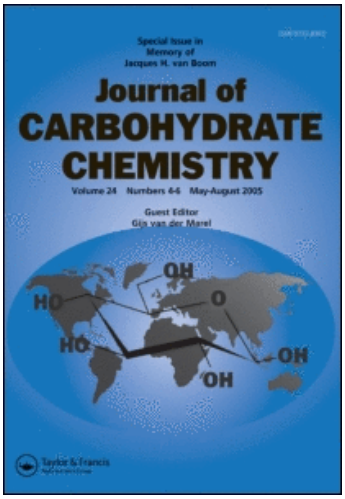

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Synthesis of Acylated Methyl 2-Acetamido-2-Deoxy-α-D-Mannopyranosides

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Synthesis of Acylated Methyl 2-Acetamido-2-Deoxy-α-D-Mannopyranosides

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2-Acetamido-2-deoxy-β-D-mannopyranose (1) was glycosylated by the Fischer method using an acidic ion-exchange resin as the catalyst to give α-methyl glycoside **2**. Selective pivaloylations of methyl 2-acetamido-2-deoxy-α-D-mannopyranoside (2) have been studied under various reaction conditions. Two partially pivaloylated products were submitted to additional acetylations. All structures were established by NMR spectroscopy. Structure of the methyl 2-acetamido-2-deoxy-3,6-di-*O*-pivaloyl-α-D-mannopyranoside (4) was determined by X-ray analysis.

Keywords Methyl 2-acetamido-2-deoxy-α-D-mannopyranosides, Acyl, Pivaloyl, Acetyl

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INTRODUCTION

In our previous reports we described the synthesis[1–3] of several series of pivaloylated and acetylated monosaccharides, and the structures of some of them[4,5] were determined by crystal structure analysis. Some of those compounds showed to be good substrates for esterases present in rabbit[6] and guinea pig[7] sera. We also observed that in several cases the pivaloyl group, which was generally regarded as not prone to acyl migrations, undergoes such migrations in neutral reaction conditions.[8] It was also proven that such migrations proceed by a mechanism involving an orthoacid intermediate, which was in the case of some pivaloylated galactopyranosides stable enough to be isolated and characterized.[8] In continuation of this work we synthesized a series of pivaloylated and acetylated derivatives of 2-acetamido-2-deoxy-D-mannopyranose (Man*N*Ac), the physiologic importance of which has been recognized and is under constant investigation. Man*N*Ac is known to be an essential component of *N*-acetylneuraminic acid, which is the parent compound of a family of sialic acids.[9] It is also a frequently occurring glycosyl residue in capsular polysaccharides and lipopolysaccharides of bacteria[10,11] and microorganisms.[12] The β-Man*N*Ac units in some saccharides have potent implications in the virulence and pathogenicity of some bacteria.[10] These and several other examples of obvious physiologic activity of compounds containing Man*N*Ac are the main reasons why the synthesis of its derivatives still remains a great challenge in carbohydrate chemistry.

RESULTS AND DISCUSSION

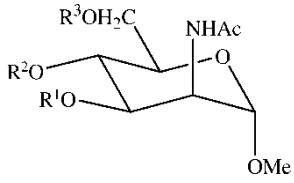
Preparation of Acylated Derivatives of 2-Acetamido-2-deoxy-β-D-mannopyranose

Glycosylation of 2-acetamido-2-deoxy-β-D-mannopyranose (**1**) by the Fischer method using an acidic ion-exchange resin (Dowex 50 H^+)[13] as a catalyst resulted in the formation of methyl 2-acetamido-2-deoxy-α-D-mannopyranoside (**2**, 46%).

Three pivaloylated derivatives were prepared by esterification of **2** with different equivalents of pivaloyl chloride in pyridine (Table 1). Acetylation of two partially pivaloylated compounds was achieved by using an excess of acetic anhydride-pyridine mixture.

Thus, pivaloylation of **2** with eight molar equivalents of pivaloyl chloride for 48 h resulted in the formation of methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-pivaloyl-α-D-mannopyranoside (**5**, 56%).

Table 1: Acylated methyl 2-acetamido-2-deoxy-α-D-mannopyranosides.



	R^1	R^2	R^3
2	H	H	H
3	H	H	Piv
4	Piv	H	Piv
5	Piv	Piv	Piv
6	Ac	Ac	Piv
7	Piv	Ac	Piv

Treatment of **2** with two molar equivalents of pivaloyl chloride for 2 h produced two partially pivaloylated compounds: methyl 2-acetamido-2-deoxy-6-*O*-pivaloyl-α-D-mannopyranoside (**3**, 14%) and methyl 2-acetamido-2-deoxy-3,6-di-*O*-pivaloyl-α-D-mannopyranoside (**4**, 43%).

The order of reactivity of hydroxyl groups was established and found to be 6-OH > 3-OH > 4-OH. It is in accord with the order of reactivity of hydroxyl groups previously assigned in acylations of methyl α-D-mannopyranoside.[2]

Acetylation of **3** and **4** produced the expected acetates **6** and **7** in high yields.

The structures of all prepared compounds were established by NMR spectroscopy and the data presented are in accord with those previously reported for other acylated *N*-acetylmannosamine derivatives.[14] However, anomeric assignment in the mannopyranose series using ^{1}H NMR spectroscopy is difficult since both anomers have similar coupling constants ($J_{1,2}$ ~1–2 Hz) and in the ^{13}C spectrum the C-1s of *N*-acetylmannosamine are almost coincidental.[14–16] Therefore, crystal structure analysis was crucial for the exact determination of the anomeric configuration of acylated derivatives of *N*-acetylmannosamine.

X-Ray Structure of 4

PLATON[17] plot of **4** is given in Figure 1. All significant bond distances and bond angles are listed in Table 2. An analysis of the C—C bond lengths within the pyranose ring shows that the bond lengths are in the range 1.501 to 1.532 Å. The anomeric C1-O1 bond is slightly shorter than the endocyclic C1-O5 and C5-O5 bonds. Analysis of the Cremer-Pople puckering parameters[18]

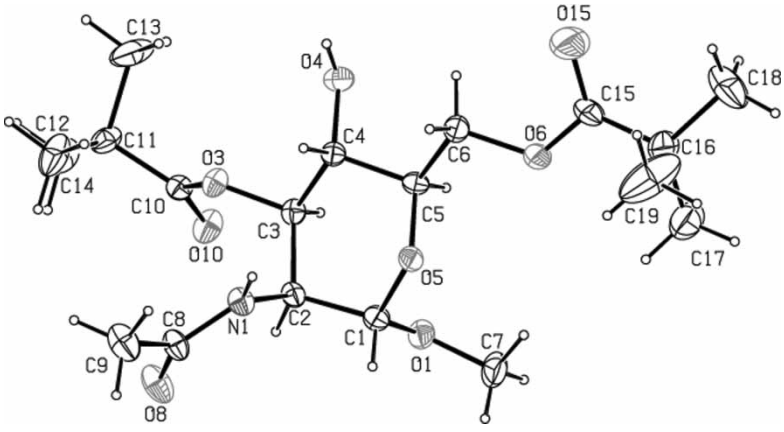


Figure 1: An ORTEP plot of **4** with the atom labeling scheme. Ellipsoids are drawn at the 10% probability level.

$Q = 0.572(6)$ Å, $\Theta = 5.8(7)^\circ$, and $\varphi = 292(6)^\circ$ showed that the molecular conformation of the pyranosyl ring is a distorted $^4C_1$. The torsion angle C5-O5-C1-O1 of $65.2(7)^\circ$ indicates the α-configuration of the anomeric centre.

In the crystal structure the molecules are connected by two intermolecular hydrogen bonds N1-H···O10[-1/2 + x, 3/2-y, -z] and O4-H···O8[-1/2 + x, 3/2-y, -z] of 2.970(6) Å and 2.816(8) Å, respectively (Fig. 2, Table 3).

Crystallographic data (excluding structure factors) for **4** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-299469. Copy of the data can be obtained, free of

Table 2: Selected bond lengths and bond angles (estimated standard deviations in parentheses).

Bonds	Length (Å)	Bonds	Angles (°)
O1-C1	1.350(8)	C1-O5-C5	112.8(5)
O3-C3	1.431(8)	O1-C1-C2	110.4(5)
O4-C4	1.444(8)	C1-C2-C3	110.3(5)
O5-C1	1.429(7)	C1-C2-N1	109.3(5)
O5-C5	1.442(8)	C2-C3-O3	111.1(5)
N1-C2	1.433(8)	C2-C3-C4	111.8(5)
C1-C2	1.532(9)	O3-C3-C4	105.0(4)
C2-C3	1.527(9)	C3-C4-C5	108.5(5)
C3-C4	1.501(8)	O4-C4-C5	108.8(5)
C4-C5	1.515(9)	O5-C5-C6	106.5(5)
C5-C6	1.503(9)	C4-C5-C6	110.3(5)
		O5-C5-C4	109.3(5)
		O6-C6-C5	107.9(5)
		O8-C8-N1	122.8(7)
		O8-C8-C9	120.3(7)

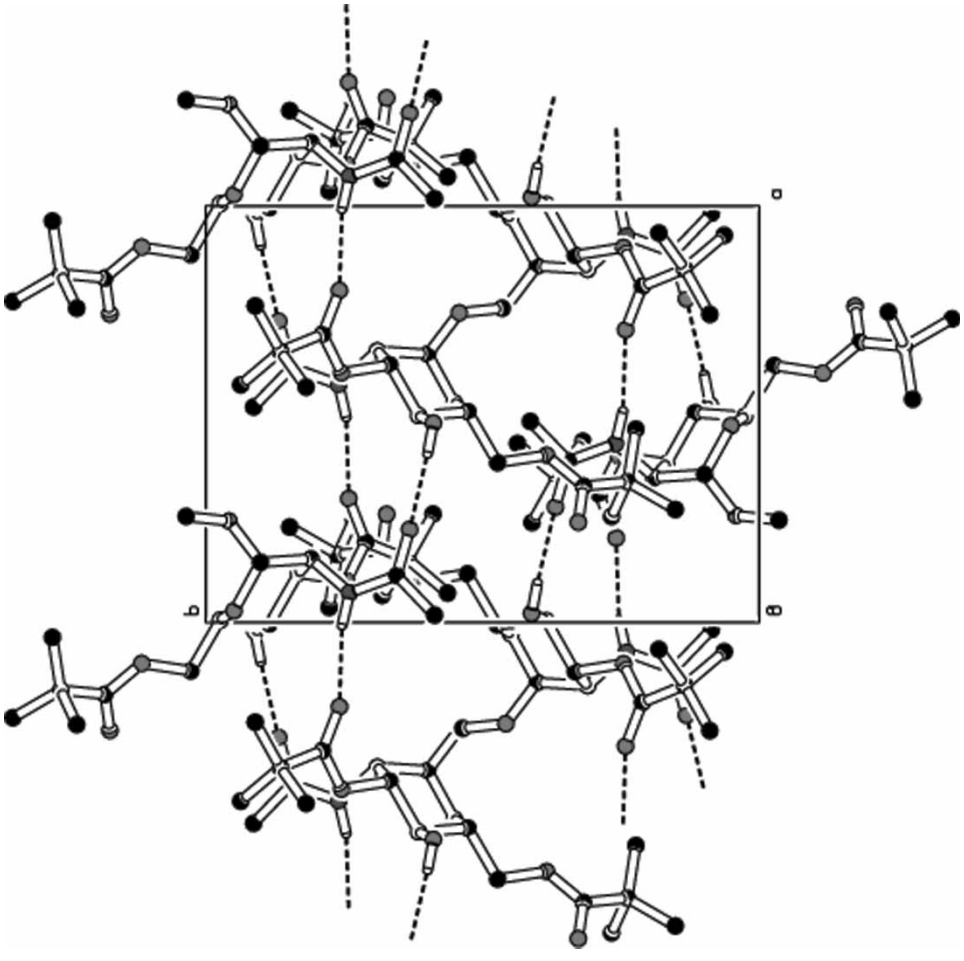


Figure 2: Hydrogen bonding in **4**.

charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-(0)1223/336-033 or e-mail: deposit@ccdc.cam.ac.uk

EXPERIMENTAL

General Methods

All solvents were reagent grade and distilled before use. 2-Acetamido-2-deoxy-β-D-mannopyranose was purchased from Sigma. Column chromatography was performed on silica gel (Merck) and TLC on Merck silica gel (60 F 254) plates (0.25 mm) with solvent A, CH_3CNH_2O (5:1); solvent B, EtOAc-C_6H_6-EtOH (2:2:1); and solvent C, EtOAc-C_6H_6 (2:1). Visualization

Table 3: Hydrogen bonding in **4** (Å, °).

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
N1-H1···O10^{i}	0.86	2.12	2.970(6)	168
O4-H4···O8^{ii}	0.82	2.09	2.816(8)	147

Symmetry transformations used to generate equivalent atoms:
i = −1/2 + x, 3/2 − y, −z.
ii= −1/2 + x, 3/2 − y, −z.

was effected by charring with H_2SO_4. Melting points were determined with a Büchi B-40 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra (300 MHz, D_2O and $CDCl_3$, internal Me_4Si) were recorded with a Bruker AV300 spectrometer. Optical rotations (in degrees) were measured using Optical Activity AA-10 Automatic Polarimeter at ~20°C using H_2O and $CHCl_3$ as solvents.

Synthesis of Mannosamine Derivatives

Methyl 2-acetamido-2-deoxy-α-D-mannopyranoside (2). 2-Acetamido-2-deoxy-β-D-mannopyranose (**1**, 200 mg, 0.9 mmol) was dissolved in anhydrous methanol (5 mL). Dry Dowex 50 (H^+) (0.25 g) was added and the reaction mixture stirred under reflux for 3 h. The ion-exchange resin was filtered off and rinsed with MeOH and the solvent was evaporated under reduced pressure. Column chromatography (solvent A) of the residue gave methyl 2-acetamido-2-deoxy-α-D-mannopyranoside **2** (114 mg, 46%); $[\alpha]_D + 50.5°$ (c 1.0, H_2O), lit.[13] +50° (c 0.9, H_2O); $R_f \sim 0.45$ (solvent A); ^{1}H NMR (D_2O): 1.86 (s, 3H, *N*Ac), 3.21 (s, 3H, *O*Me), 3.41–3.47 (m, 2H, H-4, H-6a), 3.63–3.70 (m, 2H, H-5, H-6b), 3.78 (dd, 1H, $J = 9.15$ Hz, $J = 4.77$ Hz, H-3), 4.15 (d, 1H, $J = 4.37$ Hz, H-2), 4.51 (s, 1H, H-1); ^{13}C NMR (D_2O): 22.75 (***C***H_3CO, *N*Ac), 53.30 (***C***H_3O), 55.59 (***C***-2), 61.24 (***C***-6), 67.53, 69.91, 73.00 (***C***-3, ***C***-4, ***C***-5), 100.71 (***C***-1), 175.55 (***C***═O, Ac).

Methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-pivaloyl-α-D-mannopyranoside (5). To a solution of **2** (100 mg, 0.425 mmol) in dry pyridine (1 mL) pivaloyl chloride (0.42 mL; 3.4 mmol) was added. The mixture was stirred at ambient temperature for 48 h and the reaction stopped by the addition of 96% EtOH. Water was added and the mixture of solvents evaporated under reduced pressure. The remaining traces of water were removed by codistillation with toluene. Column chromatography (solvent B) of the residue gave as a main product crystalline methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-pivaloyl-α-D-mannopyranoside **5** (120 mg, 56%); mp 180–183°C (from diisopropyl ether); $[\alpha]_D + 50.3$ (c 0.875, $CHCl_3$); $R_f \sim 0.76$ (solvent B); ^{1}H NMR ($CDCl_3$): 1.12 (s, 9H, 3-*O*Piv), 1.17 (s, 9H, 4-*O*Piv), 1.25 (s, 9H, 6-*O*Piv), 2.01 (s, 3H, *N*Ac), 3.40 (s, 3H, *O*Me), 4.00 (m, 1H, H-5), 4.1–4.2 (m, 2H, H-6a, H-6b), 4.65

(m, 1H, H-1), 4.68 (dd, 1H, $J = 4.48$ Hz, $J = 1.60$ Hz, H-2), 5.14 (t, 1H, $J = 10.19$ Hz, H-4), 5.33 (dd, 1H, $J = 10.28$ Hz, $J = 4.30$ Hz, H-3), 5.68 (d, 1H, $J = 9.57$ Hz, *N*H); ^{13}C NMR ($CDCl_3$): 23.13 (***C***H_3CO, *N*Ac), 26.90 (3 (***C***H_3)$_3$CCO, 3-, 4- and 6-*O*Piv), 38.68 (3 (CH$_3$)$_3$***C***CO, 3-, 4- and 6-*O*Piv), 49.95 (***C***H_3O), 55.17 (***C***-2), 62.05 (***C***-6), 65.26, 68.23, 68.73 (***C***-3, ***C***-4, ***C***-5), 100.09 (***C***-1), 169.48 (***C***═O, Ac), 176.83, 177.00, 177.70 (3 ***C***═O, Piv). Anal. Calcd. for $C_{24}H_{41}NO_9$: C, 59.12; H, 8.48; N, 2.87. Found: C, 59.63; H, 8.56; N, 3.01.

Methyl 2-acetamido-2-deoxy-6-*O*-pivaloyl-α-D-mannopyranoside (3) and methyl 2-acetamido-2-deoxy-3,6-di-*O*-pivaloyl-α-D-mannopyranoside (4). Pivaloylation of **2** (300 mg, 1.275 mmol) with pivaloyl chloride (0.315 mL, 2.55 mmol) in dry pyridine (3 mL) for 2 h was as described in preparation of **5**, followed by column chromatography (solvent B) of the product, gave first 3,6-dipivalate **4** (219 mg, 43%); mp 63–65°C (from ethyl acetate/ethanol); $[\alpha]_D + 45^\circ$ (c 1.0, $CHCl_3$); $R_f \sim 0.72$ (solvent B); ^{1}H NMR ($CDCl_3$): 1.19 (s, 9H, 3-*O*Piv), 1.25 (s, 9H, 6-*O*Piv), 1.99 (s, 3H, *N*Ac), 3.38 (s, 3H, *O*Me), 3.59 (t, 1H, $J = 9.92$ Hz, H-4), 3.85–3.90 (m, 1H, H-5), 4.4 (m, 2H, H-6a, H-6b), 4.57–4.63 (m, 2H, H-1, H-2), 5.15 (dd, 1H, $J = 9.88$ Hz, $J = 4.36$ Hz, H-3), 5.77 (d, 1H, $J = 9.71$ Hz, *N*H); ^{13}C NMR ($CDCl_3$): 23.07 (***C***H_3CO, *N*Ac), 26.85, 27.09 (2 (***C***H_3)$_3$CCO, 3- and 6-*O*Piv), 38.81 (2 (CH$_3$)$_3$***C***CO, 3- and 6-*O*Piv), 49.93 (***C***H_3O), 54.91 (***C***-2), 63.20 (***C***-6), 66.75, 70.38, 71.89 (***C***-3, ***C***-4, ***C***-5), 100.01 (***C***-1), 169.55 (***C***═O, Ac), 178.72 (2 ***C***═O, Piv). Anal. Calcd. for $C_{19}H_{33}NO_8$: C, 56.56; H, 8.24; N, 3.47. Found: C, 56.57; H, 8.34; N, 3.56.

Eluted next was crystalline 6-monopivalate **3** (55 mg, 14%); mp 48–50°C (from ethyl acetate/ethanol); $[\alpha]_D + 55.8^\circ$ (c 0.985, $CHCl_3$); $R_f \sim 0.4$ (solvent B); ^{1}H NMR ($CDCl_3$): 1.24 (s, 9H, 6-*O*Piv), 2.03 (s, 3H, *N*Ac), 3.37 (s, 3H, *O*Me), 3.51 (t, 1H, $J = 9.7$ Hz, H-4), 3.8 (m, 1H, H-5), 4.01–4.06 (dd, 1H, $J = 9.43$ Hz, $J = 4.43$ Hz, H-3), 4.36–4.37 (m, 3H, H-2, H-6a, H-6b), 4.65 (s, 1H, H-1), 6.33 (d, 1H, $J = 8.35$ Hz, *N*H); ^{13}C NMR ($CDCl_3$): 23.02 (***C***H_3CO, *N*Ac), 27.09 ((***C***H_3)$_3$CCO, 6-*O*Piv), 38.78 ((CH$_3$)$_3$***C***CO, 6-*O*Piv), 52.81 (***C***H_3O), 54.83 (***C***-2), 63.52 (***C***-6), 68.01, 70.06, 70.13 (***C***-3, ***C***-4, ***C***-5), 99.79 (***C***-1), 172.11 (***C***═O, Ac), 178.66 (***C***═O, Piv). Anal. Calcd. for $C_{14}H_{25}NO_7$: C, 52.65; H, 7.89; N, 4.39. Found: C, 52.25; H, 7.48; N, 4.02.

Methyl 2-acetamido-2-deoxy-3,4-di-*O*-acetyl-6-*O*-pivaloyl-α-D-mannopyranoside (6). Conventional acetylation of **3** (30 mg, 0.094 mmol) with Ac_2O-pyridine, followed by column chromatography (solvents B and C), gave 3,4-diacetate **6** (25 mg, 66%); $[\alpha]_D + 35^\circ$ (c 1.0 $CHCl_3$); $R_f \sim 0.6$ (solvent B), 0.28 (solvent C); ^{1}H NMR ($CDCl_3$): 1.26 (s, 9H, 6-*O*Piv), 1.99 (s, 3H, *N*Ac), 2.03 (s, 3H, 3-*O*Ac), 2.06 (s, 3H, 4-*O*Ac), 3.40 (s, 3H, *O*Me), 3.95–4.00 (m, 1H, H-5), 4.16–4.21 (m, 2H, H-6a, H-6b), 4.59–4.64 (m, 1H, H-2), 4.65 (s, 1H, H-1), 5.10 (t, 1H, $J = 10.13$ Hz, H-4), 5.32 (dd, 1H, $J = 10.12$ Hz, $J = 4.30$ Hz, H-3), 5.64 (d, 1H, $J = 8.98$ Hz, *N*H); ^{13}C NMR ($CDCl_3$): 20.65 (2 ***C***H_3CO, 3- and 4-*O*Ac), 23.19 (***C***H_3CO, *N*Ac), 27.05 ((***C***H_3)$_3$CCO, 6-*O*Piv), 38.76 ((CH$_3$)$_3$***C***CO, 6-*O*Piv),

50.05 (***C***H_3O), 55.16 (***C***-2), 62.18 (***C***-6), 65.83, 68.12, 69.07 (***C***-3, ***C***-4, ***C***-5), 99.82 (***C***-1), 169.75 (3 ***C***=O, Ac), 177.75 (***C***=O, Piv). Anal. Calcd. for $C_{18}H_{29}NO_9$: C, 53.59; H, 7.25; N, 3.47. Found: C, 54.01; H, 7.51; N, 3.45.

Methyl 2-acetamido-2-deoxy-4-*O*-acetyl-3,6-di-*O*-pivaloyl-α-D-manno-pyranoside (7). Likewise, **4** (85 mg, 0.21 mmol) gave the 4-acetate **7** (65 mg, 69%); $[\alpha]_D + 26^\circ$ (c 1.0 $CHCl_3$); $R_f \sim 0.66$ (solvent B), 0.51 (solvent C); ^{1}H NMR ($CDCl_3$): 1.12 (s, 9H, 3-*O*Piv), 1.25 (s, 9H, 6-*O*Piv), 2.01 (s, 3H, *N*Ac), 2.03 (s, 3H, 4-*O*Ac), 3.40 (s, 3H, *O*Me), 3.98 (m, 1H, H-5), 4.13–4.18 (m, 2H, H-6a, H-6b), 4.65 (s, 1H, H-1), 4.67–4.69 (m, 1H, H-2), 5.12 (t, 1H, $J = 10.20$ Hz, H-4), 5.33 (dd, 1H, $J = 10.22$ Hz, $J = 4.37$ Hz, H-3), 5.62 (d, 1H, $J = 9.17$ Hz, *N*H); ^{13}C NMR ($CDCl_3$): 20.66 (***C***H_3CO, 4-*O*Ac), 23.29

Table 4: Experimental details.

Crystal data		
Chemical formula	$C_{19}H_{33}NO_8$	$C_{19}H_{33}NO_8$
Chemical formula weight (M_r)	403.46	403.46
Crystal system, space group	Orthorhombic, $P2_12_12_1$	Orthorhombic, $P2_12_12_1$
a, *b*, *c* (Å)	10.6415(13), 14.1310(15), 15.4169(17)	31.776(4), 14.064(2), 14.952(2)
Z	4	12
Temperature (K)	295	100
D_x (Mg m^{-3})	1.156	1.201
Crystal form, color	Prismatic, colorless	Prismatic, colorless
Crystal size (mm)	0.45, 0.35, 0.15	0.5, 0.40, 0.21
Data collection		
Diffractometer	Xcalibur CCD	Xcalibur CCD
Data collection method	ω scan	ω scan
No. of measured, independent data	6709, 2501	13673, 10191
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.026	
θ_{max} (°)	27.5	27.0
Range of *h*, *k*, *l*	$-13 \rightarrow 9$, $-15 \rightarrow 13$, $-12 \rightarrow 20$	$-30 \rightarrow 37$, $-17 \rightarrow 17$, $-18 \rightarrow 17$
Refinement		
Refinement on	F^2	
R, *wR*, *S*	0.0836, 0.2837, 1.02	
No. of reflections and parameters used in refinement	2501, 255	
H-atom treatment	Isotropic	
Weighting scheme	1.02	
$\Delta\rho_{max}$, $\Delta\rho_{min}$, (e Å^{-3})	0.34, −0.25	

(***C***H_3CO, *N*Ac), 26.84, 27.16 (2 (***C***$H_3)_3$CCO, 3- and 6-*O*Piv), 38.74, 38.89 (2 $(CH_3)_3$***C***CO, 3- and 6-*O*Piv), 50.09 (***C***H_3O), 55.27 (***C***-2), 62.40 (***C***-6), 65.98, 68.13, 69.95 (***C***-3, ***C***-4, ***C***-5), 100.14 (***C***-1), 169.60, 169.76 (2 ***C***═O, Ac), 177.00, 177.94 (2 ***C***═O, Piv). Anal. Calcd. for $C_{21}H_{35}NO_9$: C, 56.62; H, 7.92; N, 3.14. Found: C, 56.59; H, 7.68; N, 3.12.

*X-Ray Structure Determination of **4***

The X-ray diffraction data for compound **4** were collected on the Oxford Diffraction Xcalibur 3 CCD diffractometer with monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). The measured intensity data were reduced using the CRYSALIS[19] software package. The molecular and crystal structure was solved by direct methods implemented in the program SIR97[20] and refined on F^2 with anisotropic displacement parameters for all nonhydrogen atoms (SHELXL97[21]). All hydrogen atoms were calculated and refined using the riding model. Crystal data, experimental conditions, and final refinement parameters are collected in Table 4. Since large anisotropic displacement parameters were observed for the 6-*O*-pivaloyl group, the data were also collected at 100 K. However, weak superstructure reflections at 100 K indicated tripling of the unit cell along the *a*-axis (Table 4). Unfortunately the three-unit-cell superstructure could be refined only to the *R* factor of 15.5%. Since the geometry is poor, the low-temperature structure will not be discussed here. In order to find the approximate temperature of this transition the temperature was lowered by 10 K in the range 290 to 100 K and an oscillation frame was measured at each temperature (Fig. 3). It was found that the transition is gradual and begins approx. at 160 K. The intensity of the weak superstructure reflections slowly increased as the temperature was lowered. We did not investigate

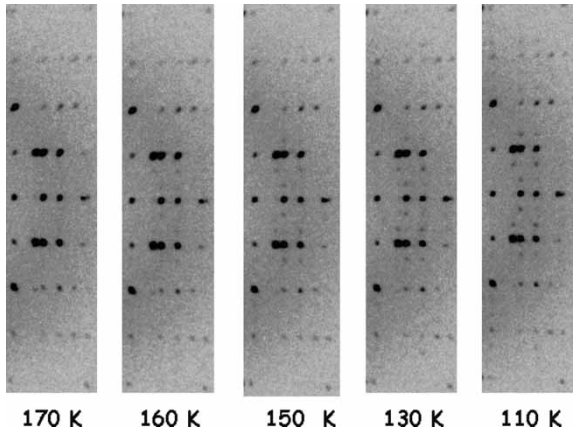


Figure 3: Partial oscillation frames along the *a*-axis showing temperature-induced superstructure phase transition in **4**.

whether hysteresis occurs. Data were also collected at 200 K but with no improvement in the final structure.

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REFERENCES

[1] Petrović, V.; Tomić, S.; Ljevaković, Đ.; Tomašić, J. Synthesis of acylated methyl β-D-xylopyranosides and their enzymic deacylations by rabbit serum esterases. Carbohydr. Res. **1997**, *302*, 13–18.

[2] Ljevaković, Đ.; Parat, D.; Tomašić, J.; Tomić, S. Syntheses and enzymatic hydrolyses of acylated methyl α-D-mannopyranosides. Croat. Chem. Acta **1995**, *68* (*3*), 477–484.

[3] Tomić, S.; Petrović, V.; Matanović, M. Synthesis, intramolecular migrations and enzymic hydrolysis of partially pivaloylated methyl α-D-mannopyranosides. Carbohydr. Res. **2003**, *338*, 491–494.

[4] Prugovečki, B.; Matković-Čalogović, D.; Petrović, V.; Tomić, S. Methyl 3,4-di-*O*-pivaloyl-β-D-xylopyranoside. Acta Cryst. **2004**, *E60*, o378–o380.

[5] Prugovečki, B.; Matković-Čalogović, D.; Petrović, V.; Tomić, S. Methyl 2,3,4-tri-*O*-pivaloyl-β-D-xylopyranoside. Acta Cryst. **2004**, *E60*, o1840–o1841.

[6] Tomić, S.; Treščec, A.; Ljevaković, Đ.; Tomašić, J. Partial purification of esterases from rabbit serum and their use in regioselective deacylations of sugars. Carbohydr. Res. **1991**, *210*, 191–198.

[7] Tomić, S.; Krstanović, M.; Tomašić, J. Isolation and properties of the guinea-pig esterases hydrolyzing esterified monosaccharides. Periodicum Biol. **1996**, *98*, 337–342.

[8] Petrović, V.; Tomić, S.; Matanović, M. Synthesis and intramolecular transesterifications of pivaloylated methyl α-D-galactopyranosides. Carbohydr. Res. **2002**, *337*, 863–867.

[9] Schauer, R. Biochemistry of sialic acid diversity. In *Carbohydrates in Chemistry and Biology. Part II Biology of Saccharides*; Ernst, B., Hart, G.W., Sinay, P., Eds.; Wiley-VCH: Weinheim, 2000; Vol. 3, 227–243.

[10] Gridley, J.J.; Osborn, H.M.I. Recent advances in the construction of β-D-mannose and β-D-mannosamine linkages. J. Chem. Soc., Perkin Trans. 1. **2000**, 1471–1491.

[11] Nilsson, M.; Norberg, T.J. Synthesis of a spacer-containing nonasaccharide fragment of *Streptococcus pneumoniae* 19F capsular polysaccharide. J. Chem. Soc., Perkin Trans. 1. **1998**, 1699–1704.

[12] Classon, B.; Garegg, P.J.; Oscarson, S.; Tidén, A.-K. Synthesis of an artificial antigen that corresponds to a disaccharide repeating unit of the capsular polysaccharide of *Haemophilus influenzae* type d. A facile synthesis of methyl 2-acetamido-2-deoxy-β-D-mannopyranoside. Carbohydr. Res. **1991**, *216*, 187–196.

[13] Nasir-ud-Din; Jeanloz, R.W. Synthesis of the 3- and 4-methyl, 3,4-dimethyl and 3,4,6-trimethyl ethers of methyl 2-acetamido-2-deoxy-α-D-mannopyranoside. Carbohydr. Res. **1973**, *28*, 243–251.

[14] Krist, P.; Kuzma, M.; Pelyvás, I.F.; Simerská, P.; Křen, V. Synthesis of 4-nitrophenyl 2-acetamido-2-deoxy-β-D-mannopyranoside and 4-nitrophenyl 2-acetamido-2-deoxy-α-D-mannopyranoside. Collect. Czech. Chem. Commun. **2003**, *68*, 801–811.

[15] Angelino, N.J.; Bernacki, R.J.; Sharma, M.; Dodson-Simmons, O.; Korytnyk, W. Versatile intermediates in the selective modification of the amino function of 2-amino-2-deoxy-D-mannopyranose and the 3-position of 2-acetamido-2-deoxy-D-mannose: potential membrane modifiers in neoplastic control. Carbohydr. Res. **1995**, *276*, 99–115.

[16] Hanchak, M.; Korytnyk, W. Studies of the epimerization of 2-acetamido-2-deoxy-D-glucopyranose: selective deuteration at C-2 of 2-acetamido-2-deoxyaldoses. Carbohydr. Res. **1976**, *52*, 219–222.

[17] Speak, A.L. *PLATON, A Multipurpose Crystallographic Tool*; Utrecht University: Utrecht, The Netherlands, **1998**.

[18] Cremer, D. On the correct usage of the Cremer-Pople puckering parameters as quantitative descriptors of ring shapes—a reply to recent criticism by Petit, Dillen and Geise. Acta Cryst. **1984**, *B40*, 498–500.

[19] Oxford Diffraction, Oxford Diffraction Ltd., Xcalibur CCD system, *CRYSALIS Software System, Version 1.17*; 2003.

[20] Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A.G.G.; Burla, M.C.; Polidori, G.; Camalli, M.; Spagna, R. *SIR 97: A Package for Crystal Structure Solution by Direct Methods and Refinement*; Roma, Italy, 1997.

[21] Sheldrick, G.M. *SHELXL97: Program for the Refinement of Crystal Structures*; Universität Göttingen: Germany, 1997.