Studies on Aminosugars. XXVIII. Synthesis of β-L-Idopyranosides through the Corresponding 5-Enopyranosides[1]

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Methyl 6-deoxy-β-L-idopyranoside (**7**), methyl 2-amino-2,6-dideoxy-β-L-idopyranoside (**13**) and methyl 3-amino-3,6-dideoxy-β-L-idopyranoside (**28**) have been prepared through the corresponding suitably protected 5-enopyranoside precursors in good yields.

As part of the investigation of the syntheses and reactions of aminosugars, the preparation and reaction of several 5-enoses were carried out. This paper reports the syntheses of 5-enoses starting from methyl α-D-glucopyranoside, methyl 2-amino-2-deoxy-α-D-glucopyranoside and methyl 3-amino-3-deoxy-α-D-glucopyranoside, and the behavior of these unsaturated sugars toward catalytic hydrogenation.

Helferich and Himmen described[2,3] the transformation of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside and methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-bromo-β-D-glucopyranoside to methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-*xylo*-hex-5-enopyranoside (**5**) and its β-D isomer, by reaction with silver fluoride in pyridine. We used the general method for the present purpose. Regarding C-6 halogeno compounds, the starting materials, Evans, Long, and Parrish[4] recently described a convenient synthesis of methyl 6-chloro-6-deoxy-α-D-glucopyranoside (**2**) by selective chlorination of the primary hydroxyl group of methyl α-D-glucopyranoside (**1**) by use of methanesulfonyl chloride in dimethylformamide (DMF). We accordingly tried the reaction of **2** with silver fluoride, but the chloro derivative hardly reacted at all with it. The corresponding bromo derivative, namely methyl 6-bromo-6-deoxy-α-D-glucopyranoside (**3**), was prepared analogously by the method of Evans *et al.* and the product was found to react with silver fluoride but not as expected. As shown by Hough and Otter[5] in the case of 5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose, it seems that the presence of free hydroxyl groups in **3** prevents the formation of an enose. **3** was therefore acetylated to the tri-*O*-acetyl derivative (**4**) and treated with silver fluoride.

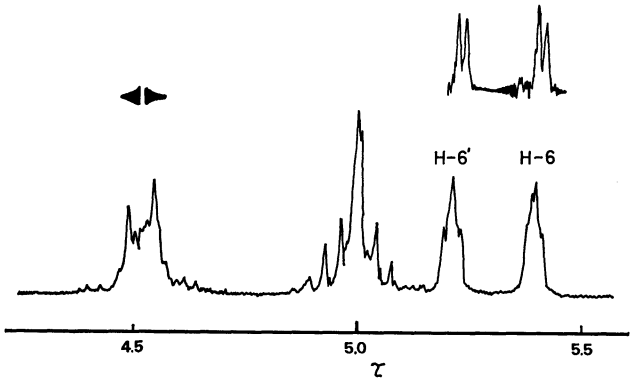

Fig. 1. The NMR Spectrum of **5** in $CDCl_3$.

By this reaction **5** was successfully prepared. The NMR spectrum (Fig. 1) of **5** showed narrow multiplets at τ 5.36 and 5.18. Irradiation at τ 4.53 resulted in the collapse of multiplets to a pair of resolved doublets (J 1.7 Hz). Small coupling is typical for terminal methylene protons supporting the structure **5**.

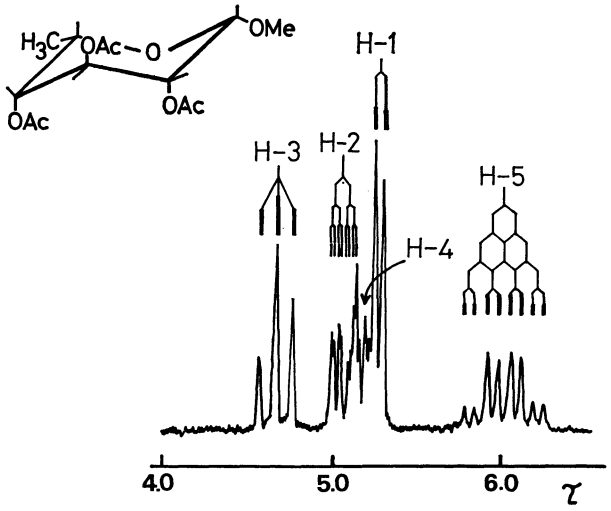

Fig 2. The NMR Spectrum of **6** in $CDCl_3$.

5-Enopyranoside (**5**) was then hydrogenated with palladium black and hydrogen to give methyl 2,3,4-tri-*O*-acetyl-β-L-idopyranoside (**6**) quantitatively. The NMR spectrum of **6** is shown in Fig. 2. The exclusive formation of β-L-idopyranoside is noteworthy in contrast with the hydrogenation of 1,2,3,4-tetra-*O*-acetyl-6-deoxy-β-D-*xylo*-hex-5-enopyranose. It has recently been reported that the latter was converted[6] into a mixture of 96% of the 6-deoxy-D-gluco and 4% of the 6-deoxy-L-ido isomer by hydrogenation with the same catalyst. Hydroboration[7] of methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside has also been reported to afford a mixture of methyl α-D-gluco and β-L-ido isomer in the ratio 1:2.5. The anomeric α-*O*-methyl group in **5**, therefore, may be the dominating cause for exclusive formation of the β-L-ido derivative in the hydrogenation with palladium black and hydrogen.

The protecting groups of **6** were finally removed in a basic condition to give methyl 6-deoxy-β-L-idopyrano-

1) A part of this paper was read at the 23rd Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1970. (See Abstract of Papers of the Meeting, Vol. III p. 1901).

2) B. Helferich and E. Himmen, *Ber.*, **61**, 1825 (1928).

3) B. Helferich and E. Himmen, *ibid.*, **62**, 2136 (1929).

4) M. E. Evans, L. Long, Jr., and F. W. Parrish, *J. Org. Chem.*, **33**, 1074 (1968).

5) L. Hough and B. Otter, *Chem. Commun.*, **1966**, 173.

6) L. Hough, R. Khan, and B. A. Otter, in "Deoxy Sugars" (Advances in Chemistry Series, No. 74), ed. by S. Hanessian, Amer. Chem. Soc., Washington (1968), p. 120.

7) J. Lehman, *Carbohyd. Res.*, **2**, 1 (1966).

side (**7**). As for 6 deoxy-L-idose, it was prepared by Meyer and Reichstein[8] and Wolfrom and Hanessian[9] from 1,2,*O*-isopropylidene-D-glucofuranose through multi-step procedures.

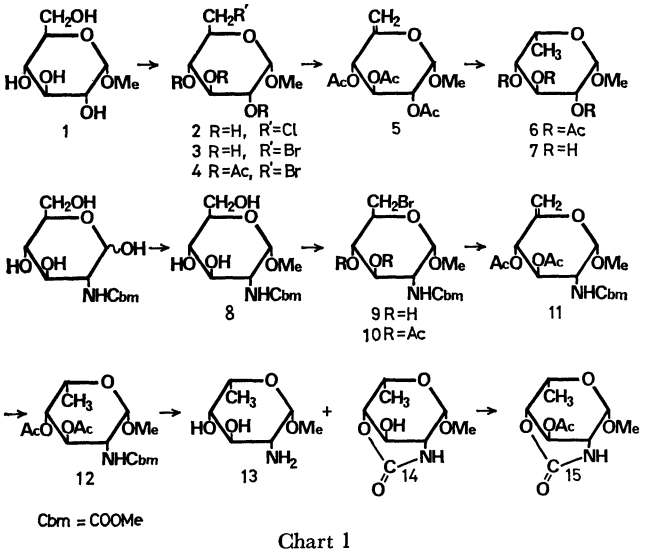

Chart 1

The above synthesis has been extended to amino-sugars, and methyl 2-amino-2,6-dideoxy-β-L-idopyranoside (**13**) has been prepared from methyl 2-deoxy-2-methoxycarbonylamino-α-D-glucopyranoside (**8**). 2-Amino-2-deoxy-D-glucose was *N*-methoxycarbonylated and then treated with hydrogen chloride in methanol to give **8** in 78% yield with no detectable formation of β-isomer. Glucoside (**8**) was brominated in a similar manner as in the preparation of **3**. The resulting 6-bromo derivative (**9**) was acetylated and then treated with silver fluoride in DMF. In this case the reaction to make 5,6-unsaturation was appreciably slower than that in the case of **5**, and methyl 3,4-di-*O*-acetyl-2,6-dideoxy-2-methoxycarbonylamido-α-D-*xylo*-hex-5-enopyranoside (**11**) was obtained in 30% yield, leaving much starting material (**10**) unchanged. In regard to the synthesis of an aminoglucoside having 5-eno structure, Kiss and Burkhardt[10] reported the preparation of methyl 4-*O*-acetyl-3-*O*-benzyl-2-benzyloxycarbonylamido-2,6-dideoxy-α-D-*xylo*-hex-5-enopyranoside from the corresponding 6-iodo precursor in a good yield.

Hydrogenation of the 5-eno derivative (**11**) gave β-L-idopyranoside (**12**) in 90% yield, and subsequent hydrolysis with 1N barium hydroxide gave methyl 2-amino-2,6-dideoxy-β-L-idopyranoside (**13**) in 56% yield. The NMR spectrum of **12** is shown in Fig. 3. In this hydrolysis, another product (**14**) was formed in 33% yield, which resisted further hydrolysis. Even after 3 hr heating at 100°C in 1N barium hydroxide solution, only half of the product was transformed to **13**. The structure of **14** was determined through the NMR spectrum (Fig. 4) of its acetyl derivative (**15**) as methyl

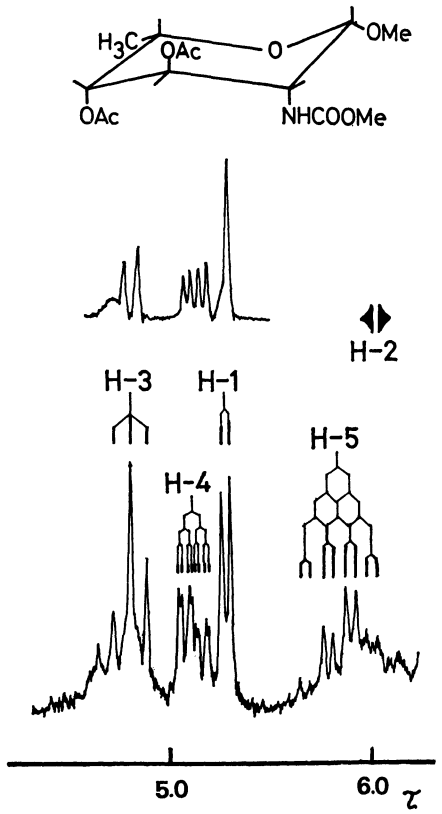

Fig. 3. The NMR spectrum of **12** in $CDCl_3$.

2-amino-2,6-dideoxy-β-L-idopyranoside 2,4-carbamate, but not 2,3-carbamate. In the NMR spectrum of **15**, H-2 resonated at τ 6.27 and appeared as double triplets (J 4.4 and 2 Hz). Double irradiation technique showed that the coupling constants relating to H-2 were $J_{2,3}$ 4 Hz, $J_{2,NH}$ 4 Hz, $J_{2,4}$ 2 Hz and $J_{2,1}$ 0 Hz. These coupling constants and others ($J_{3,4}$ 4 Hz, $J_{4,5}$ ~0 Hz) suggest that the preferred conformation of **15** is IC chair. Moreover, observation of a long-range coupling ($J_{2,4}$ 2 Hz) in **15** as well as the position of acetoxyl methyl resonance at τ 7.85, situated in the region of an axial acetoxyl methyl,[11] also support the IC conformation in which H-2 and H-4 are in di-equatorial orientation.

3-Amino-3-deoxy-D-glucose was led to the corresponding L-idopyranoside by a series of similar reactions. 3-Amino-3-deoxy-D-glucose prepared by the fermentation[12] of *Bacillus aminoglucosidicus* was *N*-methoxycarbonylated and glycosidated with hydrogen chloride - methanol to afford a mixture of α- (**16**) and β-anomer (**17**). Separation of the anomers was performed by resin column chromatography. The α-anomer was brominated in an analogous manner to those described above to give 6-bromo derivative (**18**) in 85% yield. After subsequent acetylation, the acetyl derivative (**19**) was treated with silver fluoride in pyridine. It was found that unsaturation does not

8) A. S. Meyer and T. Reichstein, *Helv. Chim. Acta*, **29**, 139 (1946); *ibid.*, **29**, 152 (1946).
9) M. L. Wolfrom and S. Hanessian, *J. Org. Chem.*, **27**, 1800 (1962).
10) J. Kiss and F. Burkhardt, *Helv. Chim. Acta*, **52**, 2622 (1969).
11) R. U. Lemieux, R. K. Kulling, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958); L. D. Hall, *Adv. Carbohyd. Chem.*, **19**, 51 (1964).
12) S. Umezawa, K. Umino, S. Shibahara, M. Hamada, and S. Omoto, *J. Antibiotics*, **20A**, 355 (1967).

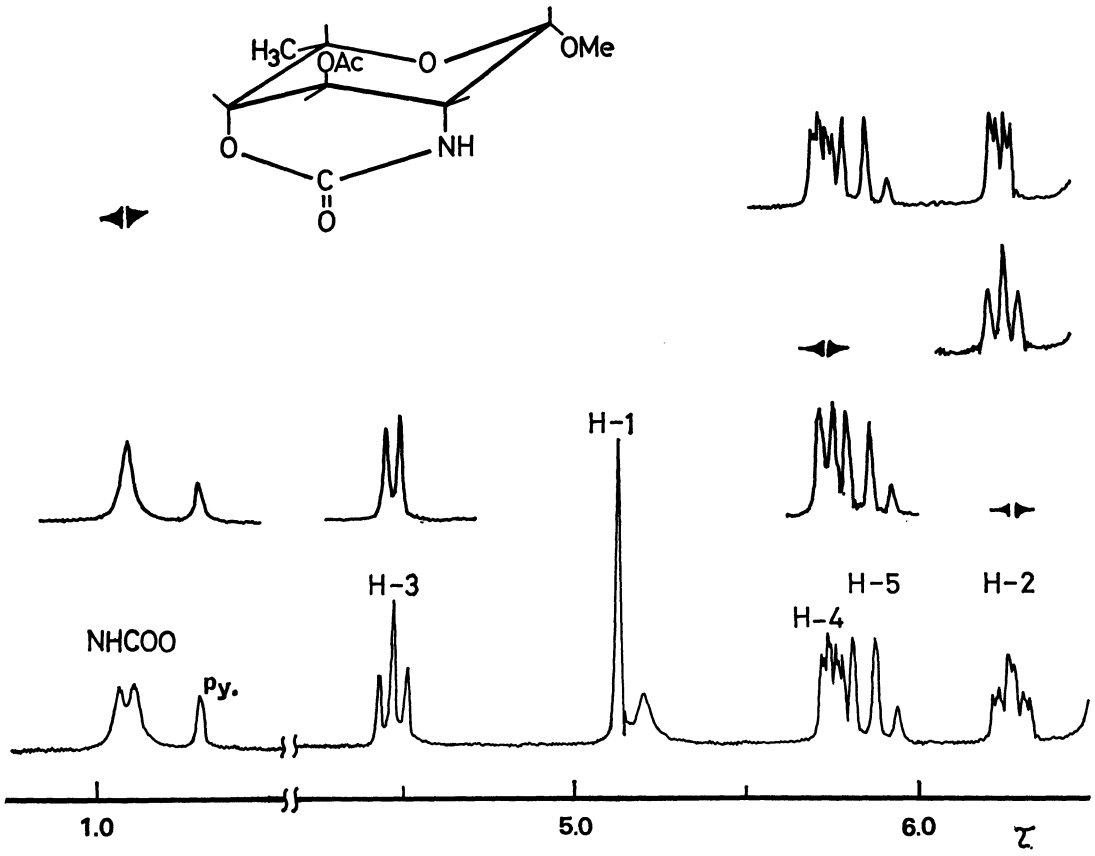

Fig. 4. The NMR spectrum of **15** in pyridine-d_5.

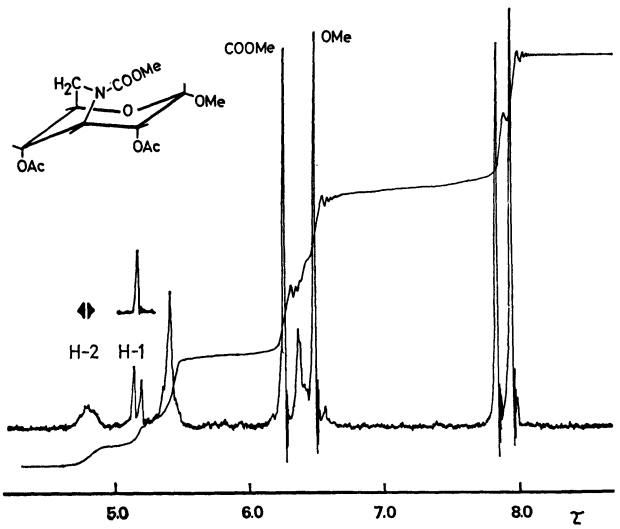

Fig. 5. The NMR spectrum of **20** in $CDCl_3$.

occur and a 3,6-imino derivative (**20**) was formed instead. No absorption ascribable to amide II was observed in its IR spectrum. The NMR spectrum indicated the presence of two axial acetyls, O–CH_3, $NCOOCH_3$, one anomeric proton and six other protons (Fig. 5). Irradiation at τ 4.80 caused the doublet of H-1 at τ 5.15 to collapse to a singlet. The broadened signal (τ 4.68—4.88) centered at τ 4.80 was therefore assigned to H-2; at the same time, the unresolved pattern and the narrow half-height width (~8 Hz) of H-2 suggested the presence of a long-range coupling between H-2 and H-4 as well as a small coupling between H-2 and H-3. These results and the presence of a narrow multiplet (τ 5.3—5.5) of H-3, 4, and 5 complex suggest the preferred conformation of **20** to be IC and, consequently, **20** has a 3,6-imino structure. Formation of structurally related 3,6-imino derivatives from suitably protected 6-*O*-mesyl or 6-*O*-tosyl precursors by the action of sodium acetate were recently

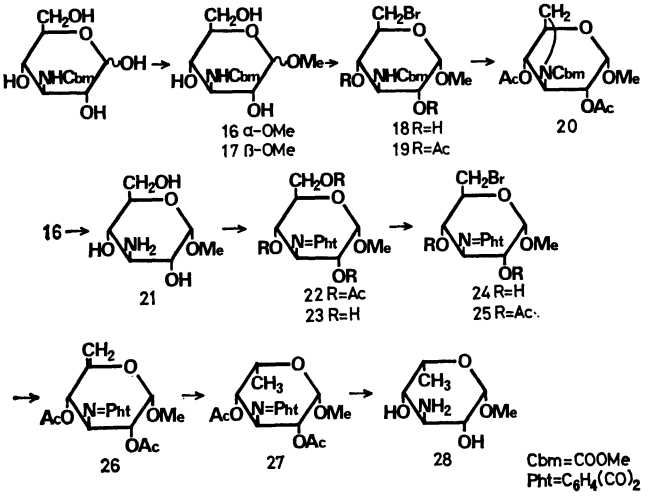

Chart 2

reported by Reckendorf *et al.*[13]

Failure of the formation of a 5,6-unsaturated compound from **19** was presumed to be due to the presence of an amino hydrogen in **19**. Accordingly, an attempt was made to use a 3-phthalimido derivative in place of **19**. Methyl 3-amino-3-deoxy-α-D-glucopyranoside (**21**) was prepared by alkaline hydrolysis of **16**, and then treated with phthalic anhydride and acetic anhydride to give an *O*-acetylated 3-phthalimido derivative (**22**). Subsequent deacetylation gave a 3-phthalimido derivative (**23**). Bromination of **23** in an analogous manner as described above gave a 6-bromo derivative (**24**), which was then acetylated. The reaction of the acetylated product (**25**) with silver fluoride proceeded smoothly, and afforded a 5,6-unsaturated compound (**26**) in 79% yield. The NMR spectrum of **26** is shown in Fig. 6. The catalytic hydrogenation of 5-enopyranoside gave β-L-ido derivative (**27**) in 87% yield. The NMR spectrum of **27** is shown in Fig. 7. The protecting

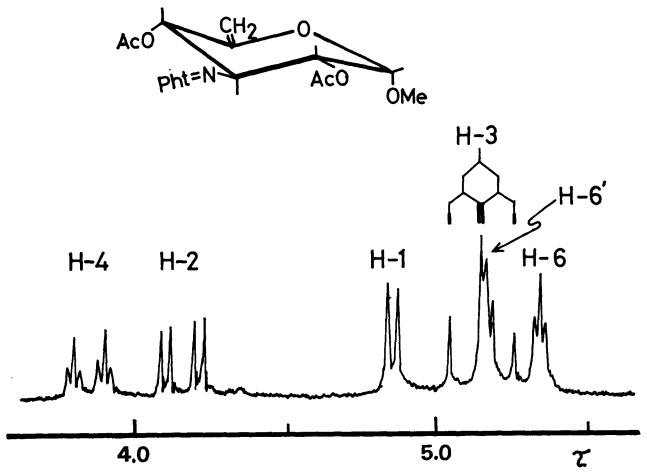

Fig. 6. The NMR Spectrum of **26** in $CDCl_3$.

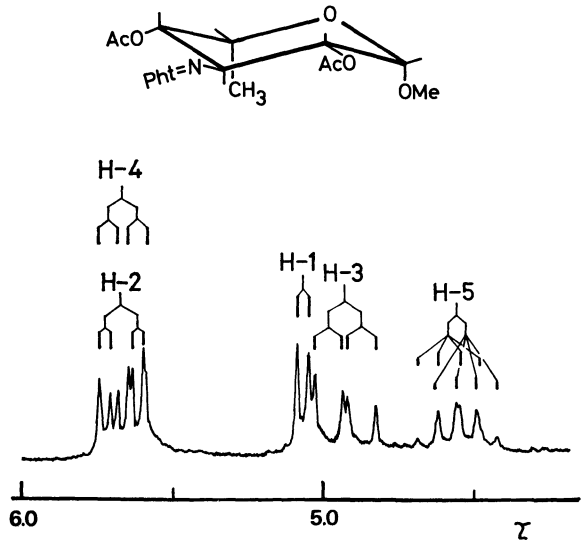

Fig 7. The NMR spectrum of **27** in $CDCl_3$.

13) W. M. zu Reckendorf, *Ber.*, **97**, 1275 (1964); W. M. zu Reckendorf and N. Wassiliadou-Micheli, *ibid.*, **103**, 37 (1970); W. M. zu Reckendorf, *ibid.*, **103**, 995 (1970).

groups of **27** were finally removed with *n*-butylamine to give methyl 3-amino-3,6-dideoxy-β-L-idopyranoside (**28**) in 77% yield.

Conformations of β-L-Ido Compounds. The NMR spectra of these final products **7**, **13**, and **28** were compared. Each proton having the same structural number of these compounds had almost the same splitting pattern and couplings. The shift-values of the corresponding protons also were in accord except for the shift-value of the proton bearing an amino group: the H-2 and H-3 protons in **13** and **28** resonated at 0.75 and 0.76 ppm higher field than that of the resonance of H-2 and H-3 of **7**, respectively. These findings show that **7**, **13**, and **28** have the same conformation. The values of the vicinal coupling constants of these compounds, $J_{1,2}$ 2, $J_{2,3}$ ~5, $J_{3,4}$ ~5 and $J_{4,5}$ 3 Hz suggested that the preferred conformation of **7**, **13**, and **28** is IC chair, but not CI. A twist-boat structure as shown by Coxon[14] was also considered, but the observation of a long-range coupling between H-2 and H-4 ($J_{2,4}$ ~1Hz) in **7** and **28** suggested that H-2 and H-4 are in diequatorial orientation and a twist-boat structure is improbable. The small $\Delta[M]_{TACu}$[15] value (+159°) of **13** also supports the view that 2-amino and 3-hydroxyl groups of **13** are not diequatorial. The results show that the structural change from α-D-gluco to β-L-ido form caused conformational change from CI to IC, and this may be responsible for the easy formation of 2,4-carbamate (**14**) from **12**. Compounds **6** and **12**, both having β-L-ido structure, also were presumed to have IC conformation. Comparison of their NMR spectra with the spectrum of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside (**6'**) support the above conclusion. On the other hand, compound **27** was presumed to have CI conformation. This is supported by a comparison of the τ-value of the C-methyl protons (τ 8.58) of **27** with the τ-values of the C-methyl protons of **6**, **7**, **12**, **13**, and **28** (τ ~8.70), suggesting that the C-methyl group of **27** is axial. The fact that only **27** of the β-L-ido derivatives has CI conformation may be interpreted by the presence of a bulky phthalimide group.

Experimental

The NMR spectra were measured with a Varian A-60D or a Varian HA-100 (at 100 MHz) spectrometer. Tetramethylsilane (τ10.00; for the solution other than deuterium oxide) and sodium 4,4-dimethyl-4-silapentane-1-sulfonate (τ 10.00; for the solution of deuterium oxide) were used as the internal standards. Thin-layer chromatography (TLC) was carried out on microscope slides coated with silica gel, and the spots were visualized with sulfonic acid. Paper chromatography (ppc) was carried out on Toyo Roshi No. 50 paper.

Methyl 6-Bromo-6-deoxy-α-D-glucopyranoside (3). To a stirred solution of methyl α-D-glucopyranoside (**1**) (1.0 g) in dry DMF (10 ml, dried over calcium hydride), mesyl bromide[16] (1.6 g) was added dropwise and the solution was

14) B. Coxon, *Carbohyd. Res.*, **1**, 357 (1966).

15) S. Umezawa, T. Tsuchiya, and K. Tatsuta, This Bulletin, **39**, 1235 (1966).

16) G. Sieber, *Ann.*, **631**, 180 (1960).

maintained at 65°C for 18 hr. On TLC with ethyl acetate-ethanol-water (45:5:3), the solution showed two spots of R_f 0.64 and 0.85 in approximately equal strength. The solution was evaporated and coevaporated with toluene to give a brown syrup which was dissolved in methanol and the solution was then neutralized with 2.4M sodium methoxide in methanol. On TLC, the spot of R_f 0.85, which was supposed to originate from an *O*-formyl by-product[4] disappeared, and a spot (R_f 0.17) corresponding to the starting material (**1**) appeared. The solution was evaporated and the residue was charged on a column of silica gel (100 g) and developed with the solvent mixture described above. The portion (180—300 m*l*) containing the substance of R_f 0.64 was evaporated to give a colorless solid which was recrystallized from ethyl acetate yielding 770 mg (58%), mp 136—137°C (lit,[17] 126—127°C), $[\alpha]_D^{20}$+126° (*c* 1, methanol) (lit,[17] +137°); IR spectrum (KBr): no peaks between 1500—2500 cm^{-1}, 940, 897, 887, 815(vw), 757, 750 (sh), and 694 cm^{-1}; NMR (in D_2O): τ 6.56 (3H s., OCH_3), 6.0—6.65 (6H), 5.18 (1H d., J 3 Hz, H-1).

Found: C, 33.00; H, 5.23; Br, 30.57%. Calcd for $C_7H_{13}O_5Br$: C, 32.70; H, 5.10; Br, 31.09%.

*Methyl 2,3,4-Tri-*O*-acetyl-6-bromo-6-deoxy-α-*D*-glucopyranoside (4).* To a solution of **3** (688 mg) in pyridine (12 m*l*), acetic anhydride (1.7 g) was added and the solution was allowed to stand overnight. A spot (R_f 0.44) appeared on TLC with benzene-ethyl acetate (6:1). After addition of a small amount of water (0.2 m*l*) followed by standing for 1 hr, the solution was evaporated and the residue was dissolved in chloroform. The solution was washed in turn, with saturated potassium hydrogensulfate solution, water, saturated sodium hydrogencarbonate solution and water, dried over sodium sulfate and evaporated to give a colorless solid. Recrystallization from ethanol yielding 956 mg (98%), mp 125—125.5° $[\alpha]_D^{20}$+121° (*c* 1, chloroform).

Found: C, 40.92; H, 5.33; Br, 20.41%. Calcd for $C_{13}H_{19}O_8Br$: C, 40.74; H, 5.00; Br, 20.86%.

IR spectrum (KBr): 1750; 931, 910(w) 880(w), 810, 752, and 682(w) cm^{-1}; NMR (in $CDCl_3$): τ 7.96, 7.92, and 7.89 (each 3H s., OAc), 6.48 (3H s., OCH_3), 5.94 (1H octet, J 3.6 and 9.7 Hz, H_{ax}-5), 4.48 (1H triplet with small splittings (~0.5 Hz), J 8.5 Hz, probably H_{ax}-3); $J_{4,5}$ 9.7 Hz, $J_{5,6}$ 3 Hz, $J_{5,6'}$ 6 Hz

*Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-α-*D*-xylo-hex-5-enopyranoside (5).* To a solution of **4** (1.01 g) in dry pyridine (12 m*l*, dried over calcium hydride), anhydrous silver fluoride (1.5 g) was added and the mixture was stirred at 50°C for 20 hr in the dark. A spot (R_f 0.72) and three weak spots (R_f 0.55, 0.50 and 0.35) appeared on TLC with benzne - ethyl acetate (3:1). The main spot showed fluorescence[18] by the sodium fluorescein-bromine test according to Stahl for double bond although it has an identical R_f-value with that of **4**. Addition of ether (50 m*l*) to the reaction mixture gave precipitates which were filtered and washed with ether. The ether layer and washings combined were evaporated and the residue was again dissolved in ether. The solution was washed successively with potassium hydrogensulfate solution, sodium hydrogencarbonate solution and water, dried over sodium sulfate and evaporated to give a solid (680 mg) which was negative to the Beilstein test for halogens. The solid was chromatogrqphed on a column of silica gel (60 g) with benzene - ethyl acetate (3:1) and the portion containing **5** was evaporated to give a residue, which was recrystallized from ethanol yielding 430 mg (54%), mp 93—94°C, $[\alpha]_D^{20}$+117° (*c* 1, chloroform) (lit,[2] +117°).

Found: C, 51.44; H, 6.15%. Calcd for $C_{13}H_{18}O_8$: C, 51.65; H, 6.00%.

IR spectrum (KBr): 1755 (s., ester), 1660 (alkene); 955 (m), 935, 907 (m), 897 (m), 872, 783, and 737 cm^{-1}; NMR (in $CDCl_3$): τ 7.95, 7.90 and 7.86 (each 3H s., OAc), 6.51 (3H s., OCH_3), 5.36 (1H m., half-height width was ~3 Hz, H-6), 5.18 (1H m., half-height width was ~4 Hz, H-6′), 4.65—5.1 (2H unresolved m.), 4.2—4.6 (2H unresolved m.). Irradiation at τ 4.53 caused the multiplets at τ 5.36 and 5.18 to collaspse to two clear-cut doublets (each has J 1.7 Hz) showing that the small coupling originated from geminal olefinic protons of H-6,6′.

*Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-β-*L*-idopyranoside (6).* A solution of **5** (100 mg) in dioxane (1.5 m*l*) was hydrogenated with palladium black and hydrogen under 50 lb/sq. inch pressure at 40°C overnight. A spot (R_f 0.45) appeared on TLC with benzene - ethyl acetate (3:1). After filtration the solution was evaporated to give a solid, which was recrystallized from ethanol yielding 98 mg (99%), mp 93.5—94°C, $[\alpha]_D^{20}$+46° (*c* 1, chloroform).

Found: C, 51.30; H, 6.31%. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63%.

IR spectrum (KBr): 1760, 1740; 972 (m), 952, 926 (m), 915, 876, 782, and 700 (m) cm^{-1}; NMR (in $CDCl_3$): τ 8.68 (3H d., J 6.7 Hz, C_5-CH_3), 7.87 (6H s., OAc), 7.86 (3H s., OAc), 6.43 (3H s., OCH_3), 5.82 (1H octet, J 6.7, 6.7, 6.7, and 3 Hz (=$J_{4,5}$), H_{eq}-5), 5.20 (1H d., $J_{1,2}$ 2.2 Hz, H-1), 5.08—5.23 (1H m., H-4), 5.02 (1H octet, J 2.2, 4.8, and ~0.8 Hz (=$J_{2,4}$), H-2), 4.69 (1H t., $J_{2,3}$=$J_{3,4}$ 4.8 Hz, H-3).

Small coupling constants of $J_{2,3}$, $J_{3,4}$ and $J_{4,5}$ and the occurrence of long-range coupling of $J_{2,4}$ suggested the preferred conformation of **6** to be IC chair. The conformtion was also substantiated by comparison of the NMR spectrum of **6** with that of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside (**6′**) prepared by hydrogenation of 6-bromo derivative (**4**).

Compound **6′**: mp 60—61°C (lit,[19] 77—78°), $[\alpha]_D^{20}$+152° (*c* 1, chloroform) (lit,[19]+153.6°, chloroform); IR spectrum (KBr): 1755; 930, 900, 893, 840 (w), and 753 cm^{-1}; NMR (in $CDCl_3$): τ 8.79 (3H d., J 6.5 Hz, C_5-CH_3), 8.00, 7.97, and 7.93 (each 3H s., OAc), 6.58 (3H, s. OCH_3), 6.05 (1H octet, J 6.5, 6.5, 6.5, and 10.0 Hz, H-5). The three equatorial acetoxy methyl protons of **6′** resonated at τ 7.93, 7.97, and 8.00, whereas those of **6** resonated at τ 7.86, 7.87, and 7.87 suggesting the presence of three axial acetoxyl groups in **6** in its preferred conformation.[12]

*Methyl 6-Deoxy-β-*L*-idopyranoside (7).* A solution of **6** (110 mg) in dry methanol (2 m*l*) was treated with sodium methoxide. After addition of a small amount of Amberlite IR-120 (H^+ form) pretreated with methanol, the solution was filtered, evaporated, and the residue was recrystallized from ethyl acetate to give a solid, 60 mg (98%), mp 81—81.5°C, $[\alpha]_D^{25}$+74° (*c* 1, water).

Found: C, 47.48; H, 7.92%. Calcd for $C_7H_{14}O_5$: C, 47.18; H, 7.92%.

IR spectrum (KBr): 1055, 1020, 1003, 970, 916, 808, and 761 cm^{-1}; NMR (in D_2O): τ 8.69 (3H d., J 6.7 Hz, C_5-CH_3), 6.45 (3H s., OCH_3), 6.35—6.52 (1H m., H-4), 6.28 (1H octet, J 5, 2, and 1 Hz, H-2), 5.97 (1H t., J 5 Hz, H-3), 5.84 (1H octet, J 6,7, 6.7, 6.7, and 3Hz, H-5), 5.20 (1H d., J 2 Hz, H-1); $J_{1,2}$ 2 Hz, $J_{2,3}$=$J_{3,4}$ 5 Hz, $J_{4,5}$ 3Hz, and $J_{2,4}$ ~1 Hz.

*Methyl 2-Deoxy-2-methoxycarbonylamido-α-*D*-glucopyranoside (8).* To a mixture of glucosamine hydrochloride (12 g) and anhyd-

17) S. Hanessian, *Carbohyd. Res.*, **2**, 86 (1966).

18) M. Ishikawa, S. Hara, T. Furuya, and Y. Nakazawa, "Thin-layer Chromatography," Nanzando Co., Japan (1963), p. 55

19) J. Compton, *J. Amer. Chem. Soc.*, **60**, 395 (1938).

rous sodium carbonate (7.75 g) in 50% aqueous acetone (200 ml), methoxycarbonyl chloride (9 ml) was added under stirring and the clear solution was allowed to stand at room temperature for 15 min. A spot (R_f 0.39) of *N*-methoxycarbonylglucosamine appeared on TLC with ethyl acetate-methanol (5:1). The solution was evaporated and the residue was dried *in vacuo*. The residue was suspended in 4% hydrogen chloride in methanol (200 ml) and the mixture was refluxed for 18 hr, whereupon a brown clear solution resulted. A new spot (R_f 0.48) appeared on TLC with the same solvent mixture as described above. The brown solution was neutralized with basic lead carbonate, centrifuged, and the supernatant layer was evaporated. The residue was then chromatographed on a column of silica gel (300 g) with ethyl acetate - methanol (5:1), and the portion containing the substance of R_f 0.48 was evaporated to give a colorless solid which was recrystallized from methanol-ether; 10.5 g (78%), mp 126—128°C $[\alpha]_D^{22}$ +135° (*c* 2, methanol).

Found: C, 42.94; H, 6.93; N, 5.75%. Calcd for $C_9H_{17}NO_7$: C, 43.01; H, 6.82; N, 5.57%.

IR spectrum (KBr): 1700, 1550; 950 (w), 940 (w), 925 (w), 900, 850, 785, 760, 720 (w), and 700 (w) cm^{-1}; NMR (in D_2O): τ 6.60 (3H s., OCH_3), 6.32 (3H s., $NHCOOC\underline{H}_3$), 6.1—6.6 (6H m., H-2,3,4,5,6,6'), 5.18 (1H d., J 2 Hz). No signal corresponding to H_{ax}-1 was observed indicating that the product was a pure α-isomer.

Methyl 6-Bromo-2,6-dideoxy-2-methoxycarbonylamido-α-D-glucopyranoside (9). Compound **8** (6.65 g) in DMF (60 ml) was treated with mesyl bromide (6.8 g) at 65°C for 15 hr. After evaporation, the residue was treated with sodium methoxide in methanol as usual, and the crude product obtained was chromatographed on a column of silica gel with benzene - methyl ethyl ketone (1:2) to separate the product (R_f 0.42) and **8** (R_f 0.22). The product was recrystallized from benzene - ethyl acetate (1:2) yielding 5.34 g (64%); mp 138—140°C, $[\alpha]_D^{25}$ +114° (*c* 0.5, methanol).

Found: C, 34.49; H, 5.03; N, 4.31; Br, 25.38%. Calcd for $C_9H_{16}NO_6Br$: C, 34.39; H, 5.14; N, 4.46; Br, 25.47%.

IR spectrum (KBr): 1730, 1530; 972, 945, 895, 772, and 717 (w) cm^{-1}; NMR (in D_2O): τ 6.56 (3H s., OCH_3), 6.30 (3H s., $NHCOOC\underline{H}_3$), 5.17 (1H d., J 2 Hz, H-1).

Methyl 3,4-Di-O-acetyl-6-bromo-2,6-dideoxy-2-methoxycarbonylamido-α-D-glucopyranoside (10). Prepared from **9** by the general procedure. Mp 104—105°C, $[\alpha]_D^{22}$ +111° (*c* 0.5, chloroform).

Found: C, 39.11; H, 4.99; N, 3.54; Br, 20.44%. Calcd for $C_{13}H_{20}NO_8Br$: C, 39.21; H, 5.06; N, 3.52; Br, 20.07%.

IR spectrum (KBr): 1760, 1730, 1535; 940, 925, 880, 780, 760, and 725 (w) cm^{-1}; NMR (in $CDCl_3$): τ 7.99 and 7.94 (each 3H s., OAc), 6.52 (3H s., OCH_3), 6.4—6.65 (2H m., H-6,6'), 6.32 (3H s., $NHCOOC\underline{H}_3$), 6.07 (1H q., J 3.5 and 10 Hz, H-2), 5.75—6.15 (1H m., H-5), 5.20 (1H d., J 3.5 Hz, H-1), τ 4.55—5.2: eight peaks which were analyzed as XABY(=$H_2H_3H_4H_5$) system: τ 5.00 (1H q., $J_{4,5}$ ~8 Hz, $J_{3,4}$ ~9.5 Hz, H-4), τ 4.77 (1H q., $J_{2,3}$ ~10 Hz, $J_{3,4}$ ~9.5 Hz, H-3).

Methyl 3,4-Di-O-acetyl-2,6-dideoxy-2-methoxycarbonylamido-α-D-xylo-hex-5-enopyranoside (11). To a solution of **10** (2.83 g) in dry pyridine (28 ml), anhydrous silver fluoride (3.3 g) was added and the mixture was stirred at 65°C for 18 hr in the dark. Two spots (R_f 0.68 and 0.62) appeard on TLC with benzene - ethyl acetate (5:2). The former spot was proved to originate from both **10** and **11** (they had the same R_f value) and the latter from a by-product, which increased with the prolongation of reaction. Ether was added to the reaction mixture and the resulting mixture was treated as in the preparation of **5**. The crude product obtained was then chromatographed on a column of silica gel (80 g) with benzene - ethyl acetate (5:2) and the portion containing **10** and **11** was evaporated to give a syrup (1.29 g) which was crystallized by addition of ethanol to give **11** (411 mg). Another crop (121 mg) was obtained from the mother liquor. Total yield was 30%. The mother liquor was proved to be constituted mainly from **10**. Attempted change in the reaction conditions could not raise the yield of **11**. Mp 85—88°C, $[\alpha]_D^{25}$ +89° (*c* 0.5, chloroform)

Found: C, 48.94; H, 6.10; N, 4.30%. Calcd for $C_{13}H_{19}NO_8$: C, 49.21; H, 6.04; N, 4.41%.

IR spectrum (KBr): 1760, 1740, 1670 (C=C), 1540; 945, 930 (w), 900 (w), 875, 852 (w), 790 (sh), 780, 748 (w), and 725 (w) cm^{-1}; NMR (in $CDCl_3$): τ 7.96 and 7.88 (each 3H s., OAc), 6.53 (3H s., OCH_3), 6.30 (3H s., $NHCOOC\underline{H}_3$), 5.85 (1H double triplets, J ~10, ~10, and 3.5 Hz, H-2), 5.38 (1H t., J ~1.8 Hz, H-6), 5.20 (1H t., J ~1.8 Hz, H-6'), 5.15 (1H d., J 3.5 Hz, H-1), ~5 (1H broad doublet, J ~10 Hz, $N\underline{H}COO$-), 4.77 (1H t., J 9.7 Hz, H-3), 4.48 (1H double triplets, J ~1.8, ~1.8, and ~10 Hz); $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.7 Hz, $J_{3,4}$ 9.7 Hz, $J_{4,6}=J_{4,6'}=J_{6,6'}$ ~1.8 Hz.

Methyl 3,4-Di-O-acetyl-2,6-dideoxy-2-methoxycarbonylamido-β-L-idopyranoside (12). Compound **11** was hydrogenated in dioxane with palladium black and hydrogen on 90% yield in a similar manner as in the preparation of **6**. Syrup, $[\alpha]_D^{22}$ +45° (*c* 1, chloroform)

Found: C, 48.73; H, 6.75; N, 4.65%. Calcd for $C_{13}H_{21}NO_8$: C, 48.90; H, 6.63; N, 4.39%.

IR spectrum (KBr): 1760, 1730, 1525; 930, 890, 860, 805, 778, 760, and 723 (w) cm^{-1}; NMR (in $CDCl_3$ at 60 and 100 MHz): τ 8.74 (3H d., J 6.7 Hz, C_5-CH_3), 7.88 and 7.90 (each 3H s., OAc), 6.48 (3H s., OCH_3), 6.30 (3H s., $NHCOOC\underline{H}_3$), 6.03 (1H unresolved m., H-2), 5.85 (1H octet, J 6.7, 6.7, 6.7, and 3 Hz, H-5), 5.27 (1H d., J ~2.5 Hz, H-1), 5.10 (1H quartet with small splittings (~0.8 Hz) and the pair in the lower field being most intense; J 3, 4.8, and ~0.8 Hz, H-4), 4.82 (1H t., J 4.8 Hz, H-3), 4.6—4.9 (1H, $N\underline{H}COO$-?); $J_{1,2}$ ~2.5 Hz, $J_{2,3}$ 4.8 Hz, $J_{3,4}$ 4.8 Hz, $J_{4,5}$ 3 Hz, $J_{2,4}$ ~0.8 Hz.

Irradiation of H-2 caused the H-1 doublet to collapse to a singlet, the H-4 octet to a quartet (J 3 and 4.8 Hz), and the H-3 triplet to a doublet. Irradiation at τ 5.85 (H-5) caused the doublet at τ 8.74 (CH_3) to collapse to a singlet, the doublet at τ 5.27 (H-1) to an incomplete doublet, and the octet at τ 5.10 (H-4) to a doublet (J 4.8 Hz). Irradiation of H-4 caused the H-5 octet to collapse to a quartet (J 6.7 Hz) and the H-3 triplet to a doublet.

Methyl 2-Amino-2,6-dideoxy-β-L-idopyranosie (13) and Methyl 2-Amino-2,6-dideoxy-β-L-idopyranoside 2,4-Carbamate (14). Compound **12** (643 mg) in 1N barium hydroxide (25 ml) was heated in a boiling water bath for 1 hr. After carbon dioxide was introduced, the mixture was heated for a while, centrifuged, and the supernatant layer was evaporated. The residual precipitates were treated with hot water several times and the solution was evaporated. The combined residues were extracted with methanol and the solution was evaporated to give a solid (~840 mg). On TLC with ethyl acetate-methanol (5:1), the solid gave two spots of R_f 0.13 (**13**, major, ninhydrin positive) and R_f 0.79 (**14**, minor, ninhydrin negative), the latter differering from the spot of the starting material (**13**, R_f 0.94). An aqueous solution of the solid was chromatographed on a column of Amberlite IRC-50 (H^+ form, 30 ml) with water. The portion containing **14** was evaporated to give a solid, 136 mg (33%), mp 177—180°C $[\alpha]_D^{25}$ +64.5° (*c* 0.8, methanol). IR spectrum (KBr): 1695; 950, 905, 893, 845, 765, 750, and 705 cm^{-1}.

Found: C, 47.24; H, 6.68; N, 6.59%. Calcd for C_8H_{13}-

NO_5: C, 47.29; H, 6.45; N, 6.89%.

The resin column was then treated with 0.3N ammonia and the solution containing **13** was evaporated to give a syrup, 198 mg (56%), R_f 0.66 (ppc with *n*-butanol-pyridine-water-acetic acid 6:4:3:1), $[\alpha]_D^{20}$ +97.4° (*c* 1.4, methanol), $\Delta[M]_{TACu}$+159°. IR spectrum (KBr): 945, 895 (w), 865, 840 (w), 775, and 700 (w) cm^{-1}.

Found: C, 47.60; H, 8.72; N, 8.12%. Calcd for $C_7H_{15}NO_4$: C, 47.45; H, 8.53; N, 7.90%.

NMR spectrum of **13** (in D_2O):τ 8.70 (3H d., *J* 6.7 Hz, C_5-CH_3), 7.03 (1H octet, *J* 4.5, 2, and 1Hz, H-2), 6.45 (3H s., OCH_3), 6.35—6.55 (1H m., H-4), 6.02 (1H t., *J* 4.5 Hz, H-3), 5.88 (1H octet, *J* 6.7, 6.7, 6.7, and 3 Hz, H-5), 5.22 (1H d., *J* 2 Hz, H-1); $J_{1,2}$ ~2 Hz, $J_{2,3}=J_{3,4}$ 4.5 Hz, $J_{4,5}$ 3 Hz, $J_{2,4}$ ~1 Hz. These coupling constants showed the preferred conformation of **13** to be IC.

Methyl 3-O-Acetyl-2-amino-2,6-dideoxy-β-L-idopyranoside 2,4-Carbamate (15). To a solution of **14** (90 mg) in pyridine (1.8 m*l*), acetic anhydride (0.08 m*l*) was added and the solution was allowed to stand overnight. On TLC with ethyl acetate, a spot (R_f 0.54) appeared accompanied by two weak spots of R_f 0.21 (**14**) and R_f 0.36. The solution was evaporated and the residue was dissolved in chloroform. The solution was washed successively with saturated potassium hydrogensulfate solution, saturated hydrogencarbonate solution and saturated sodium chloride solution, dried over sodium sulfate and evaporated to give a residue. The residue was dissolved in chloroform and the solution was passed through a short column of silica gel (3 g) with the aid of ethyl acetate and the eluate containing **15** was evaporated to give a colorless solid, 84 mg (80%). Recrystallization from ethanol, mp 165—166°C $[\alpha]_D^{24}$+26° (*c* 1.7, chloroform).

Found: C, 48.62; H, 6.15; N, 5.53%. Calcd for $C_{10}H_{15}NO_6$: C, 48.98; H, 6.17; N, 5.71%.

IR spectrum (KBr): 1755, 1725, 1700; 950, 912, 900 (sh), 885, 838 (w), 795 (w), 765 (sh), 760, 750, and 697 cm^{-1}. No peak was observed between 1475—1650 cm^{-1}; NMR (in pyridine-d_5 at 100 MHz): τ 8.63 (3H, d., *J* 6.7 Hz, C_5-CH_3), 7.85 (3H s., OAc), 6.53 (3H s., OCH_3), 6.27 (1H double triplets, *J* 4, 4, and 2 Hz, H-2), 5.85 (1H q., *J* 6.7 Hz, H-5), 5.75 (1H quartet with small splittings (*J* ~0.5 Hz), *J* 4 and 2 Hz, H-4), 5.13 (1H s., H-1), 4.47 (1H t., *J* 4 Hz, H-3), 1.08 (1H d., *J* 4 Hz, NHCOO–); $J_{1,2}$ ~0 Hz, $J_{2,3}$ 4 Hz, $J_{3,4}$ 4 Hz, $J_{4,5}$ 0—0.5 Hz, $J_{5,6}$ 6.7 Hz, $J_{NH,2}$ 4 Hz, $J_{2,4}$ 2 Hz.

Irradiation at τ 1.08 (NH) caused H-2 double triplets to collapse to a quartet (*J* 4 and 2 Hz). Irradiation of H-3 caused the H-4 multiplet to collapse to a singlet (not a quite sharp singlet), H-2 double triplets to an incomplete doublet. Irradiation of H-4 caused H-2 double triplets to collapse to a triplet (*J* 4 Hz) and H-3 triplet to a doublet (*J* 4 Hz), Irradiation of H-5 caused methyl doublet (τ 8.63) to collapse to a singlet. Irradiation of H-2 caused the H-4 multiplet to collapse to a doublet (*J* 4 Hz) and doublet of NH to a singlet.

Methyl 3-Deoxy-3-methoxycarbonylamido-α and β-D-glucopyranoside (16 and 17). Crude 3-amino-3-deoxy-α-D-glucose (2 g) obtained by fermentation[13] was dissolved in 50% aqueous acetone (40 m*l*). Anhydrous sodium carbonate (1.5 g) and methoxycarbonyl chloride (1.9 m*l*) were added successively to the solution under stirring and the mixture was stirred for 1 hr at room temperature. A ninhydrin negative spot (R_f 0.46) appeared on TLC with methyl ethyl ketone-methanol (5:1). The solution was evaporated and the residue was extracted with methanol. Evaporation of the extract gave a brown powder, which was dissolved in 4% hydrogen chloride in methanol (40 m*l*) and the solution was refluxed for 20 hr. A new spot (R_f 0.54) appeared on TLC. The resulting solution was neutralized with basic lead carbonate, filtered, and evaporated. An aqueous solution of the residue was chromatographed on a column of Dowex 1×2 (OH form, 500 m*l*) with water. From the earlier eluate (600—750 m*l*), **16** was obtained as a colorless solid which was recrystallized from ethanol-ethyl acetate yielding 803 mg, mp 178—181°C $[\alpha]_D^{20}$+152° (*c* 1, methanol); NMR (in D_2O): τ 6.55 (3H s., OCH_3), 6.32 (3H s., $NHCOOCH_3$), 5.17 (1H d., $J_{1,2}$ 3 Hz, H-1).

Found: C, 43.25; H, 7.04; N, 5.63%. Calcd for $C_9H_{17}NO_7$: C, 43.01; H, 6.82; N, 5.57%.

From the late eluate (780~930 m*l*) **17** was obtained as a colorless solid which was recrystallized from ethanol-ethyl acetate yielding 209 mg, mp 146—148°C, $[\alpha]_D^{22}$+6° (*c* 1, methanol); NMR (in D_2O): τ 6.42 (3H s., OCH_3), 6.31 (3H s., $NHCOOCH_3$), 5.54 (1H d., $J_{1,2}$ 7.5 Hz, H-1).

Found: C, 43.12; H, 6.95; N, 5.60%.

Methyl 6-Bromo-3,6-dideoxy-3-methoxycarbonylamido-α-D-glucopyranoside (18). Compound **16** (443 mg) in DMF (4.8 m*l*) was treated with mesyl bromide (570 mg) at 65°C for 15 hr. A new spot (R_f 0.62) and a very weak spot (R_f 0.25) appeared on TLC with methyl ethyl ketone. Successive de-*O*-formylation[4] gave a slight amount of starting material (**16**, R_f 0.25) in contrast to the case of **3**. Crude product obtained was purified by column chromatography with silica gel (20 g) with methyl ethyl ketone - ethyl acetate yielding a solid of 478 mg (85%), mp 197—198°C, $[\alpha]_D^{20}$+128° (*c* 0.8, methanol).

Found: C, 34.80; H, 5.16; N, 4.67, Br. 24.90%. Calcd for $C_9H_{16}NO_6Br$: C, 34.39; H, 5.14; N, 4.46; Br. 25.45%.

Methyl 2,4-Di-O-acetyl-6-bromo-3,6-dideoxy-3-methoxycarbonylamido-α-D-glucopyranoside (19). Compound **18** was acetylated in a similar manner as in the case of **3** to give **19**, mp 205—210°C, $[\alpha]_D^{20}$+95° (*c* 1, chloroform).

Found: C, 39.48; H, 5.09; N, 3.36; Br, 19.76%. Calcd for $C_{13}H_{20}NO_8Br$: C, 39.21; H, 5.06; N, 3.52; Br, 20.07%.

IR spectrum (KBr): 1750, 1710, 1550; 981, 925, 800 (w), 773(m), 760, and 710 (w) cm^{-1}; NMR (in $CDCl_3$): τ 7.91 (6H s., OAc), 6.51 (3H s., OCH_3), 6.34 (3H s., $NHCOOCH_3$), 5.96 (1H octet, *J* 3, 6, and 9.7 Hz, H_{ax} -5); No peak in the field lower than τ 4.95 was observed (compare with the spectrum of **4**).

Methyl 2,6-Di-O-acetyl-3,6-dideoxy-3,6-imino-N-methoxycarbonyl-α-D-glucopyranoside (20). A mixture of **19** (256 mg) and silver fluoride (240 mg) in dry pyridine (1.8 m*l*) was stirred at 60°C overnight in the dark. On TLC with benzene-ethyl acetate (2:1), two spots (R_f 0.18 and 0.44 (minor)) appeared but the latter was proved to be that of the starting material (**19**). The reaction mixture was extracted with ether and the organic layer was treated in a similar manner as in the preparation of **5**. The crude mixture obtained was chromatographed on a column of silica gel with benzene - ethyl acetate (2:1) and the portion containing the substance showing R_f 0.18 was evaporated to give a colorless syrup, 165 mg (80%), $[\alpha]_D^{20}$+70° (*c* 1, chloroform).

Found: C, 49.41; H, 6.20; N, 4.61%. Calcd for $C_{13}H_{19}NO_8$: C, 49.21; H, 6.04; N, 4.41%.

IR spectrum (KBr): 1750, 1715, 1540 (w); 930, 910, 880 (m), 830, 770, 725 (w), and 685 cm^{-1}; NMR (in $CDCl_3$):τ 7.91 and 7.81 (each 3H s., OAc), 6.46 (3H s., OCH_3), 6.22 (3H s., $NHCOOCH_3$), 6.3—6.6 (2H m., H-6.6′), 5.3—5.5 (3H m., H-3,4,5), 5.15 (1H d., J 3.3 Hz, H-1), 4.68—4.88 (1H unresolved broad peak having half-height width of ~8Hz, H-2).

Methyl 3-Amino-3-deoxy-α-D-glucopyranoside (21). To an aqueous solution (40 m*l*) of **16** (800 mg), barium hydroxide octahydrate (1.8 g) was added and the mixture was heated at 95°C for 1.5 hr. After introducting carbon dioxide, the

mixture was heated for a while, centrifuged, and the supernatant layer was evaporated. The residue was extracted with methanol and the solution was evaporated to give a solid which was dissolved in a small amount of methanol. Ethyl acetate was added to the solution to give ninhydrin-positive crystals (546 mg, 92%), mp 175—176°C (lit,[20] 167—168°C), $[\alpha]_D^{23}$+165° (*c* 0.6, methanol) (lit,[20] +144.4° (water)).

Methyl 2,4,6-Tri-O-acetyl-3-deoxy-3-phthalimido-α-D-glucopyranoside (22). To a solution of **21** (459 mg) in dry pyridine (9 ml), phthalic anhydride (510 mg) was added and the solution was heated at 90°C for 30 min. A phthalimido derivative (R_f 0.54 with tailing on TLC with methyl ethyl ketone - methanol 4:1) was produced. To the resulting pale yellow solution, acetic anhydride (9 ml) was added and the solution was heated at 90°C for 1 hr. A spot (R_f 0.68) appeared on TLC with benzene - ethyl acetate (5:3). The solution was evaporated and the residue was dissolved in chloroform. The solution was washed successively with potassium hydrogensulfate solution, soldium hydrogencarbonate solution, and water, dried over sodium sulfate and evaporated to give a solid. The product was dissolved in a mixture of benzene - ethyl acetate (2:1) and passed through a short column of silica gel with the aid of the same solvent mixture. The eluate was evaporated and the residue was recrystallized from ethanol yielding pale yellow crystals, 914 mg (87%), mp 175—177°C, $[\alpha]_D^{22}$+75° (*c* 1, chloroform).

Found: C, 56.13; H, 5.06; N, 3.28%. Calcd for $C_{21}H_{23}NO_{10}$: C, 56.12; H, 5.16; N, 3.12%.

IR spectrum (KBr): 1755, 1725; 732, 724 cm^{-1}; NMR (in $CDCl_3$): τ 8.11, 8.06 and 7.89 (each 3H s., OAc). It is noteworthy that two acetyl methyl protons resonated at higher field than usual. The signal at τ 7.89 seems to originate from protons of 6-*O*-acetyl (compare with the spectrum of **25**). τ 6.51 (3H s., OCH_3), 5.4—6.1 (3H m., H-5,6,6'), 5.18 (1H q., *J* 10, 11 Hz, H-3), 4.88 (1H d., *J* 3.5 Hz, H-1), 4.31 (1H, t., *J* 9.8 Hz, H-4), 4.22 (1H q., *J* 3.5, 11 Hz, H-2), 1.9—2.35 (4H m.); $J_{1,2}$ 3.5 Hz $J_{2,3}$ 11 Hz, $J_{3,4}$ 10 Hz, $J_{4,5}$ ~9.8 Hz.

Methyl 3-Deoxy-3-phthalimido-α-D-glucopyranoside (23). A solution of **22** (802 mg) in methanol was treated with sodium methoxide. A spot (R_f 0.58) appeared on TLC with ethyl acetate. The product was recrystallized from acetone yielding 570 mg (98%), mp 194—197°C, $[\alpha]_D^{22}$+103° (*c* 1, methanol); IR spectrum (KBr): 1775 (w), 1710; 970 (w), 910, 873 (w), 847 (vw), 802 (w), 777 (w), and 730 cm^{-1}.

Found: C, 55.85; H, 5.49; N, 4.02%. Calcd for $C_{15}H_{17}NO_7$: C, 55.72; H, 5.30; N, 4.33%.

Methyl 6-Bromo-3,6-dideoxy-3-phthalimido-α-D-glucopyranoside (24). To a solution of **23** (499 mg) in dry DMF (5.5 ml), mesyl bromide (770 mg) was added and the solution was heated at 65°C overnight. On TLC with benzene - ethyl acetate (1:2), two spots of R_f 0.79 (**24**) and 0.70 (an *O*-formyl compound) appeared in approximately equal color strength. The solution was evaporated and the residue was neutralized with sodium methoxide in methanol. On TLC, the spot of R_f 0.70 disappeared and a spot (R_f 0.25, **23**) appeared. In contrast to the case of the preparation of **18**, the bromination of **23** turned out to compete with *O*-formylation. The bromination procedure was repeated to raise the yield of **24**. The above methanolic solution was evaporated and the residue was coevaporated with toluene. The residue was dissolved in DMF (4.5 ml) and treated with mesyl bromide (730 mg). After the de-*O*-formylation of the resulting product with sodium methoxide in methanol, the mixture was subjected to chromatography on a column of silica gel (13 g) with benzene - ethyl acetate (1:2). From the earlier eluate (37—70 ml), **24** was obtained as a solid, which was recrystallized from benzene - ethyl acetate (3:1) yielding 360 mg (61%); mp 178—178.5°C, $[\alpha]_D^{22}$+88° (*c* 0.5, methanol); IR spectrum (KBr): 1725, 1715; 928 (w), 905, 870 (w), 802 (w), 780 (w), 726, and 717 cm^{-1}.

Found: C, 46.43; H, 4.38; N, 3.88; Br, 20.33%. Calcd for $C_{15}H_{16}NO_6Br$: C, 46.65; H, 4.18; N, 3.63; Br, 20.69%.

From the late eluate, the starting material (**23**, 120 mg) was recovered.

Methyl 2,4-Di-O-acetyl-6-bromo-3,6-dideoxy-3-phthalimido-α-D-glucopyranoside (25). Prepared from **24** by the general procedure. The final product was a syrup, which was solidified by trituration with water, mp 76.5—79.5°C, $[\alpha]_D^{23}$+49.2° (*c* 0.8, chloroform).

Found: C, 48.87; H, 4.47; N, 3.08; Br, 16.52%. Calcd for $C_{19}H_{20}NO_8Br$: C, 48.53; H, 4.29; N, 2.98; Br, 16.99%.

IR spectrum (KBr): 1755, 1725, 927, 887, 868, 798, 772 (w) and 725 (s) cm^{-1}; NMR (in $CDCl_3$): τ 8.09 and 8.07 (each 3H s., OAc), 6.47 (3H s., OCH_3), 6.4—6.6 (2H m., H-6,6'), 5.85 (1H octet, *J* 4, 6, and 10 Hz, H-5), 5.17 (1H q., *J* 10 and 11 Hz, H-3), 4.85 (1H d., *J* 3.5 Hz, H-1), 4.33 (1H t., *J* 10 Hz, H-4), 4.26 (1H q., *J* 3.5, 11 Hz, H-2), 1.9—2.35 (4H m.); $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 11 Hz, $J_{3,4}$ 10 Hz, $J_{4,5}$ 10 Hz, $J_{5,6}$ 6 Hz, $J_{5,6'}$ 4 Hz.

Methyl 2,4-Di-O-acetyl-3,6-dideoxy-3-phthalimido-α-D-xylo-hex-5-enopyranoside (26). Compound **26** was prepared from **25** in a similar manner as for the preparation of **5** from **4**. Recrystallization from ethanol gave pale yellow crystals (79%), mp 191—192°C, $[\alpha]_D^{20}$+50° (*c* 0.5, chloroform); R_f 0.52 (TLC with benzene - ethyl acetate 5:1).

Found: C, 58.68; H, 4.91; N, 3.69%. Calcd for $C_{19}H_{19}NO_8$: C, 58.61; H, 4.92; N, 3.60%.

IR spectrum (KBr): 1760, 1725, 1670 (C=C); 960, 932, 908 (w), 898, 878 (w), 845 (w), 800, and 725 (s) cm^{-1}; NMR (in $CDCl_3$ at 100 MHz): τ 8.07 and 8.03 (each 3H s., OAc), 6.50 (3H s., OCH_3), 5.35 (1H triplet with very small splittings (<0.3 Hz), *J* ~2 Hz, H-6), 5.18 (1H t., *J* ~2 Hz, H-6'), 5.16 (1H q., *J* 10 and 11 Hz, H-3), 4.85 (1H d., *J* 3 Hz, H-1), 4.16 (1H q., *J* 3 and 11 Hz, H-2), 3.85 (1H double triplets, *J* 2, 2 and 10 Hz, H-4), 1.95—2.35 (4H m.); $J_{1,2}$ 3 Hz, $J_{2,3}$ 11 Hz, $J_{3,4}$ 10 Hz, $J_{4,6}=J_{4,6'}$ ~2 Hz, $J_{6,6'}$ ~2 Hz.

Irradiation of H-4 resulted in collapse of the H-6 and H-6' triplets to two doublets (each *J* ~2 Hz), and of H-3 triplet to a doublet (*J* 11 Hz).

Methyl 2,4-Di-O-acetyl-3,6-dideoxy-3-phthalimido-β-L-idopyranoside (27). A solution of **26** (294 mg) in dioxane (3 ml) was hydrogenated with palladium black and hydrogen in a similar manner as for the preparation of **6**. A spot (R_f 0.58) appeared (the R_f of **26** was 0.62) on TLC with benzene-ethyl acetate (5:1). After filtration the solution was evaporated to give a solid which was passed through a short column of silica gel with the above solvent mixture. The eluate was evaporated to give a solid, 253 mg (87%), mp 66—69°C, $[\alpha]_D^{22}$+59° (*c* 0.9, chloroform).

Found: C, 58.17; H, 5.32; N, 3.69%. Calcd for $C_{19}H_{21}NO_8$: C, 58.31; H, 5.41; N, 3.58%.

IR spectrum (KBr): 1780, 1755, 1725; 935, 925 (sh), 907 (sh), 872 (m), 810, 800, and 725 (s) cm^{-1}: NMR (in $CDCl_3$ at 100 MHz): τ 8.58 (3H d., *J* 6.7 Hz, C_5-CH_3), 8.08 (6H s., OAc), 6.52 (3H s., OCH_3), 5.45 (1H double quartet, *J* 6.7, 6.7, 6.7 and 6 Hz, H-5), 5.06 (1H q., *J* 11 and 9 Hz, H-3), 4.93 (1H d., *J* 3.5 Hz, H-1), 4.35 (1H q., *J* 9 and 6 Hz, H-4), 4.33 (1H q., *J* 3.5 and 11 Hz, H-2); $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 11 Hz $J_{3,4}$ 9 Hz, $J_{4,5}$ 6 Hz.

Irradiation at τ 4.38 caused the H-5 multiplet to collapse to a quartet, the H-3 quartet to a broad singlet and the H-1

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doublet to a singlet. Irradiation at τ 4.33 caused the above multiplet to collapse to a quartet, the H-3 quartet to a narrow multiplet and the H-1 doublet to a sharp singlet.

Methyl 3-Amino-3,6-dideoxy-β-L-idopyranoside (28). To a solution of **27** (163 mg) in dry methanol (1.6 ml), *n*-butylamine (0.38 g) was added and the solution was refluxed for 9 hr. Evaporation of the solution gave a residue, which was extracted with ether several times. The ether-insoluble mass was dissolved in methanol, and the solution was filtered. Ether was added to the solution to give crystals of **28**, 44 mg. As the ether-soluble part still contained **28**, it was charged on a column of Amberlite IRC-50 (H^+ form) and, after washing with water, developed with 0.3N ammonia. The portion containing **28** was evaporated to give another crop (21 mg). Total yield was 77%. R_f 0.53 (ppc with *n*-butanol-pyridine-water-acetic acid 6:4:3:1); mp 146—148°C $[\alpha]_D^{21}+93°$ (*c* 1, methanol); $\Delta[M]_{TACu}-242°$.

Found: C, 47.70; H, 8.49; N, 8.13%. Calcd for $C_7H_{15}NO_4$: C, 47.45; H, 8.53; N, 7.90%.

IR spectrum (KBr): 923, 890, 808, and 760 cm^{-1}; NMR (in D_2O): Although the spectrum was not clear enough to permit detailed analysis, the pattern resembles that of methyl 6-deoxy-β-L-idopyranoside (**6**) except for the chemical shift of H-3 which resonated at 0.76 ppm higher field that than of H-3 of **6**: τ 8.67 (3H d., *J* 6.7 Hz, C_5-CH_3), 6.73 (1H t., *J* ~5 (?) Hz, H-3), 6.48 (3H s., OCH_3), 6.40—6.55 (1H m., H-4), 6.40 (1H m., H-2), 5.85 (1H octet, *J* 6.7, 6.7, 6.7, and 3 Hz, H-5), 5.23 (1H d., *J* ~2 Hz, H-1).

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