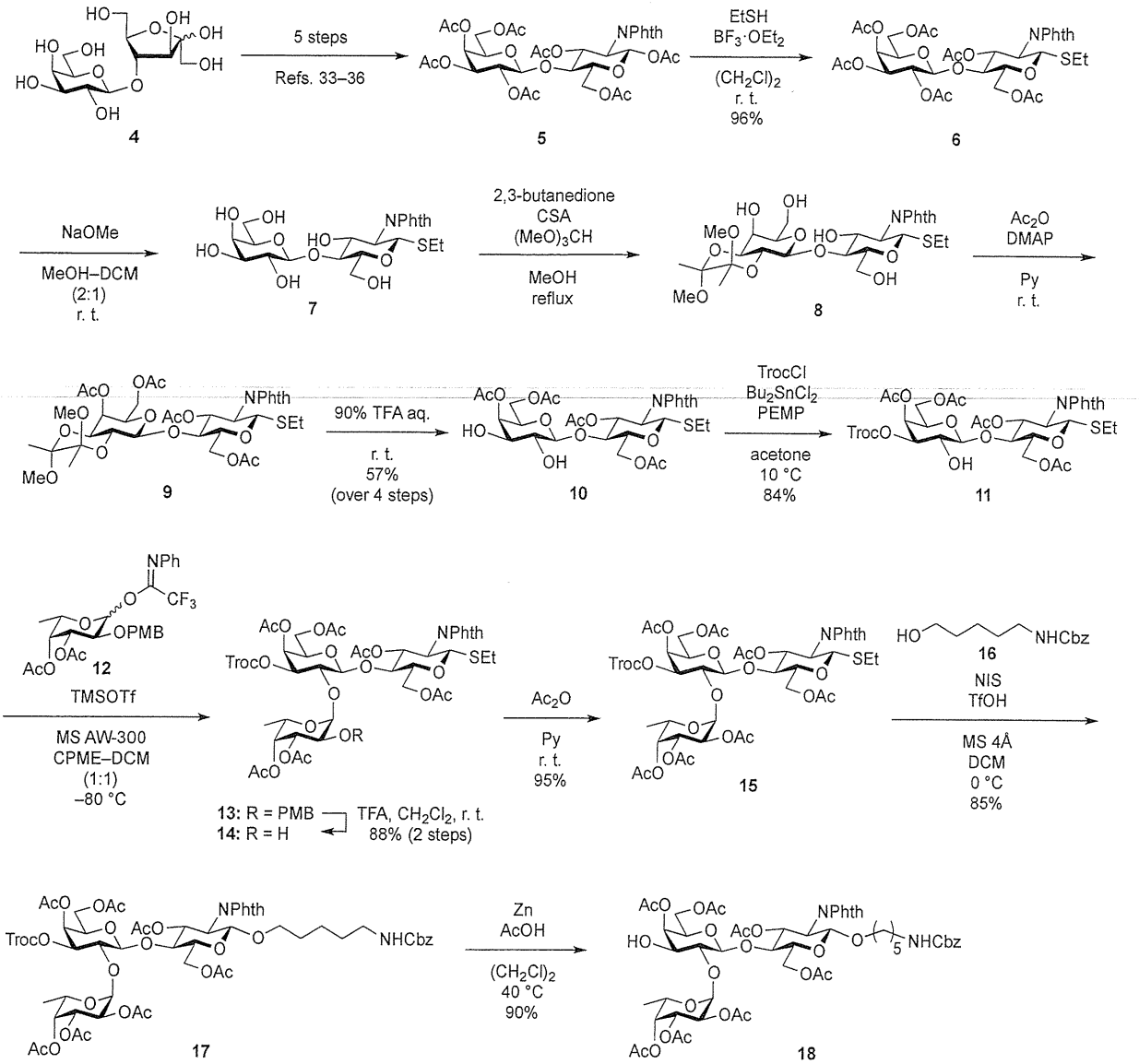
by methods in the literature [33–36]. Conversion of peracetate derivative **5** into thioglycoside form was performed in the presence of ethanethiol and $BF_3 \cdot OEt_2$ in 1,2-dichloroethane to give ethylthioglycoside **6** in 96% yield. The ethylsulfinyl group was selected in consideration of its solubility in MeOH, which was used in the next step. A phenylsulfinyl group in place of the ethylsulfinyl group resulted in poor solubility in MeOH, leading to a poor results in the deacetylation reaction. After removal of all acetyl groups in **6**, hydroxyl groups at the C2 and C3 positions of the galactose residue were simultaneously protected as a butanediacetal (BDA) [38] to afford compound **8**. In this reaction, a regioisomer of **8**, namely, a 3,4-*O*-BDA-protected by-product, was formed and these regioisomers were separated by silica gel column chromatography. However, small amounts of impurities could not be separated from **8**. Acetylation of **8** along with contaminants and subsequent hydrolysis of the BDA group afforded diol **10** as the sole product in 57% yield over the four operations. The tin-mediated selective acylation developed by Muramatsu [39] was then applied to selectively protect the C3′-OH group by the Troc group, giving the disaccharide acceptor **11** in 84% yield. Another procedure for selective protection of the C3′-OH group by treatment of TrocCl with pyridine in CH_2Cl_2 at lower temperature (−40 °C) gave **11** in somewhat lower yield (76%). For next glycosylation, the fucosyl *N*-phenyltrifluoroacetimidate **12** was designed to increase both reactivity and stability as a fucose donor. The previously used fucosyl donor, 2,3,4-tri-*O*-benzyl-protected fucosyl imidate, could be served as a good fucosyl donor, but was relatively unstable under glycosylation conditions due to its armed feature. Chemo-selectively removable PMB group was chosen as a protecting group at C2 position and electron-withdrawing acetyl groups at C3 and C4 were incorporated to suppress the armed feature by the PMB group, which could lead to stabilization of the donor. Furthermore, a more stable *N*-phenyltrifluoroacetimidate group compared to a trichloroacetimidate group was used as a leaving group [40,41]. The glycosylation of **11** with **12**, which was derived from a known fucose derivative [42] and was promoted by TMSOTf in a mixed solvent system of cyclopentylmethyl ether (CPME)–dichloromethane (1:1) [43] at −80 °C, provided trisaccharide **13**. Small amounts of contaminates remained after column chromatography. The mixture containing contaminants was used directly in the next reaction. Removal of the *p*-methoxybenzyl (PMB) group under acidic conditions allowed for purification of the newly formed trisaccharide, affording **14** with a yield of 88% over two steps. Acetylation of the liberated hydroxyl group afforded compound **15** with a yield of 95%. Next, the coupling reaction of **15** with *N*-Cbz-protected aminopentanol **16** occurred smoothly in the presence of *N*-iodosuccinimide (NIS) and TfOH [44,45] in CH_2Cl_2 at 0 °C to give the desired glycoside **17** in 85% yield. Subsequent deprotection of the Troc group by treatment with zinc and AcOH [46] in 1,2-dichloroethane at 40 °C afforded common trisaccharide derivative **18** with a yield of 90%.

For constructing the A and B antigen skeletons, it is necessary to incorporate galactosamine (for A antigen) and galactose (for B antigen) residues into trisaccharide **18** in α-linked form. Typically, α-D-galactosides are obtained by using ethereal solvents such as diethyl ether and 1,4-dioxane as well as the anomeric effect [47].

Scheme 2. Synthesis of the common trisaccharide unit.

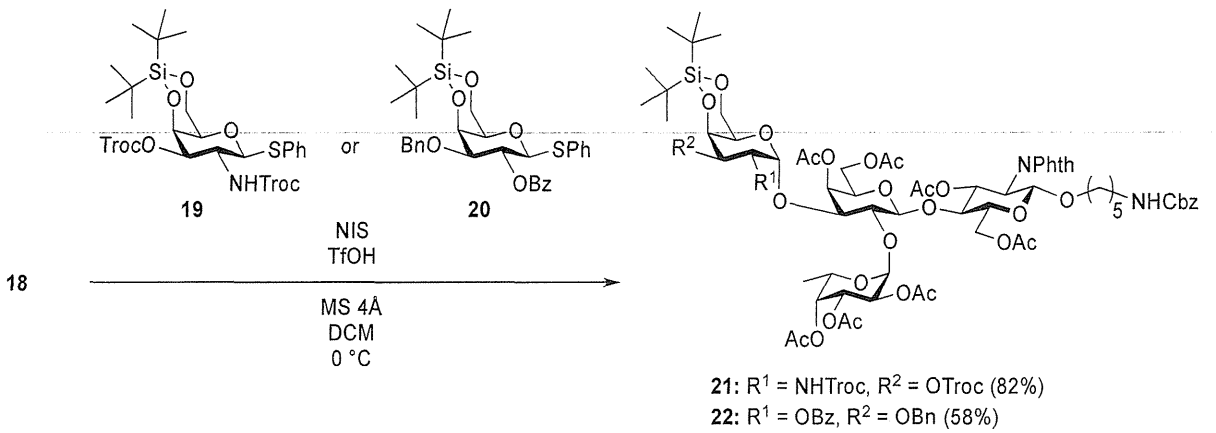


However, highly α-selectivity in such galactosylation is generally difficult and strongly dependent on various factors, such as the substrate structure, promoter, and temperature. The stereoisomers formed are often difficult to separate, which presents a serious disadvantage for synthetic studies. In 2003, we developed a reliable method for α-selective galactosidation and galactosaminidation using DTBS-protected glycosyl donors [48–51]. Notable features of the DTBS-directed α-galactosylation are excellent α-selectivity even in the presence of a neighboring participating group on the C2 oxygen or nitrogen, and the relatively greater difference between the R_f values of the α and β isomers that enables them to be more easily separated. Thus, we decided to utilize DTBS-directed α-galactosylation for the construction of the A and B antigen sequences.

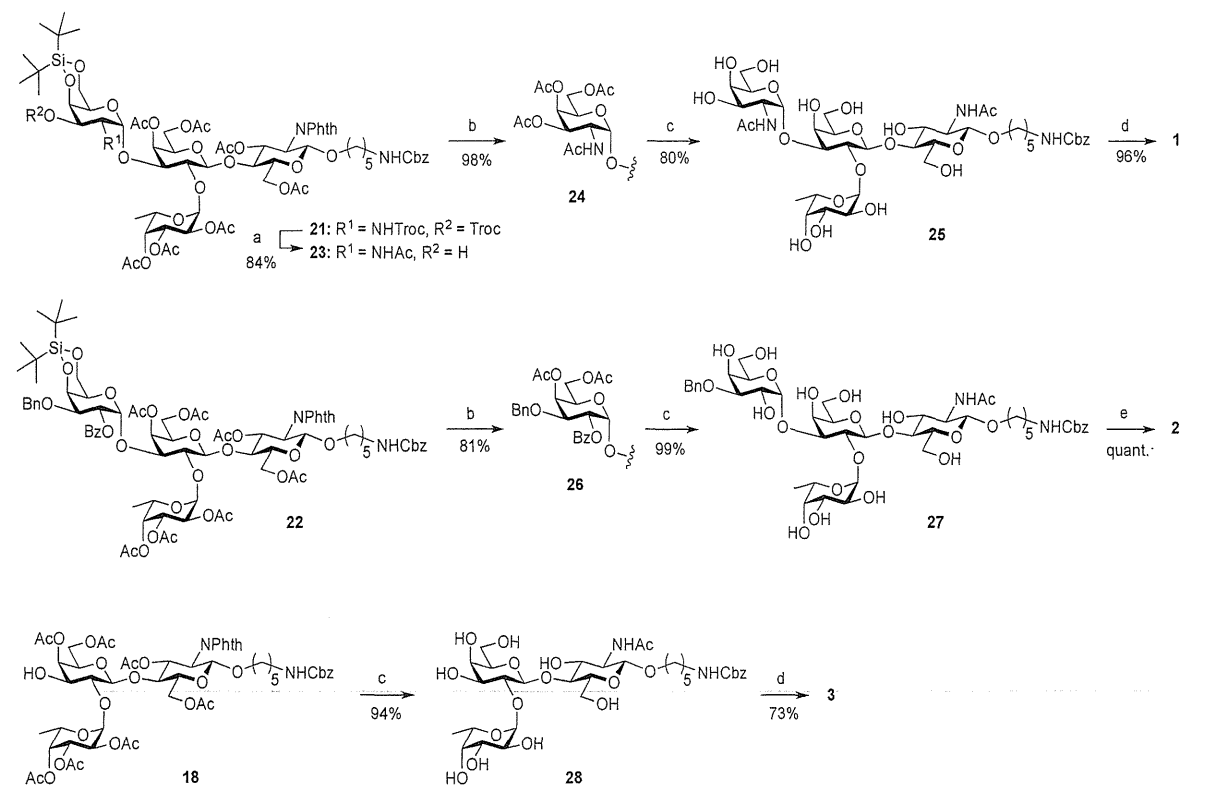
As shown in Scheme 3, trisaccharide acceptor **18** was glycosylated with galactosaminyl donor **19** [48] and galactosyl donor **20** [52] in the presence of NIS and TfOH in CH_2Cl_2 at 0 °C, giving the corresponding tetrasaccharides **21** and **22** in α-linked form in yields of 82% and 58%, respectively. In these reactions, the recovery of unreacted acceptor **18** was 9% and 22%, when **19** and **20** were used,

respectively, despite the use of 2 equiv of donor. However, other possible stereoisomers were not detected and both α-products were easy to isolate by column chromatography. To our surprise, the coupling yield of **22** was moderate. When we attempted to use the armed 2,3-di-*O*-benzyl-type galactose donor instead of **20**, the yield was not improved (41%) and many unidentified by-products were generated. The unexpectedly low reactivity of **18** as a glycosyl acceptor might arise from steric hindrance around 3-OH on the Gal residue.

Scheme 3. Assembly of A and B antigen sequences.



Scheme 4. Global deprotection sequence.



Reagents and conditions: (**a**) (i) Zn, AcOH, $(CH_2Cl)_2$, 40 °C, (ii) Ac_2O, MeOH, r.t.; (**b**) (i) TBAHF, THF, r.t. (ii) Ac_2O, Py, r.t.; (**c**) (i) $NH_2NH_2 \cdot H_2O$, EtOH, reflux, (ii) Ac_2O, MeOH, r.t.; (**d**) H_2, Pd/C, MeOH–H_2O (1:1), r.t.; (**e**) H_2, Pd/C, 1,4-dioxane–2% aq. formic acid (1:1), r.t.

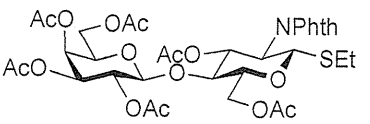
On the route to the target compounds, there is a global deprotection sequence (Scheme 4). Selective removal of the Troc groups of **21** by treatment with zinc and AcOH, followed by selective acetylation of the liberated amine of the galactosamine residue at C2 afforded **23** in 84% yield. Then, removal of the DTBS group with tributylamine hydrofluoride (TBAHF) in THF [53] followed by acetylation of the hydroxyl groups provided **24** in 98% yield over two steps. After removal of all acetyl groups on **24**, the phthalimide group at C2 of the glucosamine residue was converted to an acetamide group by sequential treatment with hydrazine hydrate in refluxing EtOH followed by selective acetylation of the free amine, affording **25** in 80% yield over three steps. Finally, the Cbz group at the terminus of the linker was removed by hydrogenolysis with Pd/C under hydrogen atmosphere, thus furnishing target **1** (A antigen) in 81% yield. Similarly, the deprotection of compounds **22** and **18** were efficiently carried out to furnish target compounds **2** (B antigen) and **3** (O antigen) in good yields.

3. Experimental

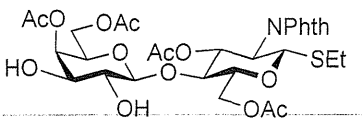
3.1. General Methods

All reactions were carried out under a positive pressure of argon, unless otherwise noted. All chemicals were purchased from commercial suppliers and used without further purification, unless otherwise noted. Molecular sieves were purchased from Nacalai Tesque, Inc. (Kyoto, Japan) and dried at 300 °C for 12 h in a muffle furnace prior to use. Solvents as reaction media such as CH_2Cl_2, MeOH, THF, DMF, and pyridine, which were tapped off from The Solvent Supply System, were purchased from Kanto Chemical Co., Inc. (Tokyo, Japan) and used without purification. TLC analysis was performed on Merck TLC (silica gel 60F254 on glass plate, Darmstadt, Germany). Compound detection was either by exposure to UV light (2536 Å) or by soak in a solution of 10% H_2SO_4 in ethanol followed by heating. Silica gel (80 mesh and 300 mesh) manufactured by Fuji Silysia Chemical Ltd. (Kasugai, Japan) was used for flash column chromatography. Quantity of silica gel was usually estimated as 100 to 200-fold weight of sample to be charged. Solvent systems in chromatography were specified in *v/v*. Evaporation and concentration were carried out *in vacuo*. ^{1}H-NMR and ^{13}C-NMR spectra were recorded with Bruker Biospin AVANCE III 500/800 spectrometers (Billerica, MA, USA). Chemical shifts in ^{1}H-NMR spectra are expressed in ppm (δ) relative to the signal of Me_4Si, adjusted to δ 0.00 ppm. Data are presented as follow: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = double of doublet, td = triple doublet, m = multiplet and/or multiple resonances), integration, coupling constant in Hertz (Hz), position of the corresponding proton. COSY methods were used to confirm the NMR peak assignments. High-resolution mass (ESI-TOF MS) spectra were run in a Bruker Daltonics micrOTOF (Billerica, MA, USA). Optical rotations were measured with a 'Horiba SEPA-300' high-sensitive polarimeter (Kyoto, Japan).

3.2. Physical Data for All New Compounds

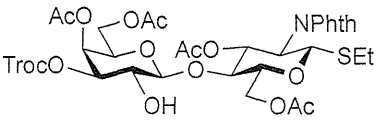


Ethyl (2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-1-thio-β-D-glucopyranoside (**6**). To a mixture of **5** (4.16 g, 5.44 mmol) in $(CH_2Cl)_2$ (27.2 mL) were added EtSH (606 μL, 8.16 mmol) and $BF_3{\cdot}OEt_2$ (1.03 mL, 8.16 mmol) at 0 °C. After stirring for 2 h at rt as the reaction was monitored by TLC (3:2 EtOAc–hexane), the reaction was quenched by the addition of crushed ice. The solution was diluted with $CHCl_3$ and subsequently washed with ice-cooled H_2O, satd aq Na_2CO_3, and brine. The organic layer was then dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (1:1 EtOAc–hexane) to give **6** (3.99 g, 96%). Spectroscopic data of **6** were identical to those reported in the literature [54].

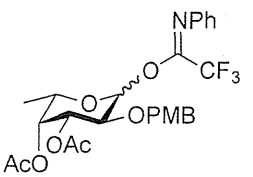


Ethyl (4,6-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-1-thio-β-D-glucopyranoside (**10**). To a solution of **6** (1.08 g, 1.41 mmol) in $MeOH/CH_2Cl_2$ (2:1, 14.1 mL) was added NaOMe (28% solution in MeOH, 31.9 μL, 141 μmol) at 0 °C. After stirring for 2 h at rt as the reaction was monitored by TLC (3:2 EtOAc–hexane), the reaction was neutralized with AcOH. After concentration, the resulting residue was diluted with $CHCl_3$ and subsequently washed with H_2O and brine. The organic layer was dried over Na_2SO_4, of which solid was filtered through cotton and the filtrate was then evaporated (giving 7). The residue was subjected to next reaction without further purification. The crude product 7 was dissolved in MeOH (28.2 mL). To the solution were added 2,3-butanedione (492 μL, 5.64 mmol), trimethyl orthoformate (1.95 mL, 17.8 mmol), and (±)-10-camphorsulfonic acid (66 mg, 282 μmol) at rt. After stirring for 20 h at reflux as the reaction was monitored by TLC (10:1 $CHCl_3$–MeOH), the reaction was quenched by the addition of triethylamine (218 μmol) and concentrated. The resulting residue was diluted with $CHCl_3$ and subsequently washed with H_2O and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated. The resulting residue was roughly purified by silica gel column chromatography (20:1 $CHCl_3$–MeOH) to give 2,3-*O*-BDA-protected product **8** along with small amounts of contaminants. The crude mixture (494 mg) was dissolved in pyridine (7.8 mL). To the solution were added Ac_2O (890 μL, 9.42 mmol) and a catalytic amount of DMAP at 0 °C. After stirring for 1 h at rt as the reaction was monitored by TLC (3:2 EtOAc–hexane), the mixture was co-evaporated with toluene. The resulting residue was diluted with EtOAc and subsequently washed with 2 M HCl, H_2O, satd aq $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (2:3 EtOAc–hexane) to give **9** (634 mg), to which suspension in H_2O (1.6 mL) was added trifluoroacetic acid (14.4 mL) at 0 °C. After stirring for 2 h at rt as the reaction was monitored by TLC (1:1 $CHCl_3$–acetone), the mixture was diluted with toluene and concentrated. The resulting residue was purified by silica gel column chromatography (7:3 $CHCl_3$–acetone) to give **10** (548 mg, 57% over four steps). $[\alpha]_D$ +18.3° (c 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.88–7.74 (m, 4H, Phth), 5.84 (dd, 1H, $J_{3,4}$ = 8.2 Hz, $J_{2,3}$ = 11.2 Hz, H-3^{GlcN}), 5.50 (d, 1H, $J_{1,2}$ = 10.6 Hz, H-1^{GlcN}), 5.28 (d, 1H, $J_{3,4}$ = 3.3 Hz, H-4^{Gal}), 4.63 (dd, 1H, $J_{5,6a}$ = 1.6 Hz, J_{gem} = 11.9 Hz, H-6a^{GlcN}), 4.40–4.29 (m, 3H, H-2^{GlcN}, H-6b^{GlcN}, H-1^{Gal}), 4.10–3.98 (m, 2H, H-6a^{Gal}, H-6b^{Gal}), 3.91–3.80 (m, 3H, H-4^{GlcN}, H-5^{GlcN}, H-5^{Gal}), 3.75–3.73 (m, 1H, H-3^{Gal}), 3.62 (d, 1H, $J_{2,OH}$ = 3.2 Hz, OH), 3.57–3.53 (m,

1H, H-2^{Gal}), 3.21 (d, 1H, $J_{3,OH}$ = 3.1 Hz, OH), 2.73–2.61 (m, 2H, SCH_2CH$_3$), 2.18–1.90 (4 s, 12H, Ac), 1.22 (t, 3H, SCH$_2$CH_3); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.2, 170.9, 170.5, 170.0, 167.7, 167.4, 134.4, 134.2, 131.6, 131.2, 123.7, 123.6, 103.1, 81.1, 72.0, 71.9, 71.7, 71.0, 68.7, 63.1, 61.5, 53.9, 29.7, 29.2, 24.6, 21.0, 20.7, 20.7, 20.6, 14.9. HRMS (ESI) *m/z*: found $[M+Na]^+$ 706.1776, $C_{30}H_{37}NO_{15}S$ calcd for $[M+Na]^+$ 706.1773.

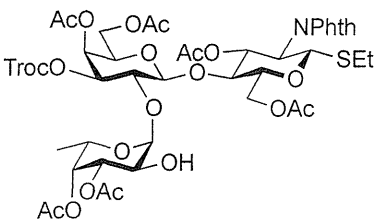


Ethyl [4,6-di-O-acetyl-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-galactopyranosyl]-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-1-thio-β-D-glucopyranoside (**11**). A solution of **10** (103 mg, 151 μmol) and dibutyltin dichloride (4.6 mg, 15.1 μmol) in acetone (3.0 mL) was stirred for 10 min at rt. To the solution were added PEMP (55 μL, 302 μmol) and TrocCl (27 μL, 196 μmol) at 10 °C. After stirring for 20 min at the same temperature as the reaction was monitored by TLC (1:2 EtOAc–toluene, 1:1 $CHCl_3$–acetone), the reaction was quenched by the addition of satd aq NH_4Cl and concentrated. The resulting residue was diluted with EtOAc and subsequently washed with H_2O and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated. The resulting residue was purified by silica gel column chromatography (2:7 EtOAc–toluene) to give **11** (108 mg, 84%). $[\alpha]_D$ +30.0° (c 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.88–7.74 (m, 4H, Phth), 5.70 (dd, 1H, $J_{3,4}$ = 8.2 Hz, $J_{2,3}$ = 10.6 Hz, H-3^{GlcN}), 5.49 (d, 1H, $J_{1,2}$ = 10.6 Hz, H-1^{GlcN}), 5.46 (d, 1H, $J_{3,4}$ = 2.9 Hz, H-4^{Gal}), 4.79 (m, 2H, H-3^{Gal}, OCH_2CCl$_3$), 4.65 (near dd, 1H, J_{gem} = 11.4 Hz, H-6a^{GlcN}), 4.44 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1^{Gal}), 4.38 (dd, 1H, $J_{5,6b}$ = 4.2 Hz, H-6b^{GlcN}), 4.31 (t, 1H, H-2^{GlcN}), 4.11–4.03 (m, 2H, H-6a^{Gal}, H-6b^{Gal}), 3.91–3.77 (m, 4H, H-4^{GlcN}, H-5^{GlcN}, H-2^{Gal}, H-5^{Gal}), 3.47 (d, 1H, $J_{2,OH}$ = 5.2 Hz, OH), 2.72–2.62 (m, 2H, SCH_2CH$_3$), 2.14–1.91 (4 s, 12H, Ac), 1.22 (t, 3H, SCH$_2$CH_3); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.2, 170.4, 170.2, 170.2, 167.8, 167.5, 153.2, 134.3, 134.3, 131.8, 131.3, 123.8, 103.3, 94.1, 81.2, 77.7, 77.3, 77.2, 72.2, 70.6, 69.2, 66.2, 63.1, 61.1, 54.0, 29.8, 24.6, 21.0, 20.7, 20.7, 20.6, 15.1. HRMS (ESI) *m/z*: found $[M+Na]^+$ 880.0823, $C_{33}H_{38}Cl_3NO_{17}S$ calcd for $[M+Na]^+$ 880.0818.



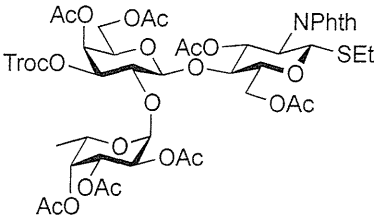
3,4-Di-O-acetyl-2-O-p-methoxybenzyl-L-fucopyranosyl N-phenyl 2,2,2-trifluoroacetimidate (**12**). To a solution of phenyl 3,4-di-*O*-acetyl-2-*O*-*p*-methoxybenzyl-1-thio-β-L-fucopyranoside [42] (1.21 g, 2.63 mmol) in acetone/H_2O (13.1 mL, 96:4) was added NBS (701 mg, 3.94 mmol) at −15 °C. After stirring for 1 h at the same temperature as the reaction was monitored by TLC (1:1 EtOAc–hexane), the reaction was quenched by the addition of satd aq $Na_2S_2O_3$ and then diluted with EtOAc, washed with H_2O and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated. The resulting residue was purified by silica gel column chromatography (2:3 EtOAc–hexane) to give the corresponding hemiacetal product (969 mg, quant.), which was then dissolved in acetone (52.6 mL). To the solution were added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (853 μL, 5.26 mmol) and

K_2CO_3 (1.82 g, 13.2 mmol) at rt. After stirring for 2.5 h at rt as the reaction was monitored by TLC (1:2 EtOAc–hexane), the reaction mixture was filtered through Celite. The filtrate and washings were concentrated. The resulting residue was purified by silica gel column chromatography (1:4 EtOAc–hexane) to give **12** (1.33 g, 94%, α/β = 1/1). $[\alpha]_D$ −81.6° (c 1.0, $CHCl_3$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.3, 170.2, 169.9, 169.8, 159.4, 159.3, 143.5, 143.2, 129.8, 129.7, 129.5, 129.3, 129.1, 128.9, 128.8, 128.6, 128.6, 128.4, 128.4, 124.3, 124.2, 119.3, 119.2, 117.2, 114.9, 114.0, 113.7, 113.7, 97.0, 93.6, 77.6, 77.2, 74.9, 74.7, 72.9, 72.6, 72.2, 70.8, 70.2, 70.0, 69.7, 67.3, 55.2, 55.1, 20.7, 20.6, 20.5, 20.5, 15.9, 15.8. ^{1}H-NMR (500 MHz, $CDCl_3$) **α-isomer**: δ 7.45–6.71 (m, 9H, Ar), 6.46 (br s, 1H, H-1), 5.35–5.31 (m, 2H, H-3, H-4), 4.75–4.59 (m, 2H, OC*H*$_2$Ar), 4.27 (br s, 1H, H-5), 3.95 (br d, 1H, H-2), 3.87–3.77 (m, 3H, OMe), 2.16–1.99 (m, 6H, Ac), 1.18–1.14 (m, 3H, H-6). **β-isomer**: δ 7.45–6.71 (m, 9H, Ar), 5.68 (br s, 1H, H-1), 5.20 (br s, 1H, H-4), 4.98 (br s, 1H, H-3) 4.75–4.59 (m, 2H, OC*H*$_2$Ar), 3.87–3.77 (m, 5H, H-2, H-5, OMe), 2.16–1.99 (m, 6H, Ac), 1.18–1.14 (m, 3H, H-6). Possible other stereoisomers were not assigned. HRMS (ESI) *m/z*: found $[M+Na]^+$ 562.1657, $C_{26}H_{28}F_3NO_8$ calcd for $[M+Na]^+$ 562.1659.

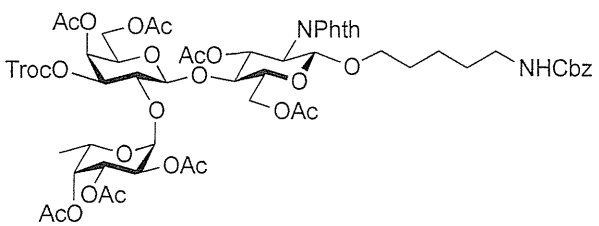


Ethyl (3,4-di-O-acetyl-α-L-fucopyranosyl)-(1→2)-[4,6-di-O-acetyl-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-galactopyranosyl]-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-1-thio-β-D-glucopyranoside (**14**). To a mixture of **11** (1.06 g, 1.24 mmol) and **12** (1.33 g, 2.47 mmol) in CPME/CH_2Cl_2 (1:1, 74.2 mL) was added 4 Å molecular sieves AW-300 (7.42 g) at rt. After stirring for 30 min, the mixture was cooled to −80 °C. TMSOTf (22 μL, 124 μmol) was then added to the mixture at −80 °C. After stirring for 5.5 h at the same temperature as the reaction was monitored by TLC (1:2 EtOAc–toluene, 1:2 EtOAc–hexane) and MALDI-TOF MS, the reaction was quenched by the addition of satd aq $NaHCO_3$. The reaction mixture was diluted with $CHCl_3$ and filtered through Celite. The filtrate was then washed with satd aq $NaHCO_3$ and H_2O. The organic layer was subsequently dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (2:7 EtOAc–toluene) to give **13** with unidentified impurity (1.66 g). The crude mixture was then dissolved in CH_2Cl_2 (44.6 mL). To the solution was added trifluoroacetic acid (5.0 mL) at 0 °C. After stirring for 40 min at rt as the reaction was monitored by TLC (1:1 EtOAc–hexane), the mixture was co-evaporated with toluene. The residue was diluted with $CHCl_3$ and subsequently washed with satd aq $NaHCO_3$ and H_2O. The organic layer was dried over Na_2SO_4, filtered, concentrated. The resulting residue was purified by silica gel column chromatography (1:2 EtOAc–toluene) to give **14** (1.18 g, 88% over two steps). $[\alpha]_D$ −38.1° (c 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.88–7.73 (m, 4H, Phth), 5.80 (t, 1H, $J_{2,3} = J_{3,4} = 10.6$ Hz, H-3^{GlcN}), 5.47–5.45 (m, 2H, H-1^{GlcN}, H-4^{Gal}), 5.29 (d, 1H, $J_{1,2} = 2.5$ Hz, H-1^{Fuc}), 5.21 (d, 1H, $J_{3,4} = 3.9$ Hz, H-4^{Fuc}), 4.99 (dd, 1H, $J_{2,3} = 10.7$ Hz, H-3^{Fuc}), 4.91 (dd, 1H, $J_{3,4} = 3.6$ Hz, $J_{2,3} = 10.1$ Hz, H-3^{Gal}), 4.75 (s, 2H, OC*H*$_2$CCl$_3$), 4.51 (dd, 1H, $J_{5,6a} = 4.2$ Hz, $J_{gem} = 12.0$ Hz, H-6a^{GlcN}), 4.33–4.31 (m, 4H, H-2^{GlcN}, H-6b^{GlcN}, H-1^{Gal}, H-5^{Fuc}), 4.17–4.09 (m, 2H, H-6a^{Gal}, H-6b^{Gal}), 3.95–3.83 (m, 5H, H-4^{GlcN}, H-5^{GlcN}, H-2^{Gal}, H-5^{Gal}, H-2^{Fuc}), 2.74–2.62 (m, 2H, SC*H*$_2$CH$_3$), 2.16–1.91 (6 s, 18H, Ac), 1.27–1.22 (m, 6H,

H-6^{Fuc}, SCH$_2$C*H*$_3$); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 170.6, 170.5, 170.3, 169.9, 169.8, 167.5, 167.2, 152.8, 134.3, 134.2, 131.6, 131.2, 123.6, 100.1, 99.6, 93.8, 81.4, 77.8, 77.2, 74.9, 73.2, 71.2, 70.7, 70.6, 67.0, 66.6, 65.7, 62.5, 60.9, 53.9, 29.6, 24.8, 20.8, 20.7, 20.6, 20.6, 20.5, 20.4, 15.6, 15.0. HRMS (ESI) *m/z*: found [M+Na]$^+$ 1110.1609, $C_{43}H_{52}Cl_3NO_{23}S$ calcd for [M+Na]$^+$ 1110.1611.

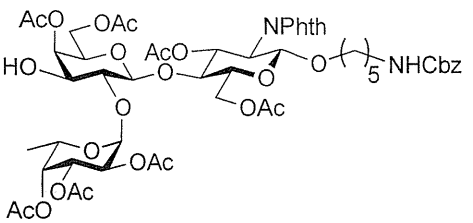


Ethyl (2,3,4-tri-O-acetyl-α-L-fucopyranosyl)-(1→2)-[4,6-di-O-acetyl-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-galactopyranosyl]-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-1-thio-β-D-glucopyranoside (**15**). To a solution of **14** (1.06 g, 975 μmol) in pyridine (4.9 mL) was added acetic anhydride (4.9 mL) at 0 °C. After stirring for 2 h at rt as the reaction was monitored by TLC (1:1 EtOAc–hexane), the reaction was quenched by addition of MeOH at 0 °C and then evaporated. The residue was diluted with CHCl$_3$, washed with 2 M HCl, H$_2$O, satd aq NaHCO$_3$, and brine, dried over Na$_2$SO$_4$, concentrated. The residue obtained was purified by silica gel column chromatography (2:3 EtOAc–hexane) to give **15** (1.05 g, 95%). [α]$_D$ −39.6° (c 1.0, CHCl$_3$); ^{1}H-NMR (500 MHz, CDCl$_3$) δ 7.86–7.73 (m, 4H, Phth), 5.79 (t, 1H, $J_{2,3} = J_{3,4} = 10.1$ Hz, H-3^{GlcN}), 5.47 (d, 1H, $J_{1,2} = 10.6$ Hz, H-1^{GlcN}), 5.43 (d, 1H, $J_{3,4} = 4.3$ Hz, H-4^{Gal}), 5.39 (d, 1H, $J_{1,2} = 3.8$ Hz, H-1^{Fuc}), 5.34 (d, 1H, $J_{3,4} = 3.9$ Hz, H-4^{Fuc}), 5.16 (dd, 1H, $J_{2,3} = 10.9$ Hz, H-3^{Fuc}), 5.07 (dd, 1H, H-2^{Fuc}), 4.88 (dd, 1H, $J_{2,3} = 9.8$ Hz, H-3^{Gal}), 4.84 (d, 1H, $J_{gem} = 11.7$ Hz, OC*H*$_2$CCl$_3$), 4.63 (d, 1H, OC*H*$_2$CCl$_3$), 4.51 (dd, 1H, $J_{5,6a} = 1.8$ Hz, $J_{gem} = 10.8$ Hz, H-6a^{GlcN}), 4.47–4.43 (m, 2H, H-1^{Gal}, H-5^{Fuc}), 4.39–4.30 (m, 2H, H-2^{GlcN}, H-6b^{GlcN}), 4.16 (dd, 1H, $J_{5,6a} = 6.6$ Hz, $J_{gem} = 11.2$ Hz, H-6a^{Gal}), 4.09 (dd, 1H, H-6b^{Gal}), 3.94 (t, 1H, H-4^{GlcN}), 3.89–3.83 (m, 3H, H-5^{GlcN}, H-2^{Gal}, H-5^{Gal}), 2.74–2.62 (m, 2H, SC*H*$_2$CH$_3$), 2.17–1.91 (7 s, 21H, Ac), 1.26–1.22 (m, 6H, H-6^{Fuc}, SCH$_2$C*H*$_3$); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 170.6, 170.5, 170.3, 170.1, 169.9, 169.7, 169.7, 167.5, 167.2, 152.7, 134.3, 134.1, 131.6, 131.2, 123.6, 100.0, 96.2, 93.8, 81.4, 77.8, 77.2, 76.9, 74.7, 72.5, 71.1, 70.7, 70.6, 67.9, 67.7, 66.4, 65.3, 62.7, 60.9, 53.8, 29.6, 24.8, 20.8, 20.6, 20.6, 20.5, 20.3, 15.5, 15.1. HRMS (ESI) *m/z*: found [M+Na]$^+$ 1152.1716, $C_{45}H_{54}Cl_3NO_{24}S$ calcd for [M+Na]$^+$ 1152.1714.



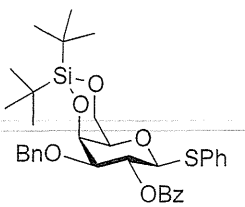
5-Benzyloxycarbonylamino-1-pentyl (2,3,4-tri-O-acetyl-α-L-fucopyranosyl)-(1→2)-[4,6-di-O-acetyl-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-galactopyranosyl]-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-β-D-glucopyranoside (**17**). A mixture of **15** (372 mg, 329 μmol) and **16** (234 mg, 988 μmol), and NIS (148 mg, 658 μmol) was exposed to high vacuum for 1 h. The mixture was dissolved in CH$_2$Cl$_2$ (13.2 mL), to which 4 Å molecular sieves (1.32 g) was added at rt. After stirring for 30 min at

rt and then for 10 min at 0 °C, TfOH (7.1 μL, 65.8 μmol) was added to the mixture. After stirring for 1 h at 0 °C as the reaction was monitored by TLC (1:1 EtOAc–hexane, 2:1 EtOAc–hexane), additional portions of NIS (148 mg, 658 μmol) and TfOH (7.1 μL, 65.8 μmol) were added to the mixture. After 8 h and 16 h, further portions of TfOH (7.1 μL of each) were added to the mixture and the stirring was continued. After stirring for total 30 h, the reaction was quenched by the addition of satd aq $NaHCO_3$. The precipitate was filtered through Celite. The filtrate was diluted with $CHCl_3$, washed with satd aq $Na_2S_2O_3$ and brine. The organic layer was subsequently dried over Na_2SO_4, concentrated and the residue was then purified by silica gel column chromatography (1:1 EtOAc–hexane) and gel filtration column chromatography (LH-20, 1:1 $CHCl_3$–MeOH) to give **17** (375 mg, 87%). $[\alpha]_D$ −41.1° (c 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.85–7.69 (m, 4H, Phth), 7.47–7.30 (m, 5H, Ph), 5.74 (dd, 1H, $J_{3,4}$ = 9.0 Hz, $J_{2,3}$ = 10.8 Hz, H-3^{GlcN}), 5.42 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-4^{Gal}), 5.40 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1^{Fuc}), 5.33 (d, 1H, $J_{3,4}$ = 3.8 Hz, H-4^{Fuc}), 5.31 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1^{GlcN}), 5.17 (dd, 1H, $J_{2,3}$ = 10.9 Hz, H-3^{Fuc}), 5.07–5.04 (m, 3H, H-2^{Fuc}, OCH_2), 4.88 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-3^{Gal}), 4.84 (d, 1H, J_{gem} = 11.6 Hz, OCH_2), 4.64–4.62 (m, 2H, $OCH_2(CH_2)_3CH_2NH$, OCH_2), 4.55 (dd, 1H, $J_{5,6a}$ = 1.8 Hz, J_{gem} = 12.1 Hz, H-6a^{GlcN}), 4.47–4.43 (m, 2H, H-1^{Gal}, H-5^{Fuc}), 4.37 (dd, 1H, $J_{5,6b}$ = 5.2 Hz, H-6b^{GlcN}), 4.24 (dd, 1H, H-2^{GlcN}), 4.16 (dd, 1H, $J_{5,6a}$ = 6.7 Hz, J_{gem} = 11.2 Hz, H-6a^{Gal}), 4.09 (dd, 1H, H-6b^{Gal}), 3.94 (t, 1H, H-4^{GlcN}), 3.88–3.79 (m, 4H, H-5^{GlcN}, H-2^{Gal}, H-5^{Gal}, $OCH_2(CH_2)_3CH_2NH$), 3.46–3.44 (m, 1H, $OCH_2(CH_2)_3CH_2NH$), 2.95–2.91 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 2.17–1.91 (7 s, 21H, Ac), 1.51–1.11 (m, 9H, H-6^{Fuc}, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.7, 170.6, 170.3, 170.2, 170.0, 169.8, 156.2, 152.8, 136.7, 134.3, 128.5, 128.1, 128.1, 123.6, 100.1, 98.1, 96.2, 93.8, 77.6, 74.8, 72.9, 72.5, 71.1, 70.6, 70.6, 70.0, 69.8, 67.9, 67.8, 66.5, 66.4, 65.3, 62.3, 61.0, 54.7, 40.8, 29.3, 28.8, 23.0, 20.9, 20.7, 20.6, 20.6, 20.4, 15.5. HRMS (ESI) *m/z*: found $[M+Na]^+$ 1327.2890, $C_{56}H_{67}Cl_3N_2O_{27}$ calcd for $[M+Na]^+$ 1327.2889.

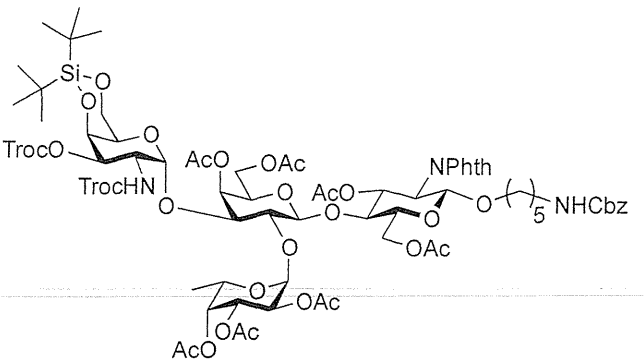


5-Benzyloxycarbonylamino-1-pentyl (2,3,4-tri-O-acetyl-α-L-fucopyranosyl)-(1→2)-(4,6-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-β-D-glucopyranoside (**18**). To a solution of **17** (289 mg, 215 μmol) in AcOH/$(CH_2Cl)_2$ (3:1, 14.3 mL) was added Zn powder (2.89 g) at rt. The reaction mixture was stirred for 1 h at 40 °C as the reaction was monitored by TLC (3:1 EtOAc–hexane). The precipitate was filtered through Celite and the filtrate was co-evaporated with toluene. The residue obtained was purified by silica gel column chromatography (3:1 EtOAc–hexane) to give **18** (233 mg, 97%). $[\alpha]_D$ −56.6° (c 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.85–7.69 (m, 4H, Phth), 7.38–7.30 (m, 5H, Ph), 5.74 (dd, 1H, $J_{3,4}$ = 9.0 Hz, $J_{2,3}$ = 10.8 Hz, H-3^{GlcN}), 5.39 (d, 1H, $J_{3,4}$ = 3.6 Hz, H-4^{Gal}), 5.33 (d, 1H, $J_{3,4}$ = 3.8 Hz, H-4^{Fuc}), 5.31 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1^{GlcN}), 5.26–5.23 (m, 2H, H-3^{Fuc}, OCH_2Ph), 5.16 (dd, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 9.9 Hz, H-2^{Fuc}), 5.07 (m, 2H, H-1^{Fuc}, OCH_2Ph), 4.65 (s, 1H, $OCH_2(CH_2)_3CH_2NH$), 4.51 (dd, 1H, $J_{5,6a}$ = 1.8 Hz, J_{gem} = 12.0 Hz, H-6a^{GlcN}), 4.42–4.37 (m, 2H, H-6b^{GlcN}, H-5^{Fuc}), 4.31 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1^{Gal}), 4.23 (dd, 1H, H-2^{GlcN}), 4.11

(m, 2H, H-6a^{Gal}, H-6b^{Gal}), 3.92 (t, 1H, $J_{4,5}$ = 9.0 Hz, H-4^{GlcN}), 3.86–3.79 (m, 4H, H-5^{GlcN}, H-3^{Gal}, H-5^{Gal}, OC*H*$_2$(CH$_2$)$_3$CH$_2$NH), 3.54 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2^{Gal}), 3.47–3.43 (m, 1H, OC*H*$_2$(CH$_2$)$_3$CH$_2$NH), 2.94–2.90 (m, 2H, OCH$_2$(CH$_2$)$_3$C*H*$_2$NH), 2.18–1.91 (7 s, 21H, Ac), 1.49–1.11 (m, 9H, H-6^{Fuc}, OCH$_2$(C*H*$_2$)$_3$CH$_2$NH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.0, 170.7, 170.7, 170.4, 170.1, 170.1, 169.9, 156.2, 136.6, 134.3, 131.4, 128.5, 128.0, 123.5, 100.1, 98.1, 97.8, 74.9, 73.0, 72.4, 71.1, 71.0, 69.9, 69.7, 69.6, 68.2, 67.7, 66.5, 65.2, 62.4, 61.5, 54.8, 40.8, 29.6, 29.3, 28.8, 23.0, 20.8, 20.7, 20.6, 20.6, 20.5, 15.7. HRMS (ESI) *m/z*: found [M+Na]$^+$ 1153.3847, $C_{53}H_{66}N_2O_{25}$ calcd for [M+Na]$^+$ 1153.3851.

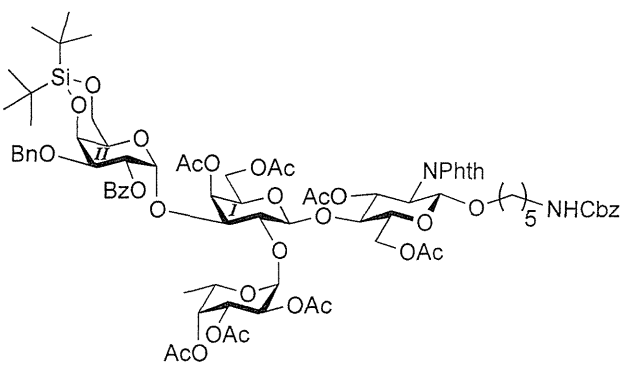


Phenyl 2-O-benzoyl-3-O-benzyl-4,6-O-di-tert-butylsilylene-1-thio-β-D-galactopyranoside (**20**). To a solution of Phenyl 3-*O*-benzyl-1-thio-*β*-D-galactopyranoside (262 mg, 724 μmol) in pyridine (7.2 mL) was added di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (260 μL, 796 μmol) at 0 °C. After stirring for 3.5 h at 0 °C as the reaction was monitored by TLC (1:1 EtOAc–hexane), benzoic anhydride (328 mg, 1.45 mmol) was added to the mixture at 0 °C. After stirring for 22 h at rt as the reaction was monitored by TLC (1:3 EtOAc–hexane), the reaction was quenched by the addition of MeOH at 0 °C. The mixture was co-evaporated with toluene. The residue obtained was diluted with EtOAc, washed with 2 M HCl, H_2O, satd aq $NaHCO_3$, and brine, dried over Na_2SO_4, concentrated. The resulting residue was purified by silica gel column chromatography (1:7 EtOAc–hexane) to give **20** (324 mg, 74%). $[\alpha]_D$ +66.9° (c 0.6, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.06–7.16 (m, 15H, Ph), 5.70 (t, 1H, $J_{1,2} = J_{2,3}$ = 9.8 Hz, H-2), 4.79 (d, 1H, H-1), 4.72 (d, 1H, J_{gem} = 12.8 Hz, OC*H*$_2$Ph), 4.60–4.57 (m, 2H, H-4, OC*H*$_2$Ph), 4.30–4.23 (m, 2H, H-6a, H-6b), 3.57 (dd, 1H, H-3), 3.40 (s, 1H, H-5), 1.16–1.08 (2 s, 18H, 2 *t*-Bu); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 165.4, 137.9, 134.4, 133.0, 132.1, 130.1, 129.9, 128.8, 128.3, 127.6, 127.5, 87.6, 79.3, 75.1, 70.0, 69.8, 69.4, 67.3, 27.6, 23.4, 20.7. HRMS (ESI) *m/z*: found [M+Na]$^+$ 629.2363, $C_{34}H_{42}O_6SSi$ calcd for [M+Na]$^+$ 629.2364.



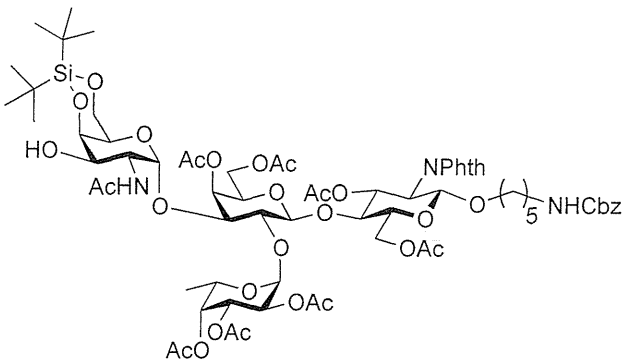
5-Benzyloxycarbonylamino-1-pentyl [2-deoxy-4,6-O-di-tert-butylsilylene-2-(2,2,2-trichloroethoxycarbamoyl)-3-O-(2,2,2-trichloroethoxycarbonyl)-α-D-galactopyranosyl]-(1→3)-[2,3,4-tri-O-acetyl-α-L-fucopyranosyl-(1→2)]-(4,6-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-β-D-

glucopyranoside (**21**). A mixture of **18** (103 mg, 91.1 μmol) and **19** (138 mg, 182 μmol), and NIS (46 mg, 364 μmol) was exposed to high vacuum for 1 h. The mixture was dissolved in CH_2Cl_2 (2.7 mL), to which 4 Å molecular sieves (273 mg) was added at rt. After stirring for 30 min at rt and then for 10 min at 0 °C, TfOH (1.9 μL, 18.2 μmol) was added to the mixture. After stirring for 3 h at 0 °C as the reaction was monitored by TLC (3:1 EtOAc–hexane, 1:1 EtOAc–hexane, 1:3 EtOAc–hexane), additional portions of NIS (23 mg) and TfOH (1.0 μL) were added to the mixture and the stirring was continued. After stirring for total 5 h, the reaction was quenched by the addition of satd aq $NaHCO_3$. The precipitate was filtered through Celite. The filtrate was diluted with $CHCl_3$, washed with satd aq $Na_2S_2O_3$ and brine. The organic layer was subsequently dried over Na_2SO_4, concentrated and the residue was then purified by silica gel column chromatography (1:1 EtOAc–hexane) to give **21** (132 mg, 82%), and 9.5 mg (9%) of **18** was recovered. $[\alpha]_D$ +23.8° (c 1.7, $CHCl_3$); ^{1}H-NMR (500 MHz, CD_3CN) δ 7.77–7.70 (m, 4H, Phth), 7.30–7.22 (m, 5H, Ph), 5.74 (d, 1H, $J_{NH,2}$ = 9.7 Hz, NH^{GalN}), 5.64 (dd, 1H, $J_{3,4}$ = 9.0 Hz, $J_{2,3}$ = 11.9 Hz, H-3^{GlcN}), 5.35 (d, 1H, $J_{3,4}$ = 2.8 Hz, H-4^{Gal}), 5.30 (m, 2H, H-1^{Fuc}, $OCH_2(CH_2)_3CH_2NH$), 5.24 (d, 1H, $J_{3,4}$ = 2.3 Hz, H-4^{Fuc}), 5.20 (d, 1H, $J_{1,2}$ = 10.8 Hz, H-1^{GlcN}), 5.08 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1^{GalN}), 5.07 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 11.0 Hz, H-2^{Fuc}), 4.97 (dd, 1H, H-3^{Fuc}), 4.93 (s, 2H, OCH_2), 4.86–4.79 (m, 2H, OCH_2), 4.78–4.68 (m, 3H, H-3^{GalN}, H-4^{GalN}, OCH_2), 4.59 (d, 1H, J_{gem} = 12.3 Hz, OCH_2), 4.41–4.28 (m, 6H, H-6a^{GlcN}, H-1^{Gal}, H-5^{Fuc}, H-2^{GalN}, H-6a^{GalN}, H-6b^{GalN}), 4.09–3.96 (m, 5H, H-2^{GlcN}, H-4^{GlcN}, H-6b^{GlcN}, H-3^{Gal}, H-6a^{Gal}), 3.92 (dd, 1H, $J_{5,6b}$ = 6.1 Hz, J_{gem} = 11.3 Hz, H-6b^{Gal}), 3.80–3.75 (m, 3H, H-5^{GlcN}, H-5^{Gal}, H-5^{GalN}), 3.65–3.61 (m, 2H, H-2^{Gal}, $OCH_2(CH_2)_3CH_2NH$), 3.39–3.34 (m, 1H, $OCH_2(CH_2)_3CH_2NH$), 2.71–2.65 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 2.18–1.80 (7 s, 21H, Ac), 1.31–0.96 (m, 27H, H-6^{Fuc}, 2 *t*-Bu, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (125 MHz, CD_3CN) δ 171.6, 171.5, 171.3, 171.2, 171.1, 155.5, 154.2, 135.7, 132.3, 129.4, 128.8, 128.7, 118.6, 118.3, 101.2, 98.9, 97.5, 96.6, 95.5, 94.4, 94.4, 79.1, 77.5, 76.6, 75.2, 74.4, 74.1, 73.5, 71.9, 71.5, 71.3, 70.8, 70.4, 69.0, 68.9, 68.6, 67.3, 66.6, 66.5, 65.7, 63.2, 62.2, 55.5, 49.4, 41.3, 30.0, 29.5, 27.9, 27.8, 23.7, 23.7, 21.5, 21.3, 21.2, 21.1, 21.0, 21.0, 20.8, 16.1. HRMS (ESI) *m/z*: found $[M+Na]^+$ 1802.3642, $C_{73}H_{95}Cl_6N_3O_{33}Si$ calcd for $[M+Na]^+$ 1802.3640.



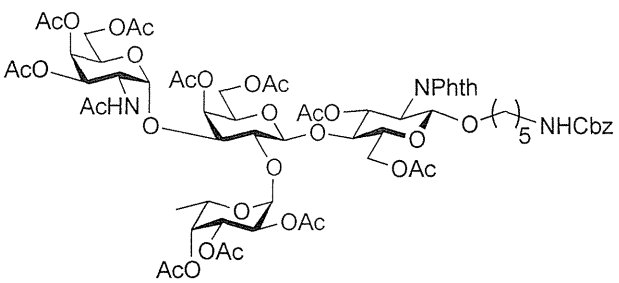
5-Benzyloxycarbonylamino-1-pentyl (2-O-benzoyl-3-O-benzyl-4,6-O-di-tert-butylsilylene-α-D-galactopyranosyl)-(1→3)-[2,3,4-tri-O-acetyl-α-L-fucopyranosyl-(1→2)]-(4,6-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-β-D-glucopyranoside (**22**). A mixture of **18** (49.7 mg, 44.0 μmol) and **20** (53.3 mg, 87.9 μmol), and NIS (22.0 mg, 176 μmol) was exposed to high vacuum for 1 h. The mixture was dissolved in CH_2Cl_2 (1.3 mL), to which 4 Å molecular sieves (132 mg) was added at rt. After stirring for 30 min at rt and then for 10 min at 0 °C, TfOH (1.0 μL, 8.79 μmol) was added to the

mixture. After stirring for 1.5 h at 0 °C as the reaction was monitored by TLC (3:1 EtOAc–hexane, 1:1 EtOAc–hexane, 1:3 EtOAc–hexane), additional portion of TfOH (1.0 μL) was added to the mixture and the stirring was continued. After stirring for total 2 h, the reaction was quenched by the addition of satd aq $NaHCO_3$. The precipitate was filtered through Celite. The filtrate was diluted with $CHCl_3$, washed with satd aq $Na_2S_2O_3$ and brine. The organic layer was subsequently dried over Na_2SO_4, concentrated and the residue was then purified by silica gel column chromatography (7:8 EtOAc–hexane) to give **22** (41.2 mg, 58%), and 10.8 mg (22%) of **18** was recovered. $[\alpha]_D$ +43.5° (c 1.3, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.96–7.21 (m, 19H, Ar), 5.70 (dd, 1H, $J_{3,4}$ = 8.7 Hz, $J_{2,3}$ = 10.9 Hz, H-3^{GlcN}), 5.64 (dd, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 10.4 Hz, H-2^{GalII}), 5.52 (d, 1H, $J_{3,4}$ = 2.3 Hz, H-4^{Fuc}), 5.41–5.40 (m, 2H, H-4^{GalI}, H-1^{GalII}), 5.34–5.33 (m, 2H, H-1^{GlcN}, H-1^{Fuc}), 5.13–5.07 (m, 4H, H-2^{Fuc}, H-3^{Fuc}, OCH_2Ph), 4.83 (d, 1H, $J_{3,4}$ = 2.1 Hz, H-4^{GalII}), 4.75 (d, 1H, J_{gem} = 12.0 Hz, OCH_2Ph), 4.63 (br s, 1H, OCH$_2$(CH$_2$)$_3$CH$_2$N*H*), 4.54 (d, 1H, OCH_2Ph), 4.47 (dd, 1H, $J_{5,6a}$ = 3.9 Hz, J_{gem} = 12.2 Hz, H-6a^{GlcN}), 4.41 (d, 1H, H-6b^{GlcN}), 4.37–4.19 (m, 5H, H-2^{GlcN}, H-1^{GalI}, H-6a^{GalI}, H-6b^{GalI}, H-5^{Fuc}), 4.13 (dd, 1H, $J_{5,6a}$ = 6.7 Hz, J_{gem} = 11.3 Hz, H-6a^{GalII}), 3.98–3.90 (m, 3H, H-4^{GlcN}, H-3^{GalII}, H-6b^{GalII}), 3.86–3.78 (m, 3H, H-5^{GlcN}, H-3^{GalI}, OCH_2(CH$_2$)$_3$CH$_2$NH), 3.69–3.63 (m, 3H, H-2^{GalI}, H-5^{GalI}, H-5^{GalII}), 3.47–3.45 (m, 1H, OCH_2(CH$_2$)$_3$CH$_2$NH), 2.93–2.89 (m, 2H, OCH$_2$(CH$_2$)$_3$CH_2NH), 2.25–1.81 (6 s, 18H, Ac), 1.47–1.11 (m, 30H, H-6^{Fuc}, 2 *t*-Bu, Ac, OCH$_2$(CH_2)$_3$CH$_2$NH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.6, 170.6, 170.4, 170.1, 170.0, 169.8, 169.2, 169.3, 165.7, 138.4, 136.6, 134.3, 133.0, 131.4, 130.2, 129.8, 128.5, 128.2, 128.1, 128.1, 127.5, 127.4, 123.5, 100.9, 98.1, 95.9, 92.7, 77.6, 74.3, 72.6, 71.1, 70.9, 70.3, 69.9, 69.7, 69.6, 68.6, 68.4, 68.1, 67.8, 66.8, 66.5, 65.4, 64.4, 62.3, 61.2, 54.6, 40.8, 29.7, 29.3, 28.8, 27.7, 27.3, 23.4, 23.0, 20.9, 20.8, 20.7, 20.6, 20.6, 19.5, 15.9. HRMS (ESI) *m/z*: found $[M+Na]^+$ 1649.6129, $C_{81}H_{102}N_2O_{31}Si$ calcd for $[M+Na]^+$ 1649.6128.



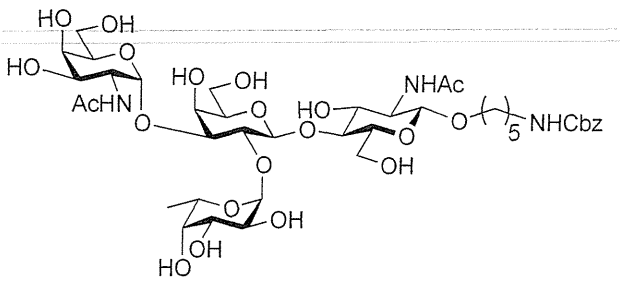
5-Benzyloxycarbonylamino-1-pentyl (2-acetamido-2-deoxy-4,6-O-di-tert-butylsilylene-α-D-galactopyranosyl)-(1→3)-[2,3,4-tri-O-acetyl-α-L-fucopyranosyl-(1→2)]-(4,6-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-β-D-glucopyranoside (**23**). To a solution of **21** (45 mg, 25.2 μmol) in CH_2Cl_2 (1.7 mL) were added AcOH (288 μL, 5.04 mmol) and Zn powder (225 mg, 3.44 mmol) at rt. After stirring for 20 min at rt as the reaction was monitored by TLC (20:1 $CHCl_3$–MeOH), another portion of Zn powder (225 mg) was added to the mixture and the stirring was continued. After 30 min, AcOH (288 μL) and CH_2Cl_2 (1.7 mL) were added to the mixture. After stirring for total 4 h, the precipitate was filtered through Celite and the filtrate was washed with satd aq $NaHCO_3$. The organic layer was subsequently dried over Na_2SO_4, concentrated and the residue obtained was then dissolved in CH_2Cl_2 (2.5 mL). To the mixture was added acetic anhydride (48 μL, 252 μmol) at 0 °C. After

stirring for 1 h at rt as the reaction was monitored by TLC (2:1 $CHCl_3$–acetone), the reaction mixture was concentrated. The resulting residue was purified by silica gel column chromatography (2:1 $CHCl_3$–acetone) to give **23** (31 mg, 84%). $[\alpha]_D$ +6.3° (c 0.6, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.85–7.70 (m, 4H, Phth), 7.38–7.26 (m, 5H, Ph), 5.76–5.69 (m, 2H, H-3^{GlcN}, NH^{GalN}), 5.45–5.43 (m, 2H, H-4^{Gal}, H-4^{Fuc}), 5.36–5.31 (m, 2H, H-1^{GlcN}, H-2^{Fuc}), 5.15–5.07 (m, 5H, H-1^{Fuc}, H-3^{Fuc}, H-1^{GalN}, OCH_2), 4.63 (br s, 1H, $OCH_2(CH_2)_3CH_2NH$), 4.50–4.43 (m, 4H, H-2^{GlcN}, H-6a^{GlcN}, H-6b^{GlcN}, H-4^{GalN}), 4.41–4.35 (m, 2H, H-1^{Gal}, H-5^{Fuc}), 4.29 (d, 1H, J_{gem} = 11.2 Hz, H-6a^{GalN}), 4.25–4.18 (m, 2H, H-2^{GalN}, H-6b^{GalN}), 4.10–4.04 (m, 2H, H-6a^{Gal}, H-6b^{Gal}), 3.95–3.92 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.9 Hz, H-4^{GlcN}), 3.89–3.72 (m, 5H, H-5^{GlcN}, H-2^{Gal}, H-3^{Gal}, H-5^{Gal}, $OCH_2(CH_2)_3CH_2NH$), 3.56–3.45 (m, 3H, H-3^{GalN}, H-5^{GalN}, $OCH_2(CH_2)_3CH_2NH$), 2.94–2.90 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 2.60 (d, 1H, $J_{3,OH}$ = 11.5 Hz, OH^{GalN}), 2.18–1.88 (8 s, 24H, Ac), 1.51–1.05 (m, 27H, H-6^{Fuc}, 2 *t*-Bu, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (125 MHz, CD_3CN) δ 170.2, 170.2, 169.9, 169.9, 169.8, 169.7, 169.6, 155.9, 137.3, 134.4, 131.0, 128.1, 127.5, 127.4, 123.1, 117.0, 99.5, 97.6, 95.6, 93.4, 73.8, 73.6, 73.1, 72.6, 72.2, 70.8, 70.4, 69.8, 69.1, 67.8, 67.7, 67.6, 67.5, 66.3, 65.3, 64.8, 64.7, 61.7, 61.1, 54.2, 53.9, 48.6, 40.0, 30.9, 29.0, 28.7, 28.4, 28.3, 26.7, 26.4, 22.5, 22.4, 21.8, 20.2, 19.9, 19.9, 19.8, 19.7, 19.7, 19.6, 19.5, 14.7. HRMS (ESI) *m/z*: found $[M+Na]^+$ 1496.5661, $C_{69}H_{95}N_3O_{30}Si$ calcd for $[M+Na]^+$ 1496.5662.

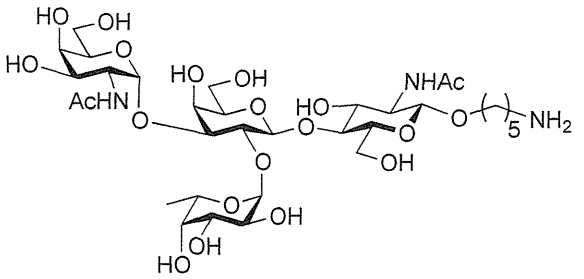


5-Benzyloxycarbonylamino-1-pentyl (2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-galactopyranosyl)-(1→3)-[2,3,4-tri-O-acetyl-α-L-fucopyranosyl-(1→2)]-(4,6-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-β-D-glucopyranoside (**24**). To a solution of **23** (31 mg, 21.2 μmol) in THF (1.1 mL) was added TBAHF 1.0 M solution (212 μL) at rt. After stirring for 40 min at rt as the reaction was monitored by TLC (10:1 $CHCl_3$–MeOH), the reaction mixture was diluted with EtOAc and washed with 2 M HCl, H_2O, satd aq $NaHCO_3$, and brine. The organic layer was then dried over Na_2SO_4 and concentrated. The residue obtained was dissolved in pyridine (1.0 mL). To the mixture was added acetic anhydride (1.0 mL) at 0 °C. After stirring for 21 h at rt as the reaction was monitored by TLC (10:1 $CHCl_3$–MeOH), the reaction was quenched by the addition of MeOH at 0 °C. The mixture was co-evaporated with toluene. The residue was diluted with EtOAc and washed with 2 M HCl, H_2O, satd aq $NaHCO_3$, and brine. The organic layer was then dried over Na_2SO_4 and concentrated. The resulting residue was purified by silica gel column chromatography (10:10:1 $CHCl_3$–toluene–MeOH) and gel filtration column chromatography (LH-20, 1:1 $CHCl_3$–MeOH) to give **24** (30 mg, 98% over two steps). $[\alpha]_D$ +2.6° (c 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.85–7.70 (m, 4H, Phth), 7.38–7.26 (m, 5H, Ph), 6.32 (br d, 1H, $J_{2,NH}$ = 6.9 Hz, NH^{GalN}), 5.76 (dd, 1H, $J_{2,3}$ = 10.8 Hz, $J_{3,4}$ = 9.2 Hz, H-3^{GlcN}), 5.50 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1^{Fuc}), 5.42 (d, 1H, $J_{3,4}$ = 1.5 Hz, H-4^{GalN}), 5.37–5.34 (m, 3H, H-4^{Gal}, H-2^{Fuc}, H-4^{Fuc}), 5.31 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1^{GlcN}), 5.22 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1^{GalN}), 5.13 (dd, 1H, $J_{3,4}$ = 3.2 Hz, $J_{2,3}$ = 11.0 Hz, H-3^{Fuc}), 5.07 (s, 2H, OCH_2Ph), 4.97 (dd, 1H,

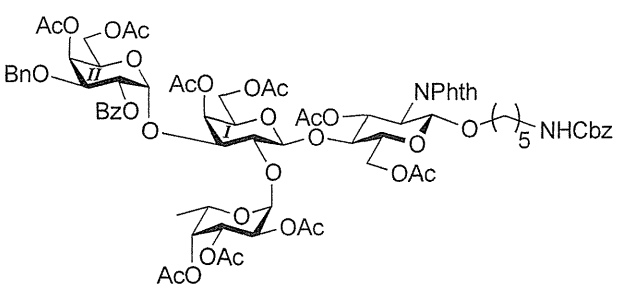
$J_{2,3}$ = 11.3 Hz, H-3^{GalN}), 4.66 (br s, 1H, $OCH_2(CH_2)_3CH_2NH$), 4.56–4.51 (m, 2H, H-6a^{GlcN}, H-5^{Fuc}), 4.48–4.43 (m, 1H, H-2^{GalN}), 4.40–4.37 (m, 2H, H-6b^{GlcN}, H-1^{Gal}), 4.24 (dd, 1H, H-2^{GlcN}), 4.17–4.14 (m, 2H, H-6a^{Gal}, H-6a^{GalN}), 4.11–4.07 (m, 2H, H-6b^{Gal}, H-6b^{GalN}), 4.03 (br d, 1H, H-5^{GalN}), 3.96 (t, 1H, $J_{4,5}$ = 9.2 Hz, H-4^{GlcN}), 3.86–3.74 (m, 5H, H-5^{GlcN}, H-2^{Gal}, H-3^{Gal}, H-5^{Gal}, $OCH_2(CH_2)_3CH_2NH$), 3.48–3.44 (m, 1H, $OCH_2(CH_2)_3CH_2NH$), 2.94–2.90 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 2.20–1.92 (11 s, 33H, Ac), 1.49–1.05 (m, 9H, H-6^{Fuc}, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.9, 170.6, 170.5, 170.4, 170.3, 170.0, 170.0, 169.9, 136.6, 134.3, 128.5, 128.1, 128.1, 123.6, 100.3, 98.1, 96.6, 77.6, 74.6, 74.5, 72.8, 71.2, 70.6, 69.9, 69.8, 68.6, 67.9, 67.4, 66.9, 66.7, 66.5, 65.3, 62.7, 62.2, 61.0, 54.7, 48.1, 40.8, 29.7, 29.3, 28.8, 23.0, 20.9, 20.7, 20.6, 20.6, 15.6. HRMS (ESI) *m/z*: found $[M+Na]^+$ 1482.4956, $C_{67}H_{85}N_3O_{33}Si$ calcd for $[M+Na]^+$ 1482.4958.



5-Benzyloxycarbonylamino-1-pentyl (2-acetamido-2-deoxy-α-D-galactopyranosyl)-(1→3)-[α-L-fucopyranosyl-(1→2)]-β-D-galactopyranosyl-(1→4)-2-acetamide-2-deoxy-β-D-glucopyranoside (**25**). To a solution of **24** (19.8 mg, 13.6 μmol) in MeOH (1.4 mL) was added NaOMe (1M solution in MeOH, 6.8 μL, 6.78 μmol) at 0 °C. After stirring for 4 h at rt as the reaction was monitored by TLC (20:12:1 $CHCl_3$–MeOH–H_2O), the reaction was neutralized with Muromac (H^+) resin. The resin was filtered out and the filtrate was concentrated. The residue obtained was then dissolved in EtOH (2.8 mL). To the solution was added $NH_2NH_2 \cdot H_2O$ (1.0 μL, 27.2 μmol) at rt. The reaction mixture was stirred at reflux as monitored by TLC (5:4:1 $CHCl_3$–MeOH–H_2O). Additional portions of $NH_2NH_2 \cdot H_2O$ (2.0 μL) was added to the mixture every 15 min (total amounts of $NH_2NH_2 \cdot H_2O$ added was 32 μL). After 6.5 h, the reaction mixture was concentrated and exposed to high vacuum for 1 h. The resulting residue was then dissolved in MeOH/CH_2Cl_2 (3:1, 4.4 mL). To the mixture was added acetic anhydride (26 μL, 272 μmol) at 0 °C. After stirring for 1.5 h at rt as the reaction was monitored by TLC (5:4:1 $CHCl_3$–MeOH–H_2O), the reaction mixture was concentrated. The residue obtained was purified by silica gel column chromatography (Iatrobeads, 9:5:0.5 $CHCl_3$–MeOH–H_2O) to give **25** (10.3 mg, 80% over three steps). $[\alpha]_D$ +4.4° (c 0.3, MeOH); ^{1}H-NMR (500 MHz, CD_3OD) δ 7.45–7.43 (m, 5H, Ph), 5.36 (d, 1H, $J_{1,2}$ = 3.9 Hz, α-anomer H), 5.15 (d, 1H, $J_{1,2}$ = 3.7 Hz, α-anomer H), 5.06 (s, 2H, OCH_2Ph), 4.52 (d, 1H, $J_{1,2}$ = 7.7 Hz, β-anomer H), 4.39 (d, 1H, $J_{1,2}$ = 8.4 Hz, β-anomer H), 4.34–4.31 (m, 1H, H-5^{Fuc}), 4.18–3.46 (m, 27H, ring H, $OCH_2(CH_2)_3CH_2NH$), 3.11–3.08 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 2.00–1.96 (2 s, 6H, Ac), 1.57–1.20 (m, 9H, H-6^{Fuc}, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (125 MHz, CD_3OD) δ 174.5, 173.5, 158.9, 138.5, 129.4, 128.9, 128.8, 102.8, 102.2, 100.3, 93.6, 78.5, 77.9, 77.2, 76.9, 74.2, 73.6, 73.5, 72.7, 71.9, 70.5, 70.5, 70.1, 69.9, 67.7, 67.3, 64.9, 63.4, 62.6, 61.8, 56.9, 51.3, 41.8, 30.5, 30.2, 24.3, 23.0, 22.7, 16.6. HRMS (ESI) *m/z*: found $[M+Na]^+$ 974.3954, $C_{41}H_{65}N_3O_{22}$ calcd for $[M+Na]^+$ 974.3952.

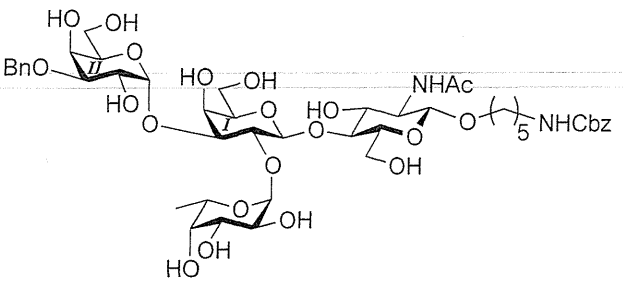


5-Amino-1-pentyl 2-acetamido-2-deoxy-α-D-galactopyranosyl-(1→3)-[α-L-fucopyranosyl-(1→2)]-β-D-galactopyranosyl-(1→4)-2-acetamide-2-deoxy-β-D-glucopyranoside (**1**). To a solution of **25** (3.2 mg, 3.36 μmol) in MeOH/H_2O (1:1, 3.2 mL) was added Pd/C (5 wt. %, 0.5 mg). After stirring for 3.5 h at rt under a hydrogen atmosphere as the reaction was monitored by TLC (5:4:1:1 $CHCl_3$–MeOH–H_2O–AcOH), additional portion of Pd/C (0.5 mg) was added to the mixture and the stirring was continued. After 12.5 h, further portion of Pd/C (0.5 mg) was added to the mixture. After stirring for total 21 h, the mixture was filtered through membrane filter. The filtrate was concentrated and the residue obtained was purified by gel filtration column chromatography (LH-20, MeOH) to give **1** (2.2 mg, 96%). $[\alpha]_D$ +4.4° (c 0.3, MeOH); ^{1}H-NMR (500 MHz, D_2O) δ 5.36 (d, 1H, $J_{1,2}$ = 4.1 Hz, α-anomer H), 5.16 (d, 1H, $J_{1,2}$ = 3.9 Hz, α-anomer H), 4.58 (d, 1H, $J_{1,2}$ = 7.7 Hz, β-anomer H), 4.47 (d, 1H, $J_{1,2}$ = 8.4 Hz, β-anomer H), 4.31–4.29 (m, 1H, H-5^{Fuc}), 4.23–3.56 (m, 27H, ring H, OCH_2(CH$_2$)$_3$CH$_2$NH), 2.98–2.95 (m, 2H, OCH$_2$(CH$_2$)$_3$CH_2NH), 2.02 (2 s, 6H, Ac), 1.67–1.22 (m, 9H, H-6^{Fuc}, OCH$_2$(CH_2)$_3$CH$_2$NH); ^{13}C-NMR (200 MHz, CD_3OD) δ 174.4, 173.6, 103.0, 102.2, 100.3, 93.5, 78.3, 77.8, 77.1, 77.0, 74.1, 73.6, 73.5, 72.7, 71.9, 70.5, 70.3, 70.0, 69.9, 67.7, 64.8, 63.4, 62.6, 61.6, 56.8, 51.2, 40.7, 33.1, 30.8, 30.5, 29.8, 28.3, 24.2, 23.8, 23.0, 22.7, 16.6, 14.5. HRMS (ESI) *m/z*: found $[M+Na]^+$ 840.3584, $C_{33}H_{59}N_3O_{20}$ calcd for $[M+Na]^+$ 840.3584

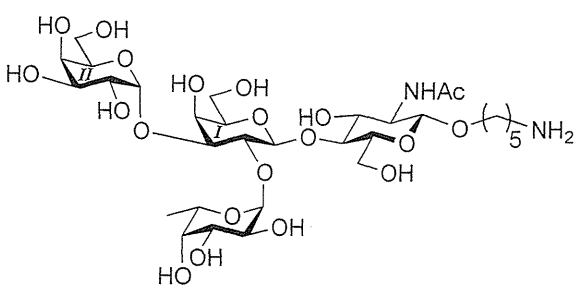


5-Benzyloxycarbonylamino-1-pentyl (4,6-di-O-acetyl-2-O-benzoyl-3-O-benzyl-α-D-galactopyranosyl)-(1→3)-[2,3,4-tri-O-acetyl-α-L-fucopyranosyl-(1→2)]-(4,6-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-acetyl-2-deoxy-2-phthalimide-β-D-glucopyranoside (**26**). Compound **22** (30.1 mg, 18.5 μmol) was converted into **26** (23.6 mg, 81%) according to the procedure described for **24**. $[\alpha]_D$ +75.3° (c 0.2, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.96–7.16 (m, 19H, Ar), 5.75 (d, 1H, $J_{3,4}$ = 1.9 Hz, H-4^{GalII}), 5.72 (dd, 1H, $J_{3,4}$ = 8.2 Hz, $J_{2,3}$ = 8.8 Hz, H-3^{GlcN}), 5.56 (d, 1H, $J_{3,4}$ = 2.6 Hz, H-4^{Fuc}), 5.42 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1^{Fuc}) 5.41 (d, 1H, $J_{3,4}$ = 2.3 Hz, H-4^{GalI}), 5.38–5.35 (m, 2H, H-1^{GalII}, H-2^{GalII}), 5.31 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1^{GlcN}), 5.22–5.17 (m, 2H, H-2^{Fuc}, H-3^{Fuc}), 5.07 (s, 2H, OCH_2Ph), 4.70 (d, 1H, J_{gem} = 11.8 Hz, OCH_2Ph), 4.64 (br s, 1H, OCH$_2$(CH$_2$)$_3$CH$_2$N*H*), 4.49–4.40 (m, 4H, H-6a^{GlcN}, H-6b^{GlcN}, H-5^{Fuc}, OCH_2Ph), 4.30 (d, 1H, $J_{1,2}$ = 7.4 Hz, H-1^{GalI}), 4.23–4.13 (m, 4H, H-2^{GlcN}, H-5^{GalII}, H-6a^{GalII}, H-6b^{GalII}), 4.08 (dd, 1H, $J_{3,4}$ = 3.2 Hz, $J_{2,3}$ = 7.2 Hz, H-3^{GalII}), 4.00 (dd, 1H, $J_{5,6a}$ = 6.7 Hz, J_{gem} = 11.3 Hz,

H-6a^{GalI}), 3.94–3.90 (m, 2H, H-4^{GlcN}, H-6b^{GalI}), 3.86–3.79 (m, 2H, H-5^{GlcN}, OCH_2(CH$_2$)$_3$CH$_2$NH), 3.76 (dd, 1H, $J_{2,3}$ = 7.4 Hz, $J_{3,4}$ = 2.9 Hz, H-3^{GalI}), 3.65 (t, 1H, H-2^{GalI}), 3.57 (t, 1H, $J_{5,6b}$ = 6.7 Hz, H-5^{GalI}), 3.48–3.43 (m, 1H, OCH_2(CH$_2$)$_3$CH$_2$NH), 2.93–2.89 (m, 2H, OCH$_2$(CH$_2$)$_3$CH_2NH), 2.24–1.83 (9 s, 27H, Ac), 1.47–1.09 (m, 9H, H-6^{Fuc}, OCH$_2$(CH_2)$_3$CH$_2$NH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.6, 170.6, 170.5, 17.3, 170.2, 170.1, 169.9, 169.8, 169.4, 165.6, 156.2, 137.8, 136.6, 134.3, 133.3, 131.4, 129.9, 129.6, 128.5, 128.4, 128.2, 128.1, 128.1, 127.9, 127.5, 123.5, 100.5, 98.1, 96.1, 77.6, 74.2, 72.7, 71.4, 71.3, 70.9, 70.1, 69.8, 69.6, 68.0, 67.8, 67.7, 67.2, 66.5, 65.2, 62.5, 62.3, 61.2, 54.6, 40.8, 29.7, 29.3, 28.8, 23.0, 20.8, 20.8, 20.7, 20.7, 20.7, 20.6, 19.8, 15.8. HRMS (ESI) *m/z*: found $[M+Na]^+$ 1593.4316, $C_{81}H_{102}N_2O_{31}Si$ calcd for $[M+Na]^+$ 1593.4318.

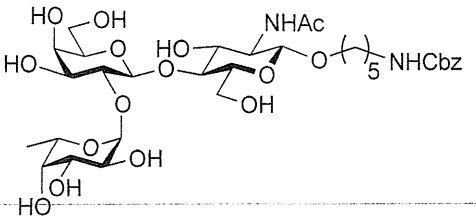


5-Benzyloxycarbonylamino-1-pentyl (3-O-benzyl-α-D-galactopyranosyl)-(1→3)-[α-L-fucopyranosyl-(1→2)]-β-D-galactopyranosyl-(1→4)-2-acetamide-2-deoxy-β-D-glucopyranoside (**27**). Compound **26** (23.3 mg, 14.8 μmol) was converted into **27** (14.7 mg, 99%) according to the procedure described for **25**. $[\alpha]_D$ −6.2° (c 0.3, MeOH); ^{1}H-NMR (500 MHz, CD_3OD) δ 7.45–7.26 (m, 10H, Ph), 5.30 (near s, 1H, α-anomer H), 5.15 (d, 1H, $J_{1,2}$ = 3.9 Hz, α-anomer H), 5.05 (s, 2H, OCH_2Ph), 4.75 (d, 1H, J_{gem} = 11.7 Hz, OCH_2Ph), 4.64 (d, 1H, OCH_2Ph), 4.53 (d, 1H, $J_{1,2}$ = 7.5 Hz, β-anomer H), 4.38 (d, 1H, $J_{1,2}$ = 8.4 Hz, β-anomer H), 4.29–4.28 (m, 1H, H-5^{Fuc}), 4.12–3.45 (m, 27H, ring H, OCH_2(CH$_2$)$_3$CH$_2$NH), 3.11–3.08 (m, 2H, OCH$_2$(CH$_2$)$_3$CH_2NH), 1.96 (s, 3H, Ac), 1.56–1.21 (m, 9H, H-6^{Fuc}, OCH$_2$(CH_2)$_3$CH$_2$NH); ^{13}C-NMR (125 MHz, CD_3OD) δ 173.5, 158.9, 139.9, 138.5, 129.4, 129.3, 129.1, 128.9, 128.8, 128.7, 102.8, 102.2, 100.2, 95.9, 79.5, 79.3, 78.6, 77.1, 76.7, 74.1, 73.6, 73.0, 72.6, 71.9, 70.5, 69.9, 69.1, 68.1, 67.6, 67.3, 65.6, 63.3, 62.6, 61.7, 56.7, 41.8, 30.5, 30.2, 24.3, 23.0, 16.6. HRMS (ESI) *m/z*: found $[M+Na]^+$ 1023.4156, $C_{46}H_{68}N_2O_{22}$ calcd for $[M+Na]^+$ 1023.4156.

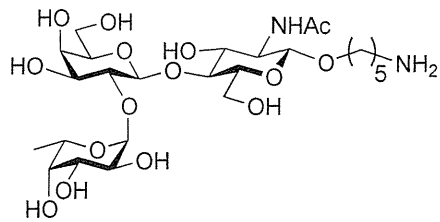


5-Amino-1-pentyl α-D-galactopyranosyl-(1→3)-[α-L-fucopyranosyl-(1→2)]-β-D-galactopyranosyl-(1→4)-2-acetamide-2-deoxy-β-D-glucopyranoside (**2**). Compound **27** (2.1 mg, 2.10 μmol) was converted into **2** (1.6 mg, quant.) according to the procedure described for **1**, except for the use of a mixed solvent (1:1, 1,4-dioxane–2% aq formic acid) as reaction media. $[\alpha]_D$ +6.3° (c 0.3, MeOH); ^{1}H-NMR (500 MHz, D_2O) δ 5.31 (d, 1H, $J_{1,2}$ = 4.1 Hz, α-anomer H), 5.22 (d, 1H, $J_{1,2}$ = 2.5 Hz,

α-anomer H), 4.59 (d, 1H, $J_{1,2}$ = 7.6 Hz, β-anomer H), 4.46 (d, 1H, $J_{1,2}$ = 8.4 Hz, β-anomer H), 4.30–3.42 (m, 28H, ring H, $OCH_2(CH_2)_3CH_2NH$), 2.98–2.95 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 2.01 (s, 3H, Ac), 1.67–1.21 (m, 9H, H-6^{Fuc}, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (200 MHz, CD_3OD) δ 173.5, 103.0, 102.2, 100.3, 96.2, 79.9, 78.5, 77.1, 76.7, 74.1, 73.8, 73.6, 73.2, 71.8, 71.4, 71.3, 70.3, 70.0, 69.9, 67.6, 65.8, 63.3, 62.6, 61.7, 56.7, 40.7, 29.8, 28.4, 24.2, 23.0, 16.5. HRMS (ESI) *m/z*: found $[M+Na]^+$ 779.3320, $C_{31}H_{56}N_2O_{20}$ calcd for $[M+Na]^+$ 779.3319.



5-Benzyloxycarbonylamino-1-pentyl α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-2-acetamide-2-deoxy-β-D-glucopyranoside (**28**). Compound **18** (19.3 mg, 17.0 μmol) was converted into **28** (12.0 mg, 94%) according to the procedure described for **25**. $[\alpha]_D$ −110.0° (c 0.2, MeOH); ^{1}H-NMR (500 MHz, CD_3OD) δ 7.34–7.28 (m, 5H, Ph), 5.22 (d, 1H, $J_{1,2}$ = 3.1 Hz, α-anomer H), 5.05 (s, 2H, OCH_2Ph), 4.48 (d, 1H, $J_{1,2}$ = 6.1 Hz, β-anomer H), 4.37 (d, 1H, $J_{1,2}$ = 8.3 Hz, β-anomer H), 4.18–4.17 (m, 1H, H-5^{Fuc}), 3.96–3.45 (m, 20H, ring H, $OCH_2(CH_2)_3CH_2NH$), 3.11–3.08 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 1.96 (s, 3H, Ac), 1.57–1.20 (m, 9H, H-6^{Fuc}, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (125 MHz, CD_3OD) δ 173.5, 158.9, 138.5, 129.4, 128.9, 128.8, 102.8, 102.5, 101.8, 79.0, 78.2, 77.1, 77.0, 76.9, 75.3, 74.1, 73.6, 71.7, 70.7, 70.5, 68.3, 67.3, 62.6, 61.6, 56.7, 41.8, 30.5, 30.2, 24.3, 23.0, 16.7. HRMS (ESI) *m/z*: found $[M+Na]^+$ 771.3156, $C_{33}H_{52}N_2O_{17}$ calcd for $[M+Na]^+$ 771.3158.



5-Amino-1-pentyl α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-2-acetamide-2-deoxy-β-D-glucopyranoside (**3**). Compound **28** (5.9 mg, 7.88 μmol) was converted into **3** (3.5 mg, 73%) according to the procedure described for **1**. $[\alpha]_D$ −76.3° (c 0.2, MeOH); ^{1}H-NMR (500 MHz, D_2O) δ 5.29 (d, 1H, $J_{1,2}$ = 3.1 Hz, α-anomer H), 4.52 (d, 1H, $J_{1,2}$ = 7.8 Hz, β-anomer H), 4.48 (d, 1H, $J_{1,2}$ = 8.2 Hz, β-anomer H), 4.22–4.20 (m, 1H, H-5^{Fuc}), 3.98–3.42 (m, 18H, ring H, $OCH_2(CH_2)_3CH_2NH$), 2.98–2.95 (m, 2H, $OCH_2(CH_2)_3CH_2NH$), 2.02 (s, 3H, Ac), 1.69–1.21 (m, 9H, H-6^{Fuc}, $OCH_2(CH_2)_3CH_2NH$); ^{13}C-NMR (200 MHz, CD_3OD) δ 173.6, 103.0, 102.5, 101.8, 79.0, 78.0, 77.1, 76.9, 75.2, 74.1, 73.6, 71.7, 70.7, 70.7, 70.2, 68.3, 62.7, 61.5, 56.6, 40.6, 39.5, 29.8, 28.2, 24.1, 23.0, 16.8. HRMS (ESI) *m/z*: found $[M+Na]^+$ 637.2791, $C_{25}H_{46}N_2O_{15}$ calcd for $[M+Na]^+$ 637.2790.

4. Conclusions

We have developed a novel approach to synthesizing human histo-blood group type 2 antigens. A lactosamine derivative served as a key building block and was efficiently prepared from lactulose via the Heyns rearrangement, a strategy that allowed us to lower the overall number of reaction steps. The introduction of galactosamine and galactose in α-linked form into the O-antigen trisaccharide was accomplished by a unique DTBS-directed α-glycosylation to afford type 2 A- and B-antigen tetrasaccharides, respectively. The present synthetic protocol can provide rapid access to various biologically relevant glycoconjugates that contain *N*-acetyl-lactosamine and ABO blood group antigens. Studies on biological applications using the synthesized antigens will be reported in due course.

Acknowledgments

The iCeMS is supported by World Premier International Research Center Initiative (WPI), MEXT, Japan. This work was financially supported in part by MEXT of Japan (a Grant-in-Aid for Scientific Research (B) No. 22380067 to M.K.). We thank Kiyoko Ito (Gifu University) for providing technical assistance and Yuji O. Kamatari (Division of Instrumental Analysis, Life Science Research Center, Gifu University) for providing technical assistance of NMR mesurement (Bruker Biospin AVANCE III 800).

Conflicts of Interest

The authors declare no conflict of interest.

References and Notes

1. Stanley, P.; Cummings, R.D. Structures Common to Different Glycans. In *Essentials of Glycobiology*, 2nd ed.; Varki, A., Cummings, R.D., Esko, J.D., Freeze, H.H., Stanley, P., Bertozzi, C.R., Hart, G.W., Etzler, M.E., Eds.; Cold Spring Harbor: New York, NY, USA, 2009; Chapter 13, pp. 175–198.
2. Ravn, V.; Dabelsteen, E. Tissue distribution of histo-blood group antigens. *APMIS* **2000**, *108*, 1–28.
3. Mollicone, R.; Gibaud, A.; Francois, A.; Ratcliffe, M.; Oriol, R. Acceptor specificity and tissue distribution of three human α-3-fucosyltransferases. *Eur. J. Biochem.* **1990**, *191*, 169–176.
4. Meloncelli, P.; Lowary, T.L. Synthesis of ABO histo-blood group type I and II antigens. *Carbohydr. Res.* **2010**, *345*, 2305–2322.
5. Landsteiner, K. Cell Antigens. In *The Specificity of Serological Reactions*; Landsteiner, K., Ed.; Dover Publications, Inc.: New York, NY, USA, 1936; pp. 75–126.
6. Williamson, L.M.; Lowe, S.; Love, E.M.; Cohen, H.; Soldan, K.; McClelland, D.B.L.; Skacel, P.; Barbara, J.A.J. Serious hazards of transfusion (SHOT) initiative: Analysis of the first two annual reports. *BMJ* **1999**, *319*, 16–19.
7. Cooper, D.K.C. Xenoantigens and xenoantibodies. *Xenotransplantation* **1998**, *5*, 6–17.
8. Reid, M.E.; Bird, G.W.G. Associations between human red cell blood group antigens and disease. *Transfus. Med. Rev.* **1990**, *4*, 47–55.
9. Anstee, D.J. The relationship between blood groups and disease. *Blood* **2010**, *115*, 4635–4643.

10. O'Donnell, J.; Laffan, M.A. The relationship between ABO histo-blood group, factor VIII and von Willebrand factor. *Transfus. Med.* **2001**, *11*, 343–351.
11. Ruiz-Palacios, G.M.; Cervantes, L.E.; Ramos, P.; Chavez-Munguia, B.; Newburg, D.S. *Campylobacter jejuni* binds intestinal H(O) antigen (Fucα1,2Galβ1,4GlcNAc), and fucosyloligosaccharides of human milk inhibit its binding and infection. *J. Biol. Chem.* **2003**, *278*, 14112–14120.
12. Rossez, Y.; Maes, E.; Darroman, T.L.; Gosset, P.; Ecobichon, C.; Curt, M.J.C.; Boneca, I.G.; Michalski, J.-C.; Robbe-Masselot, C. Almost all human gastric mucin *O*-glycans harbor blood group A, B or H antigens and are potential binding sites for *Helicobacter pylori*. *Glycobiology* **2012**, *22*, 1193–1206.
13. Lindesmith, L.; Moe, C.; Marionneau, S.; Ruvoen, N.; Jiang, X.; Lindblad, L.; Stewart, P.; LePendu, J.; Baric, R. Human susceptibility and resistance to Norwalk virus infection. *Nat. Med.* **2003**, *9*, 548–553.
14. Tan, M.; Jiang, X. Norovirus and its histo-blood group antigen receptors: An answer to a historical puzzle. *Trends Microbiol.* **2005**, *13*, 285–293.
15. Glinsky, G.V.; Ivanova, A.B.; Welsh, J.; McClelland, M. The role of blood group antigens in malignant progression, Apoptosis resistance, and metastatic behavior. *Transfus. Med. Rev.* **2000**, *14*, 326–350.
16. Pinho, S.S.; Carvalho, S.; Marcos-Pinto, R.; Magalhães, A.; Oliveira, C.; Gu, J.; Dinis-Ribeiro, M.; Carneiro, F.; Seruca, R.; Reis, C.A. Gastric cancer: Adding glycosylation to the equation. *Trends Mol. Med.* **2013**, *19*, 664–676.
17. Paulsen, H.; Kolář, Č. Synthesis of the tetrasaccharide chains of the determinants of blood group substances A and B. *Angew. Chem. Int. Ed.* **1978**, *17*, 771.
18. Korchagina, E.Y.; Ryzhov, I.M.; Byrgazov, K.A.; Popova, I.S.; Pokrovsky, S.N.; Bovin, N.V. Block synthesis of blood group tetrasaccharides B (types 1, 3 and 4). *Mendeleev Commun.* **2009**, *19*, 152–154.
19. Ryzhov, I.M.; Korchagina, E.Y.; Popova, I.S.; Bovin, N.V. Block synthesis of A tetrasaccharides (types 1, 3 and 4) related to the human ABO blood group system. *Carbohydr. Res.* **2012**, *351*, 17–25.
20. Zimmermann, P.; Greilich, U.; Schmidt, R.R. Total synthesis of a hexaosyl ceramide glycolipid acting as a receptor for macrophage migration inhibiton-factor. *Tetrahedron Lett.* **1990**, *31*, 1849–1852.
21. Udodong, U.E.; Rao, C.S.; Fraser-Reid, B. *n*-Pentenyl glycosides in the efficient assembly of the blood group substance B tetrasaccahride. *Tetrahedron* **1992**, *48*, 4713–4724.
22. Deshpande, P.P.; Kim, H.M.; Zatorski, A.; Park, T.-K.; Ragupathi, G.; Livingston, P.O.; Live, D.; Danishefsky, S.J. Strategy in oligosaccharide synthesis: An application to a concise total synthesis of the KH-1 (adenocarcinoma) antigen. *J. Am. Chem. Soc.* **1998**, *120*, 1600–1614.
23. Bovin, N.V.; Zurabyan, S.É.; Khorlin, A.Y. Stereoselectivity in glycosylation by means of 2-azido-2-desoxy-D-galactopyranose derivatives and the synthesis of the determinative oligosaccharide of blood group A, type 1. *Russ. Chem. Bull.* **1982**, *31*, 1023–1030.
24. Paulsen, H.; Kolář, Č. Synthese der tetrasaccharid-ketten der type 2 der determinanten der blutgruppensubstanzen A und B. *Tetrahedron Lett.* **1979**, *31*, 2882–2884.

25. Milat, M.-L.; Sinäy, P. Synthesis of the tetrasaccharide *O*-α-L-fucopyranosyl-(1→2)-[*O*-α-D-galactopyranosyl-(1→3)]-*O*-β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-D-glucopyranose, the antigenic determinant of human blood-group B (type 2). *Carbohydr. Res.* **1981**, *92*, 183–189.
26. Pazynina, G.V.; Tyrtysh, T.V.; Bovin, N.V. Synthesis of histo blood-group antigens A and B (type 2), xenoantigen Galα1-3Galβ1-4GlcNAc and related type 2 backbone oligosaccharides as haptens in spacered form. *Mendeleev Commun.* **2002**, *12*, 143–145.
27. Lemieux, R.U.; Driquez, H. Chemical synthesis of 2-*O*-(α-L-fucopyranosyl)-3-*O*-(α-D-galactopyranosyl)-D-galactose. Terminal structure of the blood-group B antigenic determinant. *J. Am. Chem. Soc.* **1975**, *97*, 4069–4075.
28. Lemieux, R.U.; Bock, K.; Delbaere, L.T.J.; Koto, S.; Rao, V.S. The conformations of oligosaccharides related to the ABH and Lewis human blood determinants. *Can. J. Chem.* **1980**, *58*, 631–653.
29. Lemieux, R.U.; Abbas, S.Z.; Burzynska, M.H.; Ratcliffe, R.M. Syntheses of derivatives of *N*-acetyl-D-lactosamine from D-lactal hexaacetate. Hexa-*O*-acetyl-2-deoxy-2-phthalimide-β-D-lactosyl chloride. *Can. J. Chem.* **1982**, *60*, 63–67.
30. Lemieux, R.U.; Abbas, S.Z.; Chung, B.Y. Syntheses of core chain trisaccharides related to human blood group antigenic determinants. *Can. J. Chem.* **1982**, *60*, 68–75.
31. Hindsgaul, O.; Norberg, T.; le Pendu, J.; Lemieux, R.U. Synthesis of type 2 human blood-group antigenic determinants. The H, X, and Y haptens and variations of the H type 2 determinant as probes for the combining site of the lectin I of *Ulex europaeus*. *Carbohydr. Res.* **1982**, *109*, 109–142.
32. Heyns, K.; Meinecke K.-H. Über bildung und darstellung von *d*-glucosamin aus fructose und ammoniak. *Chem. Ber.* **1953**, *86*, 1453–1462.
33. Wrodnigg, T.M.; Stütz, A.E. The Heyns rearrangement revisited: An exceptionally simple two-step chemical synthesis of D-lactosamine from lactulose. *Angew. Chem. Int. Ed.* **1999**, *38*, 827–828.
34. Stütz, A.E.; Dekany, G.; Eder, B.; Illaszewicz, C.; Wrodnigg, T.M. An exceptionally simple chemical synthesis of *O*-glycosylated D-glucosamine derivatives by Heyns rearrangement of the corresponding *O*-glycosyl fructoses. *J. Carbohydr. Chem.* **2003**, *22*, 253–265.
35. Shan, Y.; Oulaidi, F.; Lahmann, M. Lactosamine from lactulose via the Heyns arrangement: A practical protocol. *Tetrahedron Lett.* **2013**, *54*, 3960–3961.
36. Ohmae, M.; Takada, J.; Murakami, H.; Kimura, S. Rapid access to an orthogonally protected Lewis X derivative: An important building block for synthesis of Lewis antigens. *Chem. Lett.* **2011**, *40*, 438–439.
37. Depré, D.; Düffels, A.; Green, L.G.; Lenz, R.; Ley, S.V.; Wong, C.-H. Synthesis of glycans from the glycodelins: Two undeca-, two deca-, three nona-, an octa- and a heptasaccharide. *Chem. Eur. J.* **1999**, *5*, 3326–3340.
38. Hense, A.; Ley, S.V.; Osborn, H.M.I.; Owen, D.R.; Poisson, J.-F.; Warriner, S.L.; Wesson, K.E. Direct preparation of diacetals from 1,2-diketones and their use as 1,2-diol protecting groups. *J. Chem. Soc. Perkin Trans. 1* **1997**, 2023–2031, doi:10.1039/A702497E.
39. Muramatsu, W. Chemo- and regioselective monosulfonylation of nonprotected carbohydrates catalyzed by organotin dichloride under mild conditions. *J. Org. Chem.* **2012**, *77*, 8083–8091.
40. Yu, B.; Tao, H. Glycosyl trifluoroacetimidates. Part 1: Preparation and application as new glycosyl donors. *Tetrahedron Lett.* **2001**, *42*, 2405–2407.