Pergamon

Tetrahedron 55 (1999) 8397–8408

TETRAHEDRON

Passerini and Ugi Reactions of Benzyl and Acetyl Protected Isocyanoglucoses

Thomas Ziegler*, Hans-Josef Kaisers, Rolf Schlömer and Christoph Koch

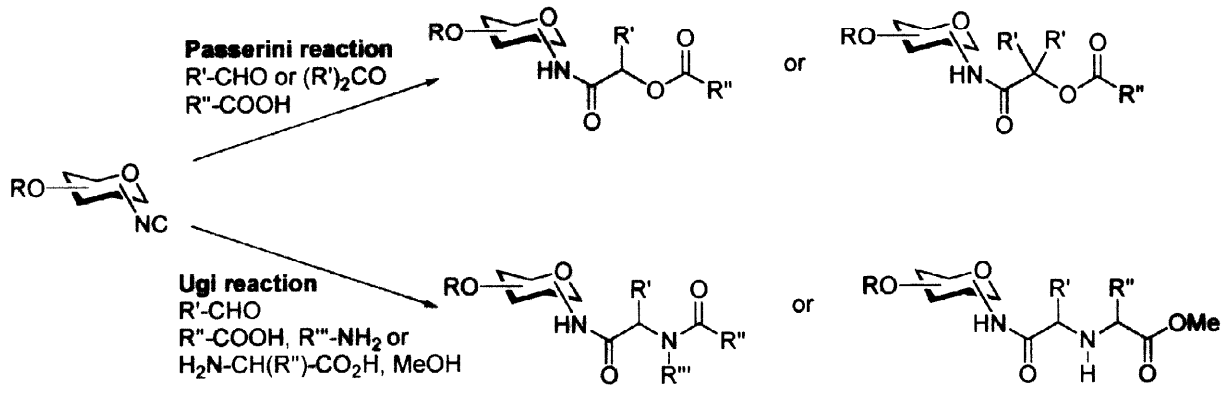
Institute of Organic Chemistry, University of Cologne, Greinstraße 4, D-50939 Cologne, Germany.

Received 29 April 1999; accepted 18 May 1999

Abstract: Acetyl and benzyl protected anomeric β-D-glucopyranosyl isonitriles and 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isocyano-β-D-glucopyranose were treated with various carbonyl compounds and carboxylic acids to give the corresponding Passerini reaction products and with *i*-butanal, carboxylic acids and amines or aminoacids to give the corresponding Ugi reaction products, respectively.

INTRODUCTION

As part of a project toward the synthesis of combinatorial libraries of glycopeptides we recently tested the potential of acetyl and benzyl protected anomeric glucosyl isonitriles in Passerini and Ugi reactions (Scheme 1).[1] Although isonitriles, in general, have found wide applications as substrates and reagents in organic synthesis, the chemistry of saccharides containing isonitrile functional groups has been examined only sporadeously yet.[2-5] Since applications of Ugi reactions for the combinatorial synthesis of peptide[6-8] and glycopeptide[9] libraries are well established and Ugi reactions of glucopyranosyloxymethyl isonitriles and 2-isocyanoethyl glucoside derivatives, respectively have been recently described for the synthesis of combinatorial libraries[10] we have now extended our previous investigation on Passerini and Ugi reactions of acetylated and benzylated anomeric glycosyl isonitriles[1] to 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isocyano-β-D-glucopyranose (**1c**). Furthermore, a comparison of the reactivity of isocyanoglucoses **1** with several aldehydes, carbonyl compounds and carboxylic acids, respectively as well as a detailed experimental procedures for Passerini and Ugi reactions of the latter will be given here.



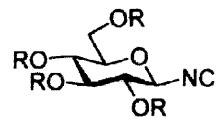
Scheme 1. Products of Passerini and Ugi reactions of isocyanoglycoses

* Fax: +49 (0) 221 470 5057; E-mail: thomas.ziegler@uni-koeln.de

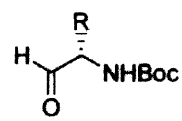
0040-4020/99/$ - see front matter
PII: S0040-4020(99)00461-5

RESULTS AND DISCUSSION

As isonitrile compounds for Passerini and Ugi reactions we chose 2,3,4,6-tetra-*O*-acetyl- (**1a**), 2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl isonitrile (**1b**), and 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isocyano-β-D-glucopyranose (**1c**). Compound **1a** was obtained from 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl azide[11] *via* subsequent hydrogenolysis, formylation and dehydration[12] as previously described. Compound **1b** was prepared from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose[13] which was first converted into the corresponding *β*-D-glucopyranosyl amine[14] followed by formylation and dehydration with diphosgene according to previously described procedures.[15] 2-Isocyanoglucose **1c** has been previously used for deoxygenations[16] and is easily accessible from 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose[17] *via* dehydration of its *N*-formyl derivative with diphosgene. Passerini reactions of isonitriles **1** afforded the condensation products **5** (Table 1) and were performed with *N*-Boc-glycinal[18] (**2a**), (*S*)-*N*-Boc-phenyl alaninal[18] (**2b**), and aldehydes and ketones **2c-f**, respectively as the carbonyl compound, and carboxylic acids **3a-d** as the acid compound. Ugi reactions of isonitriles **1** gave products **6** (Table 2) and were done with *i*-butanal **2d** as the carbonyl compound and with *N*-Boc-glycine (**3c**), and (*S*)-*N*-Boc-phenyl alanine (**3d**) as the acid compound. *n*-Propyl amine (**4a**) was used as the amine component in the case of Ugi 4 center 4 compound reactions (U-4CR) and with (*S*)-serine (**4b**) in methanol in the case of Ugi 5 center 4 compound reactions (U-5C-4CR).

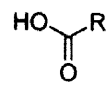


1a R = Ac
1b R = Bn

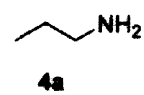


2a R = H
2b R = CH_2Ph

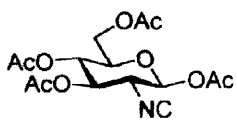
2e



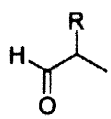
3a R = CH_3
3b R = H



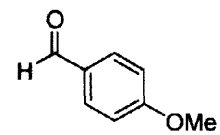
4a



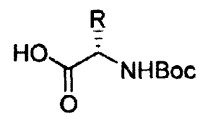
1c



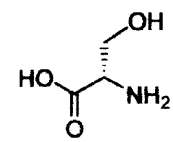
2c R = H
2d R = CH_3



2f



3c R = H
3d R = CH_2Ph



4b

In general, Passerini reactions of glycinal and phenyl alaninal derivatives **2a** and **2b** with anomeric glycosyl isonitriles **1a** and **1b**, respectively (Table 1, entries 1,2,4 and 5) proceeded significantly slower and with lower yield than the corresponding reactions with 2-isocyanoglucose **1c** (entries 8 and 9). It was evident from the TLC of the crude reaction mixture that the anomeric glucosyl isonitriles **1a** and **1b** were more sensitive under the reaction conditions (formation of products of decomposition) than isocyanide **1c**. Solely with propanal (**2c**), Passerini reaction of **1a** proceeded fast enough to give the corresponding condensation product **5c** in good yield (entry 3). Similarly, Passerini reactions of **1c** were sensitive to steric and electronic effects of the aldehyde component (entries 8-12 and 15). When isobutanal (**2d**) was used, high yields could only be obtained in special cases (entry 11) whereas aromatic aldehydes, such as **2f** (entry 15), resulted a slow reactivity. Since the diastereoselectivity of all Passerini reactions was low and separation of the formed diastereomeric products appeared to be impossible by simple chromatography, we also tested acetone (**2e**) as the carbonyl compound (entries 13 and 14). However, no reaction could be detected under conditions which have been suitable for Passerini reactions with aldehydes. When molar amounts of $ZnCl_2$ were added, TLC of

the reaction mixture showed fast consumption of the isonitrile component. However, only 15% of **5k** could be isolated with acetic acid as the carboxylic component (entry 13). When formic acid was used (entry 14), the deacylated Passerini product **5l'** was formed as the main product probably due to ester hydrolysis during work-up.

Table 1. Passerini Reactions of Isocyanoglucoses **1**.

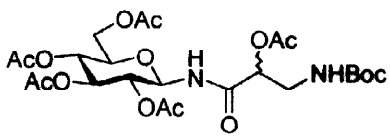
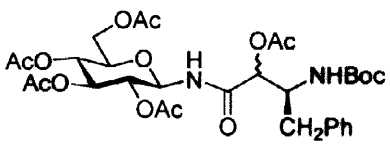
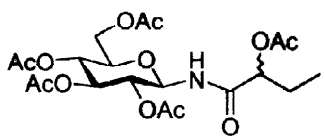
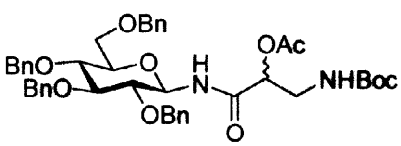
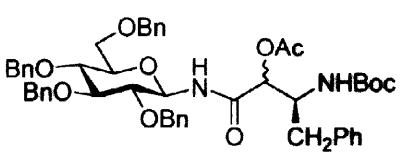
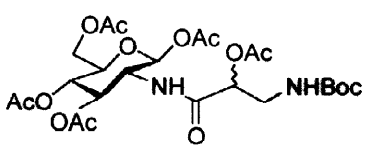
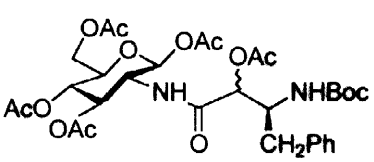
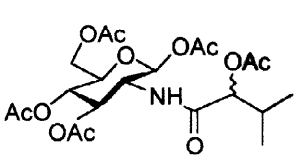
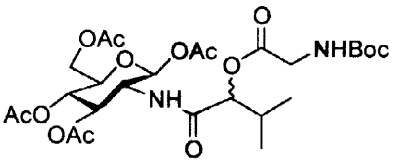
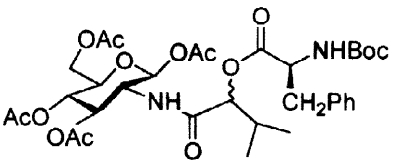
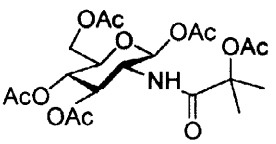
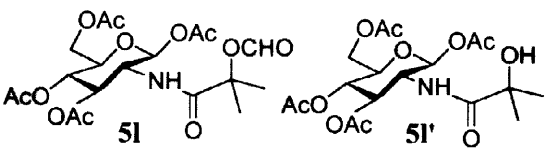
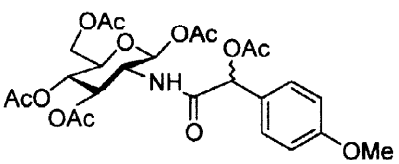
entry	R-NC	R-CHO	R-CO_2H	solvent conditions	yield d.r.	product (formula)
1	**1a**	**2a**	**3a**	CH_2Cl_2 3d RT	23% **5a** 55:45	
2	**1a**	**2b**	**3a**	CH_2Cl_2 3d RT	41% **5b** 58:42	
3	**1a**	**2c**	**3a**	CH_2Cl_2 24h RT	80% **5c** 50:50	
4	**1b**	**2a**	**3a**	CH_2Cl_2 6d RT	31% **5d** 57:43	
5	**1b**	**2b**	**3a**	CH_2Cl_2 8d RT	35% **5e** 52:48	
8	**1c**	**2a**	**3a**	CH_2Cl_2 3d RT	53% **5f** 57:43	
9	**1c**	**2b**	**3a**	CH_2Cl_2 4d RT	57% **5g** 60:40	
10	**1c**	**2d**	**3a**	CH_2Cl_2 8d RT	23% **5h** 53:47	

Table 1. Continued.

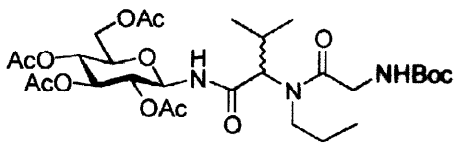
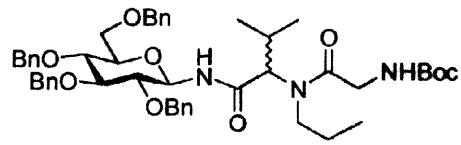
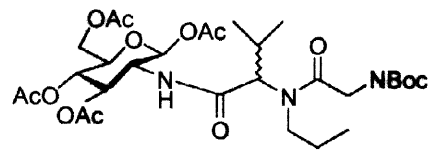
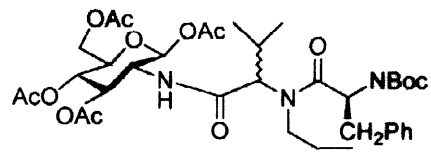
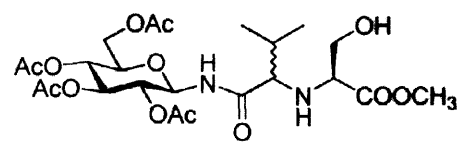
entry	R-NC	R-CHO	R-CO_2H	solvent conditions	yield d.r.	product (formula)
11	**1c**	**2d**	**3c**	CH_2Cl_2 28h RT	90% **5i** 53:47	
12	**1c**	**2d**	**3d**	CH_2Cl_2 3d RT	35% **5j** 58:42	
13	**1c**	**2e**	**3a**	CH_2Cl_2 cat. $ZnCl_2$ 5h 0 °C	15% **5k**[a]	
14	**1c**	**2e**	**3b**	acetone cat. $ZnCl_2$ 3h 0 °C	14% **5l** 44% **5l'**	 **5l** **5l'**
15	**1c**	**2f**	**3a**	CH_2Cl_2 12d RT	17% **5m** 56:44	

[a]Crude product.

In the case of Ugi reactions (Table 2) of isocyanoglucoses **1**, the differences in the reactivity of anomeric glucosyl isonitriles and 2-isocyanoglucose was not as pronounced as for the corresponding Passerini reactions. All reactions were rather slow and gave the Ugi products in low yield. Furthermore, all examples tested here did not show any significant diastereoselectivity. Compared to the U-4CR of anomeric glycosyl isonitriles **1a** and **1b**, no higher reactivity of 2-isocyanoglucose **1c** could be observed. When sterically hindered amines (*i.e.* 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl amine) were used as the amine component no condensation could be achieved at all (details not shown here). In the case of the reactions of 2-isocyanoglucose **1c** with isobutanal (**2d**), n-propyl amine (**4a**) and *N*-Boc-glycine (**3c**) or *N*-Boc-(*S*)-phenyl alanine (**3d**), respectively (Table 2, entries 3 and 4), the diastereoselectivity could not be determined quantitatively. However, as was evident from the NMR spectra of compounds **6c** and **6d**, both products appeared to be mixtures of diastereomers. These findings are in sharp contrast to the observed high diastereoselectivities of Ugi reactions with glycosyl amines as the amine component.[3,4] Here, high selectivities

were frequently found. However, it is well known from other Ugi reactions that neither the isonitrile component nor the acid component have pronounced effects on the diastereoselectivity of the reaction.[2-5,19] Ugi 5 center 4 compound reactions (U-5C-4CR)[20-22] were solely possible with glucosyl isonitrile **1a** (entry 5). When 2-isocyanoglucose **1c** was used as the isonitrile component, reaction with *i*-pronanal (**2d**) and (*S*)-serine (**4b**) in methanol resulted in complete decomposition of the starting material according to the TLC of the crude reaction mixture. This might be due to the acetyl group at the anomeric center of **1c** which can result in deacetylation under the reaction conditions. Similarly, (*S*)-alanine gave no Ugi reaction at all with all isonitriles **1** (details not shown).

Table 2. Ugi Reactions of Isocyanoglucoses **1**.

entry	R-NC	R-CHO	R-CO_2H	R-NH_2	solvent conditions	yield d.r.	product (formula)
1	**1a**	**2d**	**3c**	**4a**	CH_2Cl_2 37d RT	22% **6a** 55:45	
2	**1b**	**2d**	**3c**	**4a**	CH_2Cl_2 25d RT	35% **6b** 60:40[a]	
3	**1c**	**2d**	**3c**	**4a**	CH_2Cl_2 30d RT	31% **6c** -[b]	
4	**1c**	**2d**	**3d**	**4a**	CH_2Cl_2 18d RT	19% **6d** -[c]	
5	**1a**	**2d**	**4b**	**4b**	MeOH 11h 55°C	15% **6e** 63:37[a]	

[a] Separation of diastereomers by chromatography is possible; [b] d.r. not determined, 22% of starting material **1c** was reisolated; [c] d.r. not determined, 30% of starting material **1c** was reisolated.

Although diastereoselectivities of Passerini and Ugi reactions of isocyanoglucoses **1** were low in all examples where aldehydes have been used as the carbonyl compound, both reactions provide easy access to complex glycopeptide derivatives. Furthermore, if all components are tuned thoroughly toward their reactivity, good yields of Passerini and Ugi products, respectively can be obtained.

EXPERIMENTAL

General: The NMR data were obtained from spectra measured in $CDCl_3$ solutions (with Me_4Si as internal standard) at 25°C with a Bruker AMX 300 spectrometer. ^1H NMR signal assignments were made by first-order analysis of the spectra and by HH-COSY spectra. Of the two magnetically non-equivalent geminal protons at C-6 of the glucose residues of compounds **5** and **6**, 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 CH-COSY spectra. Signals of diastereomers in the NMR spectra of mixtures of compounds **5** and **6** were allocated as plain and italic fonts, respectively. Diastereomeric ratios (d.r.) of the products in Tables 1 and 2, respectively were determined from the ^1H NMR spectra by integration of significant signals. Optical rotations were measured at 25°C with a Perkin-Elmer automatic polarimeter, Model 241. TLC was performed on precoated plastic sheets, Polygram SIL UV_{254}, 40 x 80mm (Macherey-Nagel) using appropriately adjusted mixtures of toluene-acetone. Detection was affected by UV light, where applicable, and by charring with 5% H_2SO_4 in ethanol. CC was performed by eluting from columns of Silica Gel 60 (Merck) with appropriately adjusted mixtures of toluene/acetone. Solutions in organic solvents were dried with anhydr. Na_2SO_4 and concentrated at 2 kPa, <40°C.

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl isonitrile (**1a**): Formyl acetate (20 ml, 0.254 mol) was added at 0°C to a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl amine (9.1 g, 26 mmol), freshly prepared from 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide[11] by hydrogenation with Pd on charcoal, in ethyl acetate (250 ml), stirred for 7 h at 20°C, and concentrated. The residue (9.8 g) was dissolved in CH_2Cl_2 (250 ml), diisopropyl amine (100 ml, 0.71 mol) was added, and the mixture was cooled to 0°C. $POCl_3$ (24 ml, 0.26 mmol) was added dropwise and stirring was continued for 12 h. The mixture was poured with stirring into cold saturated aqueous $NaHCO_3$ solution (600 ml), the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried and concentrated. Chromatography (toluene/acetone 12:1) of the residue afforded **1a**[23] (6.0 g, 65%). ^1H NMR: δ = 5.17-5.05 (m, 3H, H-2,3,4), 4.82-4.78 (m, 1H, H-1), 4.17 (2dd, 2H, $J_{5,6a}$ 4.7 Hz, $J_{5,6b}$ 2.2 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a,6b), 3.75-3.69 (m, 1H, H-5); ^{13}C NMR: δ = 164.7 (CN), 79.4 (C-1), 74.6 (C-5), 72.1 (C-3), 71.0 (C-2), 67.3 (C-4), 61.3 (C-6).

2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl isonitrile (**1b**): Formyl acetate (4.4 ml, 56 mmol) was added at 0°C to a solution of 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl amine[14] (3.0 g, 6 mmol) in ethyl acetate (150 ml), stirred for 16 h at 20°C, and concentrated. The residue (3.15 g) was dissolved in CH_2Cl_2 (50 ml) and Et_3N (1.3 ml, 10 mmol) and diphosgene (0.32 ml, 6 mmol) was added at 0°C. The mixture was stirred for 2 h at 20°C, washed with water and aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (CH_2Cl_2/MeOH 10:1) of the residue gave **1b**[24] (2.54 g, 83%). ^1H NMR: δ = 7.39-7.11 (m, 20H, CH_2Ph), 4.99-4.45 (m, 9H, H-1, CH_2Ph), 3.72-3.50 (m, 5H, H-2,3,4,6a,6b), 3.47-3.41 (m, 1H, H-5).

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-isocyano-β-D-glucopyranose (**1c**): Formyl acetate (20 ml, 0.254 mol) was added at 0°C to a solution of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose[17] (8.9 g, 25.6 mmol) in ethyl acetate (300 ml), stirred for 5 h at 20°C, and concentrated. The residue (10.3 g) was dissolved in CH_2Cl_2 (200 ml) and Et_3N (9.7 ml, 67 mmol) and diphosgene (2.14 ml, 18 mmol) was added at 0°C. The mixture was stirred for 5 h at 20°C, washed with water and aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (toluene/acetone 12:1) of the residue gave **1c**[16] (8.2 g, 84%). Mp. (EtOH)

132.5°C (ref.[16] 131-132°C). ^{1}H NMR: δ = 5.80 (d, 1H, $J_{1,2}$ 8.6 Hz, H-1), 5.39 (dd, 1H, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 9.5 Hz, H-3), 5.00 (t, 1H, $J_{4,5}$ 9.5 Hz, H-4), 4.30 (dd, 1H, $J_{5,6a}$ 4.4 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.09 (dd, 1H, $J_{5,6b}$ 10.5 Hz, H-6b), 3.88 (ddd, 1H, H-5), 3.81 (d, 1H, H-2); ^{13}C NMR: δ = 162.2 (CN), 91.2 (C-1), 73.0 (C-3), 72.0 (C-5), 67.1 (C-4), 61.2 (C-6), 56.1 (C-2).

General Procedure for Passerini Reactions:. A solution of the isonitrile component **1**, aldehyde component **2** and acid component **3** in CH_2Cl_2 was stirred at RT until TLC showed complete conversion of the starting material **1** or increasing decomposition of the strating materials (Table 1). The mixture was diluted with CH_2Cl_2, washed with water, dried, and concentrated. Chromatography of the residue afforded **5**.

N-(2-Acetoxy-3-t-butoxycarbonylamido-propionyl)-2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl amine (**5a**): According to the General Procedure, **1a** (625 mg, 1.75 mmol), freshly prepared **2a**[18] (287 mg, 1.8 mmol), and **3a** (0.1 ml, 1.75 mmol) in CH_2Cl_2 (5 ml) afforded **5a** (232 mg, 23%) as a 55:45 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR: δ = 7.15 (d, 1H, J 9.0 Hz, NH), 7.04 (d, 1H, J 9.0 Hz, *NH*), 5.28 (t, 1H, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 9.5 Hz, H-3), 5.27 (t, 1H, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 9.5 Hz, *H-3*), 5.22-5.00 (m, 6H, H-1,4,CH,*1,4,CH*), 4.93 (dd, 1H, $J_{1,2}$ 9.7 Hz, H-2), 4.83 (dd, 1H, $J_{1,2}$ 9.7 Hz, *H-2*), 4.84-4.73 (m, 4H, CH_2, *CH_2*), 4.33-4.24 (m, 2H, H-6a,*6a*), 4.03 (d, 2H, H-6b,*6b*), 3.82-3.75 (m, 2H, H-5,*5*); ^{13}C NMR: δ = 78.1 (C-1,*1*), 73.7 (C-5,*5*), 72.5 (CH, *CH*), 72.3 (C-3,*3*), 70.3 (C-2,*2*), 68.0 (C-4,*4*), 61.4 (C-6,*6*), 41.4 (CH_2), 40.8 (*CH_2*). Anal. calcd for $C_{24}H_{36}N_2O_{14}$: C, 50.00; H, 6.29; N, 4.86; Found: C, 49.45; H, 6.35; N, 4.61. FAB-MS (pos.): 577 (M+H).

N-(2-Acetoxy-3-(S)-t-butoxycarbonylamido-4-phenyl-butanoyl)-2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl amine (**5b**): According to the General Procedure, **1a** (171 mg, 0.48 mmol), freshly prepared **2b**[18] (119 mg, 0.5 mmol), and **3a** (27 µl, 0.48 mmol) in CH_2Cl_2 (3 ml) afforded **5b** (130 mg, 41%) as a 58:42 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR: δ = 8.86 (d, 1H, J 9.4 Hz, NH), 8.78 (d, 1H, J 9.5 Hz, *NH*), 6.90 (d, 1H J 9.0 Hz, NH), 6.59 (d, 1H, J 9.3 Hz, *NH*), 5.51 (d, 1H, $J_{1,2}$ 9.3 Hz, H-1), 5.37 (d, 1H, $J_{1,2}$ 9.4 Hz, *H-1*), 5.34 (dd, 2H, $J_{2,3}$ 9.4 Hz, $J_{3,4}$ 9.5 Hz, H-3,*3*), 5.15 (d, 1H, J 3.7 Hz, CH), 5.02 (t, 1 H, H-2), 4.92 (m, 3H, H-*2*,4,*4*), 4.70 (d, 1H, J 4.2 Hz, *CH*), 4.01-4.22 (m, 8H, H-5,6a,*5,6a*, CH_2, *CH_2*), 4.06 (dd, 1H, $J_{5,6b}$ 2.1 Hz, $J_{6a,6b}$ 12.4 Hz, H-6b), 3.93 (d, 1H, *H-6b*); ^{13}C NMR: δ = 76.1 (C-1,*1*), 74.2 (CH), 73.9 (*CH*), 72.9 (C-5), 72.8 (*C-5*), 72.2 (C-3), 72.0 (*C-3*), 70.5 (c-2), 70.2 (*C-2*), 67.7 (C-4,*4*), 61.7 (C-6), 61.6 (*C-6*). Anal. calcd for $C_{31}H_{42}N_2O_{14}$: C, 55.85; H, 6.35; N, 4.20; Found: C, 56.07; H, 6.43; N, 4.07.

N-(2-Acetoxy-butanoyl)-2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl amine (**5c**): According to the General Procedure, **1a** (357 mg, 1.0 mmol), **2c** (58 mg, 1.0 mmol), and **3a** (56 µl, 1.0 mmol) in CH_2Cl_2 (3 ml) afforded **5c** (380 mg, 80%) as a 50:50 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR (significant signals): δ = 6.90 (d, 1H, J 9.2 Hz, NH), 6.82 (d, 1H, J 9.2 Hz, *NH*), 0.93 (t, 3H, J 7.4 Hz, CH_3), 0.84 (t, 3H, J 7.4 Hz, *CH_3*). Anal. calcd for $C_{20}H_{29}NO_{12}$: C, 50.52; H, 6.16; N, 2.95; Found: C, 50.52; H, 6.26; N, 2.80.

N-(2-Acetoxy-3-t-butoxycarbonylamido-propionyl)-2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl amine (**5d**): According to the General Procedure, **1b** (315 mg, 0.57 mmol), freshly prepared **2a**[13] (96 mg, 0.6 mmol), and **3a** (33 µl, 0.57 mmol) in CH_2Cl_2 (3 ml) afforded **5d** (135 mg, 31%) as a 57:43 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR (significant signals): δ = 6.72 (d, 1H, J 9.4 Hz, NH), 6.54 (d, 1H, J 9.6 Hz, *NH*), 1.40 (s, 9H, Boc), 1.36 (s, 9H, *Boc*); ^{13}C NMR: δ = 86.0 (C-3,*3*), 80.1 (C-2,*2*), 79.6 (C-

1,*1*), 78.8 (C-5,*5*), 77.2 (C-4,*4*), 67.9 (C-6,*6*), 41.1 (CH_2, CH_2). Anal. calcd for $C_{44}H_{52}N_2O_{10}$: C, 68.73; H, 6.82; N, 3.64; Found: C, 68.58; H, 6.78; N, 3.43.

N-(2-Acetoxy-3-(S)-t-butoxycarbonylamido-4-phenyl-butanoyl)-2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl amine (**5e**): According to the General Procedure, **1b** (608 mg, 1.1 mmol), freshly prepared **2b**[13] (261 mg, 1.1 mmol), and **3a** (65 µl, 1.1 mmol) in CH_2Cl_2 (5 ml) afforded **5e** (324 mg, 35%) as a 52:48 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR (significant signals): δ = 6.62 (d, 1H J 9.4 Hz, NH), 6.50 (d, 1H, J 9.1 Hz, *NH*), 1.35 (s, 9H, Boc), 1.28 (s, 9H, *Boc*); ^{13}C NMR: δ = 86.0 (C-3), 85.8 (*C-3*), 80.5 (C-2), 79.5 (*C-2*), 79.1 (C-1), 78.8 (*C-1*), 78.7 (C-5,*5*), 76.6 (C-4,*4*), 68.1 (C-6,*6*). Anal. calcd for $C_{51}H_{58}N_2O_{14}$: C, 71.31; H, 6.81; N, 3.26; Found: C, 71.25; H, 6.86; N, 3.10.

N-(2-Acetoxy-3-t-butoxycarbonylamido-propionyl)-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5f**): According to the General Procedure, **1c** (500 mg, 1.3 mmol), freshly prepared **2a**[13] (271 mg, 1.7 mmol), and **3a** (79 µl, 1.4 mmol) in CH_2Cl_2 (5 ml) afforded **5f** (385 mg, 53%) as a 57:43 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR: δ = 6.61 (d, 1H, NH), 6.59 (d, 1H, *NH*), 5.81 (d, 1H, $J_{1,2}$ 8.68 Hz, H-1), 5.80 (d, 1H, $J_{1,2}$ 8.82 Hz, *H-1*), 5.28 (dd, 2H, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 9.6 Hz, H-3, *H-3*), 5.14 (t, 2H, $J_{4,5}$ 9.7 Hz, H-4, *H-4*), 5.07-4.87 (m, 2H, CHOAc, *CHOAc*), 4.31-4.20 (m, 4H, H-2, *H-2*, H-6b, *H-6b*), 4.12 (dd, 2H, $J_{5,6a}$ 2.2 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a, *H-6a*), 3.88-3.84 (m, 2H, H-5, *H-5*), 3.63-3.36 (m, 4H, CH_2N, *CH_2N*), 2.17-2.03 (m, 30H, Ac, *Ac*), 1.45, 1.43 (2 s, 18H, Boc, *Boc*); ^{13}C NMR: δ = 92.3 (C-1), 92.1 (*C-1*), 72.9 (2C, CHOAc, *CHOAc*), 72.8 (C-3), 72.7 (*C-3*), 72.1 (C-5), 71.7 (*C-5*), 67.8 (C-4), 67.7 (*C-4*), 61.6 (C-6), 53.2 (C-2), 53.0 (*C-2*), 28.23 (Boc, *Boc*). Anal. calcd for $C_{24}H_{36}N_2O_{14}$: C, 50.00; H, 6.29; N, 4.86; Found: C, 49.88; H, 6.13; N, 4.80.

N-(2-Acetoxy-3-(S)-t-butoxycarbonylamido-4-phenyl-butanoyl)-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5g**): According to the General Procedure, **1c** (500 mg, 1.3 mmol), freshly prepared **2b**[13] (299 mg, 1.3 mmol), and **3a** (79 µl, 1.4 mmol) in CH_2Cl_2 (7 ml) afforded **5g** (478 mg, 57%) as a 60:40 mixture of diastereomers after chromatography (toluene/acetone 12:1). ^{1}H NMR (d_6-DMSO): δ = 8.33 (d, 1H, NH), 8.12 (d, 1H, *NH*), 7.12-7.28 (m, 10H, Ph, *Ph*), 6.87 (d, 1H, J 8.96 Hz, CHOAc), 6.61 (d, 1H, J 8.96 Hz, *CHOAc*), 5.83 (d, 1H, $J_{1,2}$ 8.67 Hz, H-1), 5 73 (d, 1H, $J_{1,2}$ 8.82 Hz, *H-1*), 5.31-5.23 (m, 2H, H-3, *H-3*), 4.88 (dd, 2H, $J_{3,4}$ 9.8 Hz, H-4, *H-4*), 4.21-3.90 (m, 8H, H-2, *H-2*, H-5, *H-5*, H-6a, *H-6a*, H-6b, *H-6b*), 2.14-1.83 (m, 30H, Ac, *Ac*), 1.26, 1.19 (2 s, 18H, Boc, *Boc*); ^{13}C NMR(d_6-DMSO): δ = 91.5 (C-1), 71.8 (C-3), 71.7 (*C-3*), 71.6 (C-5,*5*), 68.3 (C-4), 61.4 (C-6), 51.6 (C-2), 51.4 (*C-2*). Anal. calcd for $C_{31}H_{42}N_2O_{14}$: C, 55.85; H, 6.35; N, 4.20; Found: C, 55.59; H, 6.72; N, 4.09.

N-(2-Acetoxy-3-methyl-butanoyl)-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5h**): According to the General Procedure, **1c** (606 mg, 1.54 mmol), **2d** (183 µl, 2.0 mmol), and **3a** (92 µl, 1.6 mmol) in CH_2Cl_2 (7 ml) afforded **5h** (184 mg, 23%) as a 53:47 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR: δ = 6.15 (d, 2H, $J_{1,2}$ 9.7 Hz, H-1, *H-1*), 5.70 (t, 1H, $J_{2,3}$ = $J_{3,4}$ 8.68 Hz, H-3), 5,67 (t, 1H, $J_{2,3}$ = $J_{3,4}$ 8.82 Hz, *H-3*), 5,26-5,13 (m, 4H, H-4, *H-4*, NH, *NH*), 4.91 (d, 1H, J 4.7 Hz, CHOAc), 4.76 (d, 1H, J 5.4 Hz, *CHOAc*), 4.42-4.33 (m, 2H, H-2, *H-2*), 4.26 (dd, 1H, $J_{5,6b}$ 4.5 Hz, H-6b), 4.27 (dd, 1H, $J_{5,6b}$ 4.5 Hz, *H-6b*), 4.12 (dd, 2H, $J_{5,6a}$ 3.5 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a, *H-6a*), 3.82 (ddd, 2H, $J_{4,5}$ 9.7 Hz, H-5, *H-5*), 2.79-2.58 (m, 2H, $CHMe_2$, *$CHMe_2$*), 2.25-2.01 (m, 30H, Ac, *Ac*), 0.91 (ddt, 12H, Me, *Me*); ^{13}C NMR: δ = 92.4 (C-1), 92.3(*C-1*), 78.4 (CHOAc), 78.0 (*CHOAc*), 73.0 (C-5), 72.9 (*C-5*), 72.1 (C-3), 71.8 (*C-3*), 68.0 (C-4), 67.6 (*C-4*), 61.6 (C-

6), 52.3 (C-2), 52.2 (*C-2*), 30.3 ($CHMe_2$), 30.2 (*$CHMe_2$*), 18.5 (Me), 18.4 (*Me*), 16.8 (Me), 17.2 (*Me*). Anal. calcd for $C_{21}H_{31}NO_{12}$: C, 51.53; H, 6.38; N, 2.86; Found: C, 51.48; H, 6.53; N, 2.84.

N-[2-(t-Butoxycarbonylamido-acetoxy)-3-methyl-butanoyl]-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5i**): According to the General Procedure, **1c** (827 mg, 2.11 mmol), **2d** (195 µl, 2.14 mmol), and **3c** (370 mg, 2.11 mmol) in CH_2Cl_2 (5 ml) afforded **5i** (1.11 g, 90%) as a 53:47 mixture of diastereomers after chromatography (toluene/acetone 10:1). ^{1}H NMR: δ = 7.33 (d, 1H, NH), 7.16 (d, 1H, *NH*), 5.86 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 5.67 (d, 1H, $J_{1,2}$ 9.0 Hz, *H-1*), 5.34-5.24 (m, 4H, H-3, *H-3*, H-9, *H-9*), 5.10 (2dd, 2H, $J_{3,4}$ 9.4 Hz, H-4, *H-4*), 5.01 (d, 1H, J 3.5 Hz, CH-O), 4.88 (d, 1H, J 4.3 Hz, *CH-O*), 4.42-4.17 (m, 4H, H-2, *H-2*, H-6b, *H-6b*), 4.10 (dd, 2H, $J_{5,6a}$ 2.1 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a, *H-6a*), 4.00-3.70 (m, 6H, H-5, *H-5*, CH_2-N, *CH_2-N*), 2.28-2.15 (m, 2H, $HCMe_2$, *$HCMe_2$*), 2.12-1.99 (m, 24H, Ac, *Ac*), 1.49, 1.46 (2 s, 18H, Boc, *Boc*), 0.97-0.88 (m, 12H,Me, *Me*); ^{13}C NMR: δ = 92.3 (C-1), 91.9 (*C-1*), 80.8 ($C_{quart.}$), 80.7 (*$C_{quart.}$*), 79.3 (CH-O), 78.8 (*CH-O*), 72.6 (2C, C-5,5), 72.2 (C-3), 72.1 (*C-3*), 68.4 (C-4), 68.0 (*C-4*), 61.6 (C-6), 61.5 (*C-6*), 52.3 (C-2), 51.7 (*C-2*), 29.8 ($CHMe_2$, *$CHMe_2$*). Anal. calcd for $C_{26}H_{40}N_2O_{14}$: C, 51.65; H, 6.67; N, 4.63; Found: C, 51.64; H, 6.66; N, 4.46.

N-[2-(2-(S)-t-Butoxycarbonylamido-3-phenyl-propanoyl)-3-methyl-butanoyl]-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5j**): According to the General Procedure, **1c** (840 mg, 2.13 mmol), **2d** (195 µl, 2.14 mmol), and **3d** (566 mg, 2.14 mmol) in CH_2Cl_2 (8 ml) afforded **5j** (504 mg, 35%) as a 58:42 mixture of diastereomers after chromatography (toluene/acetone 12:1). ^{1}H NMR: δ = 7.58 (d, 2H, NH, *NH*), 5.82 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 5.61 (d, 1H, $J_{1,2}$ 9.0 Hz, *H-1*), 5.39-5.26 (m, 2H, H-3, *H-3*), 5.13-5.00 (m, 3H, H-4, *H-4*, CH-O), 4.84 (d, 1H, *CH-O*), 4.54-4.16 (m, 6H, H-2, *H-2*, H-6b, *H-6b*, CH-N, *CH-N*), 4.10 (2dd, 2H, H-6a, *H-6a*, $J_{5,6a}$ 2.1 Hz, $J_{6a,6b}$ 12.4 Hz), 3.85-3.78 (m, 1H, H-5, *H-5*, $J_{5,6b}$ 4.4 Hz), 3.30-2.88 (m, 4H, CH_2Ph, *CH_2Ph*), 2.36-2.23 (m, 2H, $CHMe_2$, *$CHMe_2$*), 1.99-2.17 (m, 24H, Ac, *Ac*), 1.40 (s, 18H, Boc), 1.49 (s, 18H, *Boc*); ^{13}C NMR: δ = 92.4 (C-1), 92.0 (*C-1*), 81.1 ($C_{quart.}$), 81.0 (*$C_{quart.}$*), 79.3 (CH-O), 79.0 (*CH-O*), 72.6 (2C, C-5,5), 72.6 (C-3), 72.1 (*C-3*), 68.5 (C-4), 68.4 (*C-4*), 61.7 (C-6), 61.6 (*C-6*), 52.6 (C-2), 51.5 (*C-2*). Anal. calcd for $C_{33}H_{46}N_2O_{14}$: C, 57.05; H, 6.67; N, 4.03; Found: C, 57.38; H, 6.89; N, 3.88.

N-(2-Acetoxy-2methyl-propionyl)-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5k**): According to the General Procedure, **1c** (632 mg, 1.61 mmol), **2e** (150 µl, 2.0 mmol), **3a** (100 µl, 1.7 mmol) $ZnCl_2$ 2.2M in diethylether (750 µl, 1.65 mmol) in CH_2Cl_2 (5 ml) afforded crude **5k** (111 mg, 15%), contaminated by products of decomposition. FAB-MS (pos.): 498 (M+Na), 416 (M-AcO).

N-(2-Formyloxy-2methyl-propionyl)-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5l**) *and N-(2-hydroxy-2methyl-propionyl)-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose* (**5l'**): According to the General Procedure, **1c** (925 mg, 2.35 mmol), **2e** (15 ml, 204 mmol), **3b** (95 µl, 2.42 mmol) $ZnCl_2$ 2.2M in diethylether (1.1 ml, 2.4 mmol) in acetone (15 ml) containing 4A molecular sieves (1 g) afforded at 0°C first **5l** (146 mg, 14%) after chromatography (toluene/acetone 6:1). $[\alpha]_D^{20}$ = -4.0 (*c* 1.2, $CHCl_3$); ^{1}H NMR: δ = 6.43 (d, 1H, J 9.6 Hz, NH), 5.70 (d, 2H, $J_{1,2}$ 8.8 Hz, H-1), 5.26 (dd, 1H, $J_{3,4}$ 9.7 Hz, H-3), 5.15 (t, 1H, $J_{4,5}$ 9.7 Hz, H-4), 4.38 (dd, 1H, $J_{2,3}$ 10.5 Hz, H-2), 4.27 (dd, 1H, $J_{5,6b}$ 4.9 Hz, H-6a), 4.12 (dd, 1H, $J_{6a,6b}$ 12.4 Hz, H-6b), 3.86 (ddd, 1H, $J_{5,6a}$ 2.2 Hz, H-5), 2.12-2.06 (m, 12H, Ac), 1.56 (s, Me); ^{13}C NMR: δ = 92.3 (C-1), 81.0 (C-O), 72.9 (C-5), 72.1 (C-3), 68.0 (C-4), 61.8 (C-6), 52.5 (C-2), 24.4 (2C, Me) , 20.8, 20.7, 20.6, 20.5 (Ac). Anal. calcd for $C_{19}H_{27}NO_{12}$: C, 49.43; H, 5.90; N, 3.04; Found: C, 49.83; H, 5.91; N, 2.94. Eluted next was **5l'** (450 mg, 44%). $[\alpha]_D^{20}$ = -14.1 (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ = 7.03 (d, 1H, NH), 5.82 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 5.28 (dd, 1H, $J_{2,3}$ 10.4 Hz, H-3), 5.15 (t, 1H, $J_{3,4}$ = $J_{4,5}$ 9.5 Hz, H-4), 4.32-4.22 (m, 2H, H-2, H-6a), 4.15 (dd, 1H, $J_{5,6a}$ 2.4 Hz,

$J_{6a,6b}$ 12.5 Hz, H-6b), 3.87 (ddd, 1H, $J_{5,6b}$ 4.7 Hz, H-5), 2.87 (s, 1H, OH), 2.10 (s, 6H, Ac), 2.05, 2.03 (s, 6H, Ac), 1.38 (s, 6H, Me); ^{13}C NMR: δ = 92.5 (C-1), 73.5 (C-O), 72.9 (C-3), 72.5 (C-5), 67.9 (C-4), 61.8 (C-6), 52.7 (C-2), 27.5 (2C, Me), 20.7, 20.5 (Ac). FAB-MS (pos.): 456 (M+Na), 374 (M-AcO).

N-(2-Acetoxy-2-p-methoxyphenyl-acetyl)-2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5m**): According to the General Procedure, **1c** (847 mg, 2.15 mmol), **2f** (125 µl, 2.16 mmol), and **3a** (123 µl, 2.16 mmol) in CH_2Cl_2 (10 ml) afforded **5m** (206 mg, 17%) as a 56:44 mixture of diastereomers after chromatography (toluene/acetone 6:1). ^1H NMR: δ = 8.07 (dd, 2H, Ph), 7.32 (dd, 4H, Ph, *Ph*), 6.86 (dd, 2H, *Ph*), 6.42 (d, 1H, NH, J 9.7 Hz), 6.40 (d, 1H, *NH*, J 9.7 Hz), 5.84 (s, 1H, CH-O), 5.77 (s, 1H, *CH-O*), 5.71 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 5.69 (d, 1H, $J_{1,2}$ 8,8 Hz, *H-1*), 5.25-5.08 (m, 4H, $J_{2,3}$ 9.8 Hz, $J_{4,5}$ 9.4 Hz, H-3, *H-3*, H-4, *H-4*), 4.40-4.29 (m, 2H, H-2, *H-2*), 4.27-4.21 (m, 2H, $J_{5,6b}$ 4.7 Hz, $J_{6a,6b}$ 12.5 Hz, H-6b, *H-6b*), 4.14-4.09 (m, 2H, $J_{5,6a}$ 2.1 Hz, H-6a, *H-6a*), 3.88 (s, 6H, OMe, *OMe*), 3.82-3.76 (m, 2H, H-5, *H-5*); ^{13}C NMR: δ = 92.4 (C-1), 92.2 (*C-1*), 75.4 (2C, CH-O, *CH-O*), 73.1 (2C, C-4,*4*), 72.1 (C-5), 71.7 (*C-5*), 67.8 (C-3), 67.5 (*C-3*), 61.7 (C-6), 61.6 (*C-6*), 55.3 (2C, OMe, *OMe*), 52.4 (2C, C-2, *C-2*). Anal. calcd for $C_{25}H_{31}NO_{13}$: C, 54.25; H, 5.65; N, 2.53; Found: C, 54.51; H, 5.45; N, 2.43.

General Procedure for Ugi Reactions: A solution of the isonitrile component **1**, aldehyde component **2**, acid component **3**, and amine component **4** in CH_2Cl_2 was stirred at RT until TLC showed complete conversion of the starting material **1** or increasing decomposition of the starting material (Table 2). The mixture was diluted with CH_2Cl_2, washed with water, dried, and concentrated. Chromatography of the residue afforded **6**.

N-[3-Methyl-2-(N-propyl-t-butoxycarbonylamido-acetamido)]-butanoyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl amine (**6a**): According to the General Procedure, **1a** (300 mg, 0.84 mmol), **2d** (77 µl, 0.84 mmol), **3c** (147 mg, 0.84 mmol), and **4a** (70 µl, 0.84 mmol) in CH_2Cl_2 (6.5 ml) afforded **6a** (121 mg, 22%) as a 55:45 mixture of diastereomers after chromatography (toluene/acetone 12:1). ^1H NMR: δ = 7.72 (d, 1H, J 9.4 Hz, NH), 7.56 (d, 1H, J 9.4 Hz, *NH*), 5.61-5.39 (m, 2H, NHBoc, *NHBoc*), 5.27-5.12 (m, 4H, H-1,3, *H-1,3*), 5.06-4.97 (m, 2H, H-4, *H-4*), 4.95-4.85 (m, 2H, H-2, *H-2*), 4.27-4.17 (m, 2H, H-6a, *H-6b*), 4.07-4.00 (m, 2H, H-5, *H-5*), 3.98 (m, 2H, H-6b, *H-6b*), 3.78-3.70 (m, 4H, CH_2N, *CH_2N*), 3.21-3.05 (m, 4H, CH_2N, *CH_2N*), 1.42 (s, 9H, Boc), 1.40 (s, 9H, *Boc*); ^{13}C NMR: δ = 77.9 (C-1), 77.7 (*C-1*), 73.5 (C-5), 73.4 (*C-5*), 72.9 (2C, C-3,*3*), 70.6 (C-2), 70.4 (*C-2*), 68.2 (2C, C-4,*4*), 61.7 (2C, C-6,*6*). Anal. calcd for $C_{29}H_{47}N_3O_{13}$: C, 53.94; H, 7.34; N, 6.51; Found: C, 53.40; H, 7.34; N, 6.19. FAB-MS (pos.): 646 (M+H).

N-[3-Methyl-2-(N-propyl-t-butoxycarbonylamido-acetamido)]-butanoyl 2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl amine (**6b**): According to the General Procedure, **1b** (313 mg, 0.57 mmol), **2d** (52 µl, 0.57 mmol), **3c** (100 mg, 0.57 mmol), and **4a** (47 µl, 0.57 mmol) in CH_2Cl_2 (5 ml) afforded **6b** (148 mg, 31%) as a 60:40 mixture of diastereomers after chromatography (toluene/acetone 12:1). Rechromatography (CH_2Cl_2/acetone 20:1) of the diastereomeric mixture afforded first diastereomer I (73 mg, 15%). $[\alpha]_D^{20}$ = +15.7 (*c* 0.5, $CHCl_3$); ^1H NMR: δ = 5.32 (s, 1H, NH), 5.12 (dd, 1H, $J_{1,2}$ 9.0 Hz, $J_{1,NH}$ 9.2 Hz, H-1), 3.92-3.72 (m, 2H, CH_2), 3.76-3.62 (m, 4H, H-3,5,6a,6b), 3.55-3.46 (m, 1H, H-4), 3.41-3.34 (m, 1H, H-2), 3.16-2.90 (m, 2H, NCH_2), 2.72-2.50 (m, 1H, CH), 1.89-1.72 (m, 1H, CH), 1.60-1.40 (m, 2H, CH_2), 1.45 (s, 9H, Boc); ^{13}C NMR: δ = 85.9 (C-3), 81.1 (C-2), 78.9 (C-1), 77.6 (C-5), 76.5 (C-4), 68.3 (C-6), 49.3, 42.5 (NCH_2), 28.3 ($C_{quart.}$), 26.2 (CH), 22.0 (CH_2), 19.7, 19.0, 11.1 (CH_3). Anal. calcd for $C_{49}H_{63}N_3O_9$: C, 70.23; H, 7.58; N, 5.01; Found: C, 69.74; H, 7.50; N, 4.64. FAB-MS (pos.): 839 (M+H). Eluted next was diastereomer II (49 mg, 10%). $[\alpha]_D^{20}$ = -22.3 (*c* 0.9, $CHCl_3$); ^1H NMR: δ = 5.36 (s, 1H, NH), 5.09 (dd, 1H, $J_{1,2}$ 9.0 Hz, $J_{1,NH}$ 9.3 Hz, H-1), 3.97-3.89 (m, 2H, CH_2),

3.76-3.67 (m, 4H, H-3,5,6a,6b), 3.55-3.51 (m, 1H, H-4), 3.43-3.36 (m, 1H, H-2), 3.11-3.02 (m, 2H, NCH_2), 2.56-2.41 (m, 1H, CH), 1.94-1.76 (m, 1H, CH), 1.61-1.37 (m, 2H, CH_2), 1.45 (s, 9H, Boc); ^{13}C NMR: δ = 86.3 (C-3), 81.4 (C-2), 79.5 (C-1), 78.1 (C-5), 77.0 (C-4), 68.7 (C-6), 49.0, 42.9 (NCH_2), 28.7 ($C_{quart.}$), 26.7 (CH), 22.7 (CH_2), 20.5, 19.8, 11.9 (CH_3). Anal. calcd for $C_{49}H_{63}N_3O_9$: C, 70.23; H, 7.58; N, 5.01; Found: C, 69.10; H, 7.59; N, 4.66. FAB-MS (pos.): 839 (M+H).

N-[3-Methyl-2-(N-propyl-t-butoxycarbonylamido-acetamido)]-butanoyl 2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**6c**): According to the General Procedure, **1c** (1.55 g, 4.13 mmol), **2d** (390 µl, 4.22 mmol), **3c** (746 mg, 4.17 mmol), and **4a** (350 µl, 4.2 mmol) in CH_2Cl_2 (10 ml) afforded unreacted **1c** (355 mg, 22%) and **6c** (834 mg, 31%) after chromatography (toluene/acetone 10:1). ^1H NMR: δ = 5.82 (d, 1H, $J_{1,2}$ 8.7 Hz, H-1), 5.80 (d, 1H, $J_{1,2}$ 8.7 Hz, *H-1*), 5.65 (m, 2H, NH, *NH*), 5.31 (t, 1H, $J_{3,4}$ 9.7 Hz, H-3), 5.23 (t, 1H, $J_{3,4}$ 10.1 Hz, *H-3*), 5.13-4.94 (m, 4H, $J_{4,5}$ 9.4 Hz, $J_{3,4}$ 9.4 Hz, H-4, *H-4*, CHCO, *CHCO*), 4.28 (dd, 2H, $J_{5,6b}$ 4.6 Hz $J_{6a,6b}$ 12.5 Hz, H-6a, *H-6a*), 4.18-3.92 (m, 6H, H-2, *H-2*, H-6b, *H-6b*, CH_2N, *CH_2N*), 3.84-3.80 (m, 2H, H-5, *H-5*), 3.16-3.11 (m, 4H, CH_2N, *CH_2N*), 2.58-2.46 (m, 2H, $CHMe_2$, *$CHMe_2$*), 1.49, 1.48 (2s, 9H, Boc), 1.45 (s, 9H, *Boc*); ^{13}C NMR: δ = 92.3 (C-1), 92.0 (*C-1*), 79.7 (2C, BOC), 77.4 (2C, CHNH), 71.9, 72.6 (4C, C-3,*3*,5,*5*), 68.0 (C-4), 67.9 (*C-4*), 61.6 (C-6), 61.5 (*C-6*), 53.1 (C-2), 28.4 (BOC), 28.3 (*BOC*). Anal. calcd for $C_{29}H_{47}N_3O_{13}$: C, 53.94; H, 7.34; N, 6.51; Found: C, 53.36; H, 7.33; N, 6.29. FAB-MS (pos.): 668 (M+Na), 644 (M-AcO).

N-[3-Methyl-2-(N-propyl-2-(S)-t-butoxycarbonylamido-3-phenyl-propionamido)]-butanoyl 2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**6d**): According to the General Procedure, **1c** (1.4 g, 3.72 mmol), **2d** (350 µl, 3.8 mmol), **3d** (995 mg, 3.75 mmol), and **4a** (315 µl, 3.75 mmol) in CH_2Cl_2 (10 ml) afforded unreacted **1c** (420 mg, 30%) and **6c** (514 mg, 19%) after chromatography (toluene/acetone 10:1). ^1H NMR: δ = 5.70 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 5.61 (d, 1H, $J_{1,2}$ 8.8 Hz, *H-1*), 5.33-5.00 (m, 5H, H-3, *H-3*, H-4, *H-4*, CHCO), 4.84 (d, 1H, J 3.2 Hz, *CHCO*), 4.79-4.48 (m, 2H, CHN, *CHN*), 4.33-4.20 (m, 4H, H-2, *H-2*, H-6a, *H-6a*), 4.17-4.05 (m, 2H, H-6b, *H-6b*), 3.84-3.73 (m, H-5, *H-5*), 3.32-2.85 (m, 4H, $PhCH_2$, *$PhCH_2$*), 2.69-2.38 (m, 2H, $CHMe_2$, *$CHMe_2$*); ^{13}C NMR: δ = 92.5 (2C, C-1, *C-1*), 81.1 (2C, Boc, *Boc*), 80.9 (CH), 79.8 (*CH*), 72.9, 72.6 (4C, C-5,*5*,3,*3*), 67.8 (2C, C-4,*4*), 61.5 (C-6), 52.2 (C-2), 51.9 (*C-2*), 28.4 (Boc), 28.3 (*Boc*). Anal. calcd for $C_{39}H_{53}N_3O_{13}$: C, 58.76; H, 7.26; N, 5.71; Found: C, 58.21; H, 7.20; N, 5.11. FAB-MS (pos.): 758 (M+Na), 676 (M-AcO).

N-3-Methyl-2-[(S)-2-hydoxy-1-methoxycarbonyl-1-ethyl-amino]-butanoyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl amine (**6e**): According to the General Procedure, **1a** (300 mg, 0.84 mmol), **2d** (77 µl, 0.84 mmol), **4b** (88 mg, 0.84 mmol), and triethylamine (120 µl, 0.84 mmol) in methanol (10 ml) afforded after 11h at 55°C **6e** (68 mg, 15%) as a 63:37 mixture of diastereomers after chromatography (toluene/acetone 2:1). Rechromatography (toluene/acetone 3:1) of the diastereomeric mixture afforded diastereomer I (19 mg, 4%) still contaminated by traces of diastereomer II. FAB-MS (pos.): 549 (M+H). Eluted next was pure main diastereomer II (33 mg, 7%). $[\alpha]_D^{20}$ = +17.1 (*c* 1.0, $CHCl_3$); ^1H NMR: δ = 7.57 (d, 1H, $J_{1,NH}$ 9.3 Hz, NH), 5.20, 5.25 (2d, 2H, $J_{1,2}$ 9.6 Hz, $J_{3,4}$ 10.0 Hz, H-1,3), 5.04 (t, 1H, $J_{4,5}$ 9.4 Hz, H-4), 4.93 (t, 1H, $J_{2,3}$ 9.6 Hz, H-2), 4.28 (dd, 1H, $J_{5,6a}$ 4.6 Hz, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.02 (dd, 1H, $J_{5,6b}$ 2.2 Hz, H-6b), 3.82-3.69 (m, 3H, H-5, CH_2O), 3.72 (s, 3H, CH_3), 3.26 (t, 1H, J 3.8 Hz, NCH_2), 2.93 (d, 1H, J 4.7 Hz, CH), 2.12-1.90 (m, 1H, CH), 0.96 (d, 3H, J 6.8 Hz, CH_3), 0.87 (d, 3H, J 6.9 Hz, CH_3); ^{13}C NMR: δ = 77.9 (C-1), 72.9 (C-3), 70.4 (C-4), 68.2 (C-2), 65.7 (CH), 61.7 (C-6), 61.5 (2C, C-5, NCH_2), 19.4, 17.3 (CH_3). Anal. calcd for $C_{23}H_{36}N_2O_{13}$: C, 50.36; H, 6.61; N, 5.11; Found: C, 50.02; H, 6.64; N, 4.88. FAB-MS (pos.): 549 (M+H).

ACKNOWLEDGMENT

We thank Dr. H. Schmickler, and C. Schmitz, University of Cologne for performing the NMR spectra and elemental analyses. This work was financially supported by the Fonds der Chemischen Industrie and Aventis Research & Technologies (formerly Hoechst).

REFERENCES

1. Ziegler, T.; Schlömer, R.; Koch, C., *Tetrahedron Lett.*, **1998**, *39*, 5957-5960.
2. (a) For a review of the literature up to 1983 see: Witzak, Z.J., *J. Carbohydr. Chem.*, **1984**, *3*, 359-380. (b) Witczak, Z.J., *Tetrahedron Lett.*, **1986**, *27*, 155-158.
3. Ewing, D.F.; Hiebl, J.; Humble, R.W.; Mackenzie, G.; Raynor, A.; Zbiral, E., *J. Carbohydr. Chem.*, **1993**, *12*, 923-932.
4. For the use of glycosyl amines in Ugi reactions see: Kunz, H., *Houben-Weyl*, **1996**, E 21, 1945-1952.
5. Lehnhoff, S.; Goebel, M.; Karl, R.M.; Klösel, R.; Ugi, I., *Angew. Chem.*, **1995**, *107*, 1208-1211; *Angew. Chem. Int. Ed. Engl.*, **1995**, *34*, 1104-1107.
6. Keating, T.A.; Armstrong, R.W., *J. Am. Chem. Soc.*, **1995**, *117*, 7842-7843.
7. Tempest, P.A.; Brown, S.D.; Armstrong, R.W., *Angew. Chem.*, **1996**, *108*, 689-691; *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 640-642.
8. Ugi, I.; Dömling, A.; Gruber, B.; Almstetter, M., *Croatia Chem. Acta*, **1997**, *70*, 631-647.
9. Sutherlin, D.P.; Stark, T.M.; Hughes, R.; Armstrong, R.W., *J. Org. Chem.*, **1996**, *61*, 8350-8354.
10. Lockhoff, O., *Angew. Chem.*, **1998**, *110*, 3634-3637; *Angew. Chem. Int. Ed.*, **1998**, *37*, 3436-3439.
11. Tropper, F.D.; Andersson, F.O.; Braun, S.; Roy, R., *Synthesis* **1992**, 618-620.
12. Nolte, R.J.M.; van Zomeren, J.A.J.; Zwikker, J.W., *J. Org. Chem.*, **1978**, *43*, 1972-1975.
13. Glaudemans, C.P.J; Fletcher, H.G., *Methods Carbohydr. Chem.*, **1972**, *6*, 373-376.
14. Aebischer, B.M.; Hanssen, H.W.; Vasella, A.; Schweizer, W.B., *J. Chem. Soc. Perkin Trans. 1*, **1982**, 2139-2147.
15. Ugi, I.; Skorna, G., *Angew. Chem.*, **1977**, *89*, 267-268; *Angew. Chem. Int. Ed. Engl.*, **1977**, *16*, 259.
16. Barton, D.H.R.; Bringmann, G.; Lamotte, G.; Porter, A.E.A., *J. Chem. Soc. Perkin Trans 1*, **1980**, 2657-2664.
17. Bergmann, M.; Zervas, I., *Ber. Dtsch. Chem. Ges.*, **1931**, *64*, 975-980.
18. Iizuka, I., *Chem. Pharm. Bull.*, **1990**, *38*, 2487-2493.
19. Ugi, I. in *The Peptides* (Gross, E.; Meienhofer, J., Eds.), Academic Press, New York **1980**, pp.365.
20. Demharter, A.; Hörl, W.; Herdtweck, E.; Ugi, I. *Angew. Chem.*, **1996**, *108*, 185-187; *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 173-175.
21. Ugi, I.; Demharter, A.; Hörl, W.; Schmidt, T. *Tetrahedron* **1996**, *52*, 11657-11662.
22. Ugi, I.; Hörl, W.; Hanusch-Kompa, C.; Schmidt, T.; Herdtweck, E. *Heterocycles* **1998**, *47*, 965-975.
23. Martin-Lomas, M.; Chancon-Fuertes, M.E. *Carbohydr. Res.*, **1977**, *59*, 604-606.
24. Boullanger, P.; Marmet, D.; Descotes, G. *Tetrahedron*, **1979**, *35*, 163-167.