Preparation of Ethyl 2-Azido-2-deoxy-1-thio-β-D-mannopyranosides, and their Rearrangement to 2-*S*-Ethyl-2-thio-β-D-mannopyranosylamines

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Abstract: The synthesis of ethyl 2-azido-2-deoxy-1-thio-β-D-mannopyranosides **7**–**11**, starting from appropriate synthons with *gluco* configuration, via S_N2 substitution at C(2), and their rearrangement to 2-*S*-ethyl-2-thio-β-D-mannopyranosylamines **12**–**14** are presented.

Key words: carbohydrates, D-mannosamine, thioglycosides, stereoselective synthesis, intramolecular rearrangements

2-Amino-2-deoxy-D-hexopyranosyl units (with *gluco*, *galacto*, or *manno* configuration) occur frequently in various biologically important oligosaccharides and their glycoconjugates, which have multiple biological functions and activities.[1,2] Due to the biological importance of these oligosaccharide structures, a considerable effort has been devoted to the search for efficient methods of their synthesis.[3]

β-Linked *N*-acetyl-D-mannosamine units are an integral part of a number of bacterial capsular polysaccharides[4–8] and lipopolysaccharides.[7–9] The immunological properties of capsular polysaccharides were exploited in the construction of human vaccines.[10–13] Oligosaccharides containing β- and α-linked *N*-acetyl-D-mannosamine units also seem to be potential mimics of natural ligands for activated receptor of NK cells, taking into account the fact that the binding activity of *N*-acetyl-D-mannosamine is higher than that of *N*-acetyl-D-glucosamine and in the case of chitooligomers, this activity increases with elongation of the saccharide chain.[14] Furthermore, oligosaccharides consisting of α(1→4)-linked 2-amino-2-deoxy-D-mannonopyranosyl units have an axially oriented glycosidic bond and an equatorially oriented C(4)–O bond and thus they satisfy the basic criteria for cyclization and forming of 2-amino-2-deoxy-cyclomannine analogues of cyclodextrins.[15]

However, despite the biological significance of oligosaccharides consisting of *N*-acetyl-D-mannosamine units, both the chemistry of D-mannosamine and efficient, practical methods for incorporation of the D-mannosamine motif into oligosaccharide chains remain scarce. β-D-Mannopyranosides, as well as 2-acetamido-2-deoxy-β-D-mannopyranosides, have been considered to be one of the most difficult types of *O*-glycosides to synthesize stereoselectively. This derives from their unique structural features (1,2-*cis* equatorial-oriented glycosidic bond), which do not exert any stereoelectronic control by an anomeric effect or participation of a neighboring group. Thus, from the methods so far developed for the introduction of the β-Man*p*NAc unit, the use the 2-(acyloxyimino)-2-deoxy-α-D-*arabino*-hexopyranosyl bromide as glycosyl donor proved to be superior.[12,16–18] A different method for the introduction of the β-Man*p*NAc element into the oligosaccharide chain is the *a posteriori* introduction of the azido group via S_N2 substitution at C(2) in β-linked glucosides.[11,13,19] An approach based on the use of glycosyl donors having a nonparticipating azido group at C(2) and a 1,2-*trans*-oriented leaving group, e.g., bromine[20,21] or sulfanyl,[22,23] at C(1) shows a limited β-selectivity depending on the reactivity of the OH group of the glycosyl acceptor. Therefore the formation of α-mannopyranosides is preferred with decrease of acceptor reactivity.[21,23] The synthesis of α-linked 2-acetamido-2-deoxy-D-mannopyranosides has received only little attention so far. From common glycosylation methods only Koenigs–Knorr and oxazoline methods were employed in the preparation of a few simple alkyl α-D-mannopyranosides.[24–26] These facts motivated us to focus our attention on the preparation of D-mannosamine synthons tailor-made for the stepwise synthesis of oligosaccharides consisting of α- and β(1→4)- or -(1→6)-linked 2-acetamido-2-deoxy-D-mannopyranose units.

An approach based on the introduction of the azido group as non-participating masked amino function, exploiting S_N2 substitution in position C(2) of appropriate synthons with *gluco* configuration was chosen for the synthesis of the above-mentioned D-mannosamine building units. The methods commonly used for the preparation of 2-azido-2-deoxyhexoses, based on azidonitration of glycals,[27–31] show a low *manno* stereoselectivity. Another recently used general approach is represented by the diazo transfer reaction of appropriate D-hexosamines.[22,27,28]

As the starting material for the preparation of the target ethyl 2-azido-2-deoxy-1-thio-β-D-mannopyranosides, we utilized 1,2,4,6-tetra-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranose (**1**). Compound **1** was prepared from 3-*O*-benzyl-D-

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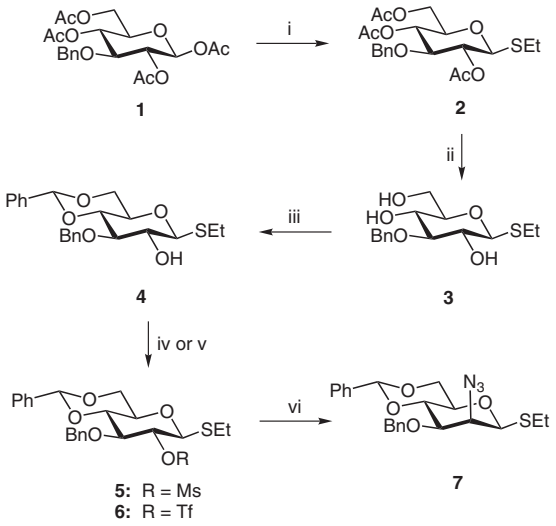
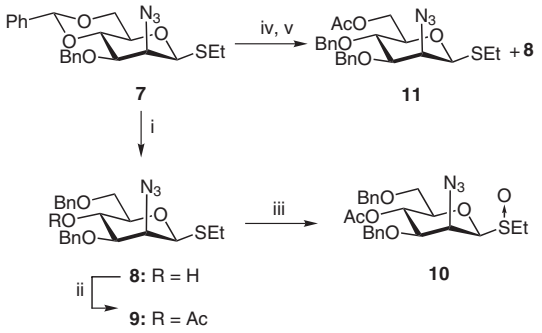


Scheme 1 *Reagents and conditions*: i) EtSH, TMSOTf, 4Å MS, CH_2Cl_2, 0 °C, 79%; ii) MeONa, MeOH, r.t., 72%; iii) α,α-dimethoxytoluene, TfOH, CH_2Cl_2, Et_3N, r.t., 84%; iv) MsCl, pyridine, 0 °C to r.t., 84%; v) Tf_2O, CH_2Cl_2–pyridine, 0 °C; vi) NaN_3, DMF, 80 °C, 82% (71% in two steps from **4** through **6**)



Scheme 2 *Reagents and conditions*: i) Et_3SiH, TFA, CH_2Cl_2, 0 °C to r.t., 72%; ii) Ac_2O, pyridine, r.t., 89%; iii) MCPBA, CH_2Cl_2, –10 °C, 81%; iv) $AlCl_3$, $BH_3{\cdot}Me_3N$, 4Å MS, CH_2Cl_2–Et_2O, 0 °C; v) AcCl, *sym*-collidine, CH_2Cl_2, –60 °C, 62% (in two steps)

glucose[32] by modification of the procedure described in the literature,[33] i.e., O-acetylation with acetic anhydride in pyridine in the presence of 4-(*N*,*N*-dimethylamino)pyridine (DMAP), instead of O-acetylation in the presence of sodium acetate, which led to a mixture of α- and β-anomers.

An efficient Lewis acid catalyzed substitution of anomeric acetate with ethanethiol requires 1,2-*trans*-acetate. For the transformation of **1** to ethyl 1-thio-β-D-glucopyranoside (**2**) (Scheme 1), trimethylsilyl trifluoromethanesulfonate, instead of $BF_3{\cdot}OEt_2$ as described in the literature,[34] was used as a promotor. Zemplén deacetylation of **2** gave ethyl 3-*O*-benzyl-1-thio-β-D-glucopyranoside (**3**) which was treated with α,α-dimethoxytoluene in the presence of a catalytic amount of trifluoromethanesulfonic acid, to afford ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**4**). *O*-Mesyl and *O*-trifluoromethanesulfonyl groups were used as leaving groups in position C(2) of **4**. Reaction of **4** with methanesulfonyl chloride in pyridine afforded crystalline 2-*O*-mesyl derivative **5**. 2-*O*-Trifluoromethanesulfonyl derivative **6**, obtained by reaction of **4** with triflic anhydride in pyridine and CH_2Cl_2 in form of an unstable syrupy product, was used for the next step without further purification. Treatment of 2-*O*-methanesulfonyl derivative **5** as well as 2-*O*-trifluoromethanesulfonyl derivative **6** with sodium azide in dry DMF at 80 °C afforded the key ethyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-mannopyranoside (**7**) in very good yields.

Reductive opening of the 4,6-*O*-benzylidene group of **7** with triethylsilane and trifluoroacetic acid in CH_2Cl_2,[35] followed by 4-O-acetylation of obtained ethyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside (**8**), gave glycosyl donor **9** designed for the synthesis of oligosaccharides consisting of (1→4)-linked 2-amino-2-deoxy-D-mannopyranosyl units (Scheme 2).

The reaction of **7** with aluminium(III) chloride and borane-trimethylamine complex in a mixture of CH_2Cl_2 and Et_2O led to a mixture of regioisomers, i.e., compound **8** and ethyl 2-azido-3,4-di-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside. The latter was isolated from the mixture as 6-*O*-acetate **11** by selective O-acetylation of its primary OH group with acetyl chloride in the presence of *sym*-collidine at –60 °C.

Attempts to activate the ethylsulfanyl group of the prepared 2-azido-2-deoxy-1-thio-β-D-mannopyranosides via a sulfonium ion by routinely used glycosylation methods, i.e., with MeOTf or dimethyl(methylthio)sulfonium triflate (DMTST) in the case of **7**, **9** and **11**, and with NIS/TfOH and in the case of **9** and **11**, were unsuccessful. Also, the conversion of these compounds to glycosyl fluorides by reaction with dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF) did not work. Methanol and cyclohexanol, respectively, were used as glycosyl acceptors. In general, β-anomers are considered to be more reactive than α-anomers.[22] The approach based on the transformation of thioglycoside to sulfoxide and its subsequent activation with Tf_2O[36] has also led to negative results. Sulfoxide **10** was prepared by oxidation of **9** with MCPBA.

The deactivation of β-oriented alkylsulfanyl and sulfoxide functionalities might be caused by significant interaction between the axially oriented azido group at C(2) and the equatorially linked sulfur at C(1) on the mannopyranose skeleton. This observation motivated us to replace the azido group at C(2) with the participating trichloroethoxycarbonylamino (NHTroc) or phthalimido (NPhth) group. The attempt to transform azides **7** and **9** into the appropriate amino derivatives was unsuccessful. Standard methods for the conversion of an azido group into an amino group, i.e., in the case of **7** and **9** by reduction with H_2S, $SnCl_2$/PhSH and Et_3N, or LAH, and in the case of **9** by reduction with H_2/PtO_2 or BH_3, led to complex mixtures. Reduction of azido derivatives **7** and **9** with triphenylphosphine gave the corresponding phosphine imides,

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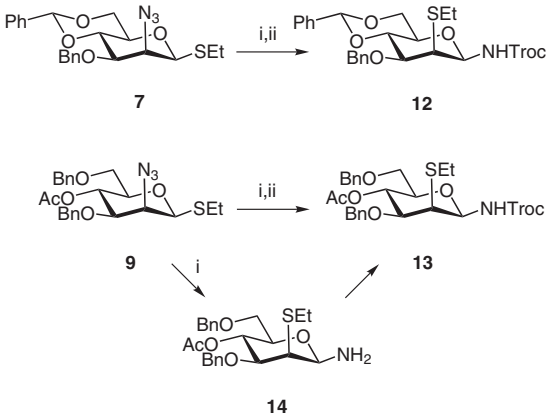


Scheme 3 *Reagents and conditions*: i) Propane-1,3-dithiol, Et_3N, pyridine–H_2O, r.t.; ii) TrocCl, pyridine, 0 °C to r.t., 79% (for **12**), 64% (for **13**), (in two steps)

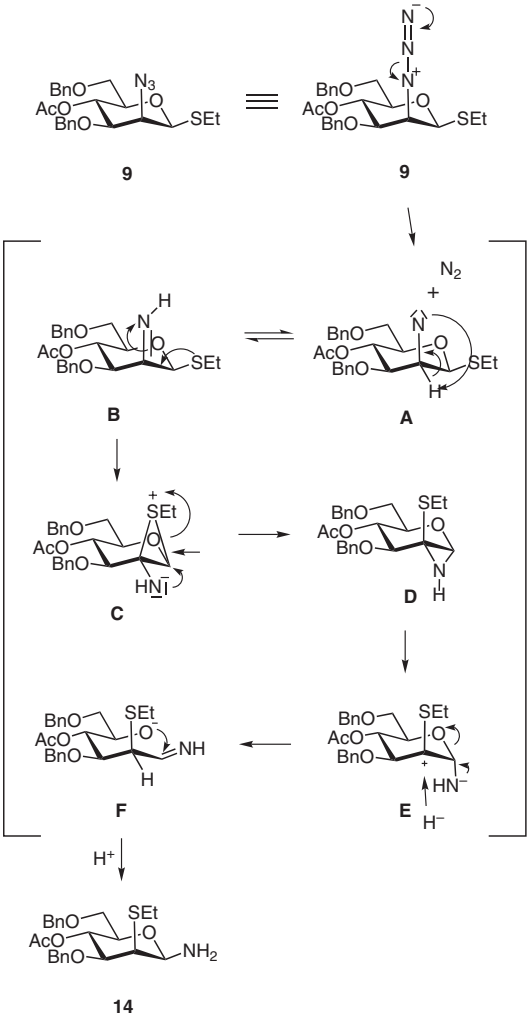
which were resistant to hydrolysis and ammonolysis,[37] as well as to direct conversion into phthalimido derivatives by their reaction with phthalic anhydride in the presence of tetrabutylammonium cyanide.[38]

On using propane-1,3-dithiol for the reduction of the azido group,[39] the reduction of derivatives **7** and **9** was followed by migration of the ethylsulfanyl group at C(1) and the amino group at C(2) with the retention of configuration in both positions. Reduction of **7** or **9** with propane-1,3-dithiol and Et_3N in a mixture of pyridine and water, and subsequent N-trocylation of the formed amino derivatives, gave 3-*O*-benzyl-4,6-*O*-benzylidene-2-*S*-ethyl-2-thio-β-D-mannopyranosyl-(2,2,2-trichloroethoxycarbonyl)amine (**12**) and 4-*O*-acetyl-3,6-di-*O*-benzyl-2-*S*-ethyl-2-thio-β-D-mannopyranosyl-(2,2,2-trichloroethoxycarbonyl)amine (**13**), respectively (Scheme 3).

Unexpected products **12** and **13** can be attributed to the formation of nitrene intermediate **A** (Scheme 4). The tautomeric form **B** can be transformed via thiiranium ion **C** into epimine **D**, which can undergo the ionization supported by the repulsion of atoms of sulfur and oxygen in pyranose rings. Intermediate **E** can be converted via imine **F** into β-glycosylamine **14** under reduction conditions. Therefore, the opening of the aziridine ring does not proceed by the Fürst–Plattner rule. The subsequent N-trocylation of glycosylamines afforded **12** and **13**, respectively. Glycosyl amine **14** was isolated from the reaction mixture before the trocylation step.

For the structure determination of key compounds **12**, **13** and **14**, the 2D homo- and heterocorelated NMR spectra and detailed analysis of coupling constants were employed. The results from 2D NMR ROESY experiments as well as those from theoretical calculation of optimum geometry using AM1 calculation supported β-configuration of the above-mentioned compounds. Characteristic H-1/H-3 and H-1/H-5 cross-peaks in ROESY NMR spectra were observed.

In summary, the synthesis of ethyl 2-azido-2-deoxy-1-thio-β-D-mannopyranosides, via S_N2 substitution at C(2)



Scheme 4 Suggested mechanism of formation of compound **14**

of appropriate synthons with *gluco* configuration, was elaborated. A significant interaction between the axially oriented azido group at C(2) and the equatorially oriented alkylsulfanyl group at C(1) on the mannopyranose skeleton was observed. It results (a) in the deactivation of the alkylsulfanyl leaving group in the glycosylation process and (b) in the migration of both substituents at C(1) and at C(2) with the retention of configuration in both positions, under conditions of reduction of the azido group to the amino group, to give 2-*S*-ethyl-2-thio-β-D-mannopyranosylamines. The acquired knowledge expands the general view of the transformations on the mannosamine skeleton.

Melting points were determined on a Kofler block and are uncorrected. Specific rotations were measured on a Perkin-Elmer 141 polarimeter at 25 °C. Elemental analyses were performed using a Perkin Elmer 2400 II instrument. NMR spectra were recorded on a Varian Unity *Inova* 400 FT spectrometer and a Bruker Avance 500 spectrometer in the FT mode in $CDCl_3$ or $(CD_3)_2SO$, using $(CH_3)_4Si$ as internal standard for ^1H NMR spectra and $CDCl_3$ ($\delta = 77.0$) or $(CD_3)_2SO$ ($\delta = 39.7$) signals as standards for ^{13}C NMR spectra. For unambiguous assignment of signals in ^{13}C NMR spectra, ^1H- and ^{13}C-heterocorrelated 2D NMR spectra were measured by gHSQC and gHMBC techniques using the standard pulse sequences deliv-

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ered by the producer of the spectrometer. The following typical parameters were used: spectral width in both f_1 and f_2 dimensions 5000 Hz and 17000 Hz, respectively, number of scans 16, number of increments in f_1 dimension 256, recycle delay 1 s, acquisition time 0.2 s, 90° pulse for ^{1}H was 12.5 μs, data matrix for processing 2048 × 2048 datapoints. For processing, shifted sinebell weighting function was used. Chemical shifts are given in ppm (δ-scale) and coupling constants (*J*) in Hz. Positive-ion FAB mass spectra were measured on a BeqG-geometry mass spectrometer ZAB-EQ (VG Analytical, Manchester, UK) using an M-Scan FAB gun (Xe, energy 8 keV) at an accelerating voltage of 8 kV. Samples were dissolved in $CHCl_3$ or MeOH, and a mixture of glycerol and thioglycerol or DMSO was used as matrix. TLC was performed on DC-Alufolien Kieselgel 60 F_{254} (Merck, Darmstadt, Germany) or Silufol UV_{254} (Kavalier, Votice, Czech Republic) silica gel sheets. Preparative chromatography was performed on a silica gel column, particle size 40–60 μm (Fluka, Neu-Ulm, Switzerland). Analytical RP HPLC was performed using a Waters instrument (PDA detector, software Milennium 32; Milford, Massachusetts, USA) equipped with a Nova-Pak C18 column (150 × 3.9 mm), particle size 4 μm. Preparative RP HPLC was performed on a column (250 × 25 mm) filled with LiChrosorb RP-18, particle size 5 μm (Merck, Darmstadt, Germany). Solvents were evaporated on a rotary vacuum evaporator at 40 °C. Analytical samples were dried at 6.5 Pa and 25 °C for 8 h. Petroleum ether is abbreviated as PE and had a bp of 40–65 °C.

Ethyl 2,4,6-Tri-*O*-acetyl-3-*O*-benzyl-1-thio-β-D-glucopyranoside (2)

To a stirred solution of 1,2,4,6-tetra-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranose[32] (**1**; 4.4 g, 10.01 mmol) and 4 Å MS (3 g) in anhyd CH_2Cl_2 (50 mL), ethanethiol (1.89 mL, 25.52 mmol) was added under Ar. The reaction mixture was cooled to 0 °C and TMSOTf (1.9 mL, 10.48 mmol) was slowly added dropwise. After 2 h the reaction mixture was filtered through celite, the filtrate was washed with sat. aq $NaHCO_3$ (2 × 20 mL) and H_2O (2 × 20 mL), dried over ($MgSO_4$) and evaporated. Crystallization from the solvent mixture toluene–heptane afforded 3.5 g (79%) of compound **2**.

Mp 112–114 °C; $[\alpha]_D$ –32.1 (*c* 0.3, $CHCl_3$) {Lit.[34] mp 88–90 °C; $[\alpha]_D^{25}$ –33.2 (*c* 0.2, $CHCl_3$)}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.2 Hz, 3 H, SCH_2CH_3), 1.97 (s, 3 H, OAc), 2.02 (s, 3 H, OAc), 2.07 (s, 3 H, OAc), 2.62–2.78 (m, 2 H, SCH_2CH_3), 3.61 (ddd, *J* = 9.9, 5.2, 2.4 Hz, 1 H, H-5), 3.71 (t, *J* = 9.2 Hz, 1 H, H-3), 4.12 (dd, *J* = 12.4, 5.3 Hz, 1 H, H-6a), 4.19 (dd, *J* = 12.4, 5.3 Hz, 1 H, H-6b), 4.40 (d, *J* = 10.1 Hz, 1 H, H-1), 4.59 (d, *J* = 11.8 Hz, 1 H), 4.64 (d, *J* = 11.6 Hz, 1 H, $C_6H_5CH_2$), 5.08 (t, *J* = 9.8 Hz, 1 H, H-2), 5.11 (t, *J* = 9.9 Hz, 1 H, H-4), 7.22–7.36 (m, 5 H, $C_6H_5CH_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 20.7, 20.8, 20.9, 23.9, 62.5, 69.6, 71.2, 74.2, 76.2, 81.5, 83.7, 127.7 (2 C), 127.8, 128.4 (2 C), 137.7, 169.3, 169.3, 170.8.

MS (FAB+): *m*/*z* (%) = 441.2 [M^+ + H].

Anal. Calcd for $C_{21}H_{28}O_8S$: C, 57.26; H, 6.41; S, 7.28. Found: C, 57.18; H, 6.42; S, 7.11.

Ethyl 3-*O*-Benzyl-1-thio-β-D-glucopyranoside (3)

Compound **2** (35.0 g, 79.45 mmol) was dissolved in a solution of sodium methoxide in MeOH (0.01 M, 1200 mL). The reaction mixture was stirred for 6 d at r.t. Then the reaction mixture was neutralized by Dowex 50 (in pyridinium form) and evaporated. Crystallization from 2-PrOH–PE afforded 18.0 g (72%) of compound **3**.

Mp 100–102 °C; $[\alpha]_D^{25}$ –67.8 (*c* 0.58, $CHCl_3$).

IR (KBr): 3498, 3435, 3307 (OH), 3087, 3064, 3025, 1497, 1452 ($PhCH_2$) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.20 (t, *J* = 7.6 Hz, 3 H, SCH_2CH_3), 2.57–2.73 (m, 2 H, SCH_2CH_3), 3.14–3.28 (m, 4 H, H-2, H-3, H-4, H-5), 3.44 (dd, *J* = 11.8, 5.8 Hz, 1 H, H-6a), 3.68 (dd, *J* = 11.8, 1.7 Hz, 1 H, H-6b), 4.32 (d, *J* = 9.4 Hz, 1 H, H-1), 4.79 (d, *J* = 11.8 Hz, 1 H), 4.83 (d, *J* = 11.8 Hz, 1 H, $C_6H_5CH_2$), 4.20–5.40 (br s, 3 H, 3 × OH), 7.20–7.25 (m, 1 H), 7.28–7.32 (m, 2 H), 7.40–7.43 (m, 2 H, $C_6H_5CH_2$).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.6, 22.9, 61.0, 69.7, 72.8, 73.9, 81.0, 85.0, 86.6, 127.0, 127.5 (2 C), 127.9 (2 C), 139.5.

MS (FAB+): *m*/*z* (%) = 337.2 [M^+ + Na].

Anal. Calcd for $C_{15}H_{22}O_5S$: C, 57.30; H, 7.05; S, 10.20. Found: C, 57.11; H, 6.98; S, 10.26.

Ethyl 3-*O*-Benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (4)

To a stirred solution of compound **3** (15.0 g, 47.70 mmol) in anhyd CH_2Cl_2 (300 mL), α,α-dimethoxytoluene (28 mL, 193.36 mmol) and TfOH (0.4 mL, 4.58 mmol) were added. After 1 h, Et_3N (1.6 mL, 11.48 mmol) was added, the reaction mixture was taken up in $CHCl_3$ (300 mL), washed with H_2O (2 × 200 mL), dried ($MgSO_4$) and evaporated. Crystallization from of EtOAc–PE afforded 16.1 g (84%) of compound **4**.

Mp 139–140 °C; $[\alpha]_D^{25}$ –61.1 (*c* 0.2, $CHCl_3$) {Lit.[34] mp 139 °C; $[\alpha]_D^{25}$ –46.2 (*c* 0.3, $CHCl_3$)}.

IR ($CHCl_3$): 3574 (OH), 654 (C–S), 1111, 1084, 1070, 1010, 994 (4,6-*O*-benzylidene), 3091, 3068, 3034, 1498, 1454, 914, 699 ($PhCH_2$) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.5 Hz, 3 H, SCH_2CH_3), 2.78–2.72 (m, 2 H, SCH_2CH_3), 3.50 (ddd, *J* = 10.2, 8.7, 5.0 Hz, 1 H, H-5a), 3.58 (t, *J* = 9.6 Hz, 1 H, H-2), 3.65–3.75 (m, 2 H, H-3, H-4), 3.78 (t, *J* = 10.4 Hz, 1 H, H-6a), 4.36 (dd, *J* = 10.5, 5.0 Hz, 1 H, H-6b), 4.47 (d, *J* = 9.8 Hz, 1 H, H-1), 4.82 (d, *J* = 11.8 Hz, 1 H), 4.98 (d, *J* = 11.8 Hz, 1 H) ($C_6H_5CH_2$), 5.58 (s, 1 H, C_6H_5CH), 7.28–7.51 (m, 10 H, $C_6H_5CH_2$, C_6H_5CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2, 24.6, 68.6, 70.8, 73.0, 74.7, 81.2, 81.5, 86.6, 101.3, 126.0 (2 C), 127.8, 128.1(2 C), 128.3 (2 C), 128.5 (2 C), 129.0, 137.2, 138.3.

MS (FAB+): *m*/*z* (%) = 403.2 [M^+ + H].

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.65; H, 6.51; S, 7.97. Found: C, 65.19; H, 6.50; S, 7.82.

Ethyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(methylsulfonyl)-1-thio-β-D-glucopyranoside (5)

A solution of **4** (1.0 g, 2.48 mmol) in pyridine (10 mL) was cooled to 0 °C and MsCl (0.39 mL, 4.97 mmol) was added dropwise. The reaction mixture was warmed gradually and then stirred at r.t. for 24 h. The reaction mixture was evaporated and the residue was diluted with CH_2Cl_2 (30 mL) and H_2O (30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried ($MgSO_4$) and evaporated. Crystallization of the residue from EtOH afforded 1.0 g (84%) of product **5**.

Mp 103–104 °C; $[\alpha]_D^{25}$ –39 (*c* 0.4, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.3 Hz, 3 H, SCH_2CH_3), 2.72–2.82 (m, 2 H, SCH_2CH_3), 3.00 (s, 3 H, OSO_2CH_3), 3.51 (ddd, *J* = 9.9, 9.2, 4.9 Hz, 1 H, H-5), 3.77 (t, *J* = 9.3 Hz, 1 H, H-4), 3.78 (t, *J* = 10.2 Hz, 1 H, H-6a), 3.86 (ddd, *J* = 9.3, 7.8, 0.8 Hz, 1 H, H-3), 4.39 (dd, *J* = 10.7, 5.0 Hz, 1 H, H-6b), 4.57 (d, *J* = 9.9 Hz, 1 H, H-1), 4.61 (dd, *J* = 10.0, 7.8 Hz, 1 H, H-2), 4.77 (d, *J* = 10.8 Hz, 1 H), 4.98 (d, *J* = 10.8 Hz, 1 H) ($C_6H_5CH_2$), 5.58 (s, 1 H, C_6H_5CH), 7.26–7.48 (m, 10 H, $C_6H_5CH_2$, C_6H_5CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7, 24.1, 39.5, 68.4, 70.4, 75.0, 79.5, 80.0, 81.6, 84.0, 101.2, 125.9 (2 C), 127.9, 128.3 (2 C), 128.3 (2 C), 128.4 (2 C), 129.1, 136.8, 137.4.

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MS (FAB+): *m*/*z* (%) = 481.2 [M^+ + H].

Anal. Calcd for $C_{23}H_{28}O_7S_2$: C, 57.48; H, 5.87; S, 13.34. Found: C, 57.44; H, 5.91; S, 13.27.

Ethyl 3-*O*-Benzyl-4,6-*O*-benzylidene-1-thio-2-*O*-[(trifluoromethyl)sulfonyl]-β-D-glucopyranoside (6) and Ethyl 2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-mannopyranoside (7)

Method A: To a stirred solution of compound **4** (1.6 g, 3.98 mmol) in anhyd CH_2Cl_2 (16 mL) and pyridine (1.6 mL) at 0 °C, Tf_2O (1.0 mL, 5.94 mmol) was added dropwise under Ar. After 30 min, the reaction mixture was treated with ice-cold sat. aq $NaHCO_3$ (10 mL), the organic layer was washed with H_2O (30 mL), dried ($MgSO_4$) and evaporated to afford **6** as a solid.

MS (FAB+): *m*/*z* (%) = 385.1 [M^+ – TfOH + H].

To a stirred solution of this residue in DMF (35 mL), NaN_3 (1.6 g, 24.61 mmol) was added and the mixture was heated to 80 °C under Ar overnight. After 16 h, the reaction mixture was taken up between toluene (100 mL) and H_2O (80 mL), the organic layer was washed with H_2O (80 mL), dried ($MgSO_4$) and evaporated. Chromatography of the residue on a silica gel column (40 g) with toluene–EtOAc (25:1) gave 1.2 g (71%) of **7** as colorless oil.

Method B: Compound **5** (1.0 g, 2.08 mmol) was dissolved in anhyd DMF (30 mL) and LiN_3 (0.25 g, 5.19 mmol) was added. The mixture was heated to 80 °C under Ar for 16 h. After cooling to r.t., the reaction mixture was concentrated, the residue was diluted with H_2O (40 mL) and extracted with CH_2Cl_2 (2 × 40 mL). The combined organic layers were dried ($MgSO_4$) and evaporated. Column chromatography on silica gel (50 g) with toluene afforded 729 mg (82%) of compound **7**.

$[\alpha]_D^{25}$ +124 (*c* 0.3, $CHCl_3$).

IR ($CHCl_3$): 2110, 1263, 566 (N_3), 3091, 3068, 3035, 1497, 1454 ($PhCH_2$) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.3 Hz, 3 H, SCH_2CH_3), 2.72 (q, *J* = 7.5 Hz, 2 H, SCH_2CH_3), 3.13 (dd, *J* = 4.0, 1.2 Hz, 1 H, H-2), 3.83 (t, *J* = 10.2 Hz, 1 H, H-4), 3.92–4.01 (m, 1 H, H-5), 4.06–4.14 (m, 2 H, H-6a, H-6b), 4.28 (dd, *J* = 10.2, 4.7 Hz, 1 H, H-3), 4.70 (d, *J* = 12.2 Hz, 1 H), 4.82 (d, *J* = 12.2 Hz, 1 H) ($C_6H_5CH_2$), 5.54 (d, *J* = 1.2 Hz, 1 H, H-1), 5.61 (s, 1 H, C_6H_5CH), 7.27–7.50 (m, 10 H, $C_6H_5CH_2$, C_6H_5CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 28.0, 50.4, 66.4, 68.4, 73.0, 74.1, 79.6, 91.8, 101.6, 126.0 (2 C), 127.6 (2 C), 127.7, 128.2 (2 C), 128.3 (2 C), 128.9, 137.3, 138.1.

MS (FAB+): *m*/*z* (%) = 428.2 [M^+ + H].

Anal. Calcd for $C_{22}H_{25}N_3O_4S$: C, 61.81; H, 5.89; N, 9.83; S, 7.50. Found: C, 61.70; H, 5.96; N, 9.92; S, 7.34.

Ethyl 2-Azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside (8) and Ethyl 6-*O*-Acetyl-2-azido-3,4-di-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside (11)

Method A: A solution of $AlCl_3$ (270 mg, 2.02 mmol) in 2 mL of (Et_2O) was added dropwise during 30 min to a stirred mixture of **7** (214 mg, 0.50 mmol), BH_3–trimethylamine complex (370 mg, 5.07 mmol) and 4Å MS in CH_2Cl_2–Et_2O (5:1, 8 mL) at 0 °C. After 1 h, the mixture was filtered through celite and 1 M H_2SO_4 (10 mL) was added to the filtrate, which was then stirred for 30 min. The organic layer was washed with sat. aq $NaHCO_3$ (10 mL), H_2O (15 mL), dried ($MgSO_4$) and evaporated. Chromatography of the residue on a silica gel column (10 g) with toluene–EtOAc (20:1) gave a mixture of **8** and 2-azido-3,4-di-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside (198 mg, 92%), which was subjected to a selective acetylation of the primary hydroxyl group before purification. The above-mentioned mixture and *sym*-collidine (133 μL, 1.01 mmol) were dissolved in anhyd CH_2Cl_2 (8 mL) and the solution was cooled to –70 °C. AcCl (38 μL, 0.5 mmol) was added and the reaction mixture was stirred for 1 h at –60 °C, then quenched with MeOH (1 mL) and allowed to attain r.t. Progress of the reaction was monitored using TLC in toluene–EtOAc (5:1). The solvent was evaporated and purification on a silica gel column (10 g) with toluene–EtOAc (20:1) gave 147 mg (62%) of **11** and 65 mg (30%) of **8**.

Method B: TFA (80 μL, 1.08 mmol) was added dropwise to a solution of compound **7** (86 mg, 0.20 mmol) and triethylsilane (160 μL, 1.00 mmol) in CH_2Cl_2 (2 mL) at 0 °C. The reaction mixture was warmed to r.t. and stirred for 1 h. Progress of the reaction was monitored using TLC with toluene–EtOAc (5:1). The mixture was diluted with EtOAc (8 mL), washed with sat. aq. $NaHCO_3$ (5 mL), H_2O (5 mL), dried ($MgSO_4$) and evaporated. Chromatography of the residue on a silica gel column (5 g) with toluene–EtOAc (12:1) afforded 62 mg (72%) of compound **8** as colorless syrup.

Compound **8**

$[\alpha]_D^{25}$ +48 (*c* 0.4, $CHCl_3$).

IR ($CHCl_3$): 3592, 3513, 1054 (OH), 2110, 1265, 567 (N_3) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.6 Hz, 3 H, SCH_2CH_3), 2.58–2.66 (m, 2 H, SCH_2CH_3), 3.09–3.13 (m, 1 H, H-2), 3.74–3.78 (m, 2 H, H-6a, H-6b), 3.88–3.91 (m, 3 H, H-3, H-4, H-5), 4.55 (d, *J* = 11.6 Hz, 1 H), 4.57 (d, *J* = 11.9 Hz, 1 H), 4.65 (d, *J* = 12.1 Hz, 1 H), 4.70 (d, *J* = 11.4 Hz, 1 H, 2 × $C_6H_5CH_2$), 5.55 (d, *J* = 1.7 Hz, 1 H, H-1), 7.27–7.40 (m, 10 H, 2 × $C_6H_5CH_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 27.1, 48.1, 67.8, 69.7, 71.8, 73.6, 73.7, 77.5, 90.7, 127.6, 127.6 (2 C), 128.1 (3 C), 128.3 (2 C), 128.6 (2 C), 137.6, 138.0.

MS (FAB+): *m*/*z* (%) = 430.1 [M^+ + H].

Anal. Calcd for $C_{22}H_{27}N_3O_4S$: C, 61.52; H, 6.34; N, 9.78; S, 7.47. Found: C, 61.49; H, 6.47; N, 9.90; S, 7.36.

Compound **11**

$[\alpha]_D^{25}$ +98 (*c* 0.4, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.3 Hz, 3 H, SCH_2CH_3), 2.06 (s, 3 H, $OCOCH_3$), 2.62–2.68 (m, 2 H, SCH_2CH_3), 3.06 (dd, *J* = 4.3, 2.6 Hz, 1 H, H-2), 3.70 (dd, *J* = 9.0, 8.6 Hz, 1 H, H-4), 3.94 (ddd, *J* = 9.0, 4.1, 2.3 Hz, 1 H, H-5), 4.06 (dd, *J* = 8.4, 4.3 Hz, 1 H, H-3), 4.28 (dd, *J* = 12.1, 4.7 Hz, 1 H, H-6a), 4.32 (dd, *J* = 11.9, 2.7 Hz, 1 H, H-6b), 4.55 (d, *J* = 11.0 Hz, 1 H), 4.63 (d, *J* = 11.4 Hz, 1 H), 4.69 (d, *J* = 11.5 Hz, 1 H), 4.86 (d, *J* = 10.8 Hz, 1 H, 2 × $C_6H_5CH_2$), 5.48 (d, *J* = 2.6 Hz, 1 H, H-1), 7.26–7.40 (m, 10 H, 2 × $C_6H_5CH_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7, 20.8, 27.2, 48.6, 62.8, 72.3 (2 C), 74.2, 74.8, 78.3, 90.4, 127.9, 128.0, (3 C), 128.1 (2 C), 128.5 (2 C), 128.5 (2 C), 137.7, 137.8.

MS (FAB+): *m*/*z* (%) = 472 [M^+ + H].

Anal. Calcd for $C_{24}H_{29}N_3O_5S$: C, 61.13; H, 6.20; N, 8.91; S, 6.80. Found: C, 61.07; H, 6.11; N, 8.77; S, 6.68.

Ethyl 4-*O*-Acetyl-2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside (9)

To a stirred solution of compound **8** (735 mg, 1.71 mmol) in anhyd pyridine (10 mL), Ac_2O (2.0 mL, 21.16 mmol) was added. The reaction mixture was stirred overnight at r.t. Progress of the reaction was monitored using TLC with toluene–EtOAc (5:1). The mixture was diluted with toluene (40 mL), washed with 1 M aq HCl (30 mL), sat. aq $NaHCO_3$ (30 mL), H_2O (2 × 30 mL), dried ($MgSO_4$) and evaporated. Chromatography of the residue on a silica gel column (15 g) in toluene–EtOAc (15:1) afforded 720 mg (89%) of compound **9**.

$[\alpha]_D^{25}$ +77 (*c* 0.2, $CHCl_3$).

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IR ($CHCl_3$): 1744, 1234, 1044 (OAc), 2111, 1263, 566 (N_3) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.5 Hz, 3 H, SCH_2CH_3), 1.96 (s, 3 H, OAc), 2.66 (q, *J* = 7.5 Hz, 2 H, SCH_2CH_3), 3.00 (t, *J* = 4.1 Hz, 1 H, H-2), 3.58 (dd, *J* = 10.8, 4.0 Hz, 1 H, H-6a), 3.63 (dd, *J* = 10.8, 5.8 Hz, 1 H, H-6b), 3.92 (dd, *J* = 7.2, 4.0 Hz, 1 H, H-3), 4.03 (ddd, *J* = 8.1, 5.8, 3.8 Hz, 1 H, H-5), 4.51 (d, *J* = 11.9 Hz, 1 H), 4.55 (d, *J* = 11.9 Hz, 1 H), 4.57 (d, *J* = 11.9 Hz, 1 H), 4.63 (d, *J* = 12.1 Hz, 1 H, 2 × $C_6H_5CH_2$), 5.21 (dd, *J* = 8.1, 7.3 Hz, 1 H, H-4), 5.45 (d, *J* = 4.1 Hz, 1 H, H-1), 7.24–7.36 (m, 10 H, 2 × $C_6H_5CH_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 20.9, 27.1, 47.9, 68.3, 68.9, 72.1, 72.8, 73.4, 76.4, 90.0, 127.6, 127.7 (4 C), 127.8, 128.3 (4 C), 137.5, 137.8, 169.6.

MS (FAB+): *m*/*z* (%) = 472 [M^+ + H].

Anal. Calcd for $C_{24}H_{29}N_3O_5S$: C, 61.13; H, 6.20; N, 8.91; S, 6.80. Found: C, 61.02; H, 6.19; N, 8.87; S, 6.67.

Ethyl 4-*O*-Acetyl-2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside *S*-Oxide (10)

To a stirred solution of compound **9** (92 mg, 0.20 mmol) in anhyd CH_2Cl_2 (4 mL), MCPBA (38 mg, 0.22 mmol) was added at –30 °C. The reaction mixture was warmed to –10 °C and stirred for 1 h. Progress of the reaction was monitored using TLC with toluene–EtOAc (2:1). After the reaction was quenched with sat. aq $NaHCO_3$ (6 mL), CH_2Cl_2 was added (10 mL). Reaction mixture was warmed to r.t., washed with H_2O (6 mL), dried ($MgSO_4$) and evaporated. The residue was purified on a silica gel column (7 g) with toluene–EtOAc (2:1) to yield 77 mg (81%) of compound **10**.

$[\alpha]_D^{25}$ +81 (*c* 0.2, $CHCl_3$).

IR ($CHCl_3$): 1045 (S=O), 1749, 1233, 1021 (OAc), 2115, 1260, 564 (N_3) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.4 Hz, 3 H, SCH_2CH_3), 1.88 (s, 3 H, OAc), 2.71 (dq, *J* = 13.2, 7.4, 7.4, 7.4 Hz, 1 H, SCH_2CH_3), 3.06 (dq, *J* = 13.2, 7.4, 7.4, 7.4 Hz, 1 H, SCH_2CH_3), 3.23 (dd, *J* = 4.5, 2.2 Hz, 1 H, H-2), 3.60 (dd, *J* = 10.9, 3.7 Hz, 1 H, H-6a), 3.64 (dd, *J* = 10.9, 5.2 Hz, 1 H, H-6b), 4.09 (dd, *J* = 9.2, 4.9 Hz, 1 H, H-3), 4.09 (ddd, *J* = 9.4, 5.2, 3.7 Hz, 1 H, H-5), 4.53 (d, *J* = 11.7 Hz, 1 H), 4.55 (s, 2 H), 4.57 (d, *J* = 11.7 Hz, 1 H, 2 × $C_6H_5CH_2$), 5.33 (dd, *J* = 9.2, 4.9 Hz, 1 H, H-4), 5.94 (d, *J* = 2.2 Hz, 1 H, H-1), 7.23–7.36 (m, 10 H, 2 × $C_6H_5CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 6.6, 20.8, 47.1, 62.3, 68.8, 69.4, 72.3, 73.4, 73.7, 74.9, 85.5, 127.6, 127.8 (2 C), 127.9 (2 C), 128.3 (3 C), 128.6 (2 C), 136.5, 137.8, 169.5.

MS (FAB+): *m*/*z* (%) = 488.2 [M^+ + H].

Anal. Calcd for $C_{24}H_{29}N_3O_6S$: C, 59.12; H, 6.00; N, 8.62; S, 6.58. Found: C, 59.16; H, 6.09; N, 8.52; S, 6.47.

3-*O*-Benzyl-4,6-*O*-benzylidene-2-*S*-ethyl-2-thio-β-D-mannopyranosyl-(2,2,2-trichloroethoxycarbonyl)amine (12)

To a stirred solution of compound **7** (640 mg, 1.50 mmol) in pyridine–H_2O (9:1, 40 mL) at r.t., 1,3-propanedithiol (2 mL, 19.92 mmol) and Et_3N (2 mL, 14.35 mmol) were added. The reaction mixture was stirred overnight. Progress of the reaction was monitored using TLC with toluene–EtOAc (5:1). The mixture was diluted with toluene (100 mL), washed with 1 M aq HCl (100 mL), sat. aq $NaHCO_3$ (100 mL), H_2O (100 mL), dried ($MgSO_4$) and evaporated. The residue was purified on a silica gel column (25 g) in toluene–$CHCl_3$ (1:4) to yield a solid residue (410 mg), which was dissolved in anhyd pyridine (25 mL). TrocCl (2.4 mL, 17.43 mmol) was added at 0 °C, the reaction mixture was warmed to r.t. and stirred for 2 h. Progress of the reaction was monitored using TLC with toluene–EtOAc (5:1). The mixture was diluted with toluene (100 mL), washed with 1 M aq HCl (2 × 50 mL), sat. aq $NaHCO_3$ (50 mL), H_2O (50 mL), dried ($MgSO_4$) and evaporated. The residue was purified on a silica gel column (25 g) in hexane–EtOAc (6:1) to yield 681 mg (79%) of compound **12**.

$[\alpha]_D^{25}$ +4 (*c* 0.5, $CHCl_3$).

^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.4 Hz, 3 H, SCH_2CH_3), 2.81 (q, *J* = 7.4 Hz, 2 H, SCH_2CH_3), 3.17 (dd, *J* = 4.2, 2.0 Hz, 1 H, H-2), 3.47 (dt, *J* = 10.0, 10.0, 4.9 Hz, 1 H, H-5), 3.74 (t, *J* = 10.4 Hz, 1 H, H-6a), 3.93 (dd, *J* = 9.6, 4.2 Hz, 1 H, H-3), 4.04 (t, *J* = 9.8 Hz, 1 H, H-4), 4.30 (dd, *J* = 10.4, 4.9 Hz, 1 H, H-6b), 4.68 (d, *J* = 12.0 Hz, 1 H, CH_2CCl_3), 4.77 (d, *J* = 12.3 Hz, 1 H, $C_6H_5CH_2$), 4.82 (d, *J* = 12.0 Hz, 1 H, CH_2CCl_3), 4.91 (d, *J* = 12.3 Hz, 1 H, $C_6H_5CH_2$), 5.26 (dd, *J* = 10.1, 2.0 Hz, 1 H, H-1), 5.60 (s, 1 H, C_6H_5CH), 6.62 (br d, *J* = 10.1 Hz, 1 H, NH), 7.27–7.51 (m, 10 H, 2 × Ph).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8, 28.6, 53.2, 68.4, 69.3, 73.3, 74.8, 77.8, 78.0, 80.0, 95.0, 101.5, 126.0, 127.7, 127.9, 128.2 (2 C), 128.5 (2 C), 128.9, 137.3, 138.1, 153.5.

MS (FAB+): *m*/*z* (%) = 576 [M^+ + H].

Anal. Calcd for $C_{25}H_{28}Cl_3NO_6S$: C, 52.05; H, 4.89; Cl, 18,44; N, 2.43; S, 5.56. Found: C, 51.96; H, 4.95; Cl, 18,31; N, 2.37; S, 5.44.

4-*O*-Acetyl-3,6-di-*O*-benzyl-2-*S*-ethyl-2-thio-β-D-mannopyranosyl-(2,2,2-trichloroethoxycarbonyl)amine (13)

To a stirred mixture of compound **9** (470 mg, 1.00 mmol) in pyridine–H_2O (9:1, 30 mL) at r.t., 1,3-propanedithiole (1.4 mL, 13.94 mmol) and Et_3N (1.4 mL, 10.04 mmol) were added. The reaction mixture was stirred overnight at r.t. Progress of the reaction was monitored using TLC with toluene–EtOAc (5:1). The mixture was diluted with toluene (60 mL), washed with 1 M aq HCl (60 mL), sat. aq $NaHCO_3$ (60 mL), H_2O (60 mL), dried ($MgSO_4$) and evaporated. The residue was purified on a silica gel column (20 g) with toluene–$CHCl_3$ (1:4) to yield a solid residue (330 mg), which was dissolved in anhyd pyridine (20 mL). TrocCl (1.8 mL, 13.07 mmol) was added at 0 °C, the reaction mixture was warmed to r.t. and stirred for 2 h. Progress of the reaction was monitored using TLC with toluene–EtOAc (5:1). The mixture was diluted with toluene (60 mL), washed with 1 M aq HCl (2 × 30 mL), sat. aq $NaHCO_3$ (30 mL), H_2O (30 mL), dried ($MgSO_4$) and evaporated. The residue was purified on a silica gel column (20 g) with hexane–EtOAc (6:1) to yield 390 mg (63%) of compound **13**.

$[\alpha]_D^{25}$ –7 (*c* 0.7, $CHCl_3$).

^1H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.3 Hz, 3 H, SCH_2CH_3), 1.91 (s, 3 H, $COCH_3$), 2.63 (dq, *J* = 12.3, 7.3, 7.3, 7.3 Hz, 1 H, SCH_2CH_3), 2.74 (dq, *J* = 12.3, 7.3, 7.3, 7.3 Hz, 1 H, SCH_2CH_3), 3.19 (dd, *J* = 4.1, 1.9 Hz, 1 H, H-2), 3.49 (dd, *J* = 10.8, 5.1 Hz, 1 H, H-6a), 3.53 (dd, *J* = 10.8, 3.5 Hz, 1 H, H-6b), 3.59 (ddd, *J* = 9.0, 5.1, 3.5 Hz, 1 H, H-5), 3.79 (dd, *J* = 9.1, 4.1 Hz, 1 H, H-3), 4.47 (d, *J* = 11.9 Hz, 1 H, $C_6H_5CH_2$), 4.50 (d, *J* = 11.9 Hz, 1 H, $C_6H_5CH_2$), 4.54 (d, *J* = 12.1 Hz, 1 H, $C_6H_5CH_2$), 4.67 (d, *J* = 12.1 Hz, 1 H, $C_6H_5CH_2$), 4.68 (d, *J* = 11.9 Hz, 1 H, CH_2CCl_3), 4.81 (d, *J* = 11.9 Hz, 1 H, CH_2CCl_3), 5.20 (dd, *J* = 10.0, 1.9 Hz, 1 H, H-1), 5.28 (t, *J* = 9.2 Hz, 1 H, H-4), 6.56 (d, *J* = 10.0 Hz, 1 H, NH), 7.23–7.38 (m, 10 H, 2 × Ph).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8, 20.9, 27.8, 51.0, 68.8, 69.3, 72.2, 73.5, 74.7, 75.6, 79.3, 79.6, 95.1, 127.6, 127.7 (2 C), 127.9 (2 C), 128.0, 128.3 (2 C), 128.5 (2 C), 137.5, 137.8, 153.5, 169.6.

MS (FAB+): *m*/*z* (%) = 620 [M^+ + H].

Anal. Calcd for $C_{27}H_{32}Cl_3NO_7S$: C, 52.22; H, 5.19; Cl, 17.13; N, 2.26; S, 5.16. Found: C, 52.18; H, 5.09; Cl, 17.01; N, 2.14; S, 5.11.

4-*O*-Acetyl-3,6-di-*O*-benzyl-2-*S*-ethyl-2-thio-β-D-mannopyranosylamine (14)

$[\alpha]_D^{25}$ –20 (*c* 0.1, $CHCl_3$).

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IR ($CHCl_3$): 3397 (NH_2), 1742, 1237, 1047 (OAc), 3090, 3067, 3032, 1497, 1455 ($PhCH_2$) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.4 Hz, 3 H, SCH_2CH_3), 1.89 (s, 3 H, $COCH_3$), 2.66 (dq, *J* = 12.0, 7.4, 7.4, 7.4 Hz, 1 H, SCH_2CH_3), 2.76 (dq, *J* = 12.0, 7.4, 7.4, 7.4 Hz, 1 H, SCH_2CH_3), 3.38 (dd, *J* = 4.2, 1.6 Hz, 1 H, H-2), 3.44 (ddd, *J* = 9.5, 6.2, 3.2 Hz, 1 H, H-5), 3.46 (dd, *J* = 11.0, 3.2 Hz, 1 H, H-6a), 3.51 (dd, *J* = 11.0, 6.2 Hz, 1 H, H-6b), 3.66 (dd, *J* = 9.5, 4.2 Hz, 1 H, H-3), 4.41 (d, *J* = 12.3 Hz, 1 H, $C_6H_5CH_2$), 4.45 (dt, *J* = 9.8, 9.8, 1.6 Hz, 1 H, H-1), 4.47 (d, *J* = 11.9 Hz, 1 H, $C_6H_5CH_2$), 4.50 (d, *J* = 11.9 Hz, 1 H, $C_6H_5CH_2$), 4.61 (d, *J* = 12.3 Hz, 1 H, $C_6H_5CH_2$), 4.76 (br d, *J* = 9.8 Hz, 2 H, NH_2), 5.12 (t, *J* = 9.5 Hz, 1 H, H-4), 7.25–7.39 (m, 10 H, 2 × $C_6H_5CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.0, 20.9, 28.1, 52.8, 69.7, 70.4, 71.6, 73.5, 75.1, 79.8, 85.7, 127.6, 127.7 (2 C), 127.8 (2 C), 127.8, 128.3 (2 C), 128.4 (2 C), 137.3, 137.4, 169.8.

MS (FAB+): *m/z* (%) = 429 [$M^+ - NH_3 + H$].

Anal. Calcd for $C_{24}H_{31}NO_5S$: C, 64.69; H, 7.01; N, 3.14; S, 7.20. Found: C, 64.84; H, 7.11; N, 3.31; S, 7.07.

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