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A novel strategy towards the synthesis of orthogonally functionalised 4-aminoglycosides

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A tethered nucleophilic substitution strategy for the stereoselective introduction of axially oriented amino functions on suitably protected gluco- and mannopyranosides is presented. The obtained oxazine is a versatile building block, which after some manipulation, could be used in the construction of highly functionalised oligosaccharides.

Introduction

The broad variety of naturally occurring carbohydrate structures originates, apart from the large number of possible interglycosidic linkages, from the wide diversity encountered in their monosaccharide constituents. Aminosugars,¹ hexapyranoses bearing diversely functionalised amino groups at different positions, represent an important category of carbohydrate units, found in numerous oligosaccharides and glycoconjugates. For instance, aminosugars are not only important as essential components of bacterial capsular polysaccharides,² but also as structural elements of aminoglycoside antibiotics.³ The biological importance of natural products containing aminosugars demands the development of efficient synthetic routes to these monosaccharides. Our focus in this field is directed towards the stereoselective introduction of C-4 amino functions cis relative to the neighbouring C-5 hydroxymethyl group of hexapyranosides.4

A convenient route to the regio- and stereoselective introduction of nitrogen substituents entails the use of tethered nitrogen nucleophiles.⁵ In this respect, allylic trichloroacetimidates have been employed in an Overman rearrangement to provide the corresponding allylic trichloroacetamides.⁶ Alternatively, IBX⁷ or NIS-mediated⁸ cyclisation of allylic trichloroacetimidates gives the corresponding trans-disposed iodo-oxazolines. In line with these studies, we here report a novel, straightforward synthesis of orthogonally protected 4-amino glycosides. A key element of our strategy is the selective introduction of a trichloroacetimidate moiety at OH-6 of partially protected gluco- and mannopyranosides. The hydroxyl at C-4 is transformed into a suitable leaving group amenable to base-induced substitution by the tethered imidate moiety to provide the corresponding oxazine. We further demonstrate that, after hydrolysis and suitable protection, the thus obtained aminoglycosides can be readily applied as building blocks in oligosaccharide synthesis.

Results and discussion

As a first example, the transformation of methyl 2,3-di-*O*-benzyl- α -D-glucopyranoside 1° into methyl 4-acetamido-6-*O*-acetyl-2,3-di-*O*-benzyl-4-deoxy- α -D-galactopyranoside 5 was undertaken (Scheme 1). Treatment of 1 with trichloro-acetonitrile (Cl₃CCN) in the presence of a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) led to the selective formation of 6-*O*-acetimidate 2 in 89% yield. Installation of the 4-*O*-triflate (Tf₂O, pyridine) followed by base-mediated cyclisation of resulting 3 gave oxazine 4 (80% yield, 2 steps), the structural integrity of which was fully established by spectro-



Scheme 1 Reagents and conditions: i, Cl_3CCN , DBU, DCM, 0 °C, 89%. ii, Tf_2O , pyr, DCM, 0 °C. iii, DiPEA, 80%. iv, 80% AcOH in H_2O , then Ac₂O, pyr, 89%.

scopic analysis. Transformation of 1 *via* a three-step one pot procedure afforded oxazine 4 in slightly improved yield (89% over 3 steps). Acidic hydrolysis of 4 and acetylation of the intermediate aminoalcohol gave methyl 4-acetamido-6-O-acetyl-2,3-di-O-benzyl-4-deoxy- α -D-galactopyranoside 5.

Next, diversely functionalised manno- and glucopyranosides were employed in the tethered nucleophilic substitution sequence (Table 1). Subjection of methyl 2,3-di-O-benzyl- α -Dmannopyranoside 6^{10} to the three-step one pot procedure afforded oxazine 7, albeit in a moderate yield (entry 1). Closer inspection of the sequence of reactions revealed that the first two steps, which entailed installation of the 6-O-imidate and 4-O-triflate functions, proceeded with equal efficiency as observed for the synthesis of its glucopyranose congener 3 (Scheme 1). Arguably, the axial oriented 2-O-benzyl group in mannopyranoside 6 may cause 1,3-diaxial strain in the transition state hampering the formation of oxazine 7. Hydrolysis and acetylation of 7 gave fully protected 4-deoxy-4-aminotaloside 8.

At this stage, we were interested in finding out whether our approach could be applied to protected thioglycosides, representing useful building blocks in the assembly of oligosaccharides (entries 2–4).¹¹ To our satisfaction, ethyl 2,3-*O*isopropylidene-1-thio- α -D-mannopyranoside 9¹² was readily transformed into oxazine 10 (entry 2). Unmasking of the oxazine ring in 10 proceeded with concomitant partial hydrolysis of the isopropylidene protecting group, leading, after acetylation, to the mixture of 4-deoxy-4-aminotalosides 11 and 12 in



^{*a*} Cl₃CCN, DBU, DCM, 0 °C, then Tf₂O, pyr, DCM, 0 °C, then D*i*PEA. ^{*b*} 80% AcOH in H₂O, then Ac₂O, pyr. ^{*c*} Isolated yields.

good overall yield. An unexpected difference in efficiency in the outcome of the three-step oxazine synthesis was observed in the case of ethyl thioglucosides 13^{13} and 14^{14} (entry 3). In both cases, selective installation of the primary trichloroacetimidate proceeded uneventfully. However, treatment of the intermediate 6-O-acetimidate in 13 with triflic anhydride and pyridine followed by DiPEA mediated cyclisation afforded oxazine 15 in a rather poor yield. The latter may be ascribed to the high nucleophilic nature of the anomeric thioacetal. A decrease in nucleophilicity¹⁵ of the thioacetal by installation of an electron withdrawing 2-O-benzoyl, as in 14, led after the triflationsubstitution sequence to formation of oxazine 16 in satisfactory yield. Analogously, application of the sequence of reactions to phenyl 2-azido-3-O-benzyl-2-deoxy-1-thio-a-D-glycoside 18,16 bearing an electron withdrawing azide at C-2, provided the 2,4diamino derivative 19 in a good yield (entry 4). Both oxazines 16 and 19 were readily hydrolysed and acetylated leading to the 4- acetamidogalactosides 17 and 20 in 61% and 94% yield, respectively.

Orthogonally protected oxazine 19 was selected as a model compound to be used both as donor and acceptor in ensuing glycosylation reactions. Diaminogalactosides possessing differently functionalised amino functions are frequently encountered in natural products, for instance as 2-acetamido-4amino-2,4,6-trideoxy-galactopyranosides present in the capsular polysaccharides of Bacteroides fragilis.² Furthermore, we recently demonstrated 17 that partially protected thioglycosides can be effectively employed as acceptor glycosides in the dehydrative condensation procedure developed by Gin et al.¹⁸ Aglycon 21 was readily obtained after acidic hydrolysis of oxazine 19 and subsequent selective reaction of the amine with N-(benzyloxycarbonyloxy)succinimide (ZOSu). Dehydrative condensation was accomplished by activating 2,3,4,6-tetra-Obenzyl- α/β -D-galactopyranose 23¹⁹ under the influence of diphenylsulfide bis(triflate) prepared in situ, followed by addition of acceptor 21 to afford the α -linked thiodisaccharide 24 in 65% yield. Next, the fully orthogonally protected thiodonor 22 was prepared by acetylation of compound 21. Activation of this highly "disarmed"¹⁵ donor was accomplished by treatment with diphenylsulfoxide (DPS)-triflic anhydride (Tf₂O)²⁰ which

was shown to be a more potent thiophilic promoter system than the analogous benzenesulfinyl piperidine (BSP)–Tf₂O²¹ combination recently developed by the Crich laboratory. Addition of methyl glucoside **25**,²² to the activated donor, smoothly afforded disaccharide **26** as an anomeric mixture in excellent yield (Scheme 2).²³

Conclusion

In summary, a new, straightforward synthetic procedure for the construction of 4-amino-4-deoxyglycosides, and their application as donors and acceptors in condensation reactions towards disaccharides, is presented. Future research will be devoted to implementation of this strategy in the synthesis of complex oligosaccharides containing aminoglycoside moieties.



Scheme 2 *Reagents and conditions:* i, 80% AcOH in H₂O, then ZOSu, pyr, rt, 95%. ii, Ac₂O, pyr, quant. iii, 23, DPS, Tf₂O, TTBP, DCM, -60 °C, then 21, 65%. iv, 22, DPS, Tf₂O, DCM, -60 °C, then 25, 95%.

Experimental

General

¹H and ¹³C NMR spectra were recorded on a Jeol JNM-FX-200 (200/50.1 MHz) and a Bruker AV-400 (400/100 MHz) spectrometer. Chemical shifts are given in ppm (δ) relative to tetramethylsilane as internal standard. Coupling constants are given in Hz. All given ¹³C spectra are proton decoupled. Mass spectra were recorded with PE/SCIEX API 165 with electronspray interface and Q-Star Applied Biosystems Q-TOF (TOFsection). Optical rotations were measured on a Propol automatic polarimeter. Traces of water in the donor and acceptor glycosides, diphenylsulfoxide and TTBP were removed by coevaporation with toluene. TTBP was synthesised as described by Crich et al.²⁴ Dichloromethane (DCM, Baker) was boiled under reflux over P2O5 for 2 h and was distilled immediately prior to use. Solvents used for flash chromatography and TLC were of technical grade and distilled before use. Flash chromatography was performed on Baker silica gel (0.063-0.200 mm). TLC-analysis was conducted on DC-fertigfolien (Schleicher & Schuell, F1500, LS254) with detection by UV-absorption (254 nm) were applicable and by spraying with 20% sulfuric acid in ethanol followed by charring at ~150 °C or by spraying with a solution of $(NH_4)_6Mo_7O_{24}$ ·H₂O (25 g l⁻¹) in 10% sulfuric acid followed by charring at ~150 °C. Free amine functions were detected by spraying with a ninhydrin solution in EtOH followed by charring at ~150 °C.

Oxazine 4

A solution of methyl 2,3-di-*O*-benzyl- α -D-glucopyranoside 1 (0.5 g; 1 mmol) in 5 ml DCM was cooled to 0 °C under an Ar

atmosphere. Subsequently trichloroacetonitrile (0.10 mL; 1.05 mmol; 1.05 eq.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (3 µL; 0.01 mmol; 0.01 eq.) were added to the solution. According to TLC analysis, all starting material was consumed after 5 min. Subsequent treatment of the reaction mixture with pyridine (0.4 mL; 5 mmol; 5 eq.) and trifluoromethanesulfonic anhydride (0.24 mL; 1.5 mmol; 1.5 eq.) afforded the triflated product in 5 min at 0 °C. Base induced cyclisation was accomplished by addition of diisopropylethylamine (1.0 mL; 5 mmol; 5 eq.) and stirring was continued for 3¹/₂ h. The reaction mixture was purified by flash chromatography (20% EtOAc-PE). Removal of the eluent gave 0.40 g (0.80 mmol; 80%) of the title compound 4 as a yellow oil. TLC: 35% EtOAc in PE. $[a]_{D}^{22}$: +63.4 (c = 1, CHCl₃). IR (cm⁻¹): 1718, 1679, 1510, 1496, 1454, 1352, 1220, 1195, 1089, 1043, 1028, 1001 ¹H NMR (400 MHz, CHCl₃): $\delta = 3.37$ (s, 3H, CH₃(OMe)), 3.62 (dd, 1H, J = 3.5 Hz, J = 10.1 Hz, H-2), 3.94 (m, 1H, H-4), 4.04 (br d, 1H, J = 2.0 Hz, H-5), 4.13 (dd, 1H, J = 10.1 Hz, J = 4.4 Hz, H-3), 4.29 (d, 1H, J = 11.8 Hz, H-6), 4.42 (dd, 1H, J = 11.8, J = 1.3 Hz, H-6), 4.60 (d, 1H, J = 3.5 Hz, H-1), 4.65 (d, 1H, J = 11.8 Hz, CHHPh); 4.77-4.88 (m, 3H, CHHPh, CH2Ph), 7.25-7.47 (m, 10H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 54.1$ (C-4), 55.7 (Me), 60.4 (C-5), 69.2 (C-6), 71.8 (CH₂(Bn)), 73.8 (CH₂(Bn)), 75.2 (C-3), 75.6 (C-2), 99.5 (C-1), 127.4-128.3 (CH(Ar)), 138.3 (C_q(Bn)), 138.9 (C_q(Bn)), 153.0 (C=NH); MS (m/z, ESI): 500 $(M + H^{+}).$

Methyl 4-acetamido-6-*O*-acetyl-2,3-di-*O*-benzyl-4-deoxy-α-D-galactopyranose 5

A solution of oxazine 4 (0.44 g; 0.89 mmol) in 5 mL 80% AcOH-H₂O was stirred for 30 min at ambient temperature. After removal of the solvent under reduced pressure, the residue was co-evaporated several times with toluene. The crude product was subsequently dissolved in 4 mL pyridine and treated with 1 mL Ac₂O. Stirring was continued for 8 h before the solvent was removed in vacuo. After co-evaporation with toluene the crude mixture was purified by flash chromatography (30% EtOAc-PE). Removal of the eluent gave 0.49 g (0.79 mmol, 89%) of the title compound 5 as a yellow oil. TLC: 35% EtOAc–PE. $[a]_{D}^{22}$: + 2.8 (c = 1, CHCl₃). IR: 1739, 1651, 1369, 1232, 1195, 1155, 1099, 1028; ¹H NMR (400 MHz, CHCl₃): $\delta = 2.04$ (s, 3H, CH₃(Ac)), 2.06 (s, 3H, CH₃(Ac)), 3.38 (s, 3H, CH₃(OMe)), 3.45–3.49 (dd, 1H, J = 4.0 Hz, J = 10.1 Hz, H-2), 3.96–4.00 (dd, 1H, J = 10.7 Hz, J = 4.7 Hz, H-3), 4.08–4.15 (m, 3H, H-5, H-6, H-6), 4.52 (d, 1H, J = 11.1 Hz, CHHPh), 4.64 (d, 1H, J = 4.0 Hz, H-1), 4.65 (d, 1H, J = 12.2 Hz, CHHPh), 4.77 (t, 1H, J = 4.4 Hz, H-4), 4.78 (d, 1H, J = 11.1 Hz, CHHPh), 4.86 (d, 1H, J = 12.2 Hz, CHHPh), 5.60 (d, 1H, J = 10.1 Hz, NH), 7.26-7.39 (m, 10H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 20.8 \text{ CH}_3(\text{Ac})), 23.5 (\text{CH}_3(\text{Ac})), 47.6 (\text{C-4}), 55.4 (\text{CH}_3-\text{CH}$ (OMe)), 63.2 (C-6), 66.7 (C-5), 71.7 (CH₂(Bn)), 73.6 (CH₂(Bn)), 75.3 (C-2), 76.0 (C-3), 98.6 (C-1), 127.7-128.4 (Ar), 137.9 (C_a(Bn)), 138.2 (C_a(Bn)), 170.5 (C=O) HRMS: (M + H) calcd for C₁₅H₃₃NO₇ 458.2101, found 458.2097.

Methyl 2,3-di-O-benzyl-6-trichloroacetimidate- α -D-glucopyranoside 2

To a stirred solution of methyl 2,3-di-*O*-benzyl- α -D-glucopyranoside **1** (1.79 g; 5 mmol) in 25 ml DCM at 0 °C was added trichloroacetonitrile (0.5 mL; 5 mmol, 1 eq.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (5 μ L; 0.05 mmol; 0.05 eq.). Stirring was allowed for 45 min after which the reaction mixture was concentrated (waterbath ~ 30 °C). Flash chromatography (20% EtOAc–PE) and removal of the eluent gave 2.23 g. (4.31 mmol, 89%) of the title compound **2** as a colourless oil. TLC: 50% EtOAc–PE. ¹H NMR (400 MHz, CHCl₃): δ = 3.39 (s, 3H, CH₃(OMe)), 3.46 (dd, 1H, *J* = 9.0 Hz, H-4), 3.50 (dd, 1H, *J* = 9.6 Hz, *J* = 3.6 Hz, H-2), 3.82 (t, 1H, *J* = 9.2 Hz, H-3), 3.87 (m, 1H, *J* = 10.1 Hz, *J* = 5.0 Hz, H-5), 4.48 (d, 1H, *J* = 11.8 Hz, H-6), 4.60 (d, 1H, J = 3.4 Hz, H-1), 4.61 (dd, 1H, J = 11.9 Hz, J = 5.0 Hz, H-6), 4.64 (d, 1H, J = 11.9 Hz, CHHPh), 4.76 (d, 2H, J = 11.6 Hz, 2 × CHHPh), 4.97 (d, 1H, J = 11.3 Hz, CHHPh), 7.29–7.37 (m, 10H, CH(Ar)), 8.23 (br s, 1H, NH); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 55.1$ (CH₃(OMe)), 68.5 (C-6), 69.6 (C-5), 70.0 (C-4), 73.2 (CH₂(Bn)), 75.6 (CH₂(Bn)), 79.6 (C-2), 81.0 (C-3), 98.1 (C-1), 127.8–128.5 (Ar), 137.9 (C_q(Bn)), 138.6 (C_q(Bn)); MS (*m*/*z*, ESI): 518.1 (M + H⁺), 540.0 (M + Na⁺).

Oxazine 7

Oxazine 7 was obtained from methyl 2,3-di-O-benzyl-a-Dmannopyranoside 6 via the same procedure as described for the conversion of compound 1 to 4. The reaction mixture was purified by flash chromatography (15% EtOAc-PE). Removal of the eluent gave 75 mg (0.15 mmol, 41%) of the title compound 7 as a yellow oil. ¹H NMR (400 MHz, CHCl₃): $\delta = 3.38$ (s, 3H, CH₃(OMe)), 3.66 (t, 1H, J = 2.6 Hz, H-2), 4.01 (m, 2H, J = 2.6 Hz, J = 4.7 Hz, H-4, H-5), 4.06 (dd, 1H, J = 4.6 Hz, J = 2.6 Hz, H-3), 4.28 (d, 1H, J = 11.2 Hz, H-6), 4.54 (dd, 1H, J = 11.5 Hz, J = 2.6 Hz, H-6), 4.66 (d, 2H, J = 12.3 Hz, 2 × CHHPh), 4.78 (d, 1H, J = 12.0 Hz, CHHPh), 4.85 (d, 1H, J = 2.7 Hz, H-1), 4.86 (d, 1H, J = 12.5 Hz, CHHPh), 7.31 (m, 10H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): δ = 52.4 (C-4), 55.4 (CH₃(OMe)), 61.4 (C-5), 68.7 (C-6), 70.9 (CH₂(Bn)), 72.7 (CH₂(Bn)), 74.1 (C-2, C-3), 101.0 (C-1), 127.6–128.4 (Ar), 138.3 (C_q(Bn)), 138.9 (C_q(Bn)), 151.8 (C=N); MS (*m*/*z*, ESI): 500.0 (M $+ \dot{H}^{+}$), 522.1 (M + Na⁺).

Methyl 4-acetamido-6-*O*-acetyl-2,3-di-*O*-benzyl-4-deoxy-α-D-talopyranoside 8

Compound 8 was prepared from oxazine 7 via the same procedure as described for the conversion of compound 4 into 5. The reaction mixture was purified by flash chromatography (20% EtOAc-PE). Removal of the eluent gave 43 mg (0.096 mmol, 64%) of the title compound 4 as a yellow oil. TLC: 40% EtOAc-PE. $[a]_D^{22}$: +36.8 (c = 0.66, CHCl₃). IR (cm⁻¹): 1739, 1670, 1515, 1454, 1369, 1230, 1114, 1041. ¹H NMR (400 MHz, CHCl₃): $\delta = 1.81$ (s, 3H, NHAc), 2.06 (s, 3H, CH₃(Ac)), 3.34 (s, 3H, CH₃(OMe)), 3.76 (m, 1H, J = 1.6 Hz, H-2), 3.81 (dd, 1H, J = 4.2 Hz, J = 3.1 Hz, H-3), 3.97 (m, 1H, H-5), 4.12 (dd, 1H, J = 8.0 Hz, J = 3.6 Hz, H-6), 4.24 (dd, 1H, J = 11.7 Hz, J = 4.2 Hz, H-6), 4.43 (d, 1H, J = 11.6 Hz, CHHPh), 4.66 (m, 1H, H-4), 4.68 (d, 2H, J = 11.2 Hz, $2 \times CH$ HPh), 4.76 (d, 1H, J = 11.0 Hz, CHHPh), 4.81 (d, 1H, J = 1.2 Hz, H-1), 6.95 (d, 1H, J = 9.3 Hz, NH), 7.30 (m, 10H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 20.8$ (CH₃(Ac)), 23.2 (CH₃(Ac)), 46.5 (C-4), 54.8 (CH₃(OMe)), 64.0 (C-6), 68.2 (C-5), 69.9 (CH₂(Bn)), 72.1 (C-3), 74.1 (CH₂(Bn)), 76.2 (C-2), 99.9 (C-1), 127.5-128.4 (Ar), 137.6 (C_q(Bn)), 137.8 (C_q(Bn)), 170.7 (C=O); HRMS: (M + H) calcd for C₁₅H₃₃NO₇ 458.2101, found 458.2174.

Oxazine 10

Oxazine 10 was obtained from ethyl 2,3-O-isopropylidene-1-thio- α -D-mannopyranoside 9 via the same procedure as described for the conversion of compound 1 into 4. The reaction mixture was purified by flash chromatography (10% EtOAc-PE). Removal of the eluent gave 216 mg (0.55 mmol, 54%) of the title compound 10 as a yellow oil. ¹H NMR (400 MHz, CHCl₃): $\delta = 1.23$ (t, 3H, J = 7.4 Hz, CH₃(SEt)), 1.27 (s, 3H, CH₃(isoprop.)), 1.47 (s, 3H, CH₃(isoprop.)), 2.62 (m, 2H, CH₂(SEt), 4.19 (d, 1H, J = 7.2 Hz, H-2), 4.23 (m, 1H, H-4), 4.27 (s, 1H, H-5), 4.28 (m, 1H, H-6), 4.35 (m, 1H, H-6), 4.67 (dd, 1H, J = 7.2 Hz, J = 3.7 Hz, H-3), 5.07 (s, 1H, H-1); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 14.7$ (CH₃(SEt)), 24.9 (CH₃-(isoprop.)), 25.4 (CH₂(SEt)), 26.1 (CH₃(isoprop.)), 49.5 (C-4), 61.1 (C-5), 67.2 (C-6), 72.0 (C-2), 76.0 (C-3), 81.4 (C-1), 110.4 (C_a(isoprop.), 154.1 (C=N); MS (*m*/*z*, ESI): 390 (M + H⁺), 412 $(M + Na^{+}).$

Ethyl 4-acetamido-6-*O*-acetyl-2,3-*O*-isopropylidene-1-thio-α-D-talopyranoside 11

Compound 11 was prepared from oxazine 10 via the same procedure as described for the conversion of compound 4 into 5. The reaction mixture was purified by column chromatography (EtOAc). Removal of the eluent gave 77 mg (0.22 mmol, 40%) of the title compound 11 as a yellow oil, together with 50 mg (0.13 mmol, 21%) ethyl 4-acetamido-2,3,6-tri-O-acetyl-1-thioα-D-talopyranoside 12. TLC: 40% EtOAc-PE. [a]_D²²: +142.0 $(c = 1, CHCl_3)$. IR (cm^{-1}) : 1739, 1666, 1519, 1373, 1235, 1211, 1083, 1037, 1002; ¹H NMR (400 MHz, CHCl₃): δ = 1.32 (t, 3H, J = 7.4 Hz, CH₃(SEt), 1.34 (s, 3H, CH₃(isoprop.)), 1.50 (s, 3H, CH₃(isoprop.)), 2.04 (s, 3H, CH₃(Ac)), 2.06 (s, 3H, CH₃(Ac)), 2.57 (m, 1H, CHH(SEt)), 2.74 (m, 1H, CHH(SEt)), 4.05 (dd, 1H, J = 5.9 Hz, J = 1.0 Hz, H-2), 4.10 (dd, 1H, J = 11.8 Hz, J = 4.1 Hz, H-6), 4.23 (d, 1H, J = 11.8 Hz, H-6), 4.34 (t, 1H, J = 5.9 Hz, H-3), 4.38 (m, 1H, H-5), 4.47 (m, 1H, H-4), 5.52 (s, 1H, H-1), 5.86 (d, 1H, J = 9.9 Hz, NH) ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 15.1$ (CH₃(SEt)), 21.6 (CH₃(Ac)), 24.3 (CH₃(Ac)), 24.8 (CH₂(SEt)), 26.2 (CH₃(isoprop.)), 27.1 (CH₃(isoprop.)), 46.5 (C-4), 64.1 (C-6), 67.5 (C-5), 72.2 (C-3), 74.6 (C-2), 80.1 (C-1), 110.0 (C_a(isoprop.), 170.5 (C=O), 171.3 (C=O); HRMS: (M + H) calcd for $C_{15}H_{26}NO_6S$ 348.1403, found 348.1434.

Ethyl 4-acetamido-2,3,6-tri-*O*-acetyl-1-thio-α-D-tallopyranoside

TLC: 40% EtOAc–PE. ¹H NMR (400 MHz, CHCl₃): $\delta = 1.30$ (t, 3H, J = 7.4 Hz, CH₃(SEt)), 2.00 (s, 3H, CH₃(Ac)), 2.04 (s, 3H, CH₃(Ac)), 2.07 (s, 3H, CH₃(Ac)), 2.20 (s, 3H, CH₃(Ac)), 2.66 (m, 2H, CH₂(SEt)), 4.12 (dd, 1H, J = 11.8 Hz, J = 4.6 Hz, H-6), 4.22 (dd, 1H, J = 11.7 Hz, J = 7.7 Hz, H-6), 4.59 (dd, 1H, J = 10.3 Hz, J = 3.6 Hz, H-4), 4.65 (m, 1H, H-5), 5.17 (t, 1H, J = 3.6 Hz, H-3), 5.21 (m, 1H, J = 3.5 Hz, H-2), 5.31 (s, 1H, H-1), 6.19 (d, 1H, J = 10.1 Hz, NH); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 14.5$ (CH₃(SEt)), 20.5 (CH₃(Ac)), 20.6 (CH₃(Ac)), 21.0 (CH₃(Ac)), 23.2 (CH₃(Ac)), 24.9 (CH₂(SEt)), 46.9 (C-4), 62.8 (C-6), 65.7 (C-2), 68.2 (C-5), 70.6 (C-3), 82.5 (C-1), 168.7 (C=O), 169.3 (C=O), 169.9 (C=O), 170.3 (C=O); MS (*m*/*z*, ESI): 414 (M + Na⁺).

Oxazine 15

Oxazine 15 was obtained from ethyl 2,3-di-O-benzyl-1-thio-β-D-glucopyranoside 13 via the same procedure as described for the conversion of compound 1 into 4. The reaction mixture was purified by flash chromatography (20% EtOAc-PE). Removal of the eluent gave 63 mg (0.12 mmol, 21%) of the title compound 15 as a yellow oil. ¹H NMR (400 MHz, CHCl₃): $\delta = 1.23$ (t, 3H, J = 7.6 Hz, CH₃(SEt)), 2.60–2.70 (m, 2H, J = 7.5 Hz, CH₂(SEt)), 3.55 (t, 1H, J = 9.2 Hz, H-2), 3.75 (dd, 1H, J = 8.9 Hz, J = 4.3 Hz, H-3), 3.83 (br s, 1H, H-5), 3.93 (br s, 1H, H-4), 4.32 (d, 1H, J = 11.7 Hz, H-6), 4.39 (d, 1H, J = 9.4 Hz, H-1), 4.55 (d, 1H, J = 10.2 Hz, H-6), 4.78–4.89 (m, 4H, $2 \times CH_2Ph$), 7.25-7.44 (m, 10H, CH(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 15.0$ (CH₃(SEt)), 22.9 (CH₂(SEt)), 53.3 (C-4), 67.4 (C-5), 67.4 (C-6), 69.4 (CH₂(Bn)), 71.6 (CH₂(Bn)), 76.6 (C-2), 80.3 (C-3), 83.9 (C-1), 127.6–133.0 (Ar), 138.1 (C_q(Bn)), 138.2 (C_a(Bn)), 154.4 (C=N); MS (*m*/*z*, ESI): 532.1 (M + H⁺), 554.1 $(M + Na^{+}).$

Oxazine 16

Oxazine **16** was obtained from ethyl 2-*O*-benzoyl-3-*O*-benzyl-1thio-β-D-glucopyranoside **14** *via* the same procedure as described for the conversion of compound **1** into **4**. The reaction mixture was purified by flash chromatography (20% EtOAc– PE). Removal of the eluent gave 63 mg (0.12 mmol, 64%) of the title compound **16** as a yellow oil. ¹H NMR (400 MHz, CHCl₃): $\delta = 1.19$ (t, 3H, J = 7.5 Hz, CH₃(SEt)), 2.67–2.75 (m, 2H, J = 7.5 Hz, CH₂(SEt)), 3.90–3.93 (dd, 1H, J = 9.4 Hz, $J = 4.2 \text{ Hz}, \text{ H-3}), 3.96 \text{ (d, 1H, } J = 2.1 \text{ Hz}, \text{ H-5}), 4.06 \text{ (br s, 1H, } \\ \text{H-4}), 4.37 \text{ (d, 1H, } J = 11.7 \text{ Hz}, \text{H-6}), 4.52 \text{ (d, 1H, } J_{1,2} = 9.5 \text{ Hz}, \\ \text{H-1}), 4.62 \text{ (dd, 1H, } J = 11.7 \text{ Hz}, J = 1.6 \text{ Hz}, \text{H-6}), 4.70 - 4.80 \text{ (dd, } \\ \text{2H, } J = 12.8 \text{ Hz}, \text{ CH}_2\text{Ph}), 5.40 \text{ (t, 1H, } J = 9.5 \text{ Hz}, J = 9.4 \text{ Hz}, \\ \text{H-3}), 7.18 - 8.03 \text{ (m, 10H, H(Ar))}; \ ^{13}\text{C} \text{ NMR} \text{ (100.8 MHz}, \\ \text{CHCl}_3): \delta = 14.7 \text{ (CH}_3(\text{SEt))}, 22.1 \text{ (CH}_2(\text{SEt))}, 53.1 \text{ (C-4)}, 67.8 \\ \text{(C-5), } 68.7 \text{ (C-2)}, 69.3 \text{ (C-6)}, 70.9 \text{ (CH}_2(\text{Bn})), 77.3 \text{ (C-3)}, 82.5 \\ \text{(C-1), } 127.6 - 133.0 \text{ (Ar)}, 129.9 \text{ (C}_q(\text{Bz})), 137.7 \text{ (C}_q(\text{Bn})), 165.0 \\ \text{(C=N)}; \text{MS} (m/z, \text{ESI}): 544.1 \text{ (M + H^+)}, 568.3 \text{ (M + Na^+)}. \\ \end{array}$

Ethyl 4-acetamido-6-*O*-acetyl-2-*O*-benzoyl-3-*O*-benzyl-4-deoxy-1-thio-β-D-galactopyranoside 17

Compound 17 was prepared from oxazine 16 via the same procedure as described for the conversion of compound 4 into 5. The reaction mixture was purified by flash chromatography (45% EtOAc-PE). Removal of the eluent gave 33 mg (0.066 mmol, 61%) of the title compound 17 as a yellow oil. TLC: 35% EtOAc-PE. $[a]_{D}^{22}$: +14.0 (c = 0.42, CHCl₃). IR (cm⁻¹): 1720, 1647, 1550, 1454, 1369, 1242; ¹H NMR (400 MHz, CHCl₃): $\delta = 1.24$ (t, 3H, J = 7.4 Hz, CH₃(SEt)), 2.07 (s, 3H, CH₃(Ac)), 2.08 (s, 3H, CH₃(Ac)), 2.65–2.71 (m, 2H, J = 7.4 Hz, CH₂(SEt)), 3.74 (dd, 1H, J = 9.7 Hz, J = 4.6 Hz, H-3, $3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, H = 3.74 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, J = 4.6 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 4.6 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 1H, } J = 9.7 \text{ Hz}, J = 3.86 \text{ (dd, 2H, } J = 3.86 \text{ (dd, 3H, } J = 3.86 \text{ (dd, 3H,$ J = 6.3 Hz, J = 1.2 Hz, H-5), 4.21 (d, 2H, J = 6.3 Hz, H-6), 4.46 (d, 1H, J = 12.6 Hz, CHHPh), 4.56 (d, 1H, J = 10.1 Hz, H-1), 4.70 (d, 1H, J = 12.6 Hz, CHHPh), 4.89–4.92 (m, 1H, H-4), 5.22 (t, 1H., J = 9.9 Hz, H-2), 5.96 (d, 1H, J = 10.1 Hz, NH), 7.09-8.01 (m, 10H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): δ = 14.9 (CH₃(SEt)), 20.8 (CH₃(Ac)), 23.3 (CH₃(Ac)), 25.2 (CH₂(SEt)), 46.6 (C-4), 63.0 (C-6), 69.9 (C-2), 70.4 (CH₂(Bn)), 76.0 (C-5), 76.6 (C-3), 84.8 (C-1), 127.6–133.2 (Ar), 129.5 (C_g(Bz)), 137.2 (C_q(Bn)), 170.4 (C=O), 170.7 (C=O) HRMS: (M + H) calcd for C₂₆H₃₂NO₇S 502.1821, found 502.1828.

Oxazine 19

Oxazine 19 was obtained from phenyl 2-azido-3-O-benzyl-2,4dideoxy-1-thio-β-D-glucopyranoside 18 via the same procedure as described for the conversion of compound 1 into 4. The reaction mixture was purified by flash chromatography (30% EtOAc-PE). Removal of the eluent gave 4.16 g (8.2 mmol, 74%) of the title compound 19 as a yellow oil. TLC: 40% EtOAc-PE. $[a]_{D}^{22}$: +46.2 (c = 1, CHCl₃). IR (cm⁻¹): 2110, 1678, 1226, 1172; ¹H NMR (400 MHz, CHCl₃): δ = 3.37 (t, 1H, J = 9.8 Hz, H-2), 3.62 (dd, 1H, J = 9.6 Hz, J = 4.4 Hz, H-3), 3.83 (dd, 1H, J = 3.7 Hz, J = 1.5 Hz, H-5), 3.88 (d, 1H, J = 4.1 Hz, H-4), 4.35 (m, 2H, J = 10.0 Hz, H-1, H-6), 4.62 (dd, 1H, J = 12.16 Hz, H-6), 4.72 (d, 1H, J = 12.1 Hz, CHHPh), 4.80 (d, 1H, J = 12.1 Hz, CHHPh), 7.26–7.55 (m, 10H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 51.8$ (C-4), 60.0 (C-5), 68.0 (C-2), 69.4 (C-6), 71.2 (CH₂(Bn)), 79.1 (C-3), 85.4 (C-1), 127.9-134.2 (Ar), 129.5 (Cq(SPh)), 137.4 (Cq(Bn)), 153.7 (C=N); MS (m/z, ESI): 513.4 (M + H⁺), 535.0 (M + Na⁺).

Phenyl 4-acetamido-6-*O*-acetyl-2-azido-3-*O*-benzyl-2,4-dideoxy-1-thio-β-D-galactopyranoside 20

Compound **20** was prepared from oxazine **19** *via* the same procedure as described for the conversion of compound **4** into **5**. The reaction mixture was purified by flash chromatography (45% EtOAc–PE). Removal of the eluent gave 1.06 g (2.27 mmol, 94%) of the title compound **20** as a yellow oil. TLC: 40% EtOAc–PE. $[a]_D^{22}$: -22.2 (c = 0.24, CHCl₃). IR (cm⁻¹): 2110, 1739, 1654, 1535, 1438, 1365, 1230, 1103, 1037; ¹H NMR (400 MHz, CHCl₃): $\delta = 1.96$ (s, 3H, CH₃(Ac)), 2.06 (s, 3H, CH₃(Ac)), 3.27 (1H, t, J = 10.0 Hz, H-2), 3.53 (dd, 1H, J = 9.7 Hz, J = 4.2 Hz, H-3), 3.74 (dd, 1H, J = 7.0 Hz, J = 5.0 Hz, H-5), 4.09–4.23 (m, 2H, H-6), 4.38 (d, 1H, J = 10.3 Hz, H-1), 4.50 (d, 1H, J = 10.8 Hz, CHHPh), 4.75 (d, 1H, J = 10.1 Hz, NH), 7.30–7.59 (m, 10H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃):

$$\begin{split} &\delta = 20.7 \; (\mathrm{CH_3(Ac)}), \; 23.3 \; (\mathrm{CH_3(Ac)}), \; 45.7 \; (\mathrm{C-4}), \; 61.2 \; (\mathrm{C-2}), \; 62.8 \\ &(\mathrm{C-6}), \; 71.4 \; (\mathrm{CH_2(Bn)}), \; 75.7 \; (\mathrm{C-5}), \; 79.4 \; (\mathrm{C-3}), \; 86.1 \; (\mathrm{C-1}), \; 128.1-133.8 \; (\mathrm{Ar}), \; 130.9 \; (\mathrm{C_q(SPh)}), \; 136.6 \; (\mathrm{C_q(Bn)}), \; 170.3 \; (\mathrm{C=O}); \\ &\mathrm{HRMS:} \; (\mathrm{M} \; + \; \mathrm{H}) \; \mathrm{calcd} \; \; \mathrm{for} \; \; \mathrm{C_{23}H_{27}N_4O_5S} \; 471.1624, \; \mathrm{found} \; 471.1745. \end{split}$$

Phenyl 4-(*N*-benzyloxycarbonyl)-amino-2-azido-3-*O*-benzyl-2,4dideoxy-1-thio-β-D-galactopyranoside 21

Oxazine 19 (0.81 g, 1.58 mmol) was stirred in 5 mL 80% AcOH in H₂O at ambient temperature. After 15 min, the clear solution was diluted with toluene, concentrated and co-evaporated several times with toluene. The crude oil was dissolved in 5 mL DCM followed by addition of NEt₃ (0.26 mL; 2.0 mmol, 1.25 eq.) and ZOSu (0.40 g; 1.6 mmol, 1.01 eq.). The reaction mixture was stirred for 8 h at room temperature before EtOAc was added. The mixture was washed with 50 mL 1M HCl. The water-layer was extracted twice with 50 mL EtOAc. The combined organic layers were dried (MgSO₄), filtered and concentrated in vacuo. Flash chromatography (50% EtOAc-PE) and removal of the eluent afforded 844 mg (1.50 mmol, 95%) of the title compound 21 as a colourless oil. TLC: 50% EtOAc-PE. $[a]_{D}^{22}$: -6.2 (c = 1, CHCl₃). IR (cm⁻¹): 2110, 1705, 1512, 1257, 1215, 1056. ¹H NMR (200 MHz, CHCl₃): δ = 3.01 (br s, 1H, OH), 3.24 (t, 1H, J = 9.9 Hz, H-2), 3.57 (m, 3H, H-3, H-6), 3.72 (m, 1H, H-5), 4.36 (m, 2H, J = 10.2 Hz, H-1, H-4), 4.50 (d, 1H J = 10.9 Hz, CHHPh), 4.68 (d, 1H, J = 11.3 Hz, CHHPh), 4.83 (d, 1H, J = 7.8 Hz, NH), 5.12 (s, 2H, CH₂(Z)); ¹³C NMR (50.4 MHz, CHCl₃): $\delta = 47.5$ (C-4), 60.5 (C-6), 61.1 (C-2), 67.0 (CH₂(Z)), 70.8 (CH₂(Bn)), 77.9 (C-5), 78.8 (C-3), 86.1 (C-1), 127.6–132.6 (Ar), 131.3 ($C_{q}(SPh)$), 135.8 ($C_{q}(Z)$), 136.6 $(C_{a}(Bn))$, 157.3 (C=O); HRMS: (M + H) calcd for $C_{27}H_{29}$ -N₄O₅S 521.1780, found 521.1829.

Phenyl 6-O-acetyl-4-(N-benzyloxycarbonyl)-amino-2-azido-3-Obenzyl-2,4-dideoxy-1-thio-β-D-galactopyranoside 22

Compound 21 (593 mg, 1.14 mmol) was dissolved in 5 mL pyridine followed by the addition of 2.5 mL Ac₂O. The reaction mixture was stirred for 2 h at room temperature. The mixture was concentrated and co-evaporated several times with toluene. After flash chromatography (30% EtOAc-PE) and removal of the eluent, 606 mg of the title compound 22 (1.14 mmol, quant.) was obtained as a colourless oil. TLC: 50% EtOAc-PE. $[a]_{D}^{22}$: -13.4 (c = 1, CHCl₃). IR (cm⁻¹): 2110, 1716, 1510, 1454, 1365, 1226, 1103, 1037; ¹H NMR (200 MHz, CHCl₃): $\delta = 2.04$ (s, 3H, CH₃(Ac)), 3.27 (t, 1H, J = 10.2 Hz, J = 9.7 Hz, H-2), 3.51 (dd, 1H, J = 9.9 Hz, J = 4.3 Hz, H-3), 3.71 (t, 1H, J = 5.8 Hz, H-5), 4.20 (m, 2H, J = 5.1 Hz, H-6), 4.34 (d, 1H, J = 10.2 Hz, CHHPh), 4.42 (m, 1H, H-4), 4.52 (d, 1H, J = 11.0 Hz, CHHPh), 4.83 (d, 2H, J = 10.6 Hz, H-1, NH), 5.08 (s, 2H, CH₂(Z)), 7.25-7.54 (m, 10H, H(Ar)); ¹³C NMR (50.4 MHz, CHCl₃): δ = 20.7 (Ac), 48.0 (C-4), 61.2 (C-2), 62.9 *C-6), 67.2 (CH₂(Z)), 71.4 (CH₂(Bn)), 75.6 (C-5), 79.6 (C-3), 86.3 (C-1), 127.9–133.4 (Ar), 131.1 ($C_q(SPh)$), 136.0 ($C_q(Z)$), 136.7 $(C_{a}(Bn))$, 156.2 (C=O(Z)), 170.5 (C=O(Ac)); MS (m/z, ESI): $563.3 (M + H^+), 585 (M + Na^+).$

Phenyl 4-(N-benzyloxycarbonyl)-amino-2-azido-3-O-benzyl-6-(2,3,4,6-tetra-O-benzyl- α/β -D-galactopyranosyl)-2-deoxy-1-thio- β -D-galactopyranoside 24

A solution of 2,3,4,6-tetra-*O*-benzyl- α/β -D-galactopyranose **23** (54 mg; 0.1 mmol), diphenylsulfoxide (40 mg; 0.2 mmol, 2 eq.) and tri-*tert*-butylpyrimidine (74 mg; 0.3 mmol, 3 eq.) in 4 ml DCM was stirred over 100 mg 4 Å activated molecular sieves for 30 min. The mixture was cooled to -78 °C before triflic acid anhydride (26 μ L; 0.15 mmol, 1.5 eq.) was added. The mixture was allowed to warm to -40 °C in 1 h followed by addition of phenyl 4-(*N*-benzyloxycarbonyl)-amino-2-azido-3-*O*-benzyl-2-deoxy-1-thio- α -D-galactopyranoside **21** (52 mg; 0.1 mmol,

1 eq.) in 1 ml DCM. Stirring was continued and the reaction mixture was allowed to warm to 0 °C. Subsequently the reaction was quenched by addition of triethylamine (0.16 mL; 2 mmol, 20 eq.). Flash chromatography (20% EtOAc-PE) and removal of the eluent afforded 66 mg of the title compound 24 (65 µmol, 65%) as a yellow oil. TLC: 50% EtOAc–PE. $[a]_{D}^{22}$: +13.2 (c = 1, CHCl₃). IR (cm⁻¹): 2110, 1716, 1496, 1454, 1215, 1096, 1030 ¹H NMR (400 MHz, CHCl₃): $\delta = 3.18$ (t, 1H, J = 10.0 Hz, H-2'), 3.45 (m, 2H, J = 6.7 Hz, J = 9.7 Hz, H-3, H-6), 3.53 (dd, 1H, J = 9.3 Hz, J = 6.4 Hz, H-6), 3.59 (q, 1H, J = 5.9 Hz, H-6'), 3.75 (m, 2H, H-5', H-6'), 3.83 (dd, 1H, J = 10.0 Hz, J = 2.7 Hz, H-3),3.89 (s, 1H, H-4), 3.95 (t, 1H, J = 6.3 Hz, H-5), 4.02 (dd, 1H, J = 10.1 Hz, J = 3.6 Hz, H-2), 4.32 (d, 1H, J = 10.0 Hz, H-1'), 4.38 (s, 1H, H-4'), 4.40 (m 2H, CH₂Ph)), 4.56 (d, 1H, J = 11.4 Hz, CHHPh), 4.69 (t, 2H, J = 13.0 Hz, CH₂Ph), 4.80 (m, 3H, CHHPh, CH₂Ph), 4.81 (d, 1H, J = 3.2 Hz, H-1'), 4.92 (d, 1H, J = 11.4 Hz, CHHPh), 5.06 (dd, 2H, J = 12.2 Hz, CH₂(Z)), 7.20-7.37 (m, 35H, H(Ar)); ¹³C NMR (100.8 MHz, CHCl₃): $\delta = 48.5$ (C-4'), 61.2 (C-3'), 67.0 (CH₂(Z)), 67.6 (C-6'), 69.1 (C-6), 69.4 (C-5'), 71.3 (CH₂(Bn)), 73.1 (CH₂(Bn)), 73.4 (CH₂-(Bn)), 73.5 (CH₂(Bn)), 74.7 (CH₂(Bn)), 74.9 (C-4), 76.5 (C-2), 76.7 (C-5), 78.9 (C-3), 79.8 (C-2'), 86.2 (C-1'), 98.2 (C-1), 124.7-133.2 (Ar), 131.5 (C_a(SPh)), 136.1-138.7 (C_a(Bn)), 156.3 (C=O); HRMS: (M + H) calcd for $C_{61}H_{63}N_4O_{10}S$ 1043.4259, found 1043, 4280.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(6-*O*-acetyl-4-(*N*-benzyloxycarbonyl)-amino-2-azido-3-*O*-benzyl-2,4-dideoxy-α/β-Dgalactopyranosyl)-α-D-glucopyranoside 26

A solution of phenyl 6-O-acetyl-4-(N-benzyloxycarbonyl)amino-2-azido-3-O-benzyl-2,4-dideoxy-1-thio-B-D-galactopyranoside 22 (53 mg; 0.1 mmol) and diphenylsulfoxide (25 mg; 0.12 mmol, 1.2 eq.) in 3 ml DCM was stirred over 100 mg activated 4 Å molecular sieves for 30 min. The mixture was cooled to -78 °C before triflic acid anhydride (22 µL; 0.13 mmol, 1.3 eq.) was added. The mixture was stirred for 5 min followed by addition of methyl 2,3,4-tri-O-benzoyl-α-D-glucopyranoside 25 (75 mg; 0.1 mmol, 1 eq.) in 1 ml DCM. The mixture was allowed to warm to 0 °C. Subsequently the reaction was quenched by addition of triethylamine (0.16 mL; 2 mmol, 20 eq.). Flash chromatography (30% EtOAc-PE) and removal of the eluent afforded 92 mg of the title compound 26 (95 µmol, 95%) as a colourless oil. TLC: 50% EtOAc-PE. IR (cm⁻¹): 2110, 1724, 1519, 1450, 1245, 1091, 1026; ¹H NMR (400 MHz, CHCl₃): $\delta = 4.27$ (d, 0.5H, J = 8.0 Hz, H-1'(β -anomer)), 4.90 (d, 0.5H, J = 3.4 Hz, H-1'(α -anomer)), 4.27 (d, 1H, J = 3.5 Hz, H-1); ¹³C NMR (100,8 MHz, CHCl₃): δ = 96.8 (C-1), 97.9 (C-1'(α -anomer)), 102.5 (C-1'(β -anomer)); HRMS: (M + H) calcd for C51H51N4O15 959.3345, found 959.3394.

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