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Chemical Modification of Lactose. VII.[1] Synthesis of 4-O-β-D-Idopyranosyl-D-glucopyranose[2]

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The title new reducing disaccharide (**12**) was synthesized starting from 1,6-anhydro-β-lactose.

Selective benzoylation of 1,6-anhydro-4′,6′-O-benzylidene-β-lactose with 4 molar equivalents of benzoyl chloride in pyridine afforded the corresponding 2,3,3′-tri-O-benzoate (**3**) in 41% yield. Sulfonylation of **3** gave 2′-O-mesylate (**4**) or 2′-O-tosylate (**6**). Treatment of **4** or **6** with 1.1 molar equivalents of sodium methoxide in boiling MeOH yielded 1,6-anhydro-4-O-(2,3-anhydro-4,6-O-benzylidene-β-D-talopyranosyl)-β-D-glucopyranose (**7**) in 50 or 66% yield. Further crop of **7** was isolated from the filtrate of **7** as the corresponding diacetate. Heating of a mixture of **7** with excess aq. KOH at 100° for 3 hr cleaved the epoxide ring of **7** *trans*-diaxially and, after acetylation, 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-β-D-idopyranosyl)-β-D-glucopyranose (**9**) was isolated in 84% yield.

Debenzylidenation of **9** followed by acetylation, and subsequent opening of the 1,6-anhydro-β-ring with titanium tetrachloride in $CHCl_3$, then treatment with mercuric acetate in glacial AcOH, afforded 1,2,3-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-idopyranosyl)-β-D-glucopyranose (**11**) in 43% yield. Deacetylation of **11** afforded the title compound (**12**) as a hygroscopic, amorphous powder which gave the crystalline tosylhydrazone.

Keywords——synthesis new reducing disaccharide; lactose selective benzoylation; idopyranosyl disaccharide; epoxide talopyranosyl; Fürst-Plattner rule; lactose chemical modification

For a long time, most disaccharides have been prepared by a) acetolysis of natural polysaccharides followed by deacetylation, b) the Koenigs-Knorr condensation of monosaccharide units followed by removal of the blocking groups, or c) isomerization of the secondary hydroxyl groups in particular disaccharides. The third method has a merit that, starting from easily available natural disaccharides and utilizing the characteristic glycosidic linkage in the molecules, new particular disaccharides can be synthesized. In addition, the prepared disaccharides may be interesting substrates from biological points of view. Recently, galacto-sucrose[4] and 4-O-α-D-galactopyranosyl-D-glucopyranose[5] were prepared from sucrose and maltose by the third method, respectively. Synthesis of lactose[6] or α-D-galactopyranosyl α-D-galactopyranoside[7] from cellobiose or α,α-treharose, respectively, has also been reported in the literature.

Reducing disaccharides having the structures in which the secondary hydroxyl groups in D-glucose moiety are isomerized have been synthesized by the route started from lactose. Namely, when lactal is oxidized with perbenzoic acid, 4-O-β-D-galactopyranosyl-D-mannopyranose is produced in a good yield.[8] The product, later designated epi-lactose, was

1) Part VI: T. Chiba, M. Haga, and S. Tejima, *Carbohyd. Res.*, **45**, 11 (1975).
2) Preliminary communication: T. Chiba and S. Tejima, *Chem. Pharm. Bull.* (Tokyo), **24**, 1684 (1976).
3) Location: *Tanabe-dori, Mizuho-ku, Nagoya, 467, Japan.*
4) P.H. Fairclough, L. Hough, and A.C. Richardson, *Carbohyd. Res.*, **40**, 285 (1975).
5) M. Mori, M. Haga, and S. Tejima, *Chem. Pharm. Bull.* (Tokyo), **23**, 1480 (1975).
6) H. Kuzuhara and S. Emoto, *Agr. Biol. Chem.*, **30**, 122 (1966).
7) G. Birch, W. Surrey, and A.C. Richardson, *J. Chem. Soc.* (*C*), **1970**, 749.
8) M. Bergmann, *Ann.*, **434**, 79 (1923); A.J. Watters and C.S. Hudson, *J. Am. Chem. Soc.*, **52**, 3472 (1930).

synthesized by condensation of 1,6-anhydro-2,3-O-isopropylidene-β-D-mannopyranose with 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide, followed by removal of the blocking groups.[9] Hudson, *et al.*[10] reported that when lactose octaacetate was treated with aluminum chloride in chloroform, neolactose, 4-O-β-D-galactopyranosyl-D-altropyranose was prepared in a satisfactory yield. However, isomerization of the secondary hydroxyl groups in D-galactose moiety of lactose has not yet been reported in the literature. In this paper, we wish to report on synthesis of the title new reducing disaccharide by chemical modification of lactose.

In the preceding paper,[1] the authors reported synthesis and identification of several partially benzoylated products of 1,6-anhydro-4',6'-O-benzylidene-β-lactose (**1**). Since these products are useful starting materials for the chemical modification of lactose and also for the synthesis of higher oligosaccharides containing lactose such as bifidus factor, a further investigation of partial benzoylation of **1** has been carried out. After several experiments, the authors elucidated that, when 4 molar equivalents of benzoyl chloride in pyridine were used at −20°, **1** afforded 1,6-anhydro-4',6'-O-benzylidene-2,3,3'-tri-O-benzoyl-β-lactose (**3**) as a major product. Compound (**3**) was characterized by a comparison with the authentic sample previously synthesized by another route, and it was easily isolated in 41 % yield through silica gel column chromatography.

On sulfonylation, **3** yielded the corresponding 2'-O-methanesulfonate (**4**) or 2'-O-*p*-toluenesulfonate (**6**) in a yield of 90 or 88%, respectively. As compared with methanesulfonylation, *p*-toluenesulfonylation of **3** proceeded very slowly. Namely, in the former case, the reaction completed within 24 hours at 5° as judged by thin-layer chromatography (TLC), while in the latter, even after 4 days at room temperature, considerable amounts of the starting material remained in the reaction mixture. Difference in their reactivities may be attributed to bulkiness of the *p*-toluenesulfonyl group.

Debenzoylation of **4** with methanolic sodium methoxide and successive acetylation afforded 2,3,3'-tri-O-acetyl-1,6-anhydro-4',6'-O-benzylidene-2'-O-methanesulfonyl-β-lactose (**5**) in 72% yield. The nuclear magnetic resonance (NMR) spectrum of **5** was consistent with the assigned composition.

Treatment of **4** or **6** with 1.1 molar equivalents of sodium methoxide in boiling methanol for 3 hours and with cooling to room temperature crystallized out 1,6-anhydro-4-O-(2,3-anhydro-4,6-O-benzylidene-β-D-talopyranosyl)-β-D-glucopyranose (**7**) in a yield of 50 or 66%, respectively. Compound (**7**), reactive to the Ross' test,[11] was easily recrystallized from methanol. On acetylation, **7** gave the corresponding 2,3-di-O-acetate (**8**) in 91% yield. Deacetylation of **8** with methanolic sodium methoxide regenerated **7** in 86% yield.

While **7** is a versatile starting material for chemical modification of 2' and 3' positions in lactose, the yield was not so satisfactory as described above. Therefore, in order to increase the yield of **7**, the contents of the filtrate from which **7** was separated by filtration were investigated.

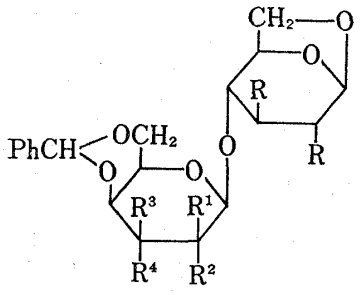
After evaporation of the solvent to dryness, the residue was acetylated to afford a sirup which showed **4** spots, *Rf* 0.48, 0.41, 0.29, and 0.19 (major), on TLC. Chromatographic separation using silica gel column yielded two crystalline materials with *Rf* 0.29 and 0.19, respectively. The faster moving component was assigned to **5** and the other to **8** by comparison with the authentic samples. The yields of **8** in the filtrate were 34% from **4** and 23% from **6**, respectively. Therefore, the total yield of **7** results in 79% from **4**, and 86% from **6**, which is almost satisfactory for preparative purpose.

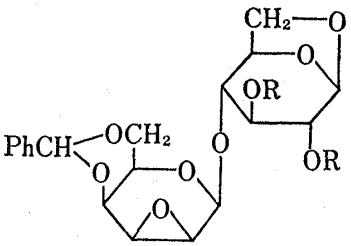
9) W.T. Haskins, R.M. Hann, and C.S. Hudson, *J. Am. Chem. Soc.*, **64**, 1490, 1852 (1942).
10) A. Kunz and C.S. Hudson, *J. Am. Chem. Soc.*, **48**, 1978, 2435 (1926); N.K. Richtmyer and C.S. Hudson, *ibid.*, **57**, 1716 (1935).
11) W.C.J. Ross, *J. Chem. Soc.*, **1950**, 2257.

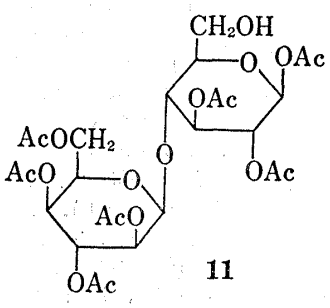
In the next step, the epoxide cleavage was proceeded as follows. A mixture of **7** with excess aqueous potassium hydroxide was heated for 3 hours at 100°. After neutralization with glacial acetic acid and removal of the solvent, the residue was acetylated to afford crystals (**9**), mp 217—218°, $[\alpha]_D^{25}$ −57°, in 84% yield. The NMR spectrum indicated the existence of one phenyl and four acetyl groups; the latter appeared as two singlets having equal integration at δ 2.11 and 2.13. While **9** had the same elemental composition with that of 2,2′,3,3′-tetra-O-acetyl-1,6-anhydro-4′,6′-O-benzylidene-β-lactose (**2**),[12] mp 228—229°, $[\alpha]_D^{25}$ +10°, which is the fully acetylated starting material in this paper, **9** was found not to be identical with **2** by comparison of their mp, optical rotation, and infrared (IR), and NMR spectra. Therefore, **9** was tentatively assigned to 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-β-D-idopyranosyl)-β-D-glucopyranose. As the ring structure of galactopyranosyl moiety in **7** is fixed with 4,6-O-benzylidene group, it is quite reasonable to assume that the epoxide ring cleaved *trans*-diaxially according to the Fürst-Plattner rule to afford **9**. Furthermore, a final structural assignment was obtained by following experiments.

Debenzylidenation of **9** and, without further purification, successive acetylation yielded 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3,4,6-tetra-O-acetyl-β-D-idopyranosyl)-β-D-glucopyranose (**10**) in 85% yield. Ring opening of the 1,6-anhydro ring in **10** by acetolysis resulted a complex mixture from which any homogeneous product could not be isolated. Probably, a considerable rupture of the glycosidic linkage might occur simultaneously. Thus, the authors had to select another method of ring opening as follows.

Reflux of **10** with titanium tetrachloride in chloroform, followed by treatment of the product with mercuric acetate in order to replace the chlorine atom by an acetoxyl group, afforded 1,2,3-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-idopyranosyl)-β-D-glucopyranose(**11**) in 50% yield together with 20% of starting material (**10**) unchanged, through silica gel column chromatography. The IR spectrum of **11** showed an absorption corresponding to the hydroxyl group at 3485 cm^{-1}.





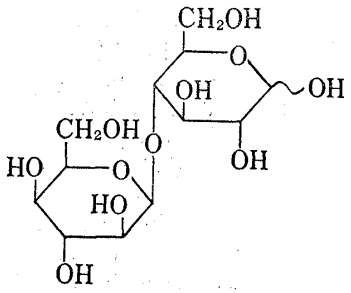


11

1: R=R²=R³=OH, R¹=R⁴=H
2: R=R²=R³=OAc, R¹=R⁴=H
3: R=R³=OBz, R¹=R⁴=H, R²=OH
4: R=R³=OBz, R¹=R⁴=H, R²=OMs
5: R=R³=OAc, R¹=R⁴=H, R²=OMs
6: R=R³=OBz, R¹=R⁴=H, R²=OTs
9: R=R¹=R⁴=OAc, R²=R³=H

7: R=H
8: R=Ac

Ac=acetyl, Bz=benzoyl, Ms=mesyl, Ph=phenyl, Ts=tosyl



12

Chart 1

12) T. Chiba, M. Haga, and S. Tejima, *Chem. Pharm. Bull.* (Tokyo), **23**, 1283 (1975).

Deacetylation of **11** with methanolic sodium methoxide afforded the title compound (**12**) as a hygroscopic, hardly sweet, amorphous powder, $[\alpha]_D^{24}$ +31°, in 95% yield. Compound (**12**) gave a hygroscopic crystalline *p*-toluenesulfonylhydrazone, mp 138—139° (decomp.), $[\alpha]_D^{19}$ −31°.

Acidic hydrolysis of **12** gave glucose and idose[13] which were identified with authentic samples by paper partition chromatography (PPC).

As mentioned in the earlier part of this paper, this is the first reported example of isomerization of the secondary hydroxyl groups in the D-galactopyranosyl moiety of lactose. The intermediates, 1,6-anhydro-4-O-(2,3-anhydro-4,6-O-benzylidene-β-D-talopyranosyl)-β-D-glucopyranose (**7**) and the corresponding 2,3-di-O-acetate (**8**) may be versatile key intermediates for chemical modification of lactose, and further studies will be reported in separated papers.

Experimental

Melting points were determined by a Yanagimoto micro melting point apparatus and uncorrected. Solutions were evaporated in a rotary evaporator below 40° under vacuum. Optical rotations were measured in a 0.5 dm tube with a Yanagimoto Model OR-10 automatic polarimeter. IR spectra were recorded with a Jasco Model IRA-2 spectrometer. NMR spectra were recorded at 100 MHz with a Jeol Model JNM-MH-100 spectrometer. Tetramethylsilane was used as the internal standard in $CDCl_3$. Chemical shifts are given on the δ scale. TLC on Kieselgel GF_{254} (E. Merck, Darmstadt, Germany) activated at 110° was performed with solvent systems (A) $CHCl_3$–acetone (3: 1, v/v), (B) $CHCl_3$–acetone (6: 1), (C) benzene–ether (1: 1), and (D) 70% iso-PrOH–AcOEt (2: 1). Detection was effected with H_2SO_4 or UV light (short wave length). Column chromatography was performed on a column of Wako-gel C-200 (Wako Pure Chemical Industries, Ltd., Osaka) as the adsorbent, with 1 g of a sample to be separated per 20 g of adsorbent. PPC was performed on Toyo Filter Paper No. 50 (Toyo Roshi Kaisha, Ltd., Tokyo) by the ascending method with (A) BuOH–pyridine–H_2O (6: 4: 3, v/v), (B) BuOH–AcOH–H_2O (25: 6: 25), and (C) BuOH–EtOH–H_2O (4: 1: 1) by the procedure of Ueda,[14] and detection was effected with alkaline silver nitrate.[15]

1,6-Anhydro-2,3,3′-tri-O-benzoyl-4′,6′-O-benzylidene-β-lactose (**3**)——To a chilled solution of 1,6-anhydro-4′,6′-O-benzylidene-β-lactose (**1**)[1,12] (14 g, 34 mmole) in dry pyridine (84 ml), benzoyl chloride (16 ml, 137.7 mmole) was added dropwise with stirring at −20°, and the stirring was continued for further 1 hr under exclusion of moisture. The mixture was left to stand overnight at 5°, treated with ice to decompose excess benzoyl chloride, and concentrated to dryness by repeated co-distillation with toluene. A solution of the residue in CH_2Cl_2 was successively washed with H_2O, 10% H_2SO_4, aq. $NaHCO_3$, and H_2O, dried (Na_2SO_4), and concentrated to dryness. The crystalline residue contained 5 components having *Rf* 0.77, 0.57 (major), 0.45, 0.21, and 0.11 on TLC (solvent B), respectively. The residue was dissolved in CH_2Cl_2 and the solution was chromatographed on a column of silica gel using CH_2Cl_2 and $CHCl_3$–acetone (20: 1, v/v) as eluants. Evaporation of the solvent from the second effluent afforded an amorphous powder which was crystallized from EtOH. Recrystallization from EtOH gave colorless needles (10 g, 41%), mp 222—223°, $[\alpha]_D^{26}$ +67° (*c*=1, $CHCl_3$). It was indistinguishable (mixed mp, IR, and TLC) from the authentic sample.[1]

1,6-Anhydro-2,3,3′-tri-O-benzoyl-4′,6′-O-benzylidene-2′-O-methanesulfonyl-β-lactose (**4**)——To a chilled solution of **3** (5 g, 6.9 mmole) in dry pyridine (50 ml) was added methanesulfonyl chloride (2.5 ml, 32.3 mmole) at −10° with stirring. After stirring for further 1 hr, the mixture was kept for 24 hr at 5°, diluted with CH_2Cl_2 (60 ml), and poured into ice-H_2O (400 ml). The organic layer was successively washed with H_2O, 10% H_2SO_4, aq. $NaHCO_3$, and H_2O, dried ($CaCl_2$), and then evaporated to dryness to give a sirup which was crystallized from EtOH. Recrystallization from EtOH gave white crystals (5 g, 90%), mp 245—246°, $[\alpha]_D^{26}$ +92° (*c*=0.9, $CHCl_3$). NMR ($CDCl_3$) δ: 2.96 (3H, s, OMs), 7.00—8.40 (20H, m, aromatic protons). TLC: *Rf* 0.69 (solvent A), 0.65 (B), 0.55 (C). *Anal.* Calcd. for $C_{41}H_{38}O_{15}S$: C, 61.34; H, 4.77. Found: C, 61.25; H, 4.67.

2,3,3′-Tri-O-acetyl-1,6-anhydro-4′,6′-O-benzylidene-2′-O-methanesulfonyl-β-lactose (**5**)——To a chilled suspension of **4** (500 mg) in dry MeOH (10 ml), methanolic 0.5M sodium methoxide (0.5 ml) was added at 5°. The mixture was stirred for 4 hr under exclusion of moisture, and kept overnight at room temperature. During the reaction period, complete deacetylation was checked by TLC. Dry Amberlite IR-120 (H^+) resin was added, and the suspension was stirred for 30 min, and then filtered. The filtrate was concentrated to dryness to give a sirup and, after washing with petr. ether (20 ml×3) to remove methyl benzoate, it was

13) E. Sorkin and T. Reichstein, *Helv. Chim. Acta*, **28**, 1 (1945).
14) M. Ueda, *Yakugaku Zasshi*, **90**, 1322 (1970).
15) W.E. Trevelyan, D.P. Procter, and J.S. Harrison, *Nature*, **166**, 444 (1950).

acetylated with Ac_2O (5 ml) and pyridine (5 ml) for 24 hr at room temperature. The mixture was evaporated by repeated co-distillation with toluene to afford a sirup which was dissolved in CH_2Cl_2 (30 ml). The CH_2Cl_2-solution was successively washed with 10% H_2SO_4, aq. $NaHCO_3$, and H_2O, dried ($CaCl_2$), and concentrated to a sirup which was crystallized from MeOH. Recrystallization from MeOH gave colorless granules (276 mg, 72%), mp 215—217°, $[\alpha]_D^{27}$ +7° (c=1.1, $CHCl_3$). NMR ($CDCl_3$) δ: 2.10, 2.13 (9H, s, 3 OAc), 3.10 (3H, s, OMs), 7.20—7.65 (5H, m, aromatic protons). TLC: *Rf* 0.41 (solvent A), 0.32 (B), 0.09 (C). *Anal.* Calcd. for $C_{26}H_{32}O_{15}S$: C, 50.65; H, 5.23. Found: C, 50.57; H, 4.97.

1,6-Anhydro-2,3,3′-tri-O-benzoyl-4′,6′-O-benzylidene-2′-O-*p*-toluenesulfonyl-β-lactose (6)——A mixture of **3** (5 g, 6.9 mmole) and *p*-toluenesulfonyl chloride (5 g, 26.2 mmole) in dry pyridine (25 ml) was stirred for 1 hr at room temperature and then kept for 4 days. After treatment with ice for decomposition of excess chloride and concentration to dryness by repeated co-distillation with toluene, the residue was dissolved in CH_2Cl_2 (100 ml). The solution was successively washed with H_2O, 10% H_2SO_4, aq. $NaHCO_3$, and H_2O, dried (Na_2SO_4), and was concentrated to afford an amorphous powder which contained a small amount of **3** on TLC (solvent B). The powder was dissolved in CH_2Cl_2 and chromatographed on a column of silica gel with $CHCl_3$–acetone (20: 1, v/v) as eluant. Evaporation of the solvent from the faster moving eluate afforded an amorphous powder which was crystallized from EtOH. Recrystallization from EtOH gave white crystals (5.35 g, 88%), mp 126—128°, $[\alpha]_D^{24}$ +133° (c=1.1, $CHCl_3$). NMR ($CDCl_3$) δ: 2.13 (3H, s, $C_6H_4CH_3$), 6.70—8.40 (24H, m, aromatic protons). TLC: *Rf* 0.87 (solvent A), 0.81 (B), 0.75 (C). *Anal.* Calcd. for $C_{47}H_{42}O_{15}S$: C, 64.23; H, 4.82. Found: C, 64.02; H, 4.70.

Evaporation of the solvent from the second effluent afforded an amorphous powder which was crystallized from EtOH. Recrystallization from EtOH gave crystals (0.3 g, 6%), mp 222—223°, indistinguishable with **3** by mixed mp, IR, and TLC.

1,6-Anhydro-4-O-(2,3-anhydro-4,6-O-benzylidene-β-D-talopyranosyl)-β-D-glucopyranose (7)——1) From **4**: To a suspension of **4** (4 g, 5 mmole) in dry MeOH (80 ml), methanolic 1M sodium methoxide (5.6 ml, 1.12 molar equivalents) was added, and the mixture was refluxed for 3 hr with stirring. After cooling to room temperature with stirring, the resulting precipitates were collected by filtration and recrystallized from MeOH to give colorless needles (0.98 g, 50%), mp 235—237°, $[\alpha]_D^{25}$ −101° (c=1.1, pyridine), the Ross' test[11] positive. TLC: *Rf* 0.03 (solvent A), 0.69 (D). *Anal.* Calcd. for $C_{19}H_{22}O_9$: C, 57.87; H, 5.62. Found: C, 57.69; H, 5.60.

The filtrate was neutralized with glacial AcOH, and, after evaporation of the solvent, the residue was acetylated with Ac_2O (15 ml) and pyridine (15 ml) overnight at room temperature. The mixture was similarly treated as for **5** to afford a sirup which showed 4 spots, *Rf* 0.48, 0.41, 0.29, and 0.19 (major) on TLC (solvent B). The sirup was dissolved in CH_2Cl_2 and chromatographed on a column of silica gel with $CHCl_3$–acetone (20: 1, v/v) as eluant. The component having *Rf* 0.29 was crystallized from MeOH. Recrystallization from MeOH gave a product (0.19 g, 6%), indistinguishable from **5** by mixed mp, IR, NMR, and TLC. The component having *Rf* 0.19 was crystallized from EtOH. Recrystallization from EtOH gave a product (0.82 g, 34%) which was indistinguishable from **8** described in the next item.

2) From **6**: Compound (**6**) (5.5 g, 6.3 mmole) was similarly treated as for **4** to afford **7** (1.64 g, 66%). After separation of **7** from the reaction mixture, the filtrate was treated as described in 1) to obtain compound (**8**) (0.70 g, 23%).

3) From **8**: Deacetylation of **8** (200 mg) with methanolic sodium methoxide in the usual way afforded **7** (142 mg, 86%).

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3-anhydro-4,6-O-benzylidene-β-D-talopyranosyl)-β-D-glucopyranose (8)——Compound (**7**) (1 g) was acetylated with Ac_2O (5 ml) and pyridine (6 ml) for 24 hr at room temperature. The mixture was similarly treated as for **5** to afford a sirup which was crystallized from EtOH. Recrystallization from EtOH gave colorless needles (1.1 g, 91%), mp 189—190°, $[\alpha]_D^{24}$ −76.5° (c=1, $CHCl_3$). NMR ($CDCl_3$) δ: 2.10, 2.14 (6H, s, 2 OAc), 7.20—7.60 (5H, m, aromatic protons). TLC: *Rf* 0.31 (solvent A), 0.19 (B), 0.03 (C). *Anal.* Calcd. for $C_{23}H_{26}O_{11}$: C, 57.74; H, 5.48. Found: C, 57.54; H, 5.32.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-β-D-idopyranosyl)-β-D-glucopyranose (9)——A mixture of **7** (1 g, 2.5 mmole) and KOH (1 g, 17.8 mmole) in H_2O (30 ml) was refluxed for 3 hr. After neutralization of excess alkali with glacial AcOH, the solution was concentrated to dryness and the residue was acetylated with Ac_2O (6 ml) and pyridine (6 ml) for 24 hr at room temperature. The mixture was similarly treated as for **5** to afford a sirup which was crystallized from EtOH. Recrystallization from EtOH gave colorless needles (1.24 g, 84%), mp 217—218°, $[\alpha]_D^{25}$ −57° (c=1.1, $CHCl_3$). NMR ($CDCl_3$) δ: 2.11, 2.13 (12H, s, 4 OAc), 7.20—7.70 (5H, m, aromatic protons). TLC: *Rf* 0.50 (solvent A), 0.35 (B), 0.13 (C). *Anal.* Calcd. for $C_{27}H_{32}O_{14}$: C, 55.86; H, 5.56. Found: C, 55.99; H, 5.37.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3,4,6-tetra-O-acetyl-β-D-idopyranosyl)-β-D-glucopyranose (10)——To a suspension of **9** (1.2 g) in dry MeOH (30 ml), Pd catalyst which was prepared from $PdCl_2$ (500 mg),[16] was added. The mixture was hydrogenated under atmospheric pressure with stirring at room temperature until theoretical amounts of hydrogen were absorbed. After removal of the catalyst and the solvent, the

16) O. Th. Schmidt and W. Staab, *Chem. Ber.*, **87**, 393 (1954).

resulting amorphous powder was acetylated with Ac_2O (6 ml) and pyridine (6 ml) as for **5** to afford a sirup which was crystallized from EtOH. Recrystallization from EtOH gave colorless needles (1.01 g, 85%), mp 146—147°, $[\alpha]_D^{25}$ −72° (c=1.2, $CHCl_3$). NMR ($CDCl_3$) δ: 2.04, 2.11, 2.13, 2.14 (18H, s, 6 OAc). TLC: *Rf* 0.49 (solvent A), 0.33 (B), 0.09 (C). *Anal.* Calcd. for $C_{24}H_{32}O_{16}$: C, 50.00; H, 5.59. Found: C, 50.08; H, 5.67.

1,2,3-Tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-idopyranosyl)-β-D-glucopyranose (11)——To a chilled solution of **10** (1 g) in dry $CHCl_3$ (14 ml) and EtOH (0.2 ml), titanium tetrachloride (2 ml) was added. Under exclusion of moisture, the mixture was refluxed for 4 hr with stirring. After cooling, the reaction mixture was poured into ice-H_2O (30 ml) with the aid of small amounts of $CHCl_3$ and ice-H_2O. The organic layer separated was washed with ice-H_2O (10 ml×3), dried ($CaCl_2$), and evaporated to dryness. The residue was dissolved in a solution of mercuric acetate (1 g) in glacial AcOH (10 ml) and the solution was kept overnight at room temperature, poured into ice-H_2O (100 ml), and the mixture was extracted with CH_2Cl_2 (20 ml×3). The extracts were combined, washed successively with aq. $NaHCO_3$ and H_2O, dried ($CaCl_2$), and evaporated to dryness. The residue was proved to be contaminated with a trace of **10** and some impurities as judged by TLC (solvent B). After dissolving in CH_2Cl_2, the solution was chromatographed on a column of silica gel with $CHCl_3$–acetone (20: 1, v/v) as eluant. Evaporation of the solvent from the faster moving eluate afforded an amorphous powder which was crystallized from EtOH. Recrystallization from EtOH gave colorless needles (0.2 g, 20%), mp 146—147°, indistinguishable with **10** by mixed mp, IR, and TLC. Evaporation of the solvent from the second effluent afforded an amorphous powder which was crystallized from EtOH. Recrystallization from EtOH gave white crystals (550 mg, 50%), mp 173—175°, $[\alpha]_D^{22}$ −33° (c=1.1, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3485 (OH). NMR ($CDCl_3$) δ: 2.03, 2.08, 2.10, 2.12 (21H, s, 7 OAc). TLC: *Rf* 0.41 (solvent A), 0.25 (B), 0.09 (C). *Anal.* Calcd. for $C_{26}H_{36}O_{18}$: C, 49.06; H, 5.70. Found: C, 48.89; H, 5.65.

4-O-β-D-Idopyranosyl-D-glucopyranose (12)——To a suspension of **11** (500 mg) in dry MeOH (10 ml), methanolic 0.5 M sodium methoxide (0.2 ml) was added at room temperature. The mixture was stirred for 1 hr under exclusion of moisture, with monitoring its complete deacetylation by TLC. Dry Amberlite IR-120 (H^+) resin was added to the reaction mixture, and the suspension was stirred for 30 min, and then filtered. The filtrate was concentrated to dryness to give a hygroscopic amorphous powder (256 mg, 95%), $[\alpha]_D^{24}$ +31° (c=1.1, H_2O). TLC: *Rf* 0.59 (solvent D). PPC: *Rf* 0.43 (solvent A), 0.24 (B), 0.13 (C). *Anal.* Calcd. for $C_{12}H_{22}O_{11}\cdot 1/2H_2O$: C, 41.03; H, 6.60. Found: C, 41.07; H, 6.95.

4-O-β-D-Idopyranosyl-D-glucopyranose Tosylhydrazone——A mixture of **12** (160 mg, 0.47 mmole) and *p*-toluenesulfonylhydrazide (88 mg, 0.47 mmole) in EtOH (3.2 ml) was refluxed for 45 min. Crystallization was induced by scratching inside of the flask and being left standing for 24 hr at room temperature. The precipitated crystals were collected by filtration and repeatedly recrystallized from MeOH–EtOH to give hygroscopic white crystals (158 mg, 66%), mp 138—139° (decomp.), $[\alpha]_D^{19}$ −31° (c=1, pyridine). TLC: *Rf* 0.80 (solvent D). *Anal.* Calcd. for $C_{19}H_{30}O_{12}N_2S\cdot 3/2H_2O$: C, 42.45; H, 6.19; N, 5.21. Found: C, 42.63; H, 6.14; N, 4.89.

PPC of Acid Hydrolyzate of Compound (12)——A mixture of **12** (50 mg) and 0.5M H_2SO_4 (3 ml) was heated at 98° for 2 hr. The hydrolyzate was neutralized with $BaCO_3$, filtered, and, after treatment with charcoal, concentrated to a thin sirup, in which glucose and idose were identified to authentic ones by PPC. PPC: *Rf* 0.42 (glucose) and 0.55 (idose) with solvent A; *Rf* 0.26 (glucose) and 0.34 (idose) with solvent B; *Rf* 0.20 (glucose) and 0.30 (idose) with solvent C.

Authentic D-idose was prepared according to the method of Sorkin and Reichstein.[13]

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