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A FACILE SYNTHESIS OF 2-METHYL-[3,4-DI-*O*-ACETYL-6-*O*-(CHLOROACETYL)-1,2-DIDEOXY-α-D-GLUCOPYRANO]-[2′,1′:4,5]-2-OXAZOLINE*

KHUSHI L. MATTA AND JOSEPH J. BARLOW
Department of Gynecology, Roswell Park Memorial Institute, Buffalo, New York 14263 (U. S. A.)
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ABSTRACT

The use of the chloroacetyl group as a protecting group has been studied for a 2-methylglyco-[2′,1′:4,5]-2-oxazoline. The reaction of chloroacetyl chloride or chloroacetic anhydride with 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-β-D-glucopyranose provided 2-acetamido-1,3,4-tri-*O*-acetyl-6-*O*-(chloroacetyl)-2-deoxy-β-D-glucopyranose which, on treatment with anhydrous ferric chloride in dichloromethane, produced the desired oxazoline. The glycosylating capability of the oxazoline has been investigated with aglycon hydroxides, to give the corresponding 2-acetamido-2-deoxy-β-D-glucopyranosides. The chloroacetyl group can be selectively removed by treatment with thiourea, and migration of *O*-acetyl groups was not observed under these conditions.

INTRODUCTION

For the past few years, *O*-acetylated 2-methylglyco-[2′,1′:4,5]-2-oxazolines have been widely employed as suitable glycosylating agents for the facile synthesis of various 1,2-*trans*-2-acetamido-2-deoxy-D-glycopyranosides[1,4–10]. In order to extend the use of the oxazoline method for the sequential synthesis of complex sugar molecules, we have focused our attention on the preparation of oxazolines having a protecting group that can be selectively removed after *O*-glycosylation, providing thereby a suitable site for the attachment of another carbohydrate unit. The chloroacetyl group was chosen as a suitable protecting group, as it has been well established that removal of this group can be accomplished by treatment with thiourea, whereas other protecting groups (such as *O*-acetyl and *O*-benzoyl) remain intact under these conditions[11,12]. In these investigations, we report a facile synthesis of 2-methyl-[3,4-di-*O*-acetyl-6-*O*-(chloroacetyl)-1,2-dideoxy-α-D-glucopyrano]-[2′,1′:4,5]-2-oxazoline.

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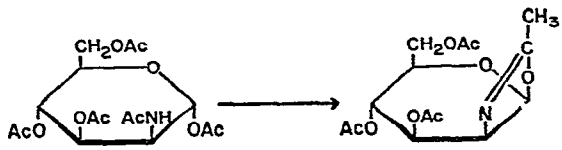
RESULTS AND DISCUSSION

Among the methods for the preparation of 2-methylglyco-[2′,1′:4,5]-2-oxazolines[1,4,8,13–15], that based upon the reaction of anhydrous ferric chloride with, for example, 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucopyranose in dichloromethane[1,4] is distinguished for its simplicity and efficiency. However, for the formation of an oxazoline under these conditions, it is essential that the anomeric *O*-acetyl group should be *trans* to the 2-acetamido group. This is supported by the fact that 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-mannopyranose[14,16] (**1**) produces



1 **2**

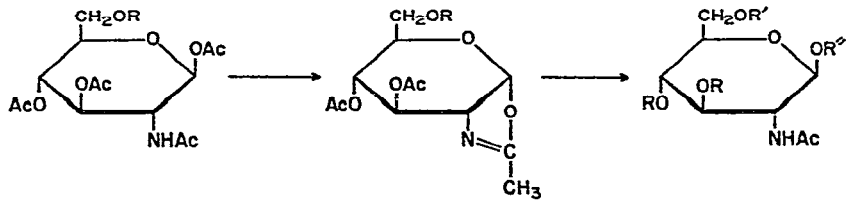
the oxazoline (**2**) in 59 percent yield under these conditions, whereas the readily available 2-acetamido-1,3,4,6-tetra-*O*-acetyl-β-D-mannopyranose[17] does not react to give **2**. Based upon these observations, 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-β-D-glucopyranose (**3**) was considered to be a suitable starting-material for the synthesis of the title oxazoline.

Compound **3** was prepared from crystalline 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-trityl-β-D-glucopyranose by treatment with hydrogen bromide in glacial acetic acid, as described by Anderson and Percival[18]. These workers established that migration of the *O*-acetyl group does not take place during removal of the trityl group. The anomeric configuration of C-1 was further established by the n.m.r. spectrum, which showed two doublets at τ 3.78 (*J* 10 Hz) for NH, and τ 4.25 (*J* 9 Hz, H-1) for the β-linkage[19].

Reaction of chloroacetyl chloride with compound **3** in anhydrous acetone containing pyridine[11] produced 2-acetamido-1,3,4-tri-*O*-acetyl-6-*O*-(chloroacetyl)-2-deoxy-β-D-glucopyranose (**4**). No difficulty was observed in the chloroacetylation with pyridine as the catalyst. In addition, the condensation of compound **3** with chloroacetic anhydride in anhydrous pyridine at 0°, as described by Cook and Maichuk[12], proceeded to give the desired compound **4**. Brief treatment of **4** with anhydrous ferric chloride in dichloromethane[1,4] produced 2-methyl-[3,4-di-*O*-acetyl-6-*O*-(chloroacetyl)-α-D-glucopyrano]-[2′,1′:4,5]-2-oxazoline (**5**), which was isolated as a syrup in 78 percent yield. The infrared and n.m.r. spectra clearly supported the structure given for the oxazoline. T.l.c. of the product showed the presence of a slight proportion of impurity; nevertheless, the compound was found to be pure enough for *O*-glycosylation with aglycon hydroxides.

The condensation of **5** with benzyl alcohol in 1:1 nitromethane–toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid produced benzyl 2-acetamido-

3,4-di-*O*-acetyl-6-*O*-(chloroacetyl)-2-deoxy-β-D-glucopyranoside (**6**) in 68 percent yield. The chloroacetyl group in **6** was removed by thiourea in pyridine–ethanol[12] to give benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**7**) in 74 percent yield. Starting from benzyl 2-acetamido-2-deoxy-β-D-glucopyranoside, Rachaman and Jeanloz[20] reported an alternative synthesis of **7** in three steps; namely, tritylation, acylation, and detritylation. The optical rotation and the melting point of our material agreed quite well with those of their compound[20], suggesting that *O*-acetyl groups had not migrated during the removal of the chloroacetyl group from **6**. In addition, the presence of a primary hydroxyl group in **7** was confirmed by its reaction with trityl chloride to give the known compound **8**.



3, R = H

4, R = $\overset{O}{\overset{\|}{C}}CH_2Cl$

5, R = $\overset{O}{\overset{\|}{C}}CH_2Cl$

5a, R = Ac

6 R = Ac, R′ = $\overset{O}{\overset{\|}{C}}CH_2Cl$, R″ = CH_2Ph

7 R = Ac, R′ = H, R″ = CH_2Ph

8 R = Ac, R′ = Tr, R″ = CH_2Ph

9 R = Ac, R′ = $\overset{O}{\overset{\|}{C}}CH_2Cl$, R″ = $(CH_2)_6NHCO_2CH_2Ph$

10 R = Ac, R′ = H, R″ = $(CH_2)_6NHCO_2CH_2Ph$

11 R = R′ = Ac, R″ = $(CH_2)_6NHCO_2CH_2Ph$

12 R = R′ = H, R″ = $(CH_2)_6NHCO_2CH_2Ph$

The glycosylating capability of **5** was also examined with 6-(benzyloxycarbonylamino)-1-hexanol[21] under similar reaction-conditions, to give compound **9** in 60 percent yield. Removal of the chloroacetyl group from **9** was effected in a similar way with thiourea, to produce **10** in 68 percent yield. In another approach, the oxazoline **5a** was treated with 6-(benzyloxycarbonylamino)-1-hexanol[21] to give **11** which, on treatment with a catalytic amount of sodium methoxide in methanol, gave 6-(benzyloxycarbonylamino)-1-hexyl 2-acetamido-2-deoxy-β-D-galactopyranoside (**12**). Treatment of compound **12** with chloro-(*p*-methoxyphenyl)diphenylmethane in anhydrous pyridine, followed by reaction with acetic anhydride, gave a crude syrup which, without further purification, was heated with dilute acetic acid to provide a compound found to be identical with the aforementioned compound **10**.

Recently, Gagnaire and Vottero[22] have prepared 3,4-di-*O*-acetyl-6-*O*-(chloroacetyl)-1,2-*O*-(1-ethoxyethylidene)-α-D-glucopyranose as a glycosylating agent. In

the present investigation, we have established the glycosylating capability of an easily accessible oxazoline.

EXPERIMENTAL

General. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. I.r. spectra were recorded with a Perkin–Elmer Model 457 spectrophotometer. N.m.r. spectra were recorded with either a Varian A-60 or HA-100 spectrometer. Optical rotations were measured with a Perkin–Elmer Model 141 Polarimeter. The purity of the compounds was examined by ascending, thin-layer chromatography (t.l.c.) conducted on plates coated with a 250-μm layer of silica gel HF-254 (Merck, Darmstadt), and the spray reagent was potassium permanganate–sulfuric acid. The solvents for t.l.c. were (*a*) 9:1 benzene–methanol, (*b*) 4:1 benzene–methanol, (*c*) 14:14:1 benzene–ether–methanol, and (*d*) 9:1 chloroform–ethanol. The elementary analyses were performed by Robertson Laboratory, Florham Park, New Jersey.

*2-Methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-β-*D*-mannopyrano)-[2′,1′:4,5]-2-oxazoline* (**2**). — A solution of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-mannopyranose[14,16] (**1**) (0.5 g) in dichloromethane (50 ml) was treated with anhydrous ferric chloride (0.5 g), and the mixture was stirred for 3 h at room temperature, washed with water (3 × 200 ml), dried (sodium sulfate), and evaporated. The residue was crystallized from ether, to give pure **2**, yield 0.25 g (59.1%), m.p. 131–133°, ν_{max}^{KBr} 1745 (OAc) and 1670 cm^{-1} (C=N); lit.[13] m.p. 132–133°; ν_{max}^{KBr} 1745 (OAc) and 1676 cm^{-1} (C=N).

*2-Acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranose* (**3**). — A cooled solution of 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-trityl-β-D-glucopyranose[18] (15 g) in glacial acetic acid (50 ml) was shaken with a cooled, 32 percent solution of hydrogen bromide in acetic acid (5 ml) for 1 min. The precipitated bromotriphenylmethane was filtered off, and the filtrate was poured into ice–water (300 ml). The mixture was refiltered, to remove unreacted trityl derivative. The clear filtrate was extracted several times with chloroform, and the extracts were combined, dried (sodium sulfate), and evaporated. Traces of acetic acid were removed by co-evaporation with toluene. The solid residue was recrystallized from chloroform–ether, to give **3**, yield 3.9 g, m.p. 175–177°, $[\alpha]_D^{23}$ +5.7° (*c* 1, water); lit.[18] m.p. 175–176°, $[\alpha]_D^{18}$ +5.5° (*c* 1.6); ν_{max}^{KBr} 3495 (OH), 3300 (NH), 1750 (OAc) 1655 (Amide I), and 1535 cm^{-1} (Amide II); n.m.r. data ($CDCl_3$): τ 3.78 (1 H, d, *J* 10 Hz, NH), 4.25 (1 H, d, *J* 9 Hz, H-1), 7.88–7.91 (9 H, 3 OAc), and 8.08 (3 H, NAc).

*2-Acetamido-1,3,4-tri-*O*-acetyl-6-*O*-(chloroacetyl)-2-deoxy-β-*D*-glucopyranose* (**4**). — *Method A.* A solution of compound **3** (0.35 g, ~1 mmole) in anhydrous acetone (30 ml) and anhydrous pyridine (0.7 ml) was cooled to 0°, and chloroacetyl chloride (0.7 ml) in anhydrous ether (5 ml) was introduced dropwise. Acetone (15 ml) was added, and the mixture was stirred for 12 h at room temperature. The mixture was diluted with cold chloroform (~200 ml), and successively washed with ice-cold

water, aqueous sodium hydrogencarbonate, and water, dried (sodium sulfate), and evaporated to a syrup which was crystallized from chloroform–ether to give **4**, yield 0.23 g (53.8%).

Method B. To a well stirred solution of **3** (1.84 g, 5.3 mmoles) in anhydrous pyridine (50 ml) at 0° was added chloroacetic anhydride (2.56 g, 15 mmoles) in small portions, and the mixture was stirred for 5 h at 0°. Cold water (20 ml) was added, and the mixture was stirred for 10 min, and evaporated to dryness under diminished pressure, the last traces of pyridine being removed by repeated co-distillation with toluene. The solid residue was then partitioned between chloroform (150 ml) and ice-cold water (150 ml). The organic layer was washed twice with ice-cold water, dried (sodium sulfate), and evaporated to a syrup which was crystallized from chloroform–ether to give **4**, yield 1.62 g (72%), m.p. 170–172°, $[\alpha]_D^{23}$ +5.3° (*c* 1, chloroform); ν_{max}^{KBr} 3350 (NH), 1750 (OAc), 1665 (Amide I), and 1540 cm^{-1} (Amide II); n.m.r. data ($CDCl_3$): τ 3.82 (1 H, d, *J* 10 Hz, NH), 4.26 (1 H, d, *J* 9 Hz), 5.88 (2 H, $COCH_2Cl$), 7.89–7.97 (9 H, 3 OAc), and 8.08 (3 H, NAc).

Anal. Calc. for $C_{16}H_{22}ClNO_{10}$: C, 45.34; H, 5.23; Cl, 8.37; N, 3.30. Found: C, 45.41; H, 5.33; Cl, 8.21; N, 3.33.

2-Methyl-[3,4-di-O-acetyl-6-O-(chloroacetyl)-1,2-dideoxy-α-D-glucopyrano]-[2',1':4,5]-2-oxazoline (**5**). — A solution of compound **4** (2.0 g) in dichloromethane (150 ml) was treated with anhydrous ferric chloride (2.0 g), and the reaction was allowed to proceed for 3 h at room temperature. The mixture was washed four times with ice-cold water, dried (sodium sulfate), and evaporated to dryness, giving a colorless syrup, yield 1.35 g (78.6%). T.l.c. of the material revealed the presence of a major component (R_F 0.6, solvent *c*), and a slow-moving, minor impurity. Crude **5** showed ν_{max}^{neat} 1750 (OAc) and 1675 cm^{-1} (C=N); n.m.r. data ($CDCl_3$): τ 4.05 (1 H, d, *J* 6.5 Hz, H-1), 5.9 (2 H, s, $C(=O)CH_2Cl$), and 7.82–7.92 (9 H, 2 OAc and $C\text{-}CH_3$).

The compound was used for the next steps without purification.

Benzyl 2-acetamido-3,4-di-O-acetyl-6-O-(chloroacetyl)-2-deoxy-β-D-glucopyranoside (**6**). — A solution of oxazoline **5** (1.8 g) in 1:1 nitromethane–toluene (40 ml) containing *p*-toluenesulfonic acid (20–25 mg) and benzyl alcohol (1 ml) was heated for 30 min at 110–115°, and cooled, and the acid was neutralized with a few drops of pyridine. The solution was evaporated to a semi-solid material; this was stirred with water (50 ml) to produce a solid which was filtered off, successively washed with water and ether, and air-dried. The material (1.9 g) was taken up in chloroform (15–20 ml), treated with carbon black, and the suspension filtered through a pad of Celite. On careful dilution with ether, the slightly colored filtrate gave **6** as crystals, yield 1.6 g (68.5%), m.p. 158–160°; ν_{max}^{KBr} 3300 (NH), 1750 (OAc), 1660 (Amide I), and 1540 cm^{-1} (Amide II); n.m.r. data ($CDCl_3$): τ 2.71 (5 H, s, C_6H_5), 4.28 (1 H, d, *J* 9 Hz, NH), 5.28 (1 H, d, *J* 8 Hz, H-1), 5.9 (2 H, s, $COCH_2Cl$), 8.0 (6 H, 2 OAc), and 8.12 (3 H, NAc).

Anal. Calc. for $C_{21}H_{26}ClNO_9$: C, 53.45; H, 5.55; Cl, 7.51; N, 2.97. Found: C, 53.30; H, 5.63; Cl, 7.81; N, 2.91.

Benzyl 2-acetamido-3,4-di-O-acetyl-2-deoxy-β-D-glucopyranoside (**7**). — A solu-

tion of compound **6** (0.5 g, 1.06 mmoles) in pyridine (12 ml) and absolute ethanol (3 ml) containing thiourea (0.1 g, 1.31 mmoles) was stirred for 30 min at 100°, cooled, and evaporated under diminished pressure, final traces of pyridine being removed by co-distillation with toluene, to give a syrup which was taken up in water, and the suspension filtered to remove unreacted compound **6**. The clear filtrate was extracted with chloroform (5 × 25 ml), and the extracts were combined, dried (sodium sulfate), and evaporated to a solid (0.35 g) which was recrystallized from chloroform–pentane to give **7**, yield 0.31 g (74%), m.p. 173–175°, $[\alpha]_D^{23}$ −28.4° (*c* 1, ethanol); ν_{max}^{KBr} 3505 (OH), 3280 (NH), 1740 (OAc), 1645 (Amide I), 1545 (Amide II), 1500, and 700 cm^{-1} (Ph); n.m.r. data ($CDCl_3$): τ 2.7 (5 H, C_6H_5), 4.19 (1 H, d, *J* 9 Hz, NH), 5.23 (1 H, d, *J* 7.5 Hz, H-1), 7.98 (6 H, 2 OAc), and 8.1 (3 H, NAc).

A portion of compound **7** (50 mg) in pyridine (1 ml) was stirred with trityl chloride (35 mg) for 3 days at room temperature. The clear solution was poured into ice-water (100 ml) with stirring, and the solid was filtered off, air-dried, and recrystallized from chloroform–hexane, to give **8**, m.p. 206–207°, lit.[20] m.p. 206–207°; ν_{max}^{KBr} 3450 (NH), 1750 (OAc), 1660 (Amide I), 1600 (Ph), 1540 (Amide II), and 700 cm^{-1} (Ph).

*6-(Benzyloxycarbonylamino)-1-hexyl 2-acetamido-3,4-di-*O*-acetyl-6-*O*-(chloroacetyl)-2-deoxy-β-*D*-glucopyranoside* (**9**). — A solution of the oxazoline **5** (1.2 g) and 6-(benzyloxycarbonylamino)-1-hexanol in 1:1 nitromethane–toluene (30 ml) was heated for 40 min at 120–130° in the presence of a catalytic amount of *p*-toluenesulfonic acid, cooled to room temperature, treated with a few drops of pyridine, and evaporated to dryness. The residue was partitioned between chloroform and water, and the aqueous layer was extracted with chloroform. The extracts were combined, washed with water, dried (sodium sulfate), treated with carbon black, the suspension filtered through a Celite pad, and the filtrate evaporated to dryness. The residue was dissolved in chloroform (25 ml), and the solution was stirred with pentane (~50 ml) to give a solid material (1.92 g); t.l.c. (solvent *d*) showed the presence of 6-(benzyloxycarbonylamino)-1-hexanol as a contaminant of **9**. A portion of the material (1.4 g) was purified by recrystallization from ethanol, to give **9**, yield 0.9 g (60.8%, based on **5**), m.p. 132–134°, $[\alpha]_D^{23}$ −6.2° (*c* 1, chloroform); ν_{max}^{KBr} 3330 (NH), 1740 (OAc), 1690 (C=O of $NHCO_2CH_2Ph$), 1660 (Amide I), 1550 (Amide II), and 700 cm^{-1} (Ph); n.m.r. data ($CDCl_3$): τ 2.68 (5 H, s, C_6H_5), 5.42 (1 H, d, *J* 8 Hz, H-1), 5.9 (2 H, s, $CO\text{-}CH_2Cl$), 7.95 (6 H, 2 OAc), 8.08 (3 H, NAc), and 8.32–8.62 (8 H, $C\text{-}CH_2$).

Anal. Calc. for $C_{28}H_{39}ClN_2O_{11}$: C, 54.67; H. 6.39; Cl, 5.76; N, 4.55. Found: C, 54.97; H, 6.39; Cl, 6.00; N, 4.53.

*6-(Benzyloxycarbonylamino)-1-hexyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside* (**10**). — A solution of the crude chloroacetyl derivative **9** (0.52 g) in pyridine (5 ml) and absolute ethanol (1 ml) was treated with thiourea (73 mg) for 40 min at 100°, cooled to room temperature, and evaporated under diminished pressure, traces of pyridine being removed by distillation with toluene. The residue was shaken with water, and then extracted with chloroform. The extract was washed

with water, dried (sodium sulfate), and evaporated. The residue was dissolved in chloroform, the solution treated with carbon black, the suspension filtered, and the filtrate evaporated to give a residue which was crystallized from chloroform–ether–pentane to give **10**, yield 0.26 g (54%, based on **5**), m.p. 153–155°, $[\alpha]_D^{23}$ −12.7° (*c* 1, chloroform); ν_{max}^{KBr} 3500 (OH), 3300 (NH), 1740 (OAc), 1685 (C=O of $NHCO_2CH_2Ph$), 1652 (Amide I), 1545–1530 (Amide II), and 700 cm^{-1} (Ph); n.m.r. data ($CDCl_3$): τ 2.62 (5 H, s, C_6H_5), 5.34 (1 H, d, *J* 8 Hz, H-1), 7.95 with a shoulder at 7.96 (6 H, 2 OAc), 8.08 (3 H, NAc), and 8.32–8.62 (8 H, C-CH_2).

Anal. Calc. for $C_{26}H_{38}N_2O_{10}$: C, 57.98; H, 7.11; N, 5.20. Found: C, 58.16; H, 6.89; N, 5.07.

Treatment of the pure chloroacetyl derivative **9** (0.76 g, 1.22 mmoles) with thiourea (0.11 g, 1.44 mmoles) under similar conditions provided pure **10** (0.45 g, 68.5% based on pure **9**).

*6-(Benzyloxycarbonylamino)-1-hexyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside* (**11**). — The reaction of the oxazoline **5a** (3.0 g) and 6-(benzyloxycarbonylamino)-1-hexanol (2.0 g) in 1:1 nitromethane–toluene (40 ml) was conducted in the presence of *p*-toluenesulfonic acid (20 mg) for 1 h at 115–120°. The mixture was cooled, a few drops of pyridine were added, and it was evaporated; the residue was stirred with a mixture of water and chloroform. The organic layer was washed with water, dried, and filtered; treatment with carbon black, followed by filtration and evaporation, provided a pale-yellow syrup which was dissolved in chloroform, and the solution diluted with ether. Slight evaporation of the solvents initiated crystallization; the suspension was diluted with more ether (40–50 ml), and cooled in ice. The crystals were filtered off, and washed with chloroform–ether, to give **11**, yield 2.9 g (54.8% based on oxazoline **5a**), m.p. 96–98°, $[\alpha]_D^{23}$ −12.0° (*c* 1, chloroform); ν_{max}^{KBr} 3320 (NH), 1740 (OAc), 1690 (C=O of $NHCO_2CH_2Ph$), 1655 (Amide I), 1550–1540 (Amide II), and 700 cm^{-1} (Ph); n.m.r. data ($CDCl_3$): τ 2.63 (5 H, C_6H_5), 5.34 (1 H, d, *J* 8 Hz, H-1), 7.90, 7.97 (9 H, 3 OAc), 8.08 (3 H, NAc), and 8.34–8.72 (8 H, C-CH_2).

Anal. Calc. for $C_{28}H_{40}N_2O_{11}$: C, 57.92; H, 6.94; N, 4.82. Found: C, 57.66; H, 7.17; N, 4.63.

*6-(Benzyloxycarbonylamino)-1-hexyl 2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**12**). — A solution of compound **11** (3.5 g) in absolute methanol (30 ml) was treated with a catalytic amount of sodium methoxide in methanol, kept overnight at 4°, made neutral with dilute acetic acid (25%), and evaporated to dryness. The residue was dissolved in hot ethanol (~20 ml), treated with carbon black, and the suspension filtered through Celite, the Celite layer then being washed with the minimal volume of ethanol. The filtrates were combined, and diluted with ether, to give **12** as an amorphous material; yield 2.18 g (76%), $[\alpha]_D^{23}$ −20° (*c* 1, ethanol); ν_{max}^{KBr} 3320–3280 (broad, OH and NH), 1685 (C=O of $NHCO_2CH_2Ph$), 1650 (Amide I), 1550–1530 (Amide II), and 700 cm^{-1} (Ph); n.m.r. data (Me_2SO-d_6): τ 2.64 (5 H, s, C_6H_5), 4.98 (2 H, O-CH_2Ph), 5.74 (1 H, d, *J* 8 Hz, H-1), 8.2 (3 H, NAc), and 8.32–8.70 (8 H, C-CH_2).

Anal. Calc. for $C_{22}H_{34}N_2O_8 \cdot H_2O$: C, 55.92; H, 7.68; N, 5.93. Found: C, 56.15; H, 7.55; N, 5.94.

Preparation of **10** *from* **12**. — A solution of compound **12** (2.36 g) in anhydrous pyridine (20 ml) was stirred with chloro(*p*-methoxyphenyl)diphenylmethane (1.95 g) for 3 days at room temperature. Acetic anhydride (12 ml) was added, and the mixture was kept for 24 h at room temperature, and then poured into ice–water (1 liter) with stirring. The aqueous layer was decanted, and the semi-solid material was restirred with water (500 ml), and extracted with chloroform (~200 ml). The extract was washed several times with water, dried, and evaporated to a syrup, 4.0 g.

A portion (1.2 g) of the crude syrup was heated with 80% acetic acid (30 ml) for 30 min at 100°, cooled, and evaporated, traces of acetic acid being removed by co-distillation with toluene. The residue was crystallized twice from chloroform–ether–pentane, to give **10** (0.4 g; 42% from **12**), m.p. 153–155°, $[\alpha]_D^{23}$ −12.3° (*c* 1, chloroform).

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