O-deacetylated arylthioglycosides of N-acetyl-d-glucosamine from 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-d-glucopyranosyl chloride and aryl thiols or disulfides. Synthetic Carbohydrate Chemistry, 341(10), 1764–1769. https://doi.org/10.1016/j.carres.2005.12.009

A highly concise preparation of O-deacetylated arylthioglycosides of *N*-acetyl-D-glucosamine from 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride and aryl thiols or disulfides

Keith A. Stubbs, Matthew S. Macauley and David J. Vocadlo*

Department of Chemistry, Simon Fraser University, 8888 University Drive, Burnaby, BC, Canada V5A 1S6

Abstract—An expedient and mild route to a range of aryl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranosides has been devised from 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride and arylthiols or aryl disulfides using phase transfer catalysis conditions. This simple procedure compresses up to three synthetic steps into a one-pot reaction, obviating the need for tedious workups and chromatography and directly furnishes crystalline materials in good yields. The procedure is compatible with a range of thiols and disulfides and may be amenable for preparing a wide range of thioglycosides with various glycons and aglycons.

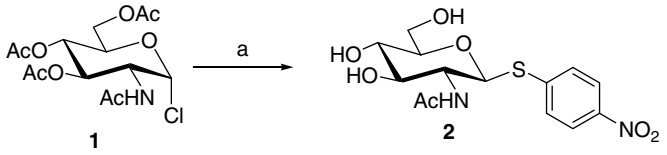
Keywords: Thioglycoside; Phase transfer reaction; Disulfides; Arylthiols; One-pot synthesis; Enzyme substrate; Enzyme inhibitor

Thioglycosides have found their place in carbohydrate chemistry and carbohydrate biology as an important tool. Such compounds have been exploited as glycosyl donors,[1] enzyme inhibitors,[2] and synthetic vaccines.[3] They have also been used in the synthesis of both glycopeptide building blocks[4] and enzyme resistant ligands[5] for affinity chromatography.[6] Selectively protected alkyl and aryl 2-acylamido-2-deoxy-1-thio-β-D-glucopyranosides, in parti- cular, have also proven useful in the synthesis of many oligosaccharides.[7–10]

For our recent work,[11,12] we needed to efficiently prepare a series of aryl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranosides for use as probes of *O*-GlcNAcase, an enzyme that cleaves terminal *N*-acetylglucosamine residues from glycoconjugates[13] One procedure that came to our attention for the preparation of aryl thioglycosides was the use of phase transfer conditions[14–17] that is convenient and uses readily accessible glycosyl halides as starting materials. Using phase transfer conditions resembling those previously reported,[18] the readily available 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride **1**[18] was treated with 4-nitrothiophenol. To our surprise, after leaving the reaction for a longer (18 h) than suggested reaction time (1–2 h), a precipitate formed that upon filtration and analysis was found to be the desired thioglycoside **2** in its fully O-deacetylated form (Scheme 1). This finding suggested to us a simple and expeditious route to fully deprotected thioglycosides that obviates the need for workup, purification and subsequent deacylation normally required after forming thioglycosides under phase transfer conditions.

Therefore, we examined the generality of these reaction conditions and accordingly set out to generate the complete desired series of aryl thioglycosides (Table 1). Aggressive mixing of chloride **1** with 1.1 equiv of the desired arylthiophenol along with benzyltriethylammonium chloride as a phase transfer reagent in a mixture of dichloromethane and 1 M sodium hydroxide for 18 h gave precipitates that, in every case (except for the thioumbelliferyl thioglycoside; see Table 1), were the desired deprotected glycosides in good yield. Simple filtration, washing of the crystals successively with dichloromethane, ethyl acetate and diethyl ether,

* Corresponding author. Tel.: +1 604 291 3530; fax: +1 604 291 3765; e-mail: dvocadlo@sfu.ca



a) 4-$O_2NC_6H_4SH$, $C_6H_5CH_2N(Cl)(C_2H_5)_3$, 1M NaOH, CH_2Cl_2

Scheme 1. Preparation of 4-nitrophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside.

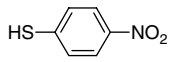
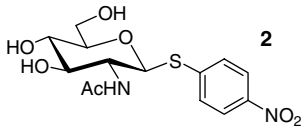
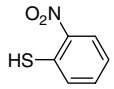
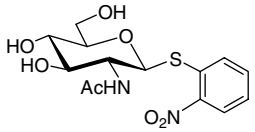
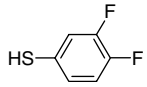
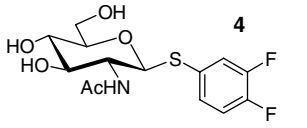
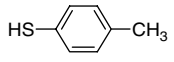
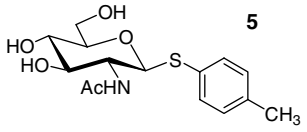
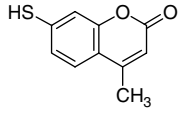
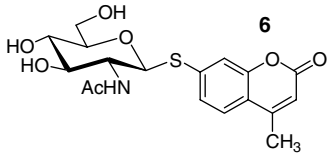
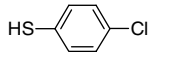
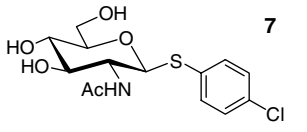
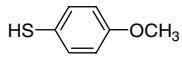
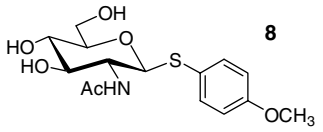
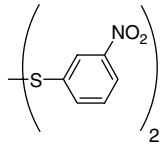
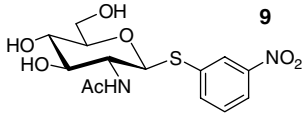
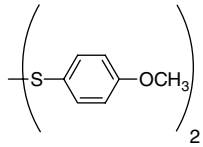
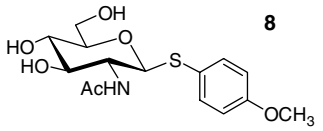
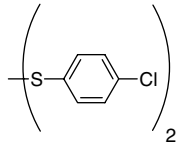
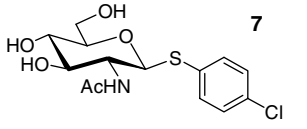
followed by air-drying gave crystalline materials. Upon analysis of these crystals we found, remarkably that most products gave satisfactory ^1H, ^{13}C NMR spectra and elemental analyses. In the few cases where analysis was not satisfactory, a simple recrystallisation of the filter cake with a mixture of ethanol and diethyl ether readily afforded the desired compound in both high purity and good yield. We can therefore compress two separate steps into a one pot reaction that yields the desired aryl glycosides in high yield and purity without the need for workup or flash column chromatography. Importantly, we noted that the initial concentration of chloride **1** is important to the success of the reaction. If the concentration is initially too high, premature precipitation can occur to yield the fully acetylated material and then, even after extended reaction times, little O-deacetylation occurs.

We speculated that the slight excess of arylthiolate (0.1 equiv) is likely to O-deacylate the saccharide to form an intermediate thioester. This thioester is, in turn, cleaved by free hydroxide to regenerate the arylthiolate, which can react again. To verify the requirement for a slight excess of arylthiolate to O-deacylate the intermediate, we subjected 4-nitrophenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucoside **2** to the same reaction conditions in the absence of any aryl thiol. Even after stirring for 48 h only a small amount of fully O-deacetylated material was observed, indicating that hydroxide is not carrying out the deacylation and supporting our supposition that the thiolate is effecting O-deacylation under these reaction conditions.

We felt that the reaction could be usefully elaborated to make direct use of disulfides, some of which are the only commercially available source of certain aryl thiols. Indeed, one of the compounds within our desired series necessitated the use of a disulfide as a starting material because the corresponding thiol is not commercially available. Consulting the literature, we found that there are two methods for preparing thiols from disulfides that could be suitably adapted to the phase transfer conditions. The first involves the reduction of a disulfide using triphenylphosphine in a dioxane/water mixture[19] and the second is based on an observation that electron poor organic disulfides react under alkaline conditions to give substoichiometric equivalents of their corresponding thiolates[20] To obtain the 3-nitrophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside **9**, the phase transfer reaction was modified for application with 3-nitrothiophenol disulfide using either triphenylphosphine in the reaction or simply relying on the alkaline reaction conditions. Quite gratifyingly, the addition of triphenylphosphine directly to the reaction mixture (pre-formation of the thiol was not required) gave the desired thioglycoside in good yield as a crystalline solid. Relying on the basic reaction conditions also gave a good yield of the desired thioglycoside, but as expected a larger excess of the disulfide is required (1.5 equiv).

After obtaining these pleasing results, we conducted a further exploration into which of the two methods used for the in situ reduction of the disulfide might be more general. We therefore attempted reactions using the electron rich 4-methoxythiophenol disulfide and the moderately electron rich 4-chlorothiophenol disulfide using both conditions; triphenylphosphine being directly added to the reaction mixture or relying on the alkaline conditions of the reaction. To some surprise no reaction was seen using either set of conditions, even after prolonged reaction times (48 h). The lack of reactivity under the simple basic conditions is surprising as it is reported that under alkaline conditions there is a good correlation of sensitivity to alkaline decomposition of disulfides to the pK_a values of the displaced thiols.[20] 4-Chlorothiophenol disulfide is reported to have a half-life of 0.5 h in a 0.125 M solution of sodium hydroxide; a time scale that is well within the time limits imposed by our conditions.[20] It is possible, however that partitioning of the disulfide between the aqueous and organic layers dramatically lowers the effective concentration of disulfide in the aqueous layer, thereby significantly slowing the reaction. However, the products were readily obtained from the disulfides in one-pot without any chromatography and only one filtration by a slight modification of the procedure. The yields are good when considering that three synthetic steps are being carried out. The disulfides can be reduced in situ with triphenylphosphine in a minimal volume of 1,4-dioxane and water after which the phase transfer reagents and solvents are added directly to the resulting mixture. This further modification does not affect the yields of the reaction and still furnishes the desired materials conveniently as pure crystalline materials (Table 1).

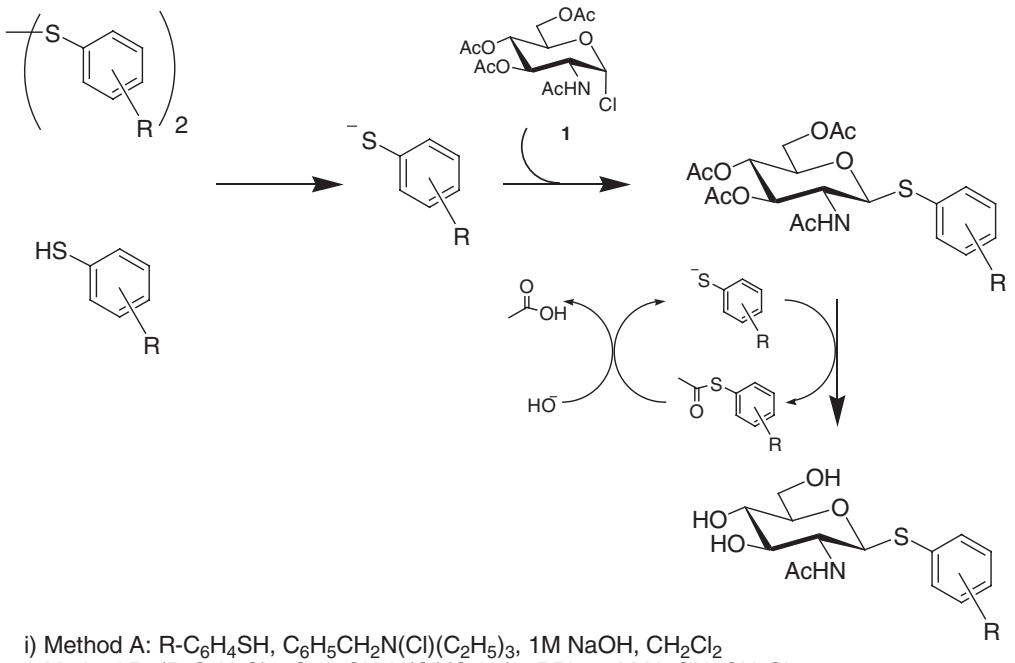
Table 1. Synthesis of aryl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranosides

Substrate	Product	Method[a] (yield, %)
	 **2**	A(76%)[21]
	 **3**	A(69%)
	 **4**	A(68%)
	 **5**	A(60%)[22]
	 **6**	A(70%)[c]
	 **7**	A(60%)
	 **8**	A(61%)
	 **9**	A(71%) B(62%)
	 **8**	A(N.R.)[b] B(N.R.) C(53%)
	 **7**	A(N.R.) B(N.R.) C(49%)

[a] Method A: No triphenylphosphine; Method B: addition of triphenylphosphine directly to the reaction; Method C: initial reduction of disulfide with triphenylphosphine before adding phase transfer reagents and compound **1**.

[b] No reaction.

[c] The yield of this reaction is reported for a two step procedure because a Zemplén deacetylation was required as the tri-*O*-acetyl intermediate prematurely precipitated under the reaction conditions.



i) Method A: R-C_6H_4SH, $C_6H_5CH_2N(Cl)(C_2H_5)_3$, 1M NaOH, CH_2Cl_2
Method B: $(R\text{-}C_6H_4S)_2$, $C_6H_5CH_2N(Cl)(C_2H_5)_3$, PPh_3, 1M NaOH, CH_2Cl_2
Method C: $(R\text{-}C_6H_4S)_2$, PPh_3, H_2O/dioxane, $C_6H_5CH_2N(Cl)(C_2H_5)_3$, 1M NaOH, CH_2Cl_2

Figure 1. Rationale for the formation of thioglycosides.

An overall rationale for the formation of the products can be given (Fig. 1). The reaction presumably proceeds by the generation of the thiolate either from the thiol (by deprotonation), or from the disulfide (either by reduction under the basic reaction conditions, by triphenylphosphine, or by pre-formation of the thiol using triphenylphosphine/dioxane/water). Interception of the thiolate by chloride **1** gives the intermediate per-O-acetylated thioglycoside. The residual thiolate in the reaction mixture (0.1 equiv) acts in a catalytic manner, transesterifying with the acetyl protecting groups on the intermediate to yield the free hydroxyl and the corresponding thioester. This thioester is readily hydrolysed by the excess hydroxide present in the reaction, thereby regenerating the thiolate for successive deacetylations.

In conclusion, an expedient, mild and stereospecific route to aryl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranosides has been achieved using modified phase transfer catalysis conditions. This simple procedure compresses up to three separate steps into a convenient one pot synthesis, obviating the need for tedious workups and flash chromatography and furnishing crystalline materials in good isolated yields. Furthermore, only a slight excess of the expensive disulfide or thiophenol is required. We envision that this method may find utility in the expedient and large-scale generation of selectively protected 2-acylamido-2-deoxy-1-thio-β-D-glycopyranosides for use in the synthesis of oligosaccharides. Further, the procedure is compatible with a range of thiols and disulfides and may be extended to a general strategy for preparing a wide range of thioglycosides with both different glycons and aglycons as well as with different protecting groups at the 2-amino position.

1. Experimental

1.1. General methods

All aryl thiols and disulfides used were purchased from Aldrich. Synthetic reactions were monitored by TLC using Merck Kieselgel 60 F_{254} aluminium-backed sheets. The compounds were detected by charring with a 10% concentrated sulfuric acid in ethanol solution and by heating. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX400 at 400 MHz (100 MHz for ^{13}C) or a Varian AS500 Unity Innova spectrometer at 500 MHz (125 MHz for ^{13}C) (chemical shifts quoted relative to $CDCl_3$, CD_3OD or $(CD_3)_2SO$ where appropriate). Elemental analyses of all synthesised compounds were performed at the Simon Fraser University Analytical Facility.

1.2. General procedures for the synthesis of aryl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranosides

1.2.1. Method A. To a mixture of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride **1**.[18] (1 equiv), benzyltriethylammonium chloride (1 equiv) and the acceptor thiophenol (1.4 equiv), sufficient dichloromethane (1 volume) was added to yield a 200 mM solution of **1**. An equal volume of 1 M NaOH

was added and the resulting mixture was stirred vigorously at room temperature (18 h). After a crystalline precipitate was observed, the solid was collected by filtration and successively washed with dichloromethane, water and diethyl ether. The resultant solid was left overnight to air dry. Recrystallisation of the solid from ethanol gave the desired thioglycosides in yields ranging from 60% to 76%. 4-Nitrophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside **2**[21] and 4-tolulyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside **5**[22] are known compounds and their physical characteristics were consistent with those found in the literature. The yield reported for 4-methylumbelliferyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside **6** is for two steps.

1.2.2. Method B. To a mixture of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride **1**.[18] (1 equiv), benzyltriethylammonium chloride (1 equiv), triphenylphosphine (1 equiv) and the acceptor thiophenol (0.7 equiv), sufficient dichloromethane (1 volume) was added and the resulting mixture treated as for Method A. Recrystallisation of the solid from ethanol gave the 3-nitrophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside **9** in a yield of 62%.

1.2.3. Method C. The thiol was prepared according to the procedure of Overman et al.[19] and the reagents for the phase transfer reaction were added as in Method A. 4-Chlorophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside **7** was prepared in a yield of 49% and 4-methoxyphenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside **8** in a yield of 53%.

1.3. 2-Nitrophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (3)

^{1}H NMR (400 MHz, (CD_3OD/$(CD_3)_2SO$)) δ 8.11 (1H, dd, $J_{H3Ar–H5Ar} = 1.2$, $J_{H3Ar–H4Ar} = 7.6$, H-3_{Ar}), 7.92 (1H, dd, $J_{H4Ar–H6Ar} = 1.2$, $J_{H5Ar–H6Ar} = 8.0$, H-6_{Ar}), 7.66 (1H, ddd, $J_{H4Ar–H5Ar} = 8.0$, H-5_{Ar}), 7.39 (1H, ddd, H-4_{Ar}), 4.97 (1H, d, $J_{H1–H2} = 10.4$, H-1), 3.92 (1H, dd, $J_{H5–H6} = 1.2$, $J_{H6–H6} = 12.4$, H-6), 3.89 (1H, dd, $J_{H2–H3} \approx J_{H3–H4} = 9.6$, H-3), 3.69 (1H, dd, $J_{H5–H6} = 6.0$, H-6), 3.54 (1H, dd, H-2), 3.48–3.38 (2H, m, H-4/H-5), 1.96 (3H, s, Ac). ^{13}C NMR (100 MHz, CD_3OD/$(CD_3)_2SO$) δ 169.1 (1C, C=O), 146.2, 135.0, 134.2, 128.5, 126.0, 125.3 (6C, Ar), 84.0 (1C, C-1), 81.1, 75.3, 70.0, 60.7, 53.9 (5C, C-2/C-3/C-4/C-5/C-6), 22.9 (1C, $COCH_3$). Anal. Calcd for $C_{14}H_{18}N_2O_7S$: C, 46.92; H, 5.06; N, 7.82. Found: C, 46.83; H, 5.03; N, 7.71.

1.4. 3,4-Difluorophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (4)

^{1}H NMR (400 MHz, CD_3OD) δ 7.51 (1H, ddd, $J_{H2Ar–H6Ar} = 2.4$, $J_{H5Ar–H6Ar} = 8.4$, $J_{H6Ar–F} = 7.6$, H-6_{Ar}), 7.32 (1H, m, H-2_{Ar}), 7.20 (1H, ddd, $J_{H5Ar–F} = 8.4$, 10.8, H-5_{Ar}), 4.72 (1H, d, $J_{H1–H2} = 8.4$, H-1), 3.89 (1H, dd, $J_{H5–H6} = 1.2$, $J_{H6–H6} = 11.6$, H-6), 3.73 (1H, dd, $J_{H2–H3} = 10.0$, H-3), 3.67 (1H, ddd, $J_{H4–H5} = 9.6$, $J_{H5–H6} = 4.4$, H-5), 3.44 (1H, dd, H-2), 3.34–3.31 (2H, m, H-4/H-6), 2.00 (3H, s, Ac). ^{13}C NMR (100 MHz, CD_3OD) δ 173.6 (1C, C=O), 151.3 (1C, dd, $J_{C–F} = 11$, 244 Hz, C-3_{Ar}), 132.0 (1C, d, $J_{C–F} = 308$ Hz, C-4_{Ar}), 132.0 (1C, d, $J_{C–F} = 13$ Hz, C-1_{Ar}), 129.8 (1C, C-6_{Ar}), 121.9 (1C, d, $J_{C–F} = 18$ Hz, C-5_{Ar}), 118.5 (1C, d, $J_{C–F} = 18$ Hz, C-2_{Ar}), 88.1 (1C, C-1), 82.2, 77.4, 71.9, 62.9, 56.1 (5C, C-2/C-3/C-4/C-5/C-6), 23.0 (1C, Ac). Anal. Calcd for $C_{14}H_{17}F_2NO_5S$: C, 48.13; H, 4.90; N, 4.01. Found: C, 48.39; H, 5.01; N, 4.15.

1.5. 4-Methylumbelliferyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (6)

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.91 (1H, d, $J_{H2–NH} = 9.2$, NH), 7.66 (1H, d, $J_{H5Ar–H6Ar} = 8.4$, H-5_{Ar}), 7.38 (1H, s, H-8_{Ar}), 7.33 (1H, d, H-6_{Ar}), 6.34 (1H, s, H-3_{Ar}), 5.20 (2H, br s, OH), 4.91 (1H, d, $J_{H1–H2} = 10.4$, H-1), 4.70 (1H, br s, OH), 3.74–3.63 (2H, br s), 3.47-3.42 (3H, br s), 3.16 (1H, br s), 2.40 (3H, s, CH_3), 1.82 (3H, s, Ac). ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 169.1, 159.5 (2C, C=O), 153.0, 152.9, 141.4, 125.3, 123.6, 117.2, 114.5, 113.4 (8C, Ar), 84.9 (1C, C-1), 81.2, 75.2, 70.1, 60.8, 54.0 (5C, C-2/C-3/C-4/C-5/C-6), 23.0 (1C, $COCH_3$), 17.9 (1C, CH_3). Anal. Calcd for $C_{18}H_{21}NO_7S$: C, 54.67; H, 5.35; N, 3.54. Found: C, 54.52; H, 5.12; N, 3.34.

1.6. 4-Chlorophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (7)

^{1}H NMR (400 MHz, CD_3OD) δ 7.49, 7.29 (4H, AA′BB′, Ar), 4.75 (1H, d, $J_{H1–H2} = 10.4$, H-1), 3.88 (1H, dd, $J_{H5–H6} = 2.0$, $J_{H6–H6} = 12.4$, H-6), 3.88 (1H, dd, $J_{H2–H3} \approx J_{H3–H4} = 10.0$, H-3), 3.70 (1H, dd, $J_{H5–H6} = 5.6$, H-6), 3.46 (1H, dd, H-2), 3.38–3.32 (2H, m, H-4/H-5), 1.99 (3H, s, Ac). ^{13}C NMR (100 MHz, CD_3OD) δ 173.5 (1C, C=O), 134.5, 134.4, 133.9, 129.9 (4C, Ar), 88.1 (1C, C-1), 82.2, 77.4, 71.9, 62.9, 56.2 (5C, C-2/C-3/C-4/C-5/C-6), 23.0 (1C, Ac). Anal. Calcd for $C_{14}H_{18}ClNO_5S$: C, 48.34; H, 5.22; N, 4.03. Found: C, 48.55; H, 5.24; N, 4.25.

1.7. 4-Methoxyphenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (8)

^{1}H NMR (400 MHz, CD_3OD) δ 7.47, 6.86 (4H, AA′BB′, Ar), 4.58 (1H, d, $J_{H1–H2} = 10.4$, H-1), 3.85 (1H, dd, $J_{H5–H6} = 2.4$, $J_{H6–H6} = 12.4$, H-6), 3.78 (3H, s, OCH_3), 3.67 (1H, dd, $J_{H2–H3} \approx J_{H3–H4} = 10.4$, H-3), 3.66 (1H, dd, $J_{H5–H6} = 5.6$, H-6), 3.43 (1H, dd, H2), 3.32 (1H, m, H-4), 3.23 (1H, ddd, $J_{H4–H5} = 9.6$, H-5), 2.01 (3H, s, Ac). ^{13}C NMR (100 MHz, CD_3OD) δ 173.5 (1C, C=O), 161.4, 136.0, 125.2, 115.4 (4C, Ar),

89.1 (1C, C-1), 82.1, 77.6, 72.0, 63.0, 56.4, 55.8 (6C, C-2/C-3/C-4/C-5/C-6/OCH_3), 23.0 (1C, Ac). Anal. Calcd for $C_{15}H_{21}NO_6S$: C, 52.46; H, 6.16; N, 4.08. Found: C, 52.56; H, 6.09; N, 4.21.

1.8. 3-Nitrophenyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (9)

^{1}H NMR (400 MHz, CD_3OD) δ 8.37 (1H, s, H-2_{Ar}), 8.10 (1H, d, $J_{H4Ar–H5Ar} = 6.8$, H-4_{Ar}), 7.87 (1H, d, $J_{H5Ar–H6Ar} = 6.4$, H-6_{Ar}), 7.54 (1H, dd, H-5_{Ar}), 4.88 (1H, d, $J_{H1–H2} = 8.4$, H-1), 3.91 (1H, dd, $J_{H5–H6} = 2.0$, $J_{H6–H6} = 10.0$, H-6), 3.81 (1H, dd, $J_{H2–H3} = 8.0$, H-3), 3.71 (1H, ddd, $J_{H4–H5} = 9.6$, $J_{H5–H6} = 2.0$, H-5), 3.50 (1H, dd, H-2), 3.41–3.37 (2H, m, H-4/H-6), 2.00 (3H, s, Ac). ^{13}C NMR (100 MHz, CD_3OD) δ 173.6 (1C, C=O), 149.7, 138.6, 137.7, 130.9, 126.0, 122.8 (6C, Ar), 87.5 (1C, C-1), 82.3, 77.3, 71.8, 62.8, 56.0 (5C, C-2/C-3/C-4/C-5/C-6), 23.0 (1C, Ac). Anal. Calcd for $C_{14}H_{18}N_2O_7S$: C, 46.92; H, 5.06; N, 7.82. Found: C, 46.79; H, 5.01; N, 7.75.

Acknowledgments

We thank the Natural Science and Engineering Research Council (NSERC) and the Canadian Protein Engineering Networks of Centres of Excellence for funding. D.J.V. is supported by the Canada Research Chairs Program as a Tier II Canada Research Chair in Chemical Glycobiology. Also M.S.M. would like to thank NSERC and the Michael Smith Foundation for Health Research for fellowships.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2005.12.009.

References

1. Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020.
2. Driguez, H. *ChemBioChem* **2001**, *2*, 311–318.
3. Bousquet, E.; Spadaro, A.; Pappalardo, M. S.; Bernardini, R.; Romeo, R.; Panza, L.; Ronisvalle, G. *J. Carbohydr. Chem.* **2000**, *19*, 527–541.
4. Thayer, D. A.; Yu, H. N.; Galan, M. C.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2005**, *44*, 4596–4599.
5. Roy, R.; Mateo-Hernandez, F.; Santoyo-Gonzales, F. *J. Org. Chem.* **2000**, *65*, 8743–8746.
6. Pazur, J. H. *Adv. Carbohydr. Chem. Biochem.* **1981**, *39*, 405–447.
7. Boons, G.-J. *Glycoscience* **2001**, *1*, 551–581.
8. Codee, J. D. C.; Litjens, R. E. J. N.; Van den Bos, L. J.; Overkleeft, H. S.; van der Marel, G. A. *Chem. Soc. Rev.* **2005**, *34*, 769–782.
9. Oscarson, S. *Carbohydr. Chem. Biol.* **2000**, *1*, 93c116.
10. Garegg, P. J. *Adv. Carbohydr. Chem. Biochem.* **1997**, *52*, 179–266.
11. Macauley, M. S.; Stubbs, K. A.; Vocadlo, D. J. *J. Am. Chem. Soc.* **2005**, *127*, 17202–17203.
12. Cetinbas, N.; Macauley, M. S.; Stubbs, K. A.; Drapala, R.; Vocadlo, D. J. *Biochemistry*, in press.
13. Dong, D. L.; Hart, G. W. *J. Biol. Chem.* **1994**, *269*, 19321–19330.
14. Tropper, F. D.; Andersson, F. O.; Grand-Maitre, C.; Roy, R. *Carbohydr. Res.* **1992**, *229*, 149–154.
15. Tropper, F. D.; Andersson, F. O.; Grand-Maitre, C.; Roy, R. *Synthesis* **1991**, 734–736.
16. Carriere, D.; Meunier, S. J.; Tropper, F. D.; Cao, S.; Roy, R. *J. Mol. Catal. A: Chem.* **2000**, *154*, 9–22.
17. Cao, S.; Meunier, S. J.; Andersson, F. O.; Letellier, M.; Roy, R. *Tetrahedron: Asymmetry* **1994**, *5*, 2303–2312.
18. Roy, R.; Tropper, F. D. *Can. J. Chem.* **1991**, *69*, 817–821.
19. Overman, L. E.; Smoot, J.; Overman, J. D. *Synthesis* **1974**, 59–60.
20. Danehy, J. P.; Parameswaran, K. N. *J. Org. Chem.* **1968**, *33*, 568–572.
21. Jones, C. S.; Shah, R. H.; Kosman, D. J.; Bahl, O. *Carbohydr. Res.* **1974**, *36*, 241–245.
22. Tsai, C. S.; Reyes-Zamora, C.; Otson, R. *Biochim. Biophys. Acta* **1971**, *250*, 172–181.