DOI: 10.1002/ejoc.200700048

Studies Directed to the Synthesis of Oligochitosans – Preparation of Building Blocks and Their Evaluation in Glycosylation Studies

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Keywords: Benzoylation / Glucosamine / Chitosan / Glycosylation

Thioglucosaminides with four different *N*-protecting groups, Troc, Phth, Alloc and PNZ could selectively be benzoylated at the C3 and C6-hydroxy groups in good yields without the requirement for low-temperature techniques. These reactions could be performed by refluxing a solution of the *N*-protected amino sugars with benzoyl chloride, 4-(dimethylamino)pyridine and pyridine in dichloromethane. The efficacy of these thioglycosides both as donors and acceptors for the construction of chitosans was evaluated. Whereas, the thioglycosides could be easily coupled to simple alcohols in excellent yields using the glycosylation promoting system *N*-iodosuccinimide and TMS triflate, these conditions could not effectuate coupling to the C4-hydroxy group possessing flanking benzoyl protecting groups. On the other hand, exploitation of Crich's *O*-glycosylation conditions involving a glycosyl triflate intermediate provided two different 1,4-linked disaccharides in good yields.

Introduction

Chitosan is a linear copolymer of β-(1,4) linked 2-acetamido-2-deoxy-D-glucopyranose (GlcNAc) and 2-amino-2-deoxy-D-glucopyranose (GlcN) as illustrated in Figure 1. The polysaccharide is produced by alkaline *N*-deacetylation of chitin, representing the second most widely distributed biopolymer on earth after cellulose. Because chitosan is enzymatically biodegradable, biocompatible and a non-toxic polymer, much interest has been focused on its biomedical, food processing, environmental and other industrial applications.[1–5] For example, chitosan has been used as a bioadhesive and permeablizer for pharmaceutical products, as well as it displays excellent properties for mucosal drug delivery. Certain chitosans exhibit antimicrobial activity and can also accelerate wound-healing processes.[6] In recent years, several studies have demonstrated the potential application of chitosan in DNA delivery systems.[7–9]

The biological properties of chitosans are nevertheless highly dependent on the chemical structure of the poly- or oligosaccharide (e.g. degree of deacetylation, GlcN/GlcNAc distribution pattern, chain length).[10] Thus structurally well-defined oligochitosans would represent important tools for studying the relationship between structure and biological activity, as well as providing information concerning the preferred enzymatic cleavage site of different chitosanases.[11] The high cost of known commercially available short-chained chitosan oligomers (di-, tri- and tetrasaccharides),[12] and there restriction in the versatility of the GlcN/GlcNAc sequences suggest that methods such as synthesis are required for accessing such compounds (Figure 1).

In this paper, we disclose our preliminary work on the way to the synthesis of chitosan oligomers, with focus on the preparation in few steps of suitably protected glucosamine derivatives for glycosylation studies.[13] In particular, we report on a modified procedure for the selective dibenzoylation of thioglycosides of a series of *N*-protected glucosamine derivatives which provides consistently good yields of the 3,6-dibenzoylated monosaccharide. Furthermore, the adaptability of these glycosyl donors/acceptors to glycosylation reactions is revealed.

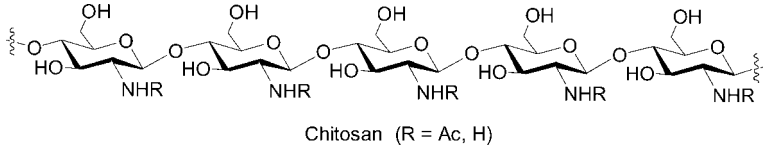

Figure 1. Structure of chitosan.

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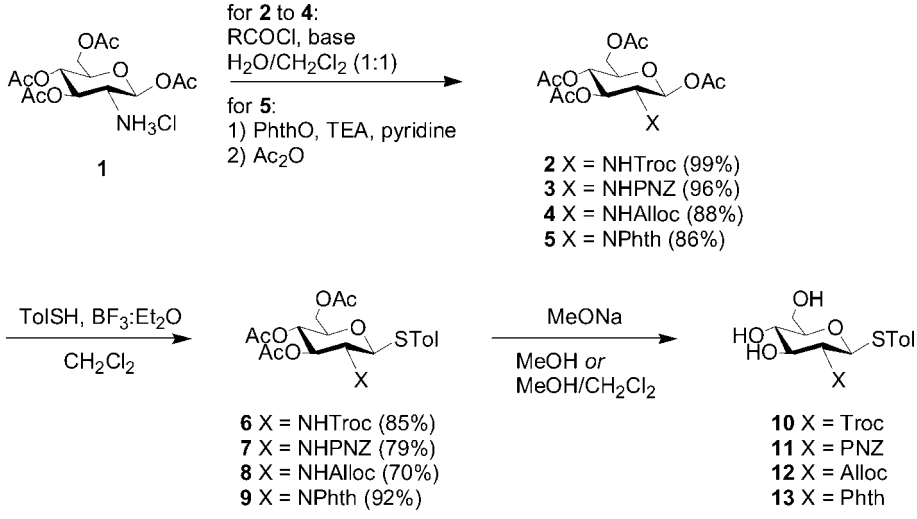
Results and Discussion

Our initial efforts to synthesize oligochitosans required the preparation of appropriately functionalized monomers that can function both as donors and acceptors in the glycosidic coupling reactions providing exclusively the β-(1,4) glycosidic linkages. Thus, the target building blocks must contain both a leaving group at the anomeric center, which can be selectively activated, and sets of orthogonal protection groups at the functionalities at C-2, C-3, C-4, and C-6. To this end, we prepared a collection of thioglucosaminides **10**–**13** with four different *N*-protecting groups in order to examine the possibility of selectively protecting the C3- and C6-hydroxy groups, as well as to test their usefulness in the glycosylations. This included the 2,2,2-trichloroethoxycarbonyl (Troc), *p*-nitrobenzyloxycarbonyl (PNZ),[14] allyloxycarbonyl (Alloc) and phthaloyl (Phth) groups, as illustrated in Scheme 1. These glycosides were synthesized by initially functionalizing the 2-amine of 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine (**1**).[15] The glycosyl acetates **2**–**5** were then subjected to a boron trifluoroetherate mediated treatment with thiocresol followed by a modified Zemplén deacetylation step affording the corresponding thioglycosides **10**–**13**. Attempts to prepare two other *N*-protected thioglucosamines as their *N*-benzyl carbamate and tetrachlorophthalamide (TCP)[16] derivatives were also undertaken. However, the Cbz protecting group failed to tolerate the thioglycosylation step, whereas the TCP group proved labile to the deacetylation protocol under various conditions. Special attention was also required for the removal of the *O*-acetyl groups in the donor containing the *N*-Troc group, as prolonged exposure to MeONa/MeOH resulted in transformation of this protecting group to the methyl carbamate.

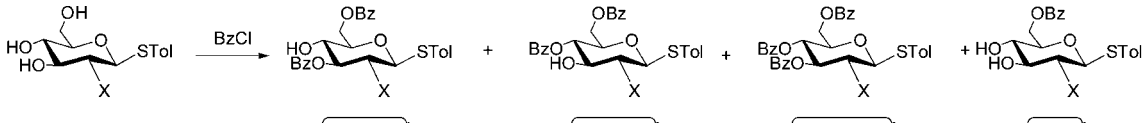
With these four thioglucosamine derivatives in hand, we then turned to investigate the possibility of selectively protecting the 3- and 6-OH groups in a single step thereby providing a short approach to glycosyl donors of glucosamine with a free 4-OH group. Hence, the standard but longer and more time-consuming three step protocol involving 4,6-benzylidene acetal formation, 3-OH group protection and regioselective opening of the benzylidene ring could be avoided. To achieve this goal, we explored the option of performing a regioselective diacylation as the least reactive hydroxy group is most often situated at C4.[17,18] However, it was noted that such a strategy would also lead to a glycosyl donor and acceptor of reduced reactivity.[19] The first attempt with the triol **10** employed 2.2 equiv. of benzoyl chloride and 2.0 equiv. dibutyltin oxide, following a procedure earlier applied for a selective 2,3,6-tri-*O*-benzoylation in the *manno* series.[20] This procedure afforded a mixture of products (Table 1, entry 1), among these the 4,6-dibenzoylated thioglycoside whereas the desired 3,6-dibenzoylated **14** was not detected. Instead a procedure by Nashed et al.[21,22] was examined, involving a dropwise addition of the benzoyl chloride to a precooled (–40 °C) solution of triol **10** in pyridine. This protocol resulted in the isolation of a small amount of the desired dibenzoate **14** (7%) along with the 4,6-dibenzoylated and the 6-benzoylated derivatives (Table 1, entry 2). Wong and co-workers have also succeeded in synthesizing 3,6-di-*O*-benzoylated glucosamines.[23] By refluxing a mixture of triol **10** or **13**, pyridine, DMAP and benzoyl chloride in excess (2.2–4.0 equiv.) in dichloromethane for 5 h, a 56% and 75% yield of **14** and **17**, respectively, was reported. Disappointingly, we could not reproduce their results, as in our hands this procedure yielded only 34% and 11% of the desired compounds along with the mono- and tribenzoylated products (Table 1, entry 3 and 4).

Optimizations of Wong's procedure were therefore performed, and by extending the reaction time, the outcome was significantly improved. TLC analysis of the reaction mixture indicated a significant amount of the mono- and tribenzoylated glucosamines formed after a reaction time of only a few hours. When heated to reflux for 2–5 d these compounds slowly disappeared with the appearance of the 3,6-dibenzoate, suggesting that a transesterification was taking place. The modified sugars **14**–**17** could be isolated in good to high yields (55% to 84%) for all the four glu-



Scheme 1. Synthesis of the *N*-protected thioglucosaminides.

Table 1. Selective benzoylation studies with thioglycosides **10**–**13**. Protocol A: 2.0 equiv. Bu_2SnO,PhMe/PhH, Dean–Stark reflux. Protocol B: pyridine, –40 °C. Protocol C: 5.0 equiv. pyridine, CH_2Cl_2, reflux. Protocol D: 0.7 equiv. DMAP, 15.0 equiv. pyridine, CH_2Cl_2, reflux.



10 X = NHTroc
11 X = NHPNZ
12 X = NHAlloc
13 X = NPhth

14 X = NHTroc
15 X = NHPNZ
16 X = NHAlloc
17 X = NPhth

Entry	X	Protocol	Equiv. BzCl	Time	3,6-diBz	4,6-diBz	3,4,6-triBz	6-Bz
1	NHTroc	A	2.2	24 h	-	+[a]	+[a]	+[a]
2	NHTroc	B	2.1	90 min	**(14)** 7 %	26%	-	+[a]
3	NHTroc	C	2.2	5 h	**(14)** 34%	-	+[b]	+[b]
4	NPhth	C	3.9	5 h	**(17)** 11%	-	+[b]	+[b]
5	NHTroc	D	2.2	4 days	**(14)** 66%	3%	-	-
6	NHPNZ	D	2.2	5 days	**(15)** 74%	-	-	-
7	NHAlloc	D	2.2	5 days	**(16)** 55%	-	-	-
8	NPhth	D	2.2	2 days	**(17)** 84%	-	-	-

[a] Identified from TLC of crude product. [b] Identified by MS of crude product.

cosamine derivatives tested (Table 1, entry 5–8). Thus, this procedure represents a potentially good alternative to the three-step protocol earlier discussed for the formation of an acceptor with an unprotected 4–OH.

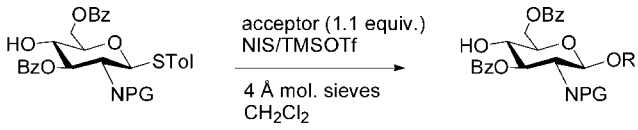
We are not entirely sure how this transesterification step may be taking place if at all, as solutions of a 1:1 mixture of the 6-*O*-benzoylated and the 3,4,6-tri-*O*-benzoylated derivatives of glucosamine (independently synthesized from **13**) in refluxing dichloromethane and in the presence pyridine and DMAP for 3 d did not lead to the formation of **17**. Addition of BzCl to this solution and continued refluxing (7 d) did lead to the formation of 3,6-di-*O*-benzoylated thioglycoside **17** but only in low yield (approx. 10%), suggesting that a simple benzoylation of the 6-*O*-benzoylated derivative at the 3-hydroxy group had occurred.

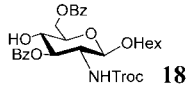
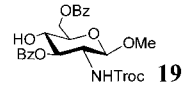
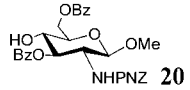
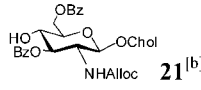
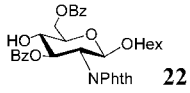
With the suitably protected thioglycosides in hand, glycosylation studies were commenced to examine the capabilities of these substrates as both glycosyl donors and acceptors. Initial work was focused on performing glycosylation without protection of the 4-hydroxy group in order to prepare the appropriate glycosyl acceptors representing the reducing end of a linear oligosaccharide. Hence, the thioglycoside **14** was subjected to NIS/TMSOTf glycosylation conditions at –18 °C in the presence of 1-hexanol or methanol generating the hexyl and methyl glycosides **18** and **19**, respectively, in high yield and with a reaction time of only 5–10 min (Table 2, entries 1 and 2).

The less reactive donor **17** also proceeded effectively, although it required higher temperatures and longer reaction time for completion (entry 5). Even though the PNZ-containing thioglycoside **15** was expected to also show a high reactivity as with **14**, its poor solubility in dichloromethane necessitated a higher reaction temperature (20 °C) and prolonged reaction times (90 min) for full conversion (entry 3). In this way, the *O*-glycosides **20** and **22** could be isolated in a yield of 72% and 83%, respectively. Finally, it is interesting to note the high reactivity of the Alloc-protected thioglycoside **16**, which provides **21** in excellent yield when reacted with 3-β-cholestanol (entry 4). This result was welcomed as Boullanger et al. had earlier demonstrated the lability of this nitrogen protecting group under BF_3-mediated glycosylation with glycosyl acetates.[24]

In order to examine the acceptor capabilities of these dibenzoylated carbohydrates, a series of NIS-based coupling attempts were made with the thioglycosides **6** and **8** bearing either a Troc or Alloc protecting group (Table 3). Thioglycoside **6** could easily be coupled to 1-hexanol and 3β-cholestanol in high yields and short reaction times (entries 1 and 2). However, all attempts to perform its coupling with the less reactive acceptor glycoside **17** bearing a free 4-OH

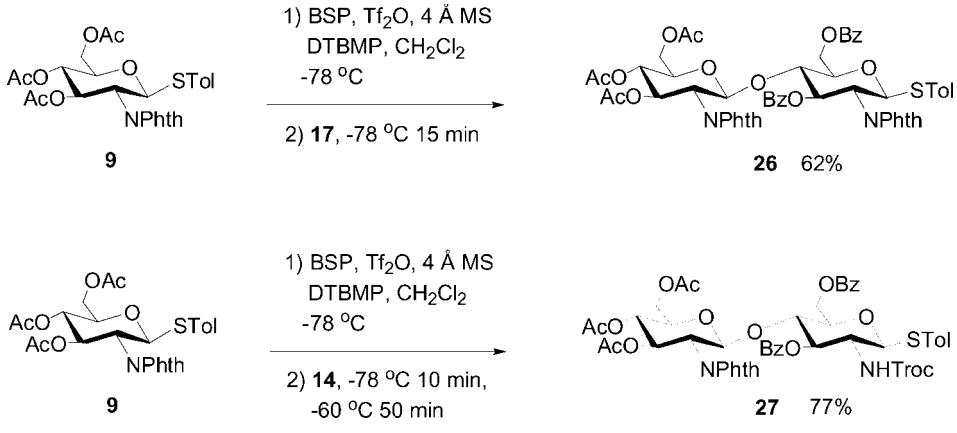
Table 2. Donor capabilities of the 3,6-dibenzoylated thioglucosaminides **14**, **15**, **16** and **17**.



Entry	Donor	Acceptor	Temp.	Time	Product	Yield[a]
1	**14**	1-hexanol	–18 °C	5 min	 **18**	97%
2	**14**	methanol	–18 °C	10 min	 **19**	82%
3	**15**	methanol	20 °C	75 min	 **20**	72%
4	**16**	3β-cholestanol	–20 °C	10 min	 **21**[b]	93%
5	**17**	1-hexanol	0 °C	90 min	 **22**	83%

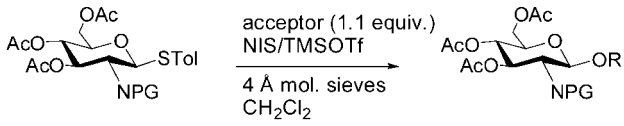
[a] All yields are based on chromatographically pure compounds. [b] Chol = 3-β-Cholestanyl.

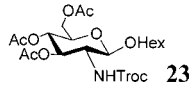
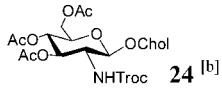
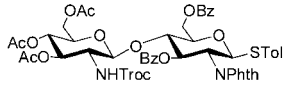
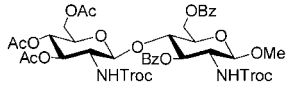
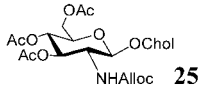
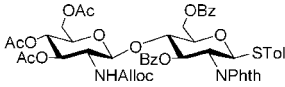
group proved futile even at high temperatures and extended reaction times (entry 3). In all cases, the glycosyl acceptor **17** was isolated. The methyl glycoside **19** was also tested with the same glycosyl donor, but again without any indication of a successful glycosylation (entry 4).[25] To increase the reactivity of the glycosyl donor, the Alloc-protection group was investigated, albeit only few studies have been reported exploiting this carbamate protecting group.[26] Again, 3β-cholestanol was employed as the acceptor for the glycosylation providing **25** in high yield (entry 5). Nevertheless, its coupling with acceptor **17** was far from satisfactory suggesting that the C4-hydroxy group with this type of glycosyl acceptors is not sufficiently reactive under the NIS/TMSOTf glycosylation conditions (entry 6).[27]



Scheme 2. Glycosylations employing Crich's conditions.

Table 3. Acceptor capabilities of the 3,6-dibenzoylated glucosamine derivatives using NIS/TMSOTf.



Entry	Donor	Acceptor	Temp.	Time	Product	Yield[a]
1	**6**	1-hexanol	0 °C	10 min	 **23**	97%
2	**6**	3β-cholestanol	0 °C	20 min	 **24** [b]	96%
3	**6**	**17**	0 °C–20 °C	overnight		0%
4	**6**	**19**	0 °C–20 °C	overnight		0%
5	**8**	3β-cholestanol	0 °C	5 min	 **25**	95%
6	**8**	**17**	0 °C–20 °C	overnight		0%

[a] All yields are based on chromatographically pure compounds. [b] Chol = 3-β-cholestanyl.

In an attempt to circumvent these coupling problems, we eventually turned to Crich's glycosylation conditions involving highly reactive glycosyl triflate intermediates.[28] This glycosylation protocol has previously been exploited for the coupling of thioglucosaminyl donors for the linear synthesis of *N*-acetylglucosamine oligosaccharides.[13a] In this case, treatment of the thioglycoside **9** with 1-benzenesulfinylpiperidine (BSP), triflic anhydride and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) in dichloromethane at –78 °C, followed by the addition of the acceptor **17** furnished after purification a good 62% yield of the disaccharide **26**. It was necessary to keep the reaction temperature low as even coupling attempts with these donors at –60 °C led to considerable decomposition. A similar coupling to the Troc-protected acceptor **14** performed at –60 °C was also successful providing the orthogonally *N*-protected disaccharide **27** in a good yield of 77% (Scheme 2).

Conclusions

In summary, we have provided a simple procedure for the selective protection of the 3- and 6-hydroxy groups of *N*-protected thioglucosaminides without the need for cold temperature techniques. These thioglycosides were effectively coupled to simple alcohols without intervention of the 4-OH. Whereas such compounds were not suitable as acceptors under NIS-glycosylation conditions due to attenuated reactivity of the 4-OH group, the use of BSP/Tf_2O proved to be compatible with both acceptor and donor possessing phthalimide and Troc protecting groups. Further work is underway to examine the use of Crich's glycosylation conditions for oligoglucosamine synthesis employing these thioglucosaminides.

Experimental Section

Unless otherwise noted all reactions were carried out under inert atmosphere. Solvents were dried according to standard procedures, reactions were monitored by thin-layer chromatography (TLC) analysis. The ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra were recorded at 100 MHz. The chemical shifts are reported in ppm downfield to TMS (δ = 0 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.16 ppm) for ^{13}C NMR spectroscopy. ^{1}H NMR spectra are reported as follows (s =

singlet, d = doublet, t = triplet, q = quartet, quin = quintet, ABspin = AB spin system, br. = broad; coupling constant(s) in Hz). Solvents were dried according to standard procedures. Flash chromatography was carried out on Merck silica gel 60 (230–400 mesh).

***p*-Methylphenyl 3,4,6-Tri-*O*-acetyl-2-deoxy-1-thio-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranoside (6):**[23] To a solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranose[24] (331 mg, 0.63 mmol) and *p*-thiocresol (119 mg, 0.96 mmol) in CH_2Cl_2 was added boron trifluoride–diethyl ether (0.11 mL, 0.87 mmol). After stirring at room temperature for 22 h the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 20 mL) and water (2 × 20 mL). The organic layer was dried with $MgSO_4$ and the solvents evaporated to dryness under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/CH_2Cl_2, 1:9) yielding **6** (315 mg, 85%) as a colorless foam. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.42 (d, J = 8.4 Hz, 2 H, Ar-H), 7.12 (d, J = 8.4 Hz, 2 H, Ar-H), 5.18 (t, J = 9.6, Hz, 1 H, 3-H), 5.12 (br. d, J = 9.6, Hz, 1 H, NH), 5.02 (t, J = 9.6 Hz, 1 H, 4-H), 4.81 (d, J = 9.6 Hz, 1-H), 4.76 (ABspin, J = 12.0 Hz, 2 H, CH_2), 4.23 (dd, J = 5.2, 12.2 Hz, 1 H, 6-H), 4.17 (dd, J = 2.4, 12.2 Hz, 1 H, 6′-H), 3.70 (ddd, J = 2.4, 5.2, 9.6 Hz, 1 H, 5-H), 3.63 (q, J = 9.6 Hz, 1 H, 2-H), 2.35 (s, 3 H, Ph-CH_3), 2.09 (s, 3 H, $COCH_3$), 2.02 (s, 3 H, $COCH_3$), 2.00 (s, 3 H, $COCH_3$) ppm.

***p*-Methylphenyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(4-nitrobenzyloxycarbonylamino)-1-thio-β-D-glucopyranoside (7):** A mixture of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(4-nitrobenzyloxycarbonylamino)-β-D-glucopyranose[14] (1.49 g, 2.84 mmol), *p*-thiocresol (498 mg, 4.01 mmol), and boron trifluoride–diethyl ether (0.43 mL, 3.4 mmol) in CH_2Cl_2 (15 mL) was stirred at room temperature for 18 h. To the dark reaction mixture was added 25 mL saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were washed with brine (25 mL), dried with $MgSO_4$ and the solvents evaporated to dryness to give a white solid. After recrystallization in ethyl acetate compound **7** was isolated as colorless crystals (1.33 g, 79%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.20 (d, J = 8.8 Hz, 2 H, Ar-H), 7.51 (d, J = 8.8 Hz, 2 H, Ar-H), 7.37 (d, J = 8.0 Hz, 2 H, Ar-H), 7.11 (d, J = 8.0 Hz, 2 H, Ar-H), 5.31–5.19 (m, 3 H, CH_2 & 3-H), 5.02 (t, J = 9.6 Hz, 1 H, 4-H), 4.98 (br. d, J = 9.6 Hz, 1 H, NH), 4.84 (d, J = 9.6 Hz, 1 H, 1-H), 4.22 (dd, J = 5.2, 12.4 Hz, 1 H, 6-H), 4.16 (dd, J = 2.4, 12.4 Hz, 1 H, 6′-H), 3.69 (m, 1 H, 5-H), 3.58 (q, J = 9.6 Hz, 1 H, 2-H), 2.35 (s, 3 H, Ph-CH_3), 2.08 (s, 3 H, $COCH_3$), 2.02 (s, 3 H, $COCH_3$), 1.96 (s, 3 H, $COCH_3$) ppm. HR-MS (ES-TOF): calcd. for $C_{27}H_{30}N_2O_{11}S$ [M + Na^+] 613.1468, found 613.1471.

***p*-Methylphenyl 3,4,6-Tri-*O*-acetyl-2-(allyloxycarbonylamino)-2-deoxy-1-thio-β-D-glucopyranoside (8):** 1,3,4,6-Tetra-*O*-acetyl-2-(allyloxycarbonylamino)-2-deoxy-β-D-glucopyranose[29] (1.98 g, 4.60 mmol) in CH_2Cl_2 (20 mL) was treated with *p*-thiocresol (803 mg, 6.47 mmol) and boron trifluoride–diethyl ether (0.70 mL, 5.53 mmol) as described for compound **6**. The product was purified by column chromatography (EtOAc/pentane, 2:3) to give **8** (1.60 g, 70%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.42 (d, J = 8.4 Hz, 2 H, Ar-H), 7.11 (d, J = 8.4 Hz, 2 H, Ar-H), 5.91 (ddd, J = 5.2, 10.4, 17.2 Hz, 1 H, CH=CH_2), 5.31 (d, J = 17.2 Hz, 1 H, CH=CH_2), 5.23 (d, J = 10.4 Hz, 1 H, CH=CH_2), 5.22 (br. s, 1 H, NH), 5.01 (t, J = 10.0 Hz, 1 H, 3-H), 4.79 (m, 2 H, 1-H & 4-H), 4.59 (d, J = 5.2 Hz, 2 H, CH_2), 4.22 (dd, J = 5.2, 12.4 Hz, 1 H, 6-H), 4.15 (dd, J = 2.4, 12.4 Hz, 1 H, 6′-H), 3.68 (ddd, J = 2.4, 5.2, 10.0 Hz, 1 H, 5-H), 3.64 (q, J = 10.0 Hz, 1 H, 2-H), 2.35 (s, 3 H, Ph-CH_3), 2.08 (s, 3 H, $COCH_3$), 2.01 (s, 6 H, 2×$COCH_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.7 (2 C), 169.6, 155.5, 138.6, 133.6 (2 C), 132.7, 129.8 (2 C), 128.3, 117.7, 86.9, 75.8, 73.6, 68.7, 65.9, 62.5, 55.0, 21.2, 20.8, 20.73, 20.66 ppm. HR-MS (ES-TOF) calcd. for $C_{23}H_{29}NO_9S$ [M + Na^+] 495.1563, found 495.1560.

***p*-Methylphenyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (9):**[23] The title compound was prepared from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose[30] (955 mg, 2.00 mmol), *p*-thiocresol (337 mg, 2.71 mmol) and boron trifluoride–diethyl ether (0.36 mL, 2.84 mmol) as described for the preparation of **6**. Column chromatography (EtOAc/CH_2Cl_2, 1:9) yielded 996 mg (92%) of **9** as colorless foam. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.88–7.86 (m, 2 H, Phth-H), 7.77–7.74 (m, 2 H, Phth-H), 7.30 (d, J = 8.0 Hz, 2 H, Tol-H), 7.07 (d, J = 8.0 Hz, 2 H, Tol-H), 5.77 (d, J = 9.6 Hz, 1 H, 3-H), 5.64 (d, J = 10.4 Hz, 1 H, 1-H), 5.12 (t, J = 9.6 Hz, 1 H, 4-H), 4.32 (t, J = 10.4 Hz, 1 H, 2-H), 4.28 (dd, J = 4.8, 12.0 Hz, 1 H, 6-H), 4.20 (dd, J = 1.2, 12.0 Hz, 1 H, 6′-H), 3.88 (ddd, J = 1.2, 4.8, 10.0 Hz, 1 H, 5-H), 2.33 (s, 3 H, Ph-CH_3), 2.10 (s, 3 H, $COCH_3$), 2.02 (s, 3 H, $COCH_3$), 1.83 (s, 3 H, $COCH_3$) ppm.

***p*-Methylphenyl 3,6-Di-*O*-Benzoyl-2-deoxy-1-thio-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranoside (14):**[23,31] To an ice-cold solution of **6** (557 mg, 0.95 mmol) in dry methanol (5 mL) and dry CH_2Cl_2 (5 mL) was added 1.0 M MeONa (0.13 mL, 0.13 mmol). The reaction was kept at 0 °C for 3 h, quenched with a small piece of dry ice and the solvents evaporated to dryness. The crude triol was taken up in CH_2Cl_2 (15 mL) and added 4-(dimethylamino)pyridine (81 mg, 0.66 mmol), dry pyridine (1.15 mL, 14.2 mmol), and freshly distilled benzoyl chloride (0.24 mL, 2.07 mmol). The reaction mixture was heated under reflux for 4 d, and then cooled to room temperature and diluted with 50 mL CH_2Cl_2. The organic phase was washed with 5% H_2SO_4 (20 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL), then dried with Na_2SO_4 and evaporated in vacuo. The product was purified by column chromatography (EtOAc/CH_2Cl_2, 1:9) to give **14** (422 mg, 66%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.00 (d, J = 8.0 Hz, 2 H, Ar-H), 7.94 (d, J = 8.0 Hz, 2 H, Ar-H), 7.60 (t, J = 8.0 Hz, 1 H, Ar-H), 7.52 (t, J = 7.6 Hz, 1 H, Ar-H), 7.43 (t, J = 7.6 Hz, 2 H, Ar-H), 7.41 (d, J = 8.0 Hz, 2 H, Ar-H), 7.34 (t, J = 8.0 Hz, 2 H, Ar-H), 6.94 (d, J = 8.0 Hz, 2 H, Ar-H), 5.62 (d, J = 9.6 Hz, 1 H, 1-H), 5.46 (t, J = 9.6 Hz, 1 H, 3-H), 4.88 (d, J = 10.0 Hz, 1 H, NH), 4.74–4.70 (m, 1 H, 6-H), 4.63 (ABspin, J = 12.0 Hz, 2 H, CH_2), 4.62 (dd, J = 5.2, 12.0 Hz, 1 H, 6′-H), 3.92 (q, J = 10.0 Hz, 1 H, 2-H), 3.86–3.76 (m, 2 H, 4-H & 5-H), 3.54 (br. s, 1 H, OH), 2.27 (s, 3 H, Ph-CH_3) ppm.

***p*-Methylphenyl 3,6-Di-*O*-Benzoyl-2-deoxy-2-(4-nitrobenzyloxycarbonylamino)-1-thio-β-D-glucopyranoside (15):** An ice-cooled suspension of **7** (501 mg, 0.85 mmol) in 20 mL methanol/CH_2Cl_2 (1:1) was added 1 M MeONa (0.13 mL, 0.13 mmol) and the reaction was stirred vigorously for 150 min. The reaction was quenched by adding a small piece of dry ice and dried by coevaporation of toluene. To the residue was added 4-(dimethylamino)pyridine (73 mg, 0.59 mmol), CH_2Cl_2 (15 mL) and pyridine (1.00 mL, 12.4 mmol). The mixture was heated to reflux, and freshly distilled benzoyl chloride (0.22 mL, 1.89 mmol) was added. The reaction was refluxed for 5 d. After cooling to room temperature the white precipitate was collected by filtration and washed repeatedly with CH_2Cl_2 and H_2O. Recrystallization in methanol gave **15** (423 mg, 74%) as colorless crystals. ^{1}H NMR ([D_6]DMSO, T = 60 °C, 400 MHz): δ = 7.99–7.90 (m, 5 H, Ar-H), 7.71 (tt, J = 1.6, 7.6 Hz, 1 H, Ar-H), 7.64–7.59 (m, 2 H, Ar-H), 7.57 (t, J = 7.6 Hz, 2 H, Ar-H), 7.47 (t, J = 7.6 Hz, 2 H, Ar-H), 7.35 (d, J = 8.4 Hz, 2 H, Ar-H), 7.30 (d,

J = 8.0 Hz, 2 H, Ar-H), 6.93 (d, J = 7.6 Hz, 2 H, Ar-H), 5.64 (d, J = 6.4 Hz, 1 H, 1-H), 5.26 (t, J = 9.2 Hz, 1 H, 3-H), 5.08 (ABspin, J = 14.0 Hz, 2 H, CH_2), 5.01 (d, J = 10.8 Hz, 1 H, NH), 4.66 (dd, J = 2.4, 10.8 Hz, 1 H, 6-H), 4.41 (dd, J = 6.8, 10.8 Hz, 1 H, 6′-H), 3.80–3.62 (m, 3 H, 2-H & 4-H & 5-H), 2.22 (s, 3 H, Ph-CH_3) ppm. HR-MS (ES-TOF) calcd. for $C_{35}H_{32}N_2O_{10}S$ [M + Na^+] 672.1778, found 672.1801.

***p*-Methylphenyl 2-(Allyloxycarbonylamino)-3,6-di-*O*-benzoyl-2-deoxy-1-thio-β-D-glucopyranoside (16):** A mixture of **8** (160 mg, 0.32 mmol) and potassium *tert*-butoxide (8.0 mg, 0.07 mmol) in dry methanol (1 mL) and CH_2Cl_2 (1 mL) was stirred at room temperature overnight. The reaction was quenched with a small piece of dry ice and the solvents were removed at reduced pressure. The crude triol **12** was treated with benzoyl chloride (85 μL, 0.73 mmol), pyridine (0.39 mL, 4.82 mmol), and 4-(dimethylamino)-pyridine (27.5 mg, 0.23 mmol) according to the procedure described for the preparation of **14**. Column chromatography (EtOAc/CH_2Cl_2, 1:9) yielded **16** (102 mg, 55%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD, 100:1, 400 MHz): δ = 8.00 (d, J = 8.0 Hz, 2 H, Ar-H), 7.96 (d, J = 7.6 Hz, 2 H, Ar-H), 7.59 (t, J = 6.8 Hz, 1 H, Ar-H), 7.53 (t, J = 6.8 Hz, 1 H, Ar-H), 7.43 (t, J = 6.8 Hz, 2 H, Ar-H), 7.40 (d, J = 8.0 Hz, 2 H, Ar-H), 7.35 (t, J = 7.6 Hz, 2 H, Ar-H), 6.91 (d, J = 8.0 Hz, 2 H, Ar-H), 5.69 (m, 1 H, CH=CH_2), 5.46 (d, J = 9.6 Hz, 1 H, 1-H), 5.38 (t, J = 9.2 Hz, 1 H, 3-H), 5.11 (d, J = 17.2 Hz, 1 H, CH=CH_2), 4.97 (d, J = 9.6 Hz, 1 H, CH=CH_2), 4.88 (d, J = 10.0 Hz, 1 H, NH), 4.72 (d, J = 12.0 Hz, 1 H, 6-H), 4.57 (dd, J = 5.6, 12.0 Hz, 1 H, 6′-H), 4.43 (d, J = 5.2 Hz, 2 H, CH_2), 3.96–3.72 (m, 3 H, 2-H & 4-H & 5-H), 2.25 (s, 3 H, Ph-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.5, 166.9, 155.8, 137.8, 133.6, 133.3, 132.7, 132.6, 130.1 (2 C), 130.0 (2 C), 129.9 (2 C), 129.8 (2 C), 129.7 (2 C), 129.2, 128.5 (3 C), 117.4, 86.9 77.9, 77.5, 69.7, 65.8, 64.1, 54.8, 21.3 ppm. HR-MS (ES-TOF) calcd. for $C_{31}H_{31}NO_8S$ [M + Na^+] 600.1668, found 600.1676.

***p*-Methylphenyl 3,6-Di-*O*-Benzoyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (17):**[23] To **9** (176 mg, 0.32 mmol) in dry MeOH (15 mL) was added 1 M MeONa (0.27 mL). The reaction mixture was stirred for 60 min at room temperature until the solution became clear, after which it was quenched with a small piece of dry ice and the solvents evaporated to dryness. The crude product in CH_2Cl_2 (15 mL) was treated with pyridine (0.39 mL, 4.82 mmol), 4-(dimethylamino)pyridine (28 mg, 0.23 mmol), and benzoyl chloride (0.10 mL, 0.86 mmol) according to the procedure described above. Column chromatography (EtOAc/CH_2Cl_2, 1:12) of the crude mixture gave 170 mg (84%) of **17** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.09 (dd, J = 1.6, 8.4 Hz, 2 H, Phth-H), 7.84–7.29 (m, 14 H, Ar-H), 6.95 (d, J = 8.0 Hz, 2 H, Ar-H), 5.98 (dd, J = 8.8, 10.4 Hz, 1 H, 3-H), 5.81 (d, J = 10.4 Hz, 1 H, 1-H), 4.77 (dd, J = 2.4, 12.4 Hz, 1 H, 6-H), 4.73 (dd, J = 4.8, 12.4 Hz, 1 H, 6′-H), 4.49 (t, J = 10.4 Hz, 1 H, 2-H), 4.02 (ddd, J = 2.4, 4.8, 8.8 Hz, 1 H, 5-H), 3.86 (ddd, J = 5.6, 8.8, 10.4 Hz, 1 H, 4-H), 3.52 (d, J = 5.6 Hz, 1 H, OH), 2.27 (s, 3 H, Ph-CH_3) ppm.

General Method for NIS/TMSOTf-Promoted Glycosylation: The thioglycoside (1 equiv.), acceptor (1.1 equiv.), and 4 Å molecular sieves in dry CH_2Cl_2 was stirred under an argon atmosphere for 30 min. The mixture was cooled to the temperature stated and *N*-iodosuccinimide (1.2 equiv.) was added followed by trimethylsilyl triflate (cat.). The reaction was followed by TLC and quenched with 1.5 mL saturated aqueous $NaHCO_3$ as soon as the donor had vanished from the reaction mixture. The reaction was heated to room temperature and a few $Na_2S_2O_3$ crystals were added followed by stirring until the solution turns colorless. The crude mixture was diluted with CH_2Cl_2 (50 mL), filtered through celite and washed with $NaHCO_3$ (saturated aqueous solution), water, and brine. The organic phase was dried with Na_2SO_4 and the solvent removed under reduced pressure. The crude product was purified by column chromatography.

1-Hexyl 3,6-Di-*O*-Benzoyl-2-deoxy-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranoside (18):[31] Thioglycoside **14** (220 mg, 0.33 mmol), 1-hexanol (45 μL, 0.36 mmol), *N*-iodosuccinimide (88 mg, 0.39 mmol in 0.60 mL CH_3CN) and trimethylsilyl triflate (20 μL, 0.11 mmol) in CH_2Cl_2 (3.0 mL) reacted for 5 min at –18 °C. Column chromatography (EtOAc/CH_2Cl_2, 1:9) gave 196 mg (92%) of **18** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.05 (d, J = 7.2 Hz, 2 H, Ar-H), 8.01 (d, J = 7.6 Hz, 2 H, Ar-H), 7.59–7.52 (m, 2 H, Ar-H), 7.43 (t, J = 7.2 Hz, 2 H, Ar-H), 7.38 (t, J = 8.0 Hz, 2 H, Ar-H), 5.55 (d, J = 9.2 Hz, 1 H, NH), 5.47 (dd, J = 8.4, 10.0 Hz, 1 H, 3-H), 4.71–4.63 (m, 3 H, 1-H & 6-H & 6′-H), 4.62 (ABspin, J = 12.0 Hz, 2 H, CH_2CCl_3), 3.91–3.80 (m, 4 H, 2-H & 4-H & 5-H & OH), 3.54–3.48 (m, 2 H, Hex-CH_2), 1.62–1.53 (m, 2 H, Hex-CH_2), 1.36–1.18 (m, 6 H, 3× Hex-CH_2), 0.85 (t, J = 7.2 Hz, 3 H, Hex-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.5, 167.3, 154.5, 133.7, 133.5, 130.2 (2 C), 130.0 (2 C), 129.8 (2 C),129.7, 129.2, 128.6 (2 C), 101.3, 95.5, 75.9, 74.5, 74.3, 70.3, 69.8, 63.9, 56.3, 31.6, 29.6, 25.6, 22.7, 14.1 ppm.

Methyl 3,6-Di-*O*-Benzoyl-2-deoxy-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranoside (19):[30] Thioglycoside **14** (104 mg, 0.16 mmol), methanol (8.6 μL, 0.21 mmol), *N*-iodosuccinimide (46 mg, 0.20 mmol in 0.25 mL CH_3CN), trimethylsilyl triflate (10 μL, 0.06 mmol) and 3-Å molecular sieves in CH_2Cl_2 (2.5 mL) reacted for 10 min at –18 °C. Column chromatography (EtOAc/CH_2Cl_2, 1:9) gave 74 mg (82%) of **18** as a colorless foam. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.06 (d, J = 7.2 Hz, 2 H, Ar-H), 8.01 (d, J = 7.2 Hz, 2 H, Ar-H), 7.58 (t, J = 7.2 Hz, 1 H, Ar-H), 7.54 (t, J = 7.6 Hz, 1 H, Ar-H), 7.44 (t, J = 7.6 Hz, 2 H, Ar-H), 7.38 (t, J = 7.2 Hz, 2 H, Ar-H), 5.58 (d, J = 9.2 Hz, 1 H, NH), 5.46 (dd, J = 8.8, 10.4 Hz, 1 H, 3-H), 4.72 (dd, J = 4.4, 12.0 Hz, 1 H, 6-H), 4.65 (dd, J = 2.4, 12.0 Hz, 1 H, 6′-H), 4.61 (ABspin, J = 12.4 Hz, 2 H, CH_2), 4.56 (d, J = 8.0 Hz, 1 H, 1-H), 3.94–3.78 (m, 3 H, 2-H & 4-H & 5-H), 3.53 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.5, 167.3, 154.7, 133.8, 133.5, 130.2 (2 C), 130.0 (2 C), 129.7, 129.1, 128.6 (4 C), 102.3, 95.5, 75.8, 74.5, 74.4, 69.6, 63.8, 57.2, 56.2 ppm.

Methyl 3,6-Di-*O*-Benzoyl-2-deoxy-2-(4-nitrobenzyloxycarbonylamino)-β-D-glucopyranoside (20): Thioglycoside **15** (81 mg, 0.12 mmol), dry methanol (6.8 μL, 0.17 mmol), *N*-iodosuccinimide (35 mg, 0.16 mmol in 0.2 mL CH_3CN) and trimethylsilyl triflate (10 μL, 0.06 mmol) in CH_2Cl_2 (2.5 mL) reacted for 50 min at room temperature. Column chromatography (EtOAc/CH_2Cl_2, 1:6) gave **20** (51 mg, 72%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.06 (dd, J = 1.2, 8.0 Hz, 2 H, Ar-H), 7.97 (dd, J = 1.6, 8.0 Hz, 2 H, Ar-H), 7.87 (br. d, J = 6.4 Hz, 2 H, Ar-H), 7.59 (tt, J = 1.6, 7.6 Hz, 1 H, Ar-H), 7.57 (tt, J = 1.2, 7.6 Hz, 1 H, Ar-H), 7.45 (t, J = 8.0 Hz, 2 H, Ar-H), 7.38 (t, J = 8.0 Hz, 2 H, Ar-H), 7.21 (br. d, J = 6.4 Hz, 2 H, Ar-H), 5.35 (t, J = 9.6 Hz, 1 H, 3-H), 5.21 (d, J = 9.6 Hz, 1 H, 1-H), 5.08 (ABspin, J = 14.0 Hz, 2 H, CH_2), 4.76 (dd, J = 4.4, 12.4 Hz, 1 H, 6-H), 4.62 (dd, J = 2.4, 12.4 Hz, 1 H, 6′-H), 4.51 (br. d, J = 7.2 Hz, 1 H, NH), 3.88 (dd, J = 9.2, 9.6 Hz, 1 H, 4-H), 3.80 (dt, J = 4.4, 9.6 Hz, 1 H, 2-H), 3.74 (ddd, J = 2.4, 4.4, 9.6 Hz, 1 H, 5-H), 3.54 (s, 3 H, OCH_3), 3.32 (br. s, 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.4, 167.3, 155.7, 147.5, 144.0, 133.9, 133.6, 130.1 (2 C), 130.0 (2 C), 129.6, 129.1, 128.7 (2 C), 128.6 (2 C), 127.7 (2 C), 123.6 (2 C), 102.4, 75.9, 74.5, 69.4, 65.3, 63.7, 57.2, 56.1 ppm. HR-MS (ES-TOF) calcd. for $C_{29}H_{28}N_2O_{11}$ [M + Na^+] 603.5292, found 603.5292.

3β-Cholestanyl 2-(Allyloxycarbonylamino)-3,6-di-*O*-benzoyl-2-deoxy-β-D-glucopyranoside (21): Thioglycoside **16** (62 mg, 0.11 mmol), 3β-cholestanol (50 mg, 0.13 mmol), *N*-iodosuccinimide (31 mg, 0.14 mmol in 0.40 mL CH_3CN), and trimethylsilyl triflate (10 μL, 0.06 mmol) in CH_2Cl_2 (3.0 mL) reacted for 10 min at –20 °C. Column chromatography (EtOAc/pentane, 1:2) yielded 83 mg (93%) of glucosaminide **21** as colorless oil. ^{1}H NMR ($CDCl_3$, T = 60 °C, 400 MHz): δ = 8.05 (t, J = 8.0 Hz, 4 H, Ar-H), 7.57 (t, J = 7.6 Hz, 1 H, Ar-H), 7.56 (t, J = 7.6 Hz, 1 H, Ar-H), 7.44 (t, J = 7.6 Hz, 2 H, Ar-H), 7.42 (t, J = 8.0 Hz, 2 H, Ar-H), 5.78 (ddt, J = 5.6, 10.8, 17.6 Hz, 1 H, CH=CH_2), 5.39 (m, 1 H, 3-H), 5.18 (d, J = 17.8 Hz, 1 H, CH=CH_2), 5.06 (d, J = 10.8 Hz, 1 H, CH=CH_2), 4.85 (d, J = 8.8 Hz, 1 H, 1-H), 4.78 (d, J = 8.0 Hz, 1 H, NH), 4.67 (ABspin, J = 9.6 Hz, 2 H, CH_2), 4.47 (m, 2 H, 6-H & 6′-H), 3.81–3.74 (m, 2 H, 4-H & 5-H), 3.69 (q, J = 8.8 Hz, 1 H, 2-H), 3.59 (sept, J = 5.2 Hz, 1 H, Chol-3-H), 3.10 (br. s, 1 H, OH), 2.10–0.50 (m, 31 H, Chol-H), 0.92 (d, J = 6.4 Hz, 3 H, Chol-CH_3), 0.88 (d, J = 6.8 Hz, 6 H, 2 Chol-CH_3), 0.77 (s, 3 H, Chol-CH_3), 0.66 (s, 3 H, Chol-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.6, 167.0, 156.0, 133.6, 133.3, 132.8, 130.2 (2 C), 130.0 (2 C), 129.9, 129.4, 128.6 (2 C), 128.5 (2 C), 117.6, 99.8, 79.6, 76.4, 74.1, 70.3, 65.8, 64.1, 56.7, 56.5, 54.5, 44.9, 42.8, 40.2, 39.7, 37.1, 36.3, 35.9, 35.7, 35.6, 34.7, 32.2, 29.5, 28.9, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.4, 18.8, 12.4, 12.2 ppm. HR-MS (ES-TOF) calcd. for $C_{51}H_{71}NO_9$ [M + Na^+] 864.5027, found 864.5018.

1-Hexyl 3,6-Di-*O*-Benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (22): Thioglycoside **17** (21 mg, 34 μmol), 1-hexanol (4.8 μL, 38 μmol), *N*-iodosuccinimide (9 mg, 40 μmol in 0.15 mL CH_3CN), and trimethylsilyl triflate (4.0 μL, 22 μmol) in CH_2Cl_2 (1.5 mL) reacted at 0 °C for 90 min. Column chromatography (EtOAc/CH_2Cl_2, 1:12) gave **22** in 83% yield (17 mg) as a colorless syrup. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.11 (d, J = 7.6 Hz, 2 H, Phth-H), 7.90 (d, J = 7.6 Hz, 2 H, Phth-H), 7.80 (m, 2 H, Ar-H), 7.69–7.66 (m, 2 H, Ar-H), 7.60 (t, J = 7.6 Hz, 1 H, Ar-H), 7.50 (t, J = 7.2 Hz, 1 H, Ar-H), 7.48 (t, J = 7.6 Hz, 2 H, Ar-H), 7.35 (t, J = 7.6 Hz, 2 H, Ar-H), 5.92 (dd, J = 8.4, 10.4 Hz, 1 H, 3-H), 5.44 (d, J = 8.4 Hz, 1 H, 1-H), 4.79 (dd, J = 4.4, 12.0 Hz, 1 H, 6-H), 4.68 (dd, J = 2.0, 12.0 Hz, 1 H, 6′-H), 4.46 (dd, J = 8.4, 10.4 Hz, 1 H, 4-H), 3.96–3.89 (m, 2 H, 2-H & 5-H), 3.85 (dt, J = 6.4, 9.6 Hz, 1 H, Hex-1-H), 3.47 (dt, J = 6.4, 9.6 Hz, 1 H, Hex-1′-H), 3.42 (br. s, 1 H, OH), 1.50–1.34 (m, 2 H, Hex-CH_2), 1.12–0.92 (m, 6 H, 3× Hex-CH_2), 0.68 (t, J = 7.2 Hz, 3 H, Hex-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.3, 167.1, 134.3 (2 C), 133.7, 133.4, 131.6 (2 C), 130.09 (2 C), 130.06 (2 C), 129.9, 129.0, 128.6 (2 C), 123.7 (2 C), 98.5, 74.6, 74.5, 70.7, 70.3, 63.8, 54.7, 31.4, 29.4, 25.6, 22.6, 14.0 ppm. HR-MS (ES-TOF) calcd. for $C_{34}H_{35}NO_9$ [M + Na^+] 624.2210, found 624.2205.

1-Hexyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranoside (23):[31] Thioglycoside **6** (92 mg, 0.16 mmol), freshly distilled 1-hexanol (22 μL, 0.18 mmol), *N*-iodosuccinimide (43 mg, 0.19 mmol) and trimethylsilyl triflate (20 μL, 11 mmol) in CH_2Cl_2 (2.0 mL) reacted at 0 °C for 10 min. Column chromatography (EtAOc/CH_2Cl_2, 1:9) yielded **23** (86 mg, 97%) as a colorless foam. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.32 (t, J = 10.0 Hz, 1 H, 3-H), 5.07 (t, J = 10.0 Hz, 1 H, 4-H), 5.05 (d, J = 9.2 Hz, 1 H, 1-H), 4.71 (ABspin, J = 12.0 Hz, 2 H, CH_2CCl_3), 4.64 (d, J = 8.0 Hz, 1 H, NH), 4.28 (dd, J = 4.8, 12.0 Hz, 1 H, 6-H), 4.13 (dd, J = 2.4, 12.0 Hz, 1 H, 6′-H), 3.87 (dt, J = 6.8, 9.6 Hz, 1 H, Hex-1-H), 3.69 (m, 1 H, 5-H), 3.59 (dt, J = 8.4, 10.0 Hz, 1 H, 2-H), 3.48 (dt, J = 6.8, 9.6 Hz, 1 H, Hex-1′-H), 2.09 (s, 3 H, $COCH_3$), 2.03 (s, 6 H, 2× $COCH_3$), 1.62–1.52 (m, 2 H, Hex-CH_2), 1.35–1.24 (m, 6 H, 3× Hex-CH_2), 0.88 (t, J = 7.2 Hz, 3 H, Hex-CH_3) ppm.

3β-Cholestanyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranoside (24):[32] Thioglycoside **6** (90 mg, 0.15 mmol), 3β-cholestanol (66 mg, 0.17 mmol), *N*-iodosuccinimide (40 mg, 0.18 mmol), and trimethylsilyl triflate (20 μL, 0.11 mmol) in CH_2Cl_2 (2.0 mL) reacted at 0 °C for 20 min. Column chromatography (EtOAc–pentane 1:4) gave **24** (125 mg, 96%) as a white powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.38 (t, J = 10.0 Hz, 1 H, 3-H), 5.12 (d, J = 8.0 Hz, 1 H, NH), 5.04 (t, J = 10.0 Hz, 1 H, 4-H), 4.81 (d, J = 8.4 Hz, 1 H, 1-H), 4.71 (ABspin, J = 12.0 Hz, 2 H, CH_2), 4.27 (dd, J = 4.8, 12.4 Hz, 1 H, 6-H), 4.10 (dd, J = 2.0, 12.4 Hz, 1 H, 6′-H), 3.69 (m, 1 H, 5-H), 3.57 (tt, J = 5.2, 11.2 Hz, 1 H, Chol-3-H), 3.48 (dt, J = 8.4, 10.0 Hz, 1 H, 2-H), 2.07 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.02 (s, 3 H, $COCH_3$), 2.00–0.54 (m, 40 H, Chol-H), 0.76 (s, 3 H, Chol-CH_3), 0.63 (s, 3H Chol-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.9, 170.7, 169.7, 154.0, 109.9, 79.7, 77.6, 71.8, 69.1, 62.4, 56.8, 56.6, 56.5, 54.5, 53.0, 44.9, 42.8, 40.2, 39.8, 37.1, 36.3, 35.9, 35.7, 35.6, 34.6, 32.2, 29.4, 29.0, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.4, 20.8 (3 C), 18.8, 12.4, 12.2 ppm.

3β-Cholestanyl 3,4,6-Tri-*O*-acetyl-2-(allyloxycarbonylamino)-2-deoxy-β-D-glucopyranoside (25): Thioglycoside **8** (90 mg, 0.18 mmol), 3β-cholestanol (92 mg, 0.24 mmol), *N*-iodosuccinimide (56 mg, 0.24 mmol in 0.40 mL CH_2Cl_2), and trimethylsilyl triflate (20 μL, 0.11 mmol) in CH_2Cl_2 (3 mL) reacted for 5 min at 0 °C. Column chromatography (EtOAc/CH_2Cl_2, 14:86) yielded **25** (131.9 mg, 95%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.90 (ddt, J = 6.0, 10.4, 17.2 Hz, 1 H, CH=CH_2), 5.32 (dd, J = 9.2, 10.8 Hz, 1 H, 3-H), 5.29 (d, J = 17.2 Hz, 1 H, CH=CH_2), 5.19 (d, J = 10.4 Hz, 1 H, CH=CH_2), 5.00 (t, J = 9.6 Hz, 1 H, 4-H), 4.75 (d, J = 8.0 Hz, 1 H, 1-H), 4.66 (d, J = 7.6 Hz, 1 H, NH), 4.56 (m, 2 H, Alloc-CH_2), 4.25 (dd, J = 5.2, 12.0 Hz, 1 H, 6-H), 4.13 (dd, J = 2.4, 12.0 Hz, 1 H, 6′-H), 3.68 (m, 1 H, 5-H), 3.57 (tt, J = 5.6, 11.2 Hz, 1 H, Chol-3-H), 3.46 (dt, J = 8.0, 9.2 Hz, 1 H, 2-H), 2.07 (s, 3 H, $COCH_3$), 2.05 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.00–0.57 (m, 46 H, Chol-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.6, 167.0, 156.0, 133.6, 133.3, 132.8, 130.2 (2 C), 130.0 (2 C), 129.9, 129.4, 128.6 (2 C), 128.5 (2 C), 117.6, 99.8, 79.6, 76.4, 74.1, 70.3, 65.8, 64.1, 56.7, 56.5, 54.5, 44.9, 42.8, 40.2, 38.7, 37.1, 36.3, 35.9, 35.7, 35.6, 34.7, 32.2, 29.5, 28.9, 28.4, 28.2, 24.4, 24.0, 23.0 (2 C), 22.7, 21.4, 18.8, 12.4, 12.2 ppm. HR-MS (ES-TOF) calcd. for $C_{51}H_{71}NO_9$ [M + Na^+] 841.5129, found 841.5124.

***p*-Methylphenyl 4-*O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-3,6-di-*O*-benzoyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (26):** Thioglycoside **9** (104 mg, 0.22 mmol), 1-benzenesulfinyl piperidine (50 mg, 0.24 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (89 mg, 0.43 mmol), and 4-Å mol. sieves in dry CH_2Cl_2 (1.5 mL) was stirred under argon for 30 min. The mixture was cooled to –78 °C and trifluoromethanesulfonic anhydride (48 μL, 0.29 mmol) was added. After 30 min, a –78 °C cold solution of **17** (203 mg, 0.33 mmol) in dry CH_2Cl_2 (0.5 mL) was added dropwise. After 15 min stirring at –78 °C, triethylamine (0.2 mL) was added and the mixture was warmed to room temperature, diluted with CH_2Cl_2 (15 mL) and filtered. The organic phase was washed with saturated aqueous $NaHCO_3$ (1 × 15 mL), and brine (1 × 15 mL), dried with Na_2SO_4, and the solvents evaporated to dryness. The product was purified by column chromatography (EtOAc/CH_2Cl_2, 1:9) to give **26** (140 mg, 62%) as a colorless foam. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.91–7.39 (m, 18 H, Ar-H), 7.15 (d, J = 8.0 Hz, 2 H, Ar-H), 6.77 (d, J = 8.0 Hz, 2 H, Ar-H), 6.11 (dd, J = 8.8, 10.0 Hz, 1 H, 3-H), 5.67 (d, J = 10.8 Hz, 1 H, 1-H), 5.61 (d, J = 8.4 Hz, 1 H, 1-H), 5.54 (dd, J = 9.2, 10.8 Hz, 1 H, 3-H), 4.96 (t, J = 10.0 Hz, 1 H, 4-H), 4.68 (dd, J = 2.0, 12.0 Hz, 1 H, 6-H), 4.27 (t, J = 10.0 Hz, 1 H, 2-H), 4.22 (dd, J = 8.4, 10.4 Hz,

1 H, 2-H), 4.11 (t, J = 10.0 Hz, 1 H, 4-H), 4.01 (dd, J = 3.6, 12.0 Hz, 1 H, 6-H), 3.92 (ddd, J = 2.0, 3.6, 10.0 Hz, 1 H, 5-H), 3.79 (dd, J = 3.6, 12.0 Hz, 1 H, 6-H), 3.45 (dd, J = 2.0, 12.0 Hz, 1 H, 6-H), 3.19 (ddd, J = 2.0, 3.6, 10.0 Hz, 1 H, 5-H), 2.18 (s, 3 H, CH_3), 1.97 (s, 3 H, CH_3), 1.86 (s, 3 H, CH_3), 1.75 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.7, 170.2, 169.3, 168.1, 167.2, 165.4, 165.1, 138.7, 134.4, 134.3, 134.2, 133.7, 133.2, 131.9, 131.3, 131.0, 129.9, 129.8, 129.7, 129.6, 129.1, 128.8, 128.4, 126.5, 123.8, 123.7, 123.6, 97.8, 82.7, 77.4, 76.5, 76.2, 73.3, 71.9, 70.5, 68.1, 62.5, 61.0, 55.1, 54.0, 21.3, 20.8, 20.6, 20.4 ppm.

***p*-Methylphenyl 4-*O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-3,6-di-*O*-benzoyl-2-deoxy-1-thio-2-(2,2,2-trichloroethyloxycarbonylamino)-β-D-glucopyranoside (27):**[31] Thioglycoside **9** (69 mg, 0.14 mmol), 1-benzenesulfinyl piperidine (34 mg, 0.16 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (65 mg, 0.32 mmol), and 4-Å mol. sieves in dry CH_2Cl_2 (2.5 mL) was stirred under argon for 90 min. The mixture was cooled to –78 °C and trifluoromethanesulfonic anhydride (27 μL, 0.16 mmol) was added. After 30 min a cold (–78 °C) solution of **14** (144 mg, 0.21 mmol) in dry CH_2Cl_2 (1.0 mL) was added dropwise. The solution was stirred at –78 °C for 10 min and then at –60 °C for 50 min. Then triethylamine (0.2 mL) was added and the mixture was warmed up to room temperature, diluted with CH_2Cl_2 (15 mL) and filtered. The organic phase was washed with saturated $NaHCO_3$ (1 × 15 mL), and brine (1 × 15 mL), dried with Na_2SO_4, and the solvents evaporated to dryness. The product was purified by column chromatography (EtOAc/CH_2Cl_2, 1:9) to give **27** (121 mg, 77%) as a colorless foam. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.09 (dd, J = 1.2, 8.4 Hz, 2 H, Ar-H), 7.79 (dd, J = 1.2, 8.4 Hz, 2 H, Ar-H), 7.64–7.24 (m, 12 H, Ar-H), 6.79 (d, J = 7.6 Hz, 2 H, Ar-H), 5.60 (d, J = 8.4 Hz, 1 H, 1-H), 5.57 (dd, J = 9.2, 10.8 Hz, 1 H, 3-H), 5.51 (dd, J = 9.2, 10.0 Hz, 1 H, 3-H), 5.25 (d, J = 10.0 Hz, 1 H, NH), 4.98 (t, J = 9.2 Hz, 1 H, 4-H), 4.62 (t, J = 10.4 Hz, 1 H), 4.61 (d, J = 10.4 Hz, 1 H, 1-H), 4.59 (ABspin, J = 12.0 Hz, 2 H, CH_2), 4.22 (dd, J = 8.4, 10.8 Hz, 1 H), 4.04 (t, J = 9.2 Hz, 1 H), 3.96 (dd, J = 4.0, 12.4 Hz, 1 H, 6-H), 3.84 (dd, J = 4.0, 12.4 Hz, 1 H, 6-H), 3.78 (d, J = 10.0 Hz, 1 H), 3.72 (ddd, J = 2.4, 4.8, 10.0 Hz, 1 H, 5-H), 3.53 (dd, J = 2.4, 12.4 Hz, 1 H, 6-H), 3.31 (ddd, J = 2.4, 3.6, 10.0 Hz, 1 H, 5-H), 2.18 (s, 3 H, Ph-CH_3), 1.96 (s, 3 H, $COCH_3$), 1.89 (s, 3 H, $COCH_3$), 1.75 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.6, 170.2, 169.3, 165.8, 165.4, 154.2, 138.6, 134.4 (2 C), 134.0 (2 C), 133.2, 131.0, 130.1 (2 C), 129.9 (2 C), 129.7 (2 C), 129.3, 128.9, 128.4, 127.5 (2 C), 123.8 (2 C), 98.0, 95.3, 86.8, 76.6, 75.8, 74.8, 74.6, 72.0, 70.5, 68.2, 62.5, 61.1, 55.6, 21.2, 20.8, 20.6, 20.4 ppm.

Supporting Information (see also the footnote of the first page of the article): NMR spectra for compounds **7**, **8** and **14**–**27**.

Acknowledgments

We are indebted to the Ministry of Science and Technology and the University of Aarhus for generous financial support.

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Received: January 20, 2007
Published Online: May 11, 2007

