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SELECTIVE PIVALOYLATION OF 2-ACETAMIDO-2-DEOXY SUGARS

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ABSTRACT

Selective pivaloylation of 2-acetamido-2-deoxy-D-glucose, its methyl α- and β-glycosides, and the methyl α-glycoside of *N*-acetyl-D-muramic acid under various conditions has been studied. The structures of the products were established by ^{1}H-n.m.r. spectroscopy and acetylation. The orders of acylation, HO-6>HO-3>HO-1>HO-4 for 2-acetamido-2-deoxy-D-glucose and HO-6>HO-3>HO-4 for its methyl glycosides, were established.

Methyl 2-acetamido-2-deoxy-3,6-di-*O*-pivaloyl-α- and -β-D-glucopyranosides and 2-acetamido-2-deoxy-1,3,4,6-tetra-*O*-pivaloyl-D-glucopyranose were hydrolysed by rabbit serum esterases.

INTRODUCTION

The utility of the pivaloyl group in the synthesis of partially pivaloylated sugar derivatives[1–6], in isomerisation studies[7], and for positional assignment of substituents in the sugar ring[8] has been reported, as well as studies of partial and total deacylations. For example, thymidine 5′-pivalate[1], a prodrug[9], expresses its biological activity after hydrolysis by plasma esterases. *O*-Pivaloyl derivatives of methyl α-D-glucopyranoside are good substrates for mammalian serum esterases.[10]. Deacylation of methyl 2,6-di-*O*-pivaloyl-α-D-glucopyranoside by rabbit serum esterases gave the 2-*O*- and 6-*O*-pivaloyl derivatives as intermediates.

We now report on the synthesis of pivaloyl derivatives of methyl 2-acetamido-2-deoxy-D-glucopyranoside (**1**), 2-acetamido-2-deoxy-D-glucopyranose (**9**), and methyl 2-acetamido-2-deoxy-3-*O*-[1-(*S*)-(methoxycarbonyl)ethyl]-α-D-glucopyranoside (methyl glycoside of muramic acid, **19**), and on their susceptibility to rabbit serum esterases.

RESULTS AND DISCUSSION

Conventional treatment of 2-acetamido-2-deoxy-D-glucose with methanolic hydrogen chloride[11] or with methanol in the presence of cation-exchange resin[12]

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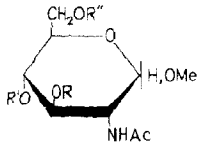
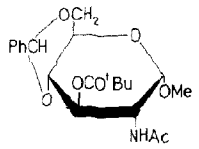
gave an ~5:1 $\alpha\beta$-mixture of methyl glycosides (**1**), which was used in the following studies.

Treatment of **1** with 3 equiv. of pivaloyl chloride in pyridine for 4 h at ambient temperature yielded an ~3.6:1 mixture of the 3,6-dipivalates **4α** and **4β** together with traces of the 3,4,6-tripivalate **6**, which were isolated by chromatography on silica gel. The ^{1}H-n.m.r. spectrum of **4α** contained, *inter alia*, signals at δ 4.72 (d, $J_{1,2}$ 3.81 Hz, H-1), 1.19 and 1.24 (2 s, 18 H, 2 CMe_3), and that of **4β** contained signals at δ 4.48 (d, $J_{1,2}$ 8.50 Hz, H-1), 1.20 and 1.22 (2 s, 18 H, 2 CMe_3). Further proof of the identity of **4α** and **4β** was provided by their conversion into the respective 4-acetates **5α** and **5β** (Table I).

Treatment of **1** with 1 equiv. of pivaloyl chloride for 40 min gave 28% of the 6-pivalate **2** together with a mixture of the 3,6-dipivalates **4α** and **4β**. Acetylation of **2** gave an $\alpha\beta$-mixture of **3** from which the α anomer was obtained crystalline.





7

2 R = R' = H, R'' = ^{t}BuCO
3 R = R' = Ac, R'' = ^{t}BuCO
4 R' = H, R = R'' = ^{t}BuCO
5 R' = Ac, R = R'' = ^{t}BuCO
6 R = R' = R'' = ^{t}BuCO
8 R = ^{t}BuCO, R' = R'' = Ac

TABLE I

^{1}H-N.M.R. DATA ($CDCl_3$, 100 MHz) FOR PIVALOYL DERIVATIVES OF METHYL 2-ACETAMIDO-2-DEOXY-D-GLUCOPYRANOSIDE

Compound	*Chemical shifts (p.p.m.)*[a]					
	Me_3C-CO_2			*AcO*		
	3	*4*	*6*	*3*	*4*	*6*
3			1.23	2.03	2.01	
4α	1.19		1.24			
4β	1.20		1.22			
5α	1.13		1.23		2.00	
5β	1.16		1.22		2.04	
6	1.13[b]	1.19[b]	1.23			
7	1.17					
8	1.13				2.00	2.11

[a]All signals are singlets. [b]Assignments could be reversed.

The reaction of **1** with 3 equiv. of pivaloyl chloride in pyridine at room temperature proceeded slowly and, after 48 h, 43% of an ~4:1 $\alpha\beta$-mixture of **6** was obtained from which the α anomer **6** was isolated crystalline. The pure anomer **6β** was obtained by the reaction of **4β** with a large excess (29 equiv.) of pivaloyl chloride at 60° and its structure was confirmed by ^{1}H-n.m.r. spectoscopy (Table I). These results showed that tri-*O*-pivaloylation of **1** required a large excess of pivaloyl chloride, prolonged reaction time, and elevated temperature, consistent with the steric hindrance of HO-4. The order of reactivity on pivaloylation (HO-6>HO-3>HO-4) was in agreement[13] with the result of selective benzoylation of methyl 2-benzamido-2-deoxy-α-D-glucopyranoside with benzoyl chloride in pyridine at −40°, for which the major product (53%) was the 3,6-dibenzoate. However, selective pivaloylation[6] of methyl α-D-glucopyranoside gave the 2,3,6- and 2,4,6-tripivalates in the ratio 1.2:1.

In order to obtain the 3-pivalate of **1**, methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[12] was treated with a slight excess of pivaloyl chloride for 36 h, and 73% of **7** was obtained. Treatment of **7** with hot dilute acetic acid produced methyl 2-acetamido-2-deoxy-3-*O*-pivaloyl-α-D-glucopyranoside which was characterised as its 4,6-diacetate **8**. The ^{1}H-n.m.r. spectra of **7** and **8** accorded with the structures assigned and were similar to that of methyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[12].

The chemical shifts of the resonances of pivaloyl groups in the ^{1}H-n.m.r. spectra of **2–8** (see Table I) followed the sequence Piv-6>Piv-4>Piv-3 and were similar to those of the corresponding resonances for methyl 2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranoside[6]. Introduction of *O*-acetyl groups in the molecule (**3**, **5**, and **8**) shifted the pivaloyl singlets to higher fields.

Pivaloylation of 2-acetamido-2-deoxy-D-glucopyranose (**9**) gave a complex mixture of products since HO-1 was available for reaction. Treatment of **9** with 4.8 equiv. of pivaloyl chloride for 24 h gave a 1:2.4 $\alpha\beta$-mixture of the 1,3,6-tri- (**16**) and 1,3,4,6-tetrapivalate (**18**) together with small amounts of **12** and **14** which were isolated by column chromatography. The ^{1}H-n.m.r. spectra of **16** and **18** contained signals for H-1 at δ 6.15–6.17 (d, $J_{1,2}$ ~3.40–3.51 Hz) and 5.62–5.63 (d, $J_{1,2}$ ~8.49–8.80 Hz) in a ratio ($\alpha\beta$ ~ 1:2) similar to that of the singlets attributed to NAc groups (Table II).

The $\alpha\beta$-mixture of **18** was resolved and the structures of the anomers were confirmed by analytical methods and the ^{1}H-n.m.r. data (Table II). The structure of **16** was confirmed by its conversion into the 4-acetate **17**.

Formation of $\alpha\beta$-mixtures of **16** and **18** in which the β anomer preponderated was unexpected since the esterification of free sugars in pyridine usually proceeds faster than mutarotation[14]. Since crystalline 2-acetamido-2-deoxy-D-glucopyranose is almost exclusively α, the above extensive formation of **16β** and **18β** may reflect steric factors associated with the bulky pivaloyl group.

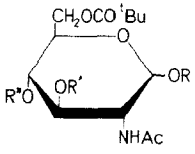
Pivaloylation of **9** for 4 h yielded a mixture of **12**, **14**, **16**, and **18** in the ratios 3.4:1:4.2:1.1. Unimolar acylation of **9** gave the 6-pivalate **10**, the 3,6-dipivalate **12**,

TABLE II

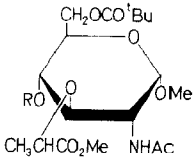
^{1}H-N.M.R. DATA ($CDCl_3$, 100 MHZ) FOR PIVALOYL DERIVATIVES OF 2-ACETAMIDO-2-DEOXY-D-GLUCOPYRANOSE

Compound	*Chemical shifts (p.p.m.)*[a]						
	Me_3C-CO_2				*AcO*		
	1	*3*	*4*	*6*	*1*[b]	*3*	*4*
11				1.21	2.18	2.05	
12		1.17		1.22			
13		1.15		1.22	2.18		2.02
14		1.13	1.15	1.22			
15		1.14	1.17	1.21	2.20		
16	1.28 1.20	1.18		1.22			
17	1.30 1.18	1.15		1.21			2.04
18α	1.30	1.15	1.18	1.21			
18β	1.19	1.14	1.15	1.22			

[a]All signals are singlets. [b]Refs. 12 and 17.



10 R = R' = R" = H
11 R = R' = R" = Ac
12 R = R" = H, R' = ^{t}BuCO
13 R = R" = Ac, R' = ^{t}BuCO
14 R = H, R' = R" = ^{t}BuCO
15 R = Ac, R' = R" = ^{t}BuCO
16 R" = H, R = R' = ^{t}BuCO
17 R" = Ac, R = R' = ^{t}BuCO
18 R = R' = R" = ^{t}BuCO



20 R = H
21 R = Ac

and **9**. The structures of **10**, **12**, and **14** were confirmed by acetylation, which gave almost pure **11α**, **13α**, and **15α** (see Experimental and Table II), and indicated that some mutarotation had occurred during the reaction.

The above results with 2-acetamido-2-deoxy-D-glucopyranose suggested the reactivity order HO-6> HO-3> HO-1> HO-4. The ^{1}H-n.m.r. spectra of **16** and **18**

allowed a ready differentiation of the two anomers on the basis of the chemical shifts of the signals assigned to the 1-pivalates and NAc groups (the signals for these groups in the α anomer are at lower field).

Only position 4 and 6 in methyl 2-acetamido-2-deoxy-3-*O*-[1-(*S*)-(methoxycarbonyl)ethyl]-α-D-glucopyranoside[15] (**19**) are available for pivaloylation. Treatment of **19** with 2 equiv. of pivaloyl chloride for 48 h gave only 32% of the 6-pivalate **20**. The ^{1}H-n.m.r. spectrum of **20** contained a resonance for a pivaloyl group at δ 1.23. The analytical and ^{1}H-n.m.r. data of the 4-acetate (**21**) of **20** were consistent with the structure proposed. Attempts to prepare the 4-pivalate of **19** failed. Treatment of **19** with up to 10 equiv. of pivaloyl chloride and a prolonged reaction time failed to yield the 4,6-dipivalate. This result corroborates[16] earlier findings that position 4 in *N*-acetyl-D-muramic acid is sterically hindered.

The derivatives **4α**, **4β**, and **18** of 2-acetamido-2-deoxy-D-glucose were each hydrolysed completely by rabbit serum esterases. Details of this work will be published elsewhere.

EXPERMENTAL

General methods. — Melting points are uncorrected. Optical rotations were determined for 1% solutions in chloroform, it not stated otherwise. Column chromatography was performed on silica gel (Merck) and t.l.c. on Kieselgel G (Merck) with *A*, ethyl acetate–benzene (proportions are given in the text); *B*, ethyl acetate–methanol (5:1); *C*, ethyl acetate–benzene–ethanol (2:2:1); *D*, ethyl acetate; and detection was effected by charring with sulphuric acid. ^{1}H-N.m.r. spectra (100 MHz, $CDCl_3$, internal Me_4Si) were recorded with a Jeol JNM FX-100 F.t. spectrometer.

Selective acylation of methyl 2-acetamido-2-deoxy-αβ-D-glucopyranoside (**1**). — To a solution of **1** (350 mg, 1.5 mmol; αβ ratio ~5:1) in dry pyridine (3.5 mL) was added pivaloyl chloride (0.55 mL, 5.4 mmol) at room temperature. The mixture was stirred for 4 h, ethanol (3 mL) was added, the solvents were evaporated, and the residue was subjected to column chromatography (solvent *A*, 2:1) to give, first, amorphous methyl 2-acetamido-2-deoxy-3,6-di-*O*-pivaloyl-α-D-glucopyranoside (**4α**; 331 mg, 54%), R_F ~0.63, $[\alpha]_D$ +52°. ^{1}H-N.m.r. data: δ 5.94 (d, *J* 9.67 Hz, NH), 5.08 (dd, 1 H, $J_{2,3}$ 10.84, $J_{3,4}$ 8.79 Hz, H-3), 4.68 (d, $J_{1,2}$ 3.53 Hz, H-1), 3.40 (s, OMe) , 1.93 (s, NAc); other signals are given in Table I.

Eluted next was methyl 2-acetamido-2-deoxy-3,6-di-*O*-pivaloyl-β-D-glucopyranoside (**4β**; 90 mg, 15%), R_F ~0.55, m.p. 162–164° (from ethyl acetate–light petroleum), $[\alpha]_D$ −5°. ^{1}H-N.m.r. data: δ 6.82 (d, *J* 9.37 Hz, NH), 4.48 (d, $J_{1,2}$ 8.50 Hz, H-1), 3.46 (s, OMe), 1.93 (s, NAc); other signals are given in Table I.

Anal. Calc. for $C_{19}H_{33}NO_8$: C, 56,56; H, 8.24; H, 3.47. Found for **4α** : C, 56.42; H, 8.48; N, 3.40; for **4β**: C, 56.81; H, 8.34; N, 3.34.

Treatment of **4α** (160 mg) with acetic anhydride–pyridine (1:1) for 16 h at room temperature afforded, after chromatography (solvent *A*, 2:1), the amorphous

4-acetate **5α** (165 mg, 94%), foam, $[\alpha]_D$ +84°. ^{1}H-N.m.r. data: δ 5.21 (d, *J* 6.05 Hz, NH), 4.72 (d, $J_{1,2}$ 3.51 Hz, H-1), 3.41 (s, OMe), 1.94 (s, NAc); other signals are given in Table I.

Anal. Calc. for $C_{21}H_{35}NO_9$: C, 56,61; H, 7.92; N, 3.41. Found: C, 56.86; H, 7.83; N, 2.98.

Acetylation of **4β** (130 mg) gave the 4-acetate **5β** (111 mg, 77%), m.p. 158–160° (from isopropyl ether–light petroleum), $[\alpha]_D$ −7°. ^{1}H-N.m.r. data: δ 6.18 (d, *J* 8.79 Hz, NH), 4.50 (d, $J_{1,2}$ 8.50 Hz, H-1), 3.48 (s, OMe), 1.94 (s, NAc); other signals are given in Table I.

Anal. Calc. for $C_{21}H_{35}NO_9$: C, 56.61; H, 7.92; N, 3.14. Found: C, 56.32; H, 8.17; N, 3.39.

*Methyl 2-acetamido-2-deoxy-6-*O*-pivaloyl-*D*-glucopyranoside* (**2**). — When the reaction of **1** (436 mg, 1.86 mmol) and pivaloyl chloride (0.23 mL, 1.86 mmol) in pyridine was conducted for 40 min at room temperature, chromatography of the product (solvent *C*) afforded **2** (170 mg, 28.6%), as a glass, $[\alpha]_D$ +47°, and a mixture of **4α** and **4β** (157 mg, 20%) in the ratio 4:1 (t.l.c.).

Acetylation of **2** in the usual manner afforded, after chromatography (solvent *C*), pure **3** (93%). Crystallisation of **3** from isopropyl ether–light petroleum gave the 3,4-diacetate **3α**, m.p. 136–138°, $[\alpha]_D$ +86°. ^{1}H-N.m.r. data: δ 6.50 (d, *J* 8 Hz, NH), 4.71 (d, $J_{1,2}$ 3.52 Hz, H-1), 3.42 (s, OMe), 1.97 (s, NAc); other signals are given in Table I.

Anal. for $C_{18}H_{29}NO_9$: C, 53.59; H, 7.25; N, 3.47. Found: C, 53.87; H, 7.56; N, 3.43.

*Methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-pivaloyl-*D*-glucopyranoside* (**6**). — *(a)* Treatment of **1** (550 mg, 2.5 mmol) as for **4**, but for 48 h at ambient temperature, and chromatography of the products (solvent *A*, 5:1) gave, first, **6αβ** (520 mg, 43%; αβ ~ 9:1). Crystallisation from ethyl acetate–light petroleum gave **6α**, m.p. 80–82°, $[\alpha]_D$ +62°. ^{1}H-N.m.r. data: δ 5.83 (d, *J* 9.67 Hz, NH), 4.72 (d, $J_{1,2}$ 3.81 Hz, H-1), 3.41 (s, OMe), 1.95 (s, NAc); other signals are given in Table I.

Anal. for $C_{24}H_{41}NO_9$: C, 59.12; H, 8.48; N, 2.87. Found: C, 59.27; H, 8.78; N, 2.80.

Eluted second was **4αβ** (430 mg, 43%; αβ ~ 9:1, based on t.l.c.).

(b) Treatment of **4β** (70 mg, 0.17 mmol) with pivaloyl chloride (0.5 mL, 4.9 mmol) in pyridine (0.5 mL) for 16 h at 60° afforded, after chromatography (solvent *A*, 2:1), amorphous **6β** (45 mg, 53%), $[\alpha]_D$ −6.8°. ^{1}H-N.m.r. data: δ 5.86 (d, *J* 9.38 Hz, NH), 4.46 (d, $J_{1,2}$ 8.80 Hz, H-1), 3.49 (s, OMe), 1.94 (s, NAc); other signals are given in Table I.

Found: C, 59.27; H, 8.36; N, 2.97.

*Methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-pivaloyl-α-*D*-glucopyranoside* (**7**) *and methyl 2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-*D*-glucopyranoside* (**8**). — A solution of methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[12] (111 mg, 0.34 mmol) in pyridine (0.7 mL) was treated with pivaloyl chloride (0.05 mL, 0.4 mmol) for 36 h at room temperature. Crystallisation

of the product from aqueous 50% ethanol gave **7** (101 mg, 73%), m.p. 165–168°, $[\alpha]_D$ −4.5°. ^{1}H-N.m.r. data: δ 7.38–7.26 (m, 5 H, Ph), 5.90 (d, *J* 9.7 Hz, NH), 5.54 (s, PhCH_2), 4.70 (d, $J_{1,2}$ 3.81 Hz, H-1), 3.37 (s, OMe), 1.94 (s, NAc); other signals are given in Table I.

Anal. Calc. for $C_{21}H_{29}NO_7$: C, 61.90; H, 7.17; N, 3.44. Found: C, 62.16; H, 7.35; N, 3.35.

A solution of **7** (100 mg, 0.25 mmol) in acetic acid (2 mL) and water (1 mL) was heated for 0.5 h at 100°, then concentrated, and the crude product was acetylated. Fast elution of the product from silica gel with solvent *A* (2:1) gave amorphous **8** (54 mg, 54%), $[\alpha]_D$ +65°. ^{1}H-N.m.r. data: δ 5.96 (d, *J* 9.67 Hz, NH), 4.73 (d, $J_{1,2}$ 3.51 Hz, H-1), 3.41 (s, OMe), 1.94 (s, NAc); other signals are given in Table I.

Anal. Calc. for $C_{18}H_{29}NO_9$: C, 53.59; H, 7.25; N, 3.47. Found: C, 53.84; H, 7.47; N, 3.35.

*2-Acetamido-2-deoxy-1,3,6-tri-*O*-pivaloyl-*(**16**) *and -1,3,4,6-tetra-*O*-pivaloyl-*D*-glucopyranose* (**18**). — To a suspension of 2-acetamido-2-deoxy-D-glucose (**9**; 1.1 g, 5 mmol) in pyridine (15 mL) was added pivaloyl chloride (2.8 mL, 24 mmol) at 4°. The mixture was stirred for 24 h at room temperature, then concentrated. Column chromatography (solvent *A*, 1:1) of the residue gave **16αβ** (402 mg, 17%), R_F ~0.49, and **18αβ** (1.14 g, 41%), R_F ~0.65. Crystallisation of **16αβ** from isopropyl ether–light petroleum gave crystalline material, m.p. 93–97°, $[\alpha]_D$ +83°. ^{1}H-N.m.r. data: δ 6.30 (d, *J* 8.5 Hz, NH), 6.15 (d, 0.33 H, $J_{1,2}$ 3.51 Hz, H-1), 5.63 (d, 0.66 H, $J_{1,2}$ 8.80 Hz, H-1), 1.89, 1.88 (2 s, 3 H, NAc); other signals are given in Table II.

Anal. Calc. for $C_{23}H_{39}NO_9$: C, 58.33; H, 8.30; N, 2.96. Found: C, 58.35; H, 8.45; N, 3.06.

Conventional acetylation of **16** (250 mg, 0.528 mmol), column chromatography of the product (solvent *A*, 1:2), and crystallisation from aqueous 50% ethanol gave the 4-acetate **17αβ** (174 mg, 64%) as needles, m.p. 127–130°, $[\alpha]_D$ +25.5°. ^{1}H-N.m.r. data: δ 6.46 (d, *J* 9.96 Hz, NH), 6.17 (d, 0.33 H, $J_{1,2}$ 3.52 Hz, H-1), 5.63 (d, 0.66 H, $J_{1,2}$ 8.78 Hz, H-1), 2.04 (s, AcO), 1.90, 1.87 (2 s, 3 H, NAc); other signals are given in Table II.

Anal. Calc. for $C_{25}H_{41}NO_{10}$: C, 58.23; H, 8.02; N, 2.72. Found: C, 58.40; H, 8.27; N, 2.67.

Crystallisation of **18αβ** twice from aqueous 50% ethanol gave **18α**, m.p. 189–190°, $[\alpha]_D$ +68°. ^{1}H-N.m.r. data: δ 6.15 (d, $J_{1,2}$ 3.81 Hz, H-1), 6.61 (d, *J* 8.79 Hz, NH), 1.90 (s, NAc); other signals are given in Table II.

Anal. Calc. for $C_{28}H_{47}NO_{10}$: C, 60.30; H, 8.50; N, 2.51. Found: C, 60.41; H, 8.74; N, 2.45.

Rechromatography of the mother liquor, followed by crystallisation from aqueous 50% ethanol, gave **18β**, m.p. 174–175°, $[\alpha]_D$ +10°. ^{1}H-N.m.r. data: δ 5.94 (d, *J* 9.96 Hz, NH), 5.62 (d, $J_{1,2}$ 8.49 Hz, H-1), 1.87 (s, NAc); other signals are given in Table II.

Found: C, 60.54; H, 8.67; N, 2.62.

*2-Acetamido-2-deoxy-3,6-di-*O*-pivaloyl-*(**12**) *and -3,4,6-tri-*O*-pivaloyl-*D*-

glucopyranose (**14**). — The reaction of **9** (1.1 g, 5 mmol) in pyridine (15 mL) with pivaloyl chloride (2.8 mL, 24 mmol) was conducted for 4 h at ambient temperature and worked-up as described for **18**. Column chromatography (solvent *A*, 2:1) of the products afforded, first, the 1,3,4,6-tetrapivalate **18** (210 mg, 7.5%), R_F ~0.80; the 1,3,6-tripivalate **16** (662 mg, 28%), R_F ~0.68; and the 3,4,6-tripivalate **14** (131 mg, 6.7%), R_F ~0.35.

Eluted next was amorphous **12** (404 mg, 21%), R_F ~0.27, $[\alpha]_D$ +20°. ^{1}H-N.m.r. data: δ 6.75 (d, J 9.38 Hz, NH), 1.96 (s, NAc); other signals are given in Table II.

Anal. Calc. for $C_{18}H_{31}NO_8$: C, 55.51; H, 8.02; N, 3.60. Found: C, 55.77; H, 8.19; N, 3.49.

Acetylation of **12** (185 mg, 0.48 mmol) for 16 h at room temperature and column chromatography (solvent *A*, 2:1) of the product gave the 1,4-diacetate **13** (211 mg, 94%), m.p. 214–216° (from aqueous 50% ethanol), $[\alpha]_D$ +87°. ^{1}H-N.m.r. data: δ 6.15 (d, $J_{1,2}$ 3.15 Hz, H-1), 1.92 (s, NAc); other signals are given in Table II.

Anal. Calc. for $C_{22}H_{35}NO_{10}$: C, 55.80; H, 7.45; N, 2.96. Found: C, 55.55; H, 7.67; N, 2.94.

Acetylation of **14** (164 mg, 0.35 mmol) and column chromatography (solvent *A*, 2:1) of the product gave the 1-acetate **15** (142 mg, 79%), m.p. 160–161° (from ethyl acetate–light petroleum), $[\alpha]_D$ +68°. ^{1}H-N.m.r. data: δ 6.14 (d, $J_{1,2}$ 3.52 Hz, H-1), 1.92 (s, NAc); other signals are given in Table II.

Anal. Calc. for $C_{25}H_{41}NO_{10}$: C, 58.23; H, 8.02; N, 2.72. Found: C, 58.42; H, 8.15; N, 3.00.

*2-Acetamido-2-deoxy-6-*O*-pivaloyl-*D*-glucopyranose* (**10**). — When **9** (1.1 g, 5 mmol) was treated with 1 equiv. (0.12 mL) of pivaloyl chloride in pyridine for 1 h at room temperature, column chromatography (solvent *A*, 2:1, followed by solvent *B*) of the product gave amorphous **10** (485 mg, 32%, eluted with solvent *B*), $[\alpha]_D$ +58°. ^{1}H-N.m.r. data (CD_3OD): δ 7.83 (d, J 7.81 Hz, NH), 2.01 (s, NAc), 1.22 (s, PivO-6).

Anal. Calc. for $C_{13}H_{23}NO_7 \cdot 0.5H_2O$: C, 49.67; H, 7.70; N, 4.46. Found: C, 49.42; H, 7.99; N, 4.76.

Conventional acetylation of **10** (107 mg, 0.35 mmol) and column chromatography (solvent *A*, 2:1) of the product afforded the 1,3,4-triacetate **11** (137 mg, 92%), m.p. 150–152°, $[\alpha]_D$ +71° (from ethyl acetate–light petroleum). ^{1}H-N.m.r. data: δ 6.17 (d, $J_{1,2}$ 3.51 Hz, H-1), 6.04 (d, J 8.92 Hz, NH); other signals are given in Table II.

Anal. Calc. for $C_{19}H_{24}NO_{10}$: C, 53.52; H, 5.67; N, 3.29. Found: C, 53.63; H, 5.85; N, 3.28.

*Methyl 2-acetamido-2-deoxy-3-[1-(S)-(methoxycarbonyl)ethyl]-6-*O*-pivaloyl-α-*D*-glucopyranoside* (**20**). — To a solution of **19**[15] (306 mg, 0.95 mmol) in pyridine (1 mL) was added pivaloyl chloride (0.26 mL, 2.1 mmol). The mixture was stirred for 20 h at room temparature. Column chromatography (solvent *A*, 2:1) of the product yielded **20** (123 mg, 32%), m.p. 118–120° (from ethyl acetate–light petroleum), $[\alpha]_D$ +82°. ^{1}H-N.m.r. data: δ 7.72 (bs, NH), 5.11 (d, $J_{1,2}$ 2.44 Hz, H-1), 4.76

(q, *J* 6.74 Hz, MeC*H*), 3.76 (s, CO_2Me), 3.34 (s, OMe), 2.05 (s, NAc), 1.42 (d, *J* 7.98 Hz, *Me*CH), and 1.23 (s, 9 H, PivO-6).

Anal. Calc. for $C_{18}H_{31}NO_9$: C, 53.32; H, 7.71; N, 3.46. Found: C, 53.62; H, 7.98; N, 3.52.

Acetylation of **20** (100 mg, 0.25 mmol) and column chromatography (solvent *A*, 2:1) of the product gave the 4-acetate **21** (80 mg, 72%) as an oil, $[\alpha]_D$ +110°. ^{1}H-N.m.r. data: δ 7.87 (bs, NH), 5.11 (d, $J_{1,2}$ 2.44 Hz, H-1), 3.79 (s, CO_2Me), 3.35 (s, OMe), 2.13 (s, AcO-4), 2.05 (s, NAc), 1.37 (d, *J* 7.2 Hz, *Me*CH), and 1.22 (s, PivO-6).

Anal. Calc. for $C_{20}H_{33}NO_{10}$: C, 53.68; H, 7.43; N, 3.13. Found: C, 53.73; H, 7.44; N, 3.15.

Enzymic deacylation of selected pivaloyl derivatives. — Solutions of **4α**, **4β**, and **18** (5 mg of each) in dimethyl sulfoxide (25 μL) were incubated with rabbit serum (0.6 mL) at 37° for 24 h. Incubation was stopped by the addition of 0.3 mL of ethanol, serum proteins were separated by centrifugation, and an aliquot of each supernatant solution was subjected to t.l.c. in solvent *A* (2:1) and acetonitrile–water (5:1). The product of each enzymic hydrolysis comigrated with 2-acetamido-2-deoxy-D-glucose.

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