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Effect of 3-Hydroxyl Group on 5,6-Epimine Formation in 1,2-O-Isopropylideneglucofuranose

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Treatment of 6-azido-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (**6b**) or its 3-O-acetyl derivative (**6a**) with $LiAlH_4$ in tetrahydrofuran gave a 5,6-epimine (**7a**) which was characterized as its acetate (**8**). In comparison with the case of the 3-O-benzyl derivative (**2**) reported earlier,[2] it was suggested that the free 3-hydroxyl group participates in the substitution of the 5-O-tosyloxy group by the formed 6-amine, decreasing the yield of 5,6-epimine. It was found that treatment of these 6-azido-5-O-tosylates with sodium borohydride and tris (α,α'-dipyridyl) cobalt (II) bromide resulted in formation of the corresponding 6-amino-5-tosylates (**10b** and **13**). Reactions of the latter with bases were also discussed.

In previous papers,[2,3] we reported syntheses of 5,6-epimino-5,6-dideoxyhexofuranoses by treatment of 6-azido-6-deoxy-5-O-tosylhexofuranoses with lithium aluminum hydride (for example, 3-O-benzyl-5,6-dideoxy-5,6-epimino-1,2-O-isopropylidene-β-L-idofuranose (**1**)

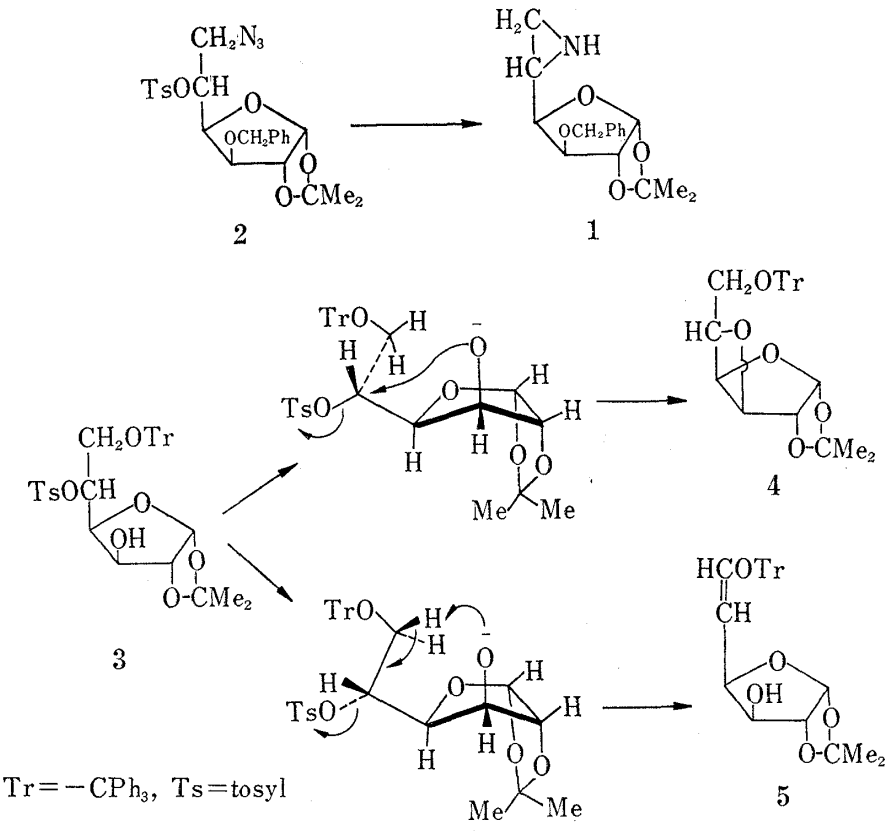

Chart 1

1) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
2) H. Saeki, T. Iwashige, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **16**, 188 (1968); H. Saeki and E. Ohki, *ibid.*, **16**, 2471 (1968).
3) H. Saeki and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **16**, 2477 (1968).

from 6-azido-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (**2**) as shown in Chart 1. This conversion includes rapid reduction of 6-azido group to 6-amino group and successive substitution of 5-tosyloxy group by the 6-amino group. Recently, Paulsen[4] also reported formation of N-amino-5,6-epimino derivatives of hexofuranoses by treatment of 5,6-dimesylates with anhydrous hydrazine. In these reactions, the 3-hydroxyl group in hexofuranoses taking part in these 5,6-epimine syntheses was blocked with benzyl group becuase of its possible unfavorable participation in these reactions. As for the participation of 3-hydroxyl function in the displacement reaction of 5-sulfonyloxy group, some examples can be found in the published papers; for instance, treatment of 1,2-O-isopropylidene-5-O-tosyl-α-D-xylofuranose with sodium methoxide gave a 3,5-anhydride (oxetan) quantitatively.[5] On treatment of 1,2-O-isopropylidene-5-O-tosyl-6-O-trityl-α-D-glucofuranose (**3**) with sodium methoxide, the 3-hydroxyl group also took part in the formation of a 3,5-anhydride[6] (**4**) and, in parallel, assisted abstraction of the 6-proton, subsequently effecting formation of a 5,6-olefin[6,7] (**5**). Further, on treatment of a 6-O-benzoyl analog of **3** with lithium aluminum hydride, removal of its 5-O-tosyloxy group was rather accelerated by the presence of free 3-hydroxyl group, and this result was assumed[8] to be due to the favorable location of the initially formed 3-O–Al–H_3 group in the supply of its hydride to the 5-position. Based on these facts, we presumed that some attempts on 5,6-epimine formation from 6-azido-6-deoxy-5-O-tosylhexofuranose with unblocked 3-hydroxyl group would be significant in view of neighboring group participation in nucleophilic displacement reaction. The present study was also urged by our failure to remove the benzyl group from **1**, which resisted catalytic hydrogenolysis and, under drastic conditions, gave a complex product with epimine–ring decomposition.

Treatment of 3-O-acetyl-1,2-O-isopropylidene-5,6-di-O-tosyl-α-D-glucofuranose[9] with sodium azide in dimethyl sulfoxide afforded 3-O-acetyl-6-azido-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (**6a**) in 77% yield. Monosubstitution of the tosyloxyl group at the terminal position by an azido group was verified in consideration of analogous examples.[2] On treatment with lithium aluminum hydride in tetrahydrofuran, **6a** gave a syrup including a desired 5,6-epimine (**7a**), which was quite unstable and was difficult to be purified by chromatography. Consequently, the product was acetylated with acetic anhydride in methanol and gave an N-acetylepimine (**7b**) which could not be crystallized. Further acetylation[10] of **7b** in pyridine gave 3-O-acetyl-5,6-acetylepimino-5,6-dideoxy-1,2-O-isopropylidene-β-L-idofuranose (**8**) as needles. The infrared spectra of **7b** and **8** exhibited an N-acetyl absorption at 1700 cm^{-1} which was characteristic for an N-acetylaziridine.[2,3,11] The structure of **8** was confirmed in the following way: **8** was also unstable to acids and, on treatment with acetic acid, was easily converted into 5-acetamido-3,6-di-O-acetyl-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose (**9a**). Hydrolysis of **9a** with barium hydroxide yielded the known 5-amino-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose[2] (**9b**). Thus, the Walden inversion at the 5-position in the formation of the 5,6-epimine was verified. The lithium aluminum hydride reduction product obtained from **6a** was acetylated with acetic anhydride in pyridine, directly affording **8** in 45% yield. A small amount of a syrupy mixture of by-products was isolated by chromatography of the fully-acetylated reaction product. Its infrared spectrum did not

4) H. Paulsen and M. Stoye, *Angew. Chem.*, **80**, 120 (1968).
5) P.A. Levene and A.L. Raymond, *J. Biol. Chem.*, **102**, 331 (1933).
6) J.G. Buchanan and E.M. Oakes, *Tetrahedron Letters*, **1964**, 2013; *Idem*, *Carbohydrate Res.*, **1**, 242 (1965); R.L. Whistler, T.J. Luttenegger, and R.M. Rowell, *J. Org. Chem.*, **33**, 396 (1968).
7) R.E. Gramera, T.R. Ingle, and R.L. Whistler, *J. Org. Chem.*, **29**, 878 (1964); *Idem*, *ibid.*, **29**, 1083 (1964).
8) E.J. Hedgley, O. Mérész, and W.G. Overend, *J. Chem. Soc.* (*C*), **1967**, 888.
9) H. Ohle, E. Euler, and R. Lichtenstein, *Ber.*, **62**, 2885 (1929).
10) Acetylation of **7b** was effected at a low temperature or for a short time; otherwise, **7b** was converted into **9a** with the epimine ring opening.
11) H.L. Spell, *Anal. Chem.*, **39**, 185 (1967).

show the presence of N-acetylepimino group, but of N-acetyl and O-acetyl groups, and its nuclear magnetic resonance (NMR) spectrum also exhibited methyl signals of acetamido and acetoxyl groups at 2—2.3 ppm, indicating that the product was composed of at least two components. Further study on this material was abandoned because of some doubt in its reproducibility and of its scarcity of the samples.

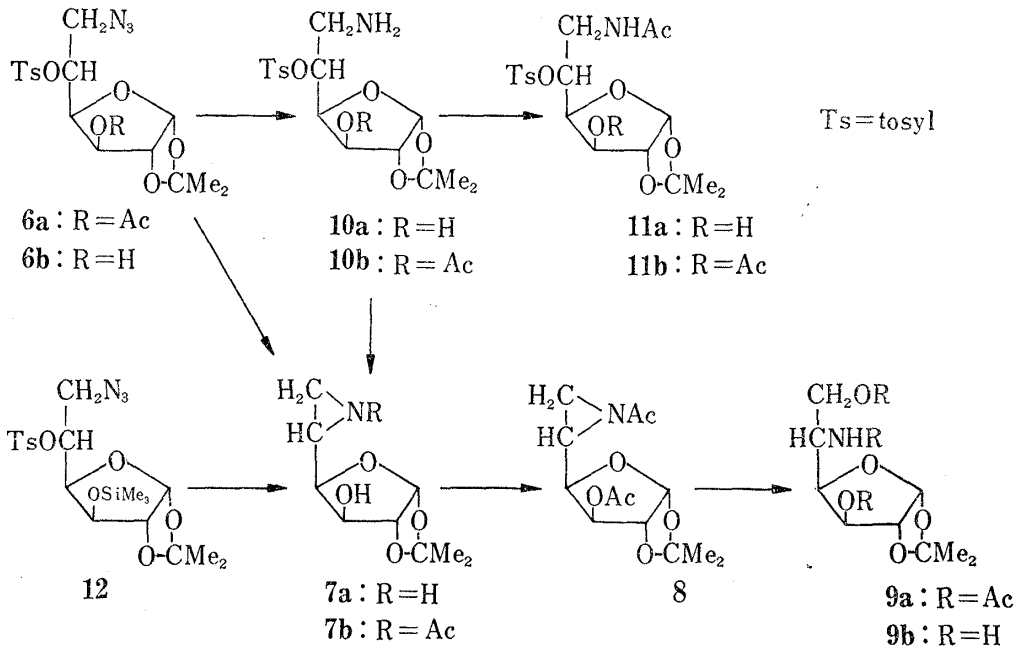

Chart 2

When ether was used as a solvent in place of tetrahydrofuran, lithium aluminum hydride reduction of **6a** gave a different result: **6a** was treated with the reagent in dry ether at room temperature and the resulting product was partitioned with ethyl acetate, methanol, and water. The component obtained from the aqueous layer gave the N-acetylepimine (**8**) in 19% yield on successive N,O-acetylation. N-Acetylation of the other product (probably **10a**) remaining in the organic layer afforded 6-acetamido-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (**11a**) in 43% yield. **11a** was further acetylated in pyridine and gave a syrupy 3-O-acetyl derivative (**11b**), and the latter was treated with a small amount of sodium methoxide in methanol, giving the parent **11a** in a good yield. On the other hand, hydrogenation of **6a** over palladium-charcoal afforded a 6-amino-5-tosylate (**10b**), which formed **11b** by acetylation. These facts showed that lithium aluminum hydride reduction of **6a** in tetrahydrofuran gave the desired 5,6-epimine, while, in ether, the reduction mainly ceased at the stage of formation of a 6-amino-5-tosylate.

Next, we examined lithium aluminum hydride reduction of 6-azido-5-tosylate (**6b**) with free 3-hydroxyl group. Treatment of 1,2-O-isopropylidene-5,6-di-O-tosyl-α-D-glucofuranose[12] with sodium azide in dimethyl sulfoxide gave **6b**, along with a 3,6-anhydride.[13] **6b** was also obtained by tosylation of 6-azido-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose[14] in a moderate yield. Treatment of **6b** with lithium aluminum hydride in tetrahydrofuran at room temperature and successive acetylation in pyridine gave **8** in 32% yield. When the reduction was carried out at a low temperature, only a small amount of the 6-acetamido-5-tosylate (**11a**) was obtained as a crystalline substance on successive N-acetylation, and further acetylation

12) H. Ohle and E. Dickhäuser, *Ber.*, **58**, 2593 (1925).
13) H. Ohle, L. von Vargha, and H. Erlbach, *Ber.*, **61**, 1211 (1928).
14) R.L. Whistler and M.L. Wolfrom (ed.), "Methods in Carbohydrate Chemistry," Vol. I, Academic Press, Inc., New York and London, 1962, p. 242.

of the remaining syrup in pyridine gave the N-acetylepimine (**8**) in a low yield. The composition of the by-products was too complicated and could not be analysed further. Thus, it was found that the yield of the 5,6-epimine from these 6-azido-5-tosylates (**6a** or **6b**) with free or acetylated 3-hydroxyl group decreases considerably in comparison with the yield (70%) of **1** from the corresponding 3-O-benzyl derivative (**2**).[2)]

After blocking of the 3-hydroxyl group of **6b** with trimethylsilyl group in the usual manner, the resulting **12** was treated with lithium aluminum hydride in tetrahydrofuran, then with water, and with acetic anhydride in pyridine to give **8** in 73% yield. Based on these facts, it may be considered that free 3-hydroxyl group influences the nucleophilic substitution of 5-tosyloxy group by 6-amine, and this would induce other feasible competing reactions, decreasing the yield of 5,6-epimine.

In 1967, Ponsold[15)] reported that treatment of α-azidoalcohol sulfonate with sodium borohydride and tris(α,α'-dipyridyl) cobalt (II) bromide successfully converted it into an aziridine without any damage to other ester or amide function. Application of this method to these 6-azido-5-tosylates seemed of interest, because it was presumed that this method results in 5,6-epimine formation without any effect on the 3-substituent. Following Ponsold's procedure, treatment of **6a** with this reagent in ethanol, followed by N-acetylation, gave **11b** in 67% yield and **11a** in 29% yield. Formation of the latter was explained as partial hydrolysis of the former by this reagent. A prolonged treatment of **6a** with this reagent, followed by N,O-acetylation, gave the 5,6-acetylepimine (**8**) in 44% yield, along with an unidentified syrup. The formation of 5,6-epimine by this reaction seemed to be the same as that with lithium aluminum hydride but, contrary to our expectation, the 3-O-acetyl group was hydrolysed. On the other hand, **6b** was treated with this reagent for a few minutes and successive N-acetylation gave **11a** in a good yield, while the same treatment for 30 min gave a disappointing result giving an unidentified syrup along with a small amount of **11a**. The same treatment of the 3-O-benzyl derivative (**2**) for 1 hr gave a 6-amine (**13**) in a good yield, which was characterized as its acetate (**14**). Prolonged treatment of **2** with this reagent at room temperature unexpectedly afforded a mixture of **13** and an unidentified material, in which the 5,6-epimine (**1**) could not be detected. Thus, the reaction of these 6-azido-5-tosylates with Ponsold's reagent gave complex results which are beyond rational interpretation. However, it may be suggested that this reagent seems to be effective for formation of 6-amino-5-sulfonate from 6-azido-5-sulfonate by a short-time treatment.[16)]

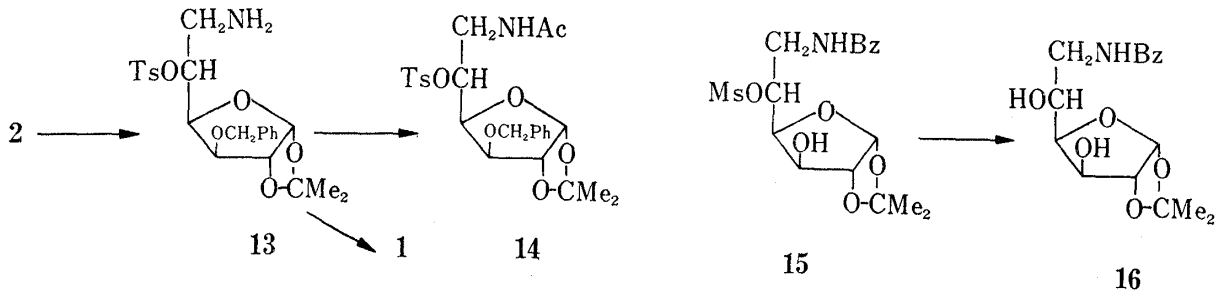

Chart 3

Finally, we would like to mention about some attempts on conversion of these 6-amino-5-tosylates thereby obtained into 5,6-epimines. Treatment of 6-amino-3-O-benzyl-5-tosylate (**13**) with lithium aluminum hydride in tetrahydrofuran gave the 5,6-epimine (**1**) in a good yield. **13** was considerably stable to sodium methoxide at room temperature, but, on treat-

15) K. Ponsold, *J. Prakt. Chem.*, **36**, 148 (1967).

16) It was reported that hydrogenation of **6b** over palladium-charcoal or Raney nickel did not give a good result for the formation of 6-amine. *cf.* W. Meyer zu Reckendorf and N. Wassiliadou-Micheli, *Chem Ber.*, **101**, 2294 (1968).

ment in boiling methanol, it also gave **1** in a good yield. In contrast, treatment of 3-O-acetyl-6-amino-5-tosylate (**10b**) with lithium aluminum hydride in tetrahydrofuran, followed by N, O-acetylation, also afforded the N-acetylepimine (**8**), but in a lower yield. On the other hand, treatment of **10b** with sodium methoxide at room temperature or under reflux did not give any epimine, but a complex reaction mixture. These facts suggest that the conversion of 6-amino-5-tosylate into 5,6-epimine was effected with lithium aluminum hydride better than with sodium methoxide and, especially in the latter case, 3-substituent probably does participate in these reactions.

Analogous problems were found in the previous work[17] which included some attempts to prepare 5,6-epimine; treatment of 6-benzamido-6-deoxy-1,2-O-isopropylidene-5-O-mesyl-α-D-glucofuranose (**15**) with sodium ethoxide afforded no epimine, but 6-benzamido-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (**16**). Presumably, one of the reasons for this result includes insufficient nucleophilicity of the nitrogen in the 6-benzamido group for attacking the neighboring carbon atom, and subsequent displacement of 5-tosyloxy group effected by participation of another functional group or by hydrolysis of sulfonic ester.[18]

The 3-O-acetyl-5,6-acetylepimine (**8**) indicated no activity against leukemia L-1210.

Experimental

Melting points are not corrected. Infrared spectra were determined on a Perkin-Elmer Model 221 or Perkin-Elmer Infracord, and NMR spectra on a Varian A-60 spectrometer. The removal of solvent *in vacuo* was accomplished by a rotating flash evaporator at 20—30 mmHg and usually at 35—50°. Plates for thin-layer chromatography were prepared with Silica Gel G (E. Merck AG). Development of spots was effected by spraying a solution of NH_4VO_3 in 50% H_2SO_4, followed by heating. Column chromatography was carried out on a column packed with silica gel (Kanto Chemical Co., Tokyo).

3-O-Acetyl-6-azido-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (6a)——A solution of 42.9 g of 3-O-acetyl-1,2-O-iospropylidene-5,6-di-O-tosyl-α-D-glucofuranose[10] and 6.0 g of NaN_3 in 170 ml of Me_2SO was stirred at 95—100° for 45 min in N_2 atmosphere. The mixture was diluted with $CHCl_3$, washed several times with H_2O, and dried (Na_2SO_4). Evaporation of the solvent *in vacuo* gave a syrup which crystallized on trituration with MeOH. The collected crystals were recrystallized from MeOH or EtOH to 20.1 g of **6a** as needles of mp 115°, $[\alpha]_D^{22}$ −43.0° (c=1.8, $CHCl_3$). The oily residue was chromatographed on silica gel, further yielding 5 g of **6a**. Total yield of **6a**, 77.4%. IR ν_{max}^{Nujol} cm^{-1}: 2100 ($-N_3$), 1750 (acetyl), 1595, 1191, 1179 (tosyl). *Anal.* Calcd. for $C_{18}H_{23}O_8N_3S$: C, 48.97; H, 5.25; N, 9.52; S, 7.26. Found: C, 49.07; H, 5.41; N, 9.37; S, 7.27.

5,6-Acetylepimino-5,6-dideoxy-1,2-O-isopropylidene-β-L-idofuranose (7a) and Its 3-O-Acetate (8) ($LiAlH_4$-Reduction of 6a in Tetrahydrofuran)——To an ice-cold solution of 500 mg of **6a** in 10 ml of tetrahydrofuran was added 100 mg of $LiAlH_4$ in one portion at 0° with stirring. The mixture was stirred for 5 min at 0° and further for 1.5 hr at room temperature. After decomposition of the excess reagent by careful addition of MeOH and successively of H_2O, the reaction mixture was filtered. To the filtrate was added 0.5 ml of Ac_2O with stirring and, after standing for a few min, the mixture was diluted with $CHCl_3$. The $CHCl_3$ solution was successively washed with H_2O, dil. $NaHCO_3$ solution, and H_2O, and dried (Na_2SO_4). Evaporation of the solvent *in vacuo* gave a crude **7a** as syrup which was dissolved in 1 ml of pyridine with cooling and 0.5 ml of Ac_2O was added. After standing for 1.5 hr at room temperature, the mixture was diluted with $CHCl_3$ and successively washed with H_2O, dil. HCl, dil. $NaHCO_3$ solution, and H_2O. The $CHCl_3$ layer was dried and evaporated *in vacuo*, leaving 198 mg of a syrup which crylstallized on trituration with EtOH–light petroleum. The crystals were collected and recrystallized from EtOH–light petroleum, yielding 120 mg (37.2%) of **8** as fine needles (or prisms), mp 124—126°, $[\alpha]_D^{22}$ −69.3° (c=1.6, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1740 (O-acetyl), 1700 (N-acetyl). *Anal.* Calcd. for $C_{13}H_{19}O_6N$: C, 54.73; H, 6.71; N, 4.91. Found: C, 54.80; H, 6.79; N, 4.80.

In the other run, the reaction mixture obtained by reduction of **6a** with $LiAlH_4$ in the same way was evaporated to dryness *in vacuo*. The resulting syrup was acetylated with Ac_2O–pyridine, and the product was dissolved in benzene and charged on a column of silica gel (20X) packed in hexane. Removal of the solvent from fractions eluted with hexane containing gradient amount of AcOEt (7:3 to 1:1, v/v) yielded **8** in 45% yield.

17) D.H. Buss, L.D. Hall, and L. Hough, *J. Chem. Soc.*, **1965**, 1616.
18) D.H. Buss, L.Hough, and A.C. Richardson, *J. Chem. Soc.*, **1963**, 5288; C.F. Gibbs, L. Hough, and A. C. Richardson, *Carbohydrate Res.*, **1**, 290 (1965); Y, Ali and A.C. Richardson, *ibid.*, **7**, 255 (1968).

6-Acetamido-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (11a) and Its 3-O-Acetate (11b) ($LiAlH_4$-Reduction of 6a in Ether)——To a suspension of 500 mg of **6a** in 25 ml of dry ether was added 80 mg of $LiAlH_4$ in one portion with stirring and the mixture was stirred for 1 hr at room temperature. After dilution with 25 ml of ether, the excess reagent was decomposed by careful addition of H_2O. The solid was collected by filtration and washed with a mixture of AcOEt–MeOH. The combined filtrate and washings were shaken with 10 ml of H_2O. The aqueous layer was extracted several times with $CHCl_3$ and the extract was dried (Na_2SO_4). Evaporation of the solvent *in vacuo* gave a syrup which was acetylated with Ac_2O in pyridine. Treatment of the reaction mixture in the usual manner yielded 61 mg (19%) of **8**, which was identified with the sample obtained as above.

The ether–AcOEt layer was dried (Na_2SO_4) and evaporated to dryness *in vacuo*, leaving a syrup which revealed one spot on thin-layer chromatogram. The syrup was dissolved in 2 ml of MeOH and 0.5 ml of Ac_2O was added. Treatment of the reaction product in the usual manner yielded 199 mg (42.5%) of **11a** as needles (from MeOH), mp 165—168° (decomp.), $[\alpha]_D^{22}$ +32.9° (c=1.6, dimethylformamide). IR ν_{max}^{Nujol} cm^{-1}: 3450 (OH), 1660, 1550 (N-acetyl), 1595. 1190, 1175 (tosyl). *Anal.* Calcd. for $C_{18}H_{25}O_8NS \cdot 1/4H_2O$: C, 51.48; H, 6.12; N, 3.34; S, 7.64. Found: C, 51.38; H, 5.99; N, 3.40; S, 7.52.

Acetylation of **11a** with Ac_2O in pyridine gave **11b** as a colorless syrup. IR ν_{max}^{liq} cm^{-1}: 1750 (O-acetyl), 1670, 1550 (N-acetyl), 1190, 1180 (tosyl).

11b (236 mg) was dissolved in 3 ml of MeOH containing a few drops of 1N NaOMe solution and the mixture was allowed to stand in a refrigerator overnight, yielding 175 mg of **11a**, mp 165—169° (decomp.), which was identified with the sample obtained as above.

5-Acetamido-3,6-di-O-acetyl-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose (9a)——A solution of 100 mg of **8** in 1 ml of AcOH was allowed to stand for 30 min at room temperature and diluted with H_2O. After neutralization with solid $NaHCO_3$, the mixture was extracted with $CHCl_3$. The extract was washed with H_2O, dried, and evaporated to dryness *in vacuo*, yielding a syrup which crystallized on trituration with ether. Thus, 37 mg of pure **9a**, mp 92—94°, $[\alpha]_D^{23}$ −14.4° (c=2.3, $CHCl_3$), and 31 mg of crude **9a** were obtained. *Anal.* Calcd. for $C_{15}H_{23}O_8N$: C, 52.17; H, 6.71; N, 4.01. Found: C, 51.84; H, 6.99; N, 4.26.

Hydrolysis of **9a** with dil. $Ba(OH)_2$ solution yielded 5-amino-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose (**9b**), mp 185°, which was identified with the authentic sample[2] by means of infrared spectrometry and mixed mp test.

3-O-Acetyl-6-amino-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (10b) and Its Treatment with $LiAlH_4$ or NaOMe——To a solution of 500 mg of **6a** in 30 ml of MeOH was added 500 mg of 5% Pd-C and a slow stream of H_2 was passed through the mixture with stirring for 1.5 hr. After the catalyst was filtered off, the mixture was evaporated to dryness *in vacuo*, leaving 426 mg of crude **10b** as a colorless thick syrup. Analytical sample was not obtained. IR ν_{max}^{liq} cm^{-1}: 3400, 1680 (amino), 1760 (acetyl), 1600, 1180 (tosyl).

10b was also obtained by treatment of **6a** with $NaBH_4$ and tris (α,α′-dipyridyl) Co (II) bromide as will be described later. Acetylation of **10b** gave **11b** quantitatively, which was identified with the sample obtained as above.

To a solution of 400 mg of crude **10b** thereby obtained in 15 ml of tetrahydrofuran was added 0.1 g of $LiAlH_4$ in one portion at 0° with stirring. The mixture was stirred at room temperature for 1.5 hr and treated in the usual manner. The resulting product was acetylated with Ac_2O–pyridine and gave 110 mg of **8** along with 30 mg of an unidentified oil. On the other hand, 300 mg of **10b** was treated with excess amount of NaOMe in MeOH at room temperature overnight and yielded a complex reaction mixture, whose acetylated product was found not to contain **8** by means of infrared spectrometry and thin-layer chromatography.

6-Azido-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (6b)——A solution of 2.65 g of 1,2-O-isopropylidene-5,6-di-O-tosyl-α-D-glucofuranose[13] and 0.38 g of NaN_3 in 15 ml of Me_2SO was stirred at 90° for 2 hr in N_2 atmosphere. When cooled, the reaction mixture was diluted with ice–water (50—60 ml) and extracted with $CHCl_3$ (30 ml×3). The $CHCl_3$ extract was washed with 40 min of H_2O, dried (Na_2SO_4), and evaporated *in vacuo*, leaving 2.03 g of a syrup. The syrup was chromatographed on 60 g of silica gel. Removal of the solvent from fractions eluted with AcOEt–benzene (1:19, v/v) gave 1.38 g (68.2%) of **6b**, along with 43 mg of the 3,6-anhydride, mp 132° (reported[14] mp 132°). Recrystallization of **6b** from AcOEt–hexane gave needles of mp 76—78°, $[\alpha]_D^{22}$ −27.4 (c=1.6, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3500 (OH), 2110 (-N_3), 1600, 1175 (tosyl).

Tosylation of 6-azido-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose[15] with 1 molar equivalent of TsCl in pyridine at room temperature for 2 days, followed by chromatography of the resulting syrup on silica gel, also gave **6b** in a moderate yield.

$LiAlH_4$-Reduction of 6b——To an ice-cold solution of 450 mg of **6b** in 10 ml of tetrahydrofuran was added 0.1 g of $LiAlH_4$ in one portion at 0° with stirring. The mixture was stirred at 0° for 5 min and further for 1.5 hr at room temperature. The analogous treatment of the reaction mixture as described for the $LiAlH_4$-reduction of **6a**, followed by acetylation, gave 101 mg (31.5%) of **8**, with 36 mg of an unidentified syrup.

In another run, the reaction mixture was allowed to stand at 0° for 2.5 hr. After decomposition of the excess reagent, filtration, and addition of Ac_2O (0.5 ml), the mixture was diluted with $CHCl_3$ and washed with dil. $NaHCO_3$ solution and H_2O. The $CHCl_3$ solution was dried and evaporated *in vacuo* giving 58 mg

of **11a** and 185 mg of a syrup. The latter syrup was treated with Ac_2O–pyridine and gave 54 mg of the 3-O-acetate of the unchanged material (**6a**), with 87 mg of a syrup which was chromatographed on 2 g of silicagel. Removal of the solvent from fractions eluted with AcOEt–hexane (1:1, v/v) gave 18 mg of **8**.

6-Azido-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-3-O-trimethylsilyl-α-D-glucofuranose(12) and Its $LiAlH_4$-Reduction——To a solution of 800 mg of **6b** and 0.5 ml of hexamethyldisilazane in 5 ml of pyridine was added 0.5 ml of Me_3SiCl. The mixture was warmed at 50° for 5 min and then allowed to stand for 30 min at room temperature. The mixture was filtered, the filtrate was evaporated to dryness *in vacuo*, and the residue was dissolved in dry benzene and filtered. Evaporation of the solvent from the benzene solution *in vacuo* gave 900 mg of **12** as a syrup, whose infrared spectrum showed no hydroxyl absorption, but trimethylsilyl absorption at *ca.* 850 cm^{-1}. **12** (700 mg) was dissolved in 20 ml of dry ether and 0.3 g of $LiAlH_4$ was added in small portions with stirring and cooling. The mixture was stirred for 2 hr at room temperature and, after decomposition of the excess reagent by the addition of H_2O, was filtered. The filtrate was evaporated to dryness *in vacuo*, giving a syrup which was acetylated with Ac_2O–pyridine. Thus, 310 mg of **8** was obtained and the yield from **6a** was 73%.

Treatment of 6-Azido-5-tosylates with $NaBH_4$ and Tris(α,α′-dipyridyl)cobalt(II) Bromide——(i) 3-O-Acetyl Derivative (**6a**): To a solution of 350 mg of **6a**, 50 mg of $CoBr_2$, and 120 mg of α,α′-dipyridyl in 50 ml of EtOH was added 0.15 g of $NaBH_4$ in one portion with stirring and, then the mixture was stirred for 30 min at room temperature. After decomposition of the excess reagent by careful addition of Ac_2O and adjusting to pH 5, the reaction mixture was diluted with 100 ml of $CHCl_3$. The solution was washed with H_2O and dried (Na_2SO_4). Evaporation of the solvent *in vacuo* afforded a syrup which crystallized on trituration with EtOH–light petroleum. The cyrstals (91 mg, 29%) were identified with the sample of **11a**.

The mother liquor left after the recrystallization of **11a** was evaporated *in vacuo* and the residue (309 mg) was chromatographed on 3 g of silicagel. Removal of the solvent from fractions eluted with AcOEt afforded 236 mg (67%) of **11b** as a syrup, which was identified with the sample obtained above by infrared spectrometry.

In the other run, the same reaction mixture was allowed to stand for 17 hr at room temperature. After decomposition of the excess reagent and adjusting to pH 5 with Ac_2O, the mixture was diluted with 150 ml $CHCl_3$. The solution was washed with H_2O and dried (Na_2SO_4). Evaporation of the solvent *in vacuo* left 263 mg of a syrup which revealed two spots on thin-layer chromatogram (AcOEt). Acetylation of the syrup with Ac_2O–pyridine yielded 100 mg (44.2%) of **8**, along with 71 mg of an unidentified syrup.

(ii) 3-Hydroxyl Derivative (**6b**): To a solution of 320 mg of **6b**, 50 mg of $CoBr_2$, and 120 mg of α,α′-dipyridyl in 40 ml of EtOH was added 150 mg of $NaBH_4$ in one portion with stirring, and the resulting mixture was allowed to stand for 5 min at room temperature. Working up as described above for **6a**, 316 mg of a crystalline product was obtained. Recrystallization from MeOH gave 270 mg of pure **11a**. Thin-layer chromatography of the mother liquor showed the absence of **7b**.

In the other run, the reaction mixture was allowed to stand for 35 min at room temperature. Working up as described above, an unidentified syrup (160 mg) was obtained along with 136 mg of **11a**.

(iii) 3-O-Benzyl Derivative (**2**): To a solution of 380 mg of **2**, 50 mg of $CoBr_2$, and 120 mg of α,α′-dipyridyl in 50 ml of EtOH was added 0.15 g of $NaBH_4$ in one portion with stirring and the mixture was allowed to stand for 1.5 hr at room temperature with stirring. After decomposition of the excess reagent by careful addition of AcOH, the mixture was diluted with 50 ml of H_2O. The solution was washed light petroleum and extracted with 150 ml of $CHCl_3$. The $CHCl_3$ layer was washed with H_2O, dried ($MgSO_4$), and evaporated *in vacuo*, giving 300 mg of a crude syrup of **13**. Acetylation of **13** thereby obtained and chromatographic purification afforded 287 mg of **14** as a thick syrup. IR $\nu_{max}^{liq.}$ cm^{-1}: 1670, 1540 (N-acetyl), 1600, 1190, 1175 (tosyl). Analytically pure samples of **13** and **14** could not be obtained.

Treatment of 6-Amino-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (13) with $LiAlH_4$ or NaOMe——The crude product of **13** (300 mg) obtained from 380 mg of **2** as described above was treated with 0.1 g of $LiAlH_4$ in 20 ml of dry ether at room temperature for 1 hr and acetylation of the resulting product with Ac_2O in MeOH gave 180 mg (69% from **2**) of an N-acetate of **1**, mp 90—92°, which was identified with the authentic sample.[2]

A solution of crude **13** (300 mg), which was also prepared from 380 mg of **2**, in 7 ml of MeOH containing 110 mg of NaOMe was refluxed for 4 hr and the resulting product was acetylated to give 181 mg of an N-acetate of **1**. Thin-layer chromatography showed contamination of a small amount of **14**.

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