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Carbohydrate Research 257 (1994) 137–143

CARBOHYDRATE RESEARCH

Note

Acylating properties of *N*-substituted 2-*C* : 1-*N*-carbonyl-2-deoxyglycopyranosylamines

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(Received March 23rd, 1993; accepted October 6th, 1993)

Recently, we reported that the unstable [2 + 2]cycloadducts (**1**) of tosyl [1,2] or trichloroacetyl [3,4] isocyanate and glycals, upon treatment with alcohols or water, underwent rapid opening of the four-membered ring at the anomeric carbon atom to afford glycosides having alkoxyl and carbamoyl functions located *anti* (Scheme 1) [1–4].

In this paper, we demonstrate that the direction of the attack of nucleophiles at 2-*C* : 1-*N*-carbonyl-2-deoxyglycopyranosylamines [5] depends on the electronegativity of the Z-substituent at the nitrogen atom. To illustrate this phenomenon, we selected four compounds (**5–8**) of α-D-*gluco* configuration, bearing an *N*-acyl substituent having less electron-withdrawing character than a sulfonyl or trichloroacetyl substituent.

The tetraacetate **5** was obtained by peracetylation of the unsubstituted compound **2** [6], whereas the *N*-acetyl (**6**), *N*-ethoxycarbonyl (**7**), and *N*-carbamoyl (**8**) derivatives were obtained by direct acylation of the β-lactam nitrogen atom in **4** with acetic anhydride, ethyl chloroformate, and trichloroacetyl isocyanate, respectively. Compound **7** could also be obtained by high-pressure [2 + 2]cycloaddition of ethoxycarbonyl isocyanate to tri-*O*-benzyl-D-glucal [7].

Compounds **5–8**, when dissolved in methanol and left overnight at room temperature, afforded the respective methyl esters **9–12** in good or moderate yield. The same direction of opening was observed when the *N*-acyl compounds **5–8** were treated with benzylamine, hexylamine, or the methyl ester of glycine. The products **9**, **10**, **13**, **14**, **17**, and **18** derived from the *N*-acetyl compounds **5** and **6** were contaminated with the corresponding *N*-deprotected compounds **3** and **4**.

Opening of the four-membered β-lactam ring at the anomeric carbon atom is an S_N type reaction and requires a good leaving group at the place of substitution.

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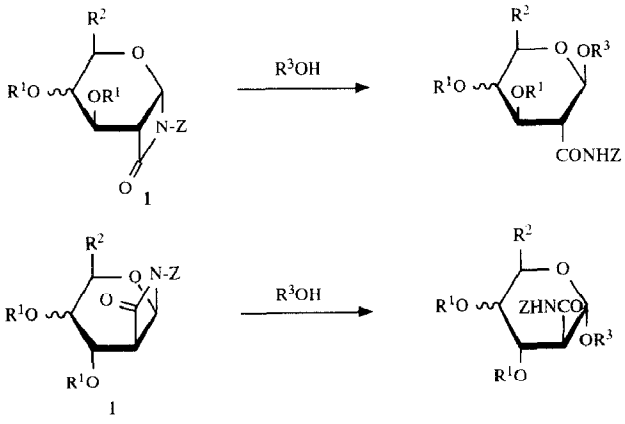
SSDI 0008-6215(93)E0389-I

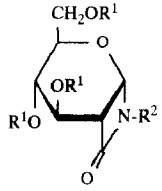


R^1= Ac, Bn; R^2= H, CH_2OR^1; R^3= Me, Et, Bn; Z= Ts, CCl_3CO

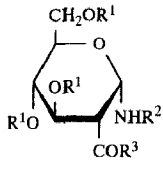
Scheme 1.

This is accomplished if the nitrogen atom bears a strong electron-withdrawing substituent such as the tosyl or trichloroacetyl group. On the other hand, opening at the β-lactam carbonyl group proceeds via an addition–elimination mechanism and requires only slight activation. Both openings are accelerated by the strain of the four-membered ring.

The opening at the β-lactam carbonyl group preserves the original configuration of the substrate, providing *N*-acylglucosylamines with α-D configuration, which are not easily accessible in other ways [8].



2 R^1= R^2= H
3 R^1= Ac, R^2= H
4 R^1= Bn, R^2= H
5 R^1= R^2= Ac
6 R^1= Bn, R^2= Ac
7 R^1= Bn, R^2= CO_2Et
8 R^1= Bn, R^2= $CONH_2$



9 R^1= R^2= Ac, R^3= OMe
10 R^1= Bn, R^2= Ac, R^3= OMe
11 R^1= Bn, R^2= CO_2Et, R^3= OMe
12 R^1= Bn, R^2= $CONH_2$, R^3= OMe
13 R^1= R^2= Ac, R^3= NHBn
14 R^1= Bn, R^2= Ac, R^3= NHBn
15 R^1= Bn, R^2= CO_2Et, R^3= NHBn
16 R^1= Bn, R^2= $CONH_2$, R^3= NHBn
17 R^1= R^2= Ac, R^3= NHC_6H_{13}
18 R^1= Bn, R^2= Ac, R^3= NHC_6H_{13}
19 R^1= Bn, R^2= CO_2Et, R^3= NHC_6H_{13}
20 R^1= Bn, R^2= $CONH_2$, R^3= NHC_6H_{13}
21 R^1= R^2= Ac, R^3= $NHCH_2CO_2Me$
22 R^1= Bn, R^2= CO_2Et, R^3= $NHCH_2CO_2Me$

Compounds **9–22** give an entry to a variety of 2-deoxy-2-*C*-acyloyl compounds of synthetic value and potential biological activity.

It is generally accepted that penicillins and other β-lactam antibiotics are bound to PBPs (penicillin-binding proteins) or to β-lactamase enzymes through the β-lactam carbonyl as the acyloyl moiety [9]. This binding requires opening of the four-membered ring at the β-lactam carbonyl group. Activation of our 2-*C*:1-*N*-carbonyl-2-deoxyglycopyranosylamines towards opening of the β-lactam ring at the carbonyl carbon atom creates a chance to find interesting biological properties of these compounds.

1. Experimental

All melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 spectropolarimeter. ^{1}H NMR spectra were recorded with Varian Gemini (200 MHz) and Bruker AM 500 (500 MHz) spectrometers, and IR spectra with a Perkin–Elmer spectrophotometer.

Column chromatography was carried out using Merck Kieselgel 70–230 or 230–400 mesh.

Compound **2** was obtained according to refs 5 and 10, compound **4** according to ref 5, and compound **5** according to ref 6.

N-*Acetyl-3,4,6-tri*-O-*benzyl-2*-C : *1*-N-*carbonyl-2-deoxy-α*-D-*glucopyranosylamine* (**6**).—β-Lactam **4** (0.137 g, 0.3 mmol) was treated with 1:2 Ac_2O–pyridine and left for 2 days. Subsequently, the mixture was poured into ice–water and extracted with ether. The extract was washed with water and brine, dried, and evaporated. The crude product was purified by column flash chromatography using hexane–EtOAc as an eluent to afford **6** (0.075 g, 50%); mp 83–84°C; $[\alpha]_D$ + 83.8° (*c* 1.4, CH_2Cl_2); ν_{max}(Nujol) 1794 (β-lactam) and 1716 cm^{-1} (C=O); ^{1}H-NMR data ($CDCl_3$): δ 2.34 (s, 3 H, Ac), 3.50 (dd, 1 H, $J_{1,2}$ 5.3, $J_{2,3}$ 3.2 Hz, H-2), 3.66 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 10.4 Hz, H-6a), 3.73 (dd, 1 H, $J_{5,6b}$ 3.7 Hz, H-6b), 3.81 (dd, 1 H, $J_{4,5}$ 7.1 Hz, H-4), 3.89 (m, 1 H, H-5), 4.13 (dd, 1 H, $J_{3,4}$ 5.6 Hz, H-3), 5.84 (d, 1 H, H-1). Anal. Calcd. for $C_{30}H_{31}NO_6$: C, 71.8; H, 6.2; N, 2.8. Found: C, 72.1; H, 6.3; N, 2.9.

3,4,6-Tri-O-*benzyl*-2-C : *1*-N-*carbonyl-2-deoxy*-N-*ethoxycarbonyl-α*-D-*glucopyranosylamine* (**7**).—To a solution of **4** (0.69 g, 1.5 mmol) and Et_3N (0.83 mL, 6 mmol) in CH_2Cl_2 (10 mL) was added ethyl chloroformate (0.57 mL, 6 mmol) with cooling and stirring. The mixture was stirred at room temperature until disappearance of the substrate. Subsequently it was evaporated to dryness and purified on a column of silica gel using 1:1 ethyl ether–hexane as eluent to afford **7** (0.61 g, 78%); mp 69–70°C; $[\alpha]_D$ + 72.2° (*c* 0.8, CH_2Cl_2); ν_{max}(Nujol) 1821 (β-lactam), and 1718 cm^{-1} (C=O); ^{1}H NMR data ($CDCl_3$): δ 1.33 (t, 3 H, CH_3), 3.49 (dd, $J_{1,2}$ 5.3, $J_{2,3}$ 3.1 Hz, H-2), 3.68 (dd, 1 H, $J_{5,6a}$ 3.2, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.74 (dd, 1 H, $J_{5,6b}$ 3.9 Hz, H-6b), 3.78 (dd, 1 H, $J_{3,4}$ 6.2, $J_{4,5}$ 7.8 Hz, H-4), 3.92 (dt, 1 H, H-5), 4.11 (dd, 1 H, H-3), 4.30 (q, 2 H, CH_2), 5.82 (d, 1 H, H-1). Anal. Calcd for $C_{31}H_{33}NO_7$: C, 70.0; H, 6.2; N, 2.6. Found: C, 69.4; H, 6.4; N, 2.6.

3,4,6-Tri-O-*benzyl*-N-*carbamoyl-2*-C : *1*-N-*carbonyl-2-deoxy-α*-D-*glucopyranosylamine* (**8**).—To a solution of **4** (0.183 g, 0.4 mmol) in dry MeCN (5 mL) was added

trichloroacetyl isocyanate (0.09 mL, 0.8 mmol) with stirring. The mixture was stirred until disappearance of the substrate (TLC). Subsequently, it was cooled to −30°C and benzylamine (0.043 mL, 0.4 mmol) was added in dry MeCN (5 mL). The temperature was allowed to rise to room temperature, and the mixture was evaporated to dryness and purified on a column of silica gel by flash chromatography using 3:7 EtOAc–hexane as eluent to afford **8** (0.14 g, 70%) as a syrup; $[\alpha]_D$ + 71.9° (*c* 1, CH_2Cl_2); ν_{max}(film) 3440, 3342 (NH), 1776 (β-lactam), and 1718 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 3.53 (ddd, 1 H, $J_{1,2}$ 5.1, $J_{2,3}$ 3.1, $J_{2,4}$ 0.6 Hz, H-2), 3.68 (dd, 1 H, $J_{5,6a}$ 3.9, $J_{6a,6b}$ 10.4 Hz, H-6a), 3.75 (dd, 1 H, $J_{5,6b}$ 3.7 Hz, H-6b), 3.83 (ddd, 1 H, $J_{3,4}$ 5.8, $J_{4,5}$ 7.0 Hz, H-4), 3.96 (dt, 1 H, H-5), 4.11 (dd, 1 H, H-3), 5.87 (d, 1 H, H-1). Anal. Calcd for $C_{29}H_{30}N_2O_6$: C, 69.3; H, 6.0; N, 5.6. Found: C, 69.0; H, 6.3; N, 5.4.

Methanolysis of compounds **5–8**: *general procedure.*—Compounds **5–8** (0.05 mmol) were each dissolved in abs MeOH (2.5 mL) and left for 48 h. Subsequently, the MeOH was evaporated and each residue was purified on a column of silica gel by flash chromatography to afford products **9–12**, respectively.

N-*Acetyl-3,4,6-tri*-O-*acetyl-2-deoxy-2*-C-*methoxycarbonyl-α*-D-*glucopyranosylamine* (**9**); 66%; mp 154–155°C; $[\alpha]_D$ + 103° (*c* 0.8, CH_2Cl_2); ν_{max}(Nujol) 3378 (NH), 1737 (ester), and 1706 cm^{-1} (NHAc); ^1H NMR data ($CDCl_3$): δ 2.02, 2.03, 2.05, 2.08 (4 s, 12 H, 4 Ac), 3.27 (dd, 1 H, $J_{1,2}$ 5.3, $J_{2,3}$ 11.4 Hz, H-2), 3.72 (s, 3 H, OMe), 3.95 (ddd, 1 H, $J_{4,5}$ 9.7, $J_{5,6a}$ 2.3, $J_{5,6b}$ 4.2 Hz, H-5), 4.06 (dd, 1 H, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.34 (dd, 1 H, H-6b), 4.99 (t, 1 H, H-4), 5.64 (dd, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 5.94 (dd, 1 H, $J_{1,NH}$ 7.7 Hz, H-1), 6.76 (bd, 1 H, NH). Anal. Calcd for $C_{16}H_{23}NO_{10}$: C, 49.35; H, 5.95; N, 3.6. Found: C, 49.3; H, 6.2; N, 3.4.

N-*Acetyl-3,4,6-tri*-O-*benzyl-2-deoxy-2*-C-*methoxycarbonyl-α*-D-*glucopyranosylamine* (**10**); 67%; mp 155–156°C; $[\alpha]_D$ + 66.9° (*c* 1, CH_2Cl_2); ν_{max}(Nujol) 3378 (NH), 1736 (ester), and 1695 cm^{-1} (C=O); ^1H-NMR data ($CDCl_3$): δ 2.01 (s, 3 H, Ac), 3.14 (dd, 1 H, $J_{1,2}$ 5.1, $J_{2,3}$ 10.8 Hz, H-2), 3.68 (s, 3 H, OMe), 3.6–3.9 (m, 4 H, H-4,5,6a,6b), 4.05 (dd, 1 H, $J_{3,4}$ 8.1 Hz, H-3), 5.79 (dd, 1 H, $J_{1,NH}$ 7.3 Hz, H-1), 6.50 (d, 1 H, NH). Anal. Calcd for $C_{31}H_{35}NO_7$: C, 69.8; H, 6.6; N, 2.6. Found: C, 69.9; H, 6.7; N, 2.2.

3,4,6-Tri-O-*benzyl-2-deoxy*-N-*ethoxycarbonyl-2*-C-*methoxycarbonyl-α*-D-*glucopyranosylamine* (**11**); 77%; mp 122–123°C; $[\alpha]_D$ + 75.6° (*c* 1.2, CH_2Cl_2); ν_{max}(Nujol) 3401 (NH), 1731 cm^{-1} (ester and NHAc); ^1H NMR data ($CDCl_3$); δ 1.24 (t, 3 H, CH_3), 3.13 (dd, 1 H, $J_{1,2}$ 5.1, $J_{2,3}$ 11.0 Hz, H-2), 3.68 (s, 3 H, OMe), 3.67–4.05 (m, 4 H, H-4,5,6a,6b), 4.02 (m, 1 H, $J_{3,4}$ 8.5 Hz, H-3), 4.13 (m, 2 H, $-CH_2-$), 4.48–4.85 (6d, 6 H, 3 benzyl), 5.64 (dd, 1 H, $J_{1,NH}$ 7.7 Hz, H-1), 5.73 (bs, 1 H, NH). Anal. Calcd for $C_{32}H_{37}NO_8$: C, 68.2; H, 6.6; N, 2.5. Found: C, 68.7; H, 6.6; N, 2.5.

3,4,6-Tri-O-*benzyl-2-deoxy-2*-C-*methoxycarbonyl-α*-D-*glucopyranosylurea* (**12**); 75%; mp 195–200°C; $[\alpha]_D$ + 89.9° (*c* 0.5, CH_2Cl_2); ν_{max}(Nujol) 1725 (ester), 1672, and 1649 cm^{-1} (urea); ^1H NMR data ($CDCl_3$): δ 3.10 (dd, 1 H, $J_{1,2}$ 4.8, $J_{2,3}$ 11.2 Hz, H-2), 3.70 (s, 3 H, OMe), 3.58–3.82 (m, 3 H, H-4,6a,6b), 3.95 (ddd, 1 H, $J_{5,6a}$ 2.1, $J_{5,6b}$ 4.0, $J_{4,5}$ 9.6 Hz, H-5), 4.09 (dd, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 4.40–4.86 (6 d, 6 H, 3 benzyl), 5.06 (bs, 2 H, NH_2), 5.41 (2, 1 H, $J_{1,NH}$ H-1), 5.78 (bd, 1 H, NH). Anal. Calcd for $C_{30}H_{34}N_2O_7$: C, 67.4; H, 6.4; N, 5.2. Found: C, 67.3; H, 6.3; N, 5.0.

Aminolysis of compounds **5–8**: *general procedure.*—Compounds **5–8** (0.05 mmol) were each dissolved in CH_2Cl_2 (1.0 mL) and treated with benzylamine or hexylamine (0.15 mmol). The mixture was left overnight at room temperature. Subsequently, the solvent was removed under reduced pressure and each crude product purified by flash column chromatography to afford products **13–20**, respectively.

N-*Acetyl-3,4,6-tri*-O-*acetyl-2*-C-(N-*benzylcarbamoyl*)-*2-deoxy-α*-D-*glucopyranosylamine* (**13**); 50%; mp 75–80°C; $[\alpha]_D$ + 51.0° (*c* 1.2, CH_2Cl_2); ν_{max}(Nujol) 1745 (ester) and 1676 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 1.89, 2.02, 2.03 (3 s, 12 H, 4 Ac), 3.09 (dd, 1 H, $J_{1,2}$ 5.2, $J_{2,3}$ 11.4 Hz, H-2), 3.9–4.1 (m, 2 H, H-5,6a), 4.25 (dd, 1 H, *J* 14.7 and 5.1 Hz, NC*H*HPh), 4.37 (dd, 1 H, $J_{5,6b}$ 4.9, $J_{6a,6b}$ 12.4 Hz, H-6b), 4.56 (dd, 1 H, *J* 6.7 Hz, NCH*H*Ph), 4.99 (t, 1 H, $J_{3,4}$ 9.4, $J_{4,5}$ 10.2 Hz, H-4), 5.66 (dd, 1 H, H-3), 5.72 (t, 1 H, $J_{1,NH}$ 5.2 Hz, H-1), 6.63 (t, 1 H, N*H*Bn), 7.11 (d, 1 H, N*H*Ac). Anal. Calcd. for $C_{22}H_{28}N_2O_9$: C, 56.9; H, 6.1; N, 6.0. Found C, 56.7; H, 6.4; N, 6.3.

N-*Acetyl-3,4,6-tri*-O-*benzyl-2*-C-(N-*benzylcarbamoyl*)-*2-deoxy-α*-D-*glucopyranosylamine* (**14**); 71%; mp 178–180°C; $[\alpha]_D$ + 27.7° (*c* 1, CH_2Cl_2); ν_{max}(Nujol) 1697 and 1652 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 2.02 (s, 3 H, Ac), 2.79 (dd, 1 H, $J_{1,2}$ 5.2, $J_{2,3}$ 10.9 Hz, H-2), 3.6–3.9 (m, 4 H, H-4,5,6a,6b), 4.17 (dd, 1 H, $J_{3,4}$ 8.4 Hz, H-3), 4.29 (dd, 1 H, *J* 14.6 and 5.1 Hz, NC*H*HPh), 4.4–4.9 (m, 7 H, NCH*H*Ph, benzyl), 5.64 (t, 1 H, $J_{1,NH}$ 4.6 Hz, H-1), 6.18 (t, 1 H, *J* 6.9 Hz, N*H*Bn). Anal. Calcd for $C_{30}H_{31}NO_6$: C, 73.0, H, 6.6; N, 4.6. Found: C, 72.5; H, 6.2; N, 4.9.

3,4,6-Tri-O-*benzyl-2*-C-(N-*benzylcarbamoyl*)-*2-deoxy*-N-*ethoxycarbonyl-α*-D-*glucopyranosylamine* (**15**); 60%; mp 163–164°C; $[\alpha]_D$ + 31.5° (*c* 1, CH_2Cl_2); ν_{max}(Nujol) 3323, 3267 (NH), 1719, and 1652 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 1.24 (t, 3 H, CH_3), 2.80 (dd, 1 H, $J_{1,2}$ 5.1, $J_{2,3}$ 10.9 Hz, H-2), 3.66 (m, 1 H, H-6a), 3.76 (t, 1 H, $J_{3,4}$ 8.6, $J_{4,5}$ 9.5 Hz, H-4), 4.04–4.17 (m, 2 H, OCH_2CH$_3$), 4.14 (dd, 1 H, H-3), 4.30 (dd, 1 H, *J* 14.7 and 5.0 Hz, NC*H*HPh), 4.12–4.84 (m, 7 H, NCH*H*Ph, benzyl), 5.52 (t, 1 H, $J_{1,NH}$ 5.3 Hz, H-1), 6.24 (t, 1 H, N*H*Bn), 6.35 (d, 1 H, N*H*CO$_2$Et). Anal. Calcd for $C_{38}H_{42}N_2O_7$: C, 71.45; H, 6.6; N, 4.4. Found: C, 71.6; H, 6.7; N, 4.3.

3,4,6-Tri-O-*benzyl-2*-C-(N-*benzylcarbamoyl*)-*2-deoxy-α*-D-*glucopyranosylurea* (**16**); 70%; mp 234–236°C; $[\alpha]_D$ + 41.2° (*c* 0.5 MeOH); ν_{max} (film) 3378, 3307, 3201 (NH), and 1642 cm^{-1} (amide). ^1H NMR data (CD_3OD): δ 2.97 (dd, 1 H, $J_{1,2}$ 5.3, $J_{3,4}$ 11.1 Hz, H-2), 3.55–3.83 (m, 4 H, H-4,5,6a,6b), 4.21 (dd, 1 H, $J_{3,4}$, 8.7 Hz, H-3), 4.32 and 4.46 (2 d, 2 H, *J* 14.5 Hz, NCH_2Ph), 4.43–4.90 (m, 6 H, benzyl), 5.58 (d, 1 H, H-1). Anal. Calcd for $C_{36}H_{39}N_3O_6$: C, 70.9; H, 6.4; N, 6.8. Found: C, 70.5; H, 6.5; N, 6.9.

N-*Acetyl-3,4,6-tri*-O-*acetyl-2-deoxy-2*-C-(N-*hexylcarbamoyl*)-*α*-D-*glucopyranosylamine* (**17**); syrup (52%); $[\alpha]_D$ + 10.6° (*c* 1.5, CH_2Cl_2); ν_{max}(film) 3351 (NH), 1729 and 1651 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 1.98, 2.02, 2.05, 2.06 (4 s, 12 H, acetyl), 3.05 (dd, 1 H, $J_{1,2}$ 5.2, $J_{2,3}$ 11.4 Hz, H-2), 3.2 (m, 2 H, NCH_2), 3.9–4.1 (m, 2 H, H-5,6a), 4.34 (dd, 1 H, $J_{5,6}$ 4.7, $J_{6a,6b}$ 12.4 Hz, H-6b), 4.99 (t, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 10.1 Hz, H-4), 5.64 (dd, 1 H, H-3), 5.69 (t, 1 H, $J_{1,NH}$ 3.6 Hz, H-1), 6.54 (t, 1 H, *J* 11.5 Hz, N*H*hexyl). Compound **17** gave inconsistent elemental analyses.

N-Acetyl-3,4-6-tri-O-benzyl-2-deoxy-2-C-(N-hexylcarbamoyl)-α-D-glucopyranosylamine (**18**); 77%; mp 132–133°C; $[\alpha]_D$ + 44.3° (*c* 0.5, CH_2Cl_2); ν_{max}(film) 3375, 3332 (NH), 1703 and 1652 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 2.02 (s, 3 H, Ac), 2.72 (dd, 1 H, $J_{1,2}$ 5.1, $J_{2,3}$ 10.8 Hz, H-2), 3.22 (m, 2 H, NCH_2), 3.74 (m, 4 H, H-4,5,6a,6b), 4.13 (dd, 1 H, $J_{3,4}$ 8.2 Hz, H-3), 4.4–4.9 (m, 6 H, benzyl), 5.58 (t, 1 H, $J_{1,NH}$ 4.6 Hz, H-1), 5.77 (t, 1 H, N*H*hexyl). Anal. Calcd for $C_{36}H_{46}N_2O_6$: C, 71.7; H, 7.7; N, 4.6. Found: C, 71.4; H, 7.8; N, 4.4.

3,4,6-Tri-O-benzyl-2-deoxy-N-ethoxycarbonyl-2-C-(N-hexylcarbamoyl)-α-D-glucopyranosylamine (**19**); syrup; $[\alpha]_D$ + 55.0° (*c* 0.5, CH_2Cl_2); ν_{max}(film) 3350, 3266 (NH), 1723 (ester), 1705 and 1656 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 2.70 (dd, 1 H, $J_{1,2}$ 5.0, $J_{2,3}$ 10.9 Hz, H-2), 3.24 (m, 2 H, NCH_2), 3.6–3.9 (m, 4 H, H-4,5,6a,6b), 4.11 (m, 3 H, OCH_2, H-3), 4.4–4.9 (m, 6 H, benzyl), 5.47 (t, 1 H, $J_{1,NH}$ 5.0 Hz, H-1), 5.74 (t, 1 H, N*H*hexyl), 6.40 (d, 1 H, N*H*CO_2Et). Anal. Calcd for $C_{37}H_{48}N_2O_7$: C, 70.2; H, 7.6; N, 4.4. Found: C, 70.2; H, 7.7; N, 4.5.

3,4,6-Tri-O-benzyl-2-deoxy-2-C-(N-hexylcarbamoyl)-α-D-glucopyranosylurea (**20**); 60%; mp 222–226°C; $[\alpha]_D$ + 52.6° (*c* 0.2, MeOH); ν_{max}(Nujol) 3381, 3330, 3207 (NH), 1647 cm^{-1} (amide); ^1H NMR data (pyridine-d_5): δ 3.39 (m, 3 H, H-2, NCH_2), 3.78 (bd, 1 H, $J_{6a,6b}$ 10.7 Hz, H-6a), 3.92 (m, 2 H, H-4,5), 4.19 (bd, 1 H, H-6b), 4.44 (dd, $J_{2,3}$ 11.0, $J_{3,4}$ 9.4 Hz, H-3), 4.46–5.06 (m, 6 H, benzyl), 6.29 (t, 1 H, *J* 12.0 Hz, H-1), 6.75 (s, 2 H, NH_2), 7.74 (bd, 1 H, N*H*CO), 9.13 (t, 1 H, N*H*hexyl). Anal. Calcd for $C_{35}H_{46}N_3O_6$: C, 69.5; H, 7.7; N, 6.95. Found: C, 69.8; H, 7.0; N, 6.4.

N-Acetyl-3,4,6-tri-O-acetyl-2-deoxy-2-C-[N-(methoxycarbonylmethyl)carbamoyl]-α-D-glucopyranosylamine (**21**).—Glycine methyl ester hydrochloride (0.04 g, 0.45 mmol) was stirred with an excess of Et_3N in THF (3 mL) for 1 h. Compound **5** (0.037 g, 0.1 mmol) was then added and the mixture was stirred for 2 days at room temperature. The solvents were removed under vacuum and the residue was purified by column chromatography to afford **21** (0.029 g, 63%); mp 194–198°C; $[\alpha]_D$ + 84.7° (*c* 1.5, CH_2Cl_2); ν_{max}(Nujol) 3389, 3307 (NH), 1743 (ester), 1702 and 1643 cm^{-1} (amide); ^1H NMR data ($CDCl_3$): δ 2.00, 2.02, 2.05, 2.07 (4 s, 12 H, 4 Ac), 3.22 (dd, 1 H, $J_{1,2}$ 5.1 and 11.5 Hz, H-2), 3.75 (s, 3 H, OMe), 3.93 (dd, 1 H, *J* 5.0 and 18.3 Hz, NC*H*HCO_2), 4.04 (m, 2 H, H-5,6a), 4.16 (dd, 1 H, *J* 6.2 Hz NCH*H*CO_2), 4.17 (dd, 1 H, $J_{5,6b}$ 4.7, $J_{6a,6b}$ 12.6 Hz, H-6b), 5.01 (t, 1 H, *J* 9.3, $J_{4,5}$ 10.1 Hz, H-4), 5.65 (dd, 1 H, H-3), 5.79 (t, 1 H, $J_{1,NH}$ 5.7 Hz, H-1), 6.92 (t, 1 H, N*H*CH_2), 7.04 (d, 1 H, N*H*Ac). Anal. Calcd for $C_{18}H_{26}N_2O_{11}$: C, 48.4; H, 5.9; N, 6.3 Found: C, 48.9; H, 6.0; N, 5.6.

3,4,6-Tri-O-benzyl-2-deoxy-N-ethoxycarbonyl-2-C-[N-(methoxycarbonylmethyl)carbamoyl]-α-D-glucopyranosylamine (**22**).—Compound **22** was obtained according to the procedure described above; syrup (61%); $[\alpha]_D$ + 62.0° (*c* 1, CH_2Cl_2); ν_{max}(Nujol) 3289 (NH), 1734 and 1653 cm^{-1} (amide). ^1H NMR data ($CDCl_3$) δ 1.23 (t, 3 H, CH_3), 2.89 (dd, 1 H, $J_{1,2}$ 4.9, $J_{2,3}$ 10.7 Hz, H-2), 3.74 (s, 3 H, OMe), 3.6–3.9 (m, 4 H, H-4,5,6a,6b), 3.98 (d, 1 H, NCH_2), 4.02–4.20 (m, 3 H, OCH_2), 5.53 (t, 1 H, $J_{1,NH}$ 5.4 Hz, 1), 6.22 (d, 1 H, N*H*CO_2Et), 6.45 (t, 1 H, N*H*CH_2). Compound **22** gave inconsistent elemental analyses.

2. Acknowledgment

This work was supported by the Polish Science Foundation grant PONT.

3. References

[1] M. Chmielewski, Z. Kałuża, C. Bełżecki, P. Sałański, J. Jurczak, and H. Adamowicz, *Tetrahedron*, 41 (1985) 2441–2449.
[2] D. Mostowicz, O. Zegrocka, and M. Chmielewski, *Carbohydr. Res.*, 212 (1991) 283–288.
[3] M. Chmielewski, Z. Kałuża, D. Mostowicz, E. Baranowska, C. Bełżecki, J.P. Jacobsen, P. Sałański, and J. Jurczak, *Tetrahedron*, 43 (1987) 4555–4563.
[4] D. Mostowicz, C. Bełżecki, and M. Chmielewski, *J. Carbohydr. Chem.*, 7 (1988) 805–810.
[5] J. Grodner, R. Urbański, C. Bełżecki and M. Chmielewski, *Pol. J. Chem.*, 66 (1992) 813–816.
[6] Z. Kałuża, M. Chmielewski, D. Sałański, and J. Jurczak, *Chem. Ber.*, 126 (1993) 265–267.
[7] M. Chmielewski, Z. Kałuża, P. Sałański, and J. Jurczak, *High Pressure Res.*, 11 (1992) 171–176.
[8] H. Paulsen and K.-W. Pflughaupt, in W. Pigman and D. Horton (Eds.), *The Carbohydrates: Chemistry and Biochemistry*, Vol. IB, Academic, London, 1980, pp. 881–927; A. Klemer and M. Kohla, *J. Carbohydr. Chem.*, 7 (1988) 785–797; A.J. Ratcliffe, P. Konradsson, and B. Fraser-Reid, *Carbohydr. Res.*, 216 (1991) 323–335.
[9] C.H. O'Callaghan and P.W. Muggleton, in E.H. Flynn (Ed.), *Cephalosporins and Penicillins*, Academic, New York, 1972, pp. 439–490; R.B. Sykes and K. Bush, in R.B. Morin and M. Gorman (Eds.), *Chemistry and Biology of β-Lactam Antibiotics*, Vol. 3, Academic, New York, 1982, pp. 155–202; D.J. Waxman and J.L. Strominger, in R.B. Morin and M. Gorman (Eds.), *Chemistry and Biology of β-Lactam Antibiotics*, Vol. 3, Academic New York, 1982, pp. 210–278.
[10] M. Chmielewski and Z. Kałuża, *Carbohydr. Res.*, 167 (1987) 143–152.