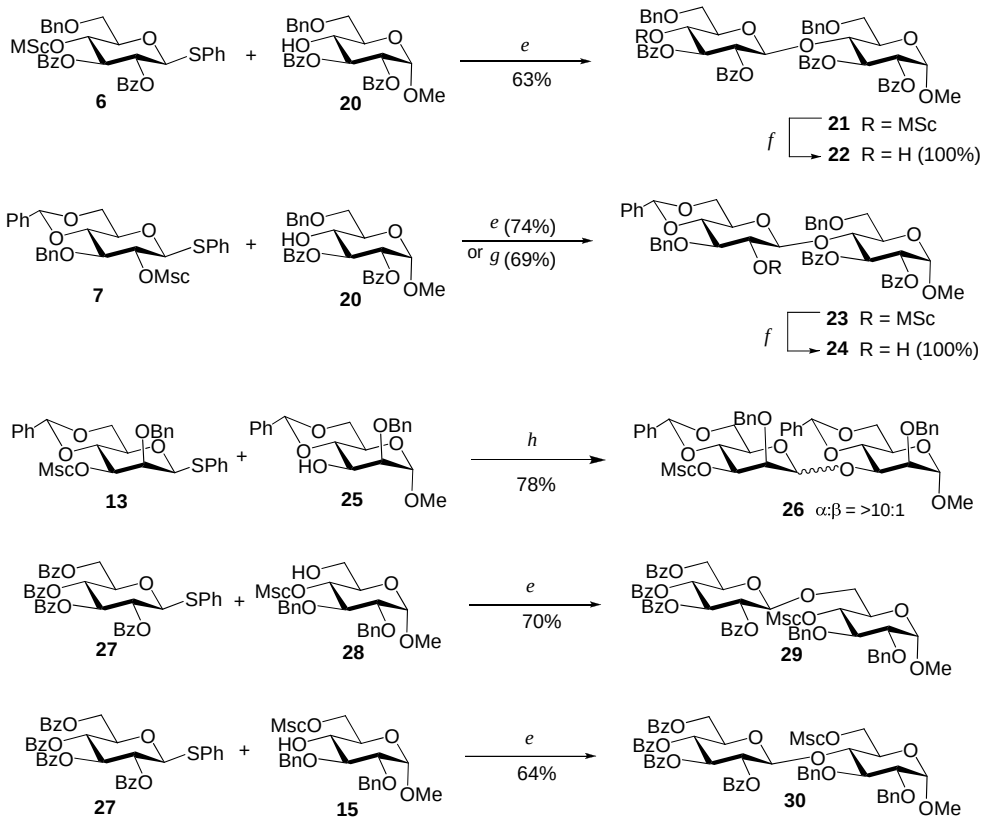


Reagents and conditions; *b*) LevOH, DMAP, EDC.HCl, DCM, 1 h, 89%; *c*) $H_2NNH_2.H_2O$, pyridine/HOAc, 5 min, 96%; *d*) DBU, DMF, 25 min.

pyridine and acetic acid. Alternatively, cleavage of the Msc group at C4-OH in **17** was accomplished with catalytic amount of DBU to provide primary alcohol **18** in 95% yield. Apart from this, 2% of 6-*O*-levulinoylated side product was isolated, originating from migration of the levulinoyl group from the secondary C4-OH to the primary C6-OH. These experiments indicate that the Msc and the Lev protective groups are orthogonal.[16]

Next the feasibility of Msc-protected carbohydrates in a set of glycosylation reactions was investigated (Scheme 2). In the first example the Msc-protected thioglucoside **6** was condensed with methyl glucoside **20** under the influence of *N*-iodosuccinimide (NIS)

Scheme 2: Glycosylation reactions using donors or acceptors containing the Msc group.



Reagents and conditions; *e*) NIS, TMSOTf, DCM, -40 ºC-RT, 1h; *f*) DBU, dioxane, 30 min; *g*) Ph_2SO, Tf_2O TTBP, DCM, -60 ºC-RT; *h*) Ph_2SO, Tf_2O TTBP, DCM, -78 ºC.

and a catalytic amount of trimethysilyltriflate (TMSOTf) to provide disaccharide **21** in 63% yield. The Msc group could be selectively removed from this disaccharide leaving all of the benzoyl functionalities untouched to give **22** in excellent yield. The second glycosylation employed thioglucose donor **7**, having the Msc group located on the C2-OH, acceptor **20** and the same activator system. The β-linked dimer **23** was obtained in 71% yield, showing that the methylsulfonylethyl carbonate provided efficient anchimeric assistance in the glycosylation reaction. When the same donor (**7**) and acceptor (**20**) were condensed, using diphenylsulfoxide (Ph_2SO) in combination with trifluoromethanesulfonic anhydride (Tf_2O)[17] and an excess tri-*tert*-butylpyrimidine (TTBP)[18] disaccharide **23** was isolated in similar yield (67%). This result indicates that the presence of the Msc carbonate at C2 excludes the unwanted formation of orthoester, even under non-acidic conditions. Treatment of dimer **23** with a catalytic amount of DBU quantitatively liberated the C2'-OH to afford **24**. Coupling of Msc-protected thiomannoside **13** with methyl mannoside **25** using the Ph_2SO/Tf_2O[19] activator system and an excess of TTBP afforded disaccharide **26** in 78% yield as an anomeric mixture (α:β >10:1), indicating that the Msc group also provides anchimeric assistance from the 3-position (for a more detailed discussion, see Chapter 4).[20] The Msc group was also tolerated when present in acceptor building blocks as shown in the next glycosylations in which the perbenzoylated *S*-phenyl glucoside **27** was coupled to both primary alcohol **28** and secondary alcohol **15** to furnish dimers **29** and **30** in 70% and 64% yield respectively.

Conclusion:

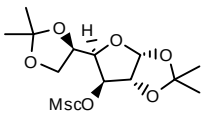
This chapter described the successful application of the methylsulfonylethoxycarbonyl (Msc) group as a non-lipophilic protecting group for hydroxyl functions in oligosaccharide synthesis. The Msc group can be introduced using standard conditions for the formation of carbonates and can be cleaved *via* β-elimination using mildly basic conditions to which commonly used ester protecting groups are stable. The Msc group is slightly more stable than the Fmoc group and is orthogonal with the levulinoyl group. The Msc group is completely stable to acid mediated glycosylation conditions, provides anchimeric assistance and excludes orthoester formation, when placed on the C2-OH of a glycosyl donor.

Experimental:

General: Dichloromethane was refluxed with P_2O_5 and distilled before use. Trifluoromethanesulfonic anhydride was distilled from P_2O_5. Traces of water in donor and acceptor glycosides, diphenylsulfoxide and TTBP were removed by co-evaporation with toluene. Molecular sieves 3Å were flame dried before use. All other chemicals (Acros, Fluka, Merck) were used as received. Column chromatography was performed on Screening Devices silica gel 60 (0.040-0.063 mm). Size exclusion chromatography was performed on Sephadex LH20 (eluent MeOH/DCM = 1/1). TLC analysis was conducted on DC-alufolien (Merck, kiesel gel 60, F_{245}). Compounds were visualized by UV absorption (245 nm), by spraying with 20% H_2SO_4 in ethanol or by spraying with a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (25g/L) and $(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$ (10g/L) in 10% $H_2SO_{4\,(aq)}$ followed by charring at ~150 ºC. IR spectra were recorded on a Shimadzu FTIR-8300 and are reported in cm^{-1}. Optical rotations were measured on a Propol automatic polarimeter. ^1H and ^{13}C NMR spectra were recorded with a Bruker AV 400 (400 MHz and 100 MHz respectively), AV 500 (500 MHz and 125 MHz respectively). NMR spectra were recorded in $CDCl_3$ unless stated otherwise. Chemical shift are relative to tetramethylsilane and are given in ppm. Coupling constants are given in Hz. All given ^{13}C spectra are proton decoupled. High resolution mass spectra were recorded on a LTQ-Orbitrap (thermo electron).

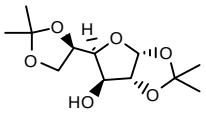
General method for the introduction of the Msc group: A solution of alcohol in DCM (0.2 M) was cooled to 0 ºC before pyridine (3 eq) was added. Methylsulfonylethoxycarbonyl chloride (Msc-Cal, 10% in DCM, 2 eq) was added drop-wise at 0 ºC over the span of 30 minutes. The reaction mixture was allowed to warm to room temperature. The reaction mixture was quenched with methanol, diluted with DCM, washed with $NaHCO_{3\,(aq)}$ and brine, dried over $MgSO_4$, filtered, concentrated and purified by silica gel column chromatography.

General method for glycosylations using NIS/TMSOTf: A solution of 1-thio-β-D-glucopyranoside (donor) and acceptor in DCM (0.05 M) was stirred over activated MS3Å for half an hour before *N*-iodosuccinimide (1.3 eq with respect to the donor) was added. The mixture was cooled to -40 ºC followed by the addition of trimethylsilyl trifluoromethanesulfonate (0.1 eq). The mixture was allowed to warm to room temperature. The reaction mixture was quenched with triethylamine (5 eq), filtered, diluted with EtOAc and washed with $Na_2S_2O_{3\,(aq)}$. The aqueous layer was extracted with EtOAc thrice, dried over $MgSO_4$, filtered, concentrated and purified by silica gel column chromatography.



1,2:5,6-di-*O*-isopropylidene-3-*O*-methylsulfonylethoxycarbonyl-α-D-glucofuranose (3): Compound **3** was prepared according to the general procedure for the introduction of the Msc group from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **2** (1.30 g, 5.0 mmol) yielding the compound **9** (1.950 g, 4.8 mmol, 95%). TLC (50% n-hexane in EtOAc): R_f = 0.45; $[\alpha]_D^{22}$: -28.6º (c = 1, DCM); IR (neat, cm^{-1}): 731, 1215, 1757; ^1H NMR (400 MHz, $CDCl_3$) δ = 1.32 (s, 6H, 2xCH_3 isopropylidene), 1.41 (s, 3H, CH_3 isopropylidene), 1.52 (s, 3H, CH_3 isopropylidene), 3.00 (s, 3H, CH_3 Msc), 3.40 (m, 2H, $MeSO_2C\underline{H}_2CH_2$-), 4.00 (m, 1H, H-6), 4.07 (m, 1H, H-6), 4.19 (m, 2H, H-4 and H-5),

4.61 (m, 3H, H-2 and $MeSO_2CH_2C\underline{H}_2$-), 5.13 (d, 1H, *J* = 2.0 Hz, H-3), 5.90 (d, 1H, *J* = 3.6 Hz, H-1); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 25.0 (CH_3 isopropylidene), 25.9 (CH_3 isopropylidene), 26.4 (CH_3 isopropylidene), 26.6 (CH_3 isopropylidene), 42.1 (CH_3 Msc), 53.3 ($MeSO_2\underline{C}H_2CH_2$-), 61.4 ($MeSO_2CH_2\underline{C}H_2$-), 66.9 (C-6), 72.0, 79.4 (C-4 and C-5), 79.9 (C-3), 82.8 (C-2), 104.8 (C-1), 109.2 (C_q isopropylidene), 112.1 (C_q isopropylidene), 153.1 (C=O Msc); HRMS $[M+H]^+$ calcd for $C_{16}H_{27}O_{10}S$ 411.13194 was found 411.13201, $[M+NH_4]^+$ calcd for $C_{16}H_{30}O_{10}SN$ 428.15849 was found 428.15854, $[M+Na]^+$ calcd for $C_{16}H_{26}O_{10}SNa$ 433.11389 was found 433.11364.

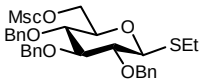


1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (2) (Cleavage of Msc from 3): Method I: To a solution of **3** (80 mg, 200 μmol) in methanol (5 ml, 0.04 M) was added sodium methoxide (1% in MeOH, 370 μl, 20 μmol, 0.1 eq) and the reaction mixture was stirred for 18 hours. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_{3\,(aq)}$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **2** (52 mg, 199 μmol, 100%).

Method II: To a solution of **3** (50 mg, 122 μmol) in DCM (2 ml, 0.06 M) was added triethylamine (500 μl, 360 μmol, 30 eq) and the reaction mixture was stirred for 20 hours. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **2** (32 mg, 122 μmol, 100%).

Method III: To a solution of **3** (50 mg, 122 μmol) in THF (3 ml, 0.04 M) was added TBAF (1 M in THF, 12.5 μl, 12 μmol, 0.1 eq) and the reaction mixture was stirred for 30 minutes. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_{3\,(aq)}$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **2** (32 mg, 121 μmol, 100%).

Method IV: To a solution of **3** (80 mg, 200 μmol) in DMF (5 ml, 0.04 M) was added DBU (0.1 M in DMF, 370 μl, 20 μmol, 0.1 eq) and the reaction mixture was stirred for 25 minutes. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **2** (52 mg, 199 μmol, 100%).

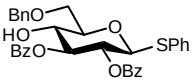


Ethyl 2,3,4-tri-*O*-benzyl-6-*O*-methylsulfonylethoxycarbonyl-1-thio-β-D-glucopyranoside (4): Compound **4** was prepared according to the general procedure for the introduction of the Msc group from ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (0.120 g, 0.242 mmol) yielding the compound **4** (0.153 g, 0.237 mmol, 98%). TLC (50% n-hexane in EtOAc): R_f = 0.5; $[\alpha]_D^{22}$: 10.0º (c = 0.8, DCM); IR (neat, cm^{-1}): 698, 1733; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.31 (t, 3H, *J* = 8.5 Hz, CH_3 Et), 2.68-2.78 (m, 2H, CH_2 Et), 2.97 (s, 3H, CH_3 Msc), 3.29-3.35 (m, 2H, $MeSO_2C\underline{H}_2CH_2$-), 3.41 (t, 1H, *J* = 9.5 Hz, H-2), 3.50 (m, 2H, H-4 and H-5), 3.70 (t, 1H, *J* = 8.5 Hz, H-3), 4.23 (dd, 1H, *J* = 5.0 Hz, *J* = 12.5 Hz, H-6), 4.42 (dd, 1H, *J* = 1.5 Hz, *J* = 12.0 Hz, H-6), 4.46 (d, 1H, *J* = 10.0 Hz, H-1),

4.53 (m, 2H, $MeSO_2CH_2C\underline{H}_2$-), 4.58 (d, 1H, *J* = 11.0 Hz, CH<u>H</u> Bn), 4.73 (d, 1H, *J* = 10.5 Hz, CH<u>H</u> Bn), 4.84 (d, 1H, *J* = 11.0 Hz, CH<u>H</u> Bn), 4.87 (d, 1H, *J* = 11.0 Hz, CH<u>H</u> Bn), 4.91 (d, 1H, *J* = 10.4 Hz, CH<u>H</u> Bn), 4.94 (d, 1H, *J* = 11.0 Hz, CH<u>H</u> Bn), 7.25-7.37 (m, 15H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 15.1 (CH_3 Et), 25.1 (CH_2 Et), 42.6 (CH_3 Msc), 53.8 ($MeSO_2\underline{C}H_2CH_2$-), 61.3 ($MeSO_2CH_2\underline{C}H_2$-), 67.2 (C-6), 75.0 ($CH_2$ Bn), 75.5 (CH_2 Bn), 75.8 (CH_2 Bn), 76.5 (C-5), 77.3 (C-4), 81.6 (C-2), 85.2 (C-1), 86.5 (C-3), 127.7-129.0 (CH arom), 137.5 (C_q Bn), 137.7 (C_q Bn), 138.2 (C_q Bn), 154.1 (C=O Msc); HRMS $[M+NH_4]^+$ calcd for $C_{33}H_{44}O_9S_2N$ 662.24520 was found 662.24536, $[M+Na]^+$ calcd for $C_{33}H_{40}O_9S_2Na$ 667.20060 was found 667.20038.

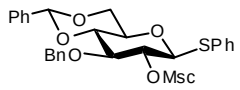
Phenyl 2,3,6-tri-*O*-benzyl-4-*O*-methylsulfonylethoxycarbonyl-1-thio-β-D-glucopyranoside (5): Compound **5** was prepared according to the general procedure for the introduction of the Msc group from phenyl 2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (0.154 g, 0.28 mmol) yielding the compound **5** (0.155 g, 0.22 mmol, 78%). TLC (50% n-hexane in EtOAc): R_f = 0.6; $[\alpha]_D^{22}$: -8.0º (c = 0.25, DCM); IR (neat, cm^{-1}): 694, 732, 1026, 1247, 1755; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.74 (s, 3H, CH_3 Msc), 3.06 (m, 2H, $MeSO_2C\underline{H}_2CH_2$-), 3.56 (t, 1H, *J* = 9.0 Hz, H-2), 3.62-3.71 (m, 4H, H-3, H-5 and 2xH-6), 4.35 (m, 2H, $MeSO_2CH_2C\underline{H}_2$-), 4.52 (m, 2H, 2xCH<u>H</u> Bn), 4.61-4.71 (m, 3H, H-1 and 2xCH<u>H</u> Bn), 4.88 (m, 3H, H-4 and 2xCH<u>H</u> Bn), 7.23-7.56 (m, 20H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 42.1 (CH_3 Msc), 53.4 ($MeSO_2\underline{C}H_2CH_2$-), 61.3 ($MeSO_2CH_2\underline{C}H_2$-), 69.6 (C-6), 73.5 ($CH_2$ Bn), 75.5 (2xCH_2 Bn), 75.7 (C-4), 76.7 (C-5), 80.5 (C-2), 84.0 (C-3), 87.6 (C-1), 127.3-132.1 (CH arom), 133.2 (C_q SPh), 137.6 (C_q Bn), 137.9 (C_q Bn), 138.0 (C_q Bn), 153.6 (C=O Msc); HRMS $[M+NH_4]^+$ calcd for $C_{37}H_{44}O_9S_2$ N 710.24520 was found 710.24548, $[M+Na]^+$ calcd for $C_{37}H_{40}O_9S_2Na$ 715.20060 was found 715.20074.

Phenyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-methylsulfonylethoxycarbonyl-1-thio-β-D-glucopyranoside (6): Compound **6** was prepared according to the general procedure for the introduction of the Msc group from phenyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-1-thio-β-D-glucopyranoside (0.160 g, 0.28 mmol) yielding the compound **6** (0.155 g, 0.21 mmol, 76%). TLC (50% n-hexane in EtOAc): R_f = 0.5; $[\alpha]_D^{22}$: +39.4º (c = 1, DCM); IR (neat, cm^{-1}): 1242, 1728; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.75 (s, 3H, CH_3 Msc), 2.97 (t, 2H, *J* = 6.0 Hz, $MeSO_2C\underline{H}_2CH_2$-), 3.72-3.79 (m, 2H, 2xH-6), 3.92 (m, 1H, H-5), 4.27 (m, 1H, $MeSO_2CH_2C\underline{H}$H-), 4.36 (m, 1H, $MeSO_2CH_2CH\underline{H}$-), 4.54 (d, 1H, *J* = 11.6 Hz, CH<u>H</u> Bn), 4.62 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 4.93 (d, 1H, *J* = 8.4 Hz, H-1), 5.17 (t, 1H, *J* = 9.6 Hz, H-4), 5.46 (t, 1H, *J* = 9.6 Hz, H-2), 5.70 (t, 1H, *J* = 9.6 Hz, H-3), 7.12-7.96 (m, 20H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.0 (CH_3 Msc), 53.4 ($MeSO_2\underline{C}H_2CH_2$-), 61.8 ($MeSO_2CH_2\underline{C}H_2$-), 68.7 (C-6), 70.1 (C-2), 73.5 (CH_2 Bn), 73.7 (C-4), 74.5 (C-3), 76.8 (C-5), 86.1 (C-1), 127.5-133.6 (CH arom), 128.9 (C_q Bz), 129.7 (C_q Bz), 131.8 (C_q SPh), 137.7 (C_q Bn), 153.2 (C=O Msc), 164.9 (C=O Bz), 165.7 (C=O Bz); HRMS $[M+NH_4]^+$ calcd for $C_{37}H_{40}O_{11}S_2$ N 738.20373 was found 738.20386, $[M+Na]^+$ calcd for $C_{37}H_{36}O_{11}S_2Na$ 743.15912 was found 743.15897.

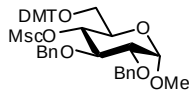


Phenyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-1-thio-β-D-glucopyranoside (Cleavage of the Msc from 6): To a solution of **6** (82 mg, 161 µmol) in DMF (8 ml, 0.02 M) was added DBU (1% in DMF, 241 µl, 16 µmol, 0.1 eq) and the reaction mixture was stirred for 1

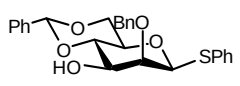
minute. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_{3\ (aq)}$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranosidurono-3,6-lactone **(**56 mg, 156 μmol, 98%).



Phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-methylsulfonylethoxycarbonyl-1-thio-β-D-glucopyranoside (7): Compound **7** was prepared according to the general procedure for the introduction of the Msc group from phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (0.460 g, 1.0 mmol) yielding the compound **7** (0.485 g, 0.81 mmol, 79%). TLC (50% n-hexane in EtOAc): R_f = 0.6; $[\alpha]_D^{22}$: -8.0º (c = 1, DCM); IR (neat, cm^{-1}): 743, 1265, 1747; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.86 (s, 3H, CH_3 Msc), 3.19-3.30 (m, 2H, $MeSO_2C\underline{H}_2CH_2$-), 3.49 (m, 1H, H-5), 3.71-3.83 (m, 3H, H-4, H-6 and H-3), 4.38 (dd, 1H, *J* = 4.8 Hz, *J* = 10.4 Hz, H-6), 4.54 (m, 1H, $MeSO_2CH_2C\underline{H}H$-), 4.59 (m, 1H, $MeSO_2CH_2CH\underline{H}$-), 4.65 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 4.73 (d, 1H, *J* = 10.0 Hz, H-1), 4.80 (t, 1H, *J* = 8.4 Hz, H-2), 4.90 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 5.56 (s, 1H, CH benzylidene), 7.24-7.49 (m, 15H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.3 (CH_3 Msc), 53.7 ($MeSO_2\underline{C}H_2CH_2$-), 61.7 ($CH_2$ $MeSO_2CH_2\underline{C}H_2$-), 68.3 (C-6), 70.5 (C-5), 74.5 (CH_2 Bn), 76.0 (C-2), 79.9 (C-3), 81.0 (C-4), 86.2 (C-1), 101.2 (CH benzylidene), 125.9-132.8 (CH arom), 131.5 (C_q SPh), 136.9 (C_q CHPh), 137.9 (C_q Bn), 153.4 (C=O Msc); HRMS $[M+H]^+$ calcd for $C_{30}H_{33}O_9S_2$ 601.15605 was found 601.15636, $[M+NH_4]^+$ calcd for $C_{30}H_{36}O_9S_2$ N 618.18260 was found 618.18264, $[M+Na]^+$ calcd for $C_{30}H_{32}O_9S_2Na$ 623.13800 was found 623.13795.

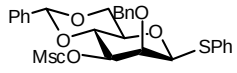


Methyl 2,3-di-*O*-benzyl-6-*O*-dimethoxytrityl-4-*O*-methylsulfonylethoxycarbonyl-α-D-glucopyranoside (8): Compound **8** was prepared according to the general procedure for the introduction of the Msc group from methyl 2,3-di-*O*-benzyl-6-*O*-dimethoxytrityl-α-D-glucopyranoside (0.750 g, 1.11 mmol) yielding the compound **8** (0.770 g, 0.87 mmol, 79%). TLC (33% EtOAc in PE): R_f = 0.4; $[\alpha]_D^{22}$: +26.4º (c = 0.5, DCM); IR (neat, cm^{-1}): 726, 1247, 1508, 1759; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.61 (s, 3H, CH_3 Msc), 2.98 (t, 2H, *J* = 6.0 Hz, $MeSO_2C\underline{H}_2CH_2$-), 3.14-3.23 (m, 2H, 2xH-6), 3.43 (s, 3H, CH_3 OMe), 3.63 (dd, *J* = 3.6 Hz, *J* = 9.6 Hz, 1H, H-2), 3.70 (s, 6H, 2xCH_3 DMT), 3.87 (m, 1H, H-5), 3.98 (t, 1H, *J* = 9.2 Hz, H-3), 4.24 (m, 2H, $MeSO_2CH_2C\underline{H}_2$-), 4.62 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 4.65 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 4.72 (d, 1H, *J* = 3.2 Hz, H-1), 4.76 (d, 1H, *J* = 11.6 Hz, CH<u>H</u> Bn), 4.86 (t, 1H, *J* = 10.0 Hz, H-4), 4.93 (d, 1H, *J* = 11.6 Hz, CH<u>H</u> Bn), 6.79-7.50 (m, 23 H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 41.6 (CH_3 Msc), 53.1 ($MeSO_2\underline{C}H_2CH_2$-), 54.8 (2x$CH_3$ DMT), 54.9 (CH_3 OMe), 60.9 ($MeSO_2CH_2\underline{C}H_2$-), 62.2 (C-6), 68.1 (C-5), 73.0 (CH_2 Bn), 75.0 (C-4), 75.1 (CH_2 Bn), 79.2 (C-3), 79.5 (C-2), 85.7 (C_q DMT), 97.5 (C-1), 112.8 (CH DMT) 126.5-129.8 (CH arom), 135.5 (C_q DMT), 137.6 (C_q Bn), 138.2 (C_q Bn), 144.3 (C_q DMT), 153.1 (C=O Msc) 158.1 (C_q DMT); HRMS $[M+Na]^+$ calcd for $C_{46}H_{50}O_{12}SNa$ 849.29152 was found 849.29230.

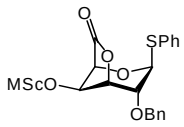


Phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-mannopyranoside (11): To a solution of phenyl 4,6-*O*-benzylidene-1-thio-β-D-mannopyranoside **(9)** (0.355 g, 1.0 mmol) in DCM (13 ml, 0.08 M) was added benzyl bromide (0.14 ml, 1.2 mmol, 1.2

eq), tetrabutylammonium sulfonate (0.067 g, 0.20 mmol, 0.2 eq) and $NaOH_{(aq)}$ (1M, 5 ml, 5.0 mmol, 5 eq). The reaction mixture was refluxed at 40 ºC for 18 hours, after which the reaction was quenched with $NH_4Cl_{(aq)}$. The mixture was diluted with EtOAc and extracted thrice with EtOAc. The combined organic layers were washed with $NH_4Cl_{(aq)}$, $NaHCO_{3\,(aq)}$, brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel chromatography to get **10** (0.071 g, 0.16 mmol, 16%), **11** (0.196 g, 0.44 mmol, 44%) and **12** (0.058 g, 0.11 mmol, 11%); TLC (33% EtAcO in PE): R_f = 0.8 (**12**), R_f = 0.6 (**10,11**); TLC (33% Et_2O in PE): R_f = 0.3 (**11**), R_f = 0.2 (**10**); (compound **10** and **12**) analytical data for the compound **10** and **12** was found in accordance to the earlier reports. (Compound **11**) $[\alpha]_D^{22}$: 21.2º (c = 1, DCM); IR (neat, cm^{-1}): 695, 1047; ^1H NMR (400 MHz, $CDCl_3$) δ = 2.56 (s, 1H, OH-3), 3.36 (m, 1H, H-5), 3.82-3.90 (m, 2H, H-3 and H-6), 3.97 (t, 1H, *J* = 9.6 Hz, H-4), 4.08 (d, 1H, *J* = 2.4 Hz, H-2), 4.29 (dd, 1H, *J* = 5.2 Hz, *J* = 10.8 Hz, H-6), 4.85 (d, 1H, *J* = 1.2 Hz, H-1), 4.85-4.97 (m, 2H, 2xCH<u>H</u> Bn), 5.53 (s, 1H, CH benzylidene), 7.24-7.37 (m, 15H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 68.3 (C-6), 71.2 (C-5), 72.8 (C-3), 76.6 (CH_2 Bn), 78.6 (C-4), 80.5 (C-2), 88.8 (C-1), 102.0 (CH benzylidene), 126.1-131.1 (CH arom), 134.7 (C_q SPh), 137.1, 137.8 (C_q CHPh and C_q Bn); CH Gated NMR (100 MHz, $CDCl_3$) δ = 88.8 (*J* = 153 Hz, C-1); HRMS $[M+Na]^+$ calcd for $C_{26}H_{26}O_5S_1Na$ 473.13932 was found 473.13904.

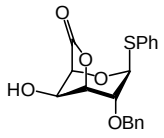


Phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-methylsulfonylethoxycarbonyl-1-thio-β-D-mannopyranoside (13): Compound **13** was prepared according to the general procedure for the introduction of the Msc group from phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-mannopyranoside (0.140 g, 0.31 mmol) yielding compound **13** (0.182 g, 0.30 mmol, 97%); TLC (50% EtOAc in PE): R_f = 0.2; $[\alpha]_D^{22}$: -42.2º (c = 1, DCM); IR (neat, cm^{-1}): 523, 1267, 1752; ^1H NMR (400 MHz, $CDCl_3$) δ = 2.75 (s, 3H, CH_3 Msc), 3.15-3.20 (m, 1H, $MeSO_2CH\underline{H}CH_2$-), 3.24-3.31 (m, 1H, $MeSO_2CH\underline{H}CH_2$-), 3.48 (m, 1H, H-5), 3.90 (t, 1H, *J* = 10.4 Hz, H-6), 4.24 (t, 1H, *J* = 9.6 Hz, H-4), 4.30 (dd, 1H, *J* = 4.8 Hz, *J* = 10.4 Hz, H-6), 4.36 (d, 1H, *J* = 2.8 Hz, H-2), 4.48 (t, 2H, *J* = 6.4 Hz, $MeSO_2CH_2C\underline{H}_2$-), 4.79 (d, 1H, *J* = 11.2 Hz, CH<u>H</u> Bn), 4.85 (d, 1H, *J* = 11.2 Hz, CH<u>H</u> Bn), 4.93-4.97 (m, 2H, H-1 and H-3), 5.53 (s, 1H, CH benzylidene), 7.24-7.42 (m, 15H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.3 (CH_3 Msc), 53.4 ($MeSO_2\underline{C}H_2CH_2$-), 61.5 ($MeSO_2CH_2\underline{C}H_2$-), 68.2 (C-6), 71.3 (C-5), 75.2 (C-4), 76.4 (CH_2 Bn), 77.7 (C-3), 78.1 (C-2), 88.6 (C-1), 101.7 (CH benzylidene), 126.0-134.0 (CH arom), 134.0 (C_q SPh), 136.9, 137.1 (C_q CHPh and C_q Bn), 153.5 (C=O); CH Gated NMR (100 MHz, $CDCl_3$) δ = 88.6 (*J* = 154 Hz, C-1); HRMS $[M+Na]^+$ calcd for $C_{30}H_{32}O_9S_2Na$ 623.13800 was found 623.13767.

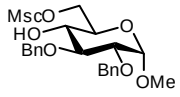


Phenyl 2-*O*-benzyl-4-*O*-methylsulfonylethoxycarbonyl-1-thio-β-D-galactopyranosidurono-3,6-lactone (14): Compound **14** was prepared according to the general procedure for the introduction of the Msc group from phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranosidurono-3,6-lactone (0.414 g, 1.16 mmol) yielding the compound **14** (0.514 g, 1.01 mmol, 88%); TLC (50% EtOAc in PE): R_f = 0.3; $[\alpha]_D^{22}$: -232.4º (c = 1.0, DCM); IR (neat, cm^{-1}): 734, 1264; ^1H NMR (400 MHz, $CDCl_3$) δ = 2.94 (s, 3H, CH_3 Msc), 3.33 (t, 2H, *J* = 5.6 Hz, $MeSO_2C\underline{H}_2CH_2$-), 4.20 (s, 1H, H-5), 4.34 (d, 1H, *J* = 4.8 Hz, H-2), 4.58 (t, 2H, *J* = 5.2 Hz, $MeSO_2CH_2C\underline{H}_2$-), 4.65 (m, 2H, 2xCH<u>H</u>

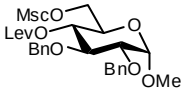
Bn), 4.99 (d, 1H, *J* = 4.8 Hz, H-3), 5.41 (s, 1H, H-4), 5.46 (s, 1H, H-1), 7.25-7.43 (m, 10H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.3 (CH_3 Msc), 53.2 ($MeSO_2\underline{C}H_2CH_2$-), 61.9 ($MeSO_2CH_2\underline{C}H_2$-), 69.8 (C-5), 72.9 ($CH_2$ Bn), 75.1 (C-4), 78.2 (C-2 and C-3), 85.9 (C-1), 128.0-132.4 (CH arom), 133.0 (C_q SPh), 136.1 (C_q Bn), 152.6 (C=O Msc), 171.2 (C-6); HRMS $[M+Na]^+$ calcd for $C_{23}H_{24}O_9S_2Na$ 531.07539 was found 531.07525.



Phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranosidurono-3,6-lactone (Cleavage of Msc from 14): To a solution of **14** (82 mg, 161 μmol) in DMF (8 ml, 0.02 M) was added DBU (1% in DMF, 241 μl, 16 μmol, 0.1 eq) and the reaction mixture was stirred for 1 minute. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_{3\ (aq)}$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranosidurono-3,6-lactone (56 mg, 156 μmol, 97%).

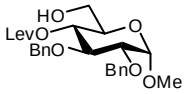


Methyl 2,3-di-*O*-benzyl-6-*O*-methylsulfonylethoxycarbonyl-α-D-glucopyranoside (15): Compound **15** was prepared according to the general procedure for the introduction of the Msc group from methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (0.214 g, 0.57 mmol) at -20 °C yielding the compound **15** (0.270 g, 0.52 mmol, 90%). TLC (50% EtOAc in PE): R_f = 0.6; $[\alpha]_D^{22}$: +49.6° (c = 1, DCM); IR (neat, cm^{-1}): 741, 1055, 1265, 1751, 2927; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.08 (bs, 1H, C4-OH), 2.99 (s, 3H, CH_3 Msc), 3.36 (t, 2H, *J* = 5.6 Hz, $MeSO_2C\underline{H}_2CH_2$-), 3.41 (s, 3H, CH_3 OMe), 3.49 (t, 1H, *J* = 9.6 Hz, H-4), 3.54 (dd, 1H, *J* = 3.6 Hz, *J* = 9.6 Hz, H-2), 3.77-3.84 (m, 2H, H-3 and H-5), 4.43 (m, 2H, 2xH-6), 4.59 (t, 2H, *J* = 6.0 Hz, $MeSO_2CH_2C\underline{H}_2$-), 4.65 (d, 1H, *J* = 3.2 Hz, H-1), 4.70 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 4.75 (d, 1H, *J* = 11.6 Hz, CH<u>H</u> Bn), 4.81 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 5.05 (d, 1H, *J* = 11.2 Hz, CH<u>H</u> Bn), 7.30-7.42 (m, 10H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.5 (CH_3 Msc), 53.7 ($MeSO_2\underline{C}H_2CH_2$-), 55.3 ($CH_3$ OMe), 61.4 ($MeSO_2CH_2\underline{C}H_2$-), 67.2 (C-6), 68.9 (C-5), 69.6 (C-4), 73.1 (CH_2 Bn), 75.4 (CH_2 Bn), 79.5 (C-2), 81.0 (C-3), 98.1 (C-1), 128.0-128.6 (CH arom), 137.8 (C_q Bn), 138.5 (C_q Bn), 154.4 (C=O Msc); HRMS $[M+NH_4]^+$ calcd for $C_{25}H_{36}O_{10}S$ N 542.20544 was found 542.20528, $[M+Na]^+$ calcd for $C_{25}H_{32}O_{10}SNa$ 547.16084 was found 547.16053.

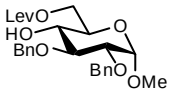


Methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-6-*O*-methylsulfonylethoxycarbonyl-α-D-glucopyranoside (17): To a solution of the compound **15** (0.196 g, 0.37 mmol) in DCM (1.8 ml, 0.2 M) was added LevOH (0.434 g, 3.74 mmol, 10 eq) and the reaction mixture was stirred for 30 minutes. A solution of EDC.HCl (0.358 g, 1.87 mmol, 5 eq) and DMAP (2 mg) in DCM (0.5 ml) was added and stirring was continued for 1 hour. The reaction mixture was diluted with DCM, washed with water, $NaHCO_{3\ (aq)}$ and brine, dried over $MgSO_4$, filtered, concentrated and purified by silica gel column chromatography to afford compound **17** (0.208 g, 3.34 mmol, 89%). TLC (10% Methanol in DCM): R_f = 0.5; $[\alpha]_D^{22}$: +34.6° (c = 1, DCM); IR (neat, cm^{-1}): 735, 1130, 1251, 1716, 1749; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.15 (s, 3H, CH_3 Lev), 2.24-2.30 (m, 1H, $MeCOCH_2CH\underline{H}COO$-), 2.44-2.50 (m, 1H, $MeCOCH_2CH\underline{H}COO$-), 2.58 (m, 1H, $MeCOCH\underline{H}CH_2COO$-), 2.70 (m, 1H, $MeCOCH\underline{H}CH_2COO$-), 2.99 (s, 3H, CH_3 Msc), 3.29 (m, 1H,

$MeSO_2CH\underline{H}CH_2$-), 3.38 (m, 4H, CH_3 OMe and $MeSO_2CH\underline{H}CH_2$-), 3.55 (dd, 1H, *J* = 3.5 Hz, *J* = 9.5 Hz, H-2), 3.86 (m, 1H, H-5), 3.93 (t, 1H, *J* = 9.5 Hz, H-3), 4.15 (dd, 1H, *J* = 2.0 Hz, *J* = 12.0 Hz, H-6), 4.32 (dd, 1H, *J* = 4.5 Hz, *J* = 12.0 Hz, H-6), 4.49 (m, 1H, $MeSO_2CH_2CH\underline{H}$-), 4.58-4.67 (m, 4H, H-1, $MeSO_2CH_2CH\underline{H}$- and 2x$CH\underline{H}$ Bn), 4.79 (d, 1H, *J* = 12.0 Hz, $CH\underline{H}$ Bn), 4.87 (d, 1H, *J* = 11.5 Hz, $CH\underline{H}$ Bn), 4.96 (t, 1H, *J* = 10.0 Hz, H-4), 7.27-7.35 (m, 10H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 27.7 ($MeCOCH_2\underline{C}H_2COO$-), 29.7 ($CH_3$ Lev), 37.8 ($MeCO\underline{C}H_2CH_2COO$-), 42.5 ($CH_3$ Msc), 53.8 ($MeSO_2\underline{C}H_2CH_2$-), 55.5 ($CH_3$ OMe), 61.5 ($MeSO_2CH_2\underline{C}H_2$-), 66.1 (C-6), 67.3 (C-3), 69.6 (C-4), 73.5 (CH_2 Bn), 75.4 (CH_2 Bn), 78.9 (C-2), 79.4 (C-5), 98.2 (C-1), 127.6-128.5 (CH arom), 137.8 (C_q Bn), 138.4 (C_q Bn), 154.0 (C=O Msc), 171.7 (C=O ($MeCOCH_2CH_2\underline{CO}O$-), 206.3 ($Me\underline{CO}CH_2CH_2COO$-); HRMS $[M+NH_4]^+$ calcd for $C_{30}H_{42}O_{12}S$ N 640.24222 was found 640.24206, $[M+Na]^+$ calcd for $C_{33}H_{38}O_{12}SNa$ 645.19762 was found 645.19721.

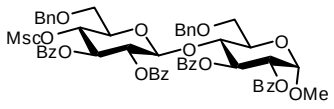


Methyl 2,3,-di-*O*-benzyl-4-*O*-levulinoyl-1-thio-α-D-glucopyranoside (18): To a solution of compound **17** (34 mg, 54 μmol) in DMF (1.1 ml, 0.04 M) was added DBU (10% in DMF, 81μl, 5.4 μmol, 0.1 eq) and the reaction mixture was stirred for 25 minutes. The reaction mixture was quenched with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_{3\ (aq)}$ and brine, dried over $MgSO_4$, filtered, concentrated and purified by silica gel column chromatography to afford the compound **17** (23.7mg, 52 μmol, 95%). TLC (66% EtOAc in toluene): R_f = 0.65; $[\alpha]_D^{22}$: +24.8° (c = 1, DCM); IR (neat, cm^{-1}): 738, 1028, 1716, 1739, 2918; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.15 (s, 3H, CH_3 Lev), 2.32 (m, 1H, $MeCOCH_2CH\underline{H}COO$-), 2.48-2.54 (m, 1H, $MeCOCH_2CH\underline{H}COO$-), 2.56-2.62 (m, 1H, $MeCOCH\underline{H}CH_2COO$-), 2.74-2.80 (m, 1H, $MeCOCH\underline{H}CH_2COO$-), 3.39 (s, 3H, CH_3 OMe), 3.56 (dd, 1H, *J* = 3.5 Hz, *J* = 9.5 Hz, H-2), 3.60-3.66 (m, 3H, H-5 and 2xH-6), 3.99 (t, 1H, *J* = 9.0 Hz, H-3), 4.61 (d, 1H, *J* = 4.0 Hz, H-1), 4.64 (d, 1H, *J* = 12.5 Hz, $CH\underline{H}$ Bn), 4.69 (d, 1H, *J* = 11.5 Hz, $CH\underline{H}$ Bn), 4.79 (d, 1H, *J* = 12.0 Hz, $CH\underline{H}$ Bn), 4.89 (m, 2H, H-4 and $CH\underline{H}$ Bn), 7.26-7.36 (m, 10H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 27.8 ($MeCOCH_2\underline{C}H_2COO$-), 29.7 ($CH_3$ Lev), 37.8 ($MeCO\underline{C}H_2CH_2COO$-), 55.4 ($CH_3$ OMe), 60.9 (C-6), 69.5 (C-3), 70.9 (C-4), 73.5 (CH_2 Bn), 75.4 (CH_2 Bn), 78.9 (C-2), 79.4 (C-5), 98.2 (C-1), 127.6-128.5 (CH arom), 137.9 (C_q Bn), 138.7 (C_q Bn), 173.2 (C=O ($MeCOCH_2CH_2\underline{CO}O$-), 206.4 ($Me\underline{CO}CH_2CH_2COO$-); HRMS $[M+NH_4]^+$ calcd for $C_{26}H_{36}O_8N$ 490.24354 was found 490.24324, $[M+Na]^+$ calcd for $C_{26}H_{32}O_8Na$ 495.19894 was found 495.19847.

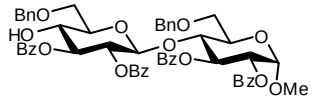


Methyl 2,3,-di-*O*-benzyl-6-*O*-levulinoyl-1-thio-α-D-glucopyranoside (19): Collected as a by-product during the synthesis of **18**; TLC (66% EtOAc in toluene): R_f = 0.8; $[\alpha]_D^{22}$: +22.6° (c = 0.3, DCM); IR (neat, cm^{-1}): 715, 1026, 1150, 1705; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.17 (s, 3H, CH_3 Lev), 2.58 (m, 2H, $MeCOCH_2C\underline{H}_2COO$-), 2.74 (t, 2H, *J* = 6.5 Hz, $MeCOC\underline{H}_2CH_2COO$-), 3.38 (s, 3H, CH_3 OMe), 3.44 (t, 1H, *J* = 9.5 Hz, H-4), 3.50 (dd, 1H, *J* = 3.5 Hz, *J* = 9.5 Hz, H-2), 3.72-3.75 (m, 1H, H-5), 3.79 (t, 1H, *J* = 9.0 Hz, H-3), 4.22 (dd, 1H, *J* = 2.0 Hz, *J* = 12.0 Hz, H-6), 4.42 (dd, 1H, *J* = 4.5 Hz, *J* = 12.0 Hz, H-6), 4.61 (d, 1H, *J* = 3.5 Hz, H-1), 4.66 (d, 1H, *J* = 12.0 Hz, $CH\underline{H}$ Bn), 4.77 (t, 2H, *J* = 11.5 Hz, 2x$CH\underline{H}$ Bn), 4.99 (d, 1H, *J* = 11.5 Hz, $CH\underline{H}$ Bn), 7.26-7.37 (m, 10H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 27.8 ($MeCOCH_2\underline{C}H_2COO$-), 29.8 ($CH_3$ Lev), 37.9 ($MeCO\underline{C}H_2CH_2COO$-), 55.2 ($CH_3$ OMe), 63.4 (C-6), 69.3 (C-5), 69.9 (C-4), 73.2 (CH_2 Bn), 75.5 (CH_2 Bn), 79.5 (C-2), 81. (C-3), 98.2 (C-1), 127.9-129.5 (CH

arom), 137.9 (C_q Bn), 138.6 (C_q Bn), 173.0 (C=O ($MeCOCH_2CH_2\underline{CO}O$-), 206.5 ($Me\underline{CO}CH_2CH_2COO$-); HRMS $[M+Na]^+$ calcd for $C_{26}H_{32}O_8Na$ 495.19894 was found 495.19849.

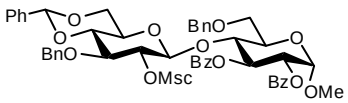


Methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-methylsulfonylethoxycarbonyl-β-D-glucopyranosyl)-α-D-glucopyranoside (21): Disaccharide **21** was prepared form donor **6** (0.113 g, 0.16 mmol, 1 eq) and acceptor **20** (0.115 g, 0.24 mmol, 1.5 eq) according to the general procedure for glycosylations as described above yielding compound **21** (0.109 g, 0.10 mmol, 63%); TLC (33% EtOAc in Toluene): R_f = 0.45; $[\alpha]_D^{22}$: +17.6º (c = 0.25, DCM); IR (neat, cm^{-1}): 707, 1247, 1724; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.70 (s, 3H, CH_3 Msc), 2.86 (t, 2H, *J* = 5.0 Hz, $MeSO_2C\underline{H_2}CH_2$-), 3.07 (dd, 1H, *J* = 5.0 Hz, *J* = 10.0 Hz, H-6'), 3.19 (dd, 1H, *J* = 4.0 Hz, *J* = 10.0 Hz, H-6'), 3.30 (s, 3H, CH_3 OMe), 3.47 (m, 1H, H-6), 3.55 (m, 1H, H-5'), 3.71 (dd, 1H, *J* = 3.0 Hz, *J* = 10.5 Hz, H-6), 3.77 (m, 1H, H-5), 4.05-4.10 (m, 2H, $MeSO_2CH_2C\underline{H}H$- and $CH\underline{H}$ Bn), 4.12 (d, 1H, *J* = 12.0, $CH\underline{H}$ Bn), 4.20-4.26 (m, 2H, H-4 and $MeSO_2CH_2CH\underline{H}$-), 4.37 (d, 1H, *J* = 12.0 Hz, $CH\underline{H}$ Bn), 4.71 (m, 2H, H-1' and $CH\underline{H}$ Bn), 4.91 (t, 1H, *J* = 9.5 Hz, H-4'), 5.10 (d, 1H, *J* = 3.5 Hz, H-1), 5.16 (dd, 1H, *J* = 4.0 Hz, *J* = 10.5 Hz, H-2), 5.35 (dd, 1H, *J* = 8.0 Hz, *J* = 10.0 Hz, H-2'), 5.46 (t, 1H, *J* = 9.5 Hz, H-3'), 5.92 (t, 1H, *J* = 9.5 Hz, H-3), 7.20-8.03 (m, 30H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 42.0 (CH_3 Msc), 53.5 ($MeSO_2C\underline{H_2}CH_2$-), 55.4 ($CH_3$ OMe), 61.4 ($MeSO_2CH_2C\underline{H_2}$-), 67.2 (C-6), 69.4 (C-6'), 69.4 (C-5), 70.7 (C-3), 71.5 (C-2'), 71.5 (C-5'), 72.0 (C-2), 73.1 (CH_2 Bn), 73.1 (C-3'), 73.6 (CH_2 Bn), 74.9 (C-4'), 75.5 (C-4), 96.9 (C-1), 100.2 (C-1'), 128.2-133.5 (CH arom), 128.9 (C_q Bz), 129.1 (C_q Bz), 130.2 (C_q Bz), 130.4 (C_q Bz), 137.7 (C_q Bn), 137.7 (C_q Bn), 153.1 (C=O Msc), 164.5 (C=O Bz), 165.2 (C=O Bz), 165.7 (C=O Bz), 165.9 (C=O Bz); HRMS $[M+NH_4]^+$ calcd for $C_{59}H_{62}O_{19}SN$ 1120.36313 was found 1120.36426, $[M+Na]^+$ calcd for $C_{59}H_{58}O_{19}SNa$ 1125.31852 was found 1125.31946.



Methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside 22 (Cleavage of Msc from 21): To a solution of **21** (90 mg, 82 µmol) in dioxane (1.5 ml, 0.05 M) was added DBU (5% in DMF, 23 µl, 8 µmol, 0.1 eq) and the reaction mixture was stirred for 30 minutes. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_{3\,(aq)}$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside **22** (78 mg, 82 µmol, 100%). TLC (33% EtOAc in Toluene): R_f = 0.66; $[\alpha]_D^{22}$: +31.8º (c = 1.0, DCM); IR (neat, cm^{-1}): 706, 1025, 1068, 1093, 1261, 1451, 1723; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.00 (dd, 1H, *J* = 5.0 Hz, *J* = 9.5 Hz, H-6'), 3.28 (m, 1H, H-6'), 3.30 (s, 3H, CH_3 OMe), 3.36 (m, 1H, H-5'), 3.46 (dd, 1H, *J* = 1.5 Hz, *J* = 10.5 Hz, H-6), 3.70 (m, 2H, H-4' and H-6), 3.75 (m, 1H, H-5), 4.18 (t, 1H, *J* = 9.5 Hz, H-4), 4.21 (m, 2H, 2x$CH\underline{H}$ Bn), 4.36 (d, 1H, *J* = 12.0 Hz, $CH\underline{H}$ Bn), 4.66 (m, 2H, H-1' and $CH\underline{H}$ Bn), 5.09 (d, 1H, *J* = 3.5 Hz, H-1), 5.16 (dd, 1H, *J* = 4.0 Hz, *J* = 10.5 Hz, H-2), 5.29 (m, 2H, H-2' and H-3'), 5.90 (t, 1H, *J* = 9.5 Hz, H-3'), 7.19-8.01 (m, 30H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 55.4 (CH_3 OMe), 67.3 (C-6), 69.5 (C-5), 70.8 (C-3), 71.0 (C-6'), 71.6 (C-2'), 72.1 (C-2), 72.3 (C-4'), 72.6 (C-5'), 73.5 (CH_2

Bn), 73.6 (CH_2 Bn), 75.5 (C-4), 75.7 (C-3'), 96.9 (C-1), 100.4 (C-1'), 127.5-133.2 (CH arom), 129.2 (C_q Bz), 129.2 (2xC_q Bz), 130.4 (C_q Bz), 137.2 (C_q Bn), 137.8 (C_q Bn), 164.8 (C=O Bz), 165.1 (C=O Bz), 165.9 (C=O Bz), 166.5 (C=O Bz); HRMS $[M+NH_4]^+$ calcd for $C_{55}H_{56}O_{15}N$ 970.36445 was found 970.36603, $[M+Na]^+$ calcd for $C_{55}H_{52}O_{15}Na$ 975.31984 was found 975.32080.

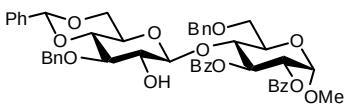


Methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-methylsulfonylethoxycarbonyl-β-D-glucopyranosyl)-α-D-glucopyranoside (23):

Method I: Disaccharide **23** was prepared form donor **7** (0.091g, 0.15 mmol, 1eq) and acceptor **20** (0.109 g, 0.22 mmol, 1.5 eq) according to the general procedure for glycosylations as described above yielding the compound **23** (0.103 g, 0.10 mmol, 71%).

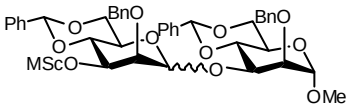
Method II: To a solution of compound **7** (0.127 g, 0.21 mmol, 1q) in DCM (4.2 ml, 0.05 M) was added diphenyl sulfoxide (0.556 g, 0.28 mmol, 1.3 eq) and tri-*tert*-butylpyrimidine (0.157 g, 0.63 mmol, 3 eq) and mixture was stirred over molecular sieve 3Å for 30 minutes. After that the mixture was brought to -60ºC and triflic acid anhydride (0.046 ml, 0.28 mmol, 1.3 eq) was added and the mixture was stirred for 15 minutes. Next a solution of compound **20** (0.156 g, 0.32 mmol, 1.5 eq) in DCM (2.1 ml, 0.15 M) was added and stirring was continued for 10 minutes. The reaction mixture was quenched with triethylamine (5 eq), diluted with DCM, washed with water and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to yield **23** (0.13 g, 0.14 mmol, 67%).

TLC (33% Toluene in EtOAc): R_f = 0.45; $[\alpha]_D^{22}$: +54.4º (c = 0.5, DCM); IR (neat, cm^{-1}): 696, 1093, 1722; ^1H NMR (500 MHz, $CDCl_3$) δ = 2.72 (t, 1H, *J* = 10.5 Hz, H-6'), 2.79 (s, 3H, CH_3 Msc), 2.98-3.03 (m, 1H, H-5'), 3.20 (t, 2H, *J* = 5.5 Hz, $MeSO_2C\underline{H}_2CH_2$-), 3.41 (m, 4H, CH_3 OMe and H-4'), 3.49 (t, 1H, *J* = 9.5 Hz, H-3'), 3.61 (dd, 1H, *J* = 5.0 Hz, *J* = 11.0 Hz, H-6'), 3.73 (d, 1H, *J* = 10.0 Hz, H-6), 3.87 (dd, 1H, *J* = 3.0 Hz, *J* = 11.0 Hz, H-6), 3.90 (m, 1H, H-5), 4.13 (t, 1H, *J* = 9.5 Hz, H-4), 4.39 (d, 1H, *J* = 8.0 Hz, H-1'), 4.47-4.57 (m, 4H, 2xCH<u>H</u> Bn and $MeSO_2CH_2C\underline{H}_2$-), 4.64 (t, 1H, *J* = 8.5 Hz, H-2'), 4.75 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 4.85 (d, 1H, *J* = 12.0 Hz, CH<u>H</u> Bn), 5.14 (d, 1H, *J* = 4.0 Hz, H-1), 5.18 (dd, 1H, *J* = 3.5 Hz, *J* = 10.0 Hz, H-2), 5.24 (s, 1H, CH Benzylidene), 5.88 (t, 1H, *J* = 10.0 Hz, H-3), 7.22-8.00 (m, 25H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 42.0 (CH_3 Msc), 53.4 ($MeSO_2\underline{C}H_2CH_2$-), 55.4 ($CH_3$ OMe), 61.3 ($MeSO_2CH_2\underline{C}H_2$-), 65.8 (C-5'), 67.5 (C-6), 67.7 (C-6'), 69.6 (C-5), 70.6 (C-3), 71.8 (C-2), 73.6 (CH_2 Bn), 73.9 (CH_2 Bn), 76.0 (C-4), 77.5 (C-2'), 78.5 (C-3'), 80.8 (C-4'), 96.9 (C-1), 100.6 (C-1'), 100.9 (CH Benzylidene), 125.9-133.2 (CH arom), 129.0 (C_q Bz), 130.2 (C_q Bz), 136.8 (C_q CHPh), 137.8 (C_q Bn), 138.1 (C_q Bn), 153.3 (C=O Msc), 165.2 (C=O Bz), 165.8 (C=O Bz); HRMS $[M+H]^+$ calcd for $C_{52}H_{55}O_{17}S$ 983.31545 was found 983.31689, $[M+NH_4]^+$ calcd for $C_{52}H_{58}O_{17}SN$ 1000.34200 was found 1000.34326, $[M+Na]^+$ calcd for $C_{52}H_{54}O_{17}SNa$ 1005.29739 was found 1005.29822.

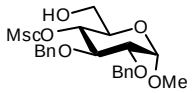


Methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-α-D-glucopyranoside (24) (Cleavage of Msc from 23): To a solution of **23** (94 mg, 96 μmol) in dioxane (1.9 ml, 0.05 M) was added DBU (1% in DMF, 71 μl, 10 μmol,

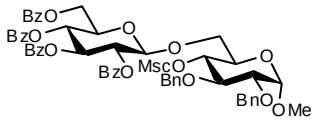
0.1 eq) and the reaction mixture was stirred for 30 minutes. The reaction mixture was neutralized with $NH_4Cl_{(aq)}$, diluted with EtOAc, washed with $NH_4Cl_{(aq)}$, $NaHCO_{3(aq)}$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-α-D-glucopyranoside **23** (78 mg, 96 μmol, 100%); TLC (33% Toluene in EtOAc): R_f = 0.6; $[\alpha]_D^{22}$: +55.2º (c = 1.0, DCM); IR (neat, cm^{-1}): 696, 709, 1026, 1067, 1277, 1722; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.72 (t, 1H, *J* = 10.4 Hz, H-6'), 2.94-2.98 (m, 1H, H-5'), 3.41 (m, 7H, CH_3 OMe, H-2', H-3', H-4' and H-6'), 3.79 (dd, 1H, *J* = 1.60 Hz, *J* = 10.8 Hz, H-6), 3.9 (m, 1H, H-5), 3.06 (dd, 1H, *J* = 2.8 Hz, *J* = 10.8 Hz, H-6), 4.14 (t, 1H, *J* = 9.2 Hz, H-4), 4.32 (d, 1H, *J* = 7.2 Hz, H-1'), 4.56 (d, 1H, *J* = 12.0 Hz, CHH Bn), 4.71 (m, 2H, 2xCHH Bn), 4.88 (d, 1H, *J* = 12.0 Hz, CHH Bn), 5.16 (m, 2H, H-1 and H-2), 5.25 (s, 1H, CH Benzylidene), 5.94 (t, 1H, *J* = 9.2 Hz, H-3), 7.25-8.00 (m, 25H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 55.4 (CH_3 OMe), 66.1 (C-5'), 67.9 (C-6'), 68.0 (C-6), 69.6 (C-5), 71.1 (C-3), 72.0 (C-2), 73.6 (CH_2 Bn), 74.3 (CH_2 Bn), 74.4 (C-2'), 80.2 (C-4'), 80.9 (C-3'), 97.0 (C-1), 100.9 (CH Benzylidene), 103.8 (C-1'), 125.9-133.2 (CH arom), 129.2 (C_q Bz), 130.3 (C_q Bz), 137.2 (C_q Benzylidene), 137.7 (C_q Bn), 138.4 (C_q Bn), 165.3 (C=O Bz), 166.0 (C=O Bz); HRMS $[M+Na]^+$ calcd for $C_{48}H_{48}O_{13}Na$ 855.29871 was found 855.29927.



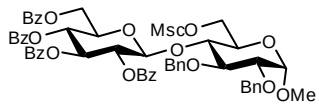
Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-methylsulfonylethoxymethyl-D-mannopyranosyl)-α-D-mannopyranoside (26): To a solution of compound **13** (0.160 g, 0.27 mmol, 1 eq) in DCM (5.3 ml, 0.05 M) was added diphenyl sulfoxide (0.070 g, 0.35 mmol, 1.3 eq) and tri-*tert*-butylpyrimidine (0.199 g, 0.80 mmol, 3 eq) and the mixture was stirred over molecular sieve 3Å for 30 minutes. After that the reaction mixture was brought to -78 ºC and triflic acid anhydride (58 μl, 0.35 mmol, 1.3 eq) was added and the mixture was stirred for 15 minutes. Next a solution of compound **25** (0.148 g, 0.40 mmol, 1.5 eq) in DCM (2.7 ml, 0.15 M) was added and stirring was continued for 18 hours at -78 ºC. The reaction mixture was quenched with triethylamine (5 eq), diluted with DCM, washed with water and extracted with DCM thrice. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to yield **26** (0.178 g, 0.21 mmol, 78%); TLC (33% Toluene in EtOAc): R_f = 0.6; IR (neat, cm^{-1}): 697, 734, 1020, 1066, 1108, 1829; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.79 (s, 3H, CH_3 Msc), 3.18-3.22 (m, 1H, $MeSO_2CHHCH_2$-), 3.27-3.33 (m, 1H, $MeSO_2CHHCH_2$-), 3.38 (s, 3H, CH_3 OMe), 3.80-3.90 (m, 5H, H-2, H-5, H-5', H-6 and H-6'), 4.05 (m, 1H, H-2'), 4.08-4.16 (m, 2H, H-4', CHH Bn), 4.20-4.29 (m, 5H, H-3, H-4, H-6, H-6' and CHH Bn), 4.37 (d, 1H, *J* = 12.0 Hz, CHH Bn), 4.48 (m, 2H, $MeSO_2CH_2$ CH_2O-), 4.76 (d, 1H, *J* = 1.5 Hz, H-1), 4.79 (s, 2H, H-1' and CHH Bn), 5.17 (dd, 1H, *J* = 3.5 Hz, *J* = 10.5 Hz, H-3'), 5.53 (s, 1H, CH Benzylidene), 5.61 (s, 1H, CH Benzylidene), 7.00-7.50 (m, 20H, H arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 42.4 (CH_3 Msc), 53.7 ($MeSO_2CH_2CH_2$-), 55.0 (CH_3 OMe), 61.4 ($MeSO_2CH_2CH_2$-), 63.8, 64.4, 77.3 (C-2, C-5 and C-5'), 68.7, 68.9 (C-6 and C-6'), 72.6 (CH_2 Bn), 73.5 (CH_2 Bn), 73.8, 79.3 (C-3 and C-4), 75.4 (C-3'), 75.7 (C-2'), 76.0 (C-4'), 99.2, (C-1'), 100.1, (C-1), 101.9 (CH Benzylidene), 102.1 (CH Benzylidene), 126.2-129.7 (CH arom), 137.2, 137.3, 137.5 (2xC_q Benzylidene and 2xC_q Bn), 153.5 (C=O Msc); CH Gated NMR (125 MHz, $CDCl_3$) δ = 99.2 (*J* = 170 Hz, C-1'), 100.1 (*J* = 182 Hz, C-1). HRMS $[M+Na]^+$ calcd for $C_{45}H_{50}O_{15}SNa$ 885.27626 was found 885.27625.



Methyl 2,3-di-*O*-benzyl-4-*O*-methylsulfonylethoxycarbonyl-α-D-glucopyranoside (28): To a solution of **8** (0.240 mg, 0.29 mmol) in DCM (2.9 ml, 0.1 M) was added EtOH (1 ml) and acetic acid (7.6 ml) and the mixture was stirred for 18 hours. The reaction mixture was neutralized with $NaHCO_{3\ (aq)}$, diluted with EtOAc, washed with $NaHCO_{3\ (aq)}$ and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel column chromatography to afford **28** (0.123 g, 0.23 mmol, 81%). TLC (50% EtOAc in PE): R_f = 0.2; $[\alpha]_D^{22}$: +37.4º (c = 1.0, DCM); IR (neat, cm^{-1}): 630, 1262, 1757; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.35 (bs, 1H, C6-OH), 2.83 (s, 3H, CH_3 Msc), 3.20-3.27 (m, 2H, $MeSO_2C\underline{H}_2CH_2$-), 3.38 (s, 3H, CH_3 OMe), 3.57 (dd, 1H, *J* = 3.6 Hz, *J* = 9.6 Hz, H-2), 3.64 (m, 3H, H-5 and 2xH-6), 3.98 (t, 1H, *J* = 9.6 Hz, H-3), 4.42-4.48 (m, 1H, $MeSO_2CH_2CH\underline{H}$-), 4.51-4.56 (m, 1H, $MeSO_2CH_2CH\underline{H}$-), 4.61 (d, 1H, *J* = 3.6 Hz, H-1), 4.62-4.66 (m, 2H, 2xCH<u>H</u> Bn), 4.76-4.83 (m, 2H, H-4 and CH<u>H</u> Bn), 4.94 (d, 1H, *J* = 11.6 Hz, CH<u>H</u> Bn), 7.26-7.35 (m, 10H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.0 (CH_3 Msc), 53.4 ($MeSO_2\underline{C}H_2CH_2$-), 55.4 ($CH_3$ OMe), 60.9 (C-6), 61.3 ($MeSO_2CH_2\underline{C}H_2$-), 69.0 (C-5), 73.4 ($CH_2$ Bn), 74.8 (C-4), 75.3 (CH_2 Bn), 78.9 (C-3), 79.3 (C-2), 98.0 (C-1), 127.4-128.4 (CH arom), 137.6 (C_q Bn), 138.4 (C_q Bn), 154.2 (C=O Msc); HRMS $[M+Na]^+$ calcd for $C_{25}H_{32}O_{10}SNa$ 547.16084 was found 547.16056.



Methyl 2,3-di-*O*-benzyl-4-*O*-methylsulfonylethoxycarbonyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (29): Disaccharide **29** was prepared form acceptor **28** (0.088 g, 0.17 mmol, 1 eq) and donor **27** (0.168 g, 0.25 mmol, 1.5 eq) according to the general procedure for glycosylations as described above yielding compound **29** (0.130 g, 0.12 mmol, 70%). TLC (50% EtOAc in PE): R_f = 0.65; $[\alpha]_D^{22}$: +39.2º (c = 1, DCM); IR (neat, cm^{-1}): 1249, 1725; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.78 (s, 3H, CH_3 Msc), 3.11-3.20 (m, 5H, CH_3 OMe and $MeSO_2C\underline{H}_2CH_2$-), 3.37-3.39 (m, 1H, H-2), 3.63 (dd, 1H, *J* = 6.4 Hz, *J* = 11.2 Hz, H-6), 3.81-3.89 (m, 2H, H-3 and H-5), 4.02 (d, 1H, *J* = 10.8 Hz, H-6), 4.17 (m, 1H, H-5'), 4.34 (m, 1H, $MeSO_2CH_2C\underline{H}H$-), 4.40-4.56 (m, 5H, H-1, H-6', $MeSO_2CH_2C\underline{H}H$- and 2xCH<u>H</u> Bn), 4.67 (m, 3H, H-4, H-6' and CH<u>H</u> Bn), 4.87 (d, 1H, *J* = 11.6 Hz, CH<u>H</u> Bn), 4.92 (d, 1H, *J* = 8.0 Hz, H-1'), 5.54 (t, 1H, *J* = 9.2 Hz, H-2'), 5.69 (t, 1H, *J* = 9.6 Hz, H-4'), 5.90 (t, 1H, *J* = 9.6 Hz, H-3'), 7.22-7.96 (m, 30H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.1 (CH_3 Msc), 53.4 ($MeSO_2\underline{C}H_2CH_2$-), 55.0 ($CH_3$ OMe), 61.2 ($MeSO_2CH_2C\underline{H}_2$-), 63.0 (C-6'), 68.0 (C-5), 68.4 (C-6), 69.6 (C-3'), 71.8 (C-2'), 72.1 (C-5'), 72.7 (C-4'), 73.2 (CH_2 Bn), 75.0 (C-4), 75.2 (CH_2 Bn), 79.0 (C-3), 79.2 (C-2), 97.5 (C-1), 101.4 (C-1'), 127.2-138.5 (CH arom), 128.7 (2xC_q Bz), 129.4 (C_q Bz), 129.7 (C_q Bz), 137.7 (C_q Bn), 138.5 (C_q Bn), 153.7 (C=O Msc), 165.0 (C=O Bz), 165.1 (C=O Bz), 165.7 (C=O Bz), 166.0 (C=O Bz); HRMS $[M+H]^+$ calcd for $C_{59}H_{59}O_{19}S$ 1103.33658 was found 1103.33850.



Methyl 2,3-di-*O*-benzyl-6-*O*-methylsulfonylethoxycarbonyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (30): Disaccharide **30** was prepared form acceptor **15** (0.068g, 0.13 mmol,

1 eq) and donor **27** (0.130 g, 0.20 mmol, 1.5 eq) according to the general procedure for glycosylations as described above yielding compound **30** (0.92 g, 0.08 mmol, 64%). TLC (50% EtOAc in PE): R_f = 0.7; $[\alpha]_D^{22}$: +46.6º (c = 1, DCM); IR (neat, cm^{-1}): 1250, 1728; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.98 (s, 3H, CH_3 Msc), 3.28 (s, 3H, CH_3 OMe), 3.30-3.38 (m, 2H, $MeSO_2C\underline{H}_2CH_2$), 3.44 (dd, 1H, *J* = 3.6 Hz, *J* = 9.6 Hz, H-2), 3.71 (m, 1H, H-5), 3.81 (t, 1H, *J* = 9.2 Hz, H-4), 3.98 (t, 1H, *J* = 9.2 Hz, H-3), 4.03 (m, 1H, H-5'), 4.23-4.32 (m, 3H, 2xH-6 and H-6'), 4.39 (dd, 1H, *J* = 3.2 Hz, *J* = 10.0 Hz, H-6'), 4.45 (m, 1H, $MeSO_2CH_2C\underline{H}H$), 4.50 (d, 1H, *J* = 3.2, H-1), 4.56-4.62 (m, 2H, $MeSO_2CH_2CH\underline{H}$ and $CH\underline{H}$ Bn), 4.71 (d, 1H, *J* = 12.0 Hz, $CH\underline{H}$ Bn), 4.91 (d, 1H, *J* = 11.2 Hz, $CH\underline{H}$ Bn), 5.06 (d, 1H, *J* = 11.6 Hz, $CH\underline{H}$ Bn), 5.10 (d, 1H, *J* = 8.0 Hz, H-1'), 5.54 (t, 1H, *J* = 9.6 Hz, H-2'), 5.66 (t, 1H, *J* = 9.6 Hz, H-4'), 5.91 (t, 1H, *J* = 9.6 Hz, H-3'), 7.16-8.00 (m, 30H, H arom); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 42.0 (CH_3 Msc), 53.5 ($MeSO_2\underline{C}H_2CH_2$), 55.4 ($CH_3$ OMe), 60.9 ($MeSO_2CH_2\underline{C}H_2$), 62.8 (C-6'), 66.1 (C-6), 67.7 (C-5), 69.4 (C-4'), 71.8 (C-5'), 72.4 (C-2'), 73.0 (C-3'), 73.4 (CH_2 Bn), 75.0 (CH_2 Bn), 78.0 (C-4), 79.1 (C-2), 79.5 (C-3), 98.0 (C-1), 100.9 (C-1'), 126.9-133.4 (CH arom), 128.7 (C_q Bz), 128.8 (2xC_q Bz), 129.5 (C_q Bz), 137.9 (C_q Bn), 138.9 (C_q Bn), 154.0 (C=O Msc), 164.9 (C=O Bz), 165.0 (C=O Bz), 165.7 (C=O Bz), 165.9 (C=O Bz); HRMS $[M+H]^+$ calcd for $C_{59}H_{59}O_{19}S$ 1103.33658 was found 1103.33871, $[M+Na]^+$ calcd for $C_{59}H_{58}O_{19}SNa$ 1125.31852 was found 1125.31962.

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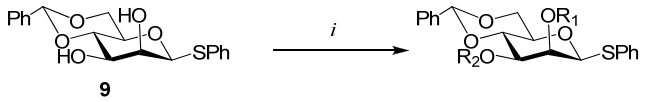
13. During the introduction and cleavage of the Fmoc, dibenzofulvene polymers can be formed which can complicate purification.

14. Phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-mannopyranoside (**11**) was obtained from phenyl-4,6-*O*-benzylidene-1-thio-β-D-mannopyranoside (**9**) as described in the experimental section.[21]



9

10 R_1 = H, R_2 = Bn (16%)
11 R_1 = Bn, R_2 = H (44%)
12 R_1 = Bn, R_2 = Bn (11%)

Reagents and conditions; *i*) BnBr, TBAS, $NaOH_{(aq)}$, DCM, 40 ºC, 18 h.

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