

Synthesis of *N*-(β -D-glucopyranosyl)- and *N*-(2-acetamido-2-deoxy- β -D-glucopyranosyl) amides as inhibitors of glycogen phosphorylase

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Abstract—2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl- and 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl azides were transformed into the corresponding per-*O*-acetylated *N*-(β -D-glucopyranosyl) amides via a PMe_3 mediated Staudinger protocol (generation of *N*-(β -D-glucopyranosyl)imino-trimethylphosphoranes followed by acylation with carboxylic acids, acid chlorides or anhydrides). The deprotected compounds obtained by Zemplén deacetylation were evaluated as inhibitors of rabbit muscle glycogen phosphorylase *b*. The best inhibitor of this series has been *N*-(β -D-glucopyranosyl) 3-(2-naphthyl)-propenoic amide ($K_i = 3.5 \mu\text{M}$).

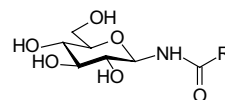
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1. Introduction

N-Glycosyl amides represent a long known class of carbohydrate derivatives readily available by acylation of glycosylamines¹ or more advantageously from glycosyl azides and carboxylic acids or their activated derivatives via an *N*-glycosyl iminophosphorane intermediate (Staudinger reaction).² Contradictory results can be found in the literature for the preparation of 2-acetamido-2-deoxy-D-glucopyranosyl derivatives by the latter procedure.^{3–5} Other methods of preparation have been surveyed and critically evaluated recently.² Nowadays growing interest in constructing *N*-glycopyranosyl amides is fuelled by the recognition of the importance of glycoproteins in which one sort of the linkages between sugar and peptide is of glycosylamide type.^{6–14} Very recently *N*-glycosyl amides have been converted

into glycosyl donors thereby rendering this functionality to be a protecting group at the anomeric centre.¹⁵

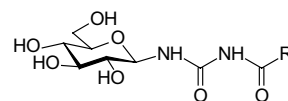
Some *N*-(β -D-glucopyranosyl) amides (e.g., A–C) were investigated as inhibitors of glycogen phosphorylase (GP) enzymes during the pioneering studies by Fleet,



A R = CH₃ K_i = 32 μM

B R = C₆H₅ K_i = 81 μM

C R = NH₂ K_i = 140 μM



D R = CH₃ K_i = 370 μM

E R = C₆H₅ K_i = 4.6 μM

F R = C₁₀H₇ K_i = 0.4 μM
(2-naphthyl)

Keywords: *N*-Glycosylamides; Inhibitors; Glycogen phosphorylase.

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Johnson and Oikonomakos exploring glucose analogue inhibitors of GP.¹⁶ Besides the academic aspects of this research inhibition of liver GP is one of several intensively investigated approaches to find novel treatments for type 2 diabetes mellitus.^{17–24}

Lately we have found that *N*-(β-D-glucopyranosyl)-*N'*-acyl urea derivatives **D** and **E** are also inhibitors of GP,²⁵ and **F** represents the most efficient glucose analogue inhibitor known to date.²⁴ A unique property for **E** and **F** is that they can also bind to the so-called new allosteric site of GP besides the catalytic centre,²⁵ which has been known to be the sole specific binding site for glucose analogues.

Based on these preliminaries we set out to prepare novel glucopyranosylamides to compare their effects on GP to those of acyl ureas having the same R group. Furthermore, in order to divert the potential inhibitors from the highly glucose specific catalytic site, 2-acetamido-2-deoxy-β-D-glucopyranosyl amides were also designed. In this paper we report on the synthesis of these glycosylamides by a modified Staudinger protocol, and enzyme assays of the deprotected derivatives.

2. Results and discussion

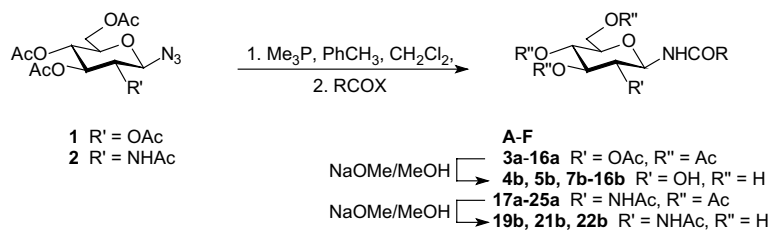
2.1. Synthesis

Acylation of *N*-glycosyl iminophosphoranes obtained from protected glycosyl azides by various phosphanes

(PPh₃, P(*n*-Bu)₃, PEt₃) was investigated in detail by several groups.^{3,4,26,27} Even the latest works demonstrate that the most widely applied PPh₃ results in variably moderate yields disregarding difficulties of work-up and purification due to the formation of P(=O)Ph₃.²⁸ Recently we have introduced the use of PMe₃ offering advantages over the above mentioned reagents:² (a) enhanced nucleophilicity of the iminophosphorane due to the small size of this phosphane allows the use of carboxylic acids as acylation agents; (b) volatility of P(=O)Me₃ ensures simplified work-up and separation of the target compound. Following this methodology and starting with per-*O*-acetylated β-D-glucopyranosyl azide (**1**) a variety of carboxylic acids (or in some cases derivatives) were used as acylating agents to give *N*-(β-D-glucopyranosyl) amides with diverse alkyl, aralkyl, aralkenyl and aralkynyl moieties (**3a**–**16a**, Table 1).

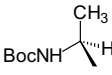
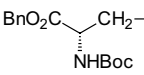
Contrary to the reported failure with PPh₃ and P(*n*-Bu)₃,⁵ the PMe₃-mediated Staudinger protocol performed well with the per-*O*-acetylated 2-acetamido-2-deoxy-β-D-glucopyranosyl azide (**2**) as well, and gave the corresponding amides **17a**–**23a** in acceptable to good yields (Table 1). It is noteworthy that reaction times were generally longer with **2** as compared to **1**. In order to demonstrate the potential of the method more complex carboxylic acids were also shown to produce glucopyranosyl amides **24a** and **25a**. Amide **25a** was prepared earlier by various acylations of the corresponding glycosylamine obtained by reduction of azide **2**.^{29–31}

Table 1. Synthesis of *N*-(β-D-glucopyranosyl)- and *N*-(2-acetamido-2-deoxy-β-D-glucopyranosyl) amides and inhibition data with RMGPb^a



Entry	Starting material	R	X	Product (yield [%])	<i>K_i</i> (μM)	IC ₅₀ (mM)
1		CH ₃		A	32 ¹⁶ 31 ³²	
2		C ₆ H ₅		B	81 ¹⁶ 144 ³²	
3		NH ₂		C	140 ¹⁶	
4		NHCOCH ₃		D	370 ²⁵	
5		NHCOC ₆ H ₅		E	4.6 ²⁵	
6		NHCOC ₁₀ H ₇ (2-naphthyl)		F	0.4 ²⁴	
7	1	<i>n</i> -C ₅ H ₁₁	OH	3a (70)		
8	1	(CH ₃) ₃ C	Cl	4a (72) 4b (96)		7.5
9	1	<i>c</i> -C ₆ H ₁₁	OH	5a (67) 5b (88)	289	
10	1	C ₁₀ H ₁₅ (1-adamantyl)	OH	6a (25)		
11	1	C ₆ H ₅ CH ₂	OH	7a^b (88) 7b (83)		1.1

Table 1 (continued)

Entry	Starting material	R	X	Product (yield [%])	K_i (μ M)	IC ₅₀ (mM)
12	1	(C ₆ H ₅) ₂ CH	OH	8a (21)	No inhibition up to 0.7mM	
13	1	C ₆ H ₅ CH ₂ CH ₂	OH	8b (17) 9a (64) 9b (99)		
14	1	C ₆ H ₅ CH=CH	OH	10a (80) 10b (87)		
15	1	C ₆ H ₅ C≡C	OH	11a (82) 11b (98)	18	4.5
16	1	4-CH ₃ -C ₆ H ₄	OH	12a (37) 12b (48)	61	
17	1	4-C ₆ H ₅ -C ₆ H ₄	OH	13a (55) 13b (85)	281	
18	1	C ₁₀ H ₇ (1-naphthyl)	OH	14a (52) 14b (75)	444	10
19	1	C ₁₀ H ₇ (2-naphthyl)	Cl	15a (62) 15b ^c (92)	10	
20	1	C ₁₀ H ₇ CH=CH (2-naphthyl)	OH	16a (71) 16b (93)	3.5	
21	2	CH ₃	OH OCOCH ₃	17a ^d (69) (68)	g	g
22	2	CF ₃	OCOCF ₃	18a (77)		
23	2	<i>n</i> -C ₁₁ H ₂₃	Cl	19a ^e (91) 19b (87)		
24	2	C ₆ H ₅	OH	20a ^f (43)	g	g
25	2	3,4,5-(CH ₃ O) ₃ -C ₆ H ₂	Cl	21a (67) 21b (78)		
26	2	C ₁₀ H ₇ (2-naphthyl)	Cl	22a (54) 22b (88)		
27	2	4-Cl-C ₆ H ₄ -O-CH ₂	OH	23a (45)		
28	2		OH	24a (73)		
29	2		OH	25a (69)		

^a Rabbit muscle glycogen phosphorylase *b*.^b This compound was obtained as a minor product (yield ~10%) together with its anomer from the reaction of **1** with PPh₃ and 2-thiopyridyl phenylacetate.³³^c Performed with KCN in MeOH.^d Prepared earlier from the corresponding glycosylamine by acetic anhydride in pyridine.^{34–37}^e Prepared earlier from the corresponding glycosylamine by dodecanoic anhydride in pyridine.³⁵^f Prepared earlier from the corresponding glycosylamine by benzoic anhydride in pyridine³⁵ or MeOH.³⁴^g Because of poor solubility of the compound the value could not be determined.

Deprotections were performed by the Zemplén method or KCN in MeOH to give compounds **4b**, **5b**, **7b–16b**, **19b**, **21b** and **22b** (Table 1).

2.2. Evaluation of the inhibitors

A comparison of inhibitors **A**, **4b** and **5b** (entries 1, 8 and 9) shows that an increase in the size of the aliphatic substituent makes the inhibition significantly weaker. Saturation of the aromatic ring of **B** (compare entries 2 and 9) as well as the presence of substituents in the 4-position of the phenyl ring (**12b** and **13b** in entries 16 and 17) also weakens the inhibition. The distance of the phenyl ring from the anomeric carbon (compare **B**, **7b** and **9b** in entries 2, 11 and 13) seems very important. Restriction of the conformational mobility of the

phenyl moiety as in **10b** and **11b** (entries 14 and 15) makes better inhibitors. The size and the orientation of the aromatic group of the amides are further decisive factors illustrated by **14b** and **15b** (entries 18 and 19). Putting together the last two structural features in **16b** results in the best inhibitor of this series (entry 20). Comparing benzoyl- (**E**) and 2-naphthoyl ureas (**F**) with amides **9b**, **10b** and **16b** (entries 5, 6, 13, 14 and 20), respectively, reveals that the presence of the acyl urea motif is essential for the strong binding. The deprotected *N*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)amide derivatives **19b**, **21b** and **22b** (entries 23, 25 and 26), proved poorly soluble to such an extent that the intended diversion of the inhibitors from the catalytic site could not be proven. X-ray crystallographic investigation of complexes of RMGPb with several inhibitors of this series is in progress.

3. Conclusion

The PMe_3 mediated Staudinger reaction of glycopyranosyl azides and carboxylic acids in the per-*O*-acetylated β -D-*gluco* and 2-acetamido-2-deoxy- β -D-*gluco* series proved to be a simple and efficient method for the preparation of a variety of the corresponding *N*-glycopyranosyl amides. Removal of the protecting groups carried out by the Zemplén-protocol furnished inhibitors of glycogen phosphorylase (GP). These compounds were tested against rabbit muscle GP and the best inhibitor constants (K_i) were in the micromolar range. It was shown that a properly positioned and large enough hydrophobic group attached to the amide moiety (as in *N*-(β -D-glucopyranosyl) 3-(2-naphthyl)propenoic amide **16b**, $K_i = 3.5 \mu\text{M}$) makes the inhibition one order of magnitude stronger than that of the best amide inhibitor known earlier (*N*-(β -D-glucopyranosyl) acetamide **A**, $K_i = 32 \mu\text{M}$). On the other hand, this compound is still much less efficient than the best known inhibitor of GP (*N*-(β -D-glucopyranosyl)-*N'*-(2-naphthoyl) urea **F**, $K_i = 0.4 \mu\text{M}$). It can be concluded that the acyl urea moiety is essential for the strong inhibition.

4. Experimental

4.1. General methods

Melting points were measured in open capillary tubes or on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter at room temperature. NMR spectra were recorded with Bruker WP 200 SY (200/50 MHz for $^1\text{H}/^{13}\text{C}$) or Avance DRX 500 (500/125 MHz for $^1\text{H}/^{13}\text{C}$) spectrometers. Chemical shifts are referenced to Me_4Si (^1H), or to the residual solvent signals (^{13}C). TLC was performed on DC-Alurolle Kieselgel 60 F₂₅₄ (Merck), and the plates were visualized by gentle heating. For column chromatography Kieselgel 60 (Merck, particle size 0.063–0.200 mm) was used. Organic solutions were dried over anhydrous MgSO_4 and concentrated in vacuo at 40–50 °C (water bath). The compounds were analyzed for C, H and N. The found percentages were within $\pm 0.4\%$ of the theoretical values.

4.2. General procedure I for the preparation of *N*-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)- (3a–16a) and *N*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) amides (17a–25a) from the corresponding azide

An azide (1 mmol of **1**³⁸ or **2**³⁹) was dissolved in dry CH_2Cl_2 (7 mL) and PMe_3 (1.04 mL of a 1 M toluene solution) was added. After cessation of the nitrogen evolution (~ 10 min) a carboxylic acid or its derivative (1 mmol, see Table 1) was added and the mixture stirred at rt for the time indicated with the particular compounds. The volatiles were removed in vacuo, and the residue was crystallized or purified by column chromatography to give the target amide. For NMR data see Tables 2–5.

4.3. General procedure II for the Zemplén-deacetylation to give compounds 4b, 5b, 7b–14b, 16b, 19b, 21b and 22b

To a solution of an acetyl protected compound in dry MeOH 1–2 drops of a ~ 1 M methanolic NaOMe solution were added, and the reaction mixture was kept at rt until completion of the transformation (TLC). Amberlyst 15 (H^+ form) was then added to remove sodium ions, the resin was filtered off, and the solvent removed in vacuo. If the residue was chromatographically not uniform it was purified by column chromatography. For NMR data see Tables 2–5.

4.4. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) hexanoic amide (3a)

Prepared by general procedure I: r. time 17 h, eluent: EtOAc–hexane 1:1, 70%, white crystals from diethyl ether–hexane, mp 84–86 °C; $[\alpha]_{\text{D}} +18$ (c 0.19, CHCl_3).

4.5. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 2,2-dimethylpropanoic amide (4a)

Prepared by general procedure I: r. time 4 d, eluent: EtOAc–hexane 1:1, 72%, white crystals, mp 165–167 °C; $[\alpha]_{\text{D}} +22$ (c 0.20, CHCl_3).

4.6. *N*-(β -D-Glucopyranosyl) 2,2-dimethylpropanoic amide (4b)

Prepared by general procedure II: r. time 2 h, 96%, syrup; $[\alpha]_{\text{D}} +4$ (c 0.25, MeOH).

4.7. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) cyclohexanecarboxamide (5a)

Prepared by general procedure I: r. time 20 h, eluent: EtOAc–hexane 1:1, 67%, white crystals, mp 178–181 °C; $[\alpha]_{\text{D}} +15$ (c 0.19, CHCl_3).

4.8. *N*-(β -D-Glucopyranosyl) cyclohexanecarboxamide (5b)

Prepared by general procedure II: r. time 20 h, 88%, white crystals, mp 206–208 °C; $[\alpha]_{\text{D}} -5$ (c 0.18, MeOH).

4.9. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) adamantane-1-carboxamide (6a)

Prepared by general procedure I: r. time 1 d, eluent: EtOAc–hexane 1:1, 25%, white crystals, mp > 350 °C; $[\alpha]_{\text{D}} +12$ (c 0.16, CHCl_3).

4.10. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) phenylacetamide (7a)

Prepared by general procedure I: r. time 17 h, eluent: EtOAc–hexane 1:1, 88%, white crystals, mp 129–132 °C (lit.³³ mp 158–159 °C); $[\alpha]_{\text{D}} -5$ (c 0.17, CHCl_3).

Table 2. ^1H NMR data for *N*-(β -D-glucopyranosyl) amides **3–16** (δ [ppm], *J* [Hz])

Compound	H-1 (<i>J</i> _{1,2})	H-2 (<i>J</i> _{2,3})	H-3 (<i>J</i> _{3,4})	H-4 (<i>J</i> _{4,5})	H-5 (<i>J</i> _{5,6})	H-6 (<i>J</i> _{6,6'})	H-6' (<i>J</i> _{5,6'})	NH (<i>J</i> _{1,NH})	OAc ^a or OH ^b	Aliphatic	Aromatic
Solvent											
3a		5.32, 5.30, 5.07, 4.93			3.83	4.32	4.08	6.48	2.09, 2.05,	2.4–2.0,	—
CDCl ₃		4 pseudo t, <i>J</i> ~9.5 Hz in each			(4.1)	(12.8)	(2.1)	(9.1)	2.04, 2.03	1.7–0.8	
4a		5.33, 5.24, 5.08, 4.95			3.82	4.34	4.07	6.44	2.09, 2.04,	1.17	—
CDCl ₃		4 pseudo t, <i>J</i> ~9.5 Hz in each			(4.2)	(12.6)	(2.1)	(9.5)	2.03, 2.02		
4b	4.73			3.7–3.6, 3.3–3.0 (m)				7.72	4.97, 4.89,	1.11	—
DMSO- <i>d</i> ₆	(8.8)							(8.8)	4.76, 4.51		
5a		5.32, 5.27, 5.07, 4.93			3.82	4.32	4.07	6.25	2.08, 2.04,	1.9–1.1	—
CDCl ₃		4 pseudo t, <i>J</i> ~9.5 Hz in each			(4.1)	(12.4)	(2.1)	(9.5)	2.03, 2.02		
5b	4.66			3.2–2.9 (m)		3.64	3.41	8.16	5.0–4.6,	2.2–1.1	—
DMSO- <i>d</i> ₆	(9.1)					(12.1, 1.5)	(4.1)	(8.2)	3.7–3.3		
6a		5.32, 5.26, 5.08, 4.95			3.82	4.33	4.07	6.39	2.09, 1.92,	2.08–2.00	—
CDCl ₃		4 pseudo t, <i>J</i> ~9.8 Hz in each			(4.1)	(12.4)	(2.1)	(9.1)	1.80	(+1 OAc)	
										1.78–1.62	
7a		5.26, 5.23, 5.03, 4.85			3.82	4.30	4.07	6.56	2.07, 2.02,	3.58, 3.49	7.4–7.2
CDCl ₃		4 pseudo t, <i>J</i> ~9.5 Hz in each			(4.5)	(12.4)	(2.1)	(9.4)	1.98, 1.84	(<i>J</i> =15.3)	
7b	4.71			3.6–3.0 (m)				8.62	5.01, 4.91,	3.39	7.34–7.18
DMSO- <i>d</i> ₆	(9.2)							(8.8)	4.90, 4.51		
8a		5.29, 5.28, 5.04, 4.85			3.81	4.33	4.06	6.44	2.07, 2.02,	4.82	7.4–7.1
CDCl ₃		4 pseudo t, <i>J</i> ~9.8 Hz in each			(4.3)	(12.5)	(2.2)	(9.3)	1.99, 1.77		
8b				4.9–4.5, 3.7–3.0 (m)				8.46	4.98, 4.87,	2.86	7.4–7.0
DMSO- <i>d</i> ₆								(8.6)	4.74, 4.50		
9a		5.30, 5.26, 5.05, 4.88			3.82	4.31	4.08	6.33	2.08, 2.03,	2.93, 2.50	7.29–7.17
CDCl ₃		4 pseudo t, <i>J</i> ~9.6 Hz in each			(4.4)	(12.5)	(1.5)	(8.8)	2.01, 1.94		
9b	4.87			3.51–3.28 (m)				—	—	2.87, 2.56,	7.32–7.21
D ₂ O	(8.8)										
10a		5.40, 5.36, 5.10, 5.00			3.88	4.34	4.10	6.42	2.08, 2.05	7.66, 6.33	7.52–7.38
CDCl ₃		4 pseudo t, <i>J</i> ~9.6 Hz in each			(4.4)	(12.5)	(2.2)	(9.6)	(2 $\times$), 2.04	(<i>J</i> =15.4)	
10b	5.12			3.94–3.49 (m)				—	—	6.61	7.60–7.45
D ₂ O	(7.4)									(<i>J</i> =15.4)	+HC=
11a		5.33, 5.32, 5.09, 5.00			3.85	4.33	4.11	6.68	2.09 (2 $\times$),	—	7.56–7.35
CDCl ₃		4 pseudo t, <i>J</i> ~9.6 Hz in each			(4.3)	(12.6)	(2.2)	(9.6)	2.05, 2.03		
11b	5.06			3.62–3.44 (m)				—	—	7.65–7.44	
D ₂ O	(8.9)										
12a		5.44, 5.38, 5.08, 5.05			3.89	4.34	4.09	7.09	2.07, 2.05	2.38	7.64, 7.22
CDCl ₃		4 pseudo t, <i>J</i> ~9.6 Hz in each			(4.1)	(12.3)	(2.3)	(9.1)	(2 $\times$), 2.03	(<i>J</i> =8.1)	
12b				5.00–4.91, 3.3.8–3.08 (m)				8.78	5.06, 5.00–4.91,	2.37	7.84, 7.29
DMSO- <i>d</i> ₆								(7.9)	4.57		(<i>J</i> =8.0)
13a		5.47, 5.41, 5.13, 5.09			3.92	4.36	4.12	7.13	2.08, 2.06	—	7.85–7.38
CDCl ₃		4 pseudo t, <i>J</i> ~9.5 Hz in each			(4.5)	(12.4)	(2.1)	(9.1)	(3 $\times$)		
13b				5.2–4.9, 3.8–3.0 (m)				8.95	5.2–4.9,	—	8.2–7.3
DMSO- <i>d</i> ₆								(8.8)	4.61		
14a		5.52, 5.42, 5.14, 5.13			3.93	4.31	4.12	7.29	2.08, 2.06	—	8.34–7.28
CDCl ₃		4 pseudo t, <i>J</i> ~9.6 Hz in each			(3.9)	(12.5)	(1.9)	(9.2)	(2 $\times$), 2.05		
14b				5.2–4.8, 3.8–3.0 (m)				9.02	5.2–4.8,	—	8.34–7.51
DMSO- <i>d</i> ₆								(8.9)	4.61		
15a		5.52, 5.42, 5.14, 5.12			3.91	4.38	4.13	7.29	2.07, 2.05	—	8.3–7.5
CDCl ₃		4 pseudo t, <i>J</i> ~9.3 Hz in each			(3.9)	(12.5)	(1.3)	(9.3)	(2 $\times$), 2.04		
15b	5.20			3.6–3.3(m)		3.88	3.71	—	—	—	8.5–7.5
CD ₃ OD	9.0					(11.5, 1.5)	(5.4)				
16a		5.44, 5.38, 5.12, 5.03			3.90	4.35	4.41	6.56	2.08, 2.06, 2.05,	6.46	7.92–7.49
CDCl ₃		4 pseudo t, <i>J</i> ~9.6 Hz in each			(4.2)	(12.5)	(2.2)	(8.8)	2.04	(<i>J</i> =15.4)	+HC=
16b	4.88			3.68–2.98 (m)				8.74	—	7.65, 6.80	8.08–7.53
DMSO- <i>d</i> ₆	(8.1)							(8.8)		(<i>J</i> =16.2)	

^a Refers to spectra of per-*O*-acetylated compounds **3a–16a**.^b Refers to spectra of deprotected compounds **b** in DMSO-*d*₆.**4.11. *N*-(β -D-Glucopyranosyl) phenylacetamide (7b)**

Prepared by general procedure II: r. time 1 d, 83%, white crystals, mp 211–213 °C; [α]_D +1 (*c* 0.19, MeOH).

4.12. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) diphenylacetamide (8a)

Prepared by general procedure I: r. time 21 h, eluent: Et-OAc–hexane 2:1, 21%, white crystals, mp 139–141 °C; [α]_D +4 (*c* 0.06, CHCl₃).

Table 3. ^1H NMR data for *N*-(2-acetamido-2-deoxy- β -D-glucopyranosyl) amides **17–25** (δ [ppm], *J* [Hz])

Compound	H-1 (<i>J</i> _{1,2})	H-2 (<i>J</i> _{2,3})	H-3 (<i>J</i> _{3,4})	H-4 (<i>J</i> _{4,5})	H-5 (<i>J</i> _{5,6})	H-6 (<i>J</i> _{6,6'})	H-6' (<i>J</i> _{5,6'})	NH	OAc, NHAc	Aliphatic	Aromatic
Solvent											
17a CDCl ₃	5.09 (8.3)	4.16 (10.2)	5.15 (9.2)	5.08 (10.2)	3.80 (4.3)	4.12 (12.5)	4.33 (2.1)	7.02 (8.0)	6.11 (8.3) 2.14, 2.12, 2.10, 2.02, 1.99	—	—
18a CDCl ₃	5.13 (9.5)	4.25 (8.8)	5.11 (8.1)	5.07 (9.6)	3.87 (4.4)	4.31 (12.5)	4.13 (2.2)	8.37 (7.4)	6.45 (8.1) 2.10 (2 $\times$), 2.06, 1.97	—	—
19a CDCl ₃	5.05 (9.9)	4.10 (10.8)	5.01 (9.5)	5.11 (9.9)	3.37 (4.4)	4.28 (12.5)	4.07 (2.2)	6.84 (8.5)	5.90 (8.2) 2.07, 2.05, 2.02, 1.92	2.15–2.09, 1.54, 1.28– 1.21, 0.86	—
19b DMSO- <i>d</i> ₆ – D ₂ O	4.77 (8.1)			3.75–2.95 (m)				—	1.79	1.49–0.77	—
20a CDCl ₃	5.23 (9.6)	4.25 (10.8)	5.09 (9.5)	5.17 (10.0)	3.82 (4.3)	4.32 (12.5)	4.11 (2.2)	7.80 (7.6)	6.03 (7.8) 2.08, 2.07, 2.05, 1.92	—	7.76, 7.51, 7.40
21a CDCl ₃	5.29 (9.5)	4.28 (9.9)	5.25 (9.5)	5.18 (8.9)	3.91 (4.2)	4.36 (12.3)	4.14	7.83 (8.4)	6.54 (8.4) 2.10 (2 $\times$), 2.07, 1.87	3.91 (2 $\times$), 3.89 (CH ₃ O)	7.10
21b D ₂ O	5.16 (9.6)	3.47 (8.8)	3.64 (9.6)	3.93 (10.3)	3.52	3.87 (12.5)	3.73 (4.6)	—	2.08	3.91 (2 $\times$), 3.81 (CH ₃ O)	7.13
22a DMSO- <i>d</i> ₆ – D ₂ O	5.50 (8.8)	4.17 (9.6)	5.25 (9.6)	4.90 (9.6)	3.95	4.22	4.03	9.20 (8.8)	2.00 (2 $\times$), 1.95, 1.72	—	8.55–7.52 +NH
22b DMSO- <i>d</i> ₆ – D ₂ O	5.18 (9.6)	3.37 (8.8)	3.58 (9.6)	3.90 (10.3)	3.45	3.80 (11.4)	3.65 (5.1)	—	1.91	—	8.39, 8.10–8.01, 7.87–7.85
23a CDCl ₃	5.08 (9.2)	4.24 (10.6)	5.07 (9.2)	5.16 (10.6)	3.82 (4.0)	4.32 (11.9)	4.13	8.05 (7.9)	5.95 (7.9) 2.12, 2.10, 2.08, 1.85	4.51, 4.38 (15.6) (COCH ₂)	7.25 (9.2), 6.90 (9.2)
24a CDCl ₃	5.21 (9.2)	4.21–4.07	5.18–5.07		3.82 (4.0)	4.29	4.21–4.07	7.40 (7.9)	6.48 (7.9) 2.08, 2.07, 2.04, 1.94	4.21–4.07 (CH ₃ CH), 1.44 (C(CH ₃) ₃)1.33 (6.6) (CH ₃ CH)	—
25a CDCl ₃	5.10– 4.98 4.98	4.12–4.04	5.10–4.98		3.74	4.28 (12.6)	4.12–4.04	7.20 (8.0) 6.01 (7.1) 5.76 (9.6)	2.08, 2.05, 2.04, 1.86	5.20, 5.11 (12.3) (OCH ₂), 4.59 (CHCH ₂), 2.86, 2.69 (4.0, 16.6) (CHCH ₂), 1.41(C(CH ₃) ₃)	7.35–7.34

4.13. *N*-(β -D-Glucopyranosyl) diphenylacetamide (8b)

Prepared by general procedure II: r. time 4 h, 20%, white crystals from MeOH, mp 186–189 °C; $[\alpha]_{\text{D}} -2$ (*c* 0.10, MeOH).

4.14. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 3-phenylpropanoic amide (9a)

Prepared by general procedure I: r. time 24 h, eluent: Et-OAc–hexane 3:1, 64%, white crystals, mp 133–136 °C; $[\alpha]_{\text{D}} -1$ (*c* 0.40, CHCl₃).

4.15. *N*-(β -D-Glucopyranosyl) 3-phenylpropanoic amide (9b)

Prepared by general procedure II: r. time 3 h, 99%, white crystals from MeOH, mp 182–185 °C; $[\alpha]_{\text{D}} +8$ (*c* 0.42, MeOH).

4.16. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 3-phenylpropenoic amide (10a)

Prepared by general procedure I: r. time 24 h, eluent: Et-OAc–hexane 1:1, 80%, white crystals, mp 177–179 °C; $[\alpha]_{\text{D}} -27$ (*c* 0.44, CHCl₃).

4.17. *N*-(β -D-Glucopyranosyl) 3-phenylpropenoic amide (10b)

Prepared by general procedure II: r. time 2 h, 87%, syrup, $[\alpha]_{\text{D}} -5$ (*c* 0.44, MeOH).

4.18. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 3-phenylpropynoic amide (11a)

Prepared by general procedure I: r. time 72 h, eluent: Et-OAc–hexane 1:2, 82%, white crystals, mp 166–169 °C; $[\alpha]_{\text{D}} -30$ (*c* 0.76, CHCl₃).

Table 4. ^{13}C NMR data for *N*-(β -D-glucopyranosyl) amides **3–16** (δ [ppm], *J* [Hz])

Compound Solvent	C-1	C-2–C-5	C-6	CO	CH ₃	Aliphatic	Aromatic
3a CDCl ₃	81.7	73.4, 72.3, 70.7, 68.6	61.7	177.9, 171.1, 170.9, 169.8, 169.6	20.7, 20.4	25.2 (1), 43.2–40.7 (4)	—
4a CDCl ₃	78.5	73.6, 72.5, 70.6, 68.2	61.6	178.6, 171, 170.5, 169.8, 169.5	20.7, 20.5	27.1 (3) 84.1 (1)	—
4b DMSO- <i>d</i> ₆	80.0	78.6, 77.6, 72.1, 70.0	60.9	177.8	—	27.2 (3), 85.6 (1)	—
5a CDCl ₃	78.0	73.5, 72.6, 70.6, 68.2	60.6	176.2, 171.0, 170.6, 169.8, 169.5	20.7, 20.6, 20.5	45.1–25.3	—
5b DMSO- <i>d</i> ₆	79.4	78.4, 77.5, 72.4, 70.0	61.0	175.5	—	43.9–25.2	—
6a CDCl ₃	78.3	73.5, 72.6, 70.6, 68.3	61.6	171.0, 170.6, 169.9, 169.6, 166.1	20.7, 20.6, 20.55	40.7–27.8	—
7a CDCl ₃	78.2	73.5, 72.6, 70.1, 68.1	61.6	171.2, 170.5 (2×), 169.7, 169.4	20.7, 20.5, 20.3	43.8	133.7–127.3
7b DMSO- <i>d</i> ₆	79.6	78.5, 77.5, 72.5, 69.9	60.8	170.4	—	42.2	135.9–126.3
8a CDCl ₃	78.4	73.6, 72.6, 70.1, 68.1	61.5	172.2, 170.6, 170.5, 169.8, 169.5	20.7, 20.5, 20.2	58.8	138.4–127.4
8b DMSO- <i>d</i> ₆	80.3	79.0, 78.0, 72.8, 70.3	61.1	171.9	—	56.8	141.4–126.5
9a CDCl ₃	78.1	73.5, 72.6, 70.5, 68.1	61.6	172.3, 170.9, 170.5, 169.8, 169.5	20.7, 20.5	38.0, 30.8	140.2–126.3
9b D ₂ O	79.8	78.0, 77.1, 72.4, 69.9	61.2	177.4	—	37.9, 31.5	141.1–127.0
10a CDCl ₃	78.5	73.6, 72.7, 70.7, 68.2	61.7	171.3, 170.6, 169.8, 169.6, 165.8	20.7, 20.6	143.3, 119.3	134.2–128.0
10b D ₂ O	80.1	78.2, 77.1, 72.5, 69.9	61.2	170.2	—	143.8, 119.8	134.6–128.8
11a CDCl ₃	78.0	73.7, 72.7, 70.3, 68.1	61.6	170.9, 170.6, 169.8, 169.5, 15.3	20.7, 20.6	87.3, 82.0	132.8–119.5
11b D ₂ O	79.4	77.7, 76.5, 71.8, 69.1	60.5	156.3	—	88.3, 81.3	132.7–127.3
12a CDCl ₃	78.2	73.4, 72.7, 70.4, 68.1	60.8	174.3, 170.7 (2×), 171.2, 169.8,	20.7, 20.6 (2×), 20.5	29.2	133.7–127.3
12b DMSO- <i>d</i> ₆	80.2	78.7, 77.6, 73, 70	61.0	166.5	—	21.0	141.4–127.6
13a CDCl ₃	78.9	73.6, 72.6, 70.8, 68.2	61.6	171.5, 170.6, 169.8, 169.6, 166.8	20.7 (2×), 20.6 (2×)	—	145.2–127.2
13b DMSO- <i>d</i> ₆	80.3	78.7, 77.6, 72.1, 70.2	61.0	166.4	—	—	143–126.4
14a CDCl ₃	78.9	73.6, 72.6, 70.8, 68.2	61.6	171.5, 170.6, 169.8, 169.5, 167.2	20.7 (2×), 20.5 (2×)	—	135–123.3
14b DMSO- <i>d</i> ₆	80.0	78.8, 77.6, 72.2, 70	61.0	168.8	—	—	134.1–124.8
15a CDCl ₃	78.9	73.6, 72.7, 70.9, 68.3	61.6	170.8, 170.5, 169.5, 167.2, 164.6	20.6 (2×), 20.5 (2×)	—	135.1–123.3
15b CD ₃ OD	81.9	79.8, 79.1, 73.9, 71.5	62.7	171.1	—	—	136.5–125.1
16a CDCl ₃	78.4	73.5, 72.7, 70.7, 68.2	61.6	171.1, 170.6, 169.8, 169.5, 165.9	20.7, 20.5	143.3, 119.4	134.1–123.4
16b DMSO- <i>d</i> ₆	79.7	78.6, 77.5, 72.6, 70.0	61.0	165.4	—	139.8, 122.4	133.5–123.4

4.19. *N*-(β -D-Glucopyranosyl) 3-phenylpropynoic amide (11b)

Prepared by general procedure II: r. time 16h, 98%, white crystals from MeOH, mp 237–240 °C (decomp.); $[\alpha]_{\text{D}} -2$ (*c* 0.38, MeOH).

4.20. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 4-methylbenzamide (12a)

Prepared by general procedure I: r. time 27h, eluent: Et-OAc–hexane 1:1, 37%, white crystals, mp 185–187 °C; $[\alpha]_{\text{D}} -19$ (*c* 0.22, CHCl₃).

Table 5. ^{13}C NMR data for *N*-(2-acetamido-2-deoxy- β -D-glucopyranosyl) amides **17–25** (δ [ppm], J [Hz])

Compound Solvent	C-1	C-2	C-3–C-5	C-6	CO	CH ₃	Aliphatic	Aromatic
17a CDCl ₃	80.5	53.6	73.7, 73.1, 67.8	61.9	176.8, 172.8, 170.7, 169.3	23.4, 23.1, 20.8, 20.7	—	—
18a CDCl ₃	80.4	53.1	73.9, 72.6, 67.7	61.6	172.4, 171.8, 170.6, 169.2, 157.9 ($J_{\text{C,F}}$ 38) (CF ₃ CO)	22.7, 20.6 (2 $\times$), 20.5	115.4 ($J_{\text{C,F}}$ 288) (CF ₃)	—
19a CDCl ₃	80.3	53.5	73.6, 73.1, 67.7	61.8	173.9, 172.0, 171.8, 170.7, 169.2	23.1, 20.9, 20.8, 20.7	36.7, 31.9, 29.6 (2 $\times$), 29.5, 29.3 (2 $\times$), 29.2, 25.2, 22.7, 14.1	—
19b DMSO- <i>d</i> ₆	78.8	54.5	78.6, 74.3, 70.4	60.9	172.4, 169.7	22.0	35.4, 31.2, 28.9 (2 $\times$), 28.8, 28.7, 28.6, 28.4, 25.0, 22.7, 13.8	—
20a CDCl ₃	82.2	54.6	74.6, 74.0, 68.7	62.7	173.5, 173.3, 171.9, 170.4, 168.6	24.0, 21.6 (2 $\times$), 21.5	—	133.0–127.3
21a CDCl ₃	80.9	60.7	73.3, 72.7, 68.0	61.7	172.2, 171.5, 170.6, 169.2, 167.3	56.1 (2 $\times$), 53.4 (CH ₃ O) 22.9, 20.6 (2 $\times$), 20.5	—	153.1 (2 $\times$), 141.2, 128.0, 104.6 (2 $\times$)
21b D ₂ O	80.8,	62.0	79.0, 75.0, 70.9	61.8	175.0, 169.9	57.4 (2 $\times$), 55.8 (CH ₃ O)23.6	—	153.9 (2 $\times$), 141.6, 129.8, 106.2 (2 $\times$)
22a CDCl ₃	78.9	52.3	73.2, 72.4, 68.4	61.8	170.0, 169.7, 169.6, 169.3, 166.6	22.6, 20.5, 20.4 (2 $\times$)	—	134.3–124.1
22b DMSO- <i>d</i> ₆	80.5	55.5	78.9, 75.0, 70.7	61.5	173.8, 169.4	23.4	—	135.6–124.7
23a CDCl ₃	79.7	52.7	73.4, 72.7, 67.8	61.6	171.7, 171.5, 170.6, 169.2, 155.7	22.7, 20.6 (2 $\times$), 20.5	67.2 (COCH ₂)	129.6, 129.4, 116.0, 115.8
24a CDCl ₃	79.9	53.5	73.5, 72.8, 68.0	61.8	173.8, 171.9, 171.5, 170.6, 169.3, 155.0	28.2 (3 $\times$), 23.0, 20.6 (2 $\times$), 20.5, 18.4	80.1 (C(CH ₃) ₃), 19.0 (CH ₃ CH)	—
25a CDCl ₃	80.1	53.2	73.5, 72.7, 67.7	61.7	172.3, 171.7, 171.3, 171.0, 170.6, 169.2, 155.5	28.2 (3 $\times$), 22.9, 20.6 (2 $\times$), 20.5	80.0 (C(CH ₃) ₃), 67.0 (OCH ₂), 50.1 (CH ₂ CH), 37.7 (CH ₂ CH)	135.6, 128.4 (2 $\times$), 128.2, 127.9

4.21. *N*-(β -D-Glucopyranosyl) 4-methylbenzamide (12b)

Prepared by general procedure II: r. time 1 h, eluent: CHCl₃–MeOH 7:1, 48%, white crystals from MeOH, mp 245–247 °C; $[\alpha]_{\text{D}} -3$ (*c* 0.21, MeOH).

4.22. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 4-phenylbenzamide (13a)

Prepared by general procedure I: r. time 4.5 d, eluent: EtOAc–hexane 1:1, 55%, white crystals, mp 210–212 °C; $[\alpha]_{\text{D}} -33$ (*c* 0.20, CHCl₃).

4.23. *N*-(β -D-Glucopyranosyl) 4-phenylbenzamide (13b)

Prepared by general procedure II: r. time 3 h, 85%, white crystals from MeOH, mp 279–280 °C; $[\alpha]_{\text{D}} +34$ (*c* 0.14, DMSO).

4.24. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 1-naphthoic amide (14a)

Prepared by general procedure I: r. time 1 d, eluent: EtOAc–hexane 1:1, 52%, white crystals from Et₂O, mp 138–140 °C; $[\alpha]_{\text{D}} +38$ (*c* 0.21, CHCl₃).

4.25. *N*-(β -D-Glucopyranosyl) 1-naphthoic amide (14b)

Prepared by general procedure II: r. time 2 h, 75%, white crystals from MeOH, mp 209–212 °C; $[\alpha]_{\text{D}} +45$ (*c* 0.16, DMSO).

4.26. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 2-naphthoic amide (15a)

Prepared by general procedure I: r. time 1 d, eluent: EtOAc–hexane 1:1, 62%, white crystals, mp 173–174 °C; $[\alpha]_{\text{D}} -30$ (*c* 0.41, MeOH).

4.27. *N*-(β -D-Glucopyranosyl) 2-naphthoic amide (15b)

Amide **15a** (150 mg) was dissolved in dry MeOH (3 mL), KCN (5 mg) was added, and the mixture kept at rt for 11 days. Amberlyst 15 (H⁺ form) was then added, and after filtration of the resin the solvent was removed in vacuo. The residue crystallized slowly from EtOH, and was recrystallized from the same solvent to give **15b** as white crystals (96 mg, 92%). Mp 177–180 °C; $[\alpha]_{\text{D}} +26$ (*c* 0.2, DMSO).

4.28. *N*-(2,3,4,6-Tetra-*O*-acetyl- β -D-glucopyranosyl) 3-(2-naphthyl)-propenoic amide (16a)

Prepared by general procedure I: r. time 24 h, eluent: EtOAc–hexane 1:1, 71%, white crystals, mp 207–209 °C; $[\alpha]_D -42$ (*c* 0.40, CHCl₃).

4.29. *N*-(β -D-Glucopyranosyl) 3-(2-naphthyl)-propenoic amide (16b)

Prepared by general procedure II: r. time 24 h, 93%, white crystals from MeOH, mp 243–246 °C; $[\alpha]_D -15$ (*c* 0.38, MeOH).

4.30. *N*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) acetamide (17a)

Prepared by general procedure I: r. time 3 d, 69%, eluent: EtOAc–MeOH 20:1, white crystals, mp 240–243 °C (lit.³⁴ mp 236–237 °C; lit.³⁵ mp 244–246 °C; lit.³⁷ mp 235 °C); $[\alpha]_D +6$ (*c* 1.02, CHCl₃) (lit.³⁴ $[\alpha]_D +18.5$ (*c* 2.0, CHCl₃); lit.³⁵ $[\alpha]_D +41$ (*c* 1.0, CHCl₃); lit.³⁷ $[\alpha]_D +18$ (*c* 0.5, pyridine)).

4.31. *N*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) trifluoroacetamide (18a)

Prepared by general procedure I: r. time 30 min, eluent: EtOAc–hexane 1:1, 56%, white crystals, mp 183–186 °C; $[\alpha]_D +6$ (*c* 1.02, CHCl₃).

4.32. *N*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) dodecanoic amide (19a)

Prepared by general procedure I: r. time 2.5 h, 91%, white crystals from EtOH, mp 178–182 °C (lit.³⁵ mp 176–178 °C); $[\alpha]_D -2$ (*c* 0.99, CHCl₃) (lit.³⁵ $[\alpha]_D -3.5$ (*c* 1.1, CHCl₃)).

4.33. *N*-(2-Acetamido-2-deoxy- β -D-glucopyranosyl) dodecanoic amide (19b)

Prepared by general procedure II: r. time 3 h, 87%, white crystals from MeOH, mp 252–255 °C; $[\alpha]_D +26$ (*c* 0.36, DMSO).

4.34. *N*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) benzamide (20a)

Prepared by general procedure I: r. time 14 days, eluent: EtOAc–MeOH 40:1, 43%, white crystals, mp 248–250 °C (lit.³⁵ mp 246–248 °C; lit.³⁴ mp 246–247 °C); $[\alpha]_D -46$ (*c* 1.02, CHCl₃) (lit.³⁵ $[\alpha]_D -37$ (*c* 0.57, CHCl₃); lit.³⁴ $[\alpha]_D -16$ (*c* 2.0, CHCl₃)).

4.35. *N*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) 3,4,5-trimethoxybenzamide (21a)

Prepared by general procedure I: r. time 1.5 h, eluent: EtOAc–hexane 4:1, 67%, white crystals, mp 233–235 °C; $[\alpha]_D -52$ (*c* 1.06, CHCl₃).

4.36. *N*-(2-Acetamido-2-deoxy- β -D-glucopyranosyl) 3,4,5-trimethoxybenzamide (21b)

Prepared by general procedure II: r. time 1 h, 78%, white crystals from MeOH, mp 268–271 °C; $[\alpha]_D -29$ (*c* 1.05, H₂O).

4.37. *N*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) 2-naphthoic amide (22a)

Prepared by general procedure I: r. time 1 day, 54%, white crystals from EtOH, mp 266–269 °C; $[\alpha]_D -34$ (*c* 1.05, DMSO).

4.38. *N*-(2-Acetamido-2-deoxy- β -D-glucopyranosyl) 2-naphthoic amide (22b)

Prepared by general procedure II: r. time 1 h, 88%, eluent: CHCl₃–MeOH 6:1, white crystals, mp 191–194 °C; $[\alpha]_D -46$ (*c* 0.38, DMSO).

4.39. *N*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) 4-chlorophenoxyacetamide (23a)

Prepared by general procedure I: r. time 3 days, 45%, eluent: toluene–EtOH 8:1, white crystals, mp 286–291 °C; $[\alpha]_D -40$ (*c* 0.42, CHCl₃).

4.40. *N*-(*N tert*-Butyloxycarbonyl-L-alanyl)-*N*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) amine (24a)

Prepared by general procedure I: r. time 8 days, 73%, eluent: toluene–EtOH 7:1, white crystals, mp 195–197 °C; $[\alpha]_D +0.5$ (*c* 0.23, CHCl₃).

4.41. *N*-[1-Benzyl-*N*-(*tert*-butyloxycarbonyl)-L-aspart-4-oyl]-*N*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl) amine (25a)

Prepared by general procedure I: r. time 4 days, 69%, eluent: EtOAc–EtOH 600:1, white crystals from EtOH, mp 165–167 °C (lit.²⁹ mp 157–158 °C); $[\alpha]_D +11$ (*c* 0.392, CHCl₃) (lit.²⁹ $[\alpha]_D +6.5$ (*c* 1, CHCl₃)).

4.42. Enzyme assays

Glycogen phosphorylase *b* was prepared from rabbit skeletal muscle according to the method of Fischer and Krebs,⁴⁰ using 2-mercaptoethanol instead of L-cysteine, and recrystallized at least three times before use. The kinetic studies with glycogen phosphorylase were performed as described previously.⁴¹ Kinetic data for the inhibition of rabbit skeletal muscle glycogen phosphorylase by monosaccharide compounds were collected using different concentrations of α -D-glucose-1-phosphate (4, 6, 8, 10, 12 and 14 mM) and constant concentrations of glycogen (1% w/v) and AMP (1 mM). The enzymatic activities were presented in the form of double-reciprocal plots (Lineweaver–Burk) applying a non-linear data-analysis program. The inhibitor constants (*K_i*) were determined by Dixon plots, by replotting the slopes from the Lineweaver–Burk plots against the

inhibitor concentrations. The means of standard errors for all calculated kinetic parameters averaged to less than 10%.^{32,42}

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