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KOENIGS–KNORR GLYCOSIDATIONS WITH 3,4,6-TRI-*O*-ACETYL-2-DEOXY-2-[(4,4-DIMETHYL-2,6-DIOXOCYCLOHEXYLIDENEMETHYL)-AMINO]-α-D-GLUCOPYRANOSYL BROMIDE*,†,§

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ABSTRACT

The title compound (**2**), readily obtained as a fairly stable, crystalline solid from 2-amino-2-deoxy-D-glucose hydrochloride through its *N*-protected derivative, 2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-D-glucopyranose, is an excellent donor of the 2-amino-2-deoxy-β-D-glucopyranosyl group. The reaction of **2** with methyl, isopropyl, allyl, and cyclohexyl alcohols in the presence of Ag_2CO_3 gave the methyl, isopropyl, allyl, and cyclohexyl β-glycosides **3**–**6** in 71–98% yields. Similar reaction with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose afforded (39%) the anticipated β-linked disaccharide *O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-β-D-glucopyranosyl]-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**7**). *N*-Deprotection of the glycosides **3**–**7** could be readily achieved by treatment with Cl_2–$CHCl_3$ or by hydrolysis in the presence of Amberlite IRA-400 (HO^-) resin, and the aminoglycosides, or their hydrochlorides, were obtained in very high yields.

INTRODUCTION

In spite of the intense research effort to develop new procedures for the synthesis of glycosides and oligosaccharides[2], the Koenigs–Knorr method[3], introduced at the beginning of the century, still remains the most generally used. Many of the disadvantages of the original procedure have been overcome in the subsequently developed variants. To this effect, Helferich's important contributions[4] to the field should be recognized. However, there are still difficulties in the

*Dedicated to Professor B. Helferich on the occasion of the 100th anniversary of his birth.

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§Protection of the Amino Group of Amino Sugars by the Acylvinyl Group, Part IV. For Part III, see ref. 1.

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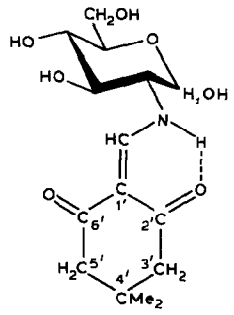
application of the method, particularly when applied to the synthesis of aminoglycosides. An important one is the need to have available relatively stable, sterically homogeneous glycosyl halides which can be easily generated and purified. Another concerns the selective protection and deprotection of the NH_2 group of the amino sugar. A variety of protecting groups, some recently introduced, have been used, but the selective removal of many of them requires rather drastic conditions with deleterious effects on the yields. This is not a problem when the *N*-protecting group (for example, the acetyl group) is present in the target aminoglycoside. In other cases, the aminoglycoside having NH_2 free or as a complex amide function (as in the synthesis[5] of analogs of lipid A) is desired, and a deprotection step is then required. In previous Parts[1,6,7] of this series we have demonstrated the utility of the 2,2-diacylvinyl group for protecting the amino group of the amino sugars during the preparation of their glycosides by the Fischer procedure. This type of protecting group can be readily introduced, and high yields of glycosides are obtained in many cases. In addition, this group can be readily removed under mild, non-acidic conditions, affording the free aminoglycosides in good overall yields. We have extended this work to glycosidation reactions under the Koenigs–Knorr conditions, and we report here on the results obtained by using the title compound.

RESULTS AND DISCUSSION

The starting material was the *N*-protected 2-amino-2-deoxy-D-glucose derivative **1**, readily obtained[1] (>75% yield) from the amino sugar hydrochloride and the readily available[8] 5,5-dimethyl-2-(phenylaminomethylene)-1,3-cyclohexanedione. Treatment of **1** with acetyl bromide at 0° afforded the title compound **2** (>85% after crystallization from CH_2Cl_2–petroleum ether), m.p. 122–125°, $[\alpha]_D$ +188° (CH_2Cl_2). This glycosyl bromide is fairly stable, and can be kept in a desiccator for several months. Its spectral properties were found to be in accordance wih the assigned structure. The u.v. spectrum had maxima at almost the same wavelengths and approximately the same intensity as those of the parent compound **1** and its tetra-*O*-acetyl derivative[1]. The i.r. spectrum of **2** exhibited the set of bands typical[9] of the intramolecularly bonded 2-alkylaminomethylene-5,5-dimethyl-1,3-cyclohexanediones. The n.m.r. spectra also showed the signals anticipated for the *N*-substituent. The anomeric proton appeared as a doublet ($J_{1,2}$ 3.8 Hz) at δ 6.49, thus indicating the α-D-configuration; this was in agreement with the $[\alpha]_D$ value observed. The ^{13}C-n.m.r. spectrum confirmed the anomeric purity.

The reaction of **2** with methyl, isopropyl, allyl, and cyclohexyl alcohols, in the presence of silver carbonate at room temperature, afforded the corresponding alkyl β-glycopyranosides **3**–**6**. The yields and diastereoselectivity of these reactions were very high. The known[1] methyl glycoside (**3**) was obtained in 98% yield (after recrystallization), and close monitoring (t.l.c.) of the glycosidation reaction indicated that it was complete in ~10 min and failed to reveal the presence of any



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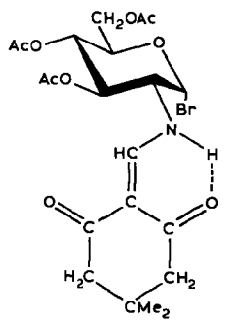
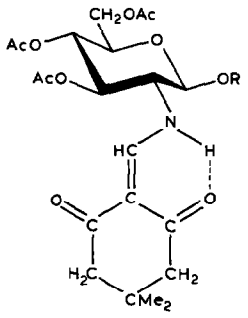
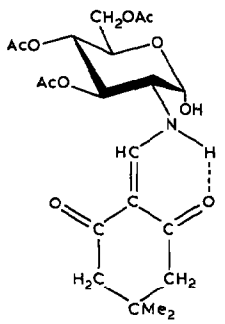


2

other product or reaction intermediate. The reaction with 2-propanol gave a quantitative yield of a mixture of **4** (subsequently isolated in a yield of >80%), and traces of a second product, probably the corresponding α anomer, having a very similar R_F. The yield of the allyl glycoside **5** was somewhat lower (71%), and the hydrolysis product of **2**, 3,4,6-tri-*O*-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-α-D-glucopyranose (**8**) was also obtained in 17% yield. The reaction with cyclohexanol was the one requiring the longest time (~2 h), and the glycoside **6** was obtained (>98%) as a chromatographically homogeneous foam which was readily purified by chromatography.





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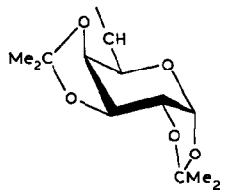
3 R = Me

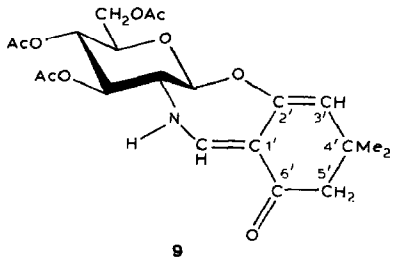
4 R = $CHMe_2$

5 R = CH_2—CH=CH_2

6 R = cyclo-C_6H_{11}

7 R =





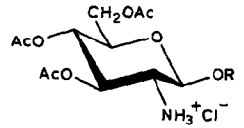
9

In order to explore the potential of **2** as a glycosyl donor in oligosaccharide synthesis, the compound was made to react with 3 molar equivalents of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in benzene, in the presence of silver carbonate, overnight at room temperature. T.l.c. then indicated formation of the disaccharide **7** and of a minor amount of the tricyclic compound **9**, an "inner enol glycoside". The two products were isolated by chromatography in 39 and ~1.5% yields, respectively. Compound **9** was better obtained when **2** was treated with silver carbonate in benzene in the absence of any alcohol; after removal of the solids, the very insoluble compound **9** readily crystallized (23.7%).

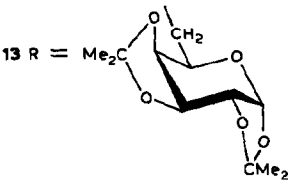
The spectral properties of **3–7** were in agreement with the structures assigned. Compound **9** had λ_{max} 248.3 and 318.6 nm, that is, at longer wavelengths than the other glycosides (λ_{max} 248.5 and 305.5 nm), in accordance with its having a more extended conjugated system. Its ^{1}H-n.m.r. spectrum showed two alkenic proton signals: one of them, a doublet ($J_{NH,H'}$ 12.4 Hz) at δ 7.29, is assigned to =C*H*–N coupled to the NH proton; the other, a singlet at δ 4.62, is assigned to H-3′. The ^{13}C-n.m.r. spectrum showed four alkenic carbon signals, two at δ 149.94 and 146.77, assigned to C-2′* and =*C*H–N, and the other two at δ 103.61 and 101.78, assigned to C-1′ and C-3′. The presence of the C=O of the aminoenone system was indicated by the band at 1665 cm^{-1} in the i.r. spectrum, and by the signal at δ 199.55 in the ^{13}C-n.m.r.; these absorptions appeared duplicated in compounds **3–6**. Other features of the spectra were consistent with structure **9**; the n.m.r. spectra of the sugar moiety were quite similar to those of compounds **3–6**, and $J_{1,2}$ (8.1 Hz) indicated the β-D-configuration.

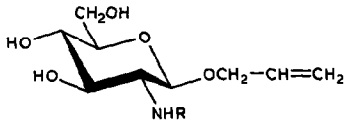
Removal of the *N*-protecting group of compounds **3, 4, 6**, and **7** was readily attained by treatment with chlorine in chloroform solution; the hydrochlorides of the *O*-acetylated glycosides readily crystallized from the reaction medium in yields >90% for the alkyl glycosides **10–12** and 85% for the disaccharide **13**. This procedure could not be applied to the allyl glycoside **5**, and the *N*-deprotection, with concomitant *O*-deacetylation, was performed by basic hydrolysis of the compound in aqueous acetone in the presence of Amberlite IRA-400 (HO$^-$) resin[6]. Allyl 2-amino-2-deoxy-β-D-glucopyranoside (**14**) was then obtained (89%) as a syrup, and was characterised as its known[10] *N*-acetyl derivative **15**.

*The numbering system used for this compound is given in formula **9**.



10 R = Me
11 R = $CHMe_2$
12 R = cyclo-C_6H_{11}

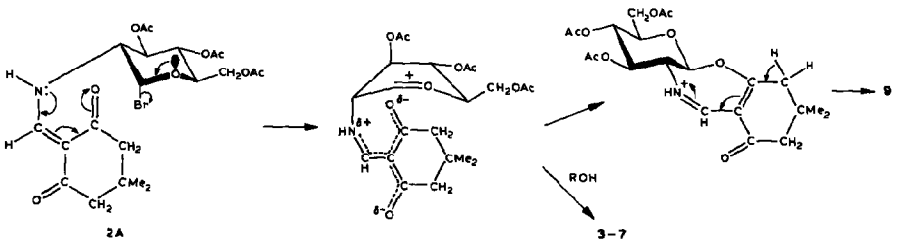




14 R = H
15 R = Ac

The high diastereoselectivity observed in these reactions, and the isolation of compound **9** in the glycosidation of the poor acceptor 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, suggest that the highly electron-delocalized[1] 4,4-dimethyl-2,6-dioxocyclohexylidenemethyl group provides anchimeric assistance as shown in Scheme 1. The glycosyl bromide **2** could adopt the non-chelated conformation **2A**, and the "inner ion pair", formed after splitting off the bromide ion, could be the reactive intermediate. The *N*-protecting group would then effectively shield the α-side of the glucopyranose ring, and the attack of the alcohol would take place from the β-side. The intramolecular attack of the C=O of the protecting group from the β-side, to yield **9**, would occur only in the absence of any alcohol or a good glycosyl acceptor, and could occur as formulated in Scheme 1. Inspection of molecular models showed that similar attack from the α-side would take place through a very congested transition state and intermediates. Our efforts to obtain, or even detect, the α anomer of **9** were unsuccessful.

In conclusion, the foregoing results demonstrate the facile preparation of β-glycosides of 2-amino-2-deoxy-D-glucose by using the readily available glycosyl bromide **2**. The procedure has the additional advantage that the *N*-protecting group can be readily removed without affecting the glycosidic linkage, and the free aminoglycosides are readily obtained in high overall yields from 2-amino-2-deoxy-D-glucose hydrochloride.



Scheme 1

EXPERIMENTAL

General methods. — Evaporations were conducted *in vacuo* at <40° (bath). Melting points were determined with a Gallenkamp melting-point apparatus and are uncorrected. Elemental analyses were made at the Instituto de Química Orgánica General, C.S.I.C., Madrid. Optical rotations were measured at room temperature with a Perkin–Elmer 241Mc polarimeter. U.v. spectra were recorded with a Perkin–Elmer Lambda 5 spectrophotometer. I.r. spectra (KBr pellets) were recorded with a Perkin–Elmer Model 1310 spectrophotometer. N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si), using a Bruker FT-80 (80 MHz) or Varian XL-200 (200 MHz) spectrometer. T.l.c. was performed on silica gel (DC-Fertigplatten, Kieselgel 60 F_{254}, Merck) with detection by u.v. light, or by charring with 50% H_2SO_4. Silica Gel 60 (Merck) was used for column chromatography.

3,4,6-Tri-O-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidene-methyl)amino]-α-D-glucopyranosyl bromide (**2**). — Freshly distilled acetyl bromide (2 mL) was slowly added to **1** (1.0 g, 1.93 mmol) at 0° through a reflux condenser, and the solution was kept for 5 h at room temperature. It was then diluted with pure CH_2Cl_2 (100 mL), successively washed at 0° with H_2O, saturated $NaHCO_3$ solution, and H_2O, dried ($MgSO_4$), and evaporated. The amorphous solid obtained (1.56 g, 99.4%) was chromatographically pure **2** (R_F 0.60 in 4:1 $CHCl_3$–MeOH). It crystallized on dissolving in CH_2Cl_2 and adding petroleum ether; yield 1.34 g (85%). The product had m.p. 122–125° (dec.), $[\alpha]_D^{20}$ +188° (*c* 1, CH_2Cl_2); $\lambda_{max}^{CH_2Cl_2}$ 242 and 305 nm (log ε 4.22 and 4.26); ν_{max}^{KBr} 3190w (NH), 1748s and 1765s (AcO), 1670s and 1605vs (C=O), and 1580s cm^{-1} (C=C–NH); ^{1}H-n.m.r. data (80 MHz, $CDCl_3$): δ 11.01 (dd, 1 H, $J_{NH,=CH}$ 14.6, $J_{NH,2}$ 9.6 Hz, N*H*), 8.00 (d, 1 H, =C*H*), 6.49 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.58–5.05 (m, 2 H, H-3,4), 4.44–4.05 (m, 3 H, 2 H-6, H-5), 3.66 (m, 1 H, H-2), 2.00, 2.05, and 2.10 (3 s, each 3 H, C*H*$_3$CO); ^{13}C-n.m.r. data (20.15 MHz): δ 88.50 (C-1), 71.20 (C-2), 73.10 (C-3), 63.85 (C-4), 67.10 (C-5), 61.10 (C-6), 157.30 (=*C*H–N), 108.90 (C-1')*, 197.95 (2 *C*=O), 51.20 (C-3',5'), 31.10 (C-4'), 28.50 (2 C*C*H$_3$), 169.30, 169.50, 170.20 (3 CH$_3$*C*O), and 20.30, 20.45, and 20.55 (3 *C*H$_3$CO).

Anal. Calc. for $C_{21}H_{28}BrNO_9$: C, 48.66; H, 5.44; Br, 15.41; N, 2.70. Found: C, 48.77; H, 5.50; Br, 15.48; N, 2.62.

General procedure for the preparation of alkyl 3,4,6-tri-O-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-β-D-glucopyranosides (**3–6**). — Compound **2** (0.5 g, 0.96 mmol) was dissolved in the appropriate alcohol (10–15 mL), and silver carbonate (0.6 g), anhydrous calcium sulfate (0.6 g), and molecular sieves Type 3A were added. The mixture was stirred for ~3 h at room temperature under dry nitrogen in the dark, and then diluted with the alcohol or

*The numbering system used for this compound and for glycosides **3–6** is given in formula **1**.

CH_2Cl_2, filtered through diatomaceous earth, and the solid washed with CH_2Cl_2. The filtrate and washings were combined, and evaporated to dryness.

Methyl glycoside **3** (0.44 g, 98%) had m.p. 151–152° (from EtOH), and was identical with an authentic sample[1].

*Isopropyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-β-*D*-glucopyranoside* (**4**). — The reaction of **2** with 2-propanol afforded an amorphous solid (0.48 g, 100%). T.l.c. in 4:1 $CHCl_3$–Me_2CO showed mainly the presence of **4** (R_F 0.70) and traces of another compound (R_F 0.65). Column chromatography (Et_2O) of this material afforded **4** (0.38 g, 80%); m.p. 60–62°, $[\alpha]_D^{20}$ +16.25° (*c* 0.8, CH_2Cl_2); λ_{max}^{EtOH} 248.4 and 305.6 nm (log ε 4.34 and 4.48); ν_{max}^{KBr} 3190w (NH), 1750s (AcO), 1655s and 1600vs (C=O), and 1575ssh cm^{-1} (C=C–NH); ^{1}H-n.m.r. data (80 MHz, $CDCl_3$): δ 11.05 (dd, 1 H, $J_{NH,=CH}$ 13.3, $J_{NH,2}$ 9.8 Hz N*H*), 8.10 (d, 1 H, =C*H*–N), 4.97–5.35 (m, 2 H, H-3,4), 4.50 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 3.70 (m, OC*H*Me_2), 4.26–3.75 (m, 3 H, 2 H-6 and H-5), 2.23 [d, 3 H, *J* 5.55 Hz, OCH(CH_3)$_2$], 1.09 [d, 3 H, OCH(CH_3)$_2$], 3.31 (m, 1 H, H-2), 2.33 and 2.38 (2 s, each 2 H, 2 H-3′ and 2 H-5′), 2.10 (s, 3 H, CH_3CO), 2.06 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), and 1.03 (s, 6 H, 2 CCH_3); ^{13}C-n.m.r. data (20.15 MHz): δ 99.90 (C-1), 68.75 (C-2), 73.65 (C-3), 64.15 (C-4), 72.15 (C-5 or C-4′), 62.30 (C-6), 159.00 (=*C*H–N), 108.55 (C-1′), 195.80 and 199.40 (2 *C*=O), 51.40 and 51.60 (C-3′,5′), 31.10 (C-4′), 28.30 and 28.70 (2 CCH_3), 169.40, 170.00, and 170.40 (3 CH_3CO), 20.40, 20.50, and 20.60 (3 *C*H_3CO), 72.35 (C-4′ or C-5), and 23.20 [CH(*C*H_3)$_2$].

Anal. Calc. for $C_{24}H_{35}NO_{10}$: C, 57.93; H, 7.09; N, 2.81. Found: C, 57.75; H, 6.76; N, 2.64.

*Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-β-*D*-glucopyranoside* (**5**) *and triacetate* **8**. — The reaction of **2** with allyl alcohol (twice distilled and then dried over molecular sieves Type 4A) gave an amorphous solid (0.45 g, 93.75%). T.l.c. in 4:1 $CHCl_3$–Me_2CO then revealed the allyl pyranoside **5** (R_F 0.53, major product) and **8** (R_F 0.30).

Column chromatography with petroleum ether and then with 9:1 Et_2O–petroleum ether afforded, first, **5** (0.34 g, 71%); m.p. 53–55°, $[\alpha]_D^{23}$ +28.75° (*c* 0.8, CH_2Cl_2); λ_{max}^{EtOH} 248.5 and 305.5 nm (log ε 4.10 and 4.35); ν_{max}^{KBr} 3190w (NH), 1760vs (AcO), 1670s and 1610vs (C=O), and 1580msh cm^{-1} (C=C–NH); ^{1}H-n.m.r. data (200 MHz, $CDCl_3$): δ 11.02 (dd, 1 H, $J_{NH,=CH}$ 13.3, $J_{NH,2}$ 8.9 Hz, N*H*), 8.07 (d, 1 H, =C*H*), 5.88–5.69 (m, 1 H, C*H*= of *O*-allyl), 5.28–5.04 (m, 3 H, H-3 and =CH_2 of *O*-allyl), 5.09 (m, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 4.52 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 3.70 (m, 1 H, $J_{5,6}$ 4.4, $J_{5,6a}$ 2.6 Hz, H-5), 4.00–4.41 (m, 4 H, $J_{6a,6b}$ −12.7 Hz, 2 H-6 and OCH_2 of *O*-allyl), 3.39 (q, 1 H, $J_{2,3}$ 8.9 Hz, H-2), 2.38 and 2.34 (2 s, each 2 H, H-3′,5′), 2.6 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO), and 1.00 (s, 6 H, 2 CCH_3).

Anal. Calc. for $C_{24}H_{33}NO_{10}$: C, 58.17; H, 6.71; N, 2.38. Found: C, 58.05; H, 6.75; N, 2.95.

Eluted second was the triacetate **8** (0.08 g, 16.6%); m.p. 172–174°, $[\alpha]_D^{20}$

+130° (*c* 0.7, $CHCl_3$); λ_{max}^{EtOH} 248.4 and 305.5 nm (log ε 4.20 and 4.45); ν_{max}^{KBr} 3420s and 3220s (OH, NH), 1755vs and 1730vs (AcO), 1660vs and 1590vs (C=O), and 1575ssh cm^{-1} (C=C–NH); ^{1}H-n.m.r. data (80 MHz, $CDCl_3$): δ 10.95 (dd, 1 H, $J_{NH,=CH}$ 14.6, $J_{NH,2}$ 9.0 Hz, N*H*), 8.10 (d, 1 H, =C*H*), 5.93 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.56–4.95 (m, 3 H, H-3, H-4, and O*H*), 4.46–4.04 (m, 3 H, 2 H-6 and H-5), 3.54 (m, 1 H, $J_{2,3}$ 9.4 Hz, H-2), 2.33 and 2.36 (2 s, each 2 H, H-3',5'), 2.00 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CO), and 1.04 (s, 6 H, 2 CCH_3).

Anal. Calc. for $C_{21}H_{29}NO_{10}$: C, 55.38; H, 6.41; N, 3.08. Found: C, 55.15; H, 6.60; N, 3.30.

*Cyclohexyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-β-*D*-glucopyranoside* (**6**). — The cyclohexyl glycoside **6** was obtained (0.50 g, 98.5%) as a chromatographically pure foam that could not be crystallized. After column chromatography, the product had m.p. 70–75°, $[\alpha]_D^{20}$ +16° (*c* 1, CH_2Cl_2); λ_{max}^{EtOH} 247.6 and 305.4 nm (log ε 4.13 and 4.29); ν_{max}^{KBr} 3190w (NH), 1750vs (AcO), 1670s and 1605vs (C=O), and 1578msh cm^{-1} (C=C–NH); ^{1}H-n.m.r. data (80 MHz, $CDCl_3$): δ 11.05 (dd, 1 H, $J_{NH,=CH}$ 13.3, $J_{NH,2}$ 8.3 Hz, N*H*), 8.1 (d, 1 H, =C*H*), 5.37–4.94 (m, 2 H, H-3,4), 4.53 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.32 (dd, 1 H, $J_{6a,6b}$ −12.2 Hz, H-6b), 4.09 (dd, 1 H, H-6a), 3.70 (ddd, 1 H, $J_{5,6b}$ 4.7, $J_{5,6a}$ 2.6 Hz, H-5), 3.50–3.18 (m, 1 H, H-2), 2.33 and 2.38 (2 s, each 2 H, H-3',5'), 2.01 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CO), 1.80–0.80 (m, 11 H, cyclo-C_6H_{11}), and 1.00 (s, 6 H, 2 CCH_3); ^{13}C-n.m.r. data (20.15 MHz): δ 99.29 (C-1), 68.61 (C-2), 72.13 (C-3), 64.08 (C-4), 71.87 (C-5), 62.08 (C-6), 158.82 (=*C*H–N), 108.36 (C-1'), 195.50 and 199.10 (2 *C*=O), 51.17 and 51.40 (C-3',5'), 31.12 (C-4'), 28.60 and 27.95 (2 CCH_3), 23.22, 23.33, 25.28, 30.86, and 32.97 (5 CH_2 of cyclo-C_6H_{11}), 78.56 (*C*H of cyclo-C_6H_{11}), 169.20, 169.79, and 170.19 (3 CH_3CO), and 20.24 (3 CH_3CO).

Anal. Calc. for $C_{27}H_{39}NO_{10}$: C, 60.32; H, 7.31; N, 2.61. Found: C, 60.00; H, 7.20; N, 2.52.

O-*[3,4,6-Tri-*O*-acetyl-2-deoxy-2-[(4,4-dimethyl-2,6-dioxocyclohexylidenemethyl)amino]-β-*D*-glucopyranosyl]-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**7**) *and 3,4,6-tri-*O*-acetyl-1,2'-anhydro-2-deoxy-2-[(2'-hydroxy-4',4'-dimethyl-6'-oxo-2'-cyclohexenylidenemethyl)amino]-β-*D*-glucopyranose* (**9**). — A solution of **2** (1.0 g, 1.93 mmol) in dry benzene (18 mL) was stirred under dry nitrogen. Anhydrous calcium sulfate (1.2 g) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (1.70 g, 6.5 mmol) in benzene (10 mL) were added. After a few minutes, silver carbonate (1.2 g) and 3A molecular sieves were added. Stirring was continued overnight at room temperature in the dark, and the mixture was processed as already described. T.l.c. in 4:1 $CHCl_3$–Me_2CO showed the formation of **7** (R_F 0.51) and of traces of **9** (R_F 0.62) and **8** (R_F 0.25). Column chromatography (Et_2O) afforded, first, the excess of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose; eluted second was a mixture (0.53 g) of **7** and **9**. Compound **9** (12 mg, 1.4%) crystallized quantitatively from the mixture. It had m.p. 245–247° (from CH_2Cl_2–EtOH); $\lambda_{max}^{CH_2Cl_2}$ 248.3, 318.6sh, and 339.6 nm (log ε 4.31, 4.23, and 4.49);

ν_{max}^{KBr} 3240w (NH), 1740vs (AcO), 1665s (C=O), 1630m (C=C), and 1580s cm^{-1} (C=C–NH); ^{1}H-n.m.r. data (200 MHz, $CDCl_3$): δ 9.45 (dd, 1 H, $J_{NH,=CH-N-}$ 12.4, $J_{NH,2}$ 8.0 Hz, N*H*), 7.29 (d, 1 H, =C*H*–N–), 5.34–5.07 (m, 2 H, H-3,4), 4.75 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 4.62 (s, 1 H, H-3'), 4.30 (dd, 1 H, $J_{5,6b}$ 5.7, $J_{6a,6b}$ −12.3 Hz, H-6b), 4.15 (dd, 1 H, $J_{5,6a}$ 2.2 Hz, H-6a), 3.83 (ddd, 1 H, $J_{4,5}$ 5.9 Hz, H-5), 3.45 (dt, 1 H, $J_{2,3}$ 10.3 Hz, H-2), 2.10 (s, 3 H, CH_3CO), 2.06 (s, 6 H, 2 CH_3CO), 1.06 (s, 3 H, CCH_3), and 1.03 (s, 3 H, CCH_3); ^{13}C-n.m.r. (50.3 MHz): δ 100.98 (C-1), 62.80 (C-2), 71.77 (C-3), 68.58 (C-4), 72.39 (C-5), 62.64 (C-6), 103.61 (C-1'), 146.77 (=*C*H–N–), 199.55 (C-6'), 52.42 (C-5'), 32.25 (C-4'), 101.78 (C-3'), 149.94 (C-2'), 31.25 and 29.74 (2 C*C*H_3), 170.04, 170.91, and 171.00 (3 CH_3*C*O),and 21.07, 21.25, and 21.24 (3 *C*H_3CO).

Anal. Calc. for $C_{21}H_{27}NO_7$: C, 57.66; H, 6.22; N, 3.20. Found: C, 57.56; H, 6.16; N, 3.00.

Evaporation of the mother liquor of **9** afforded the disaccharide **7** (0.52 g, 38.8%); m.p. 93–96° (from EtOH), $[\alpha]_D^{23}$ −11.5° (*c* 1.3, CH_2Cl_2); λ_{max}^{EtOH} 248.5 and 305.5 (log ε 4.12 and 4.20); ν_{max}^{KBr} 3190w (NH), 1750vs (AcO), 1670s and 1605vs (C=O), and 1585mh cm^{-1} (C=C–NH); ^{1}H-n.m.r. data (200 MHz, $CDCl_3$): glucosyl*; δ 11.04 (dd, 1 H, $J_{NH,=CH}$ 13.0 Hz, NH), 8.03 (d, 1 H, =CH), 5.28–4.59 (m, 2 H, H-3^2 and H-4^2), 4.61 (d, 1 H, $J_{1^2,2^2}$ 7.9 Hz, H-1^2), 4.31 (dd, 1 H, $J_{5^2,6b^2}$, $J_{6a^2,6b^2}$ −12.4 Hz, H-6b^2), 4.16 (m, 1 H, H-6a^2), 3.70 (m, 1 H, H-5^2), 3.37 (m, 1 H, H-2^2), 2.35 and 2.32 (2 s, each 2 H, H-3',5'), 2.10 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.00 (s, 3 H, CH_3CO), 1.05 (s, 3 H, CCH_3), and 1.03 (s, 3 H, CCH_3); galactose, δ 5.42 (d, 1 H, $J_{1^1,2^1}$ 5.0 Hz, H-1^1), 4.55 (dd, 1 H, $J_{2^1,3^1}$ 2.3, $J_{3^1,4^1}$ 7.9 Hz, H-3^1), 4.25 (dd, 1 H, $J_{1^1,2^1}$ 4.9 Hz, H-2^1), 4.17 (dd, 1 H, $J_{4^1,5^1}$ 1.8 Hz, H-4), 3.99 (dd, 1 H, $J_{5^1,6b^1}$ 4.1 Hz, $J_{6a^1,6b^1}$ −10.6 Hz, H-6b^1), 3.85 (m, 1 H, H-5^1), and 3.73 (m, 1 H, H-6a^1); ^{13}C-n.m.r. data (50.3 MHz): glucosyl, δ 100.90 (C-1^2), 67.90 (C-2^2), 71.70 (C-3^2), 64.05 (C-4^2), 70.80 (C-5^2), 61.60 (C-6^2), 158.80 (=*C*H–N–), 108.40 (C-1'), 195.80 and 199.10 (2 *C*=O), 51.00 and 51.10 (C-3',5'), 30.80 (C-4'), 28.20 and 28.60 (2 C*C*H_3), 169.30, 169.80, and 170.40 (3 CH_3*C*O), and 20.30, 20.40, and 20.50 (3 CH_3CO); galactose, δ 95.90 (C-1^1), 70.40 (C-2^1), 70.10 (C-3^1), 67.00 (C-4^1), 71.70 (C-5^1), 69.10 (C-6^1), 108.30 and 109.20 [2 *C*(CH_3)$_2$], and 24.10, 24.75, and 25.70 [4 C(*C*H_3)$_2$].

Anal. Calc. for $C_{33}H_{47}NO_{15}$: C, 56.80; H, 6.79; N, 2.00. Found: C, 56.70; H, 6.83; N, 1.88.

Formation of compound **9**. — A solution of **2** (0.5 g) in dry benzene (10 mL) was stirred, under nitrogen, with $AgCO_3$ (0.51 g), $CaSO_4$ (0.51 g), and molecular sieves Type 3A for 20 h. The mixture was filtered, and the filtrate evaporated to dryness. Treatment of the residue with Et_2O afforded **9** (0.10 g, 23.7%). After recrystallization from CH_2Cl_2–EtOH, it had m.p. 245–247° (dec.), and was identical with the compound already described.

Removal of the N*-protecting group.* — To a solution of methyl glycoside **3**

*Superscript 1 refers to the galactose residue, and superscript 2 to the glycosyl group.

(0.30 g) in $CHCl_3$ (2 mL) was gradually added a saturated solution of Cl_2 in $CHCl_3$ until an incipient yellow color was produced. After 15 min, the solution was evaporated, and the residue was treated with dry Et_2O, to give **10** (0.19 g, 91%); m.p. 225–228° (dec.) (lit.[11] 227–229°).

Likewise, 2-propyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranoside hydrochloride (**11**) was prepared (95%) from **4**; m.p. 234–236° (dec.) (from MeOH–Et_2O), $[\alpha]_D^{23}$ 0° (*c* 1, MeOH).

Anal. Calc. for $C_{15}H_{26}ClNO_8$: C, 46.93; H, 6.82; Cl, 9.23; N, 3.65. Found: C, 46.75; H, 6.60; Cl, 9.28; N, 3.30.

Cyclohexyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranoside hydrochloride (**12**) was prepared (98%) from **6**, and had m.p. 238–239° (dec.); $[\alpha]_D^{23}$ +8.6° (*c* 0.7, MeOH).

Anal. Calc. for $C_{18}H_{30}ClNO_8$: C, 51.00; H, 7.13; Cl, 8.36; N, 3.30. Found: C, 51.05; H, 6.75; Cl, 8.38; N, 2.98.

Likewise, *O*-(3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose hydrochloride (**13**) was obtained (85%) from **7**, and had m.p. 158–160° (dec.) (from MeOH–Et_2O); $[\alpha]_D^{23}$ +11° (*c* 1, MeOH).

Anal. Calc. for $C_{24}H_{38}ClNO_{13}$: C, 49.35; H, 6.56; Cl, 6.07; N, 2.40. Found: C, 49.25; H, 6.53; Cl, 6.20; N, 2.36.

Allyl 2-amino-2-deoxy-β-D-glucopyranoside (**14**). — A solution of **5** (0.3 g, 0.6 mmol) in 2:1 Me_2CO–H_2O (20 mL) was stirred for 30 min with Amberlite IRA-400 (HO^-) resin (14.0 g). The resin was filtered off, and washed with H_2O and Me_2CO, and the filtrates were combined, and evaporated, to give **14** (0.12 g, 89%) as a syrup; $[\alpha]_D^{23}$ +12° (*c* 1, MeOH). It was characterized as its *N*-acetyl derivative, m.p. 168–170° (lit.[10] 171–172°).

REFERENCES

1 M. G. García-Martín, C. Gasch, A. Gómez-Sánchez, M. J. Dianez, and A. López, *Carbohydr. Res.*, 162 (1987) 181–197.
2 R. R. Schmidt, *Angew. Chem., Int. Ed. Engl.*, 25 (1986) 212–235.
3 (a) H. Paulsen, *Angew. Chem., Int. Ed. Engl.*, 21 (1982) 155–173; (b) *Chem. Soc. Rev.*, 13 (1984) 15–45.
4 (a) B. Helferich and J. Goerder, *Ber.*, 73 (1940) 532–542; (b) B. Helferich and K. Weiss, *Chem. Ber.*, 89 (1956) 314–321; (c) B. Helferich and J. Zirner, *Chem. Ber.*, 95 (1962) 2604–2611.
5 M. Kiso and A. Hasegawa, *ACS Symp. Ser.*, 231 (1983) 279–299.
6 A. Gómez-Sánchez, P. Borrachero Moya, and J. Bellanato, *Carbohydr. Res.*, 135 (1984) 101–116.
7 A. Gómez-Sánchez, M. G. García-Martín, and C. Pascual, *Carbohydr. Res.*, 149 (1986) 329–345.
8 O. S. Wolfbeis and E. Ziegler, *Z. Naturforsch., Teil B*, 31 (1976) 1519–1525.
9 A. Gómez-Sánchez, M. G. García-Martín, P. Borrachero, and J. Bellanato, *J. Chem. Soc., Perkin Trans 2*, (1987) 301–306.
10 R. T. Lee and Y. C. Lee, *Carbohydr. Res.*, 37 (1974) 193–201.
11 L. Zervas and S. Konstas, *Chem. Ber.*, 93 (1969) 435–446.