Synthesis of biotinylated pentasaccharide structurally related to a fragment of glucomannan from *Candida utilis**

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The polysaccharide mannan is the main surface antigen of the cell wall of *Candida* fungi, playing an important role in the pathogenesis of diseases caused by these mycopathogens. Mannan has a complex, comb-like structure and includes a variety of structural units, with their combination varying depending on the *Candida* species and strain. Glucomannan, a polysaccharide from *Candida utilis*, contains terminal α-D-glucose residues attached to oligomannoside side chains. This paper describes the first synthesis of a pentasaccharide structurally related to *C. utilis* glucomannan fragment, which is an α-(1→2)-linked tetramannoside terminated at the non-reducing end by an α-D-glucopyranosyl residue. The pentasaccharide was obtained as a 3-aminopropyl glycoside, which made it possible to synthesize also its biotinylated derivative, suitable for various glycobiological studies. The most complicated step in the pentasaccharide synthesis was stereoselective 1,2-*cis*-glycosylation to attach the α-D-glucopyranosyl residue. This was accomplished using a glucosyl donor specially developed in our laboratory, the protecting groups of which provide the necessary α-stereoselectivity. The target biotinylated pentasaccharide thus obtained will be used in the future as a model antigen for the detection of immunodeterminant epitopes of *Candida* mannans.

Key words: *Candida utilis*, glucomannan, antigen, oligosaccharide, 1,2-*cis*-glycosylation.

The yeast-like fungus *Candida* is normally a part of natural microflora of humans; however, as a result of certain pathological processes, this microorganism can induce severe and difficult-to-cure surface (located on skin and mucous membranes) and invasive candidiases.[1,2] The invasive candidiases is the most severe disease caused by *Candida spp.,* which appears when the fungal cells penetrate into the bloodstream and spread from the focus of infection throughout the body.[2] The invasive candidiasis affects approximately 750 000 people annually all over the world and has a high lethality of up to 30—55%.[3] In Russia, more than 11 000 cases of this disease are recorded every year.[4] In 2020, due to the spread of the new coronaviral infection SARS-CoV-2, cases of COVID-19-associated invasive candidiases started to be recorded and systematized.[5] Currently, the development of acute respiratory distress syndrome and stay in the intensive care units are regarded as the main risk factors for the development of invasive candidiases associated with COVID-19.[5]

Currently, about 17 *Candida* species capable of causing the disease in humans are known, with more than 90% of all systemic candidiases being caused by *C. albicans*, *C. glabrata, C. parapsilosis, C. tropicalis*, and *C. krusei*. However, in recent years, increased morbidity and mortality due to rare *Candida* species have been observed. There are serious concerns about infectious agents such as *C. auris*, *C. utilis*, *C. lipolytica*, *C. catenulata*, and so on, which cause stubborn infections, especially in hospitalized patients with significant comorbid conditions.[6,7]

Mannan is the main surface polysaccharide component of the *Candida* cell wall.[8] This polysaccharide plays a key role as an antigen in the recognition of this pathogen by the immune system.[8,9] Normally, the interaction of immunologically active mannan fragments with pathogen-associated molecular pattern recognition receptors (DC-SIGN, Dectin-2, CD206, *etc.*) results in activation of immune cells and pathogen neutralization.[10,11] In addition, mannan is a convenient diagnostic marker for detection of invasive or another candidiasis in patients without specific symptoms.[12]

The most well-known commercial enzyme-linked immunosorbent assay used to determine mannan circulating in the blood is PLATELIA™ *Candida* Ag PLUS (Bio-Rad Laboratories, France).[13] This assay kit uses a specific monoclonal antibody, which recognizes the oligo-α-

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(1→2)-D-mannoside sequence terminated by one or two β-(1→2)-linked D-mannoside units, as shown in our recent study using a series of synthetic models.[14]

From the chemical standpoint, mannan is the carbohydrate part of the mannoprotein with a comb-like structure. Mannan structure is formed by the α-(1→6)-linked backbone, in which some mannose residues bear relatively short linear and branched oligomannoside side chains attached *via* α-(1→2)-bonds.[8,15] They can be composed of α-(1→2)-, α-(1→3)-, α-(1→6)-, and β-(1→2)-linked mannose residues and significantly differ in the size, chemical structure, and antigen properties (Fig. 1, *a*).[8] The mannan structure varies depending on the *Candida* species and strain. For example, mannan from *C. utilis* contains a unique structural unit: mannose side chains terminated by α-D-glucosyl residue (Fig. 1, *b*).[16] Due to the presence of this residue, this polysaccharide is called glucomannan.

Natural polysaccharides are too complex and heterogeneous to be used for analysis of immunobiological properties of mannans. Furthermore, the result of biotechnological growth of fungal mass and subsequent isolation of polysaccharides is poorly controllable and poorly reproducible.[17] Therefore, synthetic oligosaccharides related to the key fragments of this polysaccharide are an indispensable tool for many interdisciplinary studies of natural polysaccharide antigens.[18,19] Oligosaccharides form the basis for the development of vaccines and diagnostic kits and the search for immunodeterminant fragments of fungal cell wall polysaccharides[14,20–25] and are valuable models for the structural studies of natural fungal polysaccharides.[19,26–29]

In order to elucidate the immunological role of the glucomannan chains terminated by the α-D-glucosyl residue, we prepared spacered pentasaccharide **1** consist-

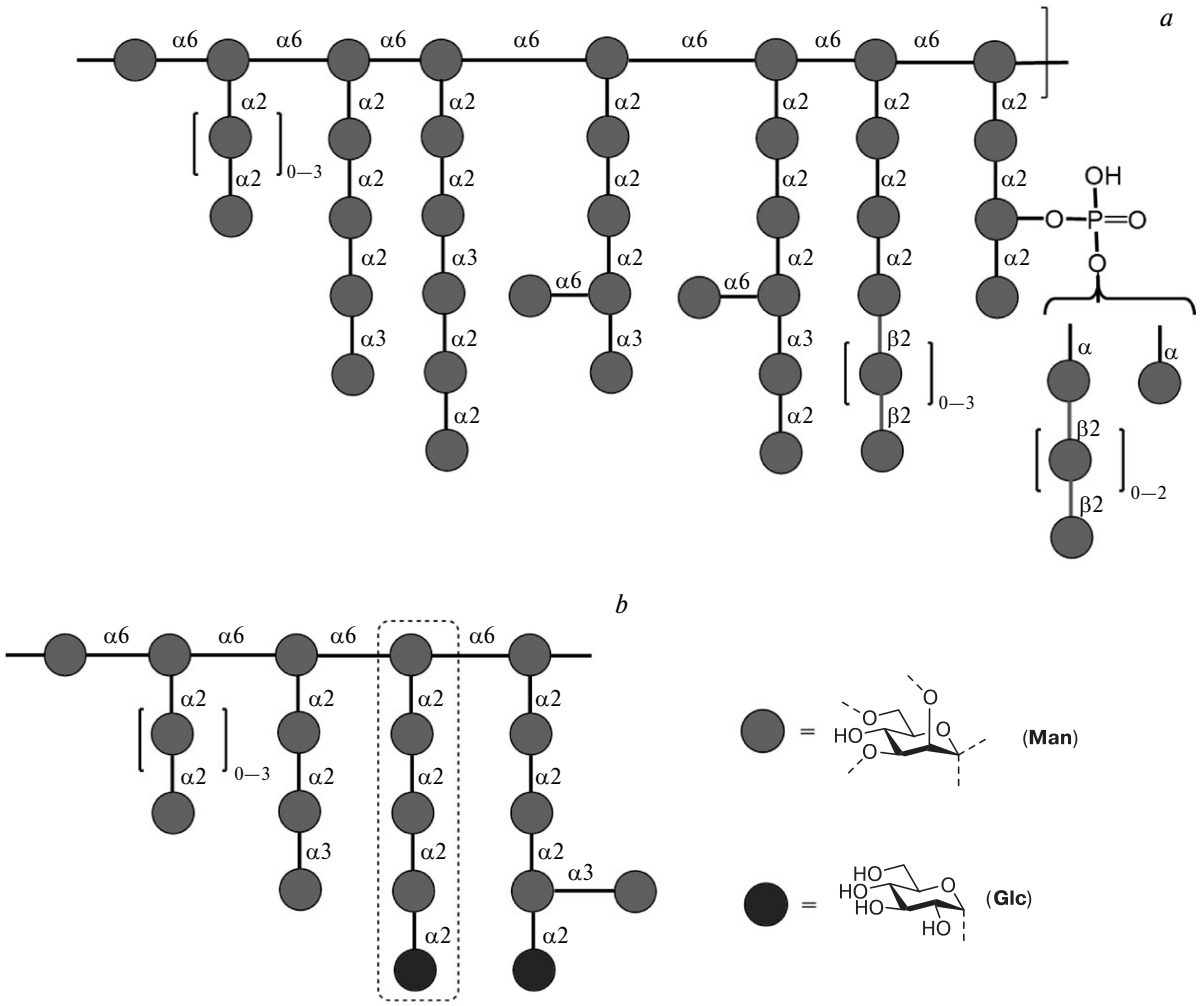


Fig. 1. Schematic structure of mannans of yeast-like fungus *Candida*. (*a*) Generalized structure of mannan of *Candida albicans* according to published data.[8,15] (*b*) Mannan structure published for *C. utilis*[16]. The dashed frame encloses the oligosaccharide fragment corresponding to pentasaccharide **1** synthesized in this study (see Fig. 2).

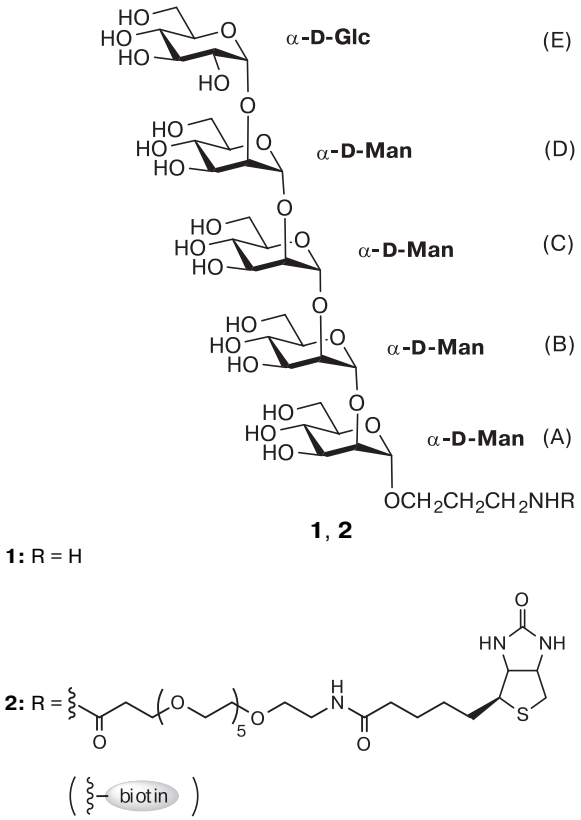


Fig. 2. Target spacered pentasaccharide **1** related to the *C. utilis* glucomannan side chain and its biotinylated derivative **2**.

ing of four α-(1→2)-linked mannose residues and terminal α-(1→ 2)-linked glucose residue at the non-reducing end of the oligosaccharide chain and its biotinylated derivative **2** (Fig. 2). This paper describes the synthesis of compounds **1** and **2**.

Results and Discussion

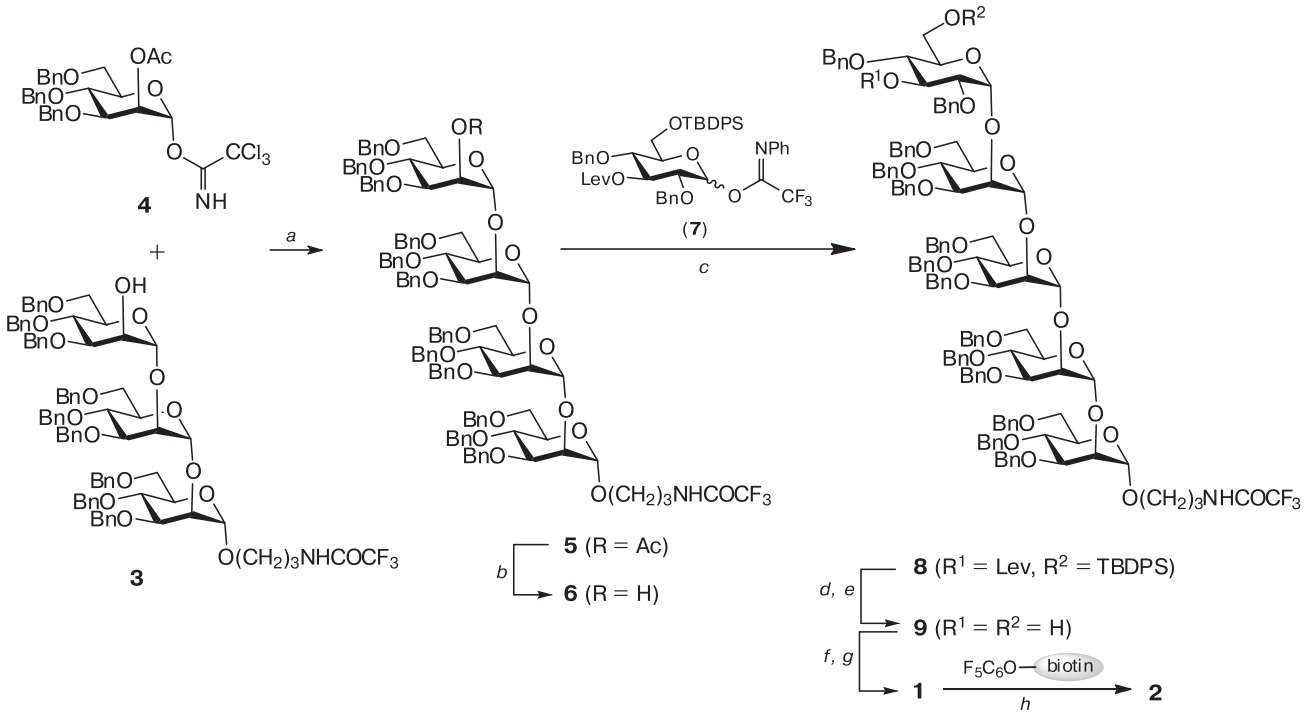
The key steps of the synthesis of spacered pentasaccharide **1** include the stereoselective formation of four glycosidic bonds. In the case of mannose moieties, the formation of α-glycosidic bond is a relatively simple task. The stereoselective formation of the 1,2-*trans*-mannosidic bond can easily be attained by using the stereocontrolling effect of the protecting group at O(2). However, α-glucosylation requires thorough selection of protecting groups and reaction conditions.[30—32] As the starting compound, we took trimannoside **3** (Scheme 1), prepared previously in our laboratory.[33] Glycosylation of this derivative by trichloroacetimidate mannosyl donor **4**[34] promoted by trimethylsilyl triflate proceeds stereoselectively to give tetramannoside **5** in a high yield. Zemplen deacetylation of compound **5** affords tetramannosyl acceptor **6**. The ^{1}H NMR spectrum of derivative **6** does not show a signal for the acetyl group, which attests to the presence of a free hydroxy group at C(2$_D$).

The selective glucosylation of compound **6** was accomplished by using glucosyl donor **7**, synthesized recently in our laboratory, at the final step of assembly of the pentasaccharide chain.[35] The use of compound **7** containing stereocontrolling protecting groups at O(3) (levulinoyl (Lev) group) and O(6) (*tert*-butyldiphenylsilyl (TBDPS) group) allows the stereospecific construction of the 1,2-*cis*-glucosidic bond. As expected, the reaction of glucosyl donor **7** with tetramannosyl acceptor **6** in the presence of *tert*-butyldimethylsilyl triflate (TBSOTf) resulted in the stereospecific formation of the α-(1→2)-glucosidic bond, thus giving protected pentasaccharide **8** in 87% yield. The α-configuration of the glucosidic bond was confirmed by the characteristic value of the spin—spin coupling constant $^3J_{H(1),H(2)}$ = 3.5 Hz between the H(1) and H(2) protons of the glucose residue.

Treatment of compound **8** with hydrazine hydrate to remove the levulinoyl protection and the subsequent removal of *tert*-butyldiphenylsilyl group on treatment with tetrabutylammonium fluoride resulted in partially deprotected pentasaccharide **9**. The benzyl and *N*-trifluoroacetyl deprotection of derivative **9** *via* successive palladium-catalyzed hydrogenolysis and alkaline treatment gave the target pentasaccharide **1**. The α-configuration of the four mannosyl residues in oligosaccharide **1** unambiguously followed from the spin—spin coupling constants between the H(1) protons and the C(1) atoms: $^1J_{C(1),H(1)}$ = 174 Hz; the α-glucosidic bond configuration was confirmed (as in the case of protected derivative **8**) by the characteristic spin—spin coupling constant $^3J_{H(1),H(2)}$ = 3.5 Hz. Biotinylation of compound **1** by treatment with activated ester of biotin derivative[36] in the presence of triethylamine gave the desired product **2** (see Scheme 1). The NMR spectra of the products (see Experimental) were fully in line with their structures.

The synthetic moieties of polysaccharides that are poorly accessible from natural sources are popular models for various glycobiological studies, which stimulates search for methods of the targeted chemical synthesis of these products.[37] Compounds **1** and **2** obtained in this study will be used, together with other oligosaccharides related to *Candida* mannans, as model antigens to determine the immunological roles of certain structural fragments of cell wall polysaccharides of this group of pathogens and also as models for the calculation of spectral (NMR) effects of glycosylation[38] in the branched oligosaccharide fragment shown in Fig. 1, *b*. The results of these studies will be published elsewhere.

Scheme 1



Reagents, conditions, and yields: *a*. TMSOTf, CH_2Cl_2, 0 °C; *b*. MeONa, CH_2Cl_2—MeOH, 20 °C, 83% (over two steps); *c*. TBSOTf, CH_2Cl_2, molecular sieves AW300, −35 °C, 87%; *d*. NH_2NH_2, pyridine—AcOH, 20 °C; *e*. TBAF, THF, 60 °C, 76% (over two steps); *f*. H_2, $Pd(OH)_2/C$, EtOAc—MeOH, 20 °C; *g*. NaOH, MeOH—H_2O, 20 °C, 50% (over two steps); *h*. Et_3N, DMF, 20 °C, 75%.

Experimental

All reactions were carried out in solvents purified by standard procedures.[39] The glycosylation was conducted in anhydrous solvent. The molecular sieves were activated before the reaction at 180 °C for 2 h in an oil pump vacuum. Thin layer chromatography was carried out on Kieselgel 60 F_{254} silica gel plates (Merck); the spots of compounds were visualized in the UV light or by spraying the plates with an orcinol solution (180 mg of orcinol in a mixture of 85 mL of water, 10 mL of orthophosphoric acid, and 5 mL of ethanol) followed by heating at ~150 °C. Column chromatography was carried out on Silica gel 60 (40—63 μm, Merck), and gel chromatography of free oligosaccharides was performed on a column with the TSK HW-40(S) gel (1.5×90 cm) in 0.1 *M* acetic acid; the eluate was analyzed using a Knauer K-2401 flow refractometer. Optical rotation was measured on a JASCO P-2000 polarimeter at 18—22 °C in the indicated solvents. NMR spectra were recorded at 25 °C on Bruker Avance 600, Bruker AM 300, and Bruker AV 400 instruments. The spectra of the protected derivatives were measured in $CDCl_3$; the spectra of unprotected oligosaccharides were recorded in D_2O; acetone was used as the internal standard (δ_H 2.225, δ_C 31.45). The signals were assigned using COSY and HSQC 2D NMR correlation procedures. In the description of the NMR spectra, the monosaccharide residues are designated by letters A, B, C, D, and E (see Fig. 2), starting from the reducing end of the oligosaccharide.

High-resolution electrospray ionization (ESI) mass spectra were measured on a Bruker micrOTOF II instrument.

3-Trifluoroacetamidopropyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (6). Trimethylsilyl triflate (18 μL, 0.093 mmol, 12 mol. % with respect to compound **4**) was added at 0 °C to a stirred mixture of trichloroacetimidate **4** (500 mg, 0.785 mmol, 1.2 equiv.) and monohydroxy glycosyl acceptor **3** (960 mg, 0.654 mmol) in dichloromethane (10 mL). The reaction mixture was stirred at 0 °C for 15 min, neutralized by adding triethylamine (0.02 mL), and concentrated *in vacuo* to give 1.26 g of crude product **5** (quantitative yield). The product was dissolved in a mixture of dichloromethane (2 mL) and methanol (5 mL) and treated with a 1 *M* solution of sodium methoxide in methanol (1 mL) at 20 °C for 4 h. The reaction mixture was neutralized by adding acetic acid (0.08 mL) and concentrated *in vacuo*. The residue was separated on silica gel using gradient elution with an acetone—toluene mixture (0→8%). This gave 1.027 g (83%) of monohydroxy derivative **6**, syrup; R_f 0.50 (toluene—acetone, 9 : 1). $[\alpha]_D$ +38 (*c* 1, $CHCl_2$). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 1.64—1.73 (m, 2 H, $OCH_2C\underline{H}_2CH_2N$); 3.16—3.28 (m, 2 H, $OCH_2CH_2C\underline{H}HN$ and $OC\underline{H}HCH_2CH_2N$); 3.32—3.42 (m, 1 H, $OCH_2CH_2CH\underline{H}N$); 3.45—3.82 (m, 13 H, $OCH\underline{H}CH_2CH_2N$, $H(6a_{A,B,C,D})$, $H(6b_{A,B,C,D})$, and $H(5_{A,B,C,D})$); 3.83—4.22 (m, 13 H, $H(2_{A,B,C,D})$, $H(3_{A,B,C,D})$, $H(4_{A,B,C,D})$ and $C\underline{H}HPh$); 4.25—4.91 (m, 23 H, 11 $C\underline{H}_2Ph$ and $CH\underline{H}Ph$); 5.00, 5.14, 5.24, and 5.30 (all s, 4 H, $H(1_{A,B,C,D})$); 6.86 (m, 1 H, NH); 7.00—7.40

(m, 60 H, 12 Ph). ^{13}C NMR (150 MHz, $CDCl_2$), δ: 28.0 ($OCH_2\underline{C}H_2CH_2N$), 37.9 ($OCH_2CH_2\underline{C}H_2N$), 65.7 ($O\underline{C}H_2CH_2CH_2N$), 68.5 ($C(2_D)$), 68.8, 69.4, 69.5, and 70.0 ($C(6_{A,B,C,D})$), 71.6, 71.7, 71.8, 71.9, 72.0, 72.2, 73.1, 73.2, 73.3, 74.3, 74.7, 74.8, 74.9, 75.0, 75.1, 75.7, and 76.1 ($C(2_{A,B,C})$, $C(4_{A,B,C,D})$, $C(5_{A,B,C,D})$, 12 $\underline{C}H_2Ph$); 79.0, 79.3, 79.7, and 80.0 ($C(3_{A,B,C,D})$), 99.0 ($C(1_A)$), 100.9(2) and 101.4 ($C(1_{B,C,D})$), 127.3, 127.4, 127.6, 127.7, 127.9, 128.1, 128.3, 128.4, 128.5, 129.6, 129.7, 133.2, 133.6, 135.9, 137.9, 138.1, 138.2, 138.4, 138.5, 138.6 (12 Ph). MS, found: *m/z* 1922.8164 $[M + Na]^+$; calculated for $C_{113}H_{120}F_3NNaO_{22}$: 1922.8152.

3-Trifluoroacetamidopropyl 2,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-3-*O*-levulinoyl-α-D-glucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (8). *tert*-Butyldimethylsilyl triflate (3.4 μL, 0.015 mmol, 18 mol.%) was added at −35 °C to a stirred mixture of *N*-phenyltrifluoroacetyl imidate **7**[35] (70 mg, 0.081 mmol, 1.9 equiv.), monohydroxy glycosyl acceptor **6** (81 mg, 0.043 mmol), and AW300 molecular sieves (120 mg) in dichloromethane (1 mL). The reaction mixture was stirred at −35 °C for 1 h, neutralized by adding triethylamine (20 μL), filtered through a Celite layer, and concentrated *in vacuo*. The residue was separated on silica gel (gradient elution with ethyl acetate—toluene (0→15%)) to give 97 mg (87%) of pentasaccharide **8**, syrup; R_f 0.48 (toluene—ethyl acetate, 8 : 2). $[\alpha]_D$ +18 (*c* 1, $CHCl_2$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.15 (s, 9 H, Me_3C); 1.63—1.74 (m, 2 H, $OCH_2C\underline{H}_2CH_2N$); 2.16 (s, 3 H, $\underline{Me}COCH_2CH_2CO$); 2.52—2.75 (m, 4 H, $MeCOC\underline{H}_2C\underline{H}_2CO$); 3.16—3.28 (m, 2 H, $OCH_2CH_2C\underline{H}HN$ and $OC\underline{H}HCH_2CH_2N$); 3.32—3.42 (m, 1 H, $OCH_2CH_2CH\underline{H}N$); 3.45 (dd, 1 H, $H(2_E)$, J = 3.5 Hz, J = 9.6 Hz); 3.55—4.90 (m, 56 H, $H(2_{A,B,C,D})$, $H(3_{A,B,C,D})$, $H(4_{A,B,C,D,E})$, $H(5_{A,B,C,D,E})$, and 14 $C\underline{H}_2Ph$), 5.02 and 5.24 (both br.s, 2 H each, $H(1_{A,B,C,D})$); 5.59 (d, 1 H, $H(1_E)$, J = 3.5 Hz); 5.74 (t, 1 H, $H(3_E)$, J = 9.6 Hz); 6.89—7.78 (m, 81 H, NH and 16 Ph). ^{13}C NMR (75 MHz, $CDCl_2$), δ: 19.6 ($Me_3\underline{C}$), 26.9 ($\underline{Me}_3C$), 28.1 ($OCH_2\underline{C}H_2CH_2N$), 28.3 ($\underline{Me}COCH_2CH_2CO$), 29.9 ($MeCOCH_2\underline{C}H_2CO$), 38.0(2) ($OCH_2CH_2\underline{C}H_2N$ and $MeCO\underline{C}H_2CH_2CO$), 65.8 ($O\underline{C}H_2CH_2CH_2N$), 69.4, 69.6, 69.7, 70.2, and 70.5 ($C(6_{A,B,C,D,E})$), 71.5,71.6, 71.7, 71.9, 72.0, 72.1, 72.4, 72.9, 73.0, 74.0, 74.7, 74.8, 75.0, 75.1, 75.4, 75.8, 76.1, and 76.4 ($C(2_{A,B,C,D,E})$, $C(3_E)$, $C(4_{A,B,C,D,E})$, $C(5_{A,B,C,D,E})$, and 14 $\underline{C}H_2Ph$); 78.7, 79.2, 79.3, and 80.8 ($C(3_{A,B,C,D})$), 96.2 ($C(1_E)$), 99.0, 100.6, and 101.6(2) ($C(1_{A,B,C,D})$), 127.2, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 129.1, 129.6, 129.7, 133.2, 133.6, 135.6, 135.9, 137.9, 138.1, 138.2, 138.3, 138.4, 138.5, 138.6, 138.7, 138.8 (16 Ph), 157.3 ($NH\underline{C}O$), 171.8 ($MeCOCH_2CH_2\underline{C}O$), 206.5 ($Me\underline{C}OCH_2CH_2CO$). MS, found: *m/z* 2601.1251 $[M + Na]^+$; calculated for $C_{154}H_{168}F_3NNaO_{29}Si$: 2601.1159.

3-Aminopropyl α-D-glucopyranosyl-(1→2)-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→2)-α-D-mannopyranoside (1). A 3 *M* solution of hydrazine hydrate in acetic acid (0.165 mL) was added to a solution of pentasaccharide **8** (97 mg, 0.037 mmol) in pyridine (1 mL). The mixture was kept at 20 °C for 20 min and diluted with dichloromethane (10 mL). The solution was washed with 1 *M* aqueous hydrochloric acid (15 mL), water (20 mL), and a saturated aqueous solution of sodium hydrogen carbonate (15 mL), dried by filtering through a cotton pad, and concentrated to dryness. The residue was dissolved in MeCN (2 mL) and treated with a 1 *M* solution of tetrabutylammonium fluoride in THF (0.1 mL) at 60 °C for 70 h. The mixture was diluted with dichloromethane (10 mL), washed with saturated brine (15 mL), and concentrated to dryness to give 64 mg (76%) of diol **9**. The product was dissolved in a mixture of ethyl acetate (0.65 mL) and methanol (3.5 mL) and hydrogenated over palladium hydroxide on carbon (130 mg, 20% Pd) for 2 h at 20 °C, with stirring in a hydrogen atmosphere at ambient pressure. The catalyst was filtered off, and the filtrate was concentrated to dryness. The residue was dissolved in a mixture of methanol (0.6 mL) and water (0.6 mL) and treated with 1 *M* aqueous NaOH (0.25 mL) at 20 °C for 1 h. The mixture was neutralized by adding acetic acid (30 μL), the solvent was evaporated to dryness, and the residue was purified by gel chromatography in 0.1 *M* aqueous acetic acid. The fractions containing the target product were freeze-dried to give 14 mg (50%) of pentasaccharide **2** as a white amorphous powder. $[\alpha]_D$ +78 (*c* 1, H_2O). ^{1}H NMR (400 MHz, D_2O), δ: 1.91—1.99 (m, 2 H, $OCH_2C\underline{H}_2CH_2N$); 3.05—3.14 (m, 2 H, $OCH_2CH_2C\underline{H}_2N$); 3.38 (t, 1 H, $H(4_E)$, J = 9.8 Hz); 3.52 (dd, 1 H, $H(2_E)$, J = 3.7 Hz, J = 10.0 Hz); 3.54—3.94 (m, 27 H, $OC\underline{H}_2CH_2CH_2N$, $H(2_A)$, $H(3_{A,B,C,D,E})$, $H(4_{A,B,C,D})$, $H(5_{A,B,C,D,E})$, $H(6a_{A,B,C,D,E})$, and $H(6b_{A,B,C,D,E})$); 4.05—4.08 (m, 3 H, $H(2_{B,C,D})$); 5.06 (s, 1 H, $H(1_A)$); 5.10 (d, 1 H, $H(1_E)$, J = 3.7 Hz); 5.24, 5.25, and 5.32 (all s, 3 H, $H(1_{B,C,D})$). ^{13}C NMR (100 MHz, D_2O, δ: 26.7 ($OCH_2\underline{C}H_2CH_2N$), 37.6 ($OCH_2CH_2\underline{C}H_2N$), 60.9, 61.1, 61.2, 61.3, and 61.4 ($C(6_{A,B,C,D,E})$), 65.2 ($O\underline{C}H_2CH_2CH_2N$), 67.1, 67.2, and 67.3(2) ($C(4_{A,B,C,D})$), 69.8 ($C(4_E)$), 72.0 ($C(2_E)$), 70.1, 70.2, 70.3, 70.5, 72.4, 72.9, 73.0, 73.3, 73.4, and 73.5 ($C(3_{A,B,C,D,E})$ and $C(5_{A,B,C,D,E})$), 78.7, 78.8, 79.0, and 79.7 ($C(2_{A,B,C,D})$), 98.4 ($C(1_A)$), 100.7(2), and 100.8 ($C(1_{B,C,D})$), 100.9 ($C(1_E)$). MS, found: *m/z* 886.3396 $[M + H]^+$; calculated for $C_{35}H_{60}NO_{26}$: 886.3398.

Biotinylated derivative 2. A 0.068 *M* solution of the activated ester of biotin derivative (52.3 μL)[36] in DMF and anhydrous Et_3N (10 μL) were added to a solution of oligosaccharide **1** (2.10 mg, 2.37 μmol) in anhydrous DMF (100 μL). The reaction mixture was stirred for 12 h at room temperature (~20 °C), and the solvent was evaporated in an oil pump vacuum. The residue was subjected to gel chromatography to give biotinylated derivative **2** (2.57 mg, 75%) as a white amorphous powder. The NMR spectrum of product **2** exhibited signals for the carbohydrate part, the chemical shifts of which almost did not differ from those for the starting 3-aminopropyl glycoside **1**, and characteristic signals of the biotinylated moiety. ^{1}H NMR (600 MHz, D_2O), δ, characteristic signals of the biotin moiety: 4.62 (dd, 1 H, H(6a), $J_{6a,3a}$ = = 8.0 Hz, $J_{6a,6}$ = 4.9 Hz); 4.42 (dd, 1 H, H(3a), $J_{6a,3a}$ = 8.0 Hz, $J_{3a,4}$ = 4.5 Hz); 3.02 (dd, 1 H, H(6), $J_{6,6'}$ = 13.1 Hz, $J_{6,6a}$ = 5.0 Hz); 2.81 (d, 1 H, H(6′), $J_{6,6'}$ = 13.0 Hz); 2.27 (t, 2 H, H(4′), $J_{3',4'}$ = 7.3 Hz). Found: *m/z* 1469.5924 $[M + Na]^+$; calculated for $C_{58}H_{102}N_4NaO_{35}S$: 1469.5938.

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This paper does not contain descriptions of studies on animals or humans.

The authors declare no competing interests.

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