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Syntheses of *p*-nitrophenyl 3- and 4-thio-β-D-glycopyranosides

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ABSTRACT

Thioglycosides have proved to be useful, enzymatically stable analogs of glycosides for structural and mechanistic studies and their synthesis is considerably simplified through the use of thioglycoligases. As part of an investigation into the use of thioglycosides as potential pharmacological chaperones, and as components of glycoproteins and glycolipids, the syntheses of *p*-nitrophenyl 3-thio-β-D-galactopyranoside, phenyl 1,4-dithio-β-D-glucopyranoside, *p*-nitrophenyl 4-thio-β-D-mannopyranoside and *p*-nitrophenyl 2-acetamido-2-deoxy-4-thio-β-D-mannopyranoside are described.

1. Introduction

Thio-oligosaccharides have proved to be very useful tools for probing carbohydrate–protein interactions within enzyme systems and have potential as therapeutics.[1,2] Generally these sulfur-containing analogs are more metabolically stable than their natural oligosaccharide counterparts due to lower rates of both acid-catalyzed and enzymatic hydrolysis.[3,4] The stability of these molecules makes them good candidates as glycosidase inhibitors and as such, thioglycosides have been used in X-ray crystallographic studies to image stable protein–carbohydrate complexes and thereby obtain valuable structural and mechanistic insights.[5,6] The replacement of natural glycosides on protein surfaces by thioglycosides would thus lead to more stable antigens for glycoconjugate vaccines and more metabolically stable therapeutic glycoproteins, with consequent therapeutic advantages.[7,8] The synthesis of thioglycosides, and their subsequent incorporation onto a protein surface, would typically require the synthesis of an appropriate thio-sugar acceptor, which is then coupled with the appropriate glycosyl donor, though it could also be carried out in a non-conventional way using 1-thiosugars as building blocks. One approach might be to first synthesize the thioglycoside-containing disaccharide conventionally, and then attach the disaccharide to the protein, but unfortunately very few suitable endo-enzymes are available for such tasks. Consequently the thiosugar acceptor must first be coupled to the protein and then the donor sugar coupled to it, with formation of the thioglycosidic linkage. While this coupling could be accomplished by chemical methods, the conditions required are generally not compatible with protein surfaces. As a result, enzymatic methods for coupling are being explored with increasing interest. Wild-type glycosyl transferases, glycosidases and mutant glycosynthases have not proved suitable for this task, but the emerging use of thioglycoligases, mutant glycosidases in which the acid/base catalyst has been replaced, has shown promise.[9–15,37] Such a strategy still requires the chemical synthesis of the thio-sugar acceptors for these enzymatic couplings. Further, in order to optimize their binding to the enzyme and to facilitate monitoring of the enzymatic coupling, they should be synthesized as thioglycosides. While a number of excellent studies have been published on the synthesis of thiosugars, these have most commonly been performed in the context of methyl glycosides. As part of a program to explore thio-disaccharides as β-galactosidase inhibitors that may function as pharmacological chaperones, we required suitable 3-thiogalactopyrano-, 4-thioglucopyrano-, 2-acetamido-2-deoxy-4-thio-mannopyrano- and 4-thio-mannopyrano- acceptor sugars. While appearing to be simple targets, these proved to be more challenging than anticipated, in part due to the need for the aryl phenyl 1,4-thio-β-D-glucopyranoside, *p*-nitrophenyl 4-thio-β-D-mannopyranoside and *p*-nitrophenyl 2-acetamido-2-deoxy-4-thio-β-D-mannopyranoside as acceptors for such coupling reactions.

2. Results and discussion

2.1. Synthesis of *p*-nitrophenyl 3-thio-β-D-galactopyranoside (12)

Previous reports demonstrated that 3-thio-β-D-galactopyranose derivatives could be synthesized from galactose by a double inversion of stereochemistry at C-3 through initial conversion of

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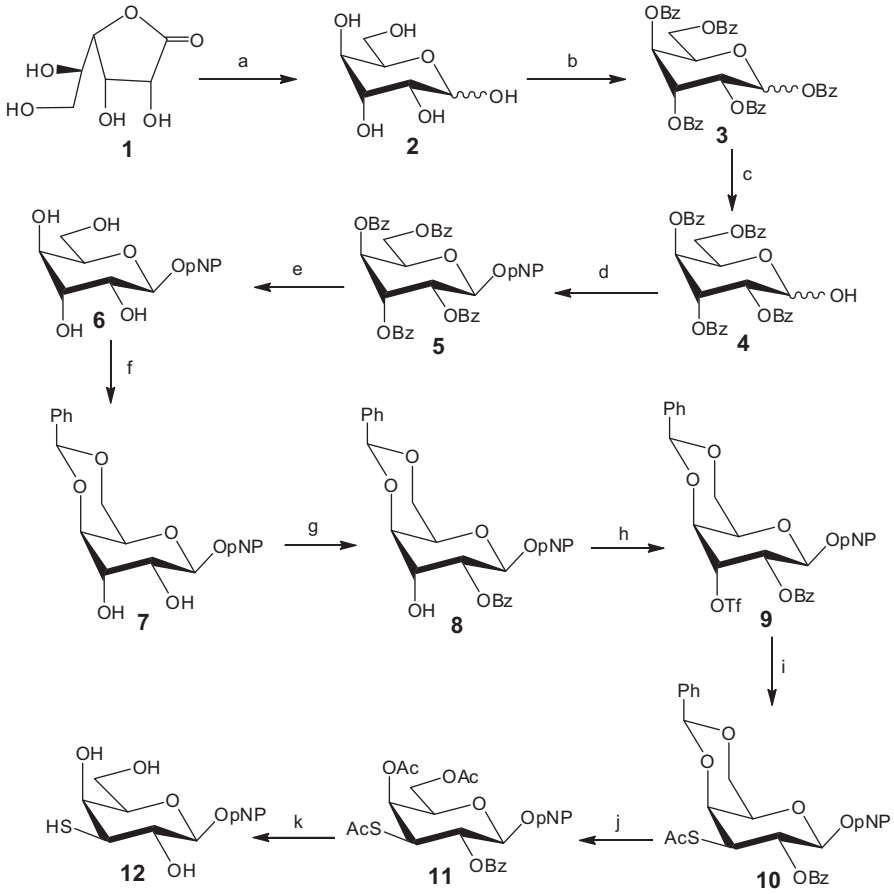
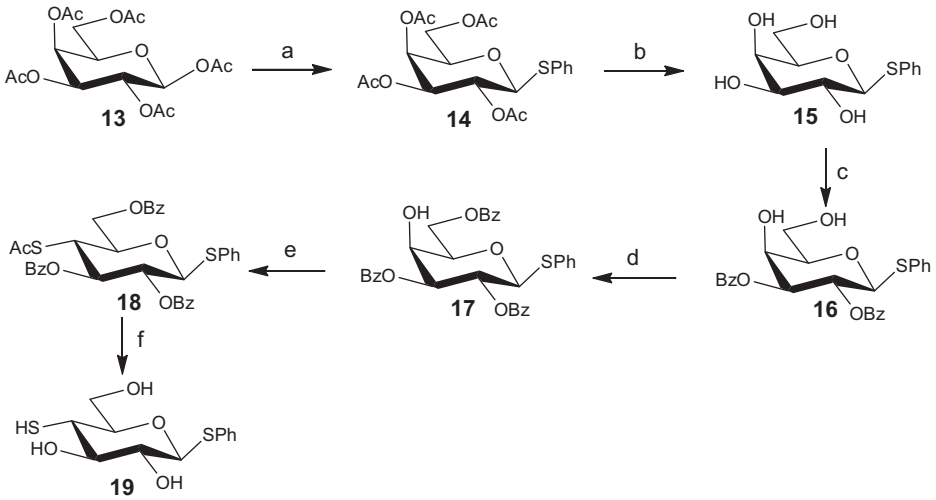
a 3-trifluoromethane sulfonyl galactopyranose derivative to its corresponding gulopyranose derivative. This is then converted to its 3-*O*-trifluoromethane sulfonyl derivative which then is subjected to thiolate displacement, generating the protected 3-thiogalactopyranose.[16,17] Our application required a *p*-nitrophenyl group to be installed at the anomeric center to improve enzyme binding, and allow easy detection during enzymatic reactions. While existing routes could have been followed, a more convenient route starting from D-gulose was developed. D-Gulose (**2**) was synthesized as reported in the literature[18] and per-benzoylated to yield **3** (Scheme 1). Conversion to the hemiacetal **4** was accomplished by treatment with HBr in acetic acid at 0 °C, followed by treatment with Ag_2CO_3 in acetone and water. Using the standard trichloroacetimidate method,[19] *p*-nitrophenol was introduced at the anomeric position, followed by removal of benzoyl groups to yield the unprotected glycopyranoside **6**.[20] In order to selectively protect hydroxyls at C4 and C6, compound **6** was reacted with benzaldehyde dimethyl acetal in DMF to give **7**, leaving 2-OH and 3-OH unprotected.[21] By taking advantage of the higher reactivity of the hydroxyl at the 2-position over that at the 3-position, selective benzoylation of **7** was accomplished with 1 equiv of benzoyl chloride to yield **8** with a free hydroxyl at the 3-position. This was converted to the very stable triflate intermediate **9** by treatment with trifluoromethanesulfonic anhydride. The mixture of products obtained in the subsequent nucleophilic displacement was highly dependent on the temperature of the reaction mixture. At room temperature, **9** reacted with potassium thioacetate very slowly to produce the desired product **10**. However, if the temperature was raised above 80 °C, the anomeric *p*-nitrophenyl group was replaced by thioacetate. The best temperature for the desired thioacetate incorporation was found to be 50 °C, though under these conditions about 5% of the anomeric thioacetate still formed during the reaction. The benzylidene group was then removed and the resulting intermediate acetylated and purified to yield **11**. Deprotection of **11** was performed under standard Zemplen conditions and after neutralization, treatment with aqueous dithiothreitol (DTT) reduced any disulfide bonds to afford the target molecule, *p*-nitrophenyl 3-thio-β-D-galactopyranoside **12**.

2.2. Synthesis of phenyl-1,4-dithio-β-D-glucopyranoside (19)

Access to the 4-thioglucopyrano- series is considerably simpler, since the precursor with inverted stereochemistry at C-4 is readily available.[16] In order to avoid any unwanted side reactions involving acetyl group participations in the activation or displacement steps, benzoyl groups, which are known to be less prone to participation, were used as protecting groups (Scheme 2). Phenyl 1-thio-β-galactopyranoside **15** was prepared from penta-*O*-acetyl galactopyranose via standard acid-catalyzed condensation followed by Zemplen deprotection.[22] Treatment of **15** with anisaldehyde dimethyl acetal in DMF at 50 °C yielded the 4,6-benzylidene derivative,[21] which was benzoylated at its 2- and 3 hydroxyls with benzoyl chloride, then its benzylidene was removed by treatment with acid to yield **16** in 76% overall yield. Selective protection of



Scheme 1. Reagents and conditions: (a) H_2O, IR-120 (H^+), $NaBH_4$, 0 °C; (b) BzCl, pyridine, 91%; (c) CH_2Cl_2, HBr/HOAc, 0 °C; acetone, H_2O, Ag_2CO_3, 90%; (d) CH_2Cl_2, TCA, DBU, −30 °C; CH_2Cl_2, $BF_3{\cdot}Et_2O$, 4-nitrophenol, molecular sieves, −30 °C; 58%; (e) CH_3OH, $NaOCH_3$, 95%; (f) DMF, CSA, benzaldehyde dimethyl acetal, 50 °C, 91%; (g) CH_2Cl_2, pyridine, BzCl, 0 °C, 79%; (h) CH_2Cl_2, pyridine, Tf_2O, 0 °C; (i) DMF, KSAc, 50 °C, 68% (two steps); (j) HOAc/H_2O = 1:1, 80 °C; Ac_2O, pyridine; 88% (two steps); (k) CH_3OH, $NaOCH_3$; DTT, H_2O, 95%.



Scheme 2. Reagents and conditions: (a) CH_2Cl_2, thiophenol, $BF_3{\cdot}Et_2O$, 0 °C, 50%; (b) CH_3OH, $NaOCH_3$, rt, 98%; (c) DMF, anisaldehyde dimethyl acetal, CSA, 50 °C; pyridine, BzCl, 0 °C to rt; AcOH, H_2O, 60 °C, 76%; (d) CH_2Cl_2, pyridine, benzoyl cyanide, rt, 86%; (e) CH_2Cl_2, pyridine, Tf_2O, 0 °C; DMPU, KSAc, rt, 70%; (f) CH_3OH, $NaOCH_3$, rt; DTT, H_2O, rt; 78%.

the primary alcohol was achieved by reaction with benzoyl cyanide at room temperature yielding **17** which was converted to its triflate by reaction with trifluoromethanesulfonic anhydride, thereby activating C-4 for nucleophilic displacement.[23] Reaction with potassium thioacetate at room temperature readily yielded **18**. Final deprotection performed under standard Zemplen conditions and treatment with DTT afforded the target molecule, phenyl-1,4-dithio-β-D-glucopyranoside **19**.

2.3. Synthesis of *p*-nitrophenyl 4-thio-β-D-mannopyranoside (27) and *p*-nitrophenyl 2-acetamido-2-deoxy-4-thio-β-D-mannopyranoside (30)

The chemical synthesis of β-mannopyranosidic linkages can be challenging due to the α-directing anomeric effects, repulsion between the C-2 axial substituent and the approaching nucleophile, and the tendency for 2-acyl neighboring group participation. While a number of solutions to this problem have been devised, an attractive route was that developed by Ramstrom involving double serial displacement of triflate leaving groups that had been installed into a partially protected sugar that was itself prepared by use of a stannylene complex. The 2,4-di-*O*-triflate formed can be subjected to regiospecific serial displacements at C-4 (with thioacetate) and then C-2 (with acetate or azide) to generate the Manno- and ManNAc derivatives.[24–26]

As Scheme 3 shows, *p*-nitrophenyl β-D-galactopyranoside (**20**) was treated with dibutyltin oxide to form a stannylene complex[27–29] across C-2/C-3 and C-4/C-6, and then reacted with benzoyl chloride to give *p*-nitrophenyl 3,6-di-*O*-benzoyl-β-D-galactopyranoside **21**.[24,30] Similar yields (60%) were obtained when the reaction was performed in methanol or toluene. While higher yields in the subsequent protection step (80%) could be obtained using acetic anhydride, unfortunately use of acetyl protecting groups resulted in lower yields (67% yield for the 4-*O*-triflate displaced with potassium thioacetate) in the double serial displacement. Reaction of **21** with trifluoromethanesufonic anhydride gave the di-*O*-triflate intermediate **22**, from which the 4-*O*-and 2-*O*-triflates can be serially displaced with nucleophiles such as potassium thioacetate or sodium acetate, based on well known relative reactivities towards displacement. Consistent with this reactivity pattern, the 2-*O*-mono-triflate intermediates **23** and **32** are stable, and can be purified by flash column chromatography.

The thioacetate intermediate **23** is very labile under the mild basic conditions encountered during the next step, liberating a free thiolate anion which underwent a number of side reactions, including attack on solvent dichloromethane yielding the chloromethyl derivative **31** (Scheme 4).[31] Consequently the acetyl group on the thiol was removed[32] and the thiol reprotected with an ethylthio group[33] to form disulfide **24**, which was very stable under most conditions. The disulfide 2-*O*-triflate **24** was individually reacted with tetrabutylammonium acetate (TBAOAc) and tetrabutylammonium azide ($TBAN_3$) in dry acetonitrile to give β-D-mannopyranosides **25a** and **25b** in good yields. The benzoyl and acetyl groups in compound **25a** were readily removed under Zemplen conditions and finally the disulfide was reduced with DTT to give the target compound *p*-nitrophenyl 4-thio-β-D-mannopyranoside **27**.

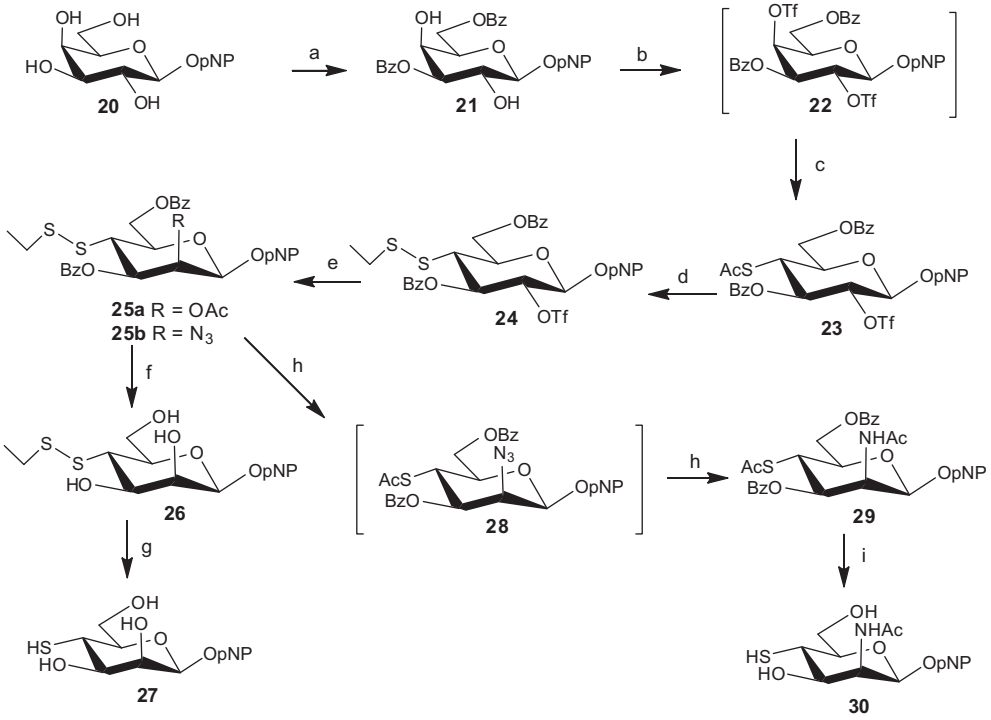
Reaction of **25b** with thioacetic acid in chloroform resulted in two sequential reactions: the disulfide was first quickly converted to the thioacetate, and then the azide was reduced and acylated.[34] If the reaction was terminated after stirring for 0.5 h, intermediate **28** could be isolated in about 90% yield. After stirring for 1 week, the ManNAc derivative **29** was obtained in 81% yield. Subsequent deprotection and reduction of **29** afforded 2-acetamido-2-deoxy-4-thio-β-D-mannopyranoside **30**.

This double serial displacement method can also be applied to the synthesis of *p*-nitrophenyl 2-acetamido-2-deoxy-β-D-mannopyranoside[35,36] (Scheme 5). Reaction of the di-*O*-triflate **22** with sodium acetate resulted in conversion to gluco-configured monotriflate **32**. Use of TBAOAc as a nucleophile in this reaction resulted in lower yields. Displacement of the second triflate with $TBAN_3$ gave **33** in good yields (91%). Reduction of the azido to the amine with triphenylphosphine,[35] followed by acetylation with acetyl chloride yielded **34**, which was deprotected under Zemplen conditions to give the desired product. This sequence is shorter and the overall yield is higher than the existing approaches.

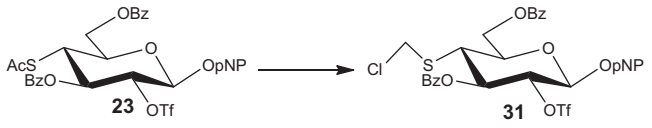
3. Experimental

3.1. General methods

All chemicals were obtained from Sigma–Aldrich Chemical Co. unless otherwise noted. Methylene chloride and pyridine were dried over CaH_2 and distilled prior to use. DMF was dried over 4 Å molecular sieves. MeOH was dried over magnesium and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on aluminum-backed sheets of Silica Gel $60F_{254}$



Scheme 3. Reagents and conditions: (a) CH_3OH, Bu_2SnO, refluxed; toluene, BzCl, 0 °C to rt, 61%; (b) CH_2Cl_2, pyridine, Tf_2O, −20 to 10 °C; (c) CH_3CN, KSAc, rt, 81%; (d) DMF, hydrazine acetate, rt; CH_2Cl_2, diethyl-*N*-(ethylsulfanyl) hydrazodicarboxylate, Et_3N, rt, 89%; (e) CH_3CN, TBAOAc, 40 °C, 82% (**25a**); CH_3CN, $TBAN_3$, 40 °C, 84% (**25b**); (f) CH_3OH, $NaOCH_3$, 86%; (g) CH_3OH/H_2O, DTT, rt, 90%; (h) $CHCl_3$, 2,6-lutidine, AcSH, 81%; (i) CH_3OH, $NaOCH_3$, rt; CH_3OH/H_2O, DTT, rt, 85%.



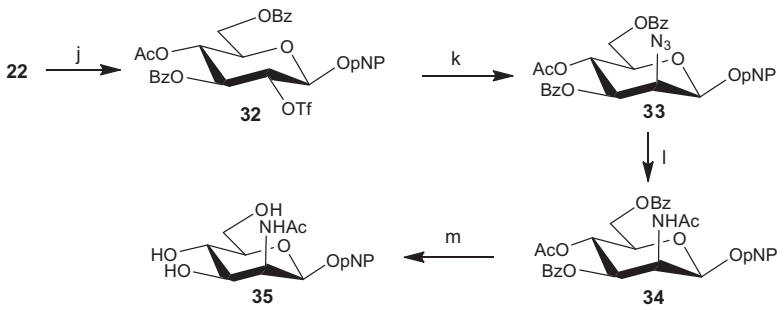
Scheme 4. Reagents and conditions: CH_2Cl_2, TASF (tris(dimethylamino)sulfur trimethylsilyl difluoride), 40 °C, 82%.

(Merck) of thickness 0.2 mm. The plates were visualized using UV light (254 nm) and/or by exposure to 10% ammonium molybdate in 2 M H_2SO_4 followed by charring. Flash column chromatography was performed using Silicycle Silica Gel 60. The NMR spectra were either recorded on a Bruker AV-400 (400 MHz) or a Bruker AV-300 (300 MHz) spectrometer. The optical rotations were recorded on a JASCO P-1010 polarimeter. Elemental analysis was carried out at the University of British Columbia microanalytical laboratory. Mass spectra were recorded by using a PE-Sciex API 300 triple quadrupole mass spectrometer equipped with an electrospray ionization (ESI) ion source.

3.2. Synthesis of *p*-nitrophenyl 3-thio-β-D-galactopyranoside (12)

3.2.1. 1,2,3,4,6-Penta-*O*-benzoyl-D-gulopyranose (3)

Benzoyl chloride (8.5 mL, 73.29 mmol, 11.0 equiv) was added in one portion at 0 °C to a mixture of D-gulopyranose (**2**, 1.2 g, 6.67 mmol) and pyridine (15 mL). The mixture was stirred overnight at 0 °C, then gradually warmed to room temperature. The reaction was quenched with MeOH (10 mL) at 0 °C, and the solvents were evaporated in vacuo to yield a residue. This residue was then dissolved in CH_2Cl_2 (100 mL), washed with 1 M HCl (50 mL), satd $NaHCO_3$ (50 mL) and brine (50 mL), and dried over $MgSO_4$. The crude product was purified by flash column chromatography (5:1 petroleum ether–EtOAc) to give **3** (4.67 g, 91%) as a white foam. ^1H NMR (β-anomer, 300 MHz, $CDCl_3$): δ 8.20–7.83 (m, 10H, Ar-H), 7.70–7.30 (m, 15H, Ar-H), 6.66 (d, 1H, $J_{1,2}$ 8.3 Hz, H-1), 6.09 (t, 1H, $J_{3,4}$ 3.9 Hz, H-3), 5.89 (dd, 1H, $J_{2,3}$ 3.4 Hz, H-2), 5.69 (dd, 1H, $J_{4,5}$ 1.7 Hz, H-4), 4.90 (m, 1H, H-5), 4.66 (dd, 1H, $J_{5,6a}$ 6.9 Hz, $J_{6a,6b}$ 11.6 Hz, H-6a), 4.55 (dd, 1H, $J_{5,6b}$ 6.0 Hz, H-6b). ESI-MS: calcd for $[C_{41}H_{32}O_{11}+Na]^+$: 723.2. Found: 723.5.



Scheme 5. Reagents and conditions: (j) toluene, 18-crown-6, NaOAc, rt, 64%; (k) CH_3CN, $TBAN_3$, 40 °C, 92%; (l) CH_2Cl_2, Ph_3P, H_2O; CH_2Cl_2, pyridine, AcCl, 0 °C; 76%; (m) CH_3OH, $NaOCH_3$, rt, 92%.

3.2.2. 2,3,4,6-Tetra-*O*-benzoyl-D-gulopyranose (4)

HBr/AcOH (2 mL, 33% w/w) was added dropwise to a solution of **3** (1.03 g, 1.47 mmol) in CH_2Cl_2 (10 mL) at 0 °C and the mixture was stirred for 0.5 h, then warmed to room temperature and stirred for 2 h. The yellow solution was diluted with CH_2Cl_2 (150 mL), washed with cold satd $NaHCO_3$ (100 mL) and brine (100 mL). The solvent was evaporated in vacuo to yield a residue that was then dissolved in acetone (20 mL) and water (4 mL) followed by treatment with Ag_2CO_3 (0.75 g). The suspension was stirred overnight at room temperature, filtered and concentrated in vacuo. The resulting residue was purified by flash column chromatography (4:1 petroleum ether–EtOAc) to give **4** (0.79 g, 90%) as a white foam. ESI-MS: calcd for $[C_{34}H_{28}O_{10}+Na]^+$: 619.2. Found: 619.3.

3.2.3. *p*-Nitrophenyl 2,3,4,6-tetra-*O*-benzoyl-β-D-gulopyranoside (5)

Under a stream of argon, TCA (trichloroacetonitrile, 0.9 mL, 8.98 mmol, 9.1 equiv) and DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene, 15 μL) were added to a solution of **4** (0.59 g, 0.99 mmol) in anhydrous CH_2Cl_2 (10 mL) and the reaction mixture was stirred for 1.5 h at −30 °C. The solvents were evaporated in vacuo to yield a pale yellow foam. A mixture of the foam, anhydrous CH_2Cl_2 (15 mL), *p*-nitrophenol (0.5 g, 3.60 mmol, 3.6 equiv) and 4 Å molecular sieves (1 g) was stirred for 20 min at room temperature under argon. The suspension was then cooled down to −30 °C, $BF_3{\cdot}Et_2O$ (50 μL) was added dropwise and the reaction mixture was stirred for 3 h under the same conditions, followed by quenching with Et_3N (1 mL). The reaction mixture was diluted with CH_2Cl_2 (100 mL), filtered through a short pad of Celite and washed with CH_2Cl_2 (50 mL). The filtrate was then washed with satd $NaHCO_3$ (100 mL) and brine (100 mL), and dried over $MgSO_4$. The crude material was purified by flash column chromatography (5:1 and 4:1 petroleum ether–EtOAc) to give **5** (410 mg, 58%) as a white solid. $[\alpha]_D^{22}$ +43.8 (*c* 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 8.18–7.91 (m, 10H, Ar-H), 7.60–7.38 (m, 12H, Ar-H), 7.15 (m, 2H, Ar-H), 6.10 (dd, 1H, $J_{3,4}$ 4.7 Hz, H-3), 5.89 (dd, 1H, $J_{2,3}$ 3.4 Hz, H-2), 5.82 (d, 1H, $J_{1,2}$ 7.3 Hz, H-1), 5.73 (dd, 1H, $J_{4,5}$ 2.1 Hz, H-4), 4.89 (m, 1H, H-5), 4.64 (m, 2H, H-6a and H-6b). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.1, 165.3, 165.2, 164.9, 161.4, 143.2, 134.2, 134.1, 133.8, 130.3, 130.1, 130.0, 129.8, 128.9, 128.7, 125.9, 116.9, 97.0, 72.3, 68.9, 68.4, 68.3, 62.9. ESI-HRMS: calcd for $[C_{40}H_{31}NO_{12}+Na]^+$: 740.1744. Found *m*/*z*: 740.1749. Anal. Calcd for $C_{40}H_{31}NO_{12}$: C, 66.94; H, 4.35; N, 1.95. Found: C, 67.05; H, 4.37; N, 1.98.

3.2.4. *p*-Nitrophenyl β-D-gulopyranoside (6)

Sodium methoxide solution (0.2 mL, 5.4 M, 1.08 mmol) was added to a solution of **5** (1.0 g, 1.39 mmol) in dry MeOH (50 mL) and the reaction mixture was stirred overnight at room temperature. The reaction mixture was then neutralized with Amberlite IR-120 (H^+) ion exchange resin, filtered, washed with MeOH and concentrated in vacuo. The residue was purified by flash column chromatography (5:1 CH_2Cl_2–CH_3OH) to give **6** (400 mg, 95%) as a white powder. ^1H NMR (300 MHz, Me_2SO-d_6): δ 8.23 (m, 2H, Ar-H), 7.23 (m, 2H, Ar-H), 5.27 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 5.16 (d, 1H, *J* 4.8 Hz, OH), 5.11 (d, 1H, *J* 6.7 Hz, OH), 4.94 (d, 1H, *J* 5.4 Hz, OH), 4.65 (t, 1H, *J* 5.6 Hz, OH), 3.96 (t, 1H, H-4), 3.85 (dd, 1H, $J_{3,4}$ 6.5 Hz, H-3), 3.77 (ddd, 1H, $J_{2,3}$ 3.2 Hz, H-2), 3.62 (br t, 1H, H-5), 3.51 (m, 2H, H-6a and H-6b). ^{13}C NMR (75 MHz, Me_2SO-d_6): δ 162.7, 141.6, 125.8, 116.5, 96.7, 74.2, 71.7, 68.9, 67.3, 60.2. ESI-HRMS: calcd for $[C_{12}H_{15}NO_8+Na]^+$: 324.0695. Found *m*/*z*: 324.0684. Anal. Calcd for $C_{12}H_{15}NO_8$: C, 47.84; H, 5.02; N, 4.65. Found: C, 47.91; H, 5.33; N, 4.47.

3.2.5. *p*-Nitrophenyl 4,6-*O*-benzylidene-β-D-gulopyranoside (7)

A mixture of **6** (1.31 g, 4.35 mmol), anhydrous DMF (20 mL), benzaldehyde dimethyl acetal (0.75 mL, 5.00 mmol, 1.1 equiv) and CSA (10-camphorsulfonic acid, 60 mg) was placed in a 100 mL round bottomed flask. This was attached to a Büchi evaporator, rotated, evacuated and lowered into a water bath at 50 °C. The suspension was rotated for 3 h under vacuum until a clear solution formed, which was checked by TLC for reaction completion. The reaction mixture was neutralized with Amberlite IR 45 (OH^-) ion exchange resin, filtered and evaporated in vacuo resulting in a residue which was purified by flash column chromatography (20:1 CH_2Cl_2–acetone) to give **7** (1.54 g, 91%) as a white solid. $[\alpha]_D^{22}$ −71.4 (*c* 2.6, Me_2CO). ^1H NMR (300 MHz, Me_2CO-d_6): δ 8.21 (m, 2H, Ar-H), 7.50 (m, 2H, Ar-H), 7.38 (m, 3H, Ar-H), 7.30 (m, 2H, Ar-H), 5.67 (s, 1H, C*H*Ph), 5.57 (d, 1H, $J_{1,2}$ 8.1 Hz, H-1), 4.77 (d, 1H, *J* 5.3 Hz, OH), 4.63 (d, 1H, *J* 2.5 Hz, OH), 4.25–3.95 (m, 6H, H-2, 3, 4, 5, 6a and 6b). ^{13}C NMR (75 MHz, Me_2CO-d_6): δ 163.8, 143.4, 139.8, 129.7, 129.0, 127.3, 126.5, 117.6 101.6, 99.6, 77.4, 71.3, 69.9, 69.0, 67.0. ESI-HRMS: calcd for $[C_{19}H_{19}NO_8+Na]^+$: 412.1008. Found *m*/*z*: 412.1000. Anal. Calcd for $C_{19}H_{19}NO_8$: C, 58.61; H, 4.92; N, 3.60. Found: C, 58.26; H, 5.05; N, 3.67.

3.2.6. *p*-Nitrophenyl 2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-gulopyranoside (8)

Under a stream of argon, benzoyl chloride (0.28 mL, 2.41 mmol, 1.0 equiv) was added dropwise to a solution of **7** (0.9 g, 2.31 mmol) in anhydrous CH_2Cl_2 (25 mL) and pyridine (4.5 mL) at 0 °C, and the mixture was stirred for 1.5 h. The reaction mixture was quenched with MeOH (2 mL), diluted with CH_2Cl_2 (100 mL), washed with satd $NaHCO_3$ (100 mL) and brine (100 mL), and dried over $MgSO_4$. The crude product was purified by flash column chromatography (1:1 petroleum ether–EtOAc) to give **8** (0.9 g, 79%) as a white solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.16 (m, 2H, Ar-H), 8.02 (m, 2H, Ar-H), 7.59 (m, 3H, Ar-H), 7.42 (m, 5H, Ar-H), 7.10 (m, 2H, Ar-H), 5.81 (d, 1H, $J_{1,2}$ 8.3 Hz, H-1), 5.68 (dd, 1H, $J_{2,3}$ 3.0 Hz, H-2), 5.63 (s, 1H, C*H*Ph), 4.53 (t, 1H, $J_{3,4}$ 3.2 Hz, H-3), 4.41 (dd, 1H, $J_{5,6a}$ 1.0 Hz, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.25 (dd, 1H, $J_{4,5}$ 0.9 Hz, H-4), 4.17 (dd, 1H, $J_{5,6b}$ 1.7 Hz, H-6b), 4.14 (m, 1H, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 162.2, 143.0, 137.5, 133.8, 130.3, 129.9, 129.5, 128.8, 128.5, 126.5, 125.9, 117.0, 101.5, 96.5, 76.0, 70.7, 69.2, 69.1, 66.3. ESI-HRMS: calcd for $[C_{26}H_{23}NO_9+Na]^+$: 516.1271. Found *m*/*z*: 516.1269. Anal. Calcd for $C_{26}H_{23}NO_9$: C, 63.28; H, 4.70; N, 2.84. Found: C, 62.93; H, 4.83; N, 2.84.

3.2.7. *p*-Nitrophenyl 3-*S*-acetyl-2-*O*-benzoyl-4,6-*O*-benzylidene-3-thio-β-D-galactopyranoside (10)

Under a stream of argon, Tf_2O (1 mL, 5.91 mmol, 4.4 equiv) was added dropwise to a solution of **8** (660 mg, 1.34 mmol) in anhydrous CH_2Cl_2 (35 mL) and pyridine (3 mL) at 0 °C, and stirred for 9 h under the same conditions. The reaction mixture was then diluted with CH_2Cl_2 (100 mL), washed with cold satd $NaHCO_3$ (50 mL) and cold brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo to yield **9** as a brown foam, which was further dried in vacuo overnight. KSAc (0.75 g, 6.58 mmol, 4.9 equiv) was then added to a solution of the dry foam in dry DMF (15 mL) and stirred for 1 h at 50 °C. The reaction mixture was diluted with CH_2Cl_2 (300 mL), washed with water (2 × 150 mL) and brine (150 mL), dried over $MgSO_4$, and concentrated in vacuo to give a residue, which was purified by flash column chromatography (2:1 petroleum ether–EtOAc) to give **10** (500 mg, 68%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (m, 2H, Ar-H), 7.94 (m, 2H, Ar-H), 7.53 (m, 3H, Ar-H), 7.39 (m, 5H, Ar-H), 7.05 (m, 2H, Ar-H), 5.74 (dd, 1H, $J_{2,3}$ 11.5 Hz, H-2), 5.59 (s, 1H, CHPh), 5.42 (d, 1H, $J_{1,2}$ 7.8 Hz, H-1), 4.40 (dd, 1H, *J* 1.2 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.34 (dd, 1H, $J_{3,4}$ 3.4 Hz, H-3), 4.23 (br d, 1H, H-4), 4.15 (dd, 1H, $J_{5,6b}$ 1.5 Hz, H-6b), 3.92 (m, 1H, H-5), 2.21 (s, 3H, CH_3CO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.8, 165.3, 161.8, 143.2, 137.3, 133.7, 130.1, 129.5, 129.4, 128.8, 128.5, 126.4, 125.9, 117.2, 101.6, 100.3, 75.7, 69.2, 69.0, 68.8, 46.8, 30.7. ESI-HRMS: calcd for $[C_{28}H_{25}NO_9S+Na]^+$:

574.1148. Found *m*/*z*: 574.1129. Anal. Calcd for $C_{28}H_{25}NO_9S$: C, 60.97; H, 4.57; N, 2.54. Found: C, 61.09; H, 4.66; N, 2.55.

3.2.8. *p*-Nitrophenyl 3-*S*-acetyl-2-*O*-benzoyl-4,6-di-*O*-acetyl-3-thio-β-D-galactopyranoside (11)

Compound **10** (610 mg, 1.10 mmol) was suspended in AcOH–H_2O (30 mL, 50% v/v), and the reaction mixture was stirred for 6 h at 80 °C. The reaction mixture was concentrated in vacuo to give a sirup which was further dried for 3 h under vacuum. Pyridine (5 mL) and Ac_2O (3 mL) were added to the syrup, and the mixture was stirred overnight at room temperature. The reaction mixture was then concentrated in vacuo, redissolved in CH_2Cl_2 (150 mL), washed with 1 M HCl (50 mL), satd $NaHCO_3$ (50 mL) and brine (50 mL), and dried over $MgSO_4$. The crude product was purified by flash column chromatography (3:1 petroleum ether–EtOAc) to give **11** (530 mg, 88%) as a white solid. $[\alpha]_D^{22}$ +45.8 (*c* 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (m, 2H, Ar-H), 7.95 (m, 2H, Ar-H), 7.56 (m, 1H, Ar-H), 7.42 (m, 2H, Ar-H), 7.03 (m, 2H, Ar-H), 5.62 (dd, 1H, $J_{2,3}$ 11.8 Hz, H-2), 5.42 (br d, 1H, H-4), 5.36 (d, 1H, $J_{1,2}$ 7.7 Hz, H-1), 4.28 (m, 1H, H-5), 4.24 (dd, 1H, $J_{3,4}$ 3.1 Hz, H-3), 4.18 (dd, 1H, $J_{5,6a}$ 5.3 Hz, $J_{6a,6b}$ 11.5 Hz, H-6a), 4.12 (dd, 1H, $J_{5,6b}$ 7.4 Hz, H-6b), 2.21 (s, 3H, CH_3CO), 2.19 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.8, 170.5, 170.1, 165.4, 161.5, 143.5, 133.9, 130.1, 129.1, 128.8, 126.0, 117.0, 100.3, 74.4, 69.0, 68.5, 62.2, 47.0, 30.7, 21.0, 20.8. ESI-HRMS: calcd for $[C_{25}H_{25}NO_{11}S+Na]^+$: 570.1046. Found *m*/*z*: 570.1046. Anal. Calcd for $C_{25}H_{25}NO_{11}S$: C, 54.84; H, 4.60; N, 2.56. Found: C, 54.80; H, 4.45; N, 2.70.

3.2.9. *p*-Nitrophenyl 3-thio-β-D-galactopyranoside (12)

Argon was bubbled through a suspension of **11** (230 mg, 0.42 mmol) in dry MeOH (15 mL) for 0.5 h at room temperature, followed by dropwise addition of sodium methoxide solution (0.2 mL, 5.4 M, 1.08 mmol, 2.6 equiv). The reaction mixture was stirred overnight under argon at room temperature, neutralized with Amberlite IR-120 (H^+) ion exchange resin, filtered, washed with MeOH and concentrated in vacuo until 5 mL of solvent remained. DTT (DL-dithiothreitol, 0.35 g in 12 mL of distilled water) was added to this solution while stirring and the reaction mixture was stirred overnight at room temperature. The solvents were evaporated in vacuo to yield a residue, which was purified by flash column chromatography (9:1 and 5:1 $CHCl_3$–CH_3OH) to give **12** (126 mg, 95%) as a white powder. $[\alpha]_D^{22}$ −3.8 (*c* 0.9, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 8.13 (m, 2H, Ar-H), 7.16 (m, 2H, Ar-H), 4.96 (d, 1H, $J_{1,2}$ 7.3 Hz, H-1), 3.79–3.61 (m, 5H, H-2, 4, 5, 6), 2.93 (br d, 1H, $J_{2,3}$ 10.4 Hz, H-3), 1.97 (s, 3H, CH_3CO). ^{13}C NMR (75 MHz, CD_3OD): δ 164.1 144.0, 126.7, 117.9, 103.4, 79.8, 73.0, 71.1, 62.8, 48.3. ESI-HRMS: Calcd for $[C_{12}H_{15}NO_7S+Na]^+$: 340.0467. Found *m*/*z*: 340.0461. Anal. Calcd for $C_{12}H_{15}NO_7S$: C, 45.42; H, 4.76; N, 4.41. Found: C, 45.20; H, 4.75; N, 4.20.

3.3. Synthesis of phenyl-1,4-dithio -β-D-glucopyranoside (19)

3.3.1. Phenyl-1-thio-β-D-galactopyranoside (15)

Compound **15** was obtained as a white solid according to the literature.[22] ^{1}H NMR (400 MHz, CD_3OD): δ 7.58 (m, 2H, Ar-H), 7.28 (m, 3H, Ar-H), 4.62 (d, 1H, $J_{1,2}$ 9.6 Hz, H-1), 3.93 (br d, 1H, H-4), 3.79 (dd, 1H, $J_{5,6a}$ 6.9 Hz, $J_{6a,6b}$ 11.8 Hz, H-6a), 3.74 (dd, 1H, $J_{5,6b}$ 5.3 Hz, H-6b), 3.65 (t, 1H, $J_{2,3}$ 9.3 Hz, H-2), 3.59 (m, 1H, H-5), 3.53 (dd, 1H, $J_{3,4}$ 3.3 Hz, H-3). ^{13}C NMR (75 MHz, CD_3OD): δ 136.2, 132.2, 130.0, 128.1, 90.4, 80.7, 76.4, 71.1, 70.5, 62.7. ESI-MS: calcd for $[C_{12}H_{16}O_5S+Na]^+$: 295.3. Found: 295.0.

3.3.2. Phenyl-1-thio-2,3-di-*O*-benzoyl-β-D-galactopyranoside (16)

A mixture of **15** (1.6 g, 5.88 mmol), anhydrous DMF (50 mL), anisaldehyde dimethyl acetal (1.5 mL, 8.82 mmol, 1.5 equiv) and CSA (26 mg) was placed in a 100 mL round bottomed flask. This was attached to a Büchi evaporator, rotated, evacuated, lowered into a water bath at 50 °C so that DMF refluxed in the vapor duct. The suspension was rotated under vacuum for 4 h until a clear solution formed, which was checked by TLC for reaction completion. The solvent was evaporated in vacuo yielding a residue. Dry pyridine (30 mL) and benzoyl chloride (3 mL, 25.84 mmol, 4.4 equiv) were added to the resulting residue at 0 °C while stirring, then gradually warmed to room temperature and stirred overnight. The reaction mixture was then poured into ice water and stirred for 0.5 h, followed by extraction with CH_2Cl_2 (2 × 100 mL). The organic phase was washed with satd $NaHCO_3$ (2 × 100 mL) and brine (100 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Acetic acid (40 mL) and water (10 mL) were added to the resulting residue and the mixture was heated to 60 °C and stirred for 2 h. After solvent evaporation, the resulting residue was purified by flash column chromatography (2:1 and 3:2 petroleum ether–EtOAc) to give **16** (2.13 g, 76%) as a white solid. $[\alpha]_D^{22}$ +92.7 (*c* 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (m, 4H, Ar-H), 7.48 (m, 4H, Ar-H), 7.30 (m, 7H, Ar-H), 5.78 (t, 1H, $J_{2,3}$ 10.0 Hz, H-2), 5.32 (dd, 1H, $J_{3,4}$ 3.0 Hz, H-3), 4.96 (d, 1H, $J_{1,2}$ 10.0 Hz, H-1), 4.41 (d, 1H, H-4), 4.02 (dd, 1H, $J_{5,6a}$ 5.9 Hz, $J_{6a,6b}$ 11.9 Hz, H-6a), 3.92 (dd, 1H, $J_{5,6b}$ 4.3 Hz, H-6b), 3.81 (m, 1H, H-5). ^{13}C NMR (75 MHz, Me_2CO-d_6): δ 166.2, 166.0, 134.9, 134.2, 134.1, 132.0, 130.8, 130.4, 130.3, 129.8, 129.5, 129.3, 128.1, 86.8, 80.1, 77.1, 69.5, 67.9, 62.1. ESI-HRMS: calcd for $[C_{26}H_{24}O_7S+Na]^+$: 503.1140. Found *m*/*z*: 503.1139. Anal. Calcd for $C_{26}H_{24}O_7S$: C, 64.99; H, 5.03. Found: C, 65.05; H, 5.15.

3.3.3. Phenyl-1-thio-2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside (17)

Under a stream of argon, benzoyl cyanide (0.83 g, 6.33 mmol, 2.1 equiv) was added to a solution of **16** (1.43 g, 2.98 mmol) in dry CH_2Cl_2 (55 mL) and dry pyridine (5.5 mL) at room temperature and the reaction mixture was stirred overnight. The reaction was quenched with MeOH (2 mL) and concentrated in vacuo. The resulting residue was purified by flash column chromatography (4:1 petroleum ether–acetone) to give **17** (1.5 g, 86%) as a white solid. $[\alpha]_D^{22}$ +19.0 (*c* 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (m, 6H, Ar-H), 7.33 (m, 14H, Ar-H), 5.85 (t, 1H, $J_{2,3}$ 10.0 Hz, H-2), 5.41 (dd, 1H, $J_{3,4}$ 2.9 Hz, H-3), 5.01 (d, 1H, $J_{1,2}$ 10.0 Hz, H-1), 4.67 (m, 2H, H-6a and H-6b), 4.43 (br d, 1H, H-4), 4.15 (m, 1H, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 166.0, 165.6, 133.6, 133.5, 133.2, 132.4, 130.1, 130.0, 129.7, 129.5, 129.0, 128.6, 128.5, 128.0, 87.0, 76.5, 75.4, 68.1, 67.8, 63.8. ESI-HRMS: calcd for $[C_{33}H_{28}O_8S+Na]^+$: 607.1403. Found *m*/*z*: 607.1397. Anal. Calcd for $C_{33}H_{28}O_8S$: C, 67.79; H, 4.83. Found: C, 68.11; H, 5.14.

3.3.4. Phenyl-1-thio-4-*S*-acetyl-2,3,6-tri-*O*-benzoyl-4-thio-β-D-galactopyranoside (18)

Under a stream of argon, Tf_2O (0.9 mL, 5.35 mmol, 2.3 equiv) was added in three portions to a solution of **17** (1.38 g, 2.36 mmol) in dry CH_2Cl_2 (20 mL) and dry pyridine (4.5 mL) at 0 °C and stirred for 1 h under the same conditions. The reaction mixture was then diluted with CH_2Cl_2 (75 mL), washed with ice cold 1 M HCl (50 mL), cold satd $NaHCO_3$ (50 mL) and cold brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo yielding a yellow residue. DMPU (1,2-dimethyl-3,4,5,6-tetra-hydro-2(1*H*)-pyrimidinone, 10 mL) and KSAc (0.82 g, 7.19 mmol, 3.0 equiv) were added to the yellow residue, and the suspension was stirred for 1.5 h at room temperature. The reaction mixture was diluted with mixed solvents (150 mL, 1:1 EtOAc–ether), washed with water (5 × 50 mL) and brine (50 mL), dried over $MgSO_4$ and concentrated in vacuo. The resulting residue was purified by flash column chromatography (4:1 and 2:1 petroleum ether–EtOAc) to give **18** (1.07 g, 70%) as a white solid. $[\alpha]_D^{22}$ +99.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR

(400 MHz, $CDCl_3$): δ 8.09–7.86 (m, 6H, Ar-H), 7.65–7.08 (m, 14H, Ar-H), 5.72 (dd, 1H, $J_{3,4}$ 10.9 Hz, H-3), 5.41 (t, 1H, $J_{2,3}$ 9.6 Hz, H-2), 4.99 (d, 1H, $J_{1,2}$ 10.0 Hz, H-1), 4.75 (dd, 1H, $J_{5,6a}$ 1.8 Hz, $J_{6a,6b}$ 12.1 Hz, H-6a), 4.51 (dd, 1H, $J_{5,6b}$ 5.9 Hz, H-6b), 4.14 (m, 1H, H-5), 4.02 (t, 1H, $J_{4,5}$ 11.1 Hz, H-4), 2.19 (s, 3H, CH_3CO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.8, 166.3, 165.9, 165.3, 133.5, 133.4, 133.1, 132.2, 130.0, 129.9, 129.4, 129.0, 128.7, 128.5, 128.3, 86.3, 77.1, 73.1, 71.7, 64.2, 44.7; 30.9. ESI-HRMS: calcd for $[C_{35}H_{30}O_8S_2+Na]^+$: 665.1280. Found *m*/*z*: 665.1287. Anal. Calcd for $C_{35}H_{30}O_8S_2$: C, 65.40; H, 4.70. Found: C, 65.67; H, 4.84.

3.3.5. Phenyl-1,4-dithio-β-D-glucopyranoside (19)

Argon was bubbled through a suspension of **18** (0.3 g, 0.47 mmol) in dry MeOH (15 mL) for 0.5 h at room temperature, followed by addition of sodium methoxide solution (0.25 mL, 5.4 M, 1.35 mmol, 2.9 equiv). The reaction mixture was stirred for 48 h under argon at room temperature, neutralized with IR-120 (H^+) ion exchange resin, filtered, washed with MeOH and concentrated in vacuo until 3 mL of solvent remained. DTT (0.36 g in 15 mL of distilled water) was added to this solution while stirring. Argon was bubbled through the reaction mixture for another half an hour, then was stirred overnight at room temperature. After concentration in vacuo, the resulting residue was purified by flash column chromatography (15:1 and 9:1 $CHCl_3$–CH_3OH) to give **19** (105 mg, 78%) as a white powder. $[\alpha]_D^{22}$ −53.4 (*c* 3.0, CH_3OH). ^1H NMR (400 MHz, CD_3OD): δ 7.50 (m, 2H, Ar-H), 7.21 (m, 3H, Ar-H), 4.58 (d, 1H, $J_{1,2}$ 9.5 Hz, H-1), 3.83 (dd, 1H, $J_{5,6a}$ 2.0 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 3.72 (dd, 1H, $J_{5,6b}$ 4.9 Hz, H-6b), 3.33 (m, 1H, H-5), 3.27–3.12 (m, 2H, H-2 and H-3), 2.69 (t, 1H, $J_{3,4}=J_{4,5}$ 10.2 Hz, H-4). ^{13}C NMR (75 MHz, CD_3OD): δ 135.3, 132.8, 130.0, 128.4, 89.4, 83.4, 80.5, 74.7, 63.5, 43.3. ESI-HRMS: calcd for $[C_{12}H_{16}O_4S_2+Na]^+$: 311.0388. Found *m*/*z*: 311.0380. Anal. Calcd for $C_{12}H_{16}O_4S_2$: C, 49.98; H, 5.59. Found: C, 49.70; H, 5.76.

3.4. Preparation of *p*-nitrophenyl 4-thio-β-D-mannopyranoside (27) and *p*-nitrophenyl 2-acetamido-2-deoxy-4-thio-β-D-mannopyranoside (30)

3.4.1. *p*-Nitrophenyl 3,6-di-*O*-benzoyl-β-D-galactopyranoside (21)

A suspension of *p*-nitrophenyl β-D-galactopyranoside (**20**, 0.70 g, 2.33 mmol) and dibutyltin oxide (1.33 g, 5.34 mmol, 2.3 equiv) in dry MeOH (70 mL) was refluxed for 2 h. The homogenous solution was concentrated and co-evaporated with toluene twice, and the resulting residue was dried under vacuum for 1 h. The residue was suspended in toluene (30 mL), and a solution of benzoyl chloride (0.59 mL, 2.2 equiv) in toluene (3 mL) was added dropwise at 0 °C with stirring under N_2, gradually warmed to room temperature and stirred overnight. The reaction mixture was diluted with ethyl acetate, cooled to 0 °C and filtered through a short pad of Celite, washed with cold ethyl acetate. After evaporation, the resulting residue was purified by flash column chromatography (10:1 CH_2Cl_2–EtOAc) to give **21** as a white solid in 61% yield (0.72 g). $[\alpha]_D^{22}$ + 12.7 (*c* 1.4, acetone). ^1H NMR (400 MHz, DMSO-d_6 + D_2O): δ 8.03 (m, 6H, Ar-H), 7.68 (m, 2H, Ar-H), 7.55 (m, 4H, Ar-H), 7.24 (m, 2H, Ar-H), 5.40 (d, 1H, $J_{1,2}$ 7.7 Hz, H-1), 5.10 (dd, 1H, $J_{3,4}$ 3.2 Hz, H-3), 4.54 (dd, 1H, $J_{5,6a}$ 8.4 Hz, $J_{6a,6b}$ 10.8 Hz, H-6a), 4.39 (m, 2H, H-5 and 6b), 4.19 (d, 1H, H-4), 4.12 (d, 1H, $J_{2,3}$ 9.6 Hz, H-2). ^{13}C NMR (100 MHz, DMSO-d_6 + D_2O): δ 167.1, 166.9, 163.3, 143.1, 135.0, 134.8, 131.3, 131.0, 130.9, 130.7, 130.1, 130.0, 126.9, 117.9 (2C), 100.9, 77.6, 74.1, 68.7, 67.1, 65.2. ESI-HRMS: calcd for $[C_{26}H_{23}NO_{10}+Na]^+$: 532.1220. Found *m*/*z*: 532.1208.

3.4.2. *p*-Nitrophenyl 4-*S*-acetyl-3,6-di-*O*-benzoyl-2-*O*-triflyl-β-D-glucopyranoside (23)

A solution of **21** (0.448 g, 0.88 mmol) in anhydrous CH_2Cl_2 (15 mL) and anhydrous pyridine (2 mL) was cooled to −20 °C, and a solution of trifluoromethanesulfonic anhydride (0.62 mL, 3.69 mmol, 4.2 equiv) in CH_2Cl_2 (5 mL) was added dropwise with stirring under N_2. The yellow solution was stirred for 2 h while allowing to gradually warm to 10 °C, diluted with CH_2Cl_2 (50 mL), washed with cold 1 M HCl (40 mL), cold satd $NaHCO_3$ (40 mL) and brine (40 mL). The organic phase was then dried over $MgSO_4$, filtered and concentrated, dried under vacuum to give a yellowish foam. To this yellow foam were added anhydrous CH_3CN (17 mL) and potassium thioacetate (0.2 g, 1.75 mmol, 2.0 equiv) under N_2. The reaction mixture was stirred at room temperature for 15 min, diluted with ethyl acetate (200 mL), washed with brine (2 × 100 mL), and dried over $MgSO_4$. After concentration, the resulting residue was purified by flash column chromatography (4:1 petroleum ether–ethyl acetate) to give **23** as a white solid in 81% yield (0.5 g). ^1H NMR (300 MHz, $CDCl_3$): δ 8.06 (m, 6H, Ar-H), 7.65 (m, 2H, Ar-H), 7.52 (m, 4H, Ar-H), 7.12 (m, 2H, Ar-H), 5.89 (t, 1H, $J_{3,4}=J_{2,3}$ 10.4 Hz, H-3), 5.39 (d, 1H, $J_{1,2}$ 7.8 Hz, H-1), 5.18 (dd, 1H, H-2), 4.78 (br d, 1H, H-6a), 4.54 (dd, 1H, $J_{5,6b}$ 7.0, $J_{6a,6b}$ 12.0, H-6b), 4.40 (m, 1H, H-5), 4.00 (t, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.7, 166.1, 165.5, 160.7, 143.8, 134.2, 134.0, 130.2 (2C), 129.9 (2C), 129.5, 128.9 (4C), 128.4, 126.0 (2C), 117.1 (2C), 118.5 (q), 97.5, 82.7, 73.4, 70.0, 63.5, 45.1, 31.0. ESI-HRMS: calcd for $[C_{29}H_{24}F_3NO_{12}S_2+Na]^+$: 722.0590. Found *m*/*z*: 722.0598.

3.4.3. *p*-Nitrophenyl 4-*S*-thioethyl-4-thio-3,6-di-*O*-benzoyl-2-*O*-triflate-β-D-gluco-pyranoside (24)

Compound **23** (0.48 g, 0.69 mmol) was dissolved in dry DMF (9 mL), and N_2 was bubbled through the solution for 15 min. To this solution was added hydrazine acetate (126 mg, 1.4 mmol, 2 equiv), and the mixture was stirred for 0.5 h at room temperature. The reaction mixture was diluted with ethyl acetate (100 mL), washed with water (50 mL) and brine (50 mL), dried over $MgSO_4$, filtered and concentrated and dried under vacuum. To the residue was added CH_2Cl_2 (25 mL), diisopropyl-*N*-ethylsulfanyl hydrazodicarboxylate (0.48 g, 1.82 mmol, 2.6 equiv) and 3 drops of ammonium hydroxide, and the mixture was stirred for 20 min at room temperature. The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with cold 1 M HCl (50 mL), cold satd $NaHCO_3$ (50 mL) and cold brine (50 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated. The resulting residue was purified by flash column chromatography (5:1 petroleum ether–ethyl acetate) to give **24** in 89% yield (438 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (m, 6H, Ar-H), 7.66 (m, 2H, Ar-H), 7.51 (m, 4H, Ar-H), 7.12 (m, 2H, Ar-H), 5.88 (t, 1H, $J_{3,4}=J_{2,3}$ 10.3 Hz, H-3), 5.38 (d, 1H, $J_{1,2}$ 7.8 Hz, H-1), 5.18 (dd, 1H, H-2), 5.05 (dd, 1H, $J_{5,6a}$ 2.0 Hz, H-6a), 4.66 (dd, 1H, $J_{5,6b}$ 7.3, $J_{6a,6b}$ 12.1, H-6b), 4.33 (m, 1H, H-5), 3.15 (t, 1H, $J_{4,5}$ 10.7 Hz, H-4), 2.78 (m, 2H, SCH_2CH_3), 1.20 (t, 3H, *J* 7.3 Hz, SCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 165.3, 160.7, 143.8, 134.1, 133.9, 130.1 (2C), 129.9 (2C), 129.5, 128.83 (2C), 128.80 (2C), 128.7, 125.9 (2C), 117.1 (2C), 118.5 (q), 97.3, 83.0, 74.6, 70.1, 63.7, 52.0, 33.8, 14.4. ESI-HRMS: calcd for $[C_{29}H_{26}F_3NO_{11}S_3+Na]^+$: 740.0518. Found *m*/*z*: 740.0526.

3.4.4. *p*-Nitrophenyl 2-*O*-acetyl-4-*S*-thioethyl-4-thio-3,6-di-*O*-benzoyl-β-D-manno-pyranoside (25a)

A mixture of **24** (165 mg, 0.23 mmol), CH_3CN (4 mL) and TBAOAc (210 mg, 0.70 mmol, 3 equiv) was stirred for 1.5 h at 40 °C under N_2. After evaporation, the resulting residue was directly purified by flash column chromatography (4:1 petroleum ether–ethyl acetate) to give **25a** in 82% yield (118 mg). $[\alpha]_D^{22}$ +14.8 (*c* 0.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (m, 6H, Ar-H), 7.63 (m, 2H, Ar-H), 7.48 (m, 4H, Ar-H), 7.06 (m, 2H, Ar-H), 5.95 (d, 1H, $J_{2,3}$ 2.7 Hz, H-2), 5.55 (dd, 1H, $J_{3,4}$ 10.9 Hz, H-3), 5.45 (s, 1H, H-1), 5.11 (dd, 1H, $J_{5,6a}$ 2.2 Hz, $J_{6a,6b}$ 11.8 Hz, H-6a), 4.65 (dd, 1H, $J_{5,6b}$ 7.7, H-6b), 4.29 (m, 1H, H-5), 3.25 (t, 1H, H-4), 2.74 (m, 2H, SCH_2CH_3), 2.21 (s, 3H, CH_3CO), 1.20 (t, 3H, *J* 7.3 Hz,

SCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 166.1, 165.5, 161.1, 143.1, 133.84, 133.76, 129.9 (2C), 129.8 (2C), 129.7, 129.1, 128.8 (2C), 128.7 (2C), 125.7 (2C), 116.7 (2C), 95.9, 74.2, 69.7, 68.3, 64.4, 46.4, 33.9, 20.9, 14.3. ESI-HRMS: calcd for $[C_{30}H_{29}NO_{10}S_2+Na]^+$: 650.1131. Found *m*/*z*: 650.1124.

3.4.5. *p*-Nitrophenyl 2-azido-2-deoxy-4-*S*-thioethyl-4-thio-3,6-di-*O*-benzoyl-β-D-mannopyranoside (25b)

A mixture of **24** (160 mg, 0.22 mmol), CH_3CN (4.5 mL) and $TBAN_3$ (190 mg, 0.67 mmol, 3 equiv) was stirred for 2 h at 40 °C under N_2. After evaporation, the resulting residue was directly purified by flash column chromatography (12:1:1 petroleum ether–ethyl acetate–acetone) to give **25b** in 84% yield (114 mg). $[\alpha]_D^{22}$ −29.4 (*c* 1.3, acetone). ^1H NMR (300 MHz, $CDCl_3$): δ 8.16 (m, 2H, Ar-H), 8.03 (m, 4H, Ar-H), 7.67 (m, 2H, Ar-H), 7.45 (m, 4H, Ar-H), 7.09 (m, 2H, Ar-H), 5.22 (dd, 1H, $J_{2,3}$ 3.2 Hz, H-3), 5.48 (s, 1H, H-1), 5.06 (br d, 1H, H-6a), 4.61 (dd, 1H, $J_{5,6b}$ 7.6 Hz, $J_{6a,6b}$ 11.8, H-6b), 4.58 (s, 1H, H-2), 4.22 (m, 1H, H-5), 3.26 (t, 1H, $J_{4,5}=J_{3,4}$ 10.6 Hz, H-4), 2.69 (m, 2H, SCH_2CH_3), 1.20 (t, 3 H, *J* 7.3 Hz, SCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.1, 165.7, 160.8, 143.2, 134.1, 133.7, 130.2 (2C), 129.8 (2C), 129.7, 128.9 (2C), 128.8, 128.7 (2C), 125.8 (2C), 116.7 (2C), 96.7, 74.4, 70.6, 64.3, 61.8, 46.5, 33.8, 14.3. ESI-HRMS: calcd for $[C_{28}H_{26}N_4O_8S_2+Na]^+$: 633.1090. Found *m*/*z*: 633.1083.

3.4.6. *p*-Nitrophenyl 4-*S*-thioethyl-4-thio-β-D-mannopyranoside (26)

A mixture of **25a** (66 mg, 0.11 mmol), dry MeOH (10 mL) and sodium methoxide solution (5.4 M, 25 μL, 1.3 equiv) was stirred for 1.5 h at room temperature under N_2, neutralized with Amberlite 120 H ion exchange resin, filtered and concentrated. The resulting residue was purified by flash column chromatography (3:2:2 petroleum ether–ethyl acetate–acetone) to give **26** in 86% yield (34 mg). $[\alpha]_D^{22}$ −25.1 (*c* 0.8, CH_3OH). ^1H NMR (300 MHz, Me_2CO-d_6): δ 8.18 (m, 2H, Ar-H), 7.26 (m, 2H, Ar-H), 5.44 (s, 1H, H-1), 4.23 (d, 1H, $J_{2,3}$ 2.6 Hz, H-2), 4.00 (m, 2H, H-3 and 6a), 3.89 (dd, 1H, $J_{5,6b}$ 4.8 Hz, $J_{6a,6b}$ 11.9 Hz, H-6b), 3.78 (m, 1H, H-5), 2.99 (t, 1H, $J_{4,5}=J_{3,4}$ 10.5 Hz, H-4), 2.81 (m, 2H, SCH_2CH_3), 1.28 (t, 3H, *J* 7.3 Hz, SCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.1, 143.2, 126.4 (2C), 117.4 (2C), 98.3, 77.5, 71.3, 70.0, 62.6, 49.4, 33.8, 14.7. ESI-HRMS: calcd for $[C_{14}H_{19}NO_7S_2+Na]^+$: 400.0501. Found *m*/*z*: 400.0490.

3.4.7. *p*-Nitrophenyl 4-thio-β-D-mannopyranoside (27)

A solution of **26** (47 mg, 0.13 mmol), MeOH (2 mL), DTT (58 mg, 3 equiv) in water (2 mL) was degassed for 0.5 h by bubbling N_2, and then NH_4OH (2 drops) was added. The reaction mixture was stirred for 1 h at room temperature and concentrated. The resulting residue was purified by flash column chromatography (30:1 CH_2Cl_2–CH_3OH) to give the product **27** (36 mg, 91%). $[\alpha]_D^{22}$ −69.7 (*c* 1.8, CH_3OH). ^1H NMR (300 MHz, CD_3OD): δ 8.24 (m, 2H, Ar-H), 7.24 (m, 2H, Ar-H), 5.39 (s, 1H, H-1), 4.09 (d, 1H, $J_{2,3}$ 2.3 Hz, H-2), 3.99 (dd, 1H, $J_{5,6a}$ 1.7 Hz, H-6a), 3.87 (dd, 1H, $J_{5,6b}$ 5.0 Hz, $J_{6a,6b}$ 12.1 Hz, H-6b), 3.58 (m, 2H, H-3 and 5), 3.07 (t, 1H, $J_{4,5}=J_{3,4}$ 10.6 Hz, H-4). ^{13}C NMR (75 MHz, CD_3OD): δ 163.6, 144.0, 126.8 (2C), 117.7 (2C), 99.1, 80.4, 76.1, 71.8, 63.4, 39.6. ESI-HRMS: calcd for $[C_{12}H_{15}NO_7S+Na]^+$: 340.0467. Found *m*/*z*: 340.0473. Anal. Calcd for $C_{12}H_{15}NO_7S$: C, 45.42; H, 4.76; N, 4.41. Found: C, 45.63; H, 5.12; N, 4.41.

3.4.8. *p*-Nitrophenyl 2-acetamido-2-deoxy-4-*S*-acetyl-4-thio-3,6-di-*O*-benzoyl-β-D-mannopyranoside (29)

A solution of **25b** (100 mg, 0.16 mmol), $CHCl_3$ (15 mL), 2,6-lutidine (154 μL, 1.3 mmol, 8 equiv) and thioacetic acid (93 μL, 1.3 mmol, 8 equiv) was stirred for a week at 65 °C under N_2. After every two days, the same amounts of fresh reagents were added. The reaction solution was cooled to room temperature, diluted with CH_2Cl_2 (50 mL), washed with 1 M HCl (30 mL), satd $NaHCO_3$ (30 mL) and brine (30 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated. The resulting residue was purified by flash column chromatography (2:1 petroleum ether–ethyl acetate) to give **29** as a white solid in 81% yield (81 mg). $[\alpha]_D^{22}$ −117.6 (*c* 0.8, $CHCl_3$). ^1H NMR (300 MHz, Me_2CO-d_6): δ 8.01 (m, 6H, Ar-H), 7.84 (d, 1H, *J* 9.5 Hz, NH), 7.65 (m, 2H, Ar-H), 7.50 (m, 4H, Ar-H), 7.21 (m, 2H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 1.2 Hz, H-1), 5.53 (dd, $J_{2,3}$ 4.0, $J_{3,4}$ 11.0 Hz, H-3), 5.16 (dd, 1H, $J_{5,6a}$ 2.3 Hz, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.57 (m, 3H, H-2, 5 and 6b), 4.11 (t, 1H, H-4), 2.35 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO). ^{13}C NMR (75 MHz, Me_2CO-d_6): δ 194.4, 171.3, 166.8, 166.3, 162.8, 143.9, 134.7, 134.6, 131.2, 130.9 (2C), 130.8 (2C), 129.9 (2C), 129.86 (2C), 126.7 (2C), 118.0 (2C), 97.1, 75.4, 72.3, 65.5, 51.2, 42.0, 31.2, 23.4. ESI-HRMS: calcd for $[C_{30}H_{28}N_2O_{10}S+Na]^+$: 631.1362. Found *m*/*z*: 631.1353.

3.4.9. *p*-Nitrophenyl 2-acetamido-2-deoxy-4-thio-β-D-mannopyranoside (30)

To a suspension of **29** (54 mg, 0.09 mmol) in dry MeOH (10 mL) was bubbled N_2 for 0.5 h, and then sodium methylate solution (5.4 M, 36 μL, 2 equiv) was added. The reaction mixture was stirred overnight at room temperature under N_2, neutralized with Amberlite IR-120 H^+ ion exchange resin, filtered and washed with MeOH, concentrated to 2 mL. To this solution was added DTT (28 mg in 1 mL of distilled water), and the solution was degassed again for another half an hour. Ammonium hydroxide (2 drops) was added, and the reaction mixture was stirred for 0.5 h at room temperature. After concentration, the resulting residue was purified by flash column chromatography (20:1 and 10:1 CH_2Cl_2–CH_3OH) to give **30** as a white solid in 85% yield (27 mg). $[\alpha]_D^{22}$ −67.8 (*c* 0.9, CH_3OH). ^1H NMR (300 MHz, CD_3OD): δ 8.19 (m, 2H, Ar-H), 7.13 (m, 2H, Ar-H), 5.46 (s, 1H, H-1), 4.68 (s, 1H, H-2), 4.00–3.59 (m, 4H, H-3, 5, 6a and 6b), 2.92 (t, 1H, $J_{3,4}=J_{4,5}$ 10.4 Hz, H-4), 2.07 (s, 3H, CH_3CO). ^{13}C NMR (75 MHz, CD_3OD): δ 174.9, 163.2, 144.2, 126.8 (2C), 117.8 (2C), 98.1, 80.4, 75.1, 62.8, 54.5, 39.8, 22.9. ESI-HRMS: calcd for $[C_{14}H_{18}N_2O_7S+Na]^+$: 381.0732. Found *m*/*z*: 381.0735. Anal. Calcd for $C_{14}H_{18}N_2O_7S$: C, 46.92; H, 5.06; N, 7.82. Found: C, 46.35; H, 5.24; N, 7.61.

3.5. Preparation of *p*-nitrophenyl 2-acetamido-2-deoxy-β-D-mannopyranoside (35)

3.5.1. *p*-Nitrophenyl 4-*O*-acetyl-3,6-di-*O*-benzoyl-2-*O*-triflate-β-D-glucopyranoside (32)

To a solution of **22** (462 mg, 0.60 mmol) in anhydrous toluene (10 mL) were added 18-crown-6 (240 mg, 0.91 mmol, 1.5 equiv) and anhydrous sodium acetate (74 mg, 0.90 mmol, 1.5 equiv), and the mixture was stirred overnight at room temperature under N_2. The reaction mixture was diluted with ethyl acetate (100 mL), washed with brine (2 × 50 mL), dried over $MgSO_4$. After concentration, the resulting residue was purified by flash column chromatography (10:1:1 petroleum ether–ethyl acetate–acetone) to give **32** as a white solid in 64% yield (261 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (m, 6H, Ar-H), 7.63 (m, 2H, Ar-H), 7.47 (m, 4H, Ar-H), 7.14 (m, 2H, Ar-H), 5.89 (t, 1H, $J_{3,4}=J_{4,5}$ 9.6 Hz, H-4), 5.45 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 5.44 (t, 1H, H-3), 5.23 (dd, 1H, $J_{2,3}$ 9.4 Hz, H-2), 4.64 (dd, 1H, $J_{5,6a}$ 2.1 Hz, H-6a), 4.51 (dd, 1H, $J_{5,6b}$ 6.6 Hz, $J_{6a,6b}$ 12.3 Hz, H-6b), 4.31 (m, 1H, H-5), 1.98 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 166.1, 165.6, 162.4, 143.9, 134.3, 134.0, 130.3 (2C), 129.9 (2C), 129.5, 128.94 (2C), 128.9 (2C), 128.3, 126.0 (2C), 117.1 (2C) (Ar-C); 118.4 (q), 97.5, 81.6, 73.0, 71.6, 68.8, 62.5, 20.6. ESI-HRMS: calcd for $[C_{29}H_{24}F_3NO_{13}S+Na]^+$: 706.0818. Found *m*/*z*: 706.0809.

3.5.2. *p*-Nitrophenyl 2-azido-2-deoxy-4-*O*-acetyl-3,6-di-*O*-benzoyl-β-D-mannopyranoside (33)

A mixture of **32** (290 mg, 0.42 mmol), CH_3CN (9 mL) and $TBAN_3$ (42 mg, 1.48 mmol, 3.5 equiv) was stirred for 3 h at 40 °C under N_2. After evaporation, the resulting residue was directly purified by flash column chromatography (3:1 petroleum ether–ethyl acetate) to give **33** in 92% yield (224 mg). $[\alpha]_D^{22}$ −8.8 (*c* 0.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (m, 6H, Ar-H), 7.63 (m, 2H, Ar-H), 7.50 (m, 4H, Ar-H), 7.11 (m, 2H, Ar-H), 5.59 (t, 1H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 5.53 (d, 1H, $J_{1,2}$ 1.1 Hz, H-1), 5.39 (dd, 1H, H-3), 4.62 (dd, 1H, $J_{5,6a}$ 2.7 Hz, H-6a), 4.56 (dd, 1H, $J_{2,3}$ 3.5 Hz, H-2), 4.49 (dd, 1H, $J_{5,6b}$ 7.3 Hz, $J_{6a,6b}$ 12.1 Hz, H-6b), 4.12 (m, 1H, H-5), 2.02 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 166.1, 165.8, 160.7, 143.3, 134.2, 133.8, 130.2 (2C), 129.9 (2C), 129.5, 128.9 (2C), 128.7 (2C), 128.6, 125.9 (2C), 116.7 (2C), 97.0, 73.2, 72.2, 65.9, 63.0, 61.6, 20.8. ESI-HRMS: calcd for $[C_{28}H_{24}N_4O_{10}+Na]^+$: 599.1390 Found *m*/*z*: 599.1378.

3.5.3. *p*-Nitrophenyl 2-acetamido-2-deoxy-4-*O*-acetyl-3,6-di-*O*-benzoyl-β-D-mannopyranoside (34)

A solution of **33** (105 mg, 0.18 mmol) and PPh_3 (75 mg, 0.29 mmol, 1.6 equiv) in CH_2Cl_2 (5 mL) was stirred for 4 h at 40 °C. Water (5 mL) was added, and the solution was stirred overnight under the same conditions. The reaction mixture was cooled to room temperature, and the two layers separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phase was concentrated and co-evaporated with toluene twice to dryness, then dried under vacuum for 0.5 h. To the residue a mixed solvent (5 mL, 1:1 pyridine–CH_2Cl_2) was added, the solution cooled to 0 °C under N_2, and acetyl chloride (0.13 mL, 1.83 mmol, 10 equiv) was added. The mixture was stirred for 2 h at 0 °C, diluted with CH_2Cl_2 (20 mL), washed with 1 M HCl (10 mL), satd $NaHCO_3$(10 mL) and brine (10 mL), and dried over $MgSO_4$. After evaporation, the resulting residue was purified by flash column chromatography (2:1 petroleum ether–ethyl acetate) to give **34** in 76% yield (82 mg). $[\alpha]_D^{22}$ −81.9 (*c* 0.9, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (m, 6H, Ar-H), 7.63 (m, 2H, Ar-H), 7.47 (m, 4H, Ar-H), 7.06 (m, 2H, Ar-H), 5.96 (d, 1H, *J* 9.1 Hz, NH), 5.59 (d, 1H, $J_{1,2}$ 2.4 Hz, H-1), 5.45 (dd, 1H, $J_{2,3}$ 4.0 Hz, H-3), 5.38 (t, 1H, $J_{3,4} = J_{4,5}$ 7.4 Hz, H-4), 5.19 (ddd, 1H, H-2), 4.67 (dd, 1H, $J_{5,6a}$ 8.3 Hz, H-6a), 4.51 (dd, 1H, $J_{5,6b}$ 3.5, $J_{6a,6b}$ 12.0 Hz, H-6b), 4.26 (m, 1H, H-5), 2.13 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 171.0, 166.8, 166.4, 162.8, 144.0, 134.8, 134.7, 131.3, 131.2, 130.9 (2C), 130.8 (2C), 129.9 (4 C), 126.8 (2C), 118.0 (2C), 97.1, 74.1, 73.2, 68.0, 64.7, 50.9, 23.3, 21.3. ESI-HRMS: calcd for $[C_{30}H_{28}N_2O_{11}+Na]^+$: 615.1591. Found *m*/*z*: 615.1584.

3.5.4. *p*-Nitrophenyl 2-acetamido-2-deoxy-β-D-mannopyranoside (35)

To the solution of **34** (60 mg, 0.1 mmol) in dry MeOH (10 mL) was added sodium methoxide solution (50 μL, 2.7 equiv), and the mixture was stirred overnight at room temperature under N_2. The solution was neutralized with Amberlite 120 (H^+) ion exchange resin, filtered and washed with MeOH. After concentration, the resulting residue was purified by flash column chromatography (20:1 and 10:1 CH_2Cl_2–CH_3OH) to give **35** as a white solid in 92% yield (32 mg). ESI-MS: calcd for $[C_{14}H_{18}N_2O_8+Na]^+$: 365.1. Found *m*/*z*: 365.0.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2010.10.001.

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