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Efficient Convergent Block Synthesis of a Pyruvated Tetrasaccharide 5-Aminopentyl Glycoside Related to *Streptococcus pneumoniae* Type 27

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Abstract: The synthesis of the 5-aminopentyl glycoside tetrasaccharide β-*D*-Glc*p*-(1→3)-4,6-carboxyethylidene-β-*D*-GlcNAc*p*-(1→3)-α-*D*-Gal*p*-(1→4)-β-*L*-Rha*p* **20**, the repeating unit of the immunodominant capsular polysaccharide of *Streptococcus pneumoniae* type 27 is described.

Gram-positive diplococci of the genus *Streptococcus pneumoniae* (Pneumococcus) are the major cause of pneumonia especially as an opportunistic disease syndrom of immunocompromized individuals or subsequent to viral infections. Furthermore, infections by *S. pneumoniae* are the leading cause of juvenile otitis media[1]. Therefore, vaccination against *S. pneumoniae* appears to be highly desirable and early attempts toward efficient vaccins that initially used heat-killed cells[2] revealed that capsular polysaccharides of *S. pneumoniae* are prone to induce immunity[3]. The currently available vaccine[4] (Pneumovax® 23) contains 23 of the more than 85 serologically distinguishable capsular polysaccharides of *S. pneumoniae*. These saccharides were chosen according to epidemiological studies of isolated bacteria[4]. However, since polysaccharides are often not very immunogenic the observed failure of pneumococcal vaccination due to the inability of patients to mount and maintain adequate antibody response is a problem[5]. In order to overcome these disadvantages of the available vaccine attempts have been undertaken to use synthetic neoglycoconjugates (oligosaccharide protein conjugates) related to pneumococci. For example, syntheses of tri- to hexasaccharides, and building blocks therefore, related to *S. pneumoniae* serotypes 1[6], 2[7], 3[8,9], 4[10], 6A[11-13], 6B[11-14], 7F[7], 8[15], 9A[16], 9V[16,17], 14[18,19], 18C[20,21], 19A[16], 19F[16,22,23], 22F[7], 23[24] and 23F[7,25,26] are described.

Our current interest in pyruvated saccharides prompted us to turn our attention toward the synthesis of oligosaccharides related to *S. pneumoniae* type 27[27]. The structure of the repeating unit of that serovar is unique for pneumococcal capsular saccharides since it contains a phosphorylcholine at position 2 of the *L*-rhamnosyl residue and a (*S*)-4,6-*O*-carboxyethylidene group (pyruvic acid acetal) at the *N*-acetyl glucosamine residue (Figure 1). Phosphorylcholine is not found among other *S. pneumoniae* serovars and a pyruvated sugar residue was solely detected so far in *S. pneumoniae* type 4[28-30] (*i.e.* 2,3-*O*-carboxyethylidene-α-*D*-Gal*p*). Furthermore it has been demonstrated that antibodies raised against the teichoic acids of *S. pneumoniae* can bind phosphorylcholine residues of the latter and equally well phosphorylcholine of capsular polysaccharides of type 27 pneumococcus[31]. In addition, immunodominant pyruvated sugar residues - like 4,6-*O*-carboxyethylidene-β-*D*-GlcNAc in type 27 pneumococcus - are thought to be responsible for cross-reactivities during serotyping[32,33]. Therefore, synthetic saccharides related to type 27 pneumococcus are attractive targets for immunological studies and synthetic vaccins.

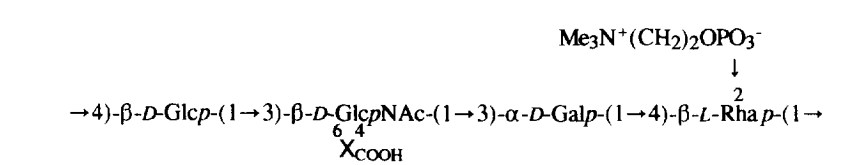
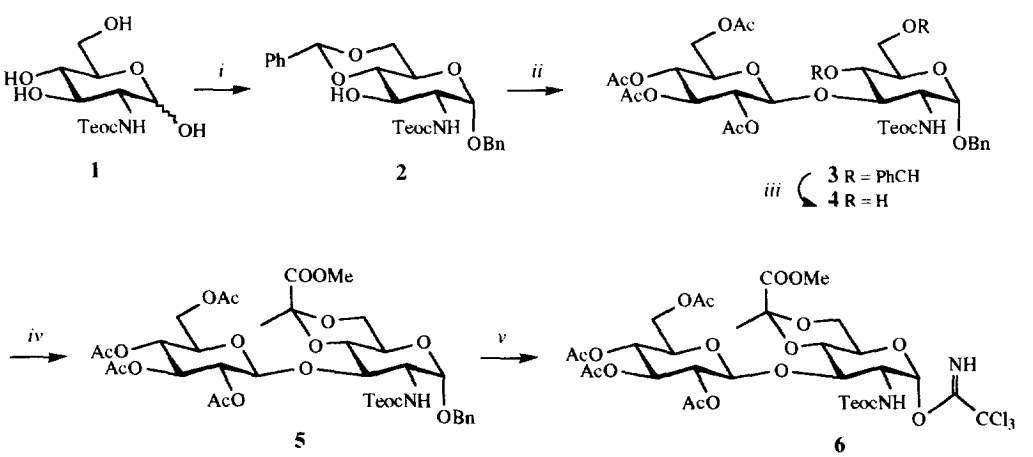


Figure 1. Repeating unit of the capsular polysaccharide of *Streptococcus pneumoniae* type 27[27].

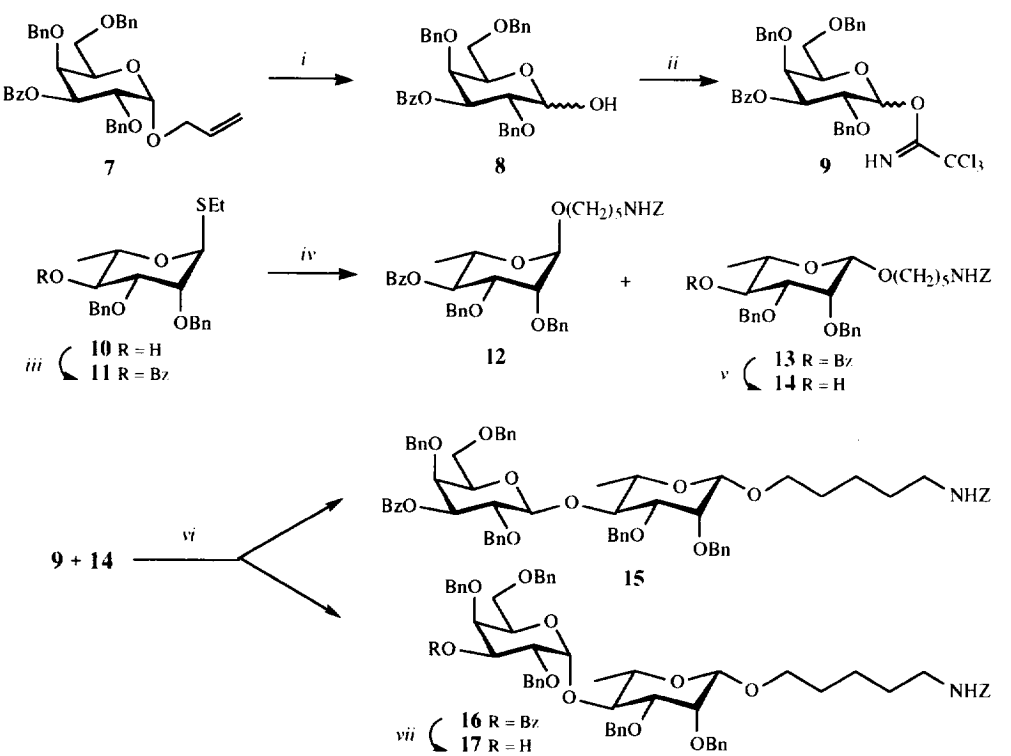
Here, the convergent block synthesis of the tetrasaccharide repeating unit of the *S. pneumoniae* type 27 polysaccharide is described. The synthetic tetrasaccharide 5-aminopentyl glycoside that does not contain a phosphorylcholine residue should be useful for the preparation of immunogenic neoglycoconjugates and for studying the immunodominant properties of the carboxyethylidene residue without disturbance of the phosphorylcholine.

For the convergent block synthesis of the pyruvated *S. pneumoniae* type 27 tetrasaccharide fragment two properly blocked disaccharide building blocks were needed - a pyruvated laminaribiosylamine donor and the 4-*O*-(α-*D*-galactopyranosyl)-β-*L*-rhamnoside acceptor. For the synthesis of the pyruvated disaccharide donor it was originally planned to glucosylate a suitably protected 4,6-pyruvated glucosamine derivative. However, all attempts to glycosylate various pyruvated acceptors failed due to the low reactivity of position 3 of the latter (no further details in the experimental). Therefore, a strategy was chosen here that introduced the pyruvic acid acetal on the disaccharide stage. Thus, 2-(2,2,2-trichloroethoxycarbonylamino)-2-deoxy-*D*-glucose[34] **1** was converted by sequential treatment with benzyl alcohol and benzaldehyde into benzyl 4,6-*O*-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-*D*-glucopyranoside **2** which was coupled with acetobromoglucose under Helferich conditions to give the disaccharide **3** (60%). The 2,2,2-trichloroethoxycarbonyl (Teoc) group was chosen as a blocking group for the amino function because Teoc-protected glucosamine imidates are excellent donors for the synthesis of β-glycosides[35] and the Teoc group can be selectively converted into the N-acetyl group without affecting pyruvic acetals[36,37]. Next, the benzylidene group of the latter was cleaved off to give the diol **4** (98%). For the introduction of the pyruvic acid acetal in **4** the acetalation procedure[38] that used acetonitrile as the solvent was applied since this method has previously been shown to proceed with high diastereoselectivity and high yield[38,39]. When **4** was treated with BF_3-ether and methyl pyruvate in acetonitrile, a complete conversion of the starting material could not be achieved. 21% of unchanged **4** was reisolated and the desired pyruvated disaccharide **5** was obtained in 48% yield. The ^{13}C NMR spectra of the latter showed a chemical shift for the CH_3 group of the pyruvic acetal of 25.7 ppm, characteristic for an equatorial position[40,41] (*i.e.* the 4,6-*O*-(1-methoxycarbonyl)ethylidene group has the (*S*) configuration). Next, the aglycon of compound **5** was split off by hydrogenolysis and the intermediate was converted without isolation into the corresponding α-trichloroacetimidate **6** (84%).



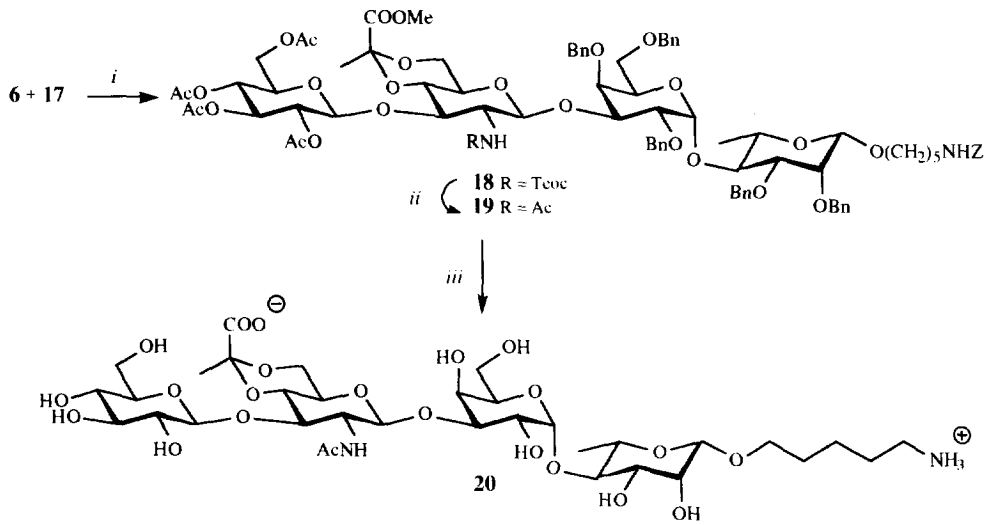
Scheme 1. *i:* 1) Benzylalcohol containing 2% HCl, 110 °C, 2.5 h; 2) PhCHO, $ZnCl_2$, 25 °C, 16 h; *ii:* acetobromoglucose, CH_3NO_2-benzene (1:1), $Hg(CN)_2$, 60 °C, 47 h; *iii:* aq. AcOH (90%), 60 °C, 90 min.; *iv:* methyl pyruvate, MeCN, BF_3-ether, 25 °C, 2 h; *v:* 1) H_2, cat. Pd-C (10%), EtOAc, 25 °C, 4 d; 2) Cl_3CCN, CH_2Cl_2, K_2CO_3, 25 °C, over night.

For the preparation of the 5-aminopentyl disaccharide acceptor the galactosyl donor **9** was needed. It was constructed to bear a 2-*O*-benzyl group in order to allow a α-selective coupling. Furthermore a 3-*O*-benzoyl group should be present as a temporary protection of that position. Starting from allyl 2,4,6-tri-*O*-benzyl-3-*O*-benzoyl-α-*D*-galactopyranoside[42] **7**, Pd-catalyzed isomerisation of the allyl group and hydrolysis of the intermediate afforded first the 1-*O*-unprotected galactose **8** (80%). Next compound **8** was transferred into the corresponding trichloroacetimidate **9**, obtained as an anomeric mixture in 89% yield. The rhamnosyl acceptor was prepared from ethyl 2,3-di-*O*-benzyl-1-thio-α-*L*-rhamnopyranoside[25] **10**. Benzoylation of position 4 gave first the fully blocked derivative **11**. For the construction of the β-rhamnosidic bond, the silver silicate procedure[43] was used. Therefore, 1-thio-rhamnoside **11** was converted *in situ* into the corresponding rhamnosyl bromide and coupled with 5-benzyloxycarbonylaminopentanol under promotion of silver silicate, to give 14% of the α-rhamnoside **12** and 59% of the desired β-rhamnoside **13**. The anomeric configuration of **12** and **13** was evident from the vicinal coupling constants of $J_{1,2}$ (1.7 Hz for **12** and 0 Hz for **13**). Next, position 4 was freed by Zemplén debenzoylation, to give **14** (88%) which was then condensed either with imidate **9**α or **9**β, affording 6% of the α-(1→4)-linked disaccharide **15** and 55% of the corresponding β-(1→4)-linked saccharide **16**. No significant difference in reactivity and anomeric selectivity was observed for **9**α and **9**β, respectively. Final debenzoylation of the latter gave the disaccharide block **17** (88%).



Scheme 2. *i:* aq. AcOH (90%), cat. $PdCl_2$, 65 °C, 22 h; *ii:* Cl_3CCN, CH_2Cl_2, K_2CO_3, 25 °C, 3.5 h, **9**α (54%), **9**β (33%); *iii:* BzCl, pyridine, 25 °C, 2 h; *iv:* 1) Br_2, CH_2Cl_2, 25 °C, 10 min.; 2) $HO(CH_2)_5NHZ$, Ag-silicate, CH_2Cl_2, 25 °C, 17 h, **12** (14%), **13** (59%); *v:* cat. NaOMe, MeOH, 25 °C, 7 d; *vi:* cat. TMSOTf, CH_2Cl_2-Et_2O (1:6), 0 °C, 1.5 h, **15** (6%), **16** (55%); *vii:* cat. NaOMe, MeOH, 25 °C, 7 d.

The superior donor properties of Teoc-protected glycosyl donors were demonstrated by the condensation of blocks **6** and **17**. TMSOTf-catalysed coupling of the latter proceeded without any formation of byproducts and afforded the blocked tetrasaccharide aminopentyl glycoside **18** in 99% yield. The anomeric configuration of the newly formed β-glycosidic bond was unambiguously proven by NMR spectroscopy that showed a coupling constant $J_{1'',2''}$ of the pyruvated glucosamine residue of 7.5 Hz and a chemical shift of 102.1 ppm for C-1''. Conversion of the Teoc group in **18** by reductive cleavage with Zn followed by reacetylation of the intermediate amine gave tetrasaccharide **19** (78%). Final deprotection of the latter by sequential removing of the acetyl groups (Zemplén), saponification of the methyl ester and hydrogenolytic cleavage of the benzyl groups, gave the free pyruvated *S. pneumoniae* type 27 tetrasaccharide fragment **20** in 97% yield.



Scheme 3. *i:* cat. TMSOTf, CH_2Cl_2, -20 °C, 1.5 h; *ii:* 1) Zn, AcOH, 25 °C, 2 h; 2) Ac_2O, pyridine, 0 °C, 2 h; *iii:* 1) cat. NaOMe, MeOH, 25 °C, 3 h; 2) NaOH, aq. MeOH, 25 °C, 4 h; 3) H_2, cat. $Pd(OH)_2$-C (10%), MeOH-H_2O-AcOH (1:1:1), 25 °C, 5 d.

EXPERIMENTAL

General. The NMR data in the experimental section were obtained from spectra measured in $CDCl_3$ solutions for blocked compounds (with Me_4Si as internal standard) and in D_2O for deblocked compounds (with MeOH as an internal standard) at 25°C with a Bruker AC 250F spectrometer. ^1H NMR signal assignments were made by first-order analysis of the spectra. Of the two magnetically non-equivalent geminal protons at C-6 of the carbohydrate residues, the one resonating at lower field was allocated H-6a and the one resonating at higher field H-6b. ^{13}C NMR assignments were made by mutual comparison of the spectra, by DEPT spectra, and by comparison with spectra of related compounds. Optical rotations were measured at 25°C with a Perkin-Elmer automatic polarimeter, Model 241. Melting points were measured with a Büchi apparatus, Model SMP-20. Thin-layer chromatography (TLC) was performed on percoated plastic sheets, Polygram SIL UV_{254}, 40 x 80mm (Macherey-Nagel) using appropriately adjusted mixtures of CCl_4-acetone for development. Detection was effected with UV light, where applicable, and by charring with 5% H_2SO_4 in EtOH. Preparative chromatography was performed by elution from columns of Silica Gel 60 (Merck). Solutions in organic solvents were dried with anhyd. Na_2SO_4, and concentrated at 2 kPa, <40°C.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside **(2)**. A suspension of 2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-*D*-glucopyranose[34] (**1**, 16.5 g, 46.5 mmol) in benzylalcohol (100 mL) containing 2 % of HCl was stirred at 110°C until a clear solution was obtained (0.5 h). The mixture was stirred for additional 2 h at 110°C, cooled to room temperature, neutralised by addition of $BaCO_3$, and filtered through a layer of Celite. The filtrate was coevaporated several times with H_2O and EtOH and dried in vacuo. The residue was mixed with benzaldehyde (40 mL) and $ZnCl_2$ (9 g), and the resulting mixture was vigorously stirred at room temperature for 16 h. Water (100 mL) and petroleum ether (250 mL) were added, and the resulting solid was collected by filtration and washed repeatedly with water and petrolether. Recrystallisation (3 times) from EtOH gave compound **2** (6.74 g, 27 %); mp 157°C; $[\alpha]_D$ +86.7° (c 0.75, DMSO); ^{1}H NMR data (d_6-DMSO): δ 5.62 (s, 1H, *H*CPh), 5.28 (d, 1H, $J_{2,NH}$ 5.9 Hz, N*H*), 4.89 (d, 1H, $J_{1,2}$ 5.9 Hz, H-1), 4.85 (d, 1H, J -12.3 Hz, PhCH_2), 4.75 (d, 1H, J -12.3 Hz, PhCH_2), 4.12-4.18 (m, 1H, H-2), 3.82 (dt, 1H, $J_{5,6a}$ 5.9 Hz, $J_{5,6b}$ 9.4 Hz, H-5), 3.54-3.75 (m, 3H, H-3, 6a, 6b), 3.52 (t, 1H, $J_{3,4}$ $J_{4,5}$ 8.9 Hz, H-4); ^{13}C NMR data (d_6-DMSO): δ 154.5 (*C*ONH), 100.8 (C_{acetal}), 96.7 (C-1), 96.1 (*C*Cl_3), 81.9 (C-4), 73.5 (*C*H_2CCl_3), 68.5 (Ph*C*H_2), 67.9 (C-6), 66.8 (C-3), 62.6 (C-5), 56.6 (C-2); Anal. calcd for $C_{23}H_{24}Cl_3NO_7$: C, 51.85; H, 4.54; Cl, 19.96; N, 2.63; Found: C, 51.97; H, 4.58; Cl, 19.73; N, 2.55.

Benzyl 4,6-O-benzylidene-2-deoxy-3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside **(3)**. A solution of benzyl 4,6-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-*D*-glucopyranoside (**2**, 4 g, 7.5 mmol) in 1:1 (v/v) nitromethane-benzene (430 mL) was boiled until 115 mL of the solvent had distilled. The temperature of the solution was adjusted to 60°C and $Hg(CN)_2$ (1.06 g) was added. A solution of 2,3,4,6-tetra-O-acetyl-α-*D*-glucopyranosyl bromide (3.13 g, 7.62 mmol) in benzene (30 mL) was added dropwise. The mixture was stirred for 7 h at 60°C and then stirred overnight at room temperature. After addition of $Hg(CN)_2$ (0.42 g) the solution was again heated to 60°C and an additional amount of acetobromoglucose (0.7 g, 1.7 mmol) in benzene (10 mL) was added slowly. The solution was stirred for further 26 h at 60° C. The mixture was washed with aq $NaHCO_3$ and twice with aqueous NaCl. The combined aqueous layers were extracted twice with CH_2Cl_2. The combined organic layers were concentrated and the residue was crystallized from acetone-hexane to afford compound **3** (3.87 g, 60%) as white crystals; mp 190°C; $[\alpha]_D$ +26.9° (c 0.85, $CHCl_3$); ^{1}H NMR data: δ 5.57 (s, 1H, *H*CPh), 5.15 (d, 1H, $J_{2,NH}$ 9.3 Hz, N*H*), 4.93-5.08 (m, 4H, H-2',3',4', CH_2CCl_3), 5.04 (d, 1H, $J_{1,2}$ 6.0 Hz, H-1), 4.73 (d, 1H, J -11.6 Hz, PhCH_2), 4.69 (d, 1H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.53 (d, 1H, J -12.1 Hz, CH_2CCl_3), 4.51 (d, 1H, J -11.6 Hz, PhCH_2), 4.23 (dd, 1H, $J_{5',6a'}$ 4.0 Hz, $J_{6a',6b'}$ -9.7 Hz, H-6a'), 4.07 (dd, 1H, $J_{5',6b'}$ 9.9 Hz, H-6b'), 3.92-4.01 (m, 3H, H-2, 3, 5'), 3.89 (dd, 1H, $J_{5,6a}$ 4.2 Hz, $J_{6a,6b}$ -9.7 Hz, H-6a), 3.79 (t, 1H, $J_{5,6b}$ 9.9 Hz, H-6b), 3.74 (t, 1H, $J_{3,4} = J_{4,5}$ 8,8 Hz, H-4), 3.33-3.60 (m, 1H, H-5), 2.03, 1.98, 2x1.96 (3s, 4x3H, 4 *C*H_3COO); ^{13}C NMR data: δ 154.0 (*C*ONH), 101.5 (C-1'), 100.6 (Ph*C*H), 97.2 (C-1), 95.4 (*C*Cl_3), 80.3 (C-4), 77.2 (C-4'), 74.7 (*C*H_2CCl_3), 72.9 (C-3'), 71.6 (C-2', 3), 70.2 (Ph*C*H_2), 68.8 (C-6), 68.0 (C-5'), 62.9 (C-5), 61.5 (C-6'), 54.6 (C-2), 20.7, 20.6 (4 *C*H_3COO). Anal. calcd for $C_{37}H_{42}Cl_3NO_{16}$: C, 51.49; H, 4.90; Cl, 12.32; N, 1.62; Found: C, 51.42; H, 4.89; Cl, 12.23; N, 1.64.

Benzyl 2-deoxy-3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside **(4)**. A solution of compound **3** (3.87 g, 4.48 mmol) in aq AcOH (90%, 220 mL) was stirred at 60°C for 90 min. Concentration of the solution, coevaporation of toluene, and chromatography (CCl_4-acetone 3:1) of the residue afforded **4** (3.43 g, 98%) as an amorphous white solid; $[\alpha]_D$ +52.2° (c 1.1, $CHCl_3$); ^{1}H NMR data: δ 5.17 (t, 2H, $J_{2',3'} = J_{3',4'} = J_{4',5'}$ 9.2 Hz, H-3',4'), 5.05 (d, 1H, $J_{2,NH}$ 8.7 Hz, N*H*), 4.90-5.01 (m, 3H, H-1, 2', CH_2), 4.72 (d, 1H, J -11.5 Hz, CH_2), 4.63 (d, 1H, $J_{1',2'}$ 7.9 Hz,

H-1'), 4.47 (d, 2H, J -11.6 Hz, 2 CH_2), 4.21 (dd, 1H, $J_{5',6a'}$ 2.3 Hz, $J_{6a',6b'}$ -12.2 Hz, H-6a'), 4.13 (dd, 1H, $J_{5',6b'}$ 6.0 Hz, H-6b'), 3.92 (dd, 1H, $J_{5,6a}$ 4.0 Hz, $J_{6a,6b}$ -9.7 Hz, H-6a), 3.64-3.88 (m, 5H, H-2, 3, 5, 5', 6b), 3.60 (t, 1H, $J_{3,4} = J_{4,5}$ 8.8 Hz, H-4), 2.08, 2.04, 2.03, 1.99 (4s, 4x3H, 4 CH_3COO); ^{13}C NMR data: δ 154.1 (*C*ONH), 101.2 (C-1'), 96.5 (C-1), 95.3 (*C*Cl_3), 83.1 (C-4), 74.7 (*C*H_2CCl_3), 72.5, 72.0, 71.5, 71.2 (C-2', 3, 3', 5'), 69.9 (Ph*C*H_2), 69.7 (C-5), 68.3 (C-4'), 62.6 (C-6), 61.9 (C-6'), 54.0 (C-2), 20.6 (4x*C*H_3COO). Anal. calcd for $C_{30}H_{38}Cl_3NO_{16}$: C, 46.50; H, 4.94; Cl, 13.72; N, 1.81; Found: C, 46.50; H,4.99; Cl, 13.64; N, 1.77.

Benzyl 2-deoxy-4,6-O-[(S)-1-(methoxycarbonyl)ethylidene]-3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside **(5).** BF_3-etherate (1.24 mL, 9.8 mmol) was added at room temperature to a solution of **4** (3.32 g, 4.28 mmol) and methyl pyruvate (0.9 mL, 9.8 mmol) in CH_3CN (7 mL) and stirred for 2 h. Though TLC showed the formation of side products the reaction was quenched although not all starting material was consumpted. The mixture was diluted with CH_2Cl_2 and washed with aq $NaHCO_3$. The organic layer was concentrated and chromatography (CCl_4-acetone 5:1) of the residue afforded first compound **5** (1.76 g, 48%); mp 177°C (acetone-hexane); $[\alpha]_D$ +55.6° (c 0.4, $CHCl_3$); ^1H NMR data: δ 5.29 (bd, 1H, $J_{2,NH}$ 8.6 Hz, N*H*), 5.11-5.21 (m, 2H, H-3', 4'), 4.90-4.99 (m, 3H, H-1, 1', 2'), 4.84 (d, 1H, J -12.1 Hz, C*H*$_2CCl_3$), 4.70 (d, 1H, J -11.8 Hz, PhC*H*$_2$), 4.63 (d, 1H, J -12.1 Hz, C*H*$_2CCl_3$), 4.48 (d, 1H, J -11.7 Hz, PhC*H*$_2$), 4.28 (dd, 1H, $J_{5',6a'}$ 2.9 Hz, $J_{6a',6b'}$ -12.1 Hz, H-6a'), 4.21 (dd, 1H, $J_{5',6b'}$ 4.0 Hz, H-6b'), 3.90-4.05 (m, 3H, H-2, 5, 5'), 3.84 (s, 3H, COOC*H*$_3$), 3.60-3.81 (m, 3H, H-3, 4, 6b), 3.77 (dd, 1H, $J_{5,6a}$ 5.7 Hz, $J_{6a,6b}$ -9.7 Hz, H-6a), 2.04, 2.03, 2.02, 2.00 (4s, 4x3H, 4 C*H*$_3$COO), 1.53 (s, 3H, C*H*$_3$); ^{13}C NMR data: δ 169.4 (*C*OOCH$_3$), 154.0 (*C*ONH), 99.2 (C_{acetal}), 98.9 (C-1'), 97.4 (C-1), 95.6 (*C*Cl_3), 75.4 (C-4), 75.1 (C-3), 74.6 (*C*H_2CCl_3), 73.3 (C-3'), 72.0 (C-5'), 71.7 (C-2'), 70.1 (Ph*C*H_2), 68.2 (C-4'), 65.2 (C-6), 62.7 (C-5), 62.0 (C-6'), 55.0 (C-2), 52.8 (COO*C*H_3), 25.7 (*C*H_3), 20.7 (4x*C*H_3COO). Anal. calcd for $C_{34}H_{42}Cl_3NO_{18}$: C, 47.54; H, 4.93; Cl, 12.38; N, 1.63; Found: C, 47.36; H, 4.87; Cl, 12.85; N, 1.63.

Further eluted was starting material **4** (0.7 g, 21%).

2-Deoxy-4,6-O-[(S)-1-(methoxycarbonyl)ethylidene]-3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl trichloroacetimidate **(6).** A suspension of **5** (1.4 g, 1.66 mmol) and a catalytic amount of Pd (10% on charcoal) in EtOAc (40 mL) and AcOH (1mL) was treated with H_2 at room temperature for 4 days. The mixture was concentrated, coevaporated with toluene and filtered over a short column of silica gel (CCl_4-acetone 4:1) to afford the crude 2-deoxy-4,6-*O*-[(*S*)-1-(methoxycarbonyl)ethylidene]-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-*D*-glucopyranose (1.22 g, 99%) which was used without further purification. A mixture of the latter (484 mg, 0.63 mmol), CCl_3CN (1.1 mL), and K_2CO_3 (550 mg) in CH_2Cl_2 was stirred at room temperature overnight. The mixture was centrifuged and decanted, and the solution was concentrated. Chromatography (CCl_4-acetone 5:1) of the residue afforded compound **6** (482 mg, 84%) as a white foam; $[\alpha]_D$ +37.6° (c 1.2, $CHCl_3$); ^1H NMR data: δ 8.71 (s, 1H, N*H*), 6.35 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.31 (bd, 1H, $J_{2,NH}$ 7.7 Hz, N*H*), 5.23 (t, 1H, $J_{3',4'}$ 9.2 Hz, H-3'), 5.15 (d, 1H, $J_{1',2'}$ 7.6 Hz, H-1'), 5.12 (t, 1H, $J_{4',5'}$ 9.6 Hz, H-4'), 4.99 (dd, 1H, $J_{2',3'}$ 8.8 Hz, H-2'), 4.83 (d, 1H, J -12.1 Hz, C*H*$_2CCl_3$), 4.61 (d, 1H, J -12.1 Hz, C*H*$_2CCl_3$), 4.18-4.31 (m, 2H, H-6a', 6b'), 4.03-4.16 (m, 3H, H-2, 5', 6a), 3.81-3.92 (m, 3H, H-3, 4, 6b), 3.87 (s, 3H, COO*C*H_3), 3.55-3.64 (m, 1H, H-5), 2.09, 2.06, 2.04, 2.01 (4s, 4x3H, 4 C*H*$_3$COO), 1.56 (s, 3H, C*H*$_3$); ^{13}C NMR data: δ 169.5 (*C*OOCH$_3$), 160.5 (*C*NH), 154,0 (*C*ONH), 99.5 (C_{acetal}), 98.0 (C-1'), 95.4 (C-1, CH_2*C*Cl_3), 90.8 (CNH*C*Cl_3), 74.6 (CH_2CCl_3), 74.3 (C-3), 74.0 (C-4), 73.1 (C-3'), 71.9 (C-2',5'), 68.2 (C-4'), 65.1 (C-5), 65.0 (C-6), 62.1 (C-6'), 54.9 (C-2), 53.0 (COO*C*H_3), 25.2 (*C*H_3), 20.7, 20.6

(4xCH_3COO). Anal. calcd for $C_{29}H_{36}Cl_6N_2O_{18}$: C, 38.14; H, 3.97; Cl, 23.29; N, 3.08; Found: C, 38.32; H, 3.95; Cl, 23.29; N, 3.04.

***3-O-Benzoyl-2,4,6-tri-O-benzyl-D-galactopyranose* (8).** A solution of allyl 3-O-benzoyl-2,4,6-tri-O-benzyl-α-*D*-galactopyranoside[42] **7** (2.52 g, 4.2 mmol) and a catalytic amount of $PdCl_2$ (50 mg) in carefully degassed aq AcOH (90%, 90 mL) was stirred for 22 h at 65°C while N_2 was bubbled through the solution. The solution was cooled to room temperature and concentrated. Chromatography (CCl_4-acetone 10:1) of the residue afforded **8** (1.87 g, 80 %) as a 3:2 α/β mixture; ^{1}H NMR data: δ 5.56 (dd, 1H, $J_{3,4}$ 3.0 Hz, H-3a); 5.38 (bt, 1H, $J_{1,2}$ 3.5 Hz, H-1α), 5.19 (dd, 1H, $J_{3,4}$ 3.1 Hz, H-3β), 4.79 (dd, 1H, $J_{1,2}$ 7.6 Hz, H-1β), 4.18 (dd, 1H, $J_{2,3}$ 10.2 Hz, H-2α), 4.14 (dd, 1H, $J_{4,5}$ <1Hz, H-4β), 4.06 (bd, 1H, $J_{4,5}$ <1Hz, H-4α), 3.91 (dd, 1H, $J_{2,3}$ 10.2 Hz, H-2β), 3.81 (bt, 1H, $J_{5,6a}$ 6.5 Hz, $J_{6a,6b}$ 6.5 Hz, H-6a), 3.73 (d, 1H, $J_{1,OH}$ 5.5 Hz, O*H*β), 3.64 (dd, 1H, $J_{5,6b}$ 9.4 Hz, H-6b), 3.46-3.67 (m, 3H, H-5a, 5b, 6a), 3.51 (dd, 1H, $J_{5,6b}$ 9.3 Hz, $J_{6a,6b}$ 6.4 Hz, H-6b), 3.32 (d, 1H, $J_{1,OH}$ 2.0 Hz, O*H*α); ^{13}C NMR data: δ 97.9 (C-1β), 91.7 (C-1α), 77.8 (C-5β), 75.6 (C-3β), 75.5 (C-3α), 75.1 (PhCH_2), 74.6 (C-2β), 74.4 (C-2α), 73.6 (PhCH_2), 73.5 (PhCH_2), 73.1 (C-4α), 73.0 (C-4β), 69.0 (C-5α), 68.7 (C-6α), 68.5 (C-6β). Anal. calcd for $C_{34}H_{34}O_7$: C, 73.63; H, 6.18; Found: C, 73.48; H, 6.18.

***3-O-Benzoyl-2,4,6-tri-O-benzyl-D-galactopyranosyl trichloroacetimidate* (9).** Treatment of **8** (1.77 g, 3.2 mmol) with trichloroacetonitrile (3.2 mL) and K_2CO_3 (3.2 g) in CH_2Cl_2 (10 mL) for 3.5 h at room temperature as described for compound **6** afforded after chromatography over a short column of silica gel (PE-ethyl acetate 3:1) **9** (1.98 g, 88.5 %) as a colorless oil.

The α/β-mixture was separated by chromatography over silica gel (PE-ethyl acetate 8:1). Eluted first was **9**α (1.2 g, 54 %). $[\alpha]_D$ +82.4 (c 0.6, $CHCl_3$); ^{1}H NMR data: δ 8.58 (s, 1H, N*H*), 6.59 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.63 (dd, 1H, $J_{3,4}$ 3.0 Hz, H-3), 4.38 (dd, 1H, $J_{2,3}$ 10.5 Hz, H-2), 4.30 (dd, 1H, $J_{4,5}$ 0.9 Hz, H-4), 4.12 (dd, 1H, $J_{5,6a}$ 7.2 Hz, $J_{6a,6b}$ -14.3 Hz, H-6a), 3.52-3.67 (m, 2H, H-5, 6b); ^{13}C NMR data: δ 161.4 (*C*NH), 94.7 (C-1), 91.3 (*C*Cl_3), 75.3, 73.4, 72.7 (3xPhCH_2), 74.9 (C-3), 73.0 (C-2, 4), 71.5 (C-5), 67.8 (C-6); Anal. calcd for $C_{36}H_{34}Cl_3NO_7$: C, 61.86; H, 4.90; Cl, 15.22; N, 2.00; Found: C, 61.43; H, 4.93; Cl, 15.73; N, 2.08.

Eluted next was **9**β (0.74 g, 33 %). $[\alpha]_D$ +70.8 (c 0.66, $CHCl_3$); ^{1}H NMR data: δ 8.7 (s, 1H, N*H*), 5.87 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 5.31 (dd, 1H, $J_{3,4}$ 3.2 Hz, H-3), 4.24 (dd, 1H, $J_{2,3}$ 10.1 Hz, H-2), 4.18 (dd, 1H, $J_{4,5}$ <1Hz, H-4), 3.97 (dd, 1H, $J_{5,6a}$=$J_{5,6b}$ 6.6 Hz, H-5), 3.67 (bd, 2H, H-6a, 6b); ^{13}C NMR data: δ 161.2 (*C*NH), 98.71 (C-1), 90.9 (*C*Cl_3), 75.6, 75.4, 74.2 (C-2, 3, 4, 5), 75.2, 74.9, 73.4 (3xPh*C*H_2); Anal. calcd for $C_{36}H_{34}Cl_3NO_7$: C, 61.86; H, 4.90; Cl, 15.22; N, 2.00; Found: C, 61.33; H, 4.89; Cl, 15.34; N, 2.11.

***Ethyl 4-O-benzoyl-2,3-di-O-benzyl-1-thio-α-L-rhamnopyranoside* (11).** Benzoyl chloride (1.32 mL) was added to an ice cooled solution of ethyl 2,3-di-O-benzyl-1-thio-α-*L*-rhamnopyranoside[25] **(10)** (2.95 g, 7.6 mmol) in pyridine (25 ml), and the solution was stirred for 2 h, poured into ice water and extracted with CH_2Cl_2. The extracts were washed with aq HCl and aq $NaHCO_3$, and concentrated. Chromatography (CCl_4-acetone 25:1) of the residue afforded **11** (3.78 g, 100 %) as a slightly yellow sirup. $[\alpha]_D$ -34.6° (c 0.8, $CHCl_3$); ^{1}H NMR data: δ 5.47 (t, 1H, $J_{4,5}$ 9.7 Hz, H-4), 5.32 (d, 1H, $J_{1,2}$ 1.4 Hz, H-1), 4.74 (s, 2H, 2xPhCH_2), 4.51 (d, 1H, J -12.2 Hz, PhCH_2), 4.38 (d, 1H, J -12.2 Hz, PhCH_2), 4.19 (dq, 1H, $J_{5,6}$ 6.2 Hz, H-5), 3.89 (dd, 1H, $J_{2,3}$ 3.0 Hz, H-2), 3.83 (dd, 1H, $J_{3,4}$ 9.6 Hz, H-3), 2.49-2.27 (m, 2H, CH_2CH$_3$), 1.27 (t, 3H, $J_{CH_2CH_3}$ 7.3 Hz, CH_2CH_3), 1.25 (d, 3H, H-6); ^{13}C NMR data: δ 82.5 (C-1), 77,0 (C-4), 76.1 (C-2), 73.7 (C-3), 72.5, 71.6 (2xPh*C*H_2), 67.4 (C-5), 25.5 (*C*H_2CH$_3$), 17.6 (C-6), 15.0 (CH_2CH_3); Anal. calcd for $C_{29}H_{32}SO_5$: C, 70.71; H, 6.55; S, 6.51; Found: C, 70.86; H, 6.58; S,6.30.

***5-[(Benzyloxycarbonyl)amino]pentyl 4-O-benzoyl-2,3-di-O-benzyl-α-L-rhamnopyranoside* (12) and *5-[(Benzyloxycarbonyl)amino]pentyl 4-O-benzoyl-2,3-di-O-benzyl-β-L-rhamnopyranoside* (13).** Bromine (0.52 mL) was added to a solution of **11** (1.69 g, 3.4 mmol) in CH_2Cl_2 (50 mL), and the solution was stirred for 10 min, concentrated and coevaporated several times of toluene to afford crude rhamnosyl bromide. A solution of the crude bromide in toluene (50 mL) was added slowly through a dropping funnel to a suspension of 5-[(benzyloxycarbonyl)amino]pentanol (3.2 g, 13.6 mmol), 4 Å molecular sieves (1.7 g) and silver silicate (2 g) in CH_2Cl_2 (50 mL), and the mixture was stirred for 17 h at room temperature in the dark. The mixture was filtered through a layer of Celite, washed with H_2O, aq $NaHCO_3$ and H_2O and concentrated. Chromatography (CCl_4-acetone 15:1) of the residue afforded first **12** (318 mg, 14 %) as a colorless oil. $[\alpha]_D$ -1.7° (c 0.9, $CHCl_3$); ^{1}H NMR data: δ 5.48 (t, 1H, $J_{4,5}$ 9.7 Hz, H-4), 5.10 (s, 2H, Z), 4.82 (d, 1H, J -12.4 Hz, PhC*H*$_2$), 4.78 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1), 4.71 (d, 1H, J -12.4 Hz, PhC*H*$_2$), 4.68-4.85 (m, 1H, N*H*), 4.56 (d, 1H, J -12.1 Hz, PhC*H*$_2$), 4.44 (d, 1H, J -12.2 Hz, PhC*H*$_2$), 3.90 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 9.7 Hz, H-3), 3.77-3.86 (m, 2H, H-2, 5), 3.64 (dt, 1H, OC*H*$_2$), 3.36 (dt, 1H, OC*H*$_2$), 3.20 (bq, 2H, 2 NHC*H*$_2$), 1.25-1.62 (m, 6H, 6 C*H*$_2$), 1.25 (d, 3H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR data: δ 165.7 (Ph*C*OO), 156.4 (*C*ONH), 98.4 (C-1), 77.2 (C-4), 74.5,73.7 (C-2, 3), 73.0 (Ph*C*H$_2$), 71.8 (Ph*C*H$_2$), 67.5 (Z), 67.0 (C-5), 66.7 (O*C*H$_2$), 41.0 (NH*C*H$_2$), 29.8, 29.0, 23.4 (3 *C*H$_2$), 17.7 (C-6); Anal. calcd for $C_{40}H_{45}NO_8$: C, 71.94; H, 6.79; N, 2.10; Found: C, 71.72; H, 6.94; N, 2.13.

Eluted next was **13** (1.33 g, 59 %). mp 83°C (acetone-hexane); $[\alpha]_D$ +75.2 (c 1, $CHCl_3$); ^{1}H NMR data: δ 5.46 (t, 1H, $J_{4,5}$ 9.7 Hz, H-4), 5.09 (s, 2H, Z), 4.89 (d, 1H, J -12.7 Hz, PhC*H*$_2$), 4.87 (d, 1H, J -12.7 Hz, PhC*H*$_2$), 4.78 (m, 1H, N*H*), 4.45 (d, 1H, J -12.5 Hz, PhC*H*$_2$), 4.39 (s, 1H, $J_{1,2}$ 0 HZ, H-1), 4.23 (d, 1H, J-12.5 Hz, PhC*H*$_2$), 3.91-4.01 (m, 2H, H-2, 5), 3.51 (dd, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 9.8 Hz, H-3), 3.36-3.57 (m, 2H, OC*H*$_2$), 3.21 (bq, 2H, 2 NHC*H*$_2$), 1.28-1.73 (m, 6H, 6 C*H*$_2$), 1.30 (d, 3H, $J_{5,6}$ 6.1 Hz, H-6); ^{13}C NMR data: δ 165.6 (Ph*C*OO), 156.4 (*C*ONH), 101.5 (C-1), 78.7 (C-4), 73.8 (Ph*C*H$_2$), 73.5, 73.2 (C-2, 3), 70.9 (C-5), 70.8 (Ph*C*H$_2$), 69.6 (Z), 66.6 (O*C*H$_2$), 41.0 (NH*C*H$_2$), 29.8, 27.3, 23.4 (3 *C*H$_2$), 17.6 (C-6); Anal. calcd for $C_{40}H_{45}NO_8$: C, 71.94; H, 6.79; N, 2.10; Found: C, 71.83; H, 6.76; N, 1.94.

***5-[(Benzyloxycarbonyl)amino]pentyl 2,3-di-O-benzyl-β-L-rhamnopyranoside* (14).** A solution of compound **13** (1.07 g, 1.6 mmol) in MeOH (50 mL) was treated with a solution of NaOMe in MeOH (1 M, 0.3 mL) for 7 d at room temperature. Dowex 2X8 (H^+-form) was added until the solution became neutral. Filtration of the mixture, concentration of the filtrate and crystallisation of the residue (acetone-hexane) gave compound **14** (790 mg, 88 %); mp 121°C ; $[\alpha]_D$ +93.7° (c 1.2, $CHCl_3$); ^{1}H NMR data: δ 5.08 (s, 2H, Z), 4.96 (d, 1H, J -12.5 Hz, PhC*H*$_2$), 4.77 (d, 1H, J -12.5 Hz, PhC*H*$_2$), 4.45 (d, 1H, J -11.8 Hz, PhC*H*$_2$), 4.37 (s, 1H, $J_{1,2}$ 0 Hz, H-1), 4.22 (d, 1H, J -11.8 Hz, PhC*H*$_2$), 3.94 (dq, 1H, $J_{5,6}$ 6.3 Hz, H-5), 3.91 (d, 1H, $J_{2,3}$ 2.7 Hz, H-2), 3.69 (t, 1H, $J_{3,4} = J_{4,5}$ 9.7 Hz, H-4), 3.41 (dt, 1H, OC*H*$_2$), 3.16-3.31 (m, 4H, H-3, OC*H*$_2$, 2 NHC*H*$_2$), 2.33 (bs, 1H, O*H*), 1.35-1.72 (m, 6H, 6 C*H*$_2$), 1.37 (d, 3H, H-6); ^{13}C NMR data: δ 101.7 (C-1), 81.6 (C-4), 74.0 (Ph*C*H$_2$), 73.1, 72.2 (C-2, 3), 71.6 (C-5), 70.8 (Ph*C*H$_2$), 69.6 (Z), 66.6 (O*C*H$_2$), 29.7, 29.4, 23.4 (3 *C*H$_2$), 17.8 (C-6); Anal. calcd for $C_{33}H_{41}NO_7$: C, 70.32; H, 7.33; N, 2.48; Found: C, 70.18; H, 7.29; N, 2.37.

***5-[(Benzyloxycarbonyl)amino]pentyl 4-O-(3-O-benzoyl-2,4,6-tri-O-benzyl-β-D-galactopyranosyl)-2,3-di-O-benzyl-β-L-rhamnopyranoside* (15) and *5-[(Benzyloxycarbonyl)amino]pentyl 4-O-(3-O-benzoyl-2,4,6-tri-O-benzyl-α-D-galactopyranosyl)-2,3-di-O-benzyl-β-L-rhamnopyranoside* (16).** To a suspension of compound **14** (914 mg, 1.62 mmol) and powdered 3 Å molecular sieves (16 g) in CH_2Cl_2 (10 mL) was added a solution of an anomeric mixture of compound **9** (1.97 g, 2.8 mmol) in

Et_2O (60 mL) and the mixture was stirred for 1.5 h. The mixture was cooled in an ice bath, TMSOTf (294 μL) was added and the mixture was stirred for 1.5 h, neutralized by addition of pyridine (1 mL), diluted with CH_2Cl_2 and filtered through a layer of Celite. The filtrate was washed with H_2O, aq $NaHCO_3$, H_2O and concentrated. Chromatography (CCl_4-acetone 10:1) of the residue afforded first compound **15** (107 mg, 6 %) as a colorless oil; $[\alpha]_D$ +49.0 (c 1.5, $CHCl_3$); ^{1}H NMR data: δ 5.20 (dd, 1H, $J_{2',3'}$ 10.3 Hz, $J_{3',4'}$ 3.2 Hz, H-3'), 5.08 (s, 2H, Z), 5.02 (d, 1H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.90 (d, 1H, J -12.7 Hz, PhCH_2), 4.83 (d,1H, J -11.6 Hz, PhCH_2), 4.74 (m, 1H, NH), 4.72 (d, 1H, J -11.8, PhCH_2), 4.62 (d, 1H, J -11.6 Hz, PhCH_2), 4.48 (d, 1H, J -11.7 Hz, PhCH_2), 4.40 (d, 1H, J -11.8 Hz, PhCH_2), 4.35 (s, 1H, $J_{1,2}$ 0 Hz, H-1), 4.23-4.32 (m, 4H, 4 PhCH_2), 4.07 (bd, 1H, $J_{4',5'}$ <1 Hz, H-4'), 3.83-3.99 (m, 3H, H-2, 3', 5), 3.50-3.76 (m, 2H, H-5', OCH_2), 3.53 (dd, 1H, $J_{5',6a'}$ 5.3 Hz, $J_{6a',6b'}$ -9.0 Hz, H-6a'), 3.40 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 9.2 Hz, H-3), 3.27-3.48 (m, 1H, OCH_2), 3.33 (dd, 1H, $J_{5',6b'}$ 6.2 Hz, H-6b'), 3.20 (bq, 2H, 2 NHCH_2), 1.36-1.68 (m, 6H, 6 CH_2), 1.41 (d, 3H, $J_{5,6}$ 6.1 Hz, H-6); ^{13}C NMR data: δ 165.8 (Ph*C*OO), 156.4 (*C*ONH), 103.0 (C-1'), 101.5 (C-1), 82.9 (C-4), 77.5, 77.2, 76.7 (C-2', 3, 3', 4'), 75.7 (C-5'), 75.0, 74.6, 73.6, 73.4, 71.9 (5xPh*C*H_2), 73.4 (C-2), 71.8 (C-5), 69.5 (Z), 68.1 (C-6'), 66.6 (O*C*H_2), 41.0 (NH*C*H_2), 29.8, 29.4, 23.4 (3 *C*H_2), 18.2 (C-6); Anal. calcd for $C_{67}H_{73}NO_{13}$: C, 73.14; H, 6.69; N, 1.27; Found: C, 72.80; H, 6.79; N, 1.25.

Eluted next was compound **16** (980 mg, 55 %); $[\alpha]_D$ +84.0° (c 1.4, $CHCl_3$); ^{1}H NMR data: δ 5.60 (dd, 1H, $J_{3',4'}$ 3.0 Hz, H-3'), 5.28 (d, 1H, $J_{1',2'}$ 3.5 Hz, H-1'), 5.08 (s, 2H, Z), 4.38 -4.93 (m, 9H, 9 PhCH_2), 4.64 (m, 1H, NH), 4.32 (s, 1H, $J_{1,2}$ 0 Hz, H-1), 4,18-4.24 (m, 2H, H-2, PhCH_2), 4.21 (dd, 1H, $J_{2',3'}$ 10.6 Hz, H-2'), 4.11 (bd, 1H, $J_{4',5'}$ <1 Hz, H-4'), 3.82-3.95 (m, 2H, H-5, 5'), 3.86 (t, 1H, $J_{3,4} = J_{4,5}$ 9.2 Hz, H-4), 3.33-3.52 (m, 4H, H-3, 6a', 2xOCH_2), 3.37 (dd, 1H, $J_{5',6b'}$ 6.2 Hz, $J_{6a',6b'}$ -9.0 Hz, H-6b'), 3.18 (bq, 2H, NHCH_2), 1.15-1.80 (m, 6H, 6xCH_2), 1.39 (d, 3H, $J_{5,6}$ 6.1 Hz, H-6); ^{13}C NMR data: δ 165.9 (Ph*C*OO), 156.4 (*C*ONH), 101.4 (C-1), 97.9 (C-1'), 80.7 (C-4), 77.9 (C-3'), 75.8 (C-5'), 75.1, 73.9, 73.7, 73.2, 71.0 (5xPh*C*H_2), 74.4 (C-2), 73.7 (C-3), 73.1 (C-2'), 69.4 (Z), 68.9 (C-5), 68.2 (C-6'), 66.6 (O*C*H_2), 41.0 (NH*C*H_2), 29.7, 29.3, 23.4 (3x*C*H_2), 18.4 (C-6); Anal. calcd for $C_{67}H_{73}NO_{13}$: C, 73.14; H, 6.69; N, 1.27; Found: C, 73.08; H, 6.64; N, 1.33.

5-[(Benzyloxycarbonyl)amino]pentyl 2,3-di-O-benzyl-4-O-(2,4,6-tri-O-benzyl-α-D-galacto-pyranosyl)-β-L-rhamnopyranoside **(17)**. Treatment of compound **16** (946 mg, 0.86 mmol) in MeOH (20 mL) with NaOMe (1 M in MeOH, 0.3 mL) for 7 days as described for compound **14** afforded after chromatography (CCl_4-acetone 5:1) compound **17** (752 mg, 88 %) as a white solid; mp 151-152°C; $[\alpha]_D$ +72.8 (c 1.2, $CHCl_3$); ^{1}H NMR data: δ 5.23 (d, 1H, $J_{1',2'}$ 3.4 Hz, H-1'), 5.08 (s, 2H, Z), 4.88 (d, 1H, J -12.5 Hz, PhCH_2), 4.56-4.73 (m, 6H, H-3', NH, 4 PhCH_2), 4.28-4.44 (m, 5H, 5 PhCH_2), 4.29 (s, 1H, $J_{1,2}$ 0 Hz, H-1), 3.83-4.09 (m, 4H, H-4, 4', 5, 5'), 3.77 (dd, 1H, $J_{2',3'}$ 10.1 Hz, H-2'), 3.27-3.55 (m, 4 H, H-6a', 6b', 2xOCH_2), 3.44 (d, 1H, $J_{2,3}$ 3.2 Hz, H-2), 3.41 (dd, 1H, $J_{3,4}$ 9.4 Hz, H-3), 3.18 (bq, 2H, 2 NHCH_2), 1.24-1.67 (m, 6H, 6xCH_2), 1.39 (d, 3H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C NMR data: δ 156.4 (*C*ONH), 101.4 (C-1), 97.2 (C-1'), 80.4 (C-4), 77.5 (C-3'), 77.0 (C-5'), 75.1, 73.9, 73.4, 73.2, 70.8 (5xPh*C*H_2), 73.7 (C-2, 3), 72.3 (C-2'), 70.1 (C-5'), 69.5 (Z), 69.1 (C-5), 68.5 (C-6'), 66.6 (O*C*H_2), 41.0 (NH*C*H_2), 29.7, 29.3, 23.3 (3 *C*H_2); Anal. calcd for $C_{60}H_{69}NO_{12}$: C, 72.34; H, 6.98; N, 1.41; Found: C, 72.37; H, 7.08; N, 1.44.

5-[(Benzyloxycarbonyl)amino]pentyl O-{2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl}-(1→3)-O-{2-deoxy-4,6-O-[(S)-1-(methoxycarbonyl)ethylidene]-2-(2,2,2-trichloroethoxycarbonyl-amino)-β-D-glucopyranosyl}-(1→3)-O-{2,4,6-tri-O-benzyl-α-D-galactopyranosyl}-(1→4)-2,3-di-O-benzyl-β-L-rhamnopyranoside **(18)**. A solution of TMSOTf (8.7 μL) in CH_2Cl_2 (5 mL) was added at -20° C to a solution of compounds **6** (262 mg, 0.29 mmol) and **17** (241 mg, 0.24 mmol) in CH_2Cl_2

(16 ml) containing 4 Å molecular sieves, and stirring was continued for 1.5 h. The mixture was neutralized with pyridine, filtered through a layer of Celite, washed with aq $NaHCO_3$ and concentrated. Chromatography of the residue (CCl_4-acetone 5:1) afforded compound **18** (416 mg, 99 %) as a colorless oil. $[\alpha]_D$ +29.8° (c 0.86, $CHCl_3$); ^{1}H NMR data: δ 5.21 (d, 1H, $J_{1',2'}$ 3.3 Hz, H-1'), 5.14 (d, 1H, $J_{2'',NH}$ 9.5 Hz, N*H*), 5.11 (t, 1H, $J_{2''',3'''} = J_{3''',4'''}$ 8.6 Hz, H-3'''), 5.08 (s, 2H, Z), 4.59-4.96 (m, 7H, H-2''', 4''', N*H*CH_2, 4 PhC*H*$_2$), 4.94 (d, 1H, $J_{1''',2'''}$ 7.5 Hz, H-1'''), 4.79 (d, 1H, J -12.0 Hz, C*H*$_2$$CCl_3$), 4.75 (d, 1H, $J_{1''',2'''}$ 7.5 Hz, H-1''), 4.62 (d, 1H, J -11.9 Hz, C*H*$_2$$CCl_3$), 4.25-4.47 (m, 9H, H-2'', 6a''', 6b''', 6 PhC*H*$_2$), 4.31 (s, 1H, $J_{1,2}$ 0 Hz, H-1), 3.80-4.13 (m, 5H, H-4', 5, 5', 5''', 6a''), 4.10 (dd, 1H, $J_{2',3'}$ 9.8 Hz, $J_{3',4'}$ 2.8 Hz, H-3'), 3.91 (t, 1H, $J_{4,5}$ 10.9 Hz, H-4), 3.84 (s, 3H, COOC*H*$_3$), 3.54-3.71 (m, 5H, H-2', 3'', 4'', 5'', 6b''), 3.24-3.64 (m, 3H, H-6a', 2 OC*H*$_2$), 3.45 (dd, 1H, $J_{3,4}$ 9.6 Hz, H-3), 3.36 (d, 1H, $J_{2,3}$ 2.8 Hz, H-2), 3.28 (dd, 1H, $J_{5',6b'}$ 5.0 Hz, $J_{6a',6b'}$ -9.8 Hz, H-6b'), 3.19 (bq, 2H, 2 NHC*H*$_2$), 2.07, 2.02, 1.99, 1.96 (4s, 4x3H, 4 C*H*$_3$COO), 1.26-1.66 (m, 6H, 6xC*H*$_2$), 1.52 (s, 3H, C*H*$_3$), 1.33 (d, 3H, $J_{5,6}$ 6.1 Hz, H-6); ^{13}C NMR data: δ 170.8, 170.4, 169.8, 169.4 (4 CH_3*C*OO), 156.4 (*C*ONH), 154.1 (*C*ONH), 102.1 (C-1''), 101.3 (C-1), 99.1 (C-1''', C_{acetal}), 96.8 (C-1'), 95.5 (*C*Cl_3), 80.6 (C-4), 78.0 (C-3'), 77.1 (C-3'', 4''), 77.0 (C-5'), 75.0 (C-2), 74.5 (*C*H$_2$$CCl_3$), 73.8, 73.2, 73.0, 70.8 (4xPh*C*H$_2$), 73.6 (C-3), 73.1 (C-2'), 72.1 (C-4'), 71.7 (C-2''', 3''', 5'''), 69.5 (Z), 69.3 (C-5), 68.7 (C-6'), 68.3 (C-4'''), 66.6 (O*C*H$_2$), 65.8 (C-5''), 64.9 (C-6''), 62.0 (C-6'''), 57.9 (C-2''), 52.8 (O*C*H$_3$), 41.0 (NH*C*H$_2$), 29.7, 29.3, 23.3 (3 *C*H$_2$), 25.3 (*C*H$_3$), 20.8 (2 *C*H_3COO), 20.6 (2 *C*H_3COO), 18.6 (C-6); Anal. calcd for $C_{87}H_{103}Cl_3N_2O_{29}$: C, 59.81; H, 5.94; Cl, 6.09; N, 1.60; Found: C, 59.09; H, 5.95; Cl, 7.71; N, 1.65.

5-[(Benzyloxycarbonyl)amino]pentyl O-{2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl}-(1→3)-O-{2-acetamido-2-deoxy-4,6-O-[(S)-1-(methoxycarbonyl)ethylidene]-β-D-glucopyranosyl}-(1→3)-O-{2,4,6-tri-O-benzyl-α-D-galactopyranosyl}-(1→4)-2,3-di-O-benzyl-β-L-rhamnopyranoside **(19).** A suspension of compound **18** (278 mg, 159 mmol) and Zn (0.75 g, 11.5 mmol) in AcOH (8.5 mL) was stirred for 2 h at room temperature, filtered through a layer of Celite, and concentrated by repeated coevaporation of toluene. The residue was dissolved in pyridine (4.5 mL), cooled in an ice bath and treated with Ac_2O (1 mL) for 2 h. The mixture was concentrated by repeated coevaporation of toluene. Chromatography (CCl_4-acetone 5:1) of the residue afforded compound **19** (201 mg, 78 %) as a white foam. $[\alpha]_D$ +39.7 (c 0.89, $CHCl_3$); ^{1}H NMR data: δ 5.48 (d, 1H, $J_{2'',NH}$ 7.6 Hz, N*H*), 5.07-5.17 (m, 2H, H-3''', H-4'''), 5.16 (d, 1H, $J_{1',2'}$ 3.6 Hz, H-1'), 5.08 (s, 2H, Z), 4.78-4.98 (m, 2H, H-1'', N*H*CH_2), 4.94 (dd, $J_{2''',3'''}$ 9.1 Hz, H-2'''), 4.90 (d, 1H, $J_{1''',2'''}$ 7.6 Hz, H-1'''), 4.81 (d, 1H, J -11.9 Hz, PhC*H*$_2$), 4.61-4.69 (m, 3H, 3 PhC*H*$_2$), 4.21-4.49 (m, 3H, H-1, 6a''', 6b'''), 4.47 (d, 1H, J -11.7 Hz, PhC*H*$_2$), 4.44 (d, 1H, J -11.3 Hz, PhC*H*$_2$), 4.40 (d, 1H, J -11.3 Hz, PhC*H*$_2$), 4.35 (d, 1H, J -11.7 Hz, PhC*H*$_2$), 4.28 (dd, 1H, $J_{2',3'}$ 9.3 Hz, $J_{3',4'}$ 3.0 Hz, H-3'), 4.22 (s, 2H, 2 PhC*H*$_2$), 3.55-4.09 (m, 9H, H-2', 2'', 3'', 4, 4', 5', 5''', 6a'', 6b''), 3.84 (s, 3H, COOC*H*$_3$), 3.72 (dq, 1H, $J_{4,5}$, H-5), 3.62 (t, 1H, $J_{3'',4''} = J_{4'',5''}$ 9.3 Hz, H-4''), 3.23-3.44 (m, 6H, H-3, 5'', 6a', 6b', 2 OC*H*$_2$), 3.32 (d, 1H, $J_{1,2}$ 0 Hz, $J_{2,3}$ 2.8 Hz, H-2), 3.18 (bq, 2H, 2 NHC*H*$_2$), 2.06, 2.02, 2.00, 1.99 (4s, 4x3H, 4 C*H*$_3$COO), 1.61 (s, 3H, C*H*$_3$CONH), 1.53 (s, 3H, C*H*$_3$), 1.25-1.61 (m, 6H, 6 C*H*$_2$), 1.34 (d, 3H, $J_{5,6}$ 6.1 Hz, H-6); ^{13}C NMR data: δ 170.8, 170.6, 170.3, 169.9, 169.4 (4 CH_3*C*OO, CH_3*C*ONH), 156.4 (*C*ONH), 101.5 (C-1''), 101.3 (C-1), 99.0 (C_{acetal}), 98.5 (C-1'''), 97.5 (C-1'), 80.9 (C-4), 79.1 (C-3'), 77.5 (C-3''), 77.2 (C-4''), 76.7 (C-5'), 75.9 (C-2), 75.2 (C-3), 74.6, 73.8, 73.4, 73.2 (4xPh*C*H$_2$), 73.6 (C-2'), 73.1 (C-5'''), 72.2 (C-4'), 72.0 (C-4'''), 71.9 (C-2'''), 71.7 (C-3'''), 69.4 (Z), 69.2 (C-5), 68.7, 68.5 (C-6'), 66.6 (O*C*H$_2$), 65.4 (C-5''), 65.0 (C-6''). 58.4 (C-2''), 52.8 (O*C*H$_3$), 41.0 (NH*C*H$_2$), 29.7, 29.3, 23.3 (3 *C*H$_2$), 25.4 (*C*H$_3$), 23.3 (*C*H$_3$CONH), 20.8 (2 *C*H_3COO), 20.6 (2 *C*H_3COO), 18.5 (C-6); Anal. calcd for $C_{86}H_{104}N_2O_{28}$: C, 64.01; H, 6.50; N, 1.74; Found: C, 64.01; H, 6.65; N, 1.54.

5-Aminopentyl O-β-D-glucopyranosyl-(1→3)-O-{2-acetamido-4,6-O-[(S)-1-carboxyethylidene]-2-deoxy-β-D-glucopyranosyl}-(1→3)-O-α-D-galactopyranosyl-(1→4)-O-β-L-rhamnopyranoside **(20).** A solution of compound **19** (181 mg, 0.112 mmol) and a catalytic amount of NaOMe in MeOH (6 mL) was kept at room temperature for 3 h. The mixture was neutralized by addition of ion-exchange resin (Lewatit, H^+-form), filtered, and concentrated. The residue was redissolved in MeOH (6 mL), 1N NaOH (1.5 mL) was added, the mixture was stirred at room temperature for 4 h, neutralized with ion exchange resin (Lewatit, H^+-form), and filtered. The filtrate was treated with a catalytic amount of $Pd(OH)_2$ (10% on charcoal) and H_2 in 1:1:1 MeOH-water-AcOH (10 mL) for 5 d, filtered, and concentrated. The residue was eluted with water from a column of Bio-Gel P2 and the carbohydrate-containing fractions were lyophilized to give **20** (92 mg, 97%); $[\alpha]_D$ -11.3 (c 0.97, H_2O); ^{13}C NMR data: δ 177.8 (*C*OOH), 106.1 (C-1''), 104.6 (C_{acetal}), 104.3 (C-1), 102.9, 102.6 (C-1', 1'''), 83.7 (C-4), 81.7 (C-3'''), 79.3, 78.3, 77.4 (C-2''', 3', 3'', 4'''), 75.6, 74.5, 74.4, 73.8, 73.2 (C-2, 3, 4'', 5, 5''), 72.5 (C-4'), 72.4 (O*C*H_2), 71.9 (C-5'), 70.3 (C-5'''), 68.6 (C-2'), 67.2 (C-6''), 63.9 (C-6'), 63.4 (C-6'''), 58.3 (C-2''), 42.3 (*C*H_2NH_2), 31.1, 29.3, 25.1 (3 *C*H_2), 27.4 (*C*H_3), 25.2 (*C*H_3CONH), 19.9 (C-6); FABMS: m/z 847.3 (M^+).

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