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Syntheses and Characterizations of 5,6-Epimino-L-altro- and -L-idofuranoses[1]

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Syntheses of methyl 2,3-di-O-benzyl-5,6-dideoxy-5,6-epimino-α-L-altrofuranoside (**4a**) and 3-O-benzyl-5,6-dideoxy-5,6-epimino-1,2-O-isopropylidene-β-L-idofuranose (**11a**) were described. It was found that an attack of nucleophiles in these epimines occurs exclusively in the terminal position with epimine ring opening.

Carbohydrate epimines are not only of chemical interest because of their potency as synthetic intermediates, but also of pharmaceutical interest in cancer chemotherapy as alkylating agents. The syntheses and characterizations of 2,3-epimino-D-manno- and -D-allopyranosides,[3] 2,3-epimino-D-ribo- and -D-lyxofuranosides,[4] 3,4-epimino-2-deoxy-D-talopyranoside (tantatively),[5] and 3,4-epimino-L-fucopyranoside[6] have already been reported, while successful approach to prepare 5,6-epimino derivatives is not yet found in earlier papers;[7] some attempts[8] were made to prepare derivatives of 5,6-dideoxy-5,6-epimino-1,2-O-isopropylidene-β-L-idofuranose (**1**) by an intramolecular displacement of a sulfonyloxy group by a neighboring nitrogen atom, in a manner analogous to that already described for preparation of 2,3-epimino derivatives of pyranosides. However, treatment of 6-benzamido-6-deoxy-1,2-O-isopropylidene-5-O-mesyl-α-D-glucofuranose (**2a**) with lithium aluminum hydride or sodium ethoxide did not afford the desired epimino derivative but 6-benzamido-6-deoxy-1,2-O-isopropylidene-α-D-glucose (**2b**). Analogous difficulty has been encountered on treatment of methyl 2,6-dibenzamido-2,6-dideoxy-5-O-mesyl-3-O-methyl-β-D-glucofuranoside with sodium ethoxide.[9] We, then, attempted a displacement reaction of the 5-O-sulfonyl group of furanosides having 6-azido group in place of 6-benzamido group, with lithium aluminum hydride, under reduction of the azide group, to yield epimino derivatives. In addition, other free hydroxyl functions were protected with benzyl group in advance, in consideration of their possible unfavorable participation in this reaction.[10,11]

1) Partly presented as preliminary communication: H. Saeki, T. Iwashige, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **16**, 188 (1968). H. Saeki and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **16**, 962 (1968).
2) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
3) J.E. Christensen and L. Goodman, *J. Am. Chem. Soc.*, **82**, 4738 (1960); R.D. Guthrie and D. Murphy, *J. Chem. Soc.*, **1963**, 5288; D.H. Buss, L. Hough, and A.C. Richardson, *J. Chem. Soc.*, **1963**, 5295; B.R. Baker and T. Neilson, *J. Org. Chem.*, **29**, 1047, 1051, 1057, 1063 (1964); W. Meyer zu Reckendorf, *Chem. Ber.*, **97**, 325 (1964); R.D. Guthrie and D. Murphy, *J. Chem. Soc.*, **1965**, 3828; D.H. Buss, L. Hough, and A.C. Richardson, *J. Chem. Soc.*, **1965**, 2736; C.F. Gibbs, L. Hough, and A.C. Richardson, *Carbohyd. Res.*, **1**, 290 (1965); B.R. Baker and T.L. Hullar, *J. Org. Chem.*, **30**, 4038 (1965).
4) B.R. Baker and T.L. Hullar, *J. Org. Chem.*, **30**, 4045 (1965); J. Cleophax, S.D. Gero, and J. Hildesheim, *Chem. Commun.*, **1968**, 94.
5) H.H. Baer and T. Neilson, *Can. J. Chem.*, **43**, 840 (1965).
6) A.D. Barford and A.C. Richardson, *Carbohyd. Res.*, **4**, 408 (1967).
7) During this work, Paulsen and Stoye (*Angew. Chem.*, **80**, 120 (1968)) reported that treatment of 3-O-benzyl-1,2-O-isopropylidene-5,6-di-O-mesyl-α-D-glucofuranose with anhydrous hydrazine yielded an N-amino-5,6-aziridine derivative (**3**).
8) D.H. Buss, L.D. Hall, and L. Hough, *J. Chem. Soc.*, **1965**, 1616.
9) W. Meyer zu Reckendorf, *Tetrahedron*, **19**, 2033 (1963).
10) R.E. Gramera, T.R. Ingle, and R.L. Whistler, *J. Org. Chem.*, **29**, 1083 (1964).
11) E.J. Hedgley, O. Mérész, and W.G. Overend, *J. Chem. Soc.* (C), **1967**, 888.

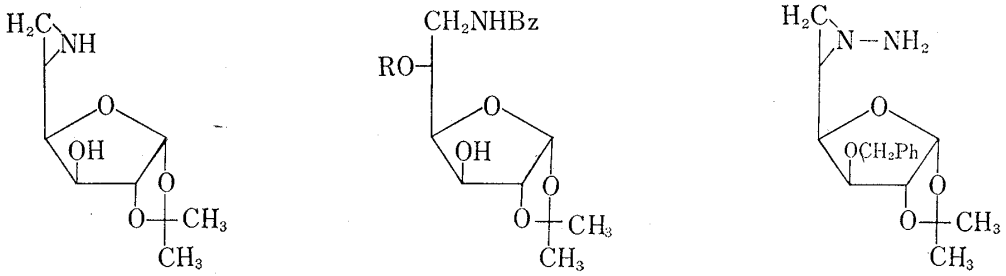


Chart 1

First, we attempted synthesis of methyl 2,3-di-O-benzyl-5,6-dideoxy-5,6-epimino-α-L-altrofuranoside (**4a**). Treatment of methyl 2,3-di-O-benzyl-5,6-di-O-tosyl-β-D-galactofuranoside[12] (**5**) with one equivalent of sodium azide in dimethyl sulfoxide (DMSO) gave a 6-azido-6-deoxy-5-O-tosyl derivative (**6**) as a syrup of $[\alpha]_D$ −42.8°, and with excess amounts of the reagent gave **6** and a 5,6-diazide (**8**). Monosubstitution of the tosyloxy group in the terminal position[13] by an azide group was verified by conversion of the known 6-azido-2,3-di-O-benzyl-6-deoxy-β-D-galactofuranoside[12] (**7**) into **6** by tosylation. Lithium aluminum hydride reduction of **6** afforded the desired methyl 2,3-di-O-benzyl-5,6-dideoxy-5,6-epimino-α-L-altrofuranoside (**4a**) as an unstable syrup, which was characterized as its syrupy acetate (**4b**) of $[\alpha]_D$ −107.3°. Formation of **4a** was supported by its infrared spectrum, which indicated the absence of tosyl or azide group, and the presence of an N–H absorption. The characteristic infrared absorption of **4b** at 1700 cm^{-1} also suggested the presence of an N-acetylaziridine ring.[14] The acetate (**4b**) was quite unstable to bases; treatment with bases for a short time or alumina column chromatography afforded the parent epimine (**4a**) under facile hydrolysis. Both **4a** and **4b** were also unstable to acids; treatment with mineral acids gave resinous mass under coloration.

A ring–opening reaction of **4b** by treatment with sodium azide in DMSO gave an uncharacterized azido-acetate (**9**), whose further short treatment with lithium aluminum hydride at a low temperature, followed by acetylation, gave methyl 5,6-diacetamido-2,3-di-O-benzyl-5,6-dideoxy-α-L-altrofuranoside (**10**) as fine needles of mp 187—188°, $[\alpha]_D$ −55.1°. **10** was identified with the sample obtained by reduction of the 5,6-diazide (**8**) with lithium aluminum hydride, followed by acetylation of the resulting diamine. The fact that **10** thus obtained by opening of the 5,6-epimino ring had an L-*altro*-configuration indicated that the ring–opening reaction proceeded by the attack of the azide ion in the terminal position.

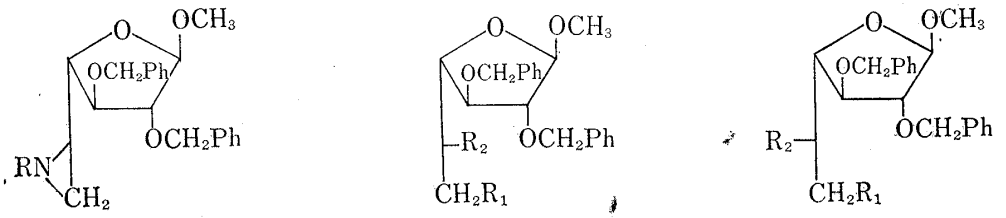
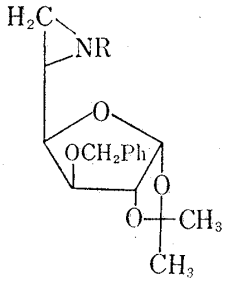


Chart 2

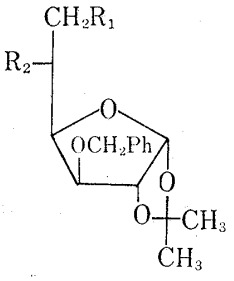
12) H. Saeki, T. Iwashige, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **16**, 2410 (1968).
13) Nucleophilic substitution of 5,6-di-O-tosylate or 5,6-di-O-mesylate of hexofuranosides occurred predominantly at the 6-position. See footnote, 8 and 9.
14) H.L. Spell, *Anal. Chem.*, **39**, 185 (1967).

On the other hand, 5,6-epimino-L-idofuranose (**11a**) was prepared in an analogous way. By following Reichstein's procedure,[15] tosylation of 3-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose(**12**)afforded 5,6-di-O-tosylate(**13**)as platelets of mp 99—99.5°(reported as syrup[15]) and 6-O-monotosylate (**14**) as a syrup. Treatment of **13** with one equivalent of sodium azide in DMSO afforded exclusively a 6-azido-6-deoxy-5-O-tosyl derivative (**15**) of mp 81.5—83°. Differing from the case of **5**, prolonged treatment of **13** with excess amounts of the reagent did not easily give a 5,6-diazide. Displacement of the tosyloxy group in the terminal position by an azide ion was also confirmed by treatment of the monotosylate (**14**) with sodium azide, followed by tosylation of the resulting 6-azide (**16**), which gave **15**.

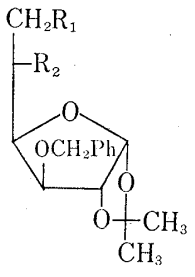
Lithium aluminum hydride reduction of **15** in ether at room temperature[16] yielded the desired 3-O-benzyl-5,6-dideoxy-5,6-epimino-1,2-O-isopropylidene-β-L-idofuranose (**11a**) as needles of mp 91.5—94°, which formed an acetate (**11b**) of mp 106—107°. The infrared spectra of **11a** and **11b** also suggested the presence of an aziridine ring. Similar to **4a** and **4b**, these epimino derivatives were also labile to acids. The acetate (**11b**) was easily hydrolysed by bases to the parent epimine (**11a**).



11a : R=H
b : R=Ac



	R_1,	R_2
12 :	OH,	OH
13 :	OTs,	OTs
14 :	OTs,	OH
15 :	N_3,	OTs
16 :	N_3,	OH
17 :	NHAc,	OH
18 :	OBz,	OTs
19 :	OCH_2Ph,	OTs



	R_1,	R_2
20 :	OAc,	NHAc
21 :	OH,	NHAc
22 :	OBz,	N_3

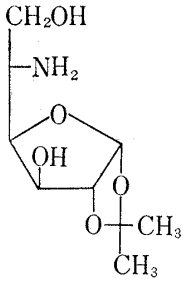


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Chart 3

In a warm acetic acid solution, **11b** was easily converted into syrupy 5-acetamido-6-O-acetyl-3-O-benzyl-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose (**20**) by opening of the epimino ring. The structure of **20** was established by methanolysis of **20** with sodium methoxide which gave a 5-acetamido-5-deoxy derivative[17] (**21**) as needles of mp 143—144°. First, **21** was not identical with 6-acetamido-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (**17**) which was supposed to be one of the possible products and which was synthesized by lithium aluminum hydride reduction of the azide (**16**), followed by acetylation in methanol. Therefore, **21** was designated as 5-acetamido-5-deoxy-L-idose derivative and also identified with the sample synthesized by an unequivocal method as follows: Treatment of 6-O-benzoyl-3-O-benzyl-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose[15] (**18**) with sodium azide[18] af-

15) A.S. Meyer and T. Reichstein, *Helv. Chim. Acta*, **29**, 152 (1946).
16) At an elevated temperature, the reduction of **15** with lithium aluminum hydride gave an unidentified complex mixture, probably including a 5-deoxy product. See the experimental.
17) It was found that uncrystallized crude **21** was unstable to a long storage, probably due to any acetyl migration, which was suggested by infrared spectrometry.
18) It was reported that the 6-benzoyloxy group of **18** had no participation in nucleophilic substitution in the 5 position. See footnote 8.

forded the 5-azide (**22**), whose lithium aluminum hydride reduction, followed by N-acetylation in methanol, gave **21**. In addition, debenzylation of **21** over palladium–charcoal with hydrogen, followed by saponification of the acetyl group yielded the known 5-amino-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose[19,20] (**23**) of mp 184—185°, which was identified with the authentic sample prepared from 3,6-di-O-benzyl-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose[10] (**19**), as described will be in the experimental.

It was concluded that nucleophiles as an acetate or azide ion caused facile ring-opening of the 5,6-epimino group in carbohydrates, exclusively with an attack in the terminal position. Analogous preparation and characterization of 5,6-deoxy-5,6-epimino-D-glucofuranose will be reported in a successive report.

These epimino carbohydrates (**4** and **11**) indicated no activity against leukemia L-1210.

Experimental

Melting points are not corrected. Infrared spectra were determined on Perkin–Elmer Model 21. Plates for thin-layer chromatography were prepared with Silica Gel G (E. Merck AG). Visualisation 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). Evaporation *in vacuo* was made in a rotary evaporator.

Methyl 6-Azido-2,3-di-O-benzyl-6-deoxy-5-O-tosyl-β-D-galactofuranoside (6) and Methyl 5,6-Diazido-2,3-di-O-benzyl-5,6-dideoxy-α-L-altrofuranoside (8)——A solution of 3.4 g of methyl 2,3-di-O-benzyl-5,6-di-O-tosyl-β-D-galactofuranoside[12] (**5**) and 0.5 g of NaN_3 in 30 ml of DMSO was heated at 90—100° for 2 hr with stirring in N_2 atmosphere. The cooled mixture was poured into H_2O and the solution was extracted with $CHCl_3$. The extract was dried over anhyd. Na_2SO_4 and evaporated *in vacuo* to dryness, giving 3.1 g of a syrup, which was chromatographed on 90 g of silica gel in column. Romoval of the solvent from fractions eluted with benzene gave 0.97 g of **8** as a colorless syrup of $[\alpha]_D^{21.5}$ −61.7° (c=5.5, $CHCl_3$). IR $\nu_{max}^{liq.}$ cm^{-1}: 2100 (-N_3). *Anal.* Calcd. for $C_{21}H_{24}O_4N_6$: C, 59.42; H, 5.70; N, 19.82. Found: C, 59.38; H, 5.67; N, 19.26.

Evaporation of the solvent from the fraction eluted with 2% (v/v) AcOEt–benzene gave 0.98 g of **6** as a colorless syrup of $[\alpha]_D^{20}$ −42.8° (c=8.5, $CHCl_3$). IR $\nu_{max}^{liq.}$ cm^{-1}: 2120 (-N_3), 1370, 1190, 1175 (-OSO_2-). *Anal.* Calcd. for $C_{28}H_{31}O_7N_3S$: C, 60.74; H, 5.64; N, 7.59; S, 5.79. Found: C, 60.81; H, 5.74; N, 7.61; S, 5.93.

To a solution of 2.36 g of methyl 6-azido-2,3-di-O-benzyl-6-deoxy-β-D-galactofuranoside[12] (7) in 20 ml of pyridine was added 1.2 g of TsCl and the mixture was allowed to stand for 3 days at room temperature. After treatment in the usual manner, the resulting product was chromatographed over 60 g of silica gel. Removal of the solvent from fractions eluted with benzene gave 0.64 g of **6** which was identified with the sample obtained earlier by thin-layer chromatography (AcOEt– benzene, 1:9 (v/v)) and infrared spectrometry.

Methyl 2,3-Di-O-benzyl-5,6-dideoxy-5,6-epimino-α-L-altrofuranoside (4a) and Its N-Acetate (4b)——To a stirred solution of 0.38 g of **6** in 10 ml of dry ether was added in portions 0.3 g of $LiAlH_4$ at 0°, and the resulting mixture was stirred for 2 hr at room temperature. After careful decomposition of an excess of the reagent by addition of H_2O and filtration, the ether layer was dried over anhyd. Na_2SO_4 and evaporated *in vacuo*, giving 0.20 g of **4a** as a colorless syrup, which revealed one spot on thin-layer chromatogram (AcOEt– benzene, 1:9 (v/v) and AcOEt). Its infrared spectrum indicated no absorption of TsO- or N_3- group, but N-H absorption. Attempted purification of **4a** for an analytical sample, using a silica gel column, was not successful because it was found to damage **4a** with coloration.

A syrupy N-acetate of **4a** (**4b**) was obtained by acetylation of **4a** with Ac_2O in MeOH, followed by silica gel column chromatography (elution with AcOEt–hexane, 3:7 (v/v)). IR $\nu_{max}^{liq.}$ cm^{-1}: 1700 (-NAc) $[\alpha]_D^{21}$ −107.3° (c=6.1, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{27}O_5N$: C, 69.50; H, 6.85; N, 3.59. Found: C, 69.27; H. 6.79; N, 3.46.

Methyl 5,6-Diacetamido-2,3-di-O-benzyl-5,6-dideoxy-α-L-altrofuranoside (10)——i) To a stirred cooled solution of 0.97 g of **7** in 10 ml of dry ether was added portionwise 0.5 g of $LiAlH_4$ and the mixture was stirred for 2 hr at room temperature. After decomposition of an excess of the reagent and filtration, the resulting organic layer was dried over anhyd. Na_2SO_4 and evaporated *in vacuo*, giving 0.53 g of 5,6-diamino-5,6-dideoxy-furanoside as a syrup, which was acetylated with a mixture of 1 ml of Ac_2O and 3 ml of pyridine. Standing of the mixture overnight yielded colorless crystals which was collected after dilution with hexane and cooling. After washing with hexane, the crystals of mp 186—188° (0.56 g) were

19) R.E. Gramera, R.M. Bruce, S. Hirase, and R.L. Whistler, *J. Org. Chem.*, **28**, 1401 (1963).
20) H. Paulsen and K. Todt, *Chem. Ber.*, **99**, 3450 (1966).

recrystallized from iso-PrOH to give **10** as fine needles of mp 187—188°, $[\alpha]_D^{20}$ −55.1° (c=2.3, $CHCl_3$). *Anal.* Calcd. for $C_{25}H_{32}O_6N_2$: C, 65.77; H, 7.07; N, 6.14. Found: C, 65.74; H, 6.98; N, 6.01.

ii) A mixture of 0.35 g of **4b**, 0.3 g of NaN_3, and 6 ml of DMSO was heated for 2 hr at 100—110°, and the colored mixture was diluted with H_2O and extracted with $CHCl_3$. The extract was dried and evaporated *in vacuo* to give 0.38 g of a colored syrup. To a solution of the syrup in 5 ml of dry ether was added in portions 0.5 g of $LiAlH_4$, and the mixture was stirred for 1 hr at room temperature. Treatment of the mixture in the usual manner afforded a pale yellow syrup which was acetylated with Ac_2O in MeOH giving a syrup which partly crystallized from iso-PrOH–hexane to afford 30 mg of **10**, mp 187—188°. These samples of **10** were identical by mixed melting point test and infrared spectrometry.

Chromatography of the mother liquor (124 mg), from which crystals of **10** were removed, gave 24 mg of the starting material (**4b**), 35 mg of a material having –OAc and –NAc groups, and 51 mg of a material having –OH and –NAc groups.

3-O-Benzyl-1,2-O-isopropylidene-5,6-di-O-tosyl-α-D-glucofuranose (13) and 3-O-Benzyl-1,2-O-isopropylidene-6-O-tosyl-α-D-glucofuranose (14)——Following the known method,[15] **13** and **14** were prepared by tosylation of 3-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose (**12**). The mixture was chromatographed on a silica gel column. Removal of the solvent from the first fractions eluted with 5% (v/v) AcOEt–benzene afforded **13** (a main component) as a syrup which crystallized on trituration with MeOH. Recrystallization from MeOH gave platelets of mp 99—99.5°, $[\alpha]_D^{20}$ −3.8 (c=3.0, $CHCl_3$) (reported[15] $[\alpha]_D^{19}$ −6.0° ±0.3°). *Anal.* Calcd. for $C_{30}H_{34}O_{10}S_2$: C, 58.24; H,5.54; S, 10.36. Found: C, 57.91; H, 5.48; S, 10.46.

For the next preparation, the syrupy mixture was directly seeded with a few crystals of **14** and the resulting precipitate was repeatedly recrystallized from MeOH.

The successive fractions eluted with the same solvent mixture, after removal of the solvent, gave **13** (a minor component) as a syrup. *Anal.* Calcd. for $C_{23}H_{28}O_8S$: C, 59.47; H, 6.08; S, 6.90. Found: C, 59.56; H, 6.45; S, 6.73.

6-Azido-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (15)——i) A mixture of 15.6 g of **13**, 1.9 g of NaN_3, and 90 ml of DMSO was heated for 1.5 hr at 90—100° in N_2 atmosphere with stirring. The mixture was diluted with a cooled aqueous NaCl solution and extracted with ether. The extract was dried over anhyd. Na_2SO_4 and evaporated *in vacuo* to give 12.5 g of a syrup which was chromatographed on 250 g of a silica gel. Removal of the solvent from the fractions eluted with 3% (v/v) AcOEt-benzene gave 11.4 g (93%) of **15** as a syrup which crystallized on standing. Recrystallization from benzene–hexane or ether afforded **15** as needles of mp 81.5—83°, $[\alpha]_D^{20}$ −41.2° (c=7.8, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 2100 (–N_3), 1190, 1180 (–O–SO_2–). *Anal.* Calcd. for $C_{23}H_{27}O_7N_3S$: C, 56.57; H, 5.56; N, 8.59; S, 6.55. Found: C, 56.54; H, 5.72; N, 8.56; S, 6.27.

ii) A mixture of 4.6 g of **14**, 1.9 g of NaN_3, and 30 ml of DMSO was treated as described for **13**. Working up in a similar way gave 3.0 g of the 6-azide (**16**) as a chromatographically pure yellow liquid, IR $\nu_{max}^{liq.}$ cm^{-1}: 3500 (–OH), 2100 (–N_3). *Anal.* Calcd. for $C_{16}H_{21}O_5N_3$: C, 57.30; H, 6.31; N, 12.53. Found: C, 57.26; H, 6.25; N, 11.50.

A mixture of 0.49 g of **16**, 0.8 g of TsCl, and 2 ml of pyridine was allowed to stand for 2 days with stirring at room temperature. Treatment in the usual manner afford 0.4 g of **15** which was identified with the sample obtained before by mixed melting point test and infrared spectrometry.

6-Acetamido-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (17)——To a solution of 3.14 g of **16** in 35 ml of dry ether was added in portions 0.8 g of $LiAlH_4$ and the mixture was stirred for 1 hr at room temperature. The syrupy 6-amino-6-deoxyfuranose obtained by treatment in the usual manner was acetylated in MeOH, giving 2.87 g of 6-acetamide (**17**). Trituration with iso-PrOH–hexane gave **17** as fine needles of mp 103—104°, $[\alpha]_D^{21}$ −5.1° (c=3.1, $CHCl_3$). *Anal.* Calcd. for $C_{18}H_{25}O_6N$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.12; H, 7.21; N, 3.81.

Hydrogenation of **17** (300 mg.) over 0.2 g of Pd-C in 20 ml of EtOH at 80 kg/cm² and 70—80° for 5.5 hr gave 211 mg (95%) of 6-acetamido-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose as needles of mp 165—166° (reported[21] mp 164—165°).

3-O-Benzyl-5,6,-dideoxy-5,6-epimino-1,2-O-isopropylidene-β-L-idofuranose (11a) and Its Acetate (11b)——To a solution of 10 g of **15** in 200 ml of dry ether was added in portions 1.4 g of $LiAlH_4$ with stirring at 0° and the mixture was stirred for 1 hr at room temperature. After decomposition of the excess reagent by dropping a small amount of H_2O carefully, the mixture was filtered and the resulting organic layer was dried over anhyd. Na_2SO_4. Evaporation of the solvent *in vacuo* afforded a syrup which crystallized on rubbing the vessel wall with a glass rod. Recrystallization of the collected crystals (4.1 g, 69%) from benzene–hexane afforded **11a** as fine needles of mp 91—94°, $[\alpha]_D^{21}$ −62.1° (c=1.8, $CHCl_3$), *Anal.* Calcd. for $C_{16}H_{21}O_4N$: C, 65.95; H, 7.25; N, 4.81. Found: C, 65.72;H, 7.24; N, 4.90.

21) F.D. Cramer, "Methods in Carbohydrate Chemistry," Vol. I, Academic Press Inc., New York and 1962, London, 1962, p. 242.

The epimine (**11a**) (2.4 g) was acetylated with 5 ml of Ac_2O in 15 ml of MeOH. After standing for 15 min at room temperature, the mixture was diluted with ice-water and, after standing for 1 hr, extracted with $CHCl_3$. The extract was washed successively with H_2O, dil. NaOH solution, and H_2O and dried over anhyd. Na_2SO_4. Evaporation of the solvent *in vacuo* and crystallization of the residual syrup from iso-PrOH–hexane gave crude crystals of **11b**. Recrystallization from iso-PrOH–hexane gave 1.7 g of needles of mp 106—107°, $[\alpha]_D^{20}$ −109.0° (c=5.0, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1700 (-NAc). *Anal.* Calcd. for $C_{18}H_{23}O_5N$: C, 64.85; H, 6,95; N, 4.20. Found: C, 64.83; H, 7.07; N, 4.15.

The combined mother liquor of crystsllization was chromatographed on a silica gel column, giving 0.3 g of **11b** as a second crop. Total yield, 2.0 g(74%).

5-Acetamido-3-O-benzyl-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose(**21**)—i) A solution of 2.0 g of **11b** in 50 ml of AcOH was warmed at 50—60° for 2 hr and the cooled mixture was diluted with H_2O. Thr mixture was neutralized with dil. Na_2CO_3 solution and extracted with $CHCl_3$. The extract was washed with dil. Na_2CO_3 solution and H_2O, and dried over anhyd. Na_2SO_4. Evaporation of the solvent *in vacuo* gave 2.4 g of a syrup(**20**), which revealed one spot on thin-layer chromatogram(AcOEt–hexane 7:3(v/v) or AcOEt). IR $\nu_{max}^{liq.}$ cm^{-1}: 3400 (N–H), 1740 (-OAc), 1660, 1540 (-NHAc). *Anal.* Calcd. for $C_{20}H_{27}O_7N$: C, 61.05; H, 6.92; N, 3.56. Found: C, 60.04; H, 6.88; N, 3.52.

The diacetate (**20**) (606 mg) was dissolved in MeOH containing a catalytic amount of NaOMe and the mixture was allowed to stand for 1 hr at room temperature. The mixture was diluted with $CHCl_3$ and washed with an aqueous NaCl solution and H_2O. After drying, the extract was evaporated *in vacuo* to give 422 mg of a syrup which crystallized on digestion with iso-PrOH–hexane. Recrystallization from the same solvent mixture yielded **21** as fine needles of mp 143—144°, $[\alpha]_D^{21}$ −7.4° (c=5.3, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3350, 3250 (-OH, -NH), 1640, 1550 (-NHAc). *Anal.* Calcd. for $C_{18}H_{25}O_6N$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.33; H, 7.23; N, 4.05.

ii) A mixture of 1.14 g of 6-O-benzoyl-3-O-benzyl-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose[15] (**18**), 0.65 g of NaN_3, and 10 ml of DMSO was heated at 130—140° for 2 hr with stirring in N_2 atmosphere. The cooled mixture was diluted with aqueous NaCl solution and extracted with ether. After being washed with H_2O and dried over anhyd. Na_2SO_4, the extract was evaporated *in vacuo* to give a brown syrup (0.52 g) which was chromatographed on 20 g of silica gel. Removal of the solvent from fractions eluted with 3% (v/v) AcOEt–benzene afforded 0.66 g of a 5-azido-benzoate (**22**). IR $\nu_{max}^{liq.}$ cm^{-1}: 2140 ($-N_3$), 1730 (-OBz).

To a solution of 0.66 g of **22** in 15 ml of dry ether was added 0.2 g of $LiAlH_4$ in portions and the mixture was stirred for 1.5 hr at room temperature. Treatment of the mixture in the usual manner gave 0.47 g of a crude 5-amino-5-deoxy derivative which was treated with Ac_2O in MeOH, giving, through chromatographic purification, 218 mg of **21**, accompanied with 83 mg of an unidentified product which was probably 5-acetamido-6-O-benzoyl-5-deoxy derivative from its infrared spectrometry.

5-Amino-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose (**23**)——i) 3-O-Benzyl-6-acetamidofuranose (**21**) (429 mg) was hydrogenated over 0.2 g of 10% Pd-C in 30 ml of EtOH at 80 kg/cm^2 and 70—80° for 5 hr. The resulting debenzylated product (300 mg) obtained by treatment in the usual manner was dissolved in 10 ml of saturated $Ba(OH)_2$ solution. The mixture was heated on a water bath for 5 hr. The cooled solution was saturated with CO_2 and the solid was centrifuged off. The supernatant was evaporated to dryness *in vacuo* below 50° to give a syrup which crystallized on digestion with ether. The collected crystals (probably a carbonate of **23**) (243 mg) were recrystallized from EtOH–ether to leaflets which were warmed at 70° under a reduced pressure of 5 mmHg for 2—3 hr to give **23** as leaflets of mp 184—185°, $[\alpha]_D^{20}$ −3.7° (c=1.1, MeOH) (reported[19] mp 178, $[\alpha]_D^{25}$ −3.0, and[20] mp 176—179°, $[\alpha]_D^{20}$ −3.4). The crystals were transformed into needles by heating at 130—150°. *Anal.* Calcd. for $C_9H_{17}O_5N$: C, 49.30; H, 7.82; N, 6.39. Found: C, 49.00; H, 7.89; N, 6.47.

ii) A mixture of 1.63 g of 3,6-di-O-benzyl-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose,[10] 0.9 g of NaN_3, and 16 ml of DMSO was heated at 120—130° for 6 hr in N_2 atmosphere with stirring. The cooled solution was treated as described before, giving 1.04 g of a syrup which was chromatographed on 30 g of silica gel. Removal of solvent from fractions eluted with 1% (v/v) AcOEt–benzene gave 0.54 g of 5-azido-5-deoxy-furanose as a syrup which revealed one spot on thin-layer chromatogram (AcOEt–benzene, 1:9 (v/v)). IR $\nu_{max}^{liq.}$ cm^{-1}: 2100 ($-N_3$). The 5-azidofuranose (538 mg) thus obtained was hydrogenated over 0.5 g of 10% Pd-C in 50 ml of EtOH at 70 kg/cm^2 and 60—70° for 5 hr. Recrystallization of the resulting crystals (103 mg) from EtOH–ether gave **23** as needles of mp 185°. These samples of **23** were identical by mixed melting point test and infrared spectrometry.

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