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Glycosylation

Conformational Lock of Glycosyl Donors Using Cyclic Carbamates

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Abstract: Axial rich glycosyl donors often display superior reactivity and stereoselectivity in glycosylations. In this study, a glucosamine glycosyl donor, locked in a $^1C_4$ conformation by a six-membered carbamate ring, i.e. an oxazinone, is synthesized and studied. The 2*N*,4*O* carbamate is synthesized in one step from the corresponding azide. The glycosylation properties were studied by glycosylating different alcohols. Derivatives of the glycosyl donor were synthesized by introducing Ac, Troc, Ts, and Ms groups on the oxazinone nitrogen. The ring opening to give the glycoside in the $^4C_1$ conformation was found to proceed smoothly using Zemplén conditions.

Introduction

Protective groups often have a decisive influence on the glycosylation reaction.[1,2] The anomeric selectivity can be directed by neighboring group participation, and the reactivity of the glycosyl donor is determined by the protective groups.[3] The connection between protective groups and reactivity was realized in the 1970s by Paulsen, who recognized that benzyl ether-protected glycosides were more reactive than the acetyl- or benzoyl-protected analogues.[4,5] Fraser-Reid utilized this finding in developing the armed-disarmed glycosylation approach.[6,7] As a rule of thumb, more electron-withdrawing (EWD) protective groups, such as esters, reduce the reactivity of the anomeric position, whereas less electron withdrawing groups, such as ethereal protective groups, do not. Besides the EWD properties of the protective group Fraser-Reid also found that introducing a benzylidene protective group reduced the reactivity and termed this effect torsional disarming.[8] The change in reactivity is strongly related to the stability of the glycosyl cation, which is the transient intermediate in most glycosylation reactions. Manipulating the reactivity of glycosyl donors has been used in one-pot oligosaccharide synthesis saving protective group manipulations.[3,9] Understanding the relationship between protective groups and anomeric reactivity is obviously important, and there have been several studies trying to pinpoint these long-range effects. Bols found that the differences in reactivity between epimeric glycosyl donors to a large extend could be explained by stereoelectronic effects.[10,11] The same effects could be confirmed in piperidine model systems, and hence provided a strong platform for understanding how to manipulate the glycosyl donor reactivities.[12–15] According to the hypothesis, axial hydroxyl groups, whether protected or not, are less deactivating compared with their equatorial counterparts. This means that developing a positive charge on the anomeric position is becoming more feasible with more axial hydroxyl groups, i.e. the axial rich glycosyl donor becomes more reactive. As the stereochemistry has been settled by nature and the protective groups only cover a certain span of reactivity, the armed-disarmed concept has its limitations. Exceeding the limitation could however be achieved by combining stereoelectronic effects with less electron-withdrawing protective groups. This led to the "superarmed" glycosyl donors,[16] where bulky silyl ether protective groups induce a conformational change leading to axial rich conformations and hence higher reactivity; often more than a thousand times more reactive than armed (perbenzylated) glycosyl donors with the same stereochemistry.[17] The same impressive rate enhancements could also be achieved by tethering the 3,6 hydroxyl groups in *manno*, *galacto* and *glucosyl* donors.[18] Surprisingly tethering the 2,4 hydroxyl groups in a glucosyl donor did not result in the same dramatic reactivity boost.[19–21] Interestingly, Demchenko found that introducing a 2-*O*-benzoyl group in a perbenzylated glucosyl donor did increase the reactivity by anchimeric assistance.[22,23] This concept, also termed superarmed,[24] was later combined with the conformationally superarming, albeit resulting in slightly less reactive glycosyl donors.[25] As mentioned, the 2,4-tethering of glycosyl donors did not increase the reactivity, which is somewhat puzzling. Furukawa et al. have used 2,4-tethring for a glucuronyl donor and found the reactions to be highly β-selective.[26] As a tethering group di-*tert*-butylsilylene was used and the bulkiness of this was supposedly responsible for shielding the α-site of the glycosyl donor. In this paper we return to 2,4 tethering, though focusing on glucosamine derivatives. Cyclic carbamates have previously been studied in glucosamine based glycosyl donors, with a few reports on the 1,2 carbamates.[27] The 2,3-carbamates have received some more attention, e.g. as a way to improve the nu-

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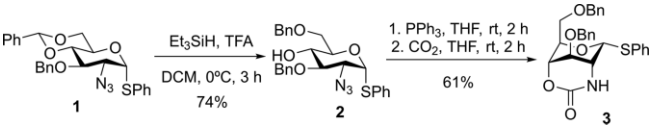
cleophilicity of the 4-OH,[28] and as glycosyl donors.[29,30] In this paper we synthesize and study the glycosylation properties of 2*N*,4*O*-tethered glucosaminyl donors.

Results and Discussion

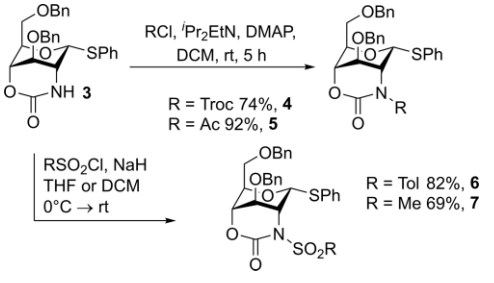
Introducing a 2,4-tethering was already studied when developing the super armed glycosyl donors, but as both the 2,4-*O*-silylene tethered, as well as the 2*N*,4*O*-carbamate tethered were cumbersome to synthesize and did not increase the reactivity as expected, these donor types were abandoned at that time. Recently, Furukawa et al. published the synthesis of 2,4-tethered glycosyl donors showing interesting stereo directing properties, which inspired us to re-evaluate the use of this tethering in glycosyl donors.[26] As a first priority, we wanted to simplify the synthesis. A key reaction was the carbamate formation from the azide and the 4-OH using PPh_3 and CO_2. This worked very efficiently on a levoglucosane derivative and hence our first approach was to investigate this reaction in an unrestricted all-equatorial 2-azido-2-deoxyglycosyl-donor. Phenyl 2-azido-3,6-di-O-benzyl-2-deoxy-1-thio-α-D-glucopyranoside **2** was synthesized from the corresponding benzylidene protected sugar **1** using known procedures.[18,31] With the mono-ol in hand the carbamate forming reaction could be investigated.[27]

The reaction sequence first involves the formation of an iminophosphorane from the reaction between PPh_3 and the azido group (Scheme 1). Upon reaction with CO_2 this is transformed into the isocyanate. In order to form the intermolecular tethering to the 4-OH, a conformational change of the pyranose ring is required. Pleasingly, the reaction yielded 63 % isolated yield, which is satisfactory taking into account the complexity and number of steps involved. The conformation of the glycosyl donor was analyzed by NMR spectroscopy, where the dihedral angles in the pyranose ring can be evaluated from the ^3J couplings. As estimated, all the coupling constants were small, in sharp contrast to the starting material, where all were ca. 8 Hz. This abrupt change confirms the change from diaxial vicinal protons to diequatorial. With access to grams of compound **3**, glycosylations could be studied. The first glycosyl acceptor, 2-methoxyethanol **8**, is a primary hydroxyl group, so steric factors are small, but its electronic features resemble a saccharide-based acceptor and hence it is a relevant model acceptor. First, the standard conditions for activating thioglycosides, i.e. NIS and TfOH, were used. Disappointingly, no product could be isolated and decomposition of the donor seemed to a problem. As a milder alternative, TfOH was exchanged by AgOTf and the amount of NIS lowered to a slight excess instead of 3 equiv. Under these conditions the primary acceptor could be glycosylated in an 86 % isolated yield and a *dr* of 1:2. To see the influence of more sterically encumbered acceptors, yet more nucleophilic than **8**, a secondary alcohol, cyclohexanol **9**, was tested next. With this acceptor, the yield took a hit down to 30 %, whereas the selectivity remained similar. Clearly, introducing another ring in the glycosyl donor makes the anomeric center less accessible, but surprisingly the glycosylation not more selective. To combine steric hindrance and electronically disarming the hindered bicyclic glycosyl acceptor diacetone-D-glucose **10** was used. The yield was again modest, but the selectivity improved to a *dr* of 1:10. The significant drop in yield when using more sterically hindered acceptors suggested that the activated glycosyl donor decomposes. A way to stabilize an intermediate could be to introduce a participating neighboring group. As the nitrogen is already a part of a ring, participation would lead to a tricyclic system, which from a geometrically point of view seems unfavorable. Especially when taken the formed positive charge, and thereby sp^2 character of the glycosyl cation into account. Introducing acetyl groups on the 2*N*,3*O*-oxazoline protected glycosyl donor was introduced by Kerns.[32,33] Kerns[34] and Oscarson[35] later realized that the anomeric selectivity was dependent on the exact amounts of catalyst used. An in situ anomerisation was later found to be the course of this.[36]



Scheme 1. Introducing the oxazinone in one-pot from the corresponding azide derivative.

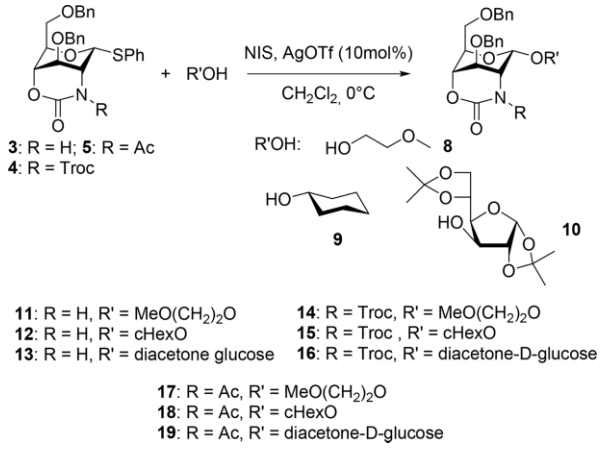
To study the influence of an additional protective group on the nitrogen we decided to introduce an acetyl, which is the most commonly used (Scheme 2). A Troc group was also introduced, as it often gives good results when used as *N*-protection in glycosylations.[37,38] Both the acetylation and the introduction of the Troc were found to give higher yield when adding 10 mol-% DMAP in DCM with DIPEA as the base, and AcCl or TrocCl as the electrophilic reagents. Introducing other electrophiles, such as Ts or Ms, did however not proceed under these milder conditions and NaH in THF or DCM had to be used affording the sulfonamides **6** and **7** (see SI for details).



Scheme 2. N-Functionalization of the oxazinone nitrogen.

Glycosylation with the acetylated donor **5** and 2-methoxyethanol **8** resulted in a low yield and there seemed not to be an influence on the anomeric selectivity, which was 1:2 again (see Scheme 3 and Table 1). Turning to the more hindered acceptors **9** and **10** furnished no product. Instead, it was observed that the *N*-acetyl had been cleaved under the reaction conditions and that the glycosylation product **12** was obtained in yields similar to the glycosylation using the donor **3**. Glycosylation using the Troc protected donor and methoxyethanol was performing slightly better, but still without a change in the anomeric selectivity. The reaction using cyclohexanol **9** gave a modest yield, but a surprisingly selective reaction. The glycosyl-

ations suggest that there is not a benefit from neighboring group participation and that the EWGs reduce the reactivity further.



Scheme 3. Glycosylation conditions and the donors and acceptors studied.

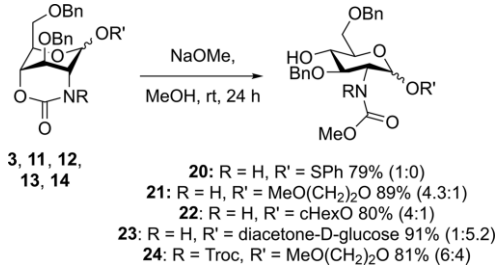
Table 1. Glycosylation reactions.

Entry	Glycosyl Donor N-*R*	Glycosyl Acceptor	Product	Yield %,[a] (*dr*)[b]
1	H	**8**	**11**	85 (66:34)
2	H	**9**	**12**	30 (65:35)
3	H	**10**	**13**	31 (91:1)
4	Troc	**8**	**14**	30 (63:37)
5	Troc	**9**	**15**	43 (100:0)
6	Troc	**10**	**16**	0
7	Ac	**8**	**17**	24 (66:34)
8	Ac	**9**	**18**	0
9	Ac	**10**	**19**	0

[a] Isolated yield. [b] Determined by NMR, specific stereochemistry was first determined after opening of the oxazinone ring. For details, see SI.

A general problem working with conformationally flipped glycosides is the assignment of the anomeric stereochemistry. In this case, for *gluco* stereochemistry, the trans-diaxial protons become trans-diequatorial, resulting in small ^3J-couplings. In order to confirm the stereochemistry beyond doubt, we decided to open the carbamate bringing the glycosides back to their $^4C_1$ conformation.

First, the glycosyl donor **3** was treated under Zemplén conditions (Scheme 4). This gave the methyl carbamate in good yield. Several attempts were made with BnOH as nucleophile, in order to synthesize a Cbz protected glycosyl donor, but neither of them afforded the desired product.



Scheme 4. Zemplén conditions to open the oxazinone.

The glycosylation products were therefore treated under Zemplén conditions to give the corresponding methyl carbamates and the unprotected 4-OH. All yields were in the range 80–91 %. The anomeric ratios could then be confirmed for the glycosides containing the methoxyethanyl and diacetone glycosyl aglycons, but rotamers caused by the methyl carbamate made assignments difficult and impossible when having the cyclohexanol aglycon and *dr* are therefore given.

From these results our initial findings working on 2,4-tethered glycosyl donors were supported. In contrast to 3,6 tethering,[18] these donors are not to be considered very reactive neither highly selective. The introduction of a 2*N*,4*O* tethering can, however, be interesting in other aspects of carbohydrate chemistry and the synthesis presented here allow easy access to this motif.

Conclusion

In conclusion, we have developed a simple and straight forward synthesis of the 2*N*,4*O* carbamate in a glucosaminyl donor. The reaction involved the in situ formation of an isocyanate from an azide and CO_2 and a subsequent ring-formation to flip the pyranose ring. The synthesized glycosyl donor was activated with NIS and AgOTf catalysis, but only demonstrated modest glycosylation properties, clearly suggesting that it is not always enough to induce a ring flip in order to boost the reactivity and selectivity of a glycosyl donor. Ring size and strain is decisive and can overrule the stereoelectronical benefit achieved by a ring flip.

Experimental Section

General working conditions

All the chemical reagents have been employed directly and no additional treatments were required. All the reactions were carried out in flame-dried flasks, under N_2 atmosphere and with dry solvents, unless otherwise stated. The anhydrous solvents were obtained from an Innovative Technology PS-MD-05 solvent drying system. The TLCs were developed in silica-coated aluminum plates (60 F254) and detection performed by UV-absorption (λ = 254 nm), and/or by moistening with a staining solution (6 % vanillin and 3 % sulfuric acid in ethanol) and subsequent charring with a heat gun. Flash column chromatography purifications were conducted with silica gel, SiO_2 (40–63 μm) as stationary phase, and HPLC-grade solvents as eluents, except heptane and petroleum ether (bp: 40–65 °C), which were acquired in technical-grade. The NMR spectra (^{1}H, ^{13}C, COSY and HSQC) were recorded on a Bruker 500 MHz spectrometer equipped with autosampler. ^{1}H-NMR spectra were recorded at 500 MHz and ^{13}C at 126 MHz. Chemical shifts are listed in ppm and the coupling constants in Hz. The NMR samples were prepared in [D]chloroform (^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm) or [D_6]DMSO (^{1}H: 2.50 ppm, ^{13}C: 39.52 ppm), and chemical shifts referenced according to the solvent peak. The HRMS samples were analyzed with a Bruker SolariX XR 7T ESI/MALDI-FT-ICR-MS spectrometer employing dithranol as matrix. The optical rotations were determined by an Anton Paar MCP 200 Circular Polarimeter and were measured at 25.0 °C and a sodium lamp (λ = 589.3 nm) was used as light source.

Phenyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-α-D-glucopyranoside (1)

To a solution of compound **SI-4** (150 mg, 0.39 mmol) in DMF (2.50 mL), BnBr (0.06 mL, 0.78 mmol, 2.0 equiv.) and NaH, as a 60 %

suspension in mineral oil (24 mg, 0.59 mmol, 1.5 equiv.) were sequentially added at 0 °C. The mixture was allowed to stir for one hour and upon completion, quenched by saturated aqueous $NaHCO_3$ (7 mL). The resulting mixture was extracted with Et_2O (3 × 20 mL), washed with H_2O (15 mL), dried with anhydrous $MgSO_4$, filtered and the solvents evaporated. The crude residue was purified by flash column chromatography in silica gel (heptane/EtOAc, 3:1) to yield pure **1** (168 mg, 0.37 mmol, 94 %; approximate yield due to the presence of impurities on the sample, which could not be removed by column chromatography) as a white solid. R_f (heptane/EtOAc, 3:1) = 0.58 ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.52–7.49 (m, 4H, Ar*H*), 7.41–7.37 (m, 6H, Ar*H*), 7.36–7.29 (m, 7H, Ar*H*), 5.60 (s, 1H, PhC*H*), 5.57 (d, *J* = 4.7, 1H, H1), 4.98 (d, *J* = 10.9 Hz, 1H, PhCH_2), 4.84 (d, *J* = 10.9 Hz, 1H, PhCH_2), 4.43 (ddd, *J* = 9.9, 9.9, 4.9 Hz, 1H, H5), 4.23 (dd, *J* = 10.4, 4.9 Hz, 1H, H6), 4.00–3.95 (m, 2H, H2, H4), 3.80–3.75 (m, 2H, H3, H6) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 137.8 (Ar), 137.2 (Ar), 133.1 (Ar), 132.6 (Ar), 129.3 (Ar), 129.3 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.1 (Ar), 126.2 (Ar), 101.6 (PhCH), 88.0 (C1), 82.9 (C3), 78.0 (C2), 75.4 (PhCH_2), 68.8 (C6), 64.0 (C5), 63.7 (C4) ppm (missing signals due to overlaps: 4 aromatic (Ar) carbon signals). The NMR spectra are in accordance with the literature.[39]

Phenyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-α-D-glucopyranoside (2)

To a stirred solution of compound **1** (600 mg, 1.20 mmol) in CH_2Cl_2 (10 mL) at 0 °C, Et_3SiH (1.0 mL, 6.48 mmol, 5.4 equiv.) was added, followed by a dropwise addition of TFA (0.5 mL, 6.48 mmol, 5.4 equiv.) during 20 minutes. The mixture was allowed to stir for three hours, after which the reaction was quenched by pouring slowly saturated aqueous $NaHCO_3$. The resulting mixture was separated, extracted with CH_2Cl_2 (15 mL), washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried with anhydrous $MgSO_4$, filtered and the solvents evaporated. The crude product was purified by flash column chromatography in silica gel (toluene/EtOAc, 9:1) to yield pure **2** (443 mg, 0.93 mmol, 74 %) as an off-white oil. R_f (EtOAc/toluene, 1:9) = 0.63 ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.53–7.51 (m, 2H, Ar*H*), 7.44–7.38 (m, 5H, Ar*H*), 7.35–7.31 (m, 7H, Ar*H*), 7.28–7.27 (m, 4H, Ar*H*), 5.58 (d, *J* = 5.4 Hz, 1H, H1), 4.96 (d, *J* = 11.1 Hz, 1H, PhCH_2), 4.85 (d, *J* = 11.3 Hz, 1H, PhCH_2), 4.59 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.51 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.34 (dd, *J* = 9.1, 4.7, 4.3 Hz, 1H, H5), 3.91 (dd, *J* = 10.2, 5.4 Hz, 1H, H2), 3.78–3.74 (m, 2H, H4, H6), 3.70–3.66 (m, 2H, H3, H6), 2.53 (bs, 1H, O*H*) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 138.0 (Ar), 137.8 (Ar), 133.5 (Ar), 132.3 (Ar), 129.2 (Ar), 128.8 (Ar), 128.6 (Ar), 128.4 (Ar), 128.3 (Ar), 128.3 (Ar), 128.0 (Ar), 127.8 (Ar), 127.8 (Ar), 87.4 (C1), 81.5 (C3), 75.6 (PhCH_2), 73.7 (PhCH_2), 72.4 (C4), 71.1 (C5), 69.8 (C6), 63.7 (C2) ppm (missing signals due to overlaps: two aromatic (Ar) carbon signals). The NMR spectra are in accordance with the literature.[39]

Phenyl 3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-*c*,*d*]-1,3-oxazin-2-one]-1-thio-α-D-glucopyranoside (3)

To a solution of compound **2** (1.149 g, 2.41 mmol) in THF (8.0 mL), PPh_3 (1.138 g, 4.34 mmol, 1.8 equiv.) was added, and the mixture was allowed to stir for 2.5 hours. Afterwards, a stream of CO_2, originated from the sublimation of dry ice through a conical flask containing $CaCl_2$ as a drying agent, was bubbled through the solution during 2.5 hours. Eventually, solvents were removed and the crude residue purified by flash column chromatography in silica gel (toluene/EtOAc, 9:1 → EtOAc) to afford pure **3** (726 mg, 0.66 mmol, 63 %) as a white brittle solid. R_f (EtOAc) = 0.65 $[\alpha]_D^{25}$ +20° (c 0.98, $CHCl_3$) Mp (not recrystallized): 47.9 °C - 51.0 °C HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{27}H_{28}NO_5S^+$ 478.16827, found 478.16823. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.53–7.51 (m, 2H, ArH), 7.35–7.30 (m, 6H, ArH), 7.28–7.26 (m, 5H, ArH), 7.23–7.21 (m, 2H, ArH), 5.78 (d, *J* = 4.9 Hz, 1H, N*H*), 5.34 (s, 1H, H1), 4.60 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.57–4.55 (m, PhCH_2, H5), 4.52 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.46 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.41 (ddd, *J* = 3.7, 2.2, 1.6 Hz, 1H, H4), 4.10 (ddd, *J* = 4.0, 4.0, 1.2 Hz, 1H, H3), 3.88 (dd, *J* = 7.7 Hz, 10.4 Hz, 1H, H6), 3.74 (dd, *J* = 6.4 Hz, 10.4 Hz, 1H, H6), 3.66–3.64 (m, 1H, H2) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 152.9 (carbamate-*C*O), 137.9 (Ar), 136.4 (Ar), 133.5 (Ar), 131.6 (Ar), 129.3 (Ar), 128.9 (Ar), 128.7 (Ar), 128.6 (Ar), 127.9 (Ar), 127.7 (Ar), 79.7 (C1), 78.1 (C5), 73.3 (PhCH_2), 72.7 (PhCH_2), 70.0 (C3), 69.8 (C4), 67.5 (C6), 51.7 (C2) ppm (missing signals due to overlaps: 5 aromatic (Ar) carbon signals).

Phenyl 3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-*c*,*d*]-1,3-oxazin-2-one]-1-thio-2-*N*-[2,2,2-trichloroethoxycarbonyl]-α-D-glucopyranoside (4)

To a stirred solution of compound **3** (40 mg, 0.11 mmol) in CH_2Cl_2 (3 mL) at 0 °C, *i*Pr_2NEt was added (60 µL, 0.32 mmol, 3.0 equiv.). Afterwards, 2,2,2-trichloroethoxycarbonyl chloride (0.43 mL, 0.31 mmol, 3.0 equiv.) and DMAP (1 mg, 1.22 mmol, 0.1 equiv.) were sequentially added, and the mixture was warmed up to room temperature. After five hours, the reaction was quenched with 1 M HCl (10 mL), washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried with anhydrous $MgSO_4$, filtered and the solvents evaporated. The crude product was purified by flash column chromatography in silica gel (EtOAc/PE, 1:1), resulting in an off-white viscous oil, which corresponded to product **4** (50 mg, 0.23 mmol, 74 %; approximate yield due to the significant presence of impurities on the sample). R_f (EtOAc/PE, 1:3) = 0.67. $[\alpha]_D^{25}$ +26° (c 0.96, $CHCl_3$) HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{30}H_{28}Cl_3NNaO_7S^+$ 674.05443, found 674.05525. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.55–7.53 (m, 2H, Ar*H*), 7.38–7.31 (m, 7H, Ar*H*), 7.28–7.24 (m, 7H, Ar*H*), 5.53 (s, 1H, H1), 5.05 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.91–4.88 (m, 2H, PhCH_2, H3), 4.66 (dd, *J* = 11.8, 14.7 Hz, 2H, CH_2CCl$_3$), 4.52 (dd, 1H, *J* = 7.1, 6.8 Hz, H5), 4.50–4.49 (m, 1H, H2), 4.47 (d, d, *J* = 12.1 Hz, 1H, PhCH_2), 4.37 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.13 (ddd, *J* = 8.0, 3.8, 2.4 Hz, H4), 3.85 (dd, *J* = 10.5, 7.6 Hz, 1H, H6), 3.75 (dd, *J* = 10.3, 6.2 Hz, 1H, H6) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 151.87 (carbamate-*C*O), 146.44 (*C*(O)OCH$_2$CCl$_3$), 137.72 (Ar), 135.93 (Ar), 133.28 (Ar), 131.85 (Ar), 129.13 (Ar), 129.12 (Ar), 129.04 (Ar), 128.90 (Ar), 128.58 (Ar), 127.98 (Ar), 127.96 (Ar), 127.64 (Ar), 94.21 (CH$_2$*C*Cl$_3$), 78.29 (C1), 77.53 (C2), 76.58 (PhCH_2), 73.36 (PhCH_2), 72.94 (*C*H$_2$CCl$_3$), 71.42 (C2), 69.39 (C4), 66.53 (C6), 54.11 (C3) ppm (missing signals due to overlaps: 3 aromatic (Ar) carbon signals).

Phenyl 2-*N*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-*c*,*d*]-1,3-oxazin-2-one]-1-thio-α-D-glucopyranoside (5)

Compound **3** (275 mg, 0.42 mmol, 1.0 equiv.) was dissolved in dry CH_2Cl_2 (4 mL) at 0 °C, followed by the addition of *i*Pr_2EtN (0.33 mL, 1.91 mmol, 4.5 equiv.) and AcCl (0.14 mL, 1.91 mmol, 4.5 equiv.). The mixture was warmed up to room temperature, and after five hours, the reaction was quenched with 1 M HCl (10 mL), washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried with anhydrous $MgSO_4$, filtered and the solvents evaporated. The crude product was purified by flash column chromatography in silica gel (toluene/EtOAc, 9:1) to yield pure **5** (200 mg, 0.39 mmol, 92 %) as a yellowish syrup. R_f (PE/EtOAc, 1:1) = 0.75. $[\alpha]_D^{25}$ +50 (c 0.11, $CHCl_3$). HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{29}H30NO_6S^+$ 520.17883, found 520.18026. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.55–7.53 (m, 2H, Ar*H*), 7.36–7.30 (m, 7H, Ar*H*), 7.25–7.16 (m, 10H, Ar*H*), 5.52 (s, 1H, H1), 5.23–5.22 (m, 1H, H2), 4.68 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.60 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.49 (dd, *J* = 7.1, 6.8 Hz, 1H, H5), 4.46 (d, *J* = 11.7 Hz, 1H, PhCH_2), 4.46 (dd, *J* = 4.0, 1.9,1H, H4), 4.36 (d, *J* = 11.8 Hz, 1H, PhCH_2), 3.98 (ddd, *J* = 4.1, 4.0, 1.2 Hz, 1H, H3), 3.85 (dd, *J* = 10.5, 7.7 Hz, 1H, H6a), 3.74 (dd, *J* = 10.5, 6.1 Hz, 1H, H6b), 2.67 (s, 1H, CH_3) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.2 (CH_3CO),

150.1 (carbamate-*C*O), 137.8 (Ar), 136.1 (Ar), 133.6 (Ar), 131.6 (Ar), 129.2 (Ar), 129.1 (Ar), 129.0 (Ar), 128.8 (Ar), 128.6 (Ar), 128.4 (Ar), 127.9 (Ar), 127.9 (Ar), 127.7 (Ar), 127.6 (Ar), 125.4 (Ar), 78.3 (C1), 77.6 (C5), 73.4 (PhCH$_2$), 72.8 (PhCH$_2$), 71.5 (C4), 69.7 (C3), 66.6 (C6), 49.9 (C2), 26.9 (CH$_3$) ppm.

Phenyl 3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-*c*,*d*]-1,3-oxazin-2-one]-2-*N*-[*p*-toluenesulfonyl]-1-thio-α-D-glucopyranoside (6)

To a solution of compound **3** (177 mg, 0.35 mmol) in THF (4.5 mL) at 0 °C, NaH, as 60wt.-% dispersion in mineral oil (55 mg, 1.49 mmol, 4.25 equiv.), and TsCl (112 mg, 0.56 mmol, 1.6 equiv.) were sequentially added. The solution was warmed up progressively to room temperature and was stirred for 5 h. Afterwards, the reaction was quenched with 1 M HCl and the resulting mixture was extracted with Et$_2$O (2 × 20 mL). The combined organic layers were washed with additional 1 M HCl (2 × 20 mL), dried with anhydrous MgSO$_4$, filtered and the solvent was removed under vacuum. The crude residue was purified by flash column chromatography (toluene) to furnish the final product **6** (183 mg, 0.29 mmol, 82 %) as a transparent syrup. R_f (EtOAc/PE, 1:1) = 0.79. $[\alpha]_D^{25}$ +39° (c 0.42, CHCl$_3$). HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{34}H_{33}NO_7S_2^+$ 632.17712, found 654.15906. ^{1}H NMR (500 MHz, [D]Chloroform) δ 8.03 (d, *J* = 8.4 Hz, 2H, tolyl-Ar*H*), 7.63–7.61 (m, 2H, tolyl-Ar*H*), 7.42–7.40 (m, 3H, Ar*H*), 7.37–7.25 (m, 15H, Ar*H*), 7.21–7.17 (m, 2H, Ar*H*), 5.52 (s, 1H, H1), 5.00 (dd, *J* = 0.7, 3.1 Hz, 1H, H2), 4.70 (d, *J* = 11.8 Hz, 1H, PhC*H*$_2$), 4.66 (d, *J* = 11.8 Hz, 1H, PhC*H*$_2$), 4.48 (d, *J* = 11.8 Hz, 1H, PhC*H*$_2$), 4.45 (m, 1H, H5), 4.40–4.38 (m, 1H, H4), 4.37 (d, *J* = 12.0 Hz, 1H, PhC*H*$_2$), 4.00–3.98 (m, 1H, H3), 3.85 (dd, *J* = 7.9, 10.5 Hz, 1H, H6), 3.72 (dd, *J* = 6.0, 10.5 Hz, 1H, H6), 2.44 (s, 3H, C*H*$_3$) ppm. ^{13}C NMR (126 MHz, CDCl$_3$) δ = 147.9 (carbamate-*C*O), 145.3 (Ar), 138.0 (Ar), 137.7 (Ar), 135.8 (Ar), 135.2 (Ar), 133.9 (Ar), 131.8 (Ar), 129.8 (Ar), 129.3 (Ar), 129.1 (Ar), 129.1 (Ar), 129.0 (Ar), 128.9 (Ar), 128.5 (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.6 (Ar), 125.4 (Ar), 78.3 (C1), 77.6 (C5), 73.3 (PhC*H*$_2$), 72.9 (PhC*H*$_2$), 71.3 (C4), 70.4 (C3), 66.6 (C6), 54.0 (C2), 21.8 (C*H*$_3$) ppm (missing signals due to overlaps: 4 aromatic carbons).

Phenyl 3,6-di-*O*-benzyl-2-deoxy-2-*N*-methylsulfonyl-2*N*,4*O*-[[2,3,4-*c*,*d*]-1,3-oxazin-2-one]-1-thio-α-D-glucopyranoside (7)

To a solution of compound **3** (63 mg, 0.13 mmol) in THF (1.0 mL) at 0 °C, NaH, as 60wt.-% dispersion in mineral oil (63 mg, 1.68 mmol, 12.7 equiv.), and MsCl (49.5 µL mg, 0.63 mmol, 4.8 equiv.) were sequentially added. The solution was warmed up progressively to room temperature and stirred for 24 h. Afterwards, the reaction was quenched carefully with 1 M HCl and the resulting mixture was extracted with Et$_2$O (2 × 20 mL). The combined organic layers were washed with additional 1 M HCl (2 × 20 mL), dried with anhydrous MgSO$_4$, filtered and the solvent was removed under vacuum. The crude residue was purified by flash column chromatography (toluene/EtOAc, 2:1) to furnish the final product **7** (48 mg, 0.09 mmol, 69 %) as a transparent syrup (since some impurities could not be removed by column chromatography, the yield is approximate). R_f (EtOAc/PE, 1:1) = 0.28. $[\alpha]_D^{25}$ −16° (c 0.064, CHCl$_3$). HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{34}H_{33}NO_7S_2^+$ 578.12776, found 578.12672. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.64–7.63 (m, 2H, Ar*H*), 7.43–7.37 (m, 7H, Ar*H*), 7.33–7.30 (m, 10H, Ar*H*), 7.26–7.25 (m, 1H, Ar*H*), 5.52–5.51 (m, 1H, H1), 4.90 (m, 1H, H3), 4.76–4.73 (m, 1H, PhC*H*$_2$), 4.69–4.66 (m, 1H, PhC*H*$_2$), 4.54 (m, 1H, H5), 4.51 (d, *J* = 11.6 Hz, 1H, PhC*H*$_2$), 4.51 (m, 1H, H2), 4.19 (d, *J* = 3.9, 7.6 Hz, 1H, H4), 3.90–3.86 (m, 1H, H6), 3.80–3.79 (m, 3H, C*H*$_3$), 3.76–3.72 (m, 1H, H6) ppm.^{13}C NMR (126 MHz, CDCl$_3$) δ = 149.0 (carbamate-*C*O), 137.7 (Ar), 135.9 (Ar), 132.8 (Ar), 132.0 (Ar), 129.3 (Ar), 129.2 (Ar), 129.2 (Ar), 129.1 (Ar), 129.0 (Ar), 128.6 (Ar), 128.4 (Ar), 128.2 (Ar), 128.0 (Ar), 128.00 (Ar), 127.6 (Ar), 125.4 (Ar), 78.0 (C1), 78.0 (C5), 73.4 (PhC*H*$_2$), 73.3 (PhC*H*$_2$), 71.7 (C2), 70.5 (C4), 66.6 (C6), 53.0 (C3), 41.7 (C*H*$_3$) ppm.

Glycosylation general procedure

To a flame-dried round-bottomed flask, the glycosyl donor (1.0 equiv.) and acceptor (1.5 equiv.) were added, coevaporated with toluene (2 × 2 mL) and dried under vacuum. Glycosyl acceptors, 2-methoxyethanol **8** and cyclohexanol **9** did not require such a procedure, as they have been dried with 3Å MS prior use. Afterwards, the reagents are dissolved in dry CH$_2$Cl$_2$ (2 mL) and 3Å MS (100 mg) were added. The resulting mixture was stirred for 1 hour at room temperature and, eventually, cooled to 0 °C. Afterwards, NIS and catalytic amounts of AgOTf were sequentially added to the solution and the reaction monitored by TLC. Upon completion, the glycosylations were quenched with Et$_3$N (0.7 mL), diluted with EtOAc and filtered through Celite. The mixture was washed with a 10wt.-% aqueous Na$_2$S$_2$O$_3$ solution (2 × 15 mL), HCl 1 M (2 × 15 mL) and saturated aqueous NaHCO$_3$ (2 × 15 mL). The organic phase was dried with anhydrous MgSO$_4$, filtered, concentrated under vacuum and purified by flash column chromatography (PE/EtOAc or toluene/EtOAc).

2-Methoxyethyl 3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-c,d]-1,3-oxazin-2-one]-D-glucopyranoside (11)

Glycosyl donor **3** (80 mg, 0.17 mmol), 2-methoxyethanol (18 mg, 0.24 mmol, 1.5 equiv.), NIS (53 mg, 0.24 mmol, 1.5 equiv.) and AgOTf (5.1 mg, 0.02 mmol, 0.1 equiv.) were used. Full conversion was observed after 45 minutes. Aqueous workup and flash column chromatography (EtOAc/PE, 1:1 → EtOAc) furnished a yellowish oil that corresponded to the mixture of anomers of the final product **11** (48 mg, 0.11 mmol, 86 %). R_f (EtOAc) = 0.28 $[\alpha]_D^{25}$ −1.1° (c 1.96, CHCl$_3$) HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{24}H_{29}NO_7Na^+$ 466.18362, found 466.18352. *dr* = 66:34 ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.36–7.32 (m, 8H, Ar*H*), 7.31–7.27 (m, 6H, Ar*H*), 7.26–7.23 (m, 4H, Ar*H*; overlapped with CHCl$_3$), 6.79 (bs, 1H, N*H*), 5.66 (d, *J* = 3.9 Hz, 1H, N*H*), 4.93 (s, 1H, H1), 4.82 (s, 1H, H1), 4.78 (d, *J* = 11.0 Hz, 1H, PhC*H*$_2$), 4.59 (d, *J* = 11.8 Hz, 1H, PhC*H*$_2$), 4.58 (d, *J* = 11.8 Hz, 1H, PhC*H*$_2$), 4.54–4.51 (m, 3H, PhC*H*$_2$, H4, H5), 4.45 (d, *J* = 11.0 Hz, 1H, PhC*H*$_2$), 4.43 (app. bs, 1H, PhC*H*$_2$), 4.41 (ddd, *J* = 1.6, 1.8, 3.6 Hz, 1H, H4), 4.34 (dd, *J* = 7.3, 7.2 Hz, 1H, H4), 4.15 (ddd, *J* = 1.1, 3.9, 3.9 Hz, 1H, H3), 4.11 (d, *J* = 3.8, 3.6 Hz, 1H, H3), 3.97–3.90 (m, 2H, H6, H6), 3.82–3.74 (m, 3H, H2, H6, H6), 3.66–3.61 (m, 2H, C*H*$_2$), 3.59–3.55 (m, 2H, C*H*$_2$), 3.54–3.53 (m, 1H, C*H*$_2$), 3.51–3.47 (m, 2H, C*H*$_2$), 3.47–3.41 (m, 2H, C*H*$_2$), 3.36 (s, 3H, C*H*$_3$), 3.29 (s, 3H, C*H*$_3$) ppm. ^{13}C NMR (126 MHz, CDCl$_3$) δ = 154.1 (carbamate-*C*O), 153.4 (carbamate-*C*O), 138.2 (*ipso*-Ar), 137.9 (*ipso*-Ar), 137.3 (*ipso*-Ar), 136.5 (*ipso*-Ar), 128.8 (Ar), 128.6 (Ar), 128.6 (Ar), 128.5 (Ar), 128.5 (Ar), 128.0 (Ar), 127.9 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 99.8 (C1), 93.5 (C1), 77.5 (C5), 75.1 (C5), 73.3 (PhC*H*$_2$), 73.2 (PhC*H*$_2$), 72.5 (PhC*H*$_2$), 71.8 (CH$_2$C*H*$_2$OMe), 71.6 (C*H*$_2$CH$_2$OMe), 71.4 (C4), 70.5 (C3), 70.2 (C6), 69.8 (C4), 68.3 (C3), 68.3 (CH$_2$C*H*$_2$OMe), 68.0 (C*H*$_2$CH$_2$OMe), 67.7 (C6), 59.1 (C*H*$_3$), 59.0 (C*H*$_3$), 50.3 (C2), 46.9 (C2) ppm (missing signals due to overlaps: 6 aromatic carbons).

Cyclohexyl 3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-c,d]-1,3-oxazin-2-one]-1-*O*-D-glucopyranoside (12)

Glycosyl donor **1** (81 mg, 0.17 mmol), cyclohexanol **9** (18 mg, 0.26 mmol, 1.5 equiv.), NIS (57 mg, 0.23 mmol, 1.4 equiv.) and AgOTf (6 mg, 0.02 mmol, 0.1 equiv.) were employed. Full conversion was observed after 45 minutes. After aqueous workup and flash column chromatography purification (EtOAc/PE, 1:3 → EtOAc), a mixture of anomers, which corresponded to product **9**, was obtained as a colorless oil (23 mg, 0.09 mmol, 30 %; approximate yield due to the presence of impurities on the sample that could not be removed

by column chromatography). R_f (EtOAc) = 0.89. $[\alpha]_D^{25}$ +6.0° (c 0.17, $CHCl_3$). HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{27}H_{34}NO_6^+$ 468.23806, found 468.23876. *dr* = 67:33. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.36–7.32 (m, 10H, Ar*H*), 7.31–7.28 (m, 7H, Ar*H*), 7.27–7.22 (m, 6H, Ar*H*; overlapped with $CHCl_3$), 6.89 (d, *J* = 5.0 Hz, 1H, N*H*), 5.54 (d, *J* = 3.9 Hz, 1H, N*H*), 4.99 (s, 1H, H1), 4.93 (s, 1H, H1), 4.79 (d, *J* = 11.0 Hz, 1H, PhCH_2), 4.63 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.57–4.45 (m, 7H, 3 × PhCH_2, H4, H5), 4.42–4.41 (m, 2H, H4, PhCH_2), 4.32 (dd, *J* = 7.5, 6.9 Hz, 1H, H5), 4.16–4.15 (m, 1H, H3), 4.12–4.10 (m, 1H, H3), 4.07 (dd, *J* = 9.5, 8.2 Hz, 1H, H6), 3.88 (dd, *J* = 6.5, 9.4 Hz, 1H, H6), 3.82–3.76 (m, 2H, H6), 3.70–3.61 (m, 3H, H2, 2 × cyclohexyl-OC*H*), 3.36–3.35 (m, 2H, H2), 1.93–1.84 (m, 2H, CH_2), 1.80–1.69 (m, 8H, CH_2), 1.55–1.47 (m, 2H, CH_2), 1.38–1.30 (m, 3H, CH_2) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 154.5 (carbamate-*C*O), 153.6 (carbamate-*C*O), 138.2 (Ar), 138.0 (Ar), 137.4 (ipso-Ar), 136.7 (ipso-Ar), 128.9 (Ar), 128.6 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.0 (Ar), 127.9 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 96.7 (C1), 90.9 (C1), 77.2 (C5), 76.4 (cyclohexyl-OCH), 75.6 (cyclohexyl-OCH), 74.8 (C5), 73.3 (PhCH_2), 72.6 (PhCH_2), 71.4 (C4), 71.3 (PhCH_2), 70.9 (C3), 70.5 (C6), 69.7 (C4), 68.4 (C3), 67.9 (C6), 51.2 (C2), 47.5 (C2), 33.6 (CH_2), 33.2 (CH_2), 31.9 (CH_2), 31.0 (CH_2), 25.8 (CH_2), 25.7 (CH_2), 24.1 (CH_2), 24.1 (CH_2), 23.8 (CH_2) ppm (missing signals due to overlaps: 9 aromatic (Ar), one benzylic (PhCH_2) and one cyclohexyl-CH_2 carbons).

3,6-Di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-c,d]-1,3-oxazin-2-one]-D-glucopyranoside (1 → 3)-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (13)

The reaction was carried out with **3** (80 mg, 0.17 mmol) as glycosyl donor, diacetone-D-glucose **10** (66 mg, 0.26 mmol, 1.5 equiv.) as glycosyl acceptor, NIS (57 mg, 0.23 mmol, 1.4 equiv.) and AgOTf (6 mg, 0.02 mmol, 0.1 equiv.). Full conversion had occurred after one hour. After aqueous workup and flash column chromatography purification (toluene/EtOAc, 3:1 → EtOAc), the mixture of anomers of the final product **13** was obtained as a colourless oil (31 mg, 0.09 mmol, 31 %) (since some impurities could not be removed by column chromatography, the yield is approximate). R_f (EtOAc) = 0.49. $[\alpha]_D^{25}$ –33° (c 0.70, $CHCl_3$). HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{33}H_{41}NO_{11}Na^+$ 650.25718, found 650.25812. *dr* = 91:9. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.36–7.27 (m, 17H, Ar*H*), 7.25–7.24 (bd, *J* = 5.3 Hz, 2H, Ar*H*), 5.87 (d, *J* = 3.9 Hz, 1H, H1′), 5.79 (d, *J* = 3.9 Hz, 1H, H1′), 5.08 (s, 1H, H1), 5.04 (1H, H1), 4.72–4.70 (m, 1H, H4), 4.66 (d, *J* = 11.0 Hz, 1H, PhCH_2), 4.58–4.56 (m, 3H, H2′, H2′, H4), 4.46 (d, *J* = 11.5 Hz, 1H, PhCH_2), 4.40–4.35 (m, 3H, H5, H5, H4′, H4′), 4.46 (dd, *J* = 9.8, 9.8 Hz, 1H, H6), 4.19–4.14 (m, 1H, H3), 4.13–4.09 (m, 3H, H3, H5′, H5′), 3.95 (dd, *J* = 4.1, 8.7 Hz, 1H, H6′), 3.84 (dd, *J* = 5.9, 9.9 Hz, 1H, H6), 3.73 (dd, *J* = 6.1, 8.6 Hz, 1H, H6′), 3.60–3.58 (m, 1H, H2), 3.47 (m, 1H, H2) ppm (missing signals due to overlaps: two H3′, one H4′, two H6, two H6′ and two benzylic (PhCH_2) protons). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 154.5 (carbamate-*C*O), 154.3 (carbamate-*C*O), 138.4 (Ar), 138.2 (Ar), 136.8 (Ar), 136.5 (Ar), 128.9 (Ar), 128.9 (Ar), 128.7 (Ar), 128.7 (Ar), 128.7 (Ar), 128.6 (Ar), 128.6 (Ar), 128.6 (Ar), 128.5 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.9 (Ar), 127.8 (Ar), 127.8 (Ar), 127.7 (Ar), 127.5 (Ar), 127.4 (Ar), 112.1 (C1′), 112.0 (C1′), 109.3 (isopropylidene-*C*), 109.3 (isopropylidene-*C*), 105.6 (isopropylidene-*C*), 104.7 (isopropylidene-*C*), 96.8 (C1), 94.6 (C1), 81.5 (C2′), 81.2 (C2′), 80.7 (C4′), 79.5 (C4′), 75.1 (C5), 74.8 (C5), 73.4 (PhCH_2), 73.1 (PhCH_2), 72.5 (PhCH_2), 72.1 (PhCH_2), 71.5 (C5′), 70.6 (C6′), 70.2 (C3), 69.6 (C6), 68.3 (C4), 67.2 (C6), 50.0 (C2), 47.5 (C2), 27.2 (isopropylidene-CH_3), 27.0 (isopropylidene-CH_3), 26.8 (isopropylidene-CH_3), 26.6 (isopropylidene-CH_3), 26.3 (isopropylidene-CH_3), 26.0 (isopropylidene-CH_3), 25.6 (isopropylidene-CH_3), 25.4 (isopropylidene-CH_3) ppm (missing signals due to overlaps: 2 aromatic (Ar), one C3, two C3′, one C4, one C5′ and one C6′ carbons).

2-Methoxyethyl 3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-c,d]-1,3-oxazin-2-one]-2-*N*-[2,2,2-trichloroethoxycarbonyl]-D-glucopyranoside (14)

The reaction was carried out with **4** (70 mg, 0.11 mmol) as glycosyl donor, 2-methoxyethanol **8** (18 mg, 0.17 mmol, 1.5 equiv.) as glycosyl acceptor, NIS (38 mg, 0.17 mmol, 1.5 equiv.) and AgOTf (5 mg, 0.01 mmol, 0.1 equiv.). Full conversion was achieved after 40 minutes. After aqueous workup flash column chromatography purification (toluene/EtOAc, 3:1 → EtOAc), the anomeric mixture of the final product **14** was obtained as a yellowish oil (50 mg, 0.04 mmol, 30 %) (some impurities could not be removed by column chromatography; the yield is approximate). R_f (EtOAc/PE, 1:1) = 0.63. $[\alpha]_D^{25}$ –6.8° (c 0.11, $CHCl_3$). HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{26}H_{32}NO_8^+$ 486.21224, found 486.21465. *dr* = 63:37. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.65–7.64 (m, 1H, Ar*H*), 7.46–7.43 (m, 1H, Ar*H*), 7.27–7.13 (m, 36H, Ar*H*; overlapped with $CHCl_3$), 4.97 (s, 1H, H1), 4.88 (s, 1H, H1), 4.84 (d, d, *J* = 11.9 Hz, *J* = 11.7 Hz, 1H, PhCH_2), 4.73 (d, d, *J* = 11.9 Hz, *J* = 11.7 Hz, 1H, PhCH_2), 4.65–4.62 (m, 2H, PhCH_2), 4.59–4.55 (m, 3H, PhCH_2, H4), 4.45–4.39 (m, 6H, H4, H5, CH_2CCl$_3$), 4.38–4.32 (dd, 4H, *J* = 17.8, 12.2 Hz, CH_2CCl$_3$), 4.25 (dd, *J* = 7.4, 7.0 Hz, 1H, H5), 4.11–4.07 (m, 2H, H3, H5), 4.03–4.01 (m, 1H, H3), 3.96 (dd, *J* = 9.6, 8.0 Hz, 1H, H6), 3.87–3.82 (m, 2H, H6), 3.80–3.76 (m, 1H, H6), 3.71–3.68 (app. d, *J* = 7.2 Hz, 1H, H6), 3.56–3.46 (m, 4H, CH_2), 3.42–3.35 (m, 4H, CH_2), 3.23 (s, 3H, CH_3), 3.21 (s, 3H, CH_3) ppm (missing signals due to overlaps: one H5 proton). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 151.1 (carbamate-*C*O), 150.9 (carbamate-*C*O), 147.3 (*C*(O)CH$_2$CCl$_3$), 146.8 (*C*(O)CH$_2$CCl$_3$), 138.0 (*ipso*-Ar), 137.7 (*ipso*-Ar), 136.8 (*ipso*-Ar), 132.3 (Ar), 129.2 (Ar), 129.0 (Ar), 128.8 (Ar), 128.7 (Ar), 128.7 (Ar), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.2 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.9 (Ar), 127.9 (Ar), 127.8 (Ar), 125.5 (Ar), 98.1 (C1), 94.4 (*C*Cl$_3$), 94.2 (*C*Cl$_3$), 93.1 (C1), 76.8 (C5), 76.4 (PhCH_2), 74.4 (C5), 73.4 (CH$_2$CCl$_3$), 73.3 (CH$_2$CCl$_3$), 73.2 (PhCH_2), 72.8 (PhCH_2), 71.9 (CH_2), 71.8 (C4), 71.6 (PhCH_2), 71.2 (CH_2), 70.8 (C4), 69.8 (C3), 69.6 (C6), 67.8 (C3), 67.8 (CH_2), 67.2 (C6), 59.0 (CH_3), 59.0 (CH_3), 53.0 (C2), 51.0 (C2) ppm (missing signals due to overlaps: one C5 carbon).

Cyclohexyl 3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-c,d]-1,3-oxazin-2-one]-2-N-[2,2,2-trichloroethoxycarbonyl]-D-glucopyranoside (15)

Glycosyl donor **4** (63 mg, 0.10 mmol), cyclohexanol **9** (15 mg, 0.15 mmol, 1.5 equiv.), NIS (43.0 mg, 0.25 mmol, 2.5 equiv.) and AgOTf (10 mg, 0.02 mmol, 0.2 equiv.) were used. Full conversion was observed after 90 minutes. The final product **15** was obtained as a yellowish oil (27 mg, 0.04 mmol, 43 %; approximate yield due to the presence of impurities on the sample that could not be removed by column chromatography), after aqueous workup and flash column chromatography purification (EtOAc/PE, 1:3 → EtOAc) as a single anomer. R_f (EtOAc) = 0.67. $[\alpha]_D^{25}$ –45° (c 0.55, $CHCl_3$). HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{26}H_{32}NO_8^+$ 486.21224, found 486.21465. *dr* = 20:1. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.37–7.32 (m, 6H, Ar*H*), 7.31–7.30 (m, 1H, Ar*H*), 7.30–7.29 (m, 1H, Ar*H*), 7.29–7.26 (m, 1H, Ar*H*), 7.24 (m, 1H, Ar*H*), 7.22 (m, 1H, Ar*H*), 5.07 (s, 1H, H1), 4.90 (dd, *J* = 15.1, 12.1 Hz, 2H, CH_2CCl$_3$), 4.81 (d, *J* = 11.3 Hz, 1H, PhCH_2), 4.67 (ddd, *J* = 3.6, 2.2, 1.7 Hz, 1H, H3), 4.59 (ddd, *J* = 3.4, 1.8, 1.8 Hz, 1H, H2), 4.54 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.45 (d, *J* = 11.2 Hz, 1H, PhCH_2), 4.41 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.34–4.31 (m, 1H, H5), 4.15 (dd, *J* = 9.3, 8.8 Hz, 1H, H6), 4.11–4.10 (m, 1H, H4), 3.87 (dd, *J* = 9.5, 6.3 Hz, 1H, H6), 3.72–3.67 (m, 1H, cyclohexyl-OC*H*), 1.90–1.85 (m, 1H, CH_2), 1.82–1.77 (m, 1H, CH_2), 1.73–1.67 (m, 2H, CH_2), 1.56–1.48 (m, 2H, CH_2) ppm (missing signals: 4 cyclohexyl CH_2 protons; expected shift: 1.39–1.21 ppm). ^{13}C NMR (126 MHz, CDCl3) δ = 151.1 (*C*O), 147.0

(C(O)OCH$_2$CCl$_3$), 138.0 (*ipso*-Ar), 136.8 (*ipso*-Ar), 128.7 (Ar), 128.5 (Ar), 128.3 (Ar), 127.9 (Ar), 127.9 (Ar), 127.8 (Ar), 95.2 (C1), 94.2 (CCl$_3$), 76.3 (cyclohexyl-OCH), 76.3 (CH$_2$CCl$_3$), 74.1 (C5), 73.4 (PhCH$_2$), 72.3 (C3), 71.6 (PhCH$_2$), 69.8 (C6), 67.8 (C5), 51.5 (C2), 33.1 (CH$_2$), 31.2 (CH$_2$), 29.9, 25.7, 24.0 (CH$_2$), 23.8 (CH$_2$) ppm (missing signals due to overlaps: 2 aromatic (Ar) and 2 cyclohexyl CH$_2$ carbons).

2-Methoxyethyl 2-*N*-acyl-3,6-di-*O*-benzyl-2-deoxy-2*N*,4*O*-[[2,3,4-c,d]-1,3-oxazin-2-one]-D-glucopyranoside (17)

The reaction was carried out with **5** (50 mg, 0.10 mmol) as glycosyl donor, methoxyethanol **8** (11 mg, 0.15 mmol, 1.5 equiv.) as glycosyl acceptor, NIS (33.8 mg, 0.15 mmol, 1.5 equiv.) and AgOTf (3 mg, 0.01 mmol, 0.1 equiv.). Full conversion was observed after 30 minutes. The aqueous workup and flash column chromatography (toluene/EtOAc, 5:1 → EtOAc) afforded the final mixture of anomers **17** as a yellowish oil (14 mg, 0.03 mmol, 24 %) (some impurities could not be removed by column chromatography; the yield is approximate). R_f (EtOAc) = 0.31. $[\alpha]_D^{25}$ –1.1° (c 0.19, CHCl$_3$). HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{26}H_{32}NO_8^+$ 486.21224, found 486.21465. *dr* = 66:34. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.35–7.33 (m, 18H, Ar*H*), 7.31–7.28 (m, 1H, Ar*H*), 7.25–7.20 (m, 9H, Ar*H*), 5.06 (s, 1H, H1), 4.95 (bs, 1H, H2), 4.86 (d, 1H, *J* = 11.2 Hz, PhCH_2) 4.71 (s, 1H, H1), 4.64–4.63 (m, 1H, H4), 4.57–4.55 (m, 2H, PhCH_2), 4.51–4.47 (m, 6H, PhCH_2, H5, H3), 4.44–4.40 (m, 3H, PhCH_2), 4.37–4.31 (m, 2H, H5), 4.15–4.14 (m, 2H, H4), 4.01–3.99 (m, 2H, H3), 3.95–3.90 (m, 4H, H6), 3.87–3.75 (m, 4H, H6), 3.61–3.55 (m, 4H, CH_2), 3.51–3.40 (m, 4H, CH_2), 3.34 (s, 3H, OCH_3), 3.29 (s, 3H, OCH_3), 2.62 (s, 3H, C(O)CH_3) ppm (missing signals due to overlaps: one H2 proton). ^{13}C NMR (126 MHz, CDCl$_3$) δ = 173.1 (C(O)CH$_3$), 154.0 (carbamate-*C*O), 150.4 (carbamate-*C*O), 138.3 (Ar), 138.1 (Ar), 137.8 (Ar), 137.1 (Ar), 136.2 (Ar), 129.7 (Ar), 129.5 (Ar), 129.1 (Ar), 129.0 (Ar), 128.9 (Ar), 128.8 (Ar), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.5 (Ar), 128.2 (Ar), 128.0 (Ar), 128.0 (Ar), 127.9 (Ar), 127.9 (Ar), 127.8 (Ar), 127.1 (Ar), 127.0 (Ar), 125.9 (Ar), 97.9 (C1), 93.7 (C1), 74.6 (C5), 73.4 (PhCH$_2$), 73.3 (PhCH$_2$), 72.6 (PhCH$_2$), 72.4 (C4), 71.7 (PhCH$_2$), 71.6 (CH$_2$), 71.5 (CH$_2$), 71.4 (CH$_2$), 71.2 (C4), 71.1 (C5), 69.7 (C6), 68.4 (C6), 68.3 (CH$_2$), 68.2 (C3), 61.7 (C3), 59.3 (OCH$_3$), 59.1 (OCH$_3$), 29.9 (C(O)CH$_3$), 27.1 (C(O)CH$_3$) ppm [missing signals due to overlaps: two C2 carbons].

Phenyl 3,6-di-*O*-benzyl-2-deoxy-2-*N*-[methoxycarbonyl]-1-thio-α-D-glucopyranose (20)

To a stirred solution of glycoside **3** (80 mg, 0.17 mmol) in dry MeOH (0.6 mL), NaOMe, as 25wt.-% solution in MeOH (0.14 mL, 0.50 mmol, 3.0 equiv.), was added. The mixture was mixture was allowed to stir at room temperature for 24 h. Once the conversion had been complete, the mixture was neutralised with Amberlite™ IR-120 resin and filtered. The solvent was eliminated under vacuum to obtain a whitish oil (68 mg, 0.13 mmol, 79 %), which corresponded to product **20**. R_f (EtOAc) = 0.85 $[\alpha]_D^{25}$ +146° (c 0.56, CHCl$_3$) HRMS (HRMS/FT-ICR): *m/z* [M + H]$^+$ Calc. for $C_{27}H_{31}NO_4S^+$ 510.19448, found 510.19486. ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.46–7.45 (m, 2H, Ar*H*), 7.38–7.30 (m, 10H, Ar*H*), 7.26–7.25 (m, 3H, Ar*H*; overlapped with CHCl$_3$), 5.60 (d, *J* = 4.1 Hz, 1H, H1), 4.84 (d, *J* = 8.8 Hz, 1H, N*H*), 4.81 (d, *J* = 11.5 Hz, 1H, PhCH_2), 4.77 (d, *J* = 11.5 Hz, 1H, PhCH_2), 4.62 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.54 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.31 (ddd, *J* = 9.3, 4.8, 4.3 Hz, 1H, H5), 4.24–4.19 (m, 1H, H2), 3.84–3.82 (m, 1H, H4), 3.80 (dd, *J* = 10.3, 4.5 Hz, 1H, H6a), 3.74 (dd, *J* = 10.3, 4.2 Hz, 1H, H6b) 3.67 (s, 3H, CH_3), 3.47 (dd, *J* = 9.8, 9.2 Hz, 1H, H3), 2.72 (bs, 1H, O*H*). ^{13}C NMR (126 MHz, CDCl$_3$) δ = 156.5 (carbamate-*C*(O)CH$_3$), 138.3 (Ar), 137.9 (Ar), 134.0 (Ar), 132.3 (Ar), 132.2 (Ar), 131.8 (Ar), 129.2 (Ar), 128.8 (Ar), 128.7 (Ar), 128.6 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 89.6 (C1), 80.3 (C3), 74.5 (PhCH$_2$), 73.8 (PhCH$_2$), 72.7 (C4), 71.5 (C5), 70.2 (C6), 54.6 (C2), 52.6 (CH$_3$) (missing signals due to overlaps: one aromatic (Ar) carbon signal).

General ring opening procedure of the glycosylation products under Zemplén conditions

The corresponding glycoside was dissolved in dry MeOH and excess NaOMe, as 25wt.-% solution in MeOH, were sequentially added. The mixture was either stirred at either room temperature or refluxed until full conversion was appreciated. The reaction was then diluted in EtOAc, washed with 1 M HCl, neutralised with aqueous saturated $NaHCO_3$, dried with anhydrous $MgSO_4$, filtered and concentrated under vacuum.

2-Methoxyethyl 3,6-di-*O*-benzyl-2-deoxy-2-*N*-[methoxycarbonyl]-D-glucopyranoside (21)

Glycoside **11** (94 mg, 0.22 mmol) was dissolved in dry MeOH (1.5 mL) and NaOMe solution (0.19 mL, 0.67 mmol, 3.0 equiv.) was added. The mixture was mixture stirred and refluxed at 45 °C for 4 hours. Eventually, a greyish oil was obtained (83 mg, 0.17 mmol, 89 %), which corresponded to product **21**. R_f (EtOAc/PE, 1:1) = 0.54 $[\alpha]_D^{25}$ +146° (c 0.61, CHCl$_3$) HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{25}H_{33}NO_8SNa^+$ 498.20984, found 498.20957. α/β = 4.3:1 ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.62–7.57 (m, 1H, Ar*H*), 7.49–7.46 (m, 1H, Ar*H*), 7.40–7.37 (m, 1H, Ar*H*), 7.31–7.19 (m, 16H, Ar*H*), 5.09 (d, *J* = 9.3 Hz, 1H, N*H*α), 4.98 (d, *J* = 7.8 Hz, 1H, N*H*β), 4.75 (d, *J* = 3.2 Hz, 1H, H1α), 4.72 (m, H1β), 4.67 (d, 2H, *J* = 11.9 Hz, PhCH_2), 4.55–4.47 (m, 3H, PhCH_2), 3.92 (ddd, *J* = 2.9, 9.7, 9.9 Hz, 1H, H2α), 3.86 (ddd, *J* = 4.3, 7.1, 8.8 Hz, 1H, H6β), 3.76–3.72 (m, 2H, H4α, H5β, H6α), 3.68 (dd, *J* = 2.4, 4.3 Hz, 2H, CH_2β), 3.65 (dd, *J* = 4.5, 8.6 Hz, 3H, CH_2α), 3.62 (bd, *J* = 1.8 Hz, 1H, H2α), 3.60 (s, 3H, C(O)CH_3α), 3.58 (s, 2H, C(O)CH_3β), 3.56–3.52 (m, 3H, H6α, CH_2α), 3.50 (bd, *J* = 3.0 Hz, 1H, H3α), 3.44–3.38 (m, 1H, H4β, H5α), 3.23 (bdd, *J* = 5.5, 3.2 Hz, 1H, H2β) 3.29 (s, 3H, OCH_3α), 3.28 (s, 2H, OCH_3β) ppm. ^{13}C NMR (126 MHz, CDCl$_3$) δ 171.3 (carbamate-*C*Oβ), 156.8 (carbamate-*C*Oα), 138.6 (Ar), 138.5 (Ar), 138.0 (Ar), 137.9 (Ar), 132.2 (Ar), 132.1 (Ar), 132.1 (Ar), 132.0 (Ar), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.5 (Ar), 128.2 (Ar), 127.9 (Ar), 127.9 (Ar), 127.8 (Ar), 127.8, 127.7 (Ar), 100.9 (C1β), 98.6 (C1α), 81.1 (C3β), 80.9 (C3α), 75.4 (C4β), 74.5 (C5α), 74.4 (PhCH$_2$), 74.0 (PhCH$_2$), 73.8 (PhCH$_2$), 73.7 (PhCH$_2$), 70.6 (C4α), 70.0 (CH$_2$), 68.7 (C6α), 67.3 (C6β), 60.5 (C5β), 59.0 (OCH$_3$α), 57.3 (OCH$_3$β), 54.4 (C2α), 52.3 (C(O)CH$_3$α), 52.2 (C(O)CH$_3$β) ppm (missing signals due to overlaps: seven aromatic, one C2β and three methoxyethyl CH$_2$ carbons).

Cyclohexyl 3,6-di-*O*-benzyl-2-deoxy-2-*N*-[methoxycarbonyl]-D-glucopyranoside (22)

Compound **12** (53 mg, 0.11 mmol) was dissolved in dry MeOH (1.5 mL) and NaOMe solution in MeOH (0.12 mL, 0.55 mmol, 5.0 equiv.) was added. The mixture was mixture stirred and refluxed at 50 °C for 24 h. Eventually, a yellowish oil was obtained (45 mg, 0.09 mmol, 80 %), which corresponded to product **22** (since some impurities could not be removed by column chromatography, the yield is approximate). R_f (EtOAc) = 0.76 $[\alpha]_D^{25}$ +2.7° (c 0.38, CHCl$_3$). HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{28}H_{37}NO_7SNa^+$ 522.24622, found 522.24535. *dr* = 79:21 ^{1}H NMR (500 MHz, [D]Chloroform) δ 7.26 (m, 10H, Ar*H*), 7.22–7.21 (m, 3H, Ar*H*), 7.19–7.18 (m, 1H, Ar*H*), 4.85 (bs, 2H, H1, H1′), 4.74 (d, *J* = 10.6 Hz, 1H, N*H*), 4.69 (bd, *J* = 11.9 Hz, 2H, PhCH_2), 4.55–4.46 (m, 3H, PhCH_2), 3.88 (bdd, *J* = 10.1, 9.6 Hz, 1H, H2), 3.79–3.77 (m, 1H, H5, H5′), 3.67–3.63 (m, 4H, H4, H4′, H6, H6′), 3.59 (bs, 3H, CH_3), 3.57 (bs, 2H, CH_3′), 3.55–3.44 (m, 3H, H3, H3′, cyclohexyl-OCH, cyclohexyl-OCH′), 1.80 (bd, *J* = 9.3 Hz, 2H, CH_2), 1.71 (bs, 1H, CH_2), 1.61 (bs, 3H, CH_2), 1.46–1.43 (m, 2H, CH_2), 1.34- 1.26 (m, 4H, CH_2), 1.06–0.94 (m, 2H, CH_2) ppm (missing signals: one N*H* proton). ^{13}C NMR (126 MHz,

$CDCl_3$) δ = 156.7 (carbamate-*C*O), 156.5 (carbamate-*C*O), 138.6 (Ar), 138.5 (Ar), 138.3 (Ar), 138.3 (Ar), 138.1 (Ar), 138.0 (Ar), 137.9 (Ar), 137.8 (Ar), 98.6 (C1′), 96.4 (C1), 81.5 (C3), 81.1 (C3′), 76.0 (cyclohexyl-OCH), 74.5 (PhCH$_2$), 73.7 (PhCH$_2$), 73.5 (PhCH$_2$), 73.5 (PhCH$_2$), 71.8 (C4), 70.9 (C6), 70.3 (C5), 70.1 (C6′), 69.8 (C5′), 69.4, 57.8, 55.2 (C2′), 54.2 (C2), 52.4 (C(O)CH$_3$), 52.3 (C(O)CH$_3$′), 37.5 (CH$_2$), 37.2 (CH$_2$), 33.5 (CH$_2$), 31.7 (CH$_2$), 25.6 (CH$_2$), 24.0 (CH$_2$) ppm (missing signals due to overlaps: two carbamate ester carbonyls (*C*(O)CH$_3$), 16 aromatic and four cyclohexyl *C*H$_2$ carbons).

3,6-*O*-benzyl-2-deoxy-2-*N*-[methoxycarbonyl]- D-glucopyranose-(1 → 3)-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (23)

Compound **13** (40 mg, 0.064 mmol) was dissolved in dry MeOH (3.0 mL) and NaOMe solution (0.08 mL, 0.34 mmol, 5.0 equiv.) was added. The mixture was mixture stirred at room temperature for 24 h. Finally, a yellowish oil was obtained (38 mg, 0.058 mmol, 91 %), which corresponded to product **23** (since some impurities could not be removed by column chromatography, the yield is approximate). R_f (EtOAc) = 0.67. $[\alpha]_D^{25}$ +2.7° (c 0.38, $CHCl_3$). HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{34}H_{45}NO_{12}SNa^+$ 682.28340, found 682.28423. α/β = 1:5.2. ^{1}H NMR (500 MHz, [D]Chloroform) δ 8.10 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.60 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.47 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.38–7.28 (m, 19H, Ar*H*), 5.85 (d, *J* = 3.5 Hz, 1H, H1′β), 5.82 (d, *J* = 3.8 Hz, 1H, H1′α), 4.82 (d, *J* = 3.5 Hz, 1H, H1α), 4.78–4.75 (m, 2H, H1β, PhC*H*$_2$), 4.72 (d, *J* = 11.7 Hz, 1H, PhC*H*$_2$), 4.63 (d, *J* = 12.2 Hz, 1H, PhC*H*$_2$), 4.59–4.50 (m, 5H, H2′, PhC*H*$_2$), 4.38 (d, *J* = 12.2 Hz, 1H, PhC*H*$_2$), 4.34–4.31 (m, 1H, H5), 4.28 (bdd, *J* = 3.5, 2.7 Hz, 1H, H3′), 4.25–4.20 (m, 1H, H3′), 4.10 (dd, *J* = 8.8, 2.9 Hz, 1H, H4′), 4.06–4.00 (m, 2H, H4, H4), 3.95 (ddd, *J* = 3.2, 6.3, 13.2 Hz, H5′), 3.89 (bs, 1H, H5′), 3.81 (dd, *J* = 3.1, 11.3 Hz, 2H, H6′), 3.73 (bd, *J* = 9.6 Hz, 1H, H6), 3.68 (s, 3H, C(O)C*H*$_3$), 3.67–3.62 (m, 5H, H3, H3, H6, H6′), 3.40 (bs, 1H, H2), 3.17 (bs, 1H, H2), 1.46 (bdd, *J* = 7.4, 7.5 Hz, 6H, C*H*$_3$), 1.30–1.16 (m, 18H, C*H*$_3$) ppm (missing signals: two N*H*, one H4′ and one H5 protons). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.5 (carbamate-*C*(O)CH$_3$), 138.2 (Ar), 137.4 (Ar), 133.7 (Ar), 130.3 (Ar), 129.6 (Ar), 128.8 (Ar), 128.8 (Ar), 128.7 (Ar), 128.7 (Ar), 128.7 (Ar), 128.7 (Ar), 128.7 (Ar), 128.6 (Ar), 128.6 (Ar), 128.3 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 112.3 (isopropylidene-*C*), 112.2 (isopropylidene-*C*), 112.1 (isopropylidene-*C*), 111.8 (isopropylidene-*C*), 105.4 (C1′), 105.2 (C1′), 83.7 (C2′), 83.0 (C3′), 82.8, 81.7, 80.5 (C3′), 80.3 (C4′), 74.8 (PhCH$_2$), 74.7 (PhCH$_2$), 74.4 (PhCH$_2$), 74.2, 74.0, 73.9 (PhCH$_2$), 73.1 (C5), 72.1, 70.4 (C6), 69.8 (C6), 68.4 (C5′), 64.6 (C6′), 57.5 (C2), 56.9 (C2), 52.6 (C(O)CH$_3$), 52.5 (C(O)CH$_3$), 32.1 (CH$_3$), 29.8 (CH$_3$), 29.5 (CH$_3$), 26.9 (CH$_3$), 26.7 (CH$_3$), 26.4 (CH$_3$), 25.4 (CH$_3$), 22.8 (CH$_3$) ppm (missing signals due to overlaps: one carbamate ester carbonyl (*C*(O)CH$_3$), 3 aromatic (Ar), C1, one C2′, two C3, two C4 and one C4′ carbons).

2-Methoxyethyl 3,6-di-*O*-benzyl-2-deoxy-2-*N*-[methoxycarbonyl]-2-*N*-[2,2,2-tricholorethoxycarbonyl]-D-glucopyranoside (24)

Compound **14** (31 mg, 0.050 mmol) was dissolved in dry MeOH (2.0 mL) and NaOMe solution (0.11 mL, 0.50 mmol, 10.0 equiv.) was added. The mixture was mixture stirred and refluxed at 50 °C for 24 h, to furnish a yellowish oil (25 mg, 0.040 mmol, 81 %), which corresponded to compound **24**. R_f (EtOAc) = 0.21 $[\alpha]_D^{25}$ +6.6° (c 0.62, DMSO) HRMS (HRMS/FT-ICR): *m/z* [M + Na]$^+$ Calc. for $C_{28}H_{34}Cl_3NO_{10}Na^+$ 672.11450, found 672.11414. *dr* = 60:40 ^{1}H NMR (500 MHz, DMSO) δ 7.79 (bd, *J* = 5.3 Hz, 2H, Ar*H*), 7.72–7.64 (m, 3H, Ar*H*), 7.36–7.22 (m, 23H, Ar*H*), 4.81 (s, 1H, H1), 4.73 (d, *J* = 11.4 Hz, 1H, PhC*H*$_2$), 4.68 (s, 1H, H1), 4.64 (d, *J* = 12.1 Hz, 1H, PhC*H*$_2$), 4.60 (d, *J* = 11.7 Hz, 1H, PhC*H*$_2$), 4.53 (d, *J* = 12.1 Hz, 1H, PhC*H*$_2$), 4.48–4.45 (m, 4H, H3), 4.40–4.39 (m, 3H, 2 × C*H*$_2$CCl$_3$), 4.15–4.09 (m, 5H, H4, H4), 3.99 (dd, *J* = 8.1, 10.0 Hz, 1H, H6), 3.86–3.78 (m, 6H, H6), 3.74 (dd, *J* = 5.2, 10.0 Hz, 3H, H6), 3.75–3.72 (m, 5H, H2), 3.65–3.64 (bd, *J* = 2.1 Hz, 4H, H2), 3.59–3.56 (m, 6H, H6), 3.52–3.41 (m, 102H, H5, 4 × methoxyethyl-C*H*$_2$), 3.22 (s, C*H*$_3$), 3.19 (s, C*H*$_3$) ppm. ^{13}C NMR (126 MHz, DMSO) δ = 152.5 (carbamate-*C*O), 152.3 (carbamate-*C*O), 138.4 (Ar), 138.3 (Ar), 138.0 (Ar), 137.5 (Ar), 128.5 (Ar), 128.4 (Ar), 128.4 (Ar), 128.3 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.6 (Ar), 127.6 (Ar), 127.6 (Ar), 99.6 (C1), 93.4 (C1), 75.3 (C4), 72.2 (CH$_2$CCl$_3$), 72.2 (CH$_2$CCl$_3$), 71.3 (PhCH$_2$), 71.2 (PhCH$_2$), 71.1 (methoxyethyl-CH$_2$), 70.6 (PhCH$_2$), 70.3 (C4), 70.2 (C6), 69.2 (C3), 68.7 (C3), 68.0, 67.7 (methoxyethyl-*C*H$_2$), 67.6, 67.1 (C6), 58.3 (OCH$_3$), 58.2 (OCH$_3$), 48.8 (C5), 45.9 (C2) ppm (missing signals due to overlaps: two Troc carbonyls, 11 aromatic, two *C*Cl$_3$, one C2, one C5 carbons and two carbamate ester methyl (C(O)CH$_3$) signals).

Keywords: Glycosylation · Conformational restriction · Cyclic carbamate · Protective groups

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