BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 41 2765—2769 (1968)

Studies of Aminosugars. XIX. Syntheses of O-Benzyl-α-halogeno Derivatives of 3-Acetamido-3-deoxy- and 6-Acetamido-6-deoxy-D-glucose[1]

Shinkiti KOTO, Takayuki TSUMURA, Yoshinori KATO and Sumio UMEZAWA

Department of Applied Chemistry, Faculty of Engineering, Keio University, Koganei-shi, Tokyo

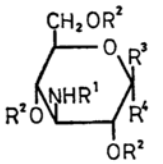
(Received May, 23, 1968)

As a part of investigation of the synthesis and reaction of 1-halogeno derivatives of amino-monosaccharides, 3-acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-α-D-glucopyranosyl chloride and 2,3,4-tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α-D-glucopyranosyl chloride have been synthesized. Attempts to prepare α-glycosides from these benzyl derivatives proved to be practical, giving cyclohexyl 3-acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-α-D-glucopyranoside and cyclohexyl 2,3,4-tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α-D-glucopyranoside as main products. Removal of the masking groups gave cyclohexyl α-glucosides of 3-amino-3-deoxy-D- and 6-amino-6-deoxy-D-glucose respectively. A number of related derivatives have been described.

1-Halogeno derivatives of masked monosaccharides are important intermediates for the synthesis of glycosides. However, the corresponding derivatives of aminosugars represents a relatively unexplored territory. In the preceding papers,[2,3] the syntheses of α-acetobromo and β-acetochloro derivatives of 3-carbobenzoxyamino-3-deoxy- and 6-carbobenzoxyamino-6-deoxy-D-glucose have been developed. This paper reports the syntheses of 3-acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-α-D-glucosyl chloride (IV) and 2,3,4-tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α-D-glucopyranosyl chloride (XII). These *O*-benzyl-α-chloro derivatives have been found to be useful for preparing α-glycosides of the aminosugars, as shown here in the preparation of cyclohexyl 3-amino-3-deoxy-α-D-glucoside (VII) and cyclohexyl 6-amino-6-deoxy-α-D-glucoside (XV).

Benzylation of methyl 3-acetamido-3-deoxy-β-D-glucopyranoside[4] with benzyl bromide in the presence of barium oxide and barium hydroxide in *N,N*-dimethylformamide (DMF) gave methyl 3-acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-β-D-glucopyranoside (II) in a 95% yield.

Hydrolysis of II with sulfuric acid in aqueous acetic acid followed by acetylation with acetic anhydride in pyridine gave 3-acetamido-1-*O*-acetyl-2,4,6-tri-*O*-benzyl-α- and β-D-glucopyranose



Ac = $-COCH_3$

Bzl = $-CH_2C_6H_5$

I R^1=Ac, R^2=R^4=H, R^3=OCH_3

II R^1=Ac, R^2=Bzl, R^3=OCH_3, R^4=H

IIIa R^1=Ac, R^2=Bzl, R^3=H, R^4=OAc

IIIb R^1=Ac, R^2=Bzl, R^3=OAc, R^4=H

IV R^1=Ac, R^2=Bzl, R^3=H, R^4=Cl

Va R^1=Ac, R^2=Bzl, R^3=H, R^4=OC_6H_{11}

Vb R^1=Ac, R^2=Bzl, R^3=OC_6H_{11}, R^4=H

VIa R^1=Ac, R^2=R^3=H, R^4=OC_6H_{11}

VIb R^1=Ac, R^2=R^4=H, R^3=OC_6H_{11}

VII R^1=H_2Cl, R^2=R^3=H, R^4=OC_6H_{11}

(IIIa and IIIb) which were separated by fractional crystallization from isopropanol and isopropyl ether, the ratio of α- to β-anomer being 1 : 1.

Chlorination of the α-anomer (IIIa) or β-anomer (IIIb) with dry hydrogen chloride in dioxane containing acetyl chloride gave 3-acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-α-D-glucopyranosyl chloride (IV) in quantitative yield.

On the other hand, the *O*-benzyl-α-chloro derivative of 6-amino-6-deoxy-D-glucose has been synthesized by an analogous route. Methyl 6-acetamido-6-deoxy-α-D-glucopyranoside[5] (VIII) was benzylated with benzyl chloride and sodium

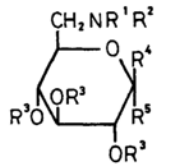
1) Part XXXV of "Studies on Antibiotics and Related Substances," by Sumio Umezawa. This paper was read before the 20th Annual Meeting of the Chemical Society of Japan, Tokyo, March, 1967. (See abstracts of the Meeting, III, p. 596).

2) Y. Ito, S. Koto and S. Umezawa, This Bulletin, **35**, 1618 (1962).

3) S. Umezawa, S. Koto and Y. Ito, *ibid.*, **36**, 183 (1963).

4) H. H. Baer, *J. Am. Chem. Soc.*, **83**, 1882 (1961).

5) F. Cramer, O. Otterbach and H. Springman, *Chem. Ber.*, **92**, 384 (1959).



Ac = -COCH$_3$

Bzl = -CH$_2$C$_6$H$_5$

VIII R^1=H, R^2=Ac, R^3=R^4=H, R^5=OCH$_3$

IX R^1=R^3=Bzl, R^2=Ac, R^4=H, R^5=OCH$_3$

X R^1=R^3=Bzl, R^2=Ac, R^4=OH, R^5=H

XI R^1=R^3=Bzl, R^2=Ac, R^4=OAc, R^5=H

XII R^1=R^3=Bzl, R^2=Ac, R^4=H, R^5=Cl

XIIIa R^1=R^3=Bzl, R^2=Ac, R^4=H, R^5=OC$_6$H$_{11}$

XIIIb R^1=R^3=Bzl, R^2=Ac, R^4=OC$_6$H$_{11}$, R^5=H

XIVa R^1=R^3=H, R^2=Ac, R^4=H, R^5=OC$_6$H$_{11}$

XIVb R^1=R^3=H, R^2=Ac, R^4=OC$_6$H$_{11}$, R^5=H

XV R^1=R^3=R^4=H, R^2=H$_2$Cl, R^5=OC$_6$H$_{11}$

hydride to give methyl 2,3,4-tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α-D-glucopyranoside (IX) in a 83% yield. It should be noted that the primary acetamido group of VIII is further benzylated. Hydrolysis of IX with sulfuric acid in aqueous acetic acid gave 2,3,4-tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-β-D-glucopyranose (X) in a 75% yield, which was converted to its acetate (XI). The acetate was chlorinated in like manner as described in the preparation of IV to give 2,3,4-tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α-glucopyranosyl chloride (XII) in a 95% yield.

Infrared spectra of the above-mentioned 1-chloro derivatives (IV and XII) of two kinds of aminomonosaccharides showed absorption near 850 cm^{-1} which is characteristic of α-configuration.

Attempts to prepare α-glycosides from IV and XII proved to be practical. When shaken with a mixture of cyclohexanol, mercuric cyanide and mercuric bromide in nitromethane, IV gave cyclohexyl 3-acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-α-D- and β-D-glucopyranoside (Va and Vb), the ratio of α- to β-anomer being 7 : 11. The similar glycosidation of XII gave cyclohexyl 2,3,4-tri-*O*-benzyl-6-(*N*-benzyl-acetamido)-6-deoxy-α-D- and β-D-glucopyranoside (XIIIa and XIIIb), the ratio of α- to β-anomer being about 47 : 5.

Hydrogenolysis over palladium black in methanol smoothly debenzylated Va and Vb to form cyclohexyl 3-acetamido-3-deoxy-α-D- and β-D-glucoside (VIa and VIb) respectively. Similar hydrogenolysis of XIIIa and XIIIb followed by de-*N*-benzylation with sodium in liquid ammonia gave cyclohexyl 6-acetamido-6-deoxy-α-D- and β-D-glucopyranoside (XIVa and XIVb) respectively.

Finally, treatment with hydrazine hydrate de-*N*-acetylated VIa and XIVa to form cyclohexyl 3-amino-3-deoxy-α-D-glucoside and cyclohexyl 6-amino-6-deoxy-α-D-glucoside, which were led to crystalline hydrochlorides (VII and XV) respectively.

Experimental

General Procedures. Thin layer chromatography (TLC) was performed on "Silica-Reider for TLC" (Dai-ich Pure Chemicals Co.). Paper chromatography was carried out on Toyo filter paper No. 51, using a solvent system of *n*-butanol, pyridine, water and acetic acid (6 : 4 : 3 : 1), ninhydrin in pyridine (0.3%) being sprayed on.

Methyl 3-Acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-β-D-glucopyranoside (II). A mixture of methyl 3-acetamido-3-deoxy-β-D-glucopyranoside (I) (5 g), benzyl bromide (50 m*l*), powdery barium oxide (37 g) and finely crushed barium hydroxide octahydrate (17 g) in DMF (100 m*l*) was vigorously stirred at about 0°C for 4 hr and then at room temperature overnight. The reaction mixture diluted with chloroform (250 m*l*) was filtered and the filtrate was dried up under reduced pressure at 60°C to afford a yellow sirup, which was extracted with ethyl acetate (200 m*l*). Evaporation of the extract, followed by treatment with cyclohexane afforded colorless crystals of II; yield, 10.2 g (95%). Recrystallized from isopropanol; mp 163—164°C, $[\alpha]_D^{18}$ +24° (*c* 1.0, chloroform), ε_{258}^{MeOH}=544 (calcd, 558), IR spectrum (KBr): 3290, 1653 and 1576 (NHAc), 1068, 747, 737 and 695 (*O*-benzyl), 907 cm^{-1} (type 2b of pyranose ring.)

Found: C, 70.88; H, 6.63; N, 2.86%. Calcd for $C_{30}H_{35}NO_6$: C, 71.27; H, 6.98; N, 2.77%.

3-Acetamido-1-*O*-acetyl-2,4,6-tri-*O*-benzyl-α- and β-D-glucopyranose (IIIa and IIIb). A mixture of II (13 g), glacial acetic acid (240 m*l*) and 2 N sulfuric acid (63 m*l*) was heated over a boiling water bath for 2 hr. To the resulting mixture was added 2 N sulfuric acid (51 m*l*) and the mixture was further heated for 13 hr. The mixture was poured into a large amount of water to give a colorless precipitate, which was collected and washed thoroughly with water; yield 9.0 g.

The hydrolysis product (8.2 g) was acetylated with acetic anhydride (50 m*l*) and pyridine (50 m*l*) at room temperature overnight. After evaporation the residue was crystallized with isopropanol to afford IIIb; 3.8 g (43%), mp 183—184°C, $[\alpha]_D^{21}$ + 8.1° (*c* 2.6, chloroform), ε_{258}^{MeOH}=534 (calcd, 558), IR spectrum (KBr): 3310, 1659 and 1552 (NHAc), 1744 and 1237 (OAc), 1102, 743 and 697 (*O*-benzyl), 892 cm^{-1} (type 2b of pyranose ring).

Found: C, 69.95; H, 6.74; N, 2.85%. Calcd for $C_{31}H_{35}NO_7$: C, 69.78; H, 6.61; N, 2.63%.

Mother liquor was concentrated and crystallized by treatment with isopropyl ether to give 3.8 g of α-isomer (43%); mp 135—136°C, $[\alpha]_D^{21}$ +62° (*c* 2.2, chloroform), ε_{258}^{MeOH}=549 (calcd, 558), IR spectrum (KBr): 3275, 1658 and 1550 (NHAc), 1757 and 1238 (OAc), 1101, 748 and 697 (*O*-benzyl), 855 cm^{-1} (type 2a of pyranose ring).

Found: C, 69.92; H, 6.67; N, 2.27%. Calcd for $C_{31}H_{35}NO_7$: C, 69.78; H, 6.61; N, 2.63%.

3-Acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-α-D-glucopyranosyl Chloride (IV). To a solution of IIIa (0.5 g) in dioxane (25 m*l*) containing dry hydrogen

chloride (4%) was added acetyl chloride (13 ml) and the mixture was kept standing at 37°C overnight in a tightly stoppered flask. After evaporation at 20°C under reduced pressure, the resulting sirup was subjected repeatedly to co-distillation with absolute toluene *in vacuo* to be freed from hydrogen chloride to give a powdery solid, which was treated with dry petroleum ether to afford the chloride IV; 0.49 g (98%), mp 143—144°C (decomp.), $[\alpha]_D^{23}$ +78° (*c* 0.7, chloroform), $\varepsilon_{258}^{AcOEt}$=530 (calcd, 558), IR spectrum (KBr): 3280, 1655 and 1550 (NHAc), 738 (C-Cl), 696 (phenyl), 856 cm^{-1} (type 2a of pyranose ring). The C=O stretching absorption of acetoxy group in IIIa completely disappeared.

Found: C, 68.01; H, 6.54; N, 2.69; Cl, 7.35%. Calcd for $C_{29}H_{32}NO_5Cl$: C, 68.30; H, 6.32; N, 2.75; Cl, 6.96%.

IIIb also gave quantitatively IV by the above-mentioned chlorination, the result being examined by TLC using a solvent system of toluene and MEK (3 : 1).

Cyclohexyl 3-Acetamido-2,4,6-tri-*O*-benzyl-3-deoxy-α- and β-D-glucopyranoside (Va and Vb). A mixture of IV (0.5 g), cyclohexanol (1.3 g), well pulverized mercuric cyanide (0.25 g) and mercuric bromide (0.35 g) in absolute nitromethane (5 ml) was shaken at 27°C for three days under anhydrous conditions. After removal of insoluble matters, the mixture was diluted with chloroform (15 ml) and washed with several 20 ml portions of 20% aqueous potassium bromide and successively twice with 20 ml portions of water. After being dried over anhydrous sodium sulfate, the solution was evaporated to dryness to give sirup, which was subjected to fractional crystallization from isopropanol. First, Va deposited and was recrystallized from isopropanol; 0.16 g (28%), mp 135—136°C, $[\alpha]_D^{28}$ +88°C (*c* 1.0, chloroform), ε_{258}^{MeOH}=539 (calcd, 558), IR spectrum (KBr): 3290, 1652 and 1567 (NHAc), 2925 and 2850 (cyclohexyl), 845 (type 2a of pyranose ring), 735 and 694 cm^{-1} (phenyl).

Found: C, 73.32; H, 7.71; N, 2.57%. Calcd for $C_{35}H_{43}NO_6$: C, 73.27; H, 7.55; N, 2.44%.

From the mother liquor β-isomer (Vb) was obtained after a few days. Recrystallized from isopropanol; yield, 0.25 g (44%), mp 179—180°C, $[\alpha]_D^{28}$ +18° (*c* 1.0, chloroform), ε_{258}^{MeOH}=541 (calcd, 558), IR spectrum (KBr): 3300, 1654 and 1568 (NHAc), 2940 2870 (cyclohexyl), 888 (type 2b of pyranose ring), 733 and 694 cm^{-1} (phenyl).

Found: C, 73.21; H, 7.69; N, 2.42%. Calcd for $C_{35}H_{43}NO_6$: C, 73.27; H, 7.55; N, 2.44%.

Cyclohexyl 3-Acetamido-3-deoxy-α-D-glucopyranoside (VIa). A sample (70 mg) of Va was hydrogenated in methanol (3 ml) containing acetic acid (0.02 ml) over palladium black (50 mg) under 3.5 atm of hydrogen pressure at room temperature. After 5 hr of hydrogenation, the catalyst was filtered off. Evaporation of the filtrate *in vacuo* gave a colorless sirup which was crystallized from acetone; yield, 36 mg (94%), mp 210—211°C, $[\alpha]_D^{23}$ +158° (*c* 1.1, methanol), IR spectrum (KBr): 2925 and 2850 (cyclohexyl), 1658 and 1563 (NHAc), 852 cm^{-1} (type 2a of pyranose ring).

Found: C, 55.64; H, 8.51; N, 4.47%. Calcd for $C_{14}H_{25}NO_6$: C, 55.44; H, 8.31; N, 4.62%.

Cyclohexyl 3-Acetamido-3-deoxy-β-D-glucopyranoside (VIb). A sample of Vb was also hydrogenated to give VIb in like manner as described above; mp 201—202°C, $[\alpha]_D^{23}$ −17°C (*c* 1.3, methanol), IR spectrum (KBr): 2930 and 2855 (cyclohexyl), 1622 and 1565 (NHAc), 888 cm^{-1} (type 2b of pyranose ring).

Found: C, 55.61; H, 8.19; N, 4.58%. Calcd for $C_{14}H_{25}NO_6$: C, 55.44; H, 8.31; N, 4.62%.

Cyclohexyl 3-Amino-3-deoxy-α-D-glucopyranoside Hydrochloride (VII). A sample (36 mg) of VIa was heated with hydrazine hydrate (1.0 ml) in a sealed tube in the boiling water for 16 hr to give a pale brown solution, which was dried up *in vacuo*. The resulting brown sirup was purified on a column of Dowex 1×2 (OH type; 10×50 mm), developing with carbon dioxide-free water. Evaporation of ninhydrin positive fractions afforded a colorless glass, 30 mg, which was took up with a small volume of water and then acidified to pH 2 with 0.1 N hydrochloric acid. After evaporation of excess acid and water, a crystalline residue remained; trituration with acetone; yield, 36 mg (72%), mp 228—230°C (decomp.), $[\alpha]_D^{23}$ +151° (*c* 0.4, water).

Found: C, 48.48; H, 8.26; N, 4.67%. Calcd for $C_{12}H_{24}NO_5Cl$: C, 48.41; H, 8.12; N, 4.71%.

On ascending paper chromatography at room temperature for 16 hr, the R_f value of VII was 0.66. When heated with 3 N hydrochloric acid at 98°C for 3 hr, VII gave 3-amino-3-deoxy-D-glucopyranose being examined by paper chromatography.

Methyl 2,3,4-Tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α-D-glucopyranoside (IX). A mixture of methyl 6-acetamido-6-deoxy-α-D-glucopyranoside (VIII) (1.0 g, finely powdered), benzyl chloride (20 ml) and sodium hydride (1.0 g) was stirred magnetically under anhydrous conditions for 2—3 hr at 125—130°C. This reaction was exothermic and the mixture became thick and then changed into a thin slurry as the reaction reached completion. Progress of the reaction was followed by TLC and measurement of volume of the evolved hydrogen gas which showed that benzylation was virtually complete after 2 hr. The reaction mixture was passed through a thick bed of Celite and the insoluble matters were washed with a large volume of dry benzene. The combined benzene filtrate and washings were washed with water, dried over anhydrous sodium sulfate and evaporated to dryness *in vacuo* at 90°C to afford a yellow sirup, which was crystallized from *n*-hexane (50 ml); colorless needles, yield, 2.1 g (83%). This product was sufficiently pure for the next preparation as described below. Recrystallization from methanol gave an analytically pure sample; mp 81—83°C, $[\alpha]_D^{25}$ +26°C (*c* 1.0, chloroform), ε_{258}^{MeOH}= 760 (calcd, 744), IR spectrum (Nujol): 1637 (NAc), 1090, 733 and 694 cm^{-1} (*O*-benzyl). No absorption appeared in the region of OH or NH stretching.

Found: C, 74.40; H, 6.77; N, 2.53%. Calcd for $C_{37}H_{41}NO_6$: C, 74.60; H. 6.94; N, 2.35%.

2,3,4-Tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-β-D-glucopyranose (X) and Its Acetate (XI). To a solution of IX (5.0 g) in glacial acetic acid (50 ml) and acetic anhydride (8 ml) was added a mixture of concentrated sulfuric acid (1.0 ml) and acetic acid (5.0 ml) at 0°C under stirring in the course of 10 min. The stirring was continued at 0°C for 1 hr under exclusion of moisture and additional 7 hr at 10—20°C. The resulting mixture was poured onto cracked pieces of ice (300 g) under stirring to separate an oily product,

which was extracted with benzene. The benzene solution was neutralized with dilute aqueous sodium bicarbonate (5%) by cautious shaking, washed with water and evaporated to give an oily product, which was not crystallizable. The product was then treated with methanolic sodium methylate (0.003%; 10 ml) at room temperature for 1 hr. After neutralization with acetic acid, the solution was evaporated to fine crystalline X; yield 3.4 g (75%). Recrystallized from methanol; mp 160—161°C, $[\alpha]_D^{18}$ +18° (*c* 1.0, chloroform), ε_{258}^{MeOH} =738 (calcd, 744), IR spectrum (Nujol): The expected absorption of OH stretching was observed at 3190 cm^{-1} and no amido II band appeared; 1624 (NAc), 734 and 696 cm^{-1} (phenyl).

Found: C, 74.51; H, 6.71; N, 2.41%. Calcd for $C_{36}H_{39}NO_6$: C, 74.35; H, 6.76; N, 2.41%.

A sample (10 g) of X was acetylated with acetic anhydride (10 ml) in pyridine (70 ml) at room temperature overnight under exclusion of moisture. The resulting mixture was evaporated to give a sirup which was crystallized with isopropanol. Recrystallized from the same solvent; mp 121—122°C, $[\alpha]_D^{25}$ +12° (*c* 1.0, chloroform), ε_{258}^{MeOH}=726 (calcd, 744), IR spectrum (Nujol): The OH stretching absorption completely disappeared; 1763 and 1240 (OAc), 1658 (NAc), 750, 735 and 701 (phenyl), 917 cm^{-1} (type 2b of pyranose ring).

Found: C, 73.49; H, 6.89; N, 2.39%. Calcd for $C_{38}H_{41}NO_7$: C, 73.17; H, 6.63; N, 2.25%.

2,3,4-Tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α-D-glucopyranosyl Chloride (XII). A solution XI (0.6 g) in a mixture of acetyl chloride (4 ml) and dioxane (23 ml) containing dry hydrogen chloride (4%) was allowed to stand at 37°C overnight in a tightly stoppered flask. After concentration *in vacuo* at 20°C, the resulting product was repeatedly co-distilled with absolute toluene until the product became an amorphous solid. Treatment with dry petroleum ether gave a colorless powder; yield 0.55 g (95%), mp 91—92°C (decomp.), $[\alpha]_D^{23}$ +70° (*c* 1.34, chloroform), $\varepsilon_{258}^{AcOEt}$=738 (calcd, 744), IR spectrum (Nujol): The C–O stretching absorption of OAc was not observed; 1652 (NAc), 845 (broad, type 2a of pyranose ring) and 699 cm^{-1} (phenyl).

Found: C, 71.65; H, 6.24; N, 2.30; Cl 6.51%. Calcd for $C_{36}H_{38}NO_5Cl$: C, 72.06; H, 6.38; N, 2.33; Cl, 5.92%.

Cyclohexyl 2,3,4-Tri-*O*-benzyl-6-(*N*-benzylacetamido)-6-deoxy-α- and β-D-glucopyranoside (XIIIa and XIIIb). A mixture of XII (0.50 g), cyclohexanol (0.25 ml), finely powdered mercuric cyanide (0.20 g) and mercuric bromide (0.23 g) in absolute nitromethane (5 ml) was shaken at 27°C for 48 hr under anhydrous conditions. The resulting pale yellow mixture was filtered and the filtrate was diluted with a large volume of chloroform. The solution was washed with three 20 ml portions of 20% aqueous potassium bromide and successively with three 20 ml portions of water. After drying over anhydrous sodium sulfate, the solution was evaporated *in vacuo* to give an oily product. TLC using a solvent system of toluene and MEK (3 : 1) showed that the product mainly consisted of two substances of R_f values 0.70 (main) and 0.65. The product was chromatographed on a silicagel column (50g) with the same solvent system to separate into the two substances; the former with R_f value 0.70 weighed 0.32 g (47%) and the latter with R_f value 0.65 was 0.04 g (5%). The analytical sample of the main product XIIIa was prepared by chromatography on a small silica-gel column; $[\alpha]_D^{22}$ +43° (*c* 1.7, chloroform), ε_{258}^{MeOH}=765 (calcd, 744), IR spectrum (KBr): 2940 (cyclohexyl), 1650 (NAc), 850 (type 2a of pyranose ring) and 696 cm^{-1} (phenyl).

Found: C, 75.76; H, 7.60; N, 2.41%. Calcd for $C_{42}H_{49}NO_6$: C, 75.99; H, 7.44; N, 2.11%.

The minor product XIIIb crystallized from methanol; mp 143.5—144.5°C, $[\alpha]_D^{27}$ +29 (*c* 1.0, chloroform), ε_{258}^{MeOH}=738 (calcd, 744); IR spectrum (KBr): 2940 (cyclohexyl), 1650 (NAc), 912 (type 2b of pyranose ring) and 695 cm^{-1} (phenyl).

Found: C, 76.46; H, 8.06; N, 2.45%. Calcd for $C_{42}H_{49}NO_6$: C, 75.99; H, 7.44; N, 2.11%.

Cyclohexyl 6-Acetamido-6-deoxy-α-D-glucopyranoside (XIVa). A sample (0.12 g) of XIIIa was hydrogenated over palladium black (0.01 g) in methanol containing a few drops of acetic acid at room temperature under 3.5 atm of hydrogen pressure for 5 hr. After removal of the catalyst, the solution was evaporated to give a sirup, which was dissolved in liquid ammonia (30 ml) and reduced by additions of several pieces of sodium until the developed blue color maintained for 15 min. After quenching the reaction with ammonium chloride (0.2 g), excess ammonia was removed by evaporation and the residue was took up in water. The solution was successively passed through a column of Amberlite IRA-410 (OH type; 5 ml) and Amberlite IR-120 (H type; 3 ml). The deionized solution was evaporated to give a colorless crystalline residue, which was further treated with acetone; yield 0.03 g (53%), mp 113—114°C, $[\alpha]_D^{23}$ +138° (*c* 1.2, methanol), IR spectrum (KBr): 1645 and 1570 (NHAc), 2935 (cyclohexyl), and 846 cm^{-1} (type 2a of pyranose ring).

Found: C, 54.81; H, 8.27; N, 4.55%. Calcd for $C_{14}H_{25}NO_6$: C, 55.43; H, 8.31; N, 4.62%.

Cyclohexyl 6-Acetamido-6-deoxy-β-D-glucopyranoside (XIVb). A sample (20 mg) of XIIIb was hydrogenated over palladium black (5 mg) in methanol containing a few drops of acetic acid at 40—45°C for 4 hr under 3.5 atm of hydrogen pressure to de-*O*-benzylate. The catalyst was filtered off and the solution was evaporated. An oily product was dissolved in liquid ammonia (30 ml) and to the solution was added small pieces of sodium until the blue color survived for 15 min. To the solution was added an excess of ammonium chloride (0.3 g) and ammonia was removed by evaporation. The product was deionized in like manner as described in the preparation of XIVa to give a colorless crystalline residue which was crystallized from acetone; yield 4.5 mg (47%), mp 163—164°C, $[\alpha]_D^{23}$ +1.5° (*c* 0.3, methanol), IR spectrum (KBr): 2850 (cyclohexyl), 1650 and 1550 (NHAc), and 893 cm^{-1} (type 2b of pyranose ring).

Found: C, 55.12; H, 8.23; N, 4.35%. Calcd for $C_{14}H_{25}NO_6$: C, 55.43; H, 8.31; N, 4.62%.

Cyclohexyl 6-Amino-6-deoxy-α-D-glucopyranoside Hydrochloride (XV). XIVa (18 mg) was heated with hydrazine hydrate (80%; 1 ml) in a sealed tube in the boiling water for 20 hr to give a pale brown solution, which was evaporated *in vacuo* at 60°C. The resulting brown sirup was purified on a column of Dowex 1×2 (OH type; 20 ml), irrigating with distilled

water. The ninhydrin-positive fractions were evaporated *in vacuo* to give a colorless glass of XV. The free base was dissolved in a small volume of water and acidified with 0.1 N hydrochloric acid to pH 4. After evaporation of excess acid and water, a crystalline residue was obtained which was treated with acetone; yield 13 mg (75%), mp 184—185°C (decomp.), $[\alpha]_D^{23}$ +120° (*c* 0.4, water).

Found: C, 48.24; H, 7.82; N, 4.84%. Calcd for $C_{12}H_{24}NO_5Cl$: C, 48.41; H, 8.12; N, 4.71%.

On the ascending paper chromatography at room temperature for 16 hr, the R_f value of XV was 0.55. When heated with 3 N hydrochloric acid at 95—98°C for 3 hr, XV afforded 6-amino-6-deoxy-D-glucopyranose, the formation of which was examined by paper chromatography.

The authors are indebted to Mr. Saburo Nakada for his microanalysis, to Mr. Yoshito Koyama for his technical assistance.