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Note

Preparation of some novel *N*-acyl derivatives of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylamine

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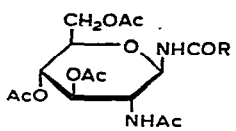
2-Acetamido-2-deoxy-D-glucosylamine residues are widely distributed in glycopeptides, glycoproteins, and proteoglycans, where they constitute a structural component linking carbohydrate to peptide or protein[1].

Under acetolysis conditions, 2-acetamido-*N*-aryl-2-deoxy-D-glycosylamines are converted into stable imidazole derivatives formed by dehydration between –NH–C=O (of the 2-acetamido group) and –NH– at C-1, without splitting the glycosylamine linkage[2,3]. The aim of the present work was to prepare 1-*N*-substituted derivatives of 2-acetamido-2-deoxy-β-D-glucopyranosylamine in order to examine the structural influence of the 1-*N*-substituent on imidazole formation. 1-*N*-*p*-Nitrobenzoyl[4], 1-*N*-isonicotinyl[4], 1-*N*-(2-acetamidoacetyl)[4], 1-*N*-(2-benzamidoacetyl)[4], 1-*N*-{2-[*N*-(benzyloxy)carbonyl]aminoacetyl}[4], 1-*N*-(L-aspart-1- or -4-oyl)[1,5–7] and 1-*N*-glutam-5-oyl[5] derivatives have been prepared by the carbodiimide method, and *N*-acetyl derivatives[4] have been prepared by acetylation with acetic anhydride.

We now report the preparation of a series of 1-*N*-(fatty acyl), 1-*N*-benzoyl, and 1-*N*-nicotinyl derivatives (**5**) of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylamine (**1**).



5 R = $-(CH_2)_nCH_3$; –Ph; $-C_5H_4N$

Compound **1** was *N*-acylated with the corresponding acid anhydride in pyridine at room temperature. As shown in Table I, the *N*-acyl derivatives were isolated in yields of 37.1–95.4%. All of the derivatives were soluble in chloroform.

The structures of these derivatives were confirmed by i.r. absorptions, n.m.r. spectra, elemental analysis, and specific rotations. The derivatives showed i.r. absorptions at ~3300 (NH), 2850–2950 (CH in fatty acyl), 1740–1750 and 1240–1250

TABLE I

PROPERTIES OF *N*-ACYL DERIVATIVES OF 2-ACETAMIDO-3,4,6-TRI-*O*-ACETYL-2-DEOXY-β-D-GLUCOPYRANOSYLAMINE

N-*Acyl group*	*Yield* (%)	*M.p.* (*degrees*)	$[\alpha]_D^{22}$ (*CHCl*$_3$) (*degrees*)	*Formula*	*Calc.*			*Found*		
					C	*H*	*N*	*C*	*H*	*N*
Acetyl[a]	78.4	244–246	+41 (*c* 1.0)	$C_{16}H_{24}N_2O_9$	49.48	6.23	7.21	49.52	6.14	7.21
Propanoyl	71.2	228.5–230	+6.0 (*c* 0.5)	$C_{17}H_{26}N_2O_9$	50.74	6.51	6.96	50.47	6.32	7.00
Butanoyl	66.8	227–228	+3.7 (*c* 1.1)	$C_{18}H_{28}N_2O_9$	51.92	6.78	6.73	51.80	6.77	6.70
Hexanoyl	92.9	223–225	+0.9 (*c* 1.1)	$C_{20}H_{32}N_2O_9$	54.04	7.26	6.30	54.25	7.29	6.40
Octanoyl	68.8	191–191.5	+1.9 (*c* 1.0)	$C_{22}H_{36}N_2O_9$	55.92	7.68	5.93	55.66	7.83	5.69
Decanoyl	73.7	182–183.5	−1.3 (*c* 1.2)	$C_{24}H_{40}N_2O_9$	57.58	8.05	5.60	57.51	8.29	5.43
Dodecanoyl	74.1	176.5–178	−3.5 (*c* 1.1)	$C_{26}H_{44}N_2O_9$	59.07	8.39	5.30	59.29	8.46	5.31
Tetradecanoyl	90.0	188.5–190	+3.3 (*c* 1.2)	$C_{28}H_{48}N_2O_9$	60.41	8.69	5.03	60.31	8.83	4.98
Hexadecanoyl	44.6	189–191	−8.2 (*c* 1.1)	$C_{30}H_{52}N_2O_9$	61.62	8.96	4.79	61.89	8.90	4.90
Octadecanoyl	41.3	189–191	−4.7 (*c* 1.1)	$C_{32}H_{56}N_2O_9$	62.72	9.21	4.57	62.47	9.12	4.54
Benzoyl[b]	95.4	246–248	−37 (*c* 0.57)	$C_{21}H_{26}N_2O_9$	55.99	5.82	6.22	56.00	5.89	6.29
Nicotinyl[c]	37.1	233–235	−5.0 (*c* 1.0)	$C_{20}H_{25}N_3O_9$	53.21	5.58	9.31	53.36	5.74	9.06

[a]Lit.[4] m.p. 241°, $[\alpha]_D^{22}$ +22.8° (*c* 1.2, pyridine). *O*-Deacetylation produced **3**, m.p. 234°, $[\alpha]_D^{20}$ +11.8° (*c* 0.76, water.) *Anal.* Calc. for $C_{10}H_{18}NO_6$: C, 45.75; H, 6.91; N, 10.68; found: C, 45.79; H, 6.89; N, 10.62; n.m.r. (D_2O): δ 2.05 (6 protons, *N*-Ac), 3.35–3.95 (7 protons, ring protons of the sugar); ν_{max}^{KBr} 3350–3250 (OH, NH), 1680 and 1660 (C=O in *N*-Ac), 1550 (NH in *N*-Ac). Lit.[4] m.p. 240–243°, $[\alpha]_D$ +43.7° (water) as the monohydrate. [b]$\lambda_{max}^{ethanol}$ 236 nm. [c]λ 255$_{max}^{ethanol}$ and 263 nm.

(C=O and C–O in *O*-acetyl), and 1640–1660 and 1530–1560 (C=O and NH in *N*-acyl), and no i.r. absorption at ~3500 cm^{-1} (OH). The *N*-benzoyl and *N*-nicotinyl derivatives showed i.r. absorptions at 730 and 700 (monosubstituted Ph) and 1600 cm^{-1} (phenyl), respectively. The 1-*N*-(fatty acyl) derivatives showed proton signals at δ 0.75–2.45 (fatty acyl), 1.95–2.10 (12 protons, acetyl-methyl), 4.9–5.4 (3 protons, H-1, H-3, and H-4), 4.20 (2 protons, H-6,6′) and 3.6–4.0 (2 protons, H-2 and H-5) in the n.m.r. spectra. The tentative assignments refer to those made for 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide[6,7] (**2**). The H-1 signal, which appeared as a doublet at δ ~5.09, was confirmed by decoupling. The $J_{1,2}$ values of 8.5–9.0 Hz observed are characteristic of the *trans*-diaxial arrangement of protons at C-1 and C-2 in the $^4C_1$(D) conformation. The β-D configuration at the anomeric center is supported by the small values of the specific rotation (Table I). The *N*-benzoyl and *N*-nicotinyl derivatives showed proton signals at δ 7.20–7.90 (5 protons, benzoyl) and 8.00–9.20 (4 protons, nicotinyl), respectively. The NH protons resonated as doublets at δ ~6.50 (1 proton) and 6.90 (1 proton), and these signals were tentatively assigned to the 2-acetamido and 1-acylamido groups, respectively[8]. The NH proton signals disappeared upon addition of D_2O. The *J* values observed (8.0–8.5 Hz) indicate the *trans* arrangement of hydrogen substituents at nitrogen in the acylamido groups and at C-1 or C-2 in the pyranose ring.

O-Deacetylation occurred on treatment of the *N*-acetyl derivatives with ammonia in methanol at room temperature, to afford 2-acetamido-1-*N*-acetyl-2-deoxy-β-D-glucopyranosylamine (**3**). 2-Amino-2-deoxy-D-glucose hydrochloride was produced on hydrolysis with 2M hydrochloric acid for 3 h at 100°.

EXPERIMENTAL

General methods. — Melting points are uncorrected. T.l.c. was performed on silica gel G, Type 60 (Merck) with 1:6 (v/v) ethanol–ethyl acetate as solvent. The other analytical methods were described in our previous paper[9].

2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosylamine (**1**). — Compound **1** was prepared from **2** by catalytic hydrogenation[4]; it showed no i.r. absorption at 2120 cm^{-1} (azide). Bis(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-amine[4] (**4**, $R_F = 0.68$) was detected by t.l.c. upon recrystallization of **1** ($R_F = 0.29$) from ethanol. Compound **1** was used without recrystallization for the *N*-acylation; it showed m.p. 156–157° and 235–238°, $[\alpha]_D^{20}$ −22° (*c* 0.5, chloroform) [lit.[4] m.p. 147–149°, $[\alpha]_D^{30}$ −14° (*c* 1.0, chloroform)]. The double melting point may result from conversion of **1** into **4** at high temperature.

General procedure for N-*acylation.* — Compound **1** (100–180 mg) was dissolved in dry pyridine (2–4 ml). The corresponding acid anhydride (1.2 mol per mol of **1**) was added, and the mixture was kept overnight at room temperature. For reactions with the higher fatty acid anhydrides (C_{12}–C_{18}), the mixture was heated for a few sec in a boiling-water bath to afford a clear solution. After completion of the reaction, the mixture was poured into ice–water (~50 ml) and the solution evaporated *in vacuo*

to dryness, with addition of portions of water several times in order to remove pyridine. The residue was crystallized and recrystallized from ethanol. For the *N*-nicotinyl derivative, the product was extracted with chloroform (3 × 20 ml), and the extract was evaporated to dryness. The residue was crystallized from ethanol.

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