Synthesis of a New Type of D-Mannosamine Glycosyl Donor and Acceptor and their Use for the Preparation of Oligosaccharides Consisting of D-Mannosamine Units Linked by α(1→4)-Glycosidic Bonds

Matyáš Turský,[a,b,1] Jan Veselý,[a] Iva Tišlerová,[a] Tomáš Trnka,[a] Miroslav Ledvina*[b]

[a] Department of Organic and Nuclear Chemistry, Faculty of Science, Charles University, Albertov 2030, 128 43 Prague 2, Czech Republic

[b] Laboratory of Glycoconjugates, Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Flemingovo nám. 2, 166 10 Prague 6, Czech Republic
Fax +420(2)20183560; E-mail: ledvina@uochb.cas.cz

Received 1 February 2008; revised 6 May 2008

Abstract: Herein, we present the synthesis of three new 2-azido-2-deoxy-D-mannopyranose building blocks that are useful in the preparation of oligosaccharides consisting of α(1→4)-linked 2-azido-2-deoxy-D-mannopyranose units. The successful utilization of these intermediates in the stepwise synthesis of the corresponding trisaccharide is also described in detail.

Key words: carbohydrates, glycosylation, oligosaccharides, D-mannosamine

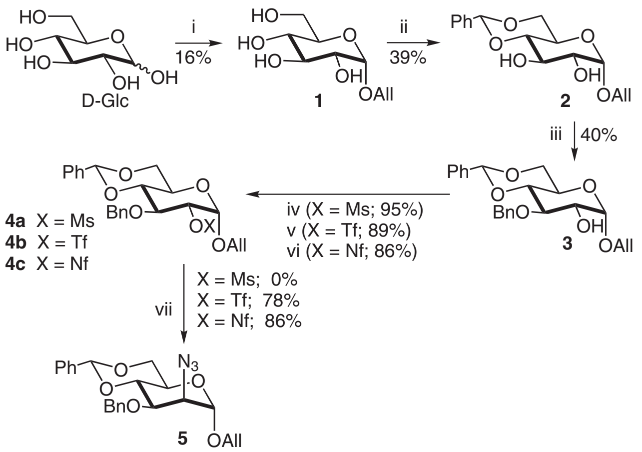
D-Hexopyranoses containing a 1,2-*trans*-(1→4)-linked 2-amino-2-deoxy-sugar motif are common functionalities in biologically important oligosaccharides and their glycoconjugates. This *trans* arrangement imparts multiple biological functions and activities.[2,3] Due to their biological significance, considerable efforts have been undertaken to enable an efficient synthetic approach to these oligosaccharides.[4,5] In contrast to the large amount of work devoted to the synthesis of homooligosaccharides with 1,2-*trans*-β(1→4)-glycosidic linkages such as 2-amino-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-galactopyranose units, to our knowledge, the synthesis of analogous oligosaccharides with a 1,2-*trans*-α(1→4)-glycosidic linkage have received little attention.[4–7] The 1,2-*cis*- as well as 1,2-*trans*-glycosidically (α- or β-) linked 2-acetamido-2-deoxy-D-mannopyranose units are the building blocks of numerous bacterial lipo- and capsular polysaccharides.[8–10] Due to the biological importance, considerable effort has been devoted to developing efficient methods for the incorporation of the D-mannosamine motif into various oligosaccharide chains. One approach, based on mannoazidopyranoside having a non-participating C(2)-azido group within the glycosyl donor, is now under intense study. This approach incorporates a masked amino functionality and stereoselection of the glycosidation reaction can be effectively controlled by steric and electronic substituent effects.[11–13] The 4,6-*O*-benzylidene-protected donors generally afford β-glycosides, and thus offers an improvement on existing methods.[11,12] While initially explained by torsional strain,[14] the significance of electronic effects of C(4) and C(6) substituents on the stereochemical outcome of glycosylation was recently reported.[13]

In 2006, we reported[15] the synthesis of ethyl 2-azido-2-deoxy-1-thio-β-D-mannopyranosides as potential building blocks for the preparation of oligosaccharides requiring (1→4)-linked 2-azido-2-deoxy-D-mannopyranose units. We demonstrated that the electronic interaction between the axially oriented azido group at C(2) and the equatorial sulfur at atom C(1) on the activated mannopyranoside led to significant deactivation of the alkylsulfanyl moiety as the desired leaving group. Attempts to transform the azido group into another suitably protected amino functionality (trichloroethoxycarbonylamino or phthalimido group) via its reduction into an amine were also unsuccessful. Unfortunately, we found that azide reduction was followed by a positional 'switch' of substituents at C(1) and at C(2) with retention of configuration at each position, to give 2-(*S*)-ethyl-2-thio-β-D-mannopyranosylamines.

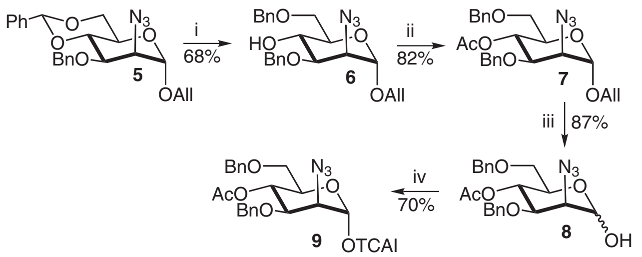
Herein we describe the synthesis of new D-mannosamine building blocks with either the trichloroacetimidate or hydroxy functionality at C(1) as a leaving group and an azide group at C(2). We also present the successful utilization of these building blocks in the convergent synthesis of trisaccharide **12**, consisting of α(1→4)-linked 2-azido-2-deoxy-D-mannopyranose units. The trichloroacetimidate[16] as well as dehydrative[17] methods were employed in parallel.

The synthetic pathway for the preparation of building blocks **6**, **8** and **9** started with known allyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**3**), which was obtained from D-glucose in three steps by a modified literature procedure (the described[18] one-pot synthesis of **2** led to an anomeric mixture of allyl 4,6-*O*-benzylidene-D-glucopyranosides that was difficult to separate by described methods). Refluxing a suspension of D-glucose in allyl alcohol catalyzed by BF_3·OEt_2 gave crystalline allyl α-D-glucopyranoside **1** in 16% yield. The benzylidene acetal **2** was formed with benzaldehyde in the presence of triethyl orthoformate and trifluoromethanesulfonic acid in a mixture of *N*,*N*-dimethylformamide and dioxane in 39% yield. Regioselective 3-*O*-benzylation was accomplished under modified (cesium fluoride) stannylene chemistry, to

SYNTHESIS 2008, No. 16, pp 2610–2616
Advanced online publication: 25.07.2008
DOI: 10.1055/s-2008-1067197; Art ID: T01808SS



Scheme 1 Synthesis of azido derivative **5**. *Reagents and conditions*: (i) AllOH, $BF_3·OEt_2$; (ii) PhCHO, $(EtO)_3CH$, TfOH, DMF–dioxane; (iii) Bu_2SnO, MeOH, then BnBr, CsF, DMF; (iv) MsCl, py; (v) Tf_2O, py, CH_2Cl_2; (vi) NfF, DIPEA, DMAP, CH_2Cl_2; (vii) LiN_3, DMF.



Scheme 2 Synthesis of glycosyl donors. *Reagents and conditions*: (i) Et_3SiH, TFA, CH_2Cl_2; (ii) Ac_2O, py; (iii) $PdCl_2$ (cat.), EtOH–MeOH; (iv) Cl_3CCN, DBU, CH_2Cl_2.

give **3** in 40% yield. Under these conditions, methyl 4,6-*O*-benzylidene-α-D-mannopyranoside yielded the 3-*O*-benzyl derivative preferentially.[19]

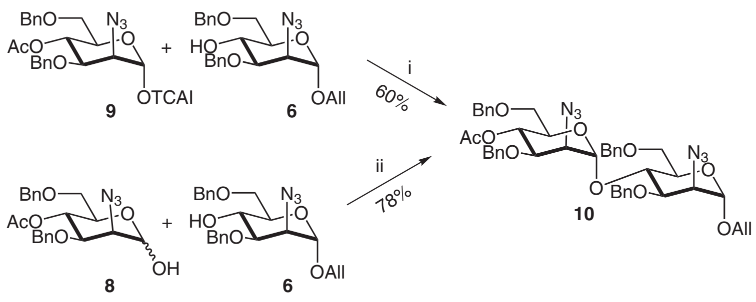
For the synthesis of the key intermediate allyl 2-azido-2-deoxy-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**5**), three sulfonates were prepared. The reaction of **3** with methanesulfonyl chloride in pyridine gave the crystalline 2-*O*-mesyl derivative **4a** in 95% yield. The trifluoromethanesulfonyl derivative **4b** was prepared by the reaction of **3** with triflic anhydride in a mixture of dichloromethane and pyridine with 89% yield. The nonafluorobutanesulfonyl derivative **4c** was obtained in 86% yield by the reaction of **3** with nonafluorobutanesulfonyl fluoride (NfF) in dichloromethane in the presence of *N*,*N*-diisopropylethylamine (DIPEA) and *N*,*N*-dimethylaminopyridine (DMAP).

Our attempts to invert the configuration at C(2) of mesylate **4a** by nucleophilic attack with lithium azide in hot *N*,*N*-dimethylformamide were unsuccessful, while the reaction of triflate **4b** and nonaflate **4c** under identical conditions gave key intermediate **5** in 78% and 86% yield, respectively (Scheme 1). Glycosyl acceptor **6** was prepared from compound **5** by reductive cleavage of the benzylidene acetal group with triethylsilane in the presence of trifluoroacetic acid (TFA) in 68% yield. Formation of the 4-*O*-benzyl ether was not observed.

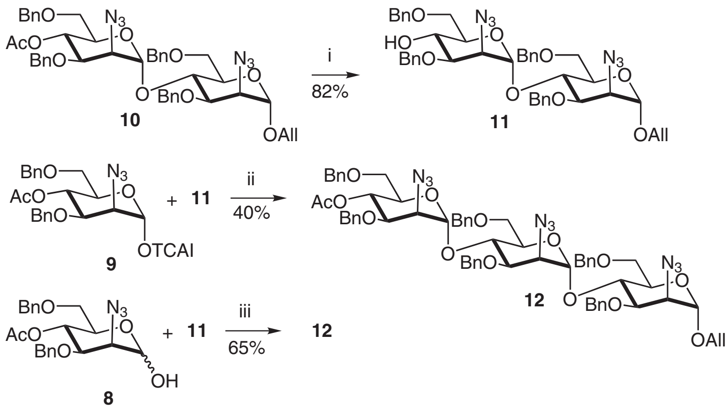
The reaction of **6** with acetic anhydride in pyridine gave the 4-*O*-acetate **7** in 82% yield. The anomeric allyl protective group was removed using a cleavage protocol, forming 1-propenyl ether using a catalytic amount of palladium(II) chloride in a methanol–ethanol mixture, yielding the glycosyl donor **8** in 87% yield. Transformation of the anomeric hydroxy group into a trichloroacetimidate [TCAI; $Cl_3CC(NH)$-] on treatment with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 0.3 equiv) in dichloromethane, afforded the α-trichloroacetimidate **9** exclusively in 70% yield (Scheme 2).

Glycosylation was performed utilizing the trichloroacetimidate protocol or the dehydrative method. The reaction of acceptor **6** with the trichloroacetimidate **9** in dichloromethane in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf; 1.1 equiv) gave the α-glycoside **10** in 60% yield. Using the dehydrative method (donor **8**, activation Ph_2SO, Tf_2O, TTBP; TTBP = 2,4,6-tri-*tert*-butyl pyrimidine), the α-linked disaccharide **10** was isolated in 78% yield. No formation of the β-glycoside was detected in either case (Scheme 3). The trisaccharide **12** was prepared in a similar manner from disaccharide **10** by a route involving Zemplén deacetylation of **10** to give **11** and subsequent glycosylation of **11** to give **12** (trichloroacetimidate method, 40% yield; dehydrative method, 65% yield), as shown in Scheme 4.

The anomeric configuration of disaccharide **10** and trisaccharide **12** were confirmed by NMR spectroscopy. In the 2D-ROESY spectra, cross-peaks between hydrogens H-1 (H-1′, H-1″) and H-3 (H-3′, H-3″) and/or H-5 (H-5′, H-5″) are absent. These cross-peaks are typical for β-configuration, where H-1, H-3 and H-5 are *syn*-axial and thus



Scheme 3 Glycosylation with donors **9** and **8**. *Reagents and conditions*: (i) TMSOTf, CH_2Cl_2; (ii) donor activation: Ph_2SO, TTBP, Tf_2O, then glycosylation: solution of acceptor in CH_2Cl_2.



Scheme 4 Synthesis of trisaccharide **12**. *Reagents and conditions*: (i) MeONa, MeOH; (ii) TMSOTf, CH_2Cl_2; (iii) donor activation: Ph_2SO, TTBP, Tf_2O, then glycosylation: solution of acceptor in CH_2Cl_2.

spatially close. Furthermore, ^3J(H–C–C–C) coupling constants can be estimated from the intensity of cross-peaks in 2D-H,C-HMBC spectra. We observed strong cross peaks between hydrogen H-1 and carbons C-3 and C-5 indicating an antiparallel arrangement of these atoms, which is possible only in the case of the α-anomer. For comparison, cross peaks between H-4 and C-2 and C-6 had much lower intensity. These atoms are in gauche arrangement.

In summary, the synthesis of 2-azido-2-deoxy-D-mannopyranosyl donors and acceptors suitable for the preparation of D-mannosamine type α(1→4)-linked oligosaccharides as well as a synthetic procedure for the build-up of the oligosaccharide chain have been developed. A combination of the influence of the electron-withdrawing character of the azido group at C(2) of glycosyl donor and a low reactivity of the OH(4) group of glycosyl acceptor, resulted in preferential formation of the α-glycosidic bond. As previously stated, it is well known that the electron-withdrawing effect of the azido group at C(2) of the glycosyl donor significantly modulates the course and facial selectivity of the glycosylation reaction, regardless of which protocol we used. Furthermore, it has been suggested that decreased reactivity of glycosyl acceptors leads preferentially to α-mannosides, and the present work supports this hypothesis.[12,20] These results lead the way to the synthesis of oligosaccharides having α(1→4)-linked D-mannosamine units which are of significant synthetic and biological interest. Possessing axial glycosidic linkages to equatorial C(4)–O bonds, the described oligosaccharides satisfy the basic criteria for cyclization, which should lead to the formation of 2-amino-2-deoxy-cyclomannin analogues of cyclodextrins.[21] Synthesis of these cyclodextrin analogues will be reported in due course.

NMR spectra were recorded on Bruker AVANCE-500, Bruker AVANCE-400 or Varian UNITY INOVA 400 instruments (^{1}H NMR at 500 or 400 MHz, respectively; ^{13}C NMR at 125 or 100 MHz, respectively) as $CDCl_3$ or D_2O solutions (referenced to TMS or solvent central peak); data are given as δ values in ppm. ESI MS were measured on a LCQ Classic (Thermo Finnigan) instrument; HR-ESI MS were measured on a Q-Tof micro (Waters) instrument. FAB mass spectra were obtained using a ZAB-EQ sector mass spectrometer (VG Analytical, Manchester) equipped with a Xe gas FAB gun. The instrument was controlled by OPUS running on AlfaStation in the Open VMS environment. Optical rotations were determined on an Autopol IV (Rudolph Research Analytical, USA) polarimeter at 589 nm at 20 °C and $[\alpha]_D$ values are given in deg·cm^2·g^{-1}. Elemental analysis (C, H, N) were performed on a PE 2400 Series II CHNS/O Analyzer (Perkin–Elmer, USA), halogens and sulfur were determined by titration methods. IR spectra were measured on a Bruker IFS-55 instrument as $CHCl_3$ solutions and wavenumbers are given in cm^{-1} (only structurally important peaks are given). Melting points were determined on a Boëtius microapparatus and are uncorrected. TLC were performed on Merck silica gel 60 F_{254} sheets with UV or carbonization detection. For column chromatography, Fluka silica gel 60 (230–400 mesh) was used. Solvents were dried and distilled from P_2O_5 (DMF, CH_2Cl_2), Mg (MeOH), KOH (pyridine) or Na (dioxane) and were stored over 4 Å MS. Glucose was dried over P_2O_5 under reduced pressure. For glycosylations, powdered 4 Å MS (Fluka) were used. Lithium azide was prepared according to the literature procedure.[22]

Allyl α-D-Glucopyranoside (1)

Dried D-glucose (80.23 g, 445.32 mmol) was refluxed in allyl alcohol (470 mL) with $BF_3 \cdot OEt_2$ (6 mL) for 4 h, then the mixture was cooled to r.t., quenched with Et_3N (50 mL), the solvent was evaporated and the residue was recrystallized from EtOAc (2 × 500 mL) to give the title compound **1**.

Yield: 15.85 g (16%); white solid; mp 97–98 °C (EtOAc) [Lit.[23] 99–100 °C (EtOAc–EtOH, 1:1)]; $[\alpha]_D$ +141 (*c* 0.3, H_2O) [Lit.[23] +140.6 (*c* 1.4, H_2O)].

^{1}H NMR (400 MHz, D_2O): δ = 5.99 (dddd, *J* = 5.5, 6.2, 10.4, 17.3 Hz, 1 H), 5.38 (qd, *J* = 1.6, 17.3 Hz, 1 H), 5.27 (tdd, *J* = 1.2, 1.7, 10.4 Hz, 1 H), 4.97 (d, *J* = 3.8 Hz, 1 H), 4.27–4.21 (m, 1 H), 4.11–4.05 (m, 1 H), 3.88–3.67 (m, 4 H), 3.57 (dd, *J* = 3.8, 9.8 Hz, 1 H), 3.41 (dd, *J* = 9.1, 9.9 Hz, 1 H). ^{1}H NMR is in agreement with literature.[24]

Allyl 4,6-*O*-Benzylidene-α-D-glucopyranoside (2)

The glycoside **1** (76.91 g, 349.2 mmol) was dissolved in anhyd DMF–dioxane (1:1, 600 mL), triethyl orthoformate (180 mL, 1.08 mol), benzaldehyde (135 mL, 1.33 mol) and TfOH (4.5 mL, 50.8 mmol) were added and the mixture was stirred at r.t. for 3 d, poured into ice-cold sat. aq $NaHCO_3$ (300 mL) and diluted with H_2O (1.5 L). The crude crystals were filtered off and recrystallized from MeOH (0.5 L) to yield **2**.

Yield: 42.15 g (39%); mp 133–135 °C ($CHCl_3$) [Lit.[18] 135–137 °C (EtOAc)]; $[\alpha]_D$ +114 (*c* 0.5, $CHCl_3$) [Lit.[18] +109.3 (*c* 1.01, $CHCl_3$)].

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.46 (m, 2 H), 7.40–7.34 (m, 3 H), 5.93 (dddd, *J* = 5.4, 6.2, 10.4, 16.8 Hz, 1 H), 5.53 (s, 1 H), 5.33 (ddd, *J* = 1.4, 2.9, 17.2 Hz, 1 H), 5.25 (br dd, *J* = 1.2, 10.4 Hz, 1 H), 4.95 (d, *J* = 4.0 Hz, 1 H), 4.30–4.22 (m, 2 H), 4.10–4.02 (m, 1 H), 3.98–3.92 (m, 1 H), 3.98–3.92 (m, 1 H), 3.73 (t, *J* = 10.2 Hz, 1 H), 3.67–3.60 (m, 1 H), 3.52–3.46 (m, 2 H), 2.83 (br d, *J* = 1.6 Hz, 1 H), 2.31 (d, *J* = 9.6 Hz, 1 H). ^{1}H NMR is in agreement with literature.[18]

Allyl 3-*O*-Benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (3)

The benzylidene acetal **2** (57.05 g, 185 mmol) was refluxed with Bu_2SnO (64.91 g, 260.7 mmol) in MeOH (900 mL) until the solid dissolved (1.5 h), then the solvent was evaporated to dryness and the residue was dissolved in anhyd DMF (650 mL). CsF (34.53 g, 227.3 mmol) and BnBr (24 mL, 202 mmol) were added and the mixture was stirred at r.t. overnight. The solvent was evaporated under reduced pressure and the residue was partitioned between brine (1 L) and $CHCl_3$ (5 × 200 mL). The combined organic layers were extracted with brine (500 mL), dried over $MgSO_4$ and the solvent was evaporated. The solid residue was crystallized (*n*-heptane–EtOH) to afford the title compound **3**.

Yield: 29.95 g (40%); white crystals; mp 137–138 °C ($CHCl_3$) (Lit.[25] 135–136 °C); $[\alpha]_D$ +87 (*c* 0.1, $CHCl_3$) [Lit.[25] +77.5 (*c* 1.11, $CHCl_3$)].

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.47 (m, 2 H), 7.41–7.24 (m, 8 H), 5.93 (dddd, *J* = 5.5, 6.2, 10.4, 16.9 Hz, 1 H), 5.57 (s, 1 H), 5.32 (ddd, *J* = 1.5, 3.0, 17.2 Hz, 1 H), 5.24 (brdd, *J* = 1.3, 10.4 Hz, 1 H), 4.97 (d, *J* = 11.6 Hz, 1 H), 4.96 (d, *J* = 3.6 Hz, 1 H), 4.80 (d, *J* = 11.6 Hz, 1 H), 4.31–4.20 (m, 2 H), 4.10–4.03 (m, 1 H), 3.92–3.82 (m, 2 H), 3.78–3.72 (m, 2 H), 3.65 (t, *J* = 9.4 Hz, 1 H), 2.29 (d, *J* = 8.0 Hz, 1 H). ^{1}H NMR is in agreement with literature.[26]

Allyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-methanesulfonyl-α-D-glucopyranoside (4a)

The benzyl ether **3** (1.0 g, 2.5 mmol) was dissolved in anhyd pyridine (10 mL) under an argon atmosphere and MsCl (0.7 mL, 9.3 mmol) was slowly added. The reaction mixture was stirred at r.t. for 24 h then toluene (60 mL) was added and the mixture was washed with cool aq HCl (1M, 3 × 20 mL), H_2O (3 × 20 mL), dried over $MgSO_4$ and evaporated. Crystallization of the residue from EtOH (15 mL) afforded the product **4a**.

Yield: 1.14 g (95%); mp 105 °C; $[\alpha]_D$ +42 (*c* 0.5, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.27–7.49 (m, 10 H, CHC_6H_5, $OCH_2C_6H_5$), 5.94 (dddd, *J* = 16.5, 10.4, 6.1, 5.3 Hz, 1 H, OCH_2CH=CH_2), 5.60 (s, 1 H, CHC_6H_5), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1 H, OCH_2CH=CH_2), 5.26 (dq, *J* = 10.4, 1.2 Hz, 1 H, OCH_2CH=CH_2), 5.10 (d, *J* = 3.8 Hz, 1 H, H-1), 4.98 (d, *J* = 11.0 Hz, 1 H, $OCH_2C_6H_5$), 4.67 (d, *J* = 11.1 Hz, 1 H, $OCH_2C_6H_5$), 4.48 (dd, *J* = 9.6, 3.8 Hz, 1 H, H-2), 4.31 (dd, *J* = 10.4, 4.9 Hz, 1 H, H-6b), 4.24 (ddt, *J* = 12.8, 5.2, 1.5 Hz, 1 H, OCH_2CH=CH_2), 4.14 (t, *J* = 9.5 Hz, 1 H, H-3), 4.11 (ddt, *J* = 13.0, 6.1, 1.2 Hz, 1 H, OCH_2CH=CH_2), 3.96 (td, *J* = 10.1, 4.9 Hz, 1 H, H-5), 3.77 (t, *J* = 10.4 Hz, 1 H, H-6a), 3.71 (t, *J* = 9.5 Hz, 1 H, H-4), 2.87 (s, 3 H, OSO_2CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 137.77, 136.99, 133.02, 129.08, 128.43 (2 × C), 128.29 (2 × C), 128.09 (2 × C), 127.97, 125.94 (2 × C), 118.45, 101.38, 96.76, 82.58, 78.76, 76.03, 75.33, 69.10, 68.80, 62.37, 38.07.

MS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{24}H_{28}NaO_8S$: 499.14; found: 499.2.

Anal. Calcd for $C_{24}H_{28}O_8S$: C, 60.49; H, 5.92; S, 6.73. Found: C, 60.27; H, 5.86; S, 6.78.

Allyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-trifluormethanesulfonyl-α-D-glucopyranoside (4b)

The benzyl ether **3** (3.61 g, 9.0 mmol) was dissolved in anhyd CH_2Cl_2 (90 mL) and anhyd pyridine (3.8 mL) under an argon atmosphere. The solution was cooled to –30 °C and Tf_2O (2.3 mL, 13.6 mmol) was added dropwise. The mixture was stirred for 20 min at –30 °C and then for 1 h at r.t., poured into ice-cold sat. aq $NaHCO_3$ (150 mL) and extracted with $CHCl_3$ (100 mL). The organic layer was dried over $MgSO_4$ and evaporated. Column chromatography on silica gel (toluene) afforded the product **4b**.

Yield: 4.31 g (89%); white solid; $[\alpha]_D$ +57 (*c* 0.4, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.27–7.49 (m, 10 H, CHC_6H_5, $OCH_2C_6H_5$), 5.90 (dddd, *J* = 16.9, 10.2, 6.4, 5.2 Hz, 1 H, OCH_2CH=CH_2), 5.57 (s, 1 H, CHC_6H_5), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1 H, OCH_2CH=CH_2), 5.29 (dq, *J* = 10.4, 1.2 Hz, 1 H, OCH_2CH=CH_2), 5.12 (d, *J* = 3.8 Hz, 1 H, H-1), 4.87 (d, *J* = 11.0 Hz, 1 H, $OCH_2C_6H_5$), 4.77 (d, *J* = 11.0 Hz, 1 H, $OCH_2C_6H_5$), 4.74 (dd, *J* = 9.5, 3.8 Hz, 1 H, H-2), 4.31 (dd, *J* = 10.4, 4.9 Hz, 1 H, H-6b), 4.25 (ddt, *J* = 12.7, 5.3, 1.2 Hz, 1 H, OCH_2CH=CH_2), 4.17 (t, *J* = 9.3 Hz, 1 H, H-3), 4.07 (ddt, *J* = 12.8, 6.6, 1.4 Hz, 1 H, OCH_2CH=CH_2), 3.95 (td, *J* = 9.9, 4.9 Hz, 1 H, H-5), 3.75 (t, *J* = 10.4 Hz, 1 H, H-6a), 3.70 (t, *J* = 9.5 Hz, 1 H, H-4).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 137.32, 136.84, 132.50, 129.14, 128.31 (4 × C), 128.23 (2 × C), 127.91, 125.94 (2 × C), 119.03, 118.40 (q, *J* = 319 Hz, CF_3SO_2), 101.44, 95.48, 83.44, 82.03, 75.33, 75.09, 69.15, 68.61, 62.45.

MS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{24}H_{25}F_3NaO_8S$: 553.11; found: 553.1.

Anal. Calcd for $C_{24}H_{25}F_3O_8S$: C, 54.34; H, 4.75; F, 10.74; S, 6.04. Found: C, 54.26; H, 4.61; F, 10.38; S, 6.12.

Allyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-(nonafluorobutanesulfonyl)-α-D-mannopyranoside (4c)

NfF (1.1 mL, 6.2 mmol) was added dropwise to a solution of **3** (0.525 g, 1.31 mmol), DMAP (0.54 g, 4.4 mmol) and DIPEA (1 mL, 5.8 mmol) in anhyd CH_2Cl_2 (6 mL) under an argon atmosphere at 0 °C. The mixture was stirred at r.t. overnight then poured into sat. aq $NaHCO_3$ (40 mL) and extracted with $CHCl_3$ (2 × 5 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. Column chromatography of the residue on silica gel (toluene–EtOAc, 20:1) afforded **4c**.

Yield: 774 mg (86%); colorless oil; $[\alpha]_D$ +42 (*c* 0.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.26 (m, 10 H, ArH), 5.90 (dddd, *J* = 5.4, 6.5, 10.3, 17.0 Hz, 1 H, OCH_2CH=CH_2), 5.57 (s, 1 H, $PhCHO_2$), 5.34 (dq, *J* = 1.5, 17.0 Hz, 1 H, OCH_2CH=CH_2), 5.27 (ddt, *J* = 1.2, 1.4, 10.3 Hz, 1 H, OCH_2CH=CH_2), 5.12 (d, *J* = 3.8 Hz, 1 H, H-1), 4.87 (d, *J* = 10.9 Hz, 1 H, CH_2-Ph), 4.81 (dd, *J* = 3.8, 9.5 Hz, 1 H, H-2), 4.78 (d, *J* = 10.9 Hz, 1 H, CH_2-Ph), 4.31 (dd, *J* = 4.9, 10.3 Hz, 1 H, H-6a), 4.25 (ddt, *J* = 1.4, 5.4, 12.6 Hz, 1 H, OCH_2CH=CH_2), 4.18 (t, *J* = 9.4 Hz, 1 H, H-3), 3.95 (ddd, *J* = 4.9, 9.7, 10.3 Hz, 1 H, H-5), 3.76 (t, *J* = 10.3 Hz, 1 H, H-6b), 3.71 (t, *J* = 9.5 Hz, 1 H, H-4).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.30, 136.86 (C_{Ar}), 132.47 (OCH_2CH=CH_2), 129.14, 128.31 (2 × C), 128.30 (2 × C), 128.25 (2 × C), 127.89, 125.95 (C_{Ar}), 119.01 (OCH_2CH=CH_2), 101.46 (CH-Ph), 95.51 (C-1), 83.58 (C-2), 82.09 (C-4), 75.35 (CH_2-Ph), 75.22 (C-3), 69.22 (OCH_2CH=CH_2), 68.63 (C-6), 62.48 (C-5).

MS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{27}H_{25}F_9NaO_8S$: 703.10; found: 702.9.

Anal. Calcd for $C_{27}H_{25}F_9O_8S$: C, 47.65; H, 3.70; F, 25.13; S, 4.71. Found: C, 47.65; H, 3.59; F, 25.04; S, 4.88.

Allyl 2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranoside (5)

Method A: LiN_3 (1.30 g, 26.5 mmol) and **4b** (4.72 g, 8.9 mmol) were dissolved in anhyd DMF (100 mL) under an argon atmosphere and the solution was heated to 120 °C for 1 h. The solvent was evaporated under reduced pressure and the residue was partitioned between H_2O (250 mL) and toluene (100 mL). The organic layer was dried over $MgSO_4$ and the solvent was evaporated. Column chromatography on silica gel (toluene) afforded the product **5**.

Yield: 2.96 g (78%); colorless viscous oil.

Method B: LiN_3 (299 mg, 6.1 mmol) and **4c** (774 mg, 1.14 mmol) were dissolved in anhyd DMF (26 mL) under an argon atmosphere and the solution was heated to 120 °C (r.t. to 120 °C in 30 min) at which time, TLC showed the reaction was complete. The mixture was cooled to r.t., diluted with brine (400 mL) and extracted with $CHCl_3$ (4 × 15 mL). The combined organic layers were extracted with brine (50 mL), dried over $MgSO_4$ and evaporated. Column chromatography of the residue on silica gel (toluene) afforded **5**.

Yield: 415 mg (86%); colorless viscous oil; $[\alpha]_D$ +40 (*c* 0.4, $CHCl_3$).

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.25–7.51 (m, 10 H, CHC_6H_5, $OCH_2C_6H_5$), 5.87 (dddd, *J* = 16.9, 10.5, 6.4, 5.4 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.62 (s, 1 H, CHC_6H_5), 5.27 (dq, *J* = 17.3, 1.7 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.22 (dq, *J* = 10.3, 1.2 Hz, 1 H, $OCH_2C_6H_5$), 4.90 (d, *J* = 12.0 Hz, 1 H, $OCH_2C_6H_5$), 4.80 (d, *J* = 1.5 Hz, 1 H, H-1), 4.74 (d, *J* = 12.2 Hz, 1 H, $OCH_2C_6H_5$), 4.09–4.27 (m, 4 H, H-3, H-5, H-6b, $OCH_2CH{=}CH_2$), 4.01 (dd, *J* = 3.2, 1.5 Hz, 1 H, H-2), 3.96 (ddt, *J* = 12.9, 6.1, 1.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 3.80–3.86 (m, 2 H, H-4, H-6a).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 138.01, 137.34, 133.04, 128.90, 128.36 (2 × C), 128.18 (2 × C), 127.67, 127.43 (2 × C), 125.97 (2 × C), 118.13, 101.52, 98.19, 79.08, 75.67, 73.28, 68.61, 68.21, 63.84, 62.74.

MS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{25}N_3NaO_5$: 446.17; found: 446.2.

Anal. Calcd for $C_{23}H_{25}N_3O_5$: C, 65.24; H, 5.95; N, 9.92. Found: C, 65.31; H, 6.03; N, 9.59.

Allyl 2-Azido-3,6-di-*O*-benzyl-2-deoxy-α-D-mannopyranoside (6)

Triethylsilane (4.4 mL, 27.9 mmol) and TFA (2.2 mL, 29.6 mmol) were added at 0 °C to a solution of **5** (2.37 g, 5.6 mmol) in anhyd CH_2Cl_2 (100 mL). The mixture was stirred at 0 °C for 2 h and then at r.t. overnight, poured into ice-cold sat. aq $NaHCO_3$ (100 mL) and extracted with $CHCl_3$ (100 mL). The organic layer was dried over $MgSO_4$ and the solvent evaporated. Column chromatography on silica gel (toluene–EtOAc, 20:1) gave the product **6**.

Yield: 1.62 g (68%); colorless viscous oil; $[\alpha]_D$ +18 (*c* 0.5, $CHCl_3$).

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.25–7.41 (m, 10 H, 2 × $OCH_2C_6H_5$), 5.87 (dddd, *J* = 17.1, 10.5, 6.3, 5.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.26 (dq, *J* = 17.1, 1.5 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.20 (dq, *J* = 10.4, 1.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 4.84 (d, *J* = 1.7 Hz, 1 H, H-1), 4.75 (d, *J* = 11.6 Hz, 1 H, $OCH_2C_6H_5$), 4.65 (d, *J* = 11.1 Hz, 1 H, $OCH_2C_6H_5$), 4.62 (d, *J* = 11.8 Hz, 1 H, $OCH_2C_6H_5$), 4.56 (d, *J* = 12.2 Hz, 1 H, $OCH_2C_6H_5$), 4.16 (ddt, *J* = 12.8, 5.0, 1.5 Hz, 1 H, $OCH_2CH{=}CH_2$), 3.89–3.99 (m, 4 H), 3.71–3.77 (m, 3 H, H-2, H-3, H-4, H-5, H-6a, H-6b, $OCH_2CH{=}CH_2$), 2.58 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 137.97, 137.52, 133.27, 128.57 (2 × C), 128.33 (2 × C), 128.05, 127.92 (2 × C), 127.60, 127.56 (2 × C), 117.80, 97.32, 79.25, 73.53, 72.44, 71.14, 69.95, 68.04, 67.90, 60.41.

MS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{27}N_3NaO_5$: 448.18; found: 448.2.

Anal. Calcd for $C_{23}H_{27}N_3O_5$: C, 64.93; H, 6.40; N, 9.88. Found: C, 64.63; H, 6.38; N, 6.65.

Allyl 4-*O*-Acetyl-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-mannopyranoside (7)

Ac_2O (4.8 mL, 50.7 mmol) was added to a solution of **6** (1.98 g, 4.6 mmol) in anhyd pyridine (60 mL). The reaction mixture was stirred at r.t. for 24 h, then diluted with toluene (200 mL) and extracted with 1 M HCl until the aqueous layer remained acidic. The organic layer was extracted with sat. aq $NaHCO_3$ (2 × 30 mL), H_2O (2 × 30 mL), dried over $MgSO_4$ and the solvent was evaporated. Column chromatography on silica gel (toluene–EtOAc, 20:1) gave the product **7**.

Yield: 1.80 g (82%); colorless liquid; $[\alpha]_D$ +53 (*c* 0.5, $CHCl_3$).

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.25–7.37 (m, 10 H, 2 × $OCH_2C_6H_5$), 5.89 (dddd, *J* = 16.6, 10.4, 6.3, 5.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.27 (dq, *J* = 17.2, 1.7 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.26 (t, *J* = 9.8 Hz, 1 H, H-4), 5.22 (dq, *J* = 10.4, 1.5 Hz, 1 H, $OCH_2CH{=}CH_2$), 4.85 (d, *J* = 1.8 Hz, 1 H, H-1), 4.69 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 4.57 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 4.52 (s, 2 H, $OCH_2C_6H_5$), 4.18 (ddt, *J* = 13.0, 5.2, 1.5 Hz, 1 H, $OCH_2CH{=}CH_2$), 4.00 (dd, *J* = 9.6, 3.7 Hz, 1 H, H-3), 3.98 (ddt, *J* = 13.0, 6.3, 1.4 Hz, 1 H, $OCH_2CH{=}CH_2$), 3.93 (dd, *J* = 3.7, 1.8 Hz, 1 H, H-2), 3.82 (ddd, *J* = 9.5, 5.3, 3.8 Hz, 1 H, H-5), 3.55 (dd, *J* = 10.7, 5.5 Hz, 1 H, H-6b), 3.51 (dd, *J* = 10.8, 3.7 Hz, 1 H, H-6a), 1.90 (s, 3 H, OAc).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 169.66, 137.93, 137.60, 133.20, 128.42 (2 × C), 128.26 (2 × C), 127.87, 127.71 (2 × C), 127.64 (2 × C), 127.54, 117.94, 97.04, 73.48, 72.27, 70.21, 69.46, 68.43, 68.19, 61.06, 20.80.

MS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{25}H_{29}N_3NaO_6$: 490.20; found: 490.3.

Anal. Calcd for $C_{25}H_{29}N_3O_6$: C, 64.23; H, 6.25; N, 8.99. Found: C, 64.56; H, 6.42; N, 8.74.

4-*O*-Acetyl-2-azido-3,6-di-*O*-benzyl-2-deoxy-α,β-D-mannopyranose (8)

A mixture of **7** (4.09 g, 8.7 mmol) and $PdCl_2$ (100 mg, 0.56 mmol) in EtOH (11 mL) and MeOH (20 mL) was stirred at r.t. overnight. $PdCl_2$ (20 mg, 0.11 mmol) was added and the mixture was stirred at r.t. for 24 h, filtered through Celite and evaporated. Column chromatography of the residue on silica gel (toluene–EtOAc, 10:1) afforded the product **8**.

Yield: 3.26 g (87%); yellowish syrup; $[\alpha]_D$ +33 (*c* 0.5, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ [major anomer (α)] = 7.37–7.26 (m, 10 H, ArH, Bn), 5.16–5.10 (m, 1 H, H-1), 5.12 (t, *J* = 9.7 Hz, 1 H, H-4), 4.67 (d, *J* = 12.1 Hz, 1 H, CH_2-Ph), 4.55 (d, *J* = 12.1 Hz, 1 H, CH_2-Ph), 4.50 (s, 2 H, CH_2-Ph), 4.03 (ddd, *J* = 2.6, 7.5, 10.1 Hz, 1 H, H-5), 3.99 (dd, *J* = 3.7, 9.3 Hz, 1 H, H-3), 3.82 (dd, *J* = 1.8, 3.5 Hz, 1 H, H-2), 3.69 (d, *J* = 3.5 Hz, 1 H, OH), 3.54 (dd, *J* = 7.6, 10.5 Hz, 1 H, H-6a), 3.43 (dd, *J* = 2.8, 10.5 Hz, 1 H, H-6b), 1.92 (s, 3 H, $OCOCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.81 (CH_3CO), 137.57, 137.45, 128.46 (2 × C), 128.36 (2 × C), 128.10 (2 × C), 127.93, 127.82, 127.69 (2 ×C, C_{Ar}, Bn), 92.61, 76.06, 73.52 (CH_2-Ph), 72.27, 69.90 (CH_2-Ph), 69.68, 68.41, 61.27, 20.81 (CH_3CO).

MS (ESI): *m/z* = 450.2 [M + Na]$^+$.

Anal. Calcd for $C_{22}H_{25}N_3O_6$: C, 61.82; H, 5.90; N, 9.83. Found: C, 61.84; H, 5.85; N, 9.54.

_O_-(4-_O_-Acetyl-2-azido-3,6-di-_O_-benzyl-2-deoxy-α-D-mannopyranosyl) Trichloroacetimidate (9)

Method A: Trichloroacetonitrile (0.8 mL, 7.97 mmol) was added to a solution of **8** (276 mg, 0.64 mmol) in anhyd toluene (20 mL) at 0 °C. A solution of DBU (0.12 mL, 0.80 mmol) in anhyd toluene (0.5 mL) was added dropwise and the mixture was stirred at 0 °C for 45 min and then at r.t. overnight. The mixture was extracted with aq. NH_4Cl (2.5 M, 20 mL) and the organic layer was washed with H_2O (20 mL), dried over $MgSO_4$ and evaporated. Column chromatography of the residue on silica gel (toluene–EtOAc, 25:1) afforded **9** (146 mg, 39%) as a yellowish viscous oil.

Method B: Compound **8** (926 mg, 2.1 mmol) was dissolved in anhyd CH_2Cl_2 (20 mL) and trichloroacetonitrile (2.3 mL, 22.9 mmol) was added. The mixture was cooled to 0 °C and DBU (80 μL, 0.56 mmol) was added dropwise. The mixture was stirred at 0 °C for 1.5 h and then for 2.5 h at r.t., then evaporated to dryness. Column chromatography of the residue on silica gel (toluene–EtOAc, 25:1) afforded **9** (868 mg, 70%) as a yellowish viscous oil.

$[\alpha]_D$ +49 (*c* 0.7, $CHCl_3$).

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.66 (s, 1 H, NH), 7.25–7.37 (m, 10 H, 2 × $OCH_2C_6H_5$), 6.20 (d, *J* = 1.8 Hz, 1 H, H-1), 5.40 (t, *J* = 9.6 Hz, 1 H, H-4), 4.66 (s, 2 H, $OCH_2C_6H_5$), 4.53 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 4.49 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 3.96–4.04 (m, 3 H, H-2, H-3, H-5), 3.54 (m, 2 H, H-6a, H-6b), 1.94 (s, 3 H, OAc).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 169.52, 159.77, 137.75, 137.11, 128.58 (2 × C), 128.27 (2 × C), 128.22, 128.17 (2 × C), 127.86 (2 × C), 127.61, 95.73, 90.63, 75.78, 73.49, 72.95, 72.73, 69.01, 67.71, 59.64, 20.82.

MS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{25}H_{29}N_3NaO_6$: 593.07; found: 593.0.

Anal. Calcd for $C_{24}H_{25}Cl_3N_4O_6$: C, 50.41; H, 4.41; Cl, 18.60; N, 9.80. Found: C, 50.52; H, 4.57; Cl, 18.43; N, 9.57.

Allyl 4-_O_-Acetyl-2-azido-3,6-di-_O_-benzyl-2-deoxy-α-D-mannopyranosyl-(1→4)-2-azido-3,6-di-_O_-benzyl-2-deoxy-α-D-mannopyranoside (10)

Method A: A mixture of compounds **9** (259 mg, 0.45 mmol) and **6** (163 mg, 0.38 mmol) in anhyd CH_2Cl_2 (8 mL) was stirred with powdered 4 Å MS (240 mg) for 30 min under an argon atmosphere. After cooling to –50 °C, TMSOTf (105 μL, 0.57 mmol) was added and the mixture was stirred at –50 °C for 2 h and then allowed to warm up to r.t. and stirred overnight. The mixture was diluted with $CHCl_3$ (10 mL) and neutralized with sat. aq $NaHCO_3$. The organic layer was extracted with H_2O (10 mL), dried over $MgSO_4$ and evaporated. Column chromatography of the residue on silica gel (toluene–EtOAc, 20:1) afforded **10** (192 mg, 60% relative to acceptor) as a yellowish oil.

Method B: A mixture of **9** (76 mg, 0.17 mmol), Ph_2SO (80 mg, 0.39 mmol) and TTBP (145 mg, 0.58 mmol) in anhyd CH_2Cl_2 (4 mL) with powdered 4 Å MS (210 mg) was stirred for 30 min at r.t. under an argon atmosphere, then cooled to –48 °C and Tf_2O (32 μL, 0.19 mmol) was added dropwise. The mixture was allowed to warm to –25 °C (in 25 min) and stirred at this temperature for 30 min. A solution of **6** (61 mg, 0.14 mmol) in anhyd CH_2Cl_2 (1 mL) was added dropwise and the mixture was warmed to r.t. (in 2 h) and stirred at r.t. overnight. The reaction was quenched with Et_3N (1 mL) and evaporated to dryness. Column chromatography of the residue on silica gel (toluene → toluene–EtOAc, 5:1) afforded **10** (94 mg, 78% relative to acceptor) as a yellowish oil.

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

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.19–7.42 (m, 20 H, 4 × $OCH_2C_6H_5$), 5.93 (dddd, *J* = 5.2, 6.2, 10.4, 17.4 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.31 (dq, *J* = 1.6, 17.4 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.25 (dq, *J* = 1.4, 10.4 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.19 (t, *J* = 9.4 Hz, 1 H, H-4′), 5.17 (d, *J* = 2.2 Hz, 1 H, H-1′), 4.87 (d, *J* = 1.8 Hz, 1 H, H-1), 4.73 (d, *J* = 11.3 Hz, 1 H, $OCH_2C_6H_5$), 4.51 (d, *J* = 12.0 Hz, 1 H, $OCH_2C_6H_5$), 4.50 (d, *J* = 11.9 Hz, 1 H, $OCH_2C_6H_5$), 4.45 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 4.44 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 4.44 (d, *J* = 11.3 Hz, 1 H, $OCH_2C_6H_5$), 4.43 (d, *J* = 12.0 Hz, 1 H, $OCH_2C_6H_5$), 4.41 (d, *J* = 11.9 Hz, 1 H, $OCH_2C_6H_5$), 4.20 (ddt, *J* = 1.5, 5.2, 12.9 Hz, 1 H, $OCH_2CH{=}CH_2$), 4.01 (dd, *J* = 1.8, 3.5 Hz, 1 H, H-2), 4.01 (ddt, *J* = 1.3, 6.2, 12.9 Hz, 1 H, $OCH_2CH{=}CH_2$), 3.99 (dd, *J* = 3.5, 9.5 Hz, 1 H, H-3), 3.95 (t, *J* = 9.5 Hz, 1 H, H-4), 3.73–3.84 (m, 3 H, H-5, H-6a, H-6b), 3.80 (dd, *J* = 3.5, 9.2 Hz, 1 H, H-3′), 3.72 (ddd, *J* = 3.5, 5.4, 9.6 Hz, 1 H, H-5′), 3.63 (dd, *J* = 2.2, 3.5 Hz, 1 H, H-2′), 3.34 (dd, *J* = 5.4, 10.6 Hz, 1 H, H-6b′), 3.37 (dd, *J* = 3.5, 10.6 Hz, 1 H, H-6a′), 1.89 (s, 3 H, OAc).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 169.6 (CH_3CO), 138.4, 137.9, 137.7, 136.8 (C_{Ar}, Bn), 133.3 ($OCH_2CH{=}CH_2$), 128.8 (2 × C), 128.4 (4 × C), 128.3 (2 × C), 128.2 (2 × C), 128.0, 127.8 (4 × C), 127.5 (2 × C), 127.4 (2 × C), 127.4 (C_{Ar}, Bn), 118.0 ($OCH_2CH{=}CH_2$), 100.1 (C-1′), 97.0 (C-1), 79.7 (C-3), 76.6 (C-3), 74.4 (C-4), 73.5, 73.2, 72.1, 71.6 (CH_2Ph), 71.3 (C-5′), 71.0 (C-5), 69.7 (C-6′), 69.5 (C-6), 68.4 (C-4′), 68.3 ($OCH_2CH{=}CH_2$), 61.0 (C-2′), 60.0 (C-2), 20.8 (CH_3CO).

MS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{45}H_{50}N_6NaO_{10}$: 857.35; found: 857.5.

Anal. Calcd for $C_{45}H_{50}N_6O_{10}$: C, 64.74; H, 6.04; N, 10.07. Found: C, 65.01; H, 6.32; N, 9.74.

Allyl 2-Azido-3,6-di-_O_-benzyl-2-deoxy-α-D-mannopyranosyl-(1→4)-2-azido-3,6-di-_O_-benzyl-2-deoxy-α-D-mannopyranoside (11)

A solution of MeONa in MeOH (0.092 M, 15 mL) was added dropwise to a solution of **10** (910 mg, 1.09 mmol) in anhyd MeOH (50 mL). The mixture was stirred for 24 h at r.t., then neutralized with Dowex-50 (pyridinium form), the solid was filtered off and the solvent was evaporated. Column chromatography of the residue on silica gel (toluene–EtOAc, 10:1) afforded **11**.

Yield: 708 mg (82%); yellowish oil; $[\alpha]_D$ +32 (*c* 0.4, $CHCl_3$).

IR ($CHCl_3$): 3600 (w), 3507 [w, br (ν OH)], 2109 [vs (ν_{as} N_3)], 1056 [s (partly ν C–OH)].

^1H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 20 H, 4 × $OCH_2C_6H_5$), 5.91 (dddd, *J* = 5.2, 6.2, 10.4, 17.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.30 (dq, *J* = 1.7, 17.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.24 (ddt, *J* = 1.2, 1.6, 10.4 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.15 (d, *J* = 1.8 Hz, 1 H, H-1′), 4.87 (d, *J* = 1.7 Hz, 1 H, H-1), 4.74 (d, *J* = 11.3 Hz, 1 H, CH_2-Ph), 4.56 (d, *J* = 11.5 Hz, 1 H, CH_2-Ph), 4.53 (d, *J* = 11.9 Hz, 1 H, CH_2-Ph), 4.51 (d, *J* = 11.5 Hz, 1 H, CH_2-Ph), 4.49 (d, *J* = 11.9 Hz, 1 H, CH_2-Ph), 4.47 (d, *J* = 12.2 Hz, 1 H, CH_2-Ph), 4.46 (d, *J* = 12.2 Hz, 1 H, CH_2-Ph), 4.43 (d, *J* = 11.3 Hz, 1 H, CH_2-Ph), 4.19 (ddt, *J* = 1.5, 5.2, 12.9 Hz, 1 H, $OCH_2CH{=}CH_2$), 4.02–3.97 (m, 4 H, $OCH_2CH{=}CH_2$, H-2, H-3, H-4), 3.91 (t, *J* = 9.5 Hz, 1 H, H-4′), 3.74–3.65 (m, 5 H, H-5, H-6a, H-6b H-3′, H5′), 3.66 (dd, *J* = 1.8, 3.5 Hz, 1 H, H-2′), 3.58 (dd, *J* = 4.8, 10.2 Hz, 1 H, H-6′a), 3.54 (dd, *J* = 4.2, 10.2 Hz, 1 H, H-6′b).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.31, 137.91, 137.65, 136.88 (C_{Ar}), 133.33 ($OCH_2CH{=}CH_2$), 128.76, 128.52, 128.35, 128.33, 128.23, 128.02, 127.96, 127.81 (2 × C), 127.65 (2 × C), 127.62, 127.42 (2 × C), 127.38 (C_{Ar}), 117.92 ($OCH_2CH{=}CH_2$), 100.28 (C-1′), 96.99 (C-1), 79.71 (C-3), 78.97 (C-3′), 74.00 (C-4), 73.61, 73.29, 72.31 (CH_2-Ph), 71.94 (C-5′), 71.63 (CH_2-Ph), 71.24 (C-5), 70.18 (C-6′), 69.42 (C-6), 68.24 ($OCH_2CH{=}CH_2$), 68.11 (C-4′), 60.37 (C-2′), 60.07 (C-2).

MS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{43}H_{48}N_6NaO_9$: 815.34; found: 815.3.

MS (HR-FAB): *m/z* [M + H]$^+$ calcd for $C_{43}H_{49}N_6O_9$: 793.3561; found: 793.3540.

Allyl 4-*O*-Acetyl-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-mannopyranosyl-(1→4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-mannopyranosyl-(1→4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-mannopyranoside (12)

Method A: A mixture of **9** (122 mg, 0.21 mmol), **11** (134 mg, 0.168 mmol) and powdered 4 Å MS (240 mg) in anhyd CH_2Cl_2 (10 mL) was stirred at r.t. for 30 min under an argon atmosphere. The mixture was cooled to –50 °C and TMSOTf (50 μL, 0.07 mmol) was added dropwise. The mixture was stirred at –50 °C for 2 h and then slowly warmed to r.t. (within 2 h) and stirred at this temperature overnight. $CHCl_3$ (15 mL) was added and the solution was washed with sat. aq $NaHCO_3$ (2 × 30 mL) and H_2O (10 mL). The organic phase was dried over $MgSO_4$ and the solvent was evaporated. Column chromatography of the residue on silica gel (toluene–EtOAc, 30:1) afforded **12** as a yellowish oil [83 mg (41% to acceptor)]; When the reaction was performed on a 0.056 mmol scale (of the acceptor), the yield was 60%.

Method B: A mixture of **8** (72 mg, 0.168 mmol), Ph_2SO (74 mg, 0.36 mmol), TTBP (135 mg, 0.54 mmol) and powdered 4 Å MS (240 mg) was stirred in anhyd CH_2Cl_2 (4 mL) under an argon atmosphere at r.t. for 20 min. After cooling to –52 °C, Tf_2O (30 μL, 0.178 mmol) was added dropwise and the mixture was warmed to –25 °C in 30 min and stirred at this temperature for 30 min. A solution of **11** (92 mg, 0.116 mmol) in anhyd CH_2Cl_2 (2 mL) was added dropwise and the mixture was warmed to r.t. in 2 h and stirred at r.t. overnight. The reaction was quenched with Et_3N (1 mL) and evaporated to dryness. Column chromatography of the residue on silica gel (toluene → toluene–EtOAc, 5:1) afforded **12** (91 mg, 65% to acceptor) as a yellowish oil

$[\alpha]_D$ +28 (*c* 0.2, $CHCl_3$).

IR ($CHCl_3$): 2110 [vs (ν_{as} N_3)], 1745 [w (ν C=O)].

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.17 (m, 30 H, 6 × $OCH_2C_6H_5$), 5.95 (dddd, *J* = 5.2, 6.2, 10.2, 17.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.33 (dq, *J* = 1.6, 17.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.29 (ddt, *J* = 1.2, 1.7, 10.2 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.20 (dd, *J* = 9.8, 10.8 Hz, 1 H, H-4″), 5.14 (d, *J* = 2.1 Hz, 1 H, H-1′), 5.12 (d, *J* = 2.2 Hz, 1 H, H-1″), 4.90 (d, *J* = 1.8 Hz, 1 H, H-1), 4.80 (d, *J* = 11.3 Hz, 1 H, CH_2-Ph), 4.53 (d, *J* = 12.0 Hz, 1 H, CH_2-Ph), 4.52 (d, *J* = 11.9 Hz, 1 H, CH_2-Ph), 4.47 (d, *J* = 11.3 Hz, 1 H, CH_2-Ph), 4.45 (d, *J* = 12.0 Hz, 1 H, CH_2-Ph), 4.45 (d, *J* = 11.3 Hz, 1 H, CH_2-Ph), 4.42 (d, *J* = 11.9 Hz, 2 H, 2 × CH_2-Ph), 4.41 (d, *J* = 12.0 Hz, 1 H, CH_2-Ph), 4.38 (d, *J* = 11.9 Hz, 1 H, CH_2-Ph), 4.37 (d, *J* = 12.0 Hz, 1 H, CH_2-Ph), 4.23 (d, *J* = 11.3 Hz, 1 H, CH_2-Ph), 4.23 (ddt, *J* = 1.5, 5.2, 12.9 Hz, 1 H, $OCH_2CH{=}CH_2$), 4.08 (dd, *J* = 1.8, 3.5 Hz, 1 H, H-2), 4.04 (dd, *J* = 3.5, 9.0 Hz, 1 H, H-3), 4.03 (ddt, *J* = 1.2, 6.2, 12.9 Hz, 1 H, $OCH_2CH{=}CH_2$), 3.94 (dd, *J* = 9.0, 9.5 Hz, 1 H, H-4), 3.90 (dd, *J* = 9.2, 9.6 Hz, 1 H, H-4′), 3.81–3.78 (m, 4 H, H-6b, H-5, H-3′, H-3″), 3.74 (ddd, *J* = 3.6, 5.1, 9.8 Hz, 1 H, H-5″), 3.70 (ddd, *J* = 1.9, 5.5, 9.2 Hz, 1 H, H-5′), 3.69 (dd, *J* = 2.1, 3.3 Hz, 1 H, H-2′), 3.66 (dd, *J* = 5.0, 11.5 Hz, 1 H, H-6a), 3.64 (dd, *J* = 2.2, 3.5 Hz, 1 H, H-2″), 3.60 (dd, *J* = 1.9, 11.0 Hz, 1 H, H-6′b), 3.52 (dd, *J* = 5.5, 11.0 Hz, 1 H, H-6′a), 3.37 (dd, *J* = 5.1, 10.6 Hz, 1 H, H-6″b), 3.35 (dd, *J* = 3.6, 10.6 Hz, 1 H, H-6″a), 1.88 (s, 3 H, CH_3CO).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.55 (CH_3CO), 138.30, 137.86, 137.70, 136.84, 136.82 (C_{Ar}), 133.33 ($OCH_2CH{=}CH_2$), 118.00 ($OCH_2CH{=}CH_2$), 100.16 (C-1′), 96.89 (C-1″), 96.95 (C-1), 79.64 (C-3), 79.32 (C-3′), 76.70 (C-3″), 74.79 (C-4), 74.02 (C-4′), 73.53, 73.41, 73.28 (CH_2-Ph), 72.12 (C-5′), 72.03, 71.52, 71.46 (CH_2-Ph), 71.43 (C-5), 70.91 (C-5″), 69.85 (C-6), 69.69 (C-6′), 69.37 (C-6″), 68.42 (C-4″), 68.36 ($OCH_2CH{=}CH_2$), 60.90 (C-2″), 59.85 (C-2), 59.81 (C-2′), 20.82 (CH_3CO).

MS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{65}H_{71}N_9NaO_{14}$: 1224.5018; found: 1224.5070.

Acknowledgment

We are thankful for the support to the Grant Agency of Czech Academy of Science (grant No. KAN200520703), Ministry of Education of the Czech Republic (project No. LC06070 and MSM 0021620857), Grant Agency of Ministry of Agriculture of the Czech Republic (grant No. QF3115/2003) and research project No. Z4 055 0506.

References

(1) Present address: Center for Sustainable and Green Chemistry, Department of Chemistry, Building 201, Technical University of Denmark, 2800 Kgs. Lyngby, Denmark.
(2) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683.
(3) Varki, A. *Glycobiology* **1993**, *3*, 97.
(4) Bongat, A. F. G.; Demchenko, A. V. *Carbohydr. Res.* **2007**, *342*, 374.
(5) Banoub, J.; Boullanger, P.; Lafont, D. *Chem. Rev.* **1992**, *92*, 1167.
(6) Gridley, J. J.; Osborn, H. M. I. *J. Chem. Soc., Perkin Trans. 1* **2000**, *10*, 1471.
(7) Veselý, J.; Ledvina, M.; Jindřich, J.; Trnka, T.; Šaman, D. *Collect. Czech. Chem. Commun.* **2004**, *69*, 1914.
(8) Beynon, L. M.; Richards, J. C.; Perry, M. B.; Kniskern, P. J. *Can. J. Chem.* **1992**, *70*, 218.
(9) Osa, Y.; Kaji, E.; Takahashi, K.; Hirooka, M.; Zen, S.; Lichtenthaler, F. W. *Chem. Lett.* **1993**, 1567.
(10) Silipo, A.; Molinaro, A.; Lanzetta, R.; Parrilli, M.; Lindner, B.; Holst, O. *Eur. J. Org. Chem.* **2004**, 1336.
(11) Litjens, R. E. J. N.; Leeuwenburgh, M. A.; van der Marel, G. A.; van Boom, J. H. *Tetrahedron Lett.* **2001**, *42*, 8693.
(12) Litjens, R. E. J. N.; van den Bos, L. J.; Codée, J. D. C.; van den Berg, R. J. B. H. N.; Overkleeft, H. S.; van der Marel, G. A. *Eur. J. Org. Chem.* **2005**, 918.
(13) van den Bos, L. J.; Duivenvoorden, B. A.; de Koning, M. C.; Filippov, D. V.; Overkleeft, H. S.; van der Marel, G. A. *Eur. J. Org. Chem.* **2007**, 116.
(14) Crich, D.; Chandrasekera, N. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 5386.
(15) Veselý, J.; Rohlenová, A.; Dýžoganová, M.; Trnka, T.; Tišlerová, I.; Šaman, D.; Ledvina, M. *Synthesis* **2006**, 699.
(16) Schmidt, R. R.; Kinzy, W. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21.
(17) Gin, D. *J. Carbohydr. Chem.* **2002**, *21*, 645.
(18) Tanaka, H.; Kawai, K.; Fujiwara, K.; Murai, A. *Tetrahedron* **2002**, *58*, 10017.
(19) Jenkins, D. J.; Potter, B. V. L. *Carbohydr. Res.* **1994**, *265*, 145.
(20) Codée, J. D. C.; van den Bos, L. J.; Litjens, R. E. J. N.; Overkleeft, H. S.; van Boeckel, C. A. A.; van Boom, J. H.; van der Marel, G. A. *Tetrahedron* **2004**, *60*, 1057.
(21) Gattuso, G.; Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev.* **1998**, *98*, 1919.
(22) Hofman-Bang, N. *Acta Chem. Scand.* **1957**, *11*, 581.
(23) Jenkins, D. J.; Potter, B. V. L. *Carbohydr. Res.* **1996**, *287*, 169.
(24) Holme, K. R.; Hall, L. D. *Carbohydr. Res.* **1992**, *225*, 291.
(25) Fukase, K.; Matsumoto, T.; Ito, N.; Yoshimura, T.; Kotani, S.; Kusumoto, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2643.
(26) Peer, A.; Vasella, A. *Helv. Chim. Acta* **1999**, *82*, 1044.