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Facile Preparation of Glycosyl Donors for Oligosaccharide Synthesis: 2-Azido-2-deoxyhexopyranosyl Building Blocks

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Abstract: Facile routes to the 2-azido-2-deoxy-1-thioglycosides **6**, **7**, **15**, and **18** and of the 2-azido-2-deoxy-4-pentenoglycoside **11**, are described. These are useful intermediates for the synthesis of oligo-saccharides containing α-D-2-amino-2-deoxy (or 2-acetamido-2-deoxy) hexosyl residues in the *galacto-*, *gluco-*, and *manno-* series.

INTRODUCTION

α-Glycosidically linked 2-amino- or 2-acetamido-2-deoxy-D-hexopyranosyl residues (*galacto-*, *gluco-*, or *manno-*) occur in a large number of carbohydrate antigens and glycoproteins. Due to the biological importance of these materials, considerable efforts have been expended in finding efficient routes to such oligosaccharide structures.[1]

Glycosidation using a 2-acetamido-2-deoxy-D-glucopyranosyl compound or the corresponding *galacto-* compound with a suitable leaving group at C-1 as the glycosyl donor will inevitably yield either a 1,2-oxazoline or a β-D-linked glycoside, due to participation at the anomeric centre by the amide group. In order to circumvent this, a masked amino function, in the form of a 2-azido-2-deoxy group has been found most useful. Several multistep routes to such starting materials have been described.[1-11] Other non-participating masked amino functions e.g. imino compounds have also been proposed.[11-13]

In contemporary block synthesis of oligosaccharides, considerable attention has been paid to the use of 4-pentenyl[14] and thio glycosides[15-16] as glycosyl donors. Based on recent work by Vasella and coworkers[17] involving a diazo transfer reaction, we now present facile routes to some 2-azido-2-deoxy thioglycosides and also to 4-pentenyl 2-azido-2-deoxy-β-D-glucopyranoside which with suitable protection in the 3,4,6-positions are useful synthons for oligosaccharide synthesis. The donors obtained by the present method are anomerically pure.

RESULTS AND DISCUSSION

2-Acetamido-1,3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranose (**1**, Scheme 1) was reacted with phenyl- or ethylthiotrimethylsilane in the presence of zinc iodide[18,19] to give compounds **2** (91%)

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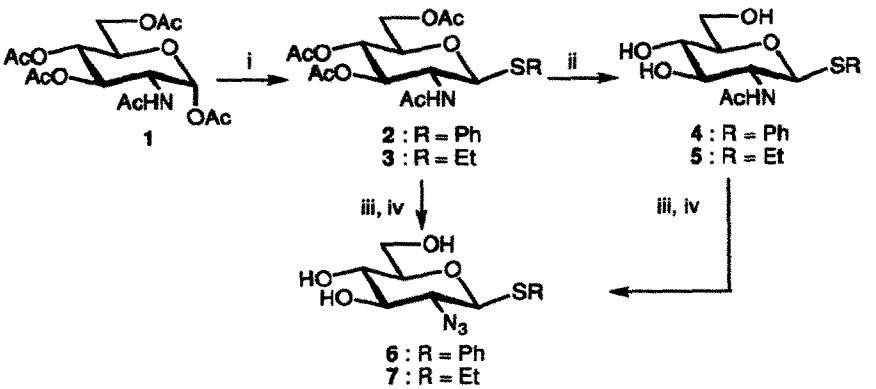
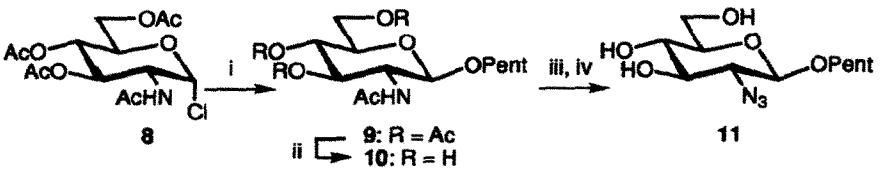
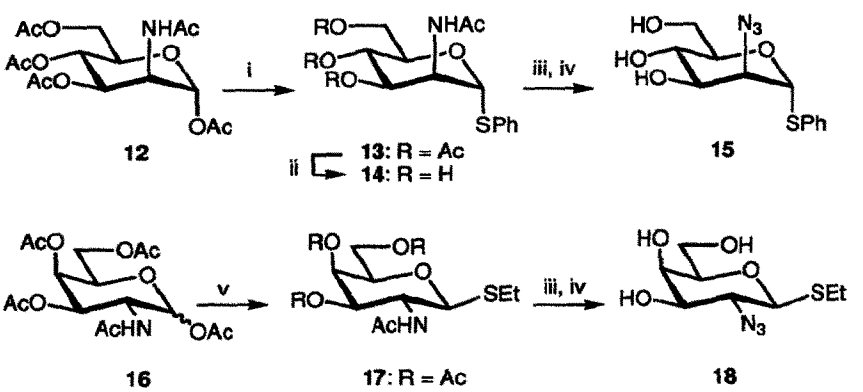


Scheme 1: (i) $RSSiMe_3$, ZnI_2, $ClCH_2CH_2Cl$, 8h, 50 °C; (ii) MeONa, MeOH; (iii) NaOH 1M, 15h, reflux; (iv) N_3OTf, DMAP, MeOH, 12h.



Scheme 2: (i) $HgBr_2$, n-pentenol, CH_2Cl_2, 10h; (ii) MeONa, MeOH; (iii) NaOH 1M, 15h, reflux; (iv) N_3OTf, DMAP, MeOH, 12h



Scheme 3: (i) $PhSSiMe_3$, ZnI_2, $ClCH_2CH_2Cl$, 8h, 50 °C; (ii) MeONa, MeOH; (iii) NaOH 1M, 15h, reflux; (iv) N_3OTf, DMAP, MeOH, 12h; (v) $EtSSiMe_3$, ZnI_2, $ClCH_2CH_2Cl$, 8h, 50 °C.

and **3** (86%) respectively. It is important that the silane and zinc iodide are added simultaneously after the solution has been warmed to 50 °C to minimize the formation of a byproduct in which the 6-*O*-acetyl group had been replaced by a thioalkyl (aryl) group. In the synthesis of **2** this product was shown to be phenyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-6-thioethyl-1-thio-β-D-glucopyranoside.[20] Compounds **2** and **3** were deacetylated to give the corresponding triols **4** and **5**. Compound **2** was also *N*-and *O*-deacetylated simultaneously and the product was treated with trifluoromethanesulfonyl azide and *N,N*-dimethylaminopyridine in dichloro-methane to yield the azido compound **6** (78%). Treatment of **5** with the same reagents yielded **7** (85% from **3**).

The glycosyl chloride **8** (Scheme 2) was used in a Helferich type glycosidation to give the 4-pentenyl glycoside **9** (85%) which was de-*O*-acetylated to give **10**, which was de-*N*-acetylated and then treated with trifluoromethanesulfonyl azide and *N,N*-dimethylaminopyridine in dichloromethane to yield **11** (79%).

The sequence **1** to **7** was repeated in the mannose series. Thus the tetraacetate **12** (Scheme 3) was routed *via* the phenyl 1-thioglycoside **13** (95%) and triol **14** into the the azido mannoside **15** (57%). A route in the galactose series similar to **1** to **6** converted tetraacetate **16** *via* **17** (83%) and then proceeded directly without isolating the intermediate acetamido triol sugar into the azido galactoside **18** (62%).

The above syntheses thus give ready access to the 2-azido-2-deoxyglycosides **6, 7, 11, 15,** and **18,** which are convenient synthons for oligosaccharide synthesis. The overall yields of these product from the starting materials **1, 8, 12, 16** ranged from 51 to 79%.

EXPERIMENTAL

General methods. All compounds, reagents and solvents were dried. Extraction: organic layers concentrated *i.v.* at or below 40°C. Qual.TLC: 0.25 mm precoated silica-gel plates (MERCK, silica-gel $60F_{254}$), HPTLC: precoated silica-gel plates (MERCK, silica-gel $60F_{254}$); detection by UV and / or spraying the plates with 8% aq. H_2SO_4 soln. followed by heating at ca 250°C. Optical rotations: recorded at room temperature with a Perkin-Elmer 241 polarimeter. Flash Chromatography (FC) : MERCK 60 (0.040-0.063 mm). ^1H- and ^{13}C-NMR Spectra: performed on a JEOL JNM-GSX 270, temp 25°C. Chemical shifts in ppm relative to TMS as internal standard. The 0.4 M TfN_3-solution was prepared according to Vasella et. al. [17] The precautions given by these authors should be noted.

Phenyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (2). A suspension of 1,3,4,6-tri-O-acetyl-2-acetamido-2-deoxy-α-D-glucopyranose(**1**) (1g, 2.57 mmol) in 1,2-dichloroethane (15 ml) was heated to 50°C before ZnI_2 (5.74g, 17.98 mmol) and then phenylthiotrimethylsilane (1.946 ml, 10.28 mmol) was added dropwise. After 8 h the mixture was diluted with CH_2Cl_2, filtered through Celite and washed with sat. aq. $NaHCO_3$ soln. and H_2O. The combined organic phases were dried (Na_2SO_4) and concentrated. FC (toluene:EtOAc 1:3) of the residue afforded **2** as white crystals (91%, 1.027 g, 2.34 mmol.). R_f = 0.37 (toluene:EtOAc 1:3). Recrystallization (EtOAc:light petroleum). m.p. = 210-212°C. $[\alpha]_D$ = -24 (*c* 1.0, $CHCl_3$). ^1H NMR

($CDCl_3$): p = 1.90, 1.91, 1.95, 1.99 (4s, 4 x $COCH_3$), 3.69 (m, 1H, H-5), 3.97 (q, H-2), 4.04.4.15 (m, 2H, 2 x H-6), 4.84 (d, 1H, $J_{1\text{-}2}$ = 10.2 Hz, H-1), 4.97, 5.20 (2t, 2H, H-3, H-4), 6.13 (d, 1H, $J_{NH\text{-}2}$ = 9.2 Hz, NH), 7.20-7.23 (m, 3H, ArH), 7.40-7.44 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$): p = 20.48 ($COCH_3$), 20.66 (2C, 3x$COCH_3$), 23.2 ($NHCOCH_3$), 53.12 (C-2), 62.32 (C-6), 68.45, 73.57, 75.51, 86.42 (C-1), 127.89, 128.80, 132.20, 132.55 (4x ArC), 169.30, 170.20, 170.57,170.87 (4 x $COCH_3$). *Anal.* Calcd for $C_{20}H_{25}O_8NS$: C, 54.66%; H, 5.73%; N, 3.19%. Found: C, 54.82%; H, 5.76%; N, 3.15%.

Ethyl 2-Acetamido-3,4,6-tetra-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (3): As described for **2**, **1** (1g, 2.57 mmol) was treated with ZnI_2 (5.74g, 17.98 mmol) and ethylthiotrimethylsilane (1.6 ml, 10.13 mmol). FC (toluene:EtOAc 1:3) gave **3** (86%, 0.864 g, 0.22 mmol) as white crystals. R_f = 0.28 (toluene:EtOAc 1:3). Recrystallization (EtOAc:light petroleum). m.p. = 194-196°C. $[\alpha]_D$ = -42 (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$): d = 1.27 (t, 3H, *J* = 7.3 Hz, SCH_2CH_3), 1.98, 2.03, 2.04, 2.08 (4s, 12H, 4 x $COCH_3$), 2.68-2.80 (m, 2H, SCH_2CH_3), 3.75 (ddd, $J_{4\text{-}5}$ =9.9 Hz, $J_{5\text{-}6}$ = 5.1 Hz, $J_{5\text{-}6}$ = 2.6 Hz, H-5), 4.04-4.16 (m, 2H, H-2, H-6), 4.25 (dd, 1H, $J_{6\text{-}6}$ = 12.1 Hz, H-6), 4.67 (d, 1H, $J_{1\text{-}2}$ = 10.2 Hz, H-1), 5.08, 5.24 (2t, 2H, H-3, H-4), 6.15 (d, 1H, *J* = 9.2 Hz, NH). ^{13}C NMR ($CDCl_3$): d = 14.71 (SCH_2CH_3), 20.52 ($COCH_3$), 20.63 (2 x $COCH_3$), 23.17 ($NHCOCH_3$), 24.09 (SCH_2CH_3), 53.16 (C-2), 62.3 (C-6), 68.51 (C-5), 73.73, 75.68, 84.16 (C-1), 169.24, 170.34, 170.61, 170.86 (4 x $COCH_3$). *Anal.* Calcd for $C_{16}H_{25}O_8NS$: C, 49.09%; H, 6.44%; N, 3.58%. Found: C, 49.10%; H, 6.35%; N, 3.58%.

Phenyl 2-Acetamido- 2-deoxy-1-thio-β-D-glucopyranoside (4). To a solution of **2** (2.74g, 6.20 mmol) in MeOH (20 ml) a catalytic amount of 1 M NaOMe soln. was added. After 3 h at r.t. the mixture was neutralized with Dowex 50 (H^+), filtered and concentrated to yield **4** quantitatively. Rf = 0.33 (EtOAc:MeOH 6:1). m.p = 196-199°C. ^1H NMR (CD_3OD): d = 1.96 (s, 1H, $COCH_3$), 3.27-3.36 (m, 2H), 3.44 (t, 1H), 3.63 (dd, 1H, $J_{5\text{-}6}$ = 5.5 Hz, $J_{6\text{-}6}$ = 12.1 Hz, H-6), 3.73 (t, 1H), 3.84 (dd, 1H, $J_{5\text{-}6}$ = 2.5 Hz, H-6), 4.75 (d, $J_{1\text{-}2}$ = 10.6 Hz, H-1), 7.21-7.28 (m, 3H, ArH), 7.44-7.48 (m, 2H, ArH). ^{13}C NMR (CD_3OD): d = 22.95 ($NHCOCH_3$), 56.32 (C-2), 62.89 (C-6), 71.89, 77.43, 82.13, 88.35 (C-1), 128.21, 129.91, 132.18, 135.88 (4 x ArC), 173.58 ($COCH_3$).

Ethyl 2-Acetamido-2-deoxy-1-thio-β-D-glucopyranoside (5). As described for **4**, a solution of **3** (0.70 g, 1.179 mmol) in MeOH (10 ml) was treated with a catalytic amount of 1 M NaOMe soln. to give quantitatively **5** as a solid. R_f = 0.18 (EtOAc:MeOH 7:1). ^1H NMR (CD_3OD): d = 1.20 (t, 3H, *J* = 7.5 Hz, SCH_2CH_3), 1.93 (s, 3H, $COCH_3$), 2.60-2.75 (m, 2H, SCH_2CH_3), 3.20-3.43 (m, 3H), 3.62 (dd, 1H, $J_{5\text{-}6}$ = 5.5 Hz, $J_{6\text{-}6}$ = 12.1 Hz, H-6), 3.70 (t, 1H, H-2)), 3.82 (dd, 1H, $J_{5\text{-}6}$ = 2.2 Hz, H-6), 4.45 (d, $J_{1\text{-}2}$ = 10.3 Hz, H-1). ^{13}C NMR (CD_3OD): d = 14.68 (SCH_2CH_3), 23.02($NHCOCH_3$), 24.03 (SCH_2CH_3), 56.35 (C-2), 62.87 (C-6), 71.94, 77.53, 82.27 86.05 (C-1), 173.31 ($COCH_3$).

Phenyl 2-Azido-2 deoxy-1-thio-β-D-glucopyranoside (6). 1) A solution of **2** (0.194 g, 0.439 mmol) in 1 M NaOH (30 ml) was refluxed at 120°C for 15 h. The reaction mixture was cooled to room temperature, neutralized with 1 M HCl and concentrated. FC of the residue using a short silica-gel column (EtOAc:MeOH:H_2O 7:2:1) gave the free amine, which was dissolved in MeOH (30 ml) and treated with 4-(dimethylamino)pyridine (DMAP) (0.06 g, 0.47 mmol). A 0.4 M TfN_3 solution in

CH_2Cl_2 (2.85 ml, 1.14 mmol) was then added dropwise. The reaction was stirred at room temperature under N_2 for 12h. The mixture was concentrated, dissolved in EtOAc and extracted with H_2O. The combined aq. layers was thoroughly extracted with EtOAc. The combined organic phases were dried (Na_2SO_4) and concentrated. FCEtOAc of the residue afforded **6** (87%, 0.114 g, 0.382 mmol) as white crystals. 2). Under identical treatment of **4** gave **6** in 78%. R_f = 0.32 (EtOAc). Recrystallization (EtOAc:light petroleum). m.p. = 112-114°C. $[\alpha]_D$ = -29 (*c* 1.0, MeOH). ^1H NMR (CD_3OD): d = 3.06 (t, H-2), 3.19-3.32 (m, 3H), 3.58 (dd, 1H, $J_{5\text{-}6}$ = 3.7 Hz, $J_{6\text{-}6}$ = 12.1 Hz, H-6), 3.77 (br.d, H-6), 4.44 (d, 1H, $J_{1\text{-}2}$ = 10.3 Hz, H-1), 7.20-7.22 (m, 3H, ArH), 7.46-7.49 (m, 2H, ArH). ^{13}C NMR (CD_3OD): d = 62.54 (C-6), 66.89, 70.97, 78.24, 81.89, 87.11 (C1), 128.94, 129.94, 133.45, 133.64 (4 x ArC). *Anal.* Calcd for $C_{12}H_{15}O_4N_3S$: C, 48.48; H, 5.08; N, 14.13. Found C, 48.54; H, 5.08; N, 14.25.

Ethyl 2-Azido-2-deoxy-1-thio-β-D-glucopyranoside (7). As described for **6**, **5** (0.30 g, 1.13 mmol) was treated with 1M NaOH to give the free amine and then DMAP (148 mg, 1.21 mmol) and a 0.4 M TfN_3-solution in CH_2Cl_2 (7.35 ml, 2.94 mmol). FC (EtOAc) afforded **7** (85%, 0.240 g, 0.96 mmol) as white crystals. R_f = 0.34 (EtOAc). Recrystallization (EtOAc:light petroleum). m.p. = 103-104°C. $[\alpha]_D$ = -68 (*c* 1.0, MeOH). ^1H NMR (CD_3OD): d = 1.29 (t, 3H, *J* = 7.5 Hz, SCH_2CH_3), 2.68-2.84 (m, 2H, SCH_2CH_3), 3.14-3.37 (m, 4H), 3.65 (dd, 1H, $J_{5\text{-}6}$ = 5.1 Hz, $J_{6\text{-}6}$ = 12.1 Hz, H-6), 3.84 (dd, 1H, $J_{5\text{-}6}$ = 2.2 Hz, H-6), 4.38 (d, 1H, $J_{1\text{-}2}$ = 10.3 Hz, H-1). ^{13}C NMR (CD_3OD): d = 15.41 (SCH_2CH_3), 25.14 (SCH_2CH_3), 62.62 (C-6), 67.92, 71.21, 78.21, 81.86, 85.08 (C-1). *Anal.* Calcd for $C_8H_{15}O_4N_3S$: C, 38.54; H, 6.06; N, 16.86. Found : C, 38.64; H, 6.01; N, 17.01.

4-Pentenyl 2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (9).
To a suspension of chloride **8** (1 g, 2.74 mmol), 4-*n* pentenol (0.566 ml, 5.48 mmol) and drierite in CH_2Cl_2 (15 ml) was added $HgBr_2$ (1.975 g, 5.48 mmol). The reaction was stirred for 12 h at r.t. The mixture was diluted with CH_2Cl_2 (20 ml), filtered through Celite and washed with sat. aq. $NaHCO_3$ soln. and H_2O. The combined organic phases were dried (Mg_2SO_4) and concentrated. FC (toluene:EtOAc 1:2) yielded **9** (85%, 965 mg, 2.33 mmol) as a white solid. R_f = 0.37(toluene:EtOAc 1:3). Recrystallization (EtOAc:light petroleum). m.p. = 133-134°. $[\alpha]_D$ = -15 (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$): d = 1.61-1.73 (m, 2H, 2 x Pent.H), 1.95-2.13 (m, 14H, 4 x $COCH_3$, 2 x Pent.H), 3.50 (dt, 1H, *J* = 9.5 Hz, *J* = 6.8 Hz, Pent.H), 3.72 (ddd, 1H, $J_{4\text{-}5}$ = 9.9 Hz, *J* = $_{5\text{-}6}$ = 4.8 Hz, $J_{5\text{-}6}$ = 2.2 Hz, H-5), 3.80-3.91 (m, 2H), 4.13 (dd, 1H, $J_{5\text{-}6}$ = 2.2 Hz, $J_{6\text{-}6}$ =12.1 Hz, H-6), 4.27 (dd, 1H, H-6), 4.69 (d, 1H, *J* = 8.4 Hz, H-1), 4.95-5.10 (m, 3H), 5.32 (t, 1H), 5.79 (ddt, 1H, *J* =16.8 Hz, *J* =10.3 Hz, *J* = 6.6 Hz, Pent.H), 5.89 (d, 1H, $J_{NH\text{-}2}$ = 8.8 Hz, H-2). ^{13}C NMR ($CDCl_3$): d = 20.56 ($COCH_3$), 20.66 (2 x $COCH_3$), 23.23 ($NHCOCH_3$), 28.52, 29.84 (2 x Pent.C), 54.69 (C-2), 62.16 (C-6), 68.72, 69.01, 71.60, 72.33, 100.64 (C-1), 114.91, 137.84 (2 x Pent.C), 169.35, 170.19, 170.68, 170.78 (4 x $COCH_3$). *Anal.* Calcd for $C_{19}H_{29}O_9N$: C, 54.93%; H, 7.04%; N, 3.37%. Found: C, 54.76%; H, 6.93%; N, 3.37%.

4-Pentenyl 2-Acetamido-2-deoxy-β-D-glucopyranoside (10). As described for **4**, a solution of **9** (900 mg, 2.17 mmol) in MeOH (10 ml) was treated with a catalytic amount of 1 M NaOMe soln. to give **10** (97%, 608 mg, 2.21mmol) as crystals. Rf = 0.18 (EtOAc:MeOH 6:1). m.p. = 186-188°.

^{1}H NMR (CD_3OD): d = 1.56-1.66 (m, 2H, 2 x Pent.H), 1.95 (s, 3H, $COCH_3$), 2.04-2.13 (m, 2H, 2 x Pent.H), 3.23-3.50 (m, 4h), 3.58-3.69 (m, 2H), 3.83-3.91 (m, 2H), 4.37 (d, 1H, *J* = 8.4 Hz, H-1), 4.90-5.02 (m, 2H, 2 x Pent.H), 5.80 (ddt, 1H, *J* = 17.2 Hz, *J* =10.3 Hz, *J* = 6.6 Hz, Pent.H). ^{13}C NMR (CD_3OD): d = 22.99 ($NHCOCH_3$), 29.98, 31.16 (2 x Pent.C), 57.42 (C-2), 62.79, 69.75, 72.12, 76.01, 77.90, 102.69 (C-1), 115.21, 139.41 (2 x Pent.C), 171.87 ($COCH_3$).

4-Pentenyl 2-Azido-2-deoxy-β-D-glucopyranoside (11). As described for **6, 10** (300 mg, 1.04 mmol) was treated with 1 M NaOH to give the free amine and then DMAP (136 mg, 1.11 mmol) and 0.4 M TfN_3-soln in CH_2Cl_2 (6.75 ml, 2.7 mmol). FC (EtOAc) afforded **11** (79%, 224 mg, 0.82mmol) as glassy solid. R_f = 0.37 (EtOAc). $[\alpha]_D$ = -10 (*c* 1.0, MeOH). ^{1}H NMR (CD_3OD): d = 1.64-1.74 (m, 2H, 2 x Pent.H), 2.12-2.20 (m, 2H, 2 x Pent.H), 3.14 (t, 1H, H-2), 3.20-3.35 (m, 4H), 3.55 (dt, J =9.9 Hz, J = 6.6 Hz, Pent.H), 3.66 (dd, 1H, J_{5-6} = 5.3 Hz, J_{6-6} =12.1 Hz, H-6), 3.84 (dd, 1H, J_{5-6} = 2.2 Hz, H-6), 3.94 (dt, J =9.9 Hz, J = 6.2 Hz, Pent.H), 4.31 (d, J_{1-2} = 7.7 Hz, H-1), 4.92-5.05 (m , 2H, 2 x Pent.H), 5.82 (ddt, 1H, *J* = 17.2 Hz, *J* =10.3 Hz, *J* = 6.6 Hz, Pent.H). *Anal.* Calcd for $C_{11}H_{19}O_5N_3$: C, 48.43%; H, 7.01%; N, 15.38%. Found: C, 48.24%; H, 6.91%; N, 15.29%.

Phenyl 2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-α-D-mannopyranoside (13). As described for **2, 12** (1 g, 2.57 mmol) was treated with ZnI_2 (5.74g, 17.98 mmol) and phenylthiotrimethylsilane (1.946 ml, 10.28 mmol). FC (toluene:EtOAc 2:3) yielded **13** (95%, 1.072 g, 2.44 mmol) as a white foam. R_f = 0.37 (toluene:EtOAc 1:3). $[\alpha]_D$ = 86 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): d = 1.99, 2.02, 2.03, 2.07 (4s, 12H, 4 x $COCH_3$), 4.05 (dd, 1H, J_{5-6} = 2.2 Hz, J_{6-6} = 12.1 Hz, H-6), 4.29 (dd, 1H, J_{5-6} = 6.6 Hz, H-6), 4.61 (ddd, 1H, J_{4-5} = 9.9 Hz, H-5), 4.87 (m, 1H, H-2), 5.18 (dd, 1H, J_{3-4} = 10.3 Hz, H-4), 5.31 (dd, 1H, J_{2-3} = 4.4 Hz, H-3), 5.44 (d, 1H, J_{1-2} = 1.1 Hz, H-1), 6.56 (d, 1H, J_{NH-2} = 8.8 Hz, NH), 7.28-7.31 (m, 3H, ArH), 7.46-7.49 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$): d = 20.39 ($COCH_3$), 20.46 (2 x $COCH_3$), 22.92 ($NHCOCH_3$), 51.11 (C-2), 62.54 (C-6), 66.32, 68.95, 69.30, 86.51 (C-1), 127.75, 128.89, 131.75, 132.64 (4 x ArC), 169.64, 169.80, 169.88, 170.34 (4 x $COCH_3$). Anal. Calcd for $C_{20}H_{25}O_8NS$: C, 54.66%; H, 5.73%; N, 3.19%. Found: C, 55.27%; H, 5.74%; N, 2.98%.

Phenyl 2-Acetamido-2-deoxy-1-thio-α-D-mannopyranoside (14). As described for **3**, a solution of **13** (900 mg, 2.05 mmol) in MeOH (15 ml) was treated with a catalytic amount 1 M NaOMe to give **14** quantitatively. R_f = 0.28 (EtOAc:MeOH 6:1). m.p. =101-103°C. ^{1}H NMR (CD_3OD): d = 1.96 (s, 1H, $COCH_3$), 3.27-3.36 (m, 2H), 3.44 (t, 1H), 3.63 (dd, 1H, J_{5-6} = 5.5 Hz, J_{6-6} = 12.1 Hz, H-6), 3.73 (t, 1H), 3.84 (dd, 1H, J_{5-6} = 2.5 Hz, H-6), 4.75 (d, J_{1-2} = 10.6 Hz, H-1), 7.21-7.28 (m, 3H, ArH), 7.44-7.48 (m, 2H, ArH). ^{13}C NMR (CD_3OD): d = 22.95 ($NHCOCH_3$), 56.32 (C-2), 62.89 (C-6), 71.89, 77.43, 82.13, 88.35 (C-1), 128.21, 129.91, 132.18, 135.88 (4 x ArC), 173.58 ($COCH_3$).

Phenyl 2-Azido-2-deoxy-1-thio-α-D-mannopyranoside (15). As described for **5, 14** (0.470 g, 1.50 mmol) was treated with 1 M NaOH (50 ml) to yield the free amine and then DMAP (0.197g, 1.605 mmol) and a 0.4 M solution of TfN_3 in CH_2Cl_2 (9.76 ml, 3.90 mmol). FC (EtOAc) afforded **15** (57%, 0.255g, 0.855 mmol) as a colorless oil. R_f = 0.55 (EtOAc). $[\alpha]_D$ = 113 (*c* 1.0, MeOH). ^{1}H NMR (CD_3OD): d = 3.67-3.77 (m, 2H, H-4, H-6), 3.80 (dd, 1H, J_{5-6} = 2.2 Hz, J_{6-6} = 12.1 Hz, H-6), 3.96 (dd,

J_{2-3} = 3.7 Hz, J_{3-4} = 9.2 Hz,H-3), 4.05 (ddd, J_{4-5} = 9.5 Hz, J_{5-6} = 5.5 Hz, H-5), 4.14 (dd, J_{1-2} = 1.6 Hz, H-2), 5.48 (br.d, H-1). ^{13}C NMR (CD_3OD): d = 62.38 (C-6), 66.99, 68.75, 73.04, 75.71, 87.85 (C-1), 128.81, 130.13, 133.15, 135.17 (4 x ArC). *Anal.* Calcd for $C_{12}H_{15}O_4N_3S$: C, 48.47%; H, 5.08%; N, 14.13%. Found: C, 48.21%; H, 5.09%; N, 14.14%.

Ethyl 2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-galactopyranoside (17). As described for **2**, **16** (1.0 g, 2.57 mmol) was treated with ZnI_2 (5.74g, 17.98 mmol) and ethylthiotrimethylsilane (1.6 ml, 10.13 mmol). FC (toluene:EtOAc 1:3) yielded **17** (83%, 834 mg, 2.13 mmol) as crystals. R_f = 0.30 (toluene:EtOAc 1:4). Recrystallization (EtOAc:light petroleum). m.p. = 191-194°C. $[\alpha]_D$ = -34 (*c* 1.0, MeOH). ^1H NMR ($CDCl_3$): d = 1.29 (t, *J* = 7.5 Hz, SCH_2CH_3), 1.98, 2.00, 2.05, 2.16 (4s, 12H, 4 x $COCH_3$), 2.68-2.80 (m, 2H, SCH_2CH_3), 3.99 (t, 1H), 4.08-4.28 (m, 3H), 4.73 (d, J_{1-2} = 10.2 Hz, H-1), 5.21 (dd, J_{2-3} = 10.6 Hz, J_{3-4} = 3.1 Hz, H-3), 5.40 (d, H-4), 6.40 (d, J_{NH-2} = 9.2 Hz, NH).
^{13}C NMR ($CDCl_3$): d = 14.68 (SCH_2CH_3), 20.52 (3 x $COCH_3$), 23.14 ($NHCOCH_3$), 24.14 (SCH_2CH_3), 49.33 (C-2), 61.65 (C-6), 66.87, 71.11, 74.08, 84.46 (C-1), 170.18 ($COCH_3$), 170.29 (2 x $COCH_3$), 170.34 ($COCH_3$). *Anal.* Calcd for $C_{16}H_{25}O_8NS$: C, 49.09%; H, 6.44%; N, 3.58%. found: C, 49.08%; H, 6.40%; N, 3.51%.

Ethyl 2-Azido-2-deoxy-1-thio-β-D-galactopyranoside (18). A solution of **17** (0.228 g, 0.583 mmol) in 1 M NaOH (35 ml) was treated as described for **6** . Before FC the well-dried residue was suspended in dry MeOH and filtered through a glasfilter. The filter was washed twice with small amounts of dry MeOH. FC (EtOAc:MeOH:H_2O 6:3:1) using a short silica-gel column (insoluble material stayed on the top of the column) yielded the free amine, which was used without further purification. The amine was dissolved in MeOH (35 ml) and treated with DMAP (0.076 g, 0.624 mmol) and a 0.4 M TfN_3-solution in CH_2Cl_2 (3.79 ml, 1.52 mmol) as described for **6**. The reaction mixture was concentrated and purified by FC (EtOAc) to yield **18** (62%, 0.090 g, 0.361 mmol) as a solid. R_f = 0.28 (EtOAc). $[\alpha]_D$ = -15 (*c* 1.0, MeOH). ^1H NMR (CD_3OD): d = 1.29 (t, 3H, J = 7.4 Hz, SCH_2CH_3), 2.66-2.84 (m, 2H, SCH_2CH_3), 3.43-3.52 (m, 3H), 3.67 (dd, J_{5-6} = 5.1 Hz, J_{6-6} =10.4 Hz, H-6), 3.74 (dd, J_{5-6} = 7.0 Hz, H-6), 3.84 (d, J_{3-4} = 1.5 Hz, H-4), 4.33 (second order, H-1). ^{13}C NMR (CD_3OD): d = 15.54 (SCH_2CH_3), 25.17 (SCH_2CH_3), 62.57 (C-6), 65.35, 69.80, 75.11, 80.62, 85.61 (C-1).

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20. The byproducts were characterized after the deprotection step and the diazotransfer reaction, because at this stage the two products could be more easily separated by FC.

^{13}C NMR Internal standard CD_3OD=49.0 ^1H NMR Internal standard TMS *Phenyl 2-azido-2-deoxy-6-thiophenyl-1-thio-β-D-glucopyranoside* ^{13}C NMR (CD_3OD): d = 26.6 (C-6), 66.9, 73.8, 78.1, 80.3, 87.3 (C-1), 126.9, 133.9 (12 x ArC). ^1H NMR (CD_3OD): d = 3,02-3.20(m, 2H), 3.28-3.53 (m, 4H), 4.48 (d, J=9.9 Hz, H-9), 7.14-7.53(10H, aromatic H). DEPTD-EXPERIMENT showed that the signal at 36.6 ppm in ^{13}C belonged to C-6. Accurate FAB-MS.calcd for $C_{18}H_{19}O_3N_3S_2$: 389.0868 found 389.0875 ± 0.007. Only the characteristic signals for the compounds below are listed. *Ethyl 2-azido-2-deoxy-6-thio-ethyl-1-thio-β-D-glucopyranoside.* ^{13}C NMR (CD_3OD): d = 15.1, 15.6 (2 x SCH_2CH_3), 25.2, 27.7 (2 x SCH_2CH3), 33.9 (C-6). *Ethyl 2-azido-deoxy-6-thioethyl-1-thio-β-D-galactopyranoside.* ^{13}C NMR (CD_3OD): d = 15.2, 15.6 (2 x SCH_2CH_3), 25.4, 27.4 (2 x SCH_2CH_3), 32.8 (C-6). ^1H NMR (CD_3OD): d = 1.24 (t, 3H, J=6.3 Hz, SCH_2CH_3), 1.30 (t, 3H, J=6.5 Hz, SCH_2CH_3), 2.81-2.67 (m, 4H).

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