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Stereoselective Synthesis of Glycosides and Anomeric Azides of Glucosamine

Carlo Unverzagt and Horst Kunz

Mainz, Institut für Organische Chemie, Johannes Gutenberg-Universität

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Dedicated to Professor H. G. O. Becker on the Occasion of his 70th Birthday

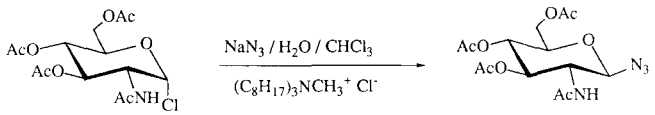
Abstract. The β-azide of O-acetyl protected N-acetyl glucosamine is efficiently accessible via a phase-transfer-catalyzed reaction of the corresponding glycosyl chloride with sodium azide. The azido group revealed to be a useful anomeric protection for modifications of the protecting group pattern of the glucosamine unit. Exchange of the O-acyl groups by 4-methoxybenzylidene and 4-methoxybenzyl (Mpm) protection delivered regioselectively blocked glucosaminyl azide derivatives. In contrast, the N-phthaloyl protected glucosaminyl azide was obtained quantitatively from the corresponding glycosyl fluoride via a boron trifluoride-promoted reaction with trimethylsilyl azide. N-Phthaloyl glucosaminyl fluoride was also revealed to be useful in the synthesis of β-glucosamine glycosides and saccharides. Chitobiosyl azide **21** carrying a selctively removable 6-O-Mpm protection was synthesized from the O-acetyl protected N-phthaloyl glucosaminyl bromide and N-acetylglucosaminyl azide **13** as an acceptor selectively deblocked at O-4.

The β-N-glycosidic bond between N-acetylglucosamine and asparagine constitutes the characteristic linkage region of the majority of N-glycoproteins which are carriers of manifold functions in biological selectivity [1]. The β-1-amino derivatives of N-acetyl glucosamine required for the synthesis of the GlcNAc-asparagine conjugates are usually obtained by hydrogenolysis of the corresponding azides. The O-acetyl protected glucosaminyl-β-azide was successfully synthesized by reaction of the α-chloride **1** with sodium azide in formamide at elevated temperature [2, 3]. However, this procedure failed in the chitobiose series, and highly explosive silver azide was needed to obtain the chitobiosyl azide [4].

We here report on new and improved routes to α- and β-azides of glucosamine, and on the subsequent transformation of their protecting group pattern. The report includes the use of glucosaminyl fluorides and bromides for the synthesis of glycosides and chitobiose derivatives required for the chemical construction of complex N-glycopeptides [5].

β-1-Azides of Glucosamine Derivatives

A convenient and efficient synthesis of 2-acetamido-3, 4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl azide **2** was achieved by reaction of 2-acetamido-3, 4, 6-tri-O-acetyl-2-deoxy-α-D-glucopyranosyl chloride **1** [6] with sodium azide in chloroform/water in the presence of the phase-transfer catalyst tri-n-capryl-methyl-ammonium chloride (Aliquat 336) [7].

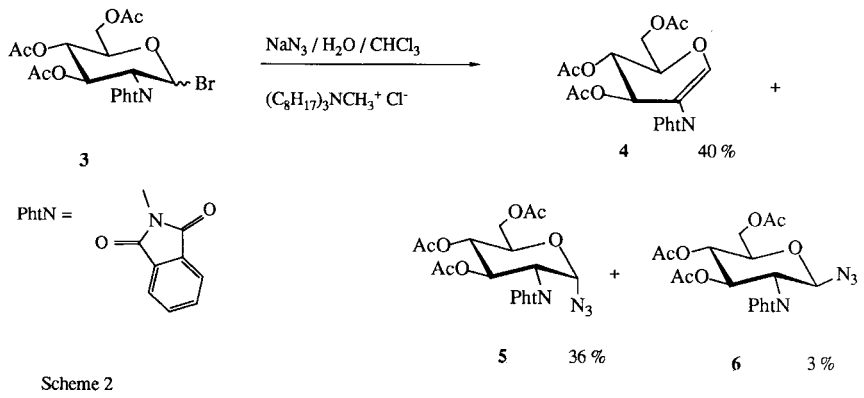


1 2 88 %

Scheme 1

Since the acetamido group often causes undesired side reactions in subsequent tranformations of compounds like **2**, the N-phthaloyl protected glucosaminyl azide is also of interest. However, the analogous phase-transfer-catalyzed reaction of O-acetylated N-phthaloyl glucosaminyl bromide **3** [8] with sodium azide delivered a mixture of products. The major component was glycal **4**. Among the desired azides, α-anomer **5** surprisingly exceeded β-anomer **6** by a ratio of 12 : 1 (Scheme 2).

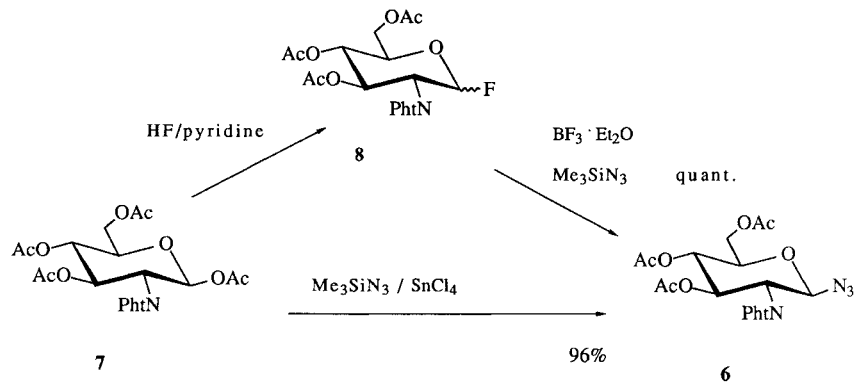
In contrast to glycosyl bromide **3**, the corresponding N-phthaloyl glucosaminyl fluoride **8** quantitatively delivered the pure β-anomeric N-phthaloyl glucosaminyl



Scheme 2

azide **6** via a BF_3 etherate promoted reaction [9, 10] with trimethylsilyl azide. Glycosyl fluoride **8** is easily accessible from the peracetylated N-phthaloyl glucosamine **7** by treatment with HF/pyridine complex [9].

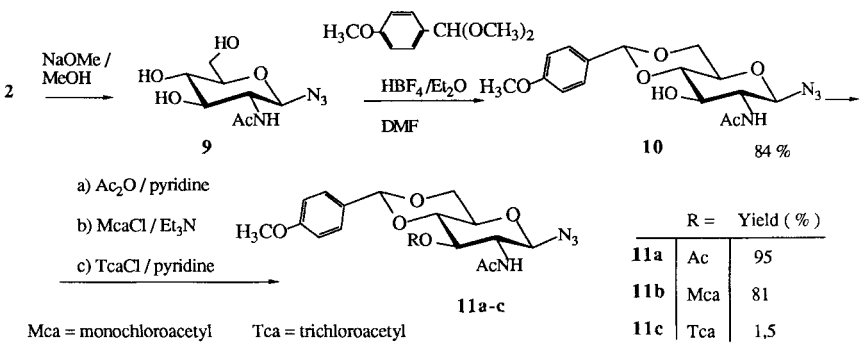
Alternatively, the β-acetate **7** was reacted with trimethylsilyl azide/$SnCl_4$ [11] furnishing β-azide **6** with equal efficiency.



Scheme 3

Use of the Azido Group as a Protected Anomeric Amino Group

Anomeric azido functions show a reliable stability under different reaction conditions. Thus, Zemplén transesterification of the N-acetyl glucosaminyl azide **2** resulted in the selective deacetylation without affecting the azide [12]. The OH-deblocked compound **9** was subjected to acid-catalyzed introduction of the 4,6-(4-methoxybenzylidene)-acetal protection [13] to give the derivative **10** without destruction of the anomeric azide. Compound **10** not only constitutes a glucosamine derivative selectively unblocked at the 3-OH group, but also allows a variety of transformations to other regioselectively deprotected glucosamine derivatives. Acylation with acetic acid anhydride/pyridine,

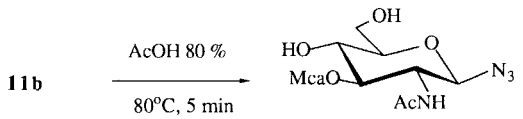


	R =	Yield (%)
11a	Ac	95
11b	Mca	81
11c	Tca	1,5

Scheme 4

monochloroacetyl chloride/triethylamine or trichloroacetyl chloride/pyridine, respectively, delivered the corresponding 3-O-acyl derivatives **11**. Whereas the acetyl **11a** and the monochloroacetyl (Mca) derivative **11b** were isolated in high yield, the trichloroacetyl analog **11c** mainly hydrolyzed during chromatographic purification.

Treatment of **11b** with 80 % acetic acid at 80 °C for 5 min resulted in the removal of the 4-methoxybenzylidene group to give **12**, which is useful in further reactions differentiating between 6-and 4-position.



12 91 %

Scheme 5

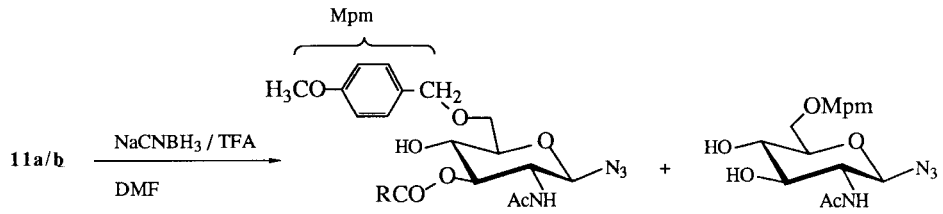
The fully protected compounds **11a, b** can be selectively deblocked at the 4-position by regioselective reductive opening [14] of the 4-methoxybenzylidene acetal [13] using sodium cyanoborohydride/trifluoroacetic acid in dimethylformamide. The 3-O-acetyl derivative **11a** gave the desired product **13** in high yield, whereas the reaction of **11b** was accompanied by extensive dechloroacetylation. The compound **14** deblocked at 4-OH was isolated only in low yield besides the derivative **15**.

Sodium cyanoborohydride in combination with trimethylsilyl chloride influences the regioselective opening of the methoxybenzylidene group in favour of the 4-O-Mpm compound. However, for derivative **11b**, low yield (13 %) and low selectively (5 : 2) was found.

The more favourable preparation of the glucosaminyl azide **17** carrying an unblocked 6-OH group was performed by acetylation of **13** to form the 3,4-di-O-acetyl compound **16** and subsequent deprotection in the 6-position via oxidative cleavage of the Mpm group by using ceric ammonium nitrate in acetonitrile/water [13]. The desired product **17** was isolated in high yield. It should be noticed, that the Mpm ether can be removed selectively in the presence of the azido function needed in the synthesis of fucosylated N-glycopeptides [5].

Compound **17** is sensitive to 4→6 acetyl shift, especially when it is kept in contact with silica gel for longer time. After 3 days coated on silica gel, **17** disappeared completely, and only the 3,6-di-O-acetyl derivative **18** was isolated by chromatography.

These results illustrate that the azido moiety is useful as a protected anomeric amino equivalent and allows the synthesis of glucosaminyl azides selectively deblocked at 3- (**18**), 4- (**13, 18**) or 6-position (**17**).



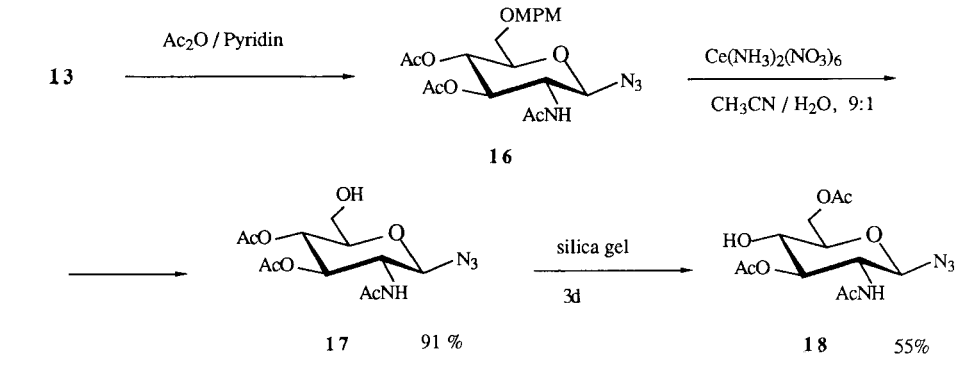
13 RCO = Ac , 86%

14 RCO = Mca, 35%

15 -

15 45%

Scheme 6



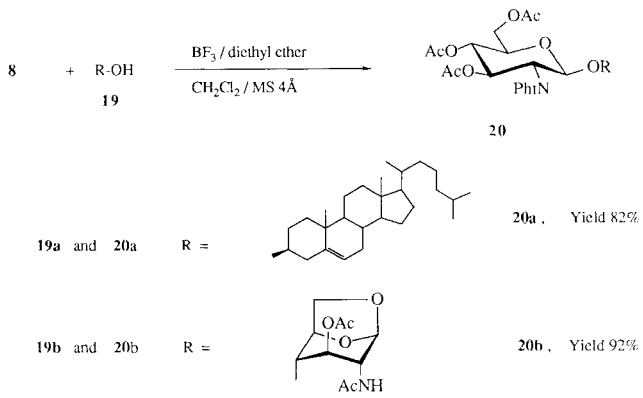
17 91 %

18 55%

Scheme 7

Synthesis of N-Phthaloyl Glucosamine Glycosides and Chitobiosyl Azides

The phthaloyl protected glucosaminyl fluoride **8** was considered a useful glycosyl donor in the construction of chitobiose derivatives. However, the borontrifluoride-promoted reaction of **8** with the azide **13** as an acceptor selectively unprotected at the 4-OH group resulted in fast cleavage of the acid-sensitive 4-methoxybenzyl ether and was not of practical use. Other acceptors, e.g. cholesterol **19a** or the 1,6-anhydro N-acetylglucosamine derivative **19b** [15], reacted with the glycosyl fluoride **8** under homogeneous conditions in short times to give the β-glycosides **20** in high yield and complete stereoselectivity.



Scheme 8

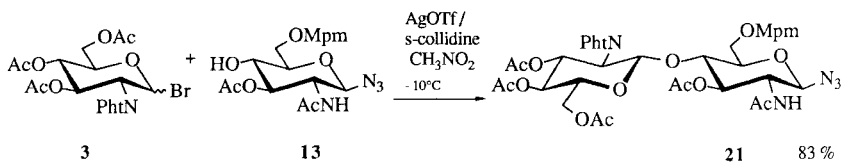
In respect of the construction of complex glycopeptides [5], the use of the chitobiosyl derivative **20b** as an intermediate is not favourable. A more rapid access to a selectively protected chitobiosyl azide was found by condensation of 6-O-Mpm and 4-O-acetyl protected glucosaminyl azide **13** with N-phthaloyl glucosaminyl bromide **3** in the presence of silver triflate/collidine in nitromethane [8] at −10 °C furnishing the chitobiosyl azide **21** in high yield.

The efficient formation of the disaccharide **21** corroborates results of Haraldsson et al. [16] and Krepinsky et al. [17] who demonstrated Mpm protected acceptors as useful components in glycosylation reactions. Further investigations revealed that the 3-O-acyl group has also a strong influence on these processes. Attempts to glycosylate the 3-O-Mca protected acceptor **14** using glycosyl donor **3** under identical conditions surprisingly resulted in the efficient formation of the O-glycosyl imidate **22**.

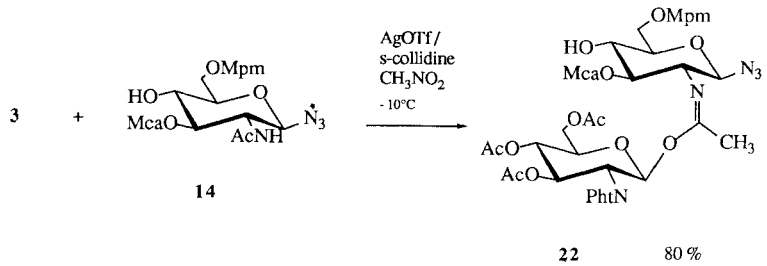
The structure of imidate **22** was proven inevitably by NMR spectroscopy. The ^{1}H-NMR spectrum of **22** shows no signal of an amide proton, but a free 4-OH group. The signal of H-1′ is remarkably shifted downfield (δ = 6.59 ppm), whereas the signal of C-1′ in the ^{13}C NMR spectrum shows a highfield shift, both indicating an O-acyl-type substituent (imidate) at the anomeric position of the N-phthaloyl glucosamine portion. The different behaviour of the glycosyl acceptors **13** and **14** illustrates that the protecting group pattern can modulate the reactivity of the hydroxyl groups in a complex way.

The anomeric azido group tolerates many modifications in the protecting group pattern of carbohydrates and, as the synthesis of the selectively deprotectable chitobiosyl azide **21** was efficiently achieved on the basis of this chemistry, decisive preconditions for the chemical synthesis of N-glycopeptides with oligosaccharide side chains [5] are provided by the methodology described. Furthermore, the anomeric azide not only constitutes a useful protected form of an anomeric amine, but also was proved as an activable leaving group in glycosylation reactions after its transformation to the triazole group [18].

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.



Scheme 9



Scheme 10

Experimental

Melting points were determined using a Büchi apparatus (according to Dr. Tottoli) and are uncorrected. Optical rotation values were measured with a Perkin Elmer polarimeter 241.400 MHz ^{1}H and 100.6 MHz ^{13}C NMR spectra were recorded using a Bruker AM 400 (tetramethylsilane as the internal standard). Flash chromatography was carried out on silica gel Kieselgel 60 (0.04 – 0.063 mm) purchased from E. Merck, Darmstadt, Germany. T.l.c. was recorded using silica gel Kieselgel 60 – F^{254} (E. Merck, Darmstadt, Germany). Indication was performed by u.v. light or using a mixture (1 : 1) of 2N H_2SO_4 and a solution of 3-methoxyphenol (0.2 %) in ethanol.

2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl Azide (**2**)

A solution of 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranosyl chloride [6] (20.1 g, 55 mmol) and tri-n-capryl methylammonium chloride (0.5 g, 2.5 mmol) in chloroform (200 ml) was stirred vigorously with an aqueous solution (50 ml) of sodium azide (5 g, 76 mmol) for 2 days. After separation of the chloroform solution the solvent was evaporated in vacuo. The residue crystallized after addition of diethyl ether (300 ml) and was collected by filtration. Recrystallization from ethyl acetate/light petroleum ether yielded glycosyl azide **2** as colourless needles. Yield: 88 %; mp. 164 °C (lit. [2]: mp. 160 – 161 °C); $[\alpha]_D^{22}$ −44.8 (c 1, $CHCl_3$) (lit. [2]: $[\alpha]_D^{22} = -40$, (c 1.0, $CHCl_3$).

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α, β-D-glucopyranosyl bromide **3** was synthesized according to the procedure described in [8]. Recrystallization from dichloromethane/diisopropyl ether delivered **3** as a 1 : 1 mixture of the anomers. Yield: 80 – 90 %; mp. 131 °C (lit. [8] mp. (α-anomer) 122 – 123 °C.

^{1}H NMR (DMSO-d_6): δ = 6.85 (d, $J_{1,2}$ = 3.4 Hz, H-1α); 6.53 (d, $J_{1,2}$ = 9.6 Hz, H-1β).

Phasetransfer Reaction of 3 with Sodium Azide

The glycosyl bromide **3** (1 g, 2 mmol) and tri-n-capryl methylammonium chloride (0.1 g, 0.5 mmol) were dissolved in dichloromethane (10 ml) and vigorously stirred with an aqueous solution (5 ml) of sodium azide (0.5 g, 7.5 mmol) for 2 days. The organic layer was dried ($MgSO_4$) and evaporated in vacuo. Flash chromatography on silica gel (80 g) using light petroleum ether/ethyl acetate (2 : 1) furnished a mixture (12 : 1) of the anomeric azides **5** and **6** and the elimination product **4**.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-1,5-anhydro-D-arabino-hexenitol (**4**)

Yield: 334 mg (40 %); FD-MS: m/z = 417 (M + 1).
^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.9 (m, 4H, Ar); 7.06 (s, 1H, H-1); 5.38 (d, $J_{3,4.}$ = 3.6 Hz, 1H, H-3); 5.21 (dd, $J_{4,5}$ = 4.6 Hz, 1H, H-4); 4.64 (m, 1H, H-5); 4.42 (dd, $J_{vic.}$ = 7.2 Hz, J_{gem} = 12.2 Hz, 1H, H-6a); (dd, J_{vic} = 3.6 Hz, 1H, H-6b); 2.09; 2.07; 1.85 (3s, 9H, OAc).
^{13}C-NMR (D MSO-d_6): δ [ppm]: 169.8 – 167.1 C = O; 148.0 C-1; 134.6 C-4/5 Ar; 131.2 C-1/2 Ar; 123.3 C-2/6 Ar; 104.9 C-2; 60.5 C-6; 20.42; 20.39; 20.17 OAc.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α/β-D-glucopyranosyl Azide (**5**) *and* (**6**)

Yield: 360 mg (39 %); $[\alpha]_D^{22}$ = + 194.8 (c 1, CH_2Cl_2).

$C_{20}H_{20}N_4O_9$	Calcd.	C 52.18	H 4.38	N 12.12
(460.4)	Found	C 52.29	H 4.61	N 11.94

NMR signals of the α-anomer **5** (Content of β-anomer 8 %).
^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.9 (m, 4H, Ar); 6.23 (dd, $J_{2,3}$ = 11.5 Hz, $J_{3,4}$ = 9.1 Hz, 1H, H-3); 5.84 (d, $J_{1,2}$ = 4 Hz, 1H, H-1); 4.99 (dd, $J_{4,5}$ = 10 Hz, 1H, H-4); 4.5 (dd, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 11.5 Hz, 1H, H-2); 4.32 – 4.25 (m, 2H, H-5, H-6a); 4,1 (m, 1H, H-6b); 2.03; 1.96; 1.78 (3s, 9H, OAc).
^{13}C NMR (DMSO-d_6): δ [ppm]: 169.9 – 166.9 C = O; 134.4 C-4/5 Ar; 130.8 C-1/2 Ar; 123.3 C-2/6 Ar; 86.7 C-1; 61.5 C-6; 52.1 C-2; 20.35; 20.26; 20.15 OAc.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α, β-D-glucopyranosyl Fluoride (**8**)

The 1,3,4,6-tetra-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside **7** (2 g, 4.19 mmol) was dissolved in HF/pyridine (5 ml, 65 – 70 % HF) at room temperature. After completion of the reaction (20 – 40 h, t.l.c. control, light petroleum ether/ethyl acetate 2 : 1) the solution was poured into a mixture of ice (100 g) and dichloromethane (100 ml). The aqueous layer was extracted twice with dichloromethane (100 ml), and the combined organic solutions were washed twice with 1N HCl (100 ml) and with 1N $KHCO_3$. After drying with $MgSO_4$ and evaporation of the solvent in vacuo, the residue was recrystallized from diisopropyl ether.
Yield: 1.5 g (82 %); mp. 80 – 90 °C; $[\alpha]_D^{22}$ = + 138.5 °C (c 0.5 = dichloromethane);
R_f = 0.3 (light petroleum ether/ethyl acetate 2 : 1).

$C_{20}H_{20}NO_9F$	Calcd.	C 54.90	H 4.61	N 3.20
(437.4)	Found	C 54.91	H 4.61	N 3.15

According to the ^{1}H NMR spectrum, the obtained anomeric mixture contained 73 % of the α-anomer.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α-D-glucopyranosyl Fluoride

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.9 (m, 4H, Ar); 6.29 (dd, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 9.2 Hz, 1H, H-3); 5.91 (dd, $J_{1,2}$ = 2.6 Hz, $J_{1,F}$ = 51.8 Hz, 1H, H-1a); 5.15 (m, 1H, H-4); 4.62 (ddd, $J_{2,F}$ = 30.3 Hz, 1H, H-2); 4.35 – 4.1 (m, 3H, H-5, H-6a/b); 2.04; 1.99; 1.80 (3s, 9H, OAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.9 – 166.8 C = O; 134.8 C-4/5 Ar; 130.7 C-1/2 Ar; 123.4 C-2/6 Ar; 105.14 (d, $J_{C\text{-}1,F}$ = 230 Hz) C-1; 69.6 C-4; 68.5 C – 3; 66.2 C-5; 61.3 C-6; 52.0 (d, $J_{C\text{-}2,F}$ = 29.4 Hz) C – 2; 22.7 – 19.9 OAc.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Fluoride

^{1}H-NMR (DMSO – d_6): δ [ppm]: 7.9 (m, 4H, Ar); 6.15 (dd, $J_{1,2}$ = 7.8 Hz, $J_{1,F}$ = 52.7 Hz, 1H, H-1b); 5.7 (dd, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 9.3 Hz, 1H, H-3); 5.14 (m, 1H, H-4); 4.35 – 4.1 (m, 4H, H-2, H-5, H-7a/b); 2.05; 2.00; 1.81 (3s, 9H, OAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.9 – 166.8, C = O; 135.1 C-4/5 Ar; 130.5 C-1/2 Ar; 123.6 C-2/6 Ar; 104.13 (d, $J_{C\text{-}1,F}$ = 210 Hz) C-1; 71.18 (d, $J_{4,F}$ = 5.6 Hz) C-4; 69.0 (d, $J_{3,F}$ = 10.4 Hz) C-3; 67.3 C-5; 61.4 C-6; 53.0 (d, $J_{C\text{-}2,F}$ = 24.1 Hz) C-2; 22.7 – 19.9 OAc.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Azide (**6**)

a) from glycosyl fluoride **8**

To a solution of the protected glycosaminyl fluoride **8** (50 mg, 0.11 mmol) and trimethylsilyl azide (0.1 ml) in dry dichloromethane (2 ml) was added borontrifluoride-etherate (0.05 ml). After 30 min the mixture was diluted with dichloromethane (50 ml) and extraced twice with 1N $KHCO_3$ (50 ml). The organic layer was dried ($MgSO_4$) and evaporated in vacuo.

Yield: 52.6 mg (quantitative), amorphous; $[\alpha]_D^{22} = -21.0°$ (C 0.25, CH_2Cl_2);

$R_f = 0.56$ (light petroleum ether/ethyl acetate 1 : 1).

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.9 (m, 4H, Ar); 5.77 (d, $J_{1,2} = 9.6$ Hz, 1H, H-1); 5.65 (dd, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 9.3$ Hz, 1H, H-3); 5.06 (dd, $J_{4,5} = 9.3$ Hz, 1H, H-4); 4.3 – 4.05 (m, 4H, H-2, H-5, H-7a/b); 2.04; 1.99; 1.78 (3s, 9H, OAc).

b) from β-acetate **7**

To a solution of the tetra-O-acetyl N-phthaloyl glucosamine **7** [8] (1 g, 2.1 mmol) in dry dichloromethane (20 ml) was added trimethylsilyl azide (0.5 ml) and tin tetrachloride (0.1 ml). After 30 min the reaction mixture was diluted with dichloromethane (100 ml) and extracted twice with 1N $KHCO_3$ (100 ml). The dried organic layer ($MgSO_4$) was evaporated in vacuo. Yield: 960 mg (97 %).

2-Acetamido-2-deoxy-β-D-glucopyranosyl Azide (**9**)

was obtained from the acetylated compound **2** by treatment with sodium methoxide/methanol according to ref. [12].

2-Acetamido-2-deoxy-4,6-O-(4-methoxybenzylidene)-β-D-glucopyranosyl Azide (**10**)

To a solution of the N-acetylglucosaminyl azide **9** (11.7 g, 50 mmol) in dimethylformamide (270 ml) were added p-methoxybenzaldehyde dimethylacetal (8.7 ml, 58 mmol) and tetrafluoroboric acid (54 % in diethyl ether). After complete conversion of **9** (4 h, t.l.c. control, $CHCl_3$/MeOH 10 : 1), the mixture was neutralized by addition of triethylamine (7.6 ml, 54 mmol). The solvent was evaporated in high vacuum and the residue was crystallized by trituration with water/dichloromethane 1 : 1 (400 ml). The precipitate was collected by filtration, washed with diethyl ether and dried. Additional amounts of **10** were isolated from the dichloromethane solution after concentration and precipitation using diethyl ether. The crude product was recrystallyzed from CH_2Cl_2/MeOH 10 : 1. Yield: 15.3 g (84 %); mp. 194 °C; $[\alpha]_D^{22} = -76.5$ °C (c 0.5, CH_2Cl_2/MeOH 1 : 1); $R_f = 0.45$ ($CHCl_3$/MeOH 10 : 1).

$C_{16}H_{20}N_4O_6$	Calcd.	C 52.74	H 5.53	N 15.38
(364.4)	Found	C 52.71	H 5.70	N 15.32

^{1}H-NMR (DMSO – d_6): δ [ppm]: 7.97 (d, $J_{2,NH} = 8.6$ Hz, 1H, NH); 7.35; 6.92 (2m, 4H, Ar); 5.56 (s, 1H, Ar – CH =); 5.43 (d, $J_{3,OH} = 6$ Hz, 1H, OH-3); 4.58 (d, $J_{1,2} = 9$ Hz, 1H, H-1); 4.2 (dd, $J_{vic} = 4$ Hz, $J_{gem} = 11$ Hz, 1H, H-7a); 3.76 – 3.45 (m, 5H, H-2, H-3, H-4, H-5, H-7b); 3.73 (s, 3H, CH_3O); 1.85 (s, 3H, NAc).

^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.4 C = O; 159.5 C-p Ar; 129.9 C-i Ar; 127.5 C-o Ar; 113.2 C-m Ar; 100.58 Ar-CH = ; 88.7 C-1; 67.5 C-6; 55.45 C-2; 55.02 CH_3O; 22.8 NAc.

2-Acetamido-3-O-acetyl-2-deoxy-4,6-O-(4-methoxybenzylidene)-β-D-glucopyranosyl Azide (**11 a**)

To a solution of **10** (3.17 g, 9 mmol) in pyridine (20 ml) at 0 °C was added acetic acid anhydride (10 ml). After several minutes precipitation of the product occurred. After stirring for 8 h, the solution was concentrated in vacuo three times, each after addition of toluene (50 ml). The crude product was dissolved in dichlormethane (150 ml) and extracted with 1N HCl, water and 1N $KHCO_3$ (100 ml in each case). After drying with $MgSO_4$ and evaporation of the solvent in vacuo, the residue was stirred with diethyl ether, and the crystalline **11 a** was collected by filtration.

Yield: 3.5 g (95 %); mp 198 °C; $[\alpha]_D^{22} = 108.5°$ (c 1, CH_2Cl_2); $R_f = 0.65$ ($CHCl_3$/MeOH 10 : 1).

$C_{18}H_{22}N_4O_7$	Calcd.	C 53.20	H 5.46	N 13.79
(364.4)	Found	C 53.40	H 5.46	N 13.76

^{1}H-NMR (DMSO-d_6): δ [ppm]: 8.1 (d, $J_{2,NH} = 9.3$ Hz, 1H, NH); 7.29; 6.91 (2m, 4H, Ar); 5.59 (s, 1H, Ar-CH =); 5.14 (dd, $J_{2,3} = J_{3,4} = 9.3$ Hz, 1H, H-3); 4.87 (d, $J_{1,2} = 9.3$ Hz, 1H, H-1); 4.24 (dd, $J_{vic} = 4.8$ Hz, $J_{gem} = 10$ Hz, 1H, H-7a); 3.9 – 3.65 (m, 4H, H-2, H-4, H-5, H-7b); 3.75 (s, 3H, CH_3O); 1.96 (s, 3H, OAc); 1.81 (s, 3H, NAc).

^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.5; 169.4 C = O; 159.6 C-p Ar; 129.5 C-i Ar; 127.3 C-o Ar; 113.4 C-m Ar; 100.3 Ar-CH = ; 88.2 C-1; 67.2 C-6; 55.0 CH_3O; 53.1 C-2; 22.5 NAc; 20.3 OAc.

2-Acetamido-2-deoxy-4,6-O-(4-methoxybenzylidene)-3-O-monochloroacetyl-β-D-glucopyranosyl Azide (**11 b**)

To a suspension of **10** (810 mg, 2 mmol) and triethylamine (1.4 ml) in dichloromethane (20 ml) at – 15 °C was added dropwise monochloroacetyl chloride (0.35 ml) dissolved in dichloromethane (10 ml). After 2 – 3 h at room temperature, the reaction was completed (t.l.c., $CHCl_3$/MeOH 10 : 1). The mixture was diluted with dichloromethane (100 ml) and extracted with 1N HCl, water and 1N $KHCO_3$ (100 ml in each case). After drying with $MgSO_4$ and evaporation of the solvent in vacuo, a colorless residue remained. Yield: 0.79 g (81 %); mp. 196 °C; $[\alpha]_D^{22} = -75.9$ °C (c 1, CH_2Cl_2/MeOH 1 : 1);

$R_f = 0.65$ ($CHCl_3$/MeOH 10 : 1).

$C_{18}H_{21}N_4O_7Cl$	Calcd.	C 49.05	H 4.80	N 12.71
(440.8)	Found	C 48.97	H 4.81	N 12.61

200 MHz-^{1}H-NMR (DMSO-d_6): δ [ppm]: 8.15 (d, $J_{2,NH} = 9.3$ Hz, 1H, NH); 7.30; 6.9 (2m, 4H, Ar); 5.59 (s, 1H, Ar-CH =); 5.22 (dd, $J_{2,3} = J_{3,4} = 9.6$ Hz, 1H, H-3); 4.9 (d, $J_{1,2} = 9.3$ Hz, 1H, H-1); 4.43; 4.27 (2d, $J_{gem} = 15$ Hz, 2H, CH_2Cl); 4.27 (m, 1H, H-7a); 3.95 – 3.65 (m, 4H, H-2, H-4, H-5, H-7b); 3,73 (s, 3H, CH_3O); 1.81 (s, 3H, NAc).

50.3 MHz-^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.6; 166.8 C = O; 159.6 C-p Ar; 129.4 C-i Ar; 127.3 C-o Ar; 113,4 C-m Ar; 100.3 Ar-CH = ; 88.2 C-1; 67.2 C-6; 55.1 CH_3O; 53.0 C-2; 40.7 CH_2Cl; 22.5 NAc.

2-Acetamido-2-deoxy-4,6-O-(4-methoxybenzylidene)-3-O-trichloroacetyl-β-D-glucopyranosyl Azide (**11 c**)

To a solution of **10** (2.84 g, 8 mmol) in pyridine (10 ml) at – 20 °C was added dropwise trichloroacetyl chloride (3 ml). After 1 h the solution was diluted with dichloromethane (150 ml) and extracted with 1N HCl (500 ml), water and 1N $KHCO_3$ (100 ml). Drying with $MgSO_4$ and evaporation of the solvent gave a brown remainder, which was pu-

rified by chromatography on silca gel (50 g, light petroleum ether/ethyl acetate 2 : 1).
Yield: 60 mg (1.5 %), yellow solid; mp. 158 °C; $[\alpha]_D^{22} = -76.1$ °C (c 1, dichloromethane).

$C_{18}H_{19}N_4O_7Cl_3$	Calcd.	C 42.41	H 3.76	N 10.99
(709.7)	Found.	C 42.32	H 3.94	N 10.93

^{1}H-NMR (DMSO-d_6): δ [ppm]: 8.3 (d, $J_{2,NH} = 9.4$ Hz, 1H, NH); 7.25; 6.92 (2m, 4H, Ar); 5.64 (s, 1H, Ar-CH=); 5.28 (dd, $J_{2,3} = J_{3,4} = 9.9$ Hz, 1H, H-3); 4.87 (d, $J_{1,2} = 9.9$ Hz, 1H, H-1); 4.29 (dd, $J_{vic} = 4.2$ Hz, $J_{gem} = 9.4$ Hz, 1H, H-7a); 4.1 (ddd, 1H, H-2); 4.02 (m, 1H, H-4); 3.9 – 3.7 (m, 2H, H-5, H-7b); 3.73 (s, 3H, CH_3O); 1.81 (s, 3H, NAc).

2-Acetamido-2-deoxy-3-O-monochloroacetyl-β-D-glucopyranosyl Azide (**12**)

A suspension of **11b** (1 g, 2.27 mmol) in acetic acid/water 4 : 1 (20 ml) was stirred at 80 °C. The reaction was finished, 5 minutes after the suspension had cleared. The acetic acid was evaporated in vacuo and acetonitrile (3 × 20 ml) was distilled off the residue. Chromatography (silica gel, 50 g in CH_2Cl_2/MeOH 10 : 1) furnished compound **12** which was crystallized from methanol/diisopropyl ether.
Yield: 666 mg (91 %); mp 135 – 142 °C; $[\alpha]_D^{22} = -74{,}5$ °C (c 0.5, MeOH); $R_f = 0.3$ ($CHCl_3$/MeOH 5 : 1).

$C_{10}H_{15}N_4O_6$	Calcd.	C 37.22	H 4.69	N 17.36
(322.7)	Found	C 37.29	H 4.74	N 17.34

^{1}H-NMR (DMSO-d_6): δ [ppm]: 8.0 (d, $J_{2,NH} = 9.3$ Hz, 1H, NH); 5.5 (m, 1H, OH); 4.9 (dd, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 9.6$ Hz, 1H, H-3); 4.78 (m, 1H, OH); 4.68 (d, $J_{1,2} = 9.3$ Hz, 1H, H-1); 4.32; 4.24 (2d, 2H, CH_2Cl); 3.8 – 3.3 (m, 5H, H-2, H-4, H-5, H-7a/b); 1.76 NAc.
^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.3; 166.9 C=O; 87.7 C-1; 60.2 C-6; 52.6 C-2; 41.0 CH_2Cl; 22.5 NAc.

2-Acetamido-3-O-acetyl-2-deoxy-6-O-(4-methoxybenzyl)-β-D-glucopyranosyl Azide (**13**)

To a stirred mixture of **11a** (15.4 g, 36 mmol), $NaCNBH_3$ (11.1 g, 180 mmol) and powdered molecular sieves 4 Å (30 g) in DMF (280 ml) at – 10 °C was added dropwise a solution of trifluoroacetic acid (27.6 ml, 0.36 mol) in DMF (210 ml). After completion of the reaction (20 h, t. l. c. control, $CHCl_3$/MeOH 10 : 1) the solvent was evaporated in high vacuum. The residue was dissolved in dichloromethane (500 ml) and filtered through a pad of Celite. The organic layer was extracted with 1N $KHCO_3$ (250 ml), dried with $MgSO_4$ and evaporated to dryness. Traces of DMF were removed from the oily residue in high vacuum. Compound **13** was purified by flash chromatography on silica gel (150 g) in CH_2Cl_2/MeOH (40 : 1) and was recrystallized from ethyl acetate/light petroleum ether.
Yield: 12.7 g (86 %); mp. 133 °C; $[\alpha]_D^{22} = -76.8$ °C (c 1, CH_2Cl_2); $R_f = 0.45$($CHCl_3$/MeOH 10 : 1).

$C_{18}H_{24}N_4O_7$	Calcd.	C 52.94	H 5.92	N 13.71
(408.4)	Found	C 52.88	H 5.90	N 13.87

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.97 (d, $J_{2,NH} = 9.4$ Hz, 1H, NH); 7.37; 6.9 (2m, 4H, Ar); 5.55 (d, $J_{4,OH} = 6{,}1$ Hz, 1H, OH-4); 4.85 (dd, $J_{2,3} = 1.04$ Hz, $J_{3,4} = 9.1$ Hz, 1H, H-3); 4.7 (d, $J_{1,2} = 9.3$ Hz, 1H, H-1); 4,45 (s, 2H, CH_2O); 3.73 (s, 3H, CH_3O); 3.73 – 3.64 (m, 2H, H-2, H-7a); 3.6 – 3.53 (m, 2H, H-5, H-7b); 3.37 (ddd, $J_{4,5} = 9.1$ Hz, 1H, H-4); 1.98 (s, 3H, OAc); 1.77 (s, 3H, NAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.7; 169.2 C=O; 158.7 C-p Ar; 130.3 C-i Ar; 129.0 C-o Ar; 113.6 C-m Ar; 87.6 C-1; 72.0 CH_2O; 68.7 C-6; 55.0 CH_3O; 52.8 C-2; 22.5 NAc; 20.6 OAc.

Reaction of **11b** *with Sodium Cyanoborohydride/Trifluoroacetic Acid*

A mixture of **11b** (3 g, 7.4 mmol), $NaCNBH_3$ (2.3 g, 37 mmol) and powdered molecular sieves 4 Å (6 g) in DMF (50 ml) and trifluoracetic acid (5.7 ml, 74 mmol) in DMF (45 ml) was reacted according to the procedure described for **13**. Flash chromatography on silica gel (100 g) in CH_2Cl_2/MeOH 40 : 1 yielded compounds **14** and **15**.

2-Acetamido-2-deoxy-6-O-(4-methoxybenzyl)-3-O-monochloroacetyl-β-D-glucopyranosyl Azide (**14**)

Yield: 1.01 g (35 %); mp. 132 °C (ethyl acetate/light petroleum ether/diisopropyl ether); $[\alpha]_D^{22} = -64.9$ °C (c 1, dichloromethane); $R_f = 0.45$ ($CHCl_3$/MeOH 10 : 1).

$C_{18}H_{23}ClN_4O_7$	Calcd.	C 48.82	H 5.24	N 12.65
(442.9)	Found	C 48.66	H 5.43	N 12.49

^{1}H-NMR (DMSO-d_6): δ [ppm]: 8.03 (d, $J_{2,NH} = 9.3$ Hz, 1H, NH); 7.25; 6.89 (2m, 4H, Ar); 5.63 (d, $J_{4,OH} = 5.8$ Hz, 1H, OH-4); 4.92 (dd, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 9.1$ Hz, 1H, H-3); 4.7 (d, $J_{1,2} = 9.3$ Hz, 1H, H-1); 4.44 (s, 2H, CH_2O); 4.34; 4.25 (2d, $J_{gem} = 15.2$ Hz, 2H, CH_2Cl); 3.76 – 3.69 (m, 2H, H-2, H-7a); 3.73 (s, 3H, CH_3O); 3.68 – 3.53 (m, 2H, H-5, H-7b); 3,44 (ddd, $J_{4,5} = 9.1$ Hz, 1H, H-4); 1.77 (s, 3H, NAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.3; 166.8 C=O; 158.6 C-p Ar; 130.2 C-i Ar; 129.0 C-o Ar; 113.6 C-m Ar; 87.5 C-1; 72.0 CH_2O; 68.5 C-6; 55.0 CH_3O; 52.5 C-2; 41.0, CH_2Cl; 22.5 NAc.

2-Acetamido-2-deoxy-6-O-(4-methoxybenzyl)-β-D-glucopyranosyl Azide (**15**)

Yield: 1.22 g (45 %); mp.: 142 °C (methanol/diisopropyl ether); $[\alpha]_D^{22} = -25.22$ °C (c 1, methanol);
$R_f = 0.25$ ($CHCl_3$/MeOH 10 : 1).

$C_{16}H_{22}N_4O_6$	Calcd.	C 52.45	H 6.05	N 15.29
(366.4)	Found	C 52.30	H 6.10	N 15.07

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.85 (d, $J_{2,NH} = 9.2$ Hz, 1H, NH); 7.24; 6.89 (2m, 4H, Ar); 5.3; 5.14 (2m, 2H, OH-3/4); 4,92 (dd, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 9.1$ Hz, 1H, H-3); 4.42 (s, 2H, CH_2O); 4.39 (d, $J_{1,2} = 9.3$ Hz, 1H, H-1); 3,73 (s, 3H, CH_3O); 3.69 (dd, $J_{vic} = 1.2$ Hz, $J_{gem} = 10.9$ Hz, 1H, H-7a); 3.55 – 3.1 (m, 5H, H-2, H-3, H-4, H-5, H-7b); 1.83 (s, 3H, NAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.3 C=O; 158.6 C-p Ar; 130.0 C-i Ar; 129 C-o Ar; 113.5 C-m Ar; 88.2 C-1; 71.9 CH_2O; 69.1 C-6; 54.9 CH_3O; 54.8 C-2; 22.8 NAc.

2-Acetamido-3,4-di-O-acetyl-2-deoxy-6-O-(4-methoxybenzyl)-β-D-glucopyranosyl Azide (**16**)

To **13** (2 g, 4.9 mmol) dissolved in pyridine (20 ml) were added 10 ml of acetic acid anhydride at 0 °C. After stirring for 8 h at room temperature, the mixture was concentrated in vacuo, and toluene (3 × 50 ml) was distilled off the residue in vacuo. The crude product was dissolved in dichloromethane (100 ml) and extracted with 1N HCl, water and 1N $KHCO_3$ (50 ml of each) and dried with $MgSO_4$. After evaporation of the solvent in vacuo, the residue was recrystallized from ethyl acetate/light petroleum ether.

Yield: 2.2 g (95 %); mp.: 144 °C; $[\alpha]_D^{22} = -12.4$ °C (c 1, dichloromethane); $R_f = 0.7$ ($CHCl_3$/MeOH 10 : 1).

$C_{20}H_{26}N_4O_8$	Calcd.	C 53.33	H 5.82	N 12.44
(450.5)	Found	C 53.29	H 5.78	N 12.44

^{1}H-NMR (DMSO-d_6): δ [ppm]: 8.06 (d, $J_{2,NH} = 9.2$ Hz, 1H, NH); 7.22; 6.89 (2m, 4H, Ar); 5.06 (dd, $J_{2,3} = J_{3,4} = 9.8$ Hz, 1H, H-3); 4.89 (dd, $J_{4,5} = 9.8$ Hz, 1H, H-4); 4,84 (d, $J_{1,2} = 9.7$ Hz, 1H, H-1); 4.43; 4.34 (2d, $J_{gem} = 11.5$ Hz, 2H, CH_2O); 3.9 (m, 1H, H-5); 3.78 (ddd, 1H, H-2); 3.73 (s, 3H, CH_3O); 3.51 (dd, $J_{vic} = 2.3$ Hz, $J_{gem} = 11.2$ Hz, 1H, H-7a); 3,45 (dd, $J_{vic} = 4.8$ Hz, 1H, H-7b); 1.90 (s, 6H, OAc); 1,78 (s, 3H, NAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.5 – 169.0 C=O; 158.7 C-p Ar; 129.8 C-i Ar; 129.2 C-o Ar; 113.5 C-m Ar; 87.5 C-1; 72.0 CH_2O; 67.7 C-6; 55.0 CH_3O; 52.6 C-2; 22.5 NAc; 20.3; 20.2 OAc.

2-Acetamido-3,4-di-O-acetyl-2-deoxy-β-D-glucopyranosyl Azide (**17**)

A solution of 1 g (2.2 mmol) of **16** in 10 ml of acetonitrile/water (9 : 1) was stirred with ceric ammonium nitrate (1 g). After the reaction was complete (t.l.c. control, $CHCl_3$/MeOH 10 : 1) additional 20 ml of acetonitrile were added, and the solvent was evaporated in vacuo. The residue was purified by flash chromatography on 30 g of silica gel in CH_2Cl_2/MeOH 15 : 1.
Yield: 667 mg (91 %), amorphous; $[\alpha]_D^{22} = -26.8$ °C (c 0.25, MeOH); $R_f = 0{,}35$ ($CHCl_3$/MeOH 10 : 1).

$C_{12}H_{18}N_4O_7$	Calcd.	C 43.64	H 5.49	N 16.96
(330.4)	Found	C 43.63	H 5.61	N 16.72

^{1}H-NMR (DMSO-d_6): δ [ppm]: 8.04 (d, $J_{2,NH} = 9.4$ Hz, 1H, NH); 5.06 (dd, $J_{2,3} = 10.1$ Hz, $J_{3,4} = 9.7$ Hz, 1H, H-3); 4.84 (dd, $J_{4,5} = 9.7$ Hz, 1H, H-4); 4.80 (d, $J_{1,2} = 9.4$ Hz, 1H, H-1); 3.78 (ddd, 1H, H-2); 3.7 (m, 1H, H-5); 3,52 (dd, $J_{vic} = 2$ Hz, $J_{gem} = 12.2$ Hz, 1H, H-7a); 3.4 (dd, $J_{vic} = 5.1$ Hz, 1H, H-7b); 1.96; 1.90 (2s, 6H, OAc); 1.78 (s, 3H, NAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 170.0 – 169.0 C=O; 87.6 C-1; 59.9 C-6; 52.6 C-2; 22.5 NAc; 20.3; 20.2 OAc.

2-Acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl Azide (**18**)

A solution of 0.5 g (1.1 mmol) of **16** in 10 ml of acetonitrile/water (9 : 1) was stirred with ceric ammonium nitrate (1 g). After the end of the reaction (t.l.c. control, $CHCl_3$/MeOH 10 : 1), silica gel (3 g) was added. The mixture was concentrated in vacuo and the residue finally dried in high vacuum. After a period of 3 d, **18** was obtained by flash chromatography on silica gel (20 g) in CH_2Cl_2/MeOH 15 : 1.
Yield: 200 mg (55 %); amorphous; $[\alpha]_D^{22} = -56.8$ °C (c 1, methanol); $R_f = 0.5$ ($CHCl_3$/MeOH 10 : 1).

$C_{12}H_{18}N_4O_7$	Calcd.	C 43.64	H 5.49	N 16.96
(330.4)	Found	C 43.63	H 5.61	N 16.72

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.98 (d, $J_{2,NH} = 9.4$ Hz, 1H, NH); 5.67 (d, $J_{4,OH} = 6$ Hz, 1H, OH-4); 4.85 (dd, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 9.4$ Hz, 1H, H-3); 4.72 (d, $J_{1,2} = 9.4$ Hz, 1H, H-1); 4.32 (dd, $J_{vic} = 1.5$ Hz, $J_{gem} = 12.3$ Hz, 1H, H-7a); 4,1 (dd, $J_{vic} = 6$ Hz, 1H, H-7b); 3.73 – 3.63 (m, 2H, H-2, H-5); 3.41 (ddd, $J_{4,5} = 9.4$ Hz, 1H, H-4); 2.04; 1.96 (2s, 6H, OAc); 1.76 (s, 3H, NAc).
^{13}C-NMR (DMSO-d_6): δ [ppm]: 170.0 – 169.0 C=O; 87.6 C-1; 62.8 C-6; 52.6 C-2; 22.5 NAc; 20.6; 20.5 OAc.

Cholesteryl-3, 4, 6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**20a**)

Cholesterol **19a** (200 mg, 0.52 mmol), glycosyl fluoride **8** (100 mg, 0.23 mmol) and 100 mg of powdered molecular sieves 4 Å were stirred in dichloromethane (4 ml) for 30 min. After addition of borontrifluoride etherate (5 drops) the reaction was monitored by t.l.c. (light petroleum ether/ethyl acetate 2 : 1). After the consumption of fluoride **8**, dichloromethane (100 ml) was added and the solution was extracted with 100 ml of 1N $KHCO_3$. After drying with $MgSO_4$ and concentration in vacuo, the remaining residue was stirred with pyridine/acetic acid anhydride (2 : 1, 10 ml) for 10 h. Repeated distillation with toluene (3 × 40 ml) gave a residue that was purified by flash chromatography on 50 g of silica gel in light petroleum ether/ethyl acetate 7 : 1.
Yield: 150 mg (82 %), amorphous; $[\alpha]_D^{22} = +24.5$ °C (c 0.25, dichloromethane); $R_f = 0.7$ (light petroleum ether/ethyl acetate 2 : 1).

$C_{47}H_{65}NO_{10}$	Calcd.	C 70.21	H 8.15	N 1.74
(804.0)	Found	C 69.91	H 8.22	N 2.02

^{1}H-NMR (DMSO-d_6/$CDCl_3$ 1 : 1): δ [ppm]: 7.8 (m, 4H, Ar); 5.6 (dd, $J_{2,3} = 10.7$ Hz, $J_{3,4} = 9.2$ Hz, 1H, H-3); 5.41 (d, $J_{1,2} = 8.5$ Hz, 1H, H-1); 4.98 (dd, $J_{4,5} = 10$ Hz, 1H, H-4); 4.25 (dd, $J_{vic} = 4.8$ Hz, $J_{gem} = 12.2$ Hz, 1H, H-7a); 4.1 – 3.95 (m, 3H, H-2, H-5, H-7b); 2.00; 1.97; 1.76 (3s, 9H, OAc); 0.58 (s, 3H, CH_3 Chol).

2-Acetamido-4-O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-3-O-acetyl-1,6-anhydro-2-deoxy-D-glucopyranose (**20b**)

2-Acetamido-3-O-acetyl-1,6-anhydro-2-deoxy-β-D-glucopyranose **19b** [15] (50 mg, 0.2 mmol), 150 mg (0.34 mmol) of glycosyl fluoride **8** and 150 mg of powdered molecular sieves 4 Å were stirred in 4 ml of dry dichloromethane for 30 minutes. Borontrifluoride etherate (5 drops) was added and the reaction was monitored by t.l.c. (ethyl acetate). After the fluoride **8** had disappeared, dichloromethane (100 ml) was added and the solution was extracted with 100 ml of 1N $KHCO_3$. Subsequent drying with $MgSO_4$ and concentration of the organic layer in vacuo, gave a residue that was purified by flash chromatography on 50 g of silica gel in ethyl acetate.
Yield: 124 mg (92 %), amorphous; $[\alpha]_D^{22} = -23.8$ °C (c 0.5, dichloromethane); $R_f = 0.4$ (ethyl acetate).

$C_{30}H_{34}N_2O_{15}$	Calcd.	C 54.38	H 5.17	N 4.23
(662.6)	Found	C 54.42	H 5.25	N 4.15

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.9 (m, 4H, Ar); 6.88 (d, $J_{2,NH} = 8.5$ Hz, 1H, NH); 5.69 (dd, $J_{2',3'} = 10.7$ Hz, $J_{3',4'} = 9.2$ Hz, 1H, H-3'); 5.55 (d, $J_{1',2'} = 8.6$ Hz, 1H, H-1'); 5.0 (m, 2H, H-1, H-4'); 4.8 (s, 1H, H-3); 4.3 – 4.15 (m, 3H, H-2', H-5, H-7a'); 4.05 – 3.95 (m, 2H, H-5', H-7b'); 3.88 (d, $J_{gem.} = 7.7$ Hz, 1H, H-7a); 3.65 (s, 1H, H-4); 3.55 (d, 1H, H-2); 3.47 (dd, $J_{vic} = 5.9$ Hz, 1H, H-7b); 2.01; 1.99; 1.89 (3s, 9H, OAc); 1.82 (s, 3H, NAc) 1.78 (s, 3H, OAc').
^{13}C-NMR (DMSO-d_6): δ [ppm]: 170.2 – 167.8 C=O; 135.2 C-4/5 Ar; 130.4 C-1/2 Ar; 123.7 C-2/6 Ar; 100.0 C-1; 96.8 C-1'; 64.6 C-6; 62.0 C-6; 54.4 C-2'; 49.6 C-2; 22.5 NAc; 21.0; 20.6; 20.3 OAc.

2-Acetamido-4-O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-3-O-acetyl-2-deoxy-6-O-(4-methoxybenzyl)-β-D-glucopyranosyl Azide (**21**)

To a solution of 2-acetamido-3-O-acetyl-2-deoxy-6-O-(4-methoxybenzyl)-β-D-glucopyranosyl azide **13** (2 g, 4.89 mmol) and 4.98 g (10 mmol) of 3, 4, 6-tri-O-acetyl-2-deoxy-2-phthalimido-glucopyranosyl bromide [8] **3** in dry nitromethane (15 ml) maintained at −10 °C was added dropwise a solution of 2.55 g (10 mmol) of silver trifluoromethanesulfonate and 1.21 g (10 mmol) of sym-collidine in 10 ml of dry nitromethane. After educt **13** was completely converted (t.l.c., $CHCl_3$/MeOH 10 : 1), the mixture was diluted with dichloromethane and filtered through a pad of Celite. The filtrate was extracted with 1N HCl (100 ml) and 1N $KHCO_3$ (100 ml), dried with $MgSO_4$ and concentrated in vacuo. The residue was purified twice by flash chromatography on 100 g of silica gel first in acetone/light petroleum ether (1 : 2) and subsequently in CH_2Cl_2/MeOH (50 : 1).
Yield: 3.41 g (83 %) amorphous solid; $[\alpha]_D^{22} = -17.5$ °C (c 0.5, dichloromethane); $R_f = 0.75$ ($CHCl_3$/MeOH 10 : 1).

$C_{38}H_{43}N_5O_{16}H_2O$	Calcd.	C 52.94	H 5.92	N 13.71
(843.8)	Found:	C 52.88	H 5.90	N 13.87

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.96 − 7.86 (m, 5H, Ar Pht, NH); 7.08; 6.87 (2m, 4H, Ar MPM); 5.61 (dd, $J_{2',3'}$ = 10.7 Hz, $J_{3',4'}$ = 9.2 Hz, 1H, H-3′); 5.34 (d, $J_{1',2'}$ = 8.3 Hz, 1H, H-1′); 4.97 (dd, $J_{3',4'}$ = 9.1 Hz, $J_{4',5'}$ = 10 Hz, 1H, H-4′); 4.93 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 9.2 Hz, 1H, H-3); 4.63 (d, $J_{1,2}$ = 9.4 Hz, 1H, H-1); 4.32 (dd, J_{vic} = 4 Hz, J_{gem} = 11.4 Hz, 1H, H-7a′); 4.17; 4.14 (2d, J_{gem} = 11.4 Hz, 2H, CH_2O); 3.97 − 3.9 (m, 2H, H-7b′, H-2′); 3.85 − 3.78 (m, 2H, H-4, H-5′); 3.74 (s, 3H, CH_3O); 3.66 (ddd, $J_{2,NH}$ = 9.4 Hz, 1H, H-2); 3.58 (m, 1H, H-5); 3.34 (dd, J_{vic} = 1.7 Hz, J_{gem} = 10.5 Hz, 1H, H-7a); 3.25 (dd, J_{vic} = 4.6 Hz, 11H, H-7b); 2.0; 1.99; 1.97 (3s, 9H, OAc); 1.75 (s, 6H, NAc, OAc).

2-(O-3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-acetimido-2-deoxy-3-O-monochloroacetyl-6-O-(4-methoxybenzyl)-β-D-glucopyranosyl Azide (**22**)

2-Acetamido-2-deoxy-6-O-(4-methoxybenzyl)-3-O-monochloroacetyl-β-D-glucopyranosyl azide (**14**) (100 mg, 0.226 mmol) was reacted with **3** [8] as has been described above for the analogous reaction of **13**. The product was purified by chromatography on 20 g of silica gel in light petroleum ether/ethyl acetate 2 : 1 and by recrystallization from dichloromethane/diisopropyl ether.
Yield: 155 mg (80 %); mp.: 171 °C; $[\alpha]_D^{22} = +21.3$ °C (c 0.5, dichloromethane); $R_f = 0.8$ ($CHCl_3$/MeOH 10 : 1).

$C_{38}H_{42}ClN_5O_{16}$	Calcd.	C 53.07	H 4.92	N 8.14
(860.1)	Found	C 53.00	H 5.20	N 8.27

^{1}H-NMR (DMSO-d_6): δ [ppm]: 7.92 − 7.82 (m, 4H, Ar Pht); 7.23; 6.88 (2m, 4H, Ar MPM); 6.59 (d, $J_{1',2'}$ = 8.9 Hz, 1H, H-1′); 5.78 (dd, $J_{2',3'}$ = 10.4 Hz, $J_{3',4'}$ = 9.6 Hz, 1H, H-3′); 5.52 (d, $J_{4',OH}$ = 5.7 Hz, 1H, OH-4′); 5.05 (dd, $J_{3',4'}$ = $J_{4',5'}$ = 9.6 Hz, 1H, H-4′); 4.95 (dd, $J_{2,3} = J_{3,4}$ = 9.4 Hz, 1H, H-3); 4.66 (d, $J_{1,2}$ = 8.5 Hz, 1H, H-1); 4.41 (m, 2H, CH_2O); 4.35 − 4.2 (m, 4H, CH_2Cl, H-2′, H-7a′); 4.08 (m, 1H, H-7b′) 3.85 (m, 1H, H-5′); 3.74 − 3.65 (m, 5H, CH_3O, H-5, H-7a); 3.53 (dd, J_{vic} = 5.2 Hz, J_{gem} = 11.2 Hz, 1H, H-7b); 3.44 (ddd, 1H, H-4); 3.16 (dd, $J_{2,3}$ = 9.7 Hz, 1H, H-2); 2.03; 2.00 (2s, 6H, OAc); 1.80; 1.77 (2s, 6H, N = C-CH_3, OAc).

^{13}C-NMR (DMSO-d_6): δ [ppm]: 169.9 − 161.7 C = O, C = N; 158.7 C-p MPM; 134.9 C-4/5 Pht; 130.6 C-1/2 Pht; 120.2 C-i MPM; 129.1 C-o MPM; 123.4 C-3/6 Pht; 113.5 C-m MPM; 89.4; 88.7 C-1, C-1′; 72.0 CH_2O; 68.5 C-6; 61,1 C-6′; 55,0; 53,4 CH_3O, C-2′, C-2; 40.2 CH_2Cl; 22.5 NAc; 20.3; 20.2; 19.9 OAc; 14.9 = C-CH_3.

References

[1] For review, see: a) J. Montreuil, Adv. Carbohydr. Chem. Biochem. **37** (1980), 157; b) H. Kunz: Angew. Chem. **99** (1987) 297; Angew. Chem., Int. Ed. Engl. **26** (1987) 294
[2] A. Yamamoto, C. Miyashita, H. Tsukamoto, Chem. Pharm. Bull. (Tokyo) **13** (1965) 1041
[3] H. Kunz, H. Kauth, Liebigs Ann. Chem. **1983**, 337
[4] M. Spinola, R.W. Jeanloz, J. Biol. Chem. **245** (1970) 4158
[5] H. Kunz, C. Unverzagt, Angew. Chem. **100** (1988) 1763; Angew. Chem., Int. Ed. Engl. **27** (1988) 1697
[6] D. Horton, M.L. Wolfram, J. Org. Chem. **27** (1962) 1794
[7] For the synthesis of the corresponding chitobiosyl azide, see: H. Kunz, H. Waldmann, Angew. Chem. **97** (1985) 885; Angew. Chem., Int. Ed. Engl. **24** (1985)
[8] R.U. Lemieux, T. Takeda, B.Y. Chung, ACS Symp. Ser. **39** (1976) 90; In contrast to results reported in this article, the N-phthaloyl glucosamine bromide **3** was not obtained as the pure β anomer, but as a mixture of anomers
[9] H. Kunz, W. Sager, Helv. Chim. Acta **68** (1985) 283; W. Sager: Diplomarbeit, Universität Mainz, 1983
[10] K.C. Nicolaou, A. Chuchulowsky, R.E. Dolle, J.L. Randall, J. Chem. Soc., Chem. Commun. **1984**, 1155
[11] H. Paulsen, Z. Györgydeak, M. Friedmann, Chem. Ber. **107** (1974) 1590
[12] L. Szilagyi, Z. Györgydeak, Carbohydr. Res. **143** (1985) 21
[13] R. Johansson, B. Samuelsson, J. Chem. Soc., Perkin Trans I **1984**, 2371
[14] P.J. Garegg, H. Hultberg, S. Wallin, Carbohydr. Res. **108** (1982) 97
[15] S. Oguri, S. Tejima, Chem. Pharm. Bull. **29** (1981) 1629
[16] J. Arnarp, M. Haraldsson, J. Lönngren, J. Chem. Soc., Perkin Trans I **1985**, 535
[17] H.H. Lee, D.A. Schwartz, J.F. Harris, J.P. Carver, J.J. Krepinsky, Can. J. Chem. **64** (1986) 1912
[18] W. Bröder, H. Kunz, Synlett **1990**, 251

Address for correspondence:

Prof. Dr. H. Kunz
Institut für Organische Chemie der
Johannes Gutenberg-Universität Mainz
J.-J.-Becher-Weg 18 − 20
W-6500 Mainz, Bundesrepublik Deutschland