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# Deoxysugar Synthesis. II.[1] Deoxygenations of Methyl 2,6-Dibenzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside

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The 3-*p*-toluenesulfonate (**4**) of methyl 2,6-dibenzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside was treated with sodium borohydride in dimethyl sulfoxide, giving 3-deoxy- and 4-deoxy-α-D-*ribo*-hexopyranosides (**10** and **11**) in a ratio of 1:5. On the other hand, analogous treatment of the 4-*p*-toluenesulfonate (**5**) afforded the *allo*-3,4-epoxide (**19**). Further, related study was described.

In connection with our studies in the field of aminoglycoside antibiotics,[3] it deemed expedient to develop a method for the removal of a 3- or 4-hydroxyl function in 2,6-diamino-2,6-dideoxy-α-D-glucopyranoside, which is an important structural unit of aminoglycoside antibiotics.[4] Thus, among several approaches attempted along this line, the metal hydride reduction of the 3- or 4-sulfonate or 3,4-anhydride of the diaminoglucoside derivatives was found to provide certain deoxy compounds which forms the topic of this paper.

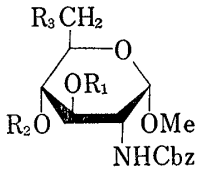
Methyl 2,6-dibenzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside (**1**) was selected for this study and prepared in quantity from the known methyl 2-benzyloxycarbonylamino-2-deoxy-6-O-tosyl-α-D-glucopyranoside[5] (**2**) in the following way.[6] Treatment of **2** with sodium azide in dimethyl sulfoxide (DMSO) gave the 6-azide (**3**) which was converted into the starting material (**1**) on reduction with lithium aluminum hydride or zinc followed by N-benzyloxycarbonylation.

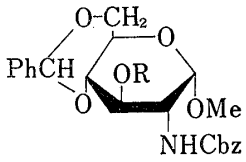
Tosylation of the dibenzyloxycarbonylaminoglucoside (**1**) with two molar equivalents of *p*-toluenesulfonyl chloride (TsCl) in pyridine afforded a mixture containing the 3-sulfonate (**4**), the 4-sulfonate (**5**), and the 3,4-disulfonate in relative ratio of 7:3:1, each of which was isolated by chromatography over silica gel. Predominant formation of the 3-sulfonate (**4**) is supposedly due to the greater activity of the 3-hydroxy group for esterification and parallels the preceding observation on other related compounds.[7] The structures of these sulfonates were clarified based on an alternative synthesis of the 3-sulfonate (**4**) which was carried out by an unequivocal process as follows. Tosylation of methyl 4,6-O-benzylidene-2-benzyloxycarbonylamino-2-deoxy-α-D-glucopyranoside[8] (**6**) gave its 3-sulfonate (**7**) which was converted into the 3,6-disulfonate (**8**) by acid hydrolysis and successive tosylation of the 6-hydroxy group. Treat-

1) Part I: S. Oida, H. Saeki, Y. Ohashi, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **23**, 1547 (1975).
2) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
3) H. Saeki, Y. Shimada, Y. Ohashi, M. Tajima, S. Sugawara, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **22**, 1145 (1974); H. Saeki, Y. Shimada, S. Sugawara, and E. Ohki, *J. Antibiotics*, **28**, 530 (1975).
4) S. Hanessian and T.H. Haskell, "The Carbohydrates, Chemistry and Biochemistry," Vol. IIA, ed. by W. Pigmand and D. Horton, Academic Press, New York & London, 1970, p. 139; S. Umezawa, "Advances in Carbohydrate Chemistry and Biochemistry," Vol. 30, ed. by R.S. Tipson and D. Horton, Academic Press, N.Y., San Francisco & London, 1974, p. 111.
5) A.B. Foster, M. Stacy, and S.V. Vardheim, *Acta Chem. Scand.*, **13**, 281 (1959).
6) *cf.* K.L. Rinehart, Jr., M. Hichens, K. Striegler, K.R. Rover, and S. Tatsuoka, *J. Am. Chem. Soc.*, **83**, 2964 (1961); W. Meyer zu Reckendorf and W.A. Bonner, *Chem. Ber.*, **96**, 2017 (1963).
7) M.W. Horner, L. Hough, and A.C. Richardson, *J. Chem. Soc.* (*C*), **1970**, 1336; R. Khan and L. Hough, *Carbohyd. Res.*, **24**, 141 (1972); Y. Takagi, T. Miyake, T. Tsuchiya, S. Umezawa, and H. Umezawa, *J. Antibiotics*, **26**, 403 (1973).
8) S. Akiya and T. Osawa, *Yakugaku Zasshi*, **76**, 1276 (1956).

ment of the disulfonate (**8**) with sodium azide gave the 6-azide (**9**) without a substitution at the 3-tosyloxy group. Reduction of **9** with lithium aluminum hydride followed by N-benzyloxycarbonylation resulted in a formation of the 3-sulfonate (**4**) which was identified with the major product obtained by tosylation of **1**.

In 1969, Bell, *et al.*[9] reported that treatment of several sulfonates with sodium borohydride in DMSO or diglyme furnishes a useful method for the reductive fission of their carbon–oxygen bonds; and this method has recently been used with carbohydrate derivatives for removal of a primary sulfonyloxy group.[10] Herein, we undertook the application of this method to these secondary sulfonates (**4** and **5**) obtained as above.




**1**: $R_1=R_2=H$, $R_3=NHCbz$
**2**: $R_1=R_2=H$, $R_3=OTs$
**3**: $R_1=R_2=H$, $R_3=N_3$
**4**: $R_1=Ts$, $R_2=H$, $R_3=NHCbz$
**5**: $R_1=H$, $R_2=Ts$, $R_3=NHCbz$
**8**: $R_1=Ts$, $R_2=H$, $R_3=OTs$
**9**: $R_1=Ts$, $R_2=H$, $R_3=N_3$

**6**: R=H
**7**: R=Ts

Ph=phenyl
Cbz=$COOCH_2C_6H_5$

Chart 1

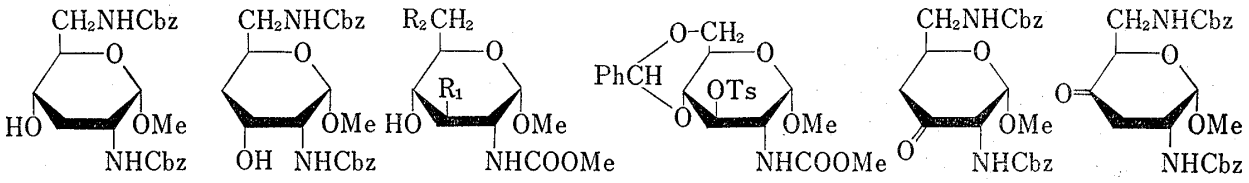
When the 3-sulfonate (**4**) was treated with sodium borohydride in DMSO at 80°, two deoxygenated compounds, methyl 2,6-dibenzyloxycarbonylamino-2,3,6-trideoxy-α-D-*ribo*-hexopyranoside (**10**) and its 2,4,6-trideoxy isomer (**11**) were obtained in a ratio of 1:5. Both were acetylated to give the corresponding acetates whose mass spectra and nuclear magnetic resonance (NMR) spectra exhibited data reflecting a molecular formula corresponding to a monodeoxy mono-O-acetyl derivative of the starting material (**1**). These analyses, however, did not give any reliable data for structural elucidation. Consequently, their structures were confirmed on the basis of the following synthetic study.

First, an authentic sample of the minor deoxygenated product (**10**) was prepared by an unequivocal route and identified. 4,6-O-Benzylidenation of methyl 2-deoxy-2-methoxycarbonylamino-α-D-glucopyranoside[11] (**12**) followed by tosylation gave the 3-sulfonate[12] (**13**). Removal of the benzylidene group from **13** with acid and treatment of the resulting 3-sulfonate (**14**) with sodium iodide in hot N,N-dimethylformamide (DMF) afforded a 3-iodide (**15**).[13] Hydrogenation of **15** over Raney nickel gave methyl 2,3-dideoxy-2-methoxycarbonylamino-α-D-*ribo*-hexopyranoside (**16**) which was identified with the sample derived from the known 4,6-O-isopropylidene derivative of **16**.[1] Compound **16** was converted into the desired compound **10** by a sequence of reactions; 6-O-tosylation, displacement of the 6-tosyloxy group with sodium azide, hydrogenation over palladium on charcoal, alkaline hydrolysis and N-benzyloxycarbonylation.

On the other hand, the structure of the major deoxygenated product (**11**) was determined as follows. Oxidation of **11** with DMSO and acetic anhydride[14] afforded a ketone (**17**) which was different from the 4-ketone (**18**) analogously prepared from the minor product (**10**). This fact suggests that the major product (**11**) was a 4-deoxy derivative of the starting material (**1**). Although the configuration at C-3 in **11** was still ambiguous, it was assumed that the formation of a 4-deoxy product can be illustrated by an initial participation of the 4-hydroxy group

9) H.M. Bell, C.W. Vanderslice, and A. Spehar, *J. Org. Chem.*, **34**, 3923 (1969).
10) H. Weidmann, N. Wolf, and W. Timpe, *Carbohyd. Res.*, **24**, 184 (1972); L.M. Lerner, *ibid.*, **36**, 392 (1974).
11) D. Ikeda, T. Tsuchiya, and S. Umezawa, *Bull. Chem. Soc., Japan*, **44**, 2529 (1971).
12) Sodium borohydride reduction of the 3-sulfonate (**13**) or displacement reaction with an iodide was attempted; but it was found that **13** was quite inert under these reaction conditions.
13) In the case of using the N-benzyloxycarbonyl analog of **14**, the displacement reaction of its 3-tosyloxy group was not successful.
14) J.D. Albright and L. Goldman, *J. Am. Chem. Soc.*, **87**, 4214 (1965).

in a displacement of the 3-tosyloxy group to give a 4,3-epoxide which is subject to a hydride attack at C-4. Therefore, we next attempted a preparation of an epoxide from the 3-sulfonate (**4**) and examined its ring opening reaction[15] in order to certify the structure of the 4-deoxy product (**11**).




**10** **11** **12**: $R_1$=OH, $R_2$=OH **13** **17** **18**

**14**: $R_1$=OTs, $R_2$=OH

**15**: $R_1$=I,[a] $R_2$=OH

**16**: $R_1$=H, $R_2$=OH

Cbz=$COOCH_2C_6H_5$

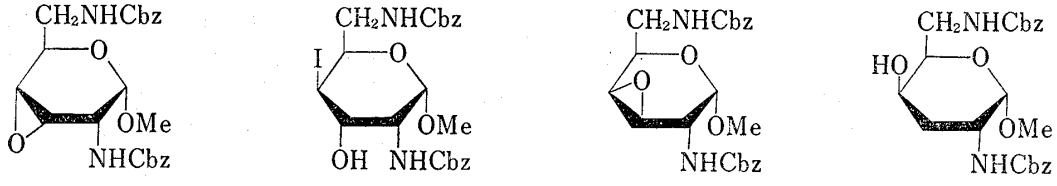
Ph=phenyl

Chart 2

*a*) configuration uncertain

Treatment of the 3-sulfonate (**4**) with sodium methoxide in methanol afforded the D-*allo*-epoxide (**19**) slowly but in a good yield. Contrary to our expectation, **19** was found to be inert to further reduction with sodium borohydride in DMSO; however, lithium aluminum hydride reduction of **19** resulted in the formation of the same 4-deoxy compound (**11**) that was obtained by sodium borohydride reduction of the 3-sulfonate (**4**). Further, treatment of the epoxide (**19**) with hydrogen iodide and hydrogenolysis of the subsequent iodohydrin (**20**) over Raney nickel afforded the same 4-deoxy compound (**11**). These results indicate that lithium aluminum hydride reduction of the *allo*-epoxide (**19**) proceeded under a hydride attack, preferentially at its 4-position (diaxial opening), to give methyl 2,6-dibenzyloxycarbonylamino-2,4,6-trideoxy-α-D-*ribo*-hexopyranoside (**11**) and the iodohydrin formation from **19** was also conducted under diaxial opening of the epoxide ring to give the 4-iodo-D-gulo derivative (**20**). Thus, the structure of the 4-deoxy compound (**11**) mainly obtained by the reduction of the 3-sulfonate (**4**) was conclusively confirmed. These facts suggest that the borohydride reduction of **4** does not always imply a simple displacement of the tosyloxy group by a hydride, due to the significant participation by the neighboring hydroxyl group. As for the formation of the 3-deoxy product (**10**) from **4**, it is not obvious so far whether it occurred *via* hydride attack of the epoxide intermediate at C-3 or by direct substitution of the 3-tosyloxy group with hydride.

In contrast to the case of the 3-sulfonate (**4**), analogous treatment of the 4-sulfonate (**5**) with sodium borohydride did not give a deoxygenated product, but resulted in a facile formation of the D-*galacto*-epoxide (**21**), suggesting that the reagent reacted simply as a base in this case. Actually, the same epoxide (**21**) was easily obtained by treatment of the 4-sulfonate (**5**) with




**19** **20** **21** **22**

Cbz=$COOCH_2C_6H_5$

Chart 3

15) N.R. Williams, "Advances in Carbohydrate Chemistry and Biochemistry," Vol. 25, ed. by R.S. Tipson and D. Horton, Academic Press, N.Y. & London, 1970, p. 109.

sodium methoxide in methanol. Lithium aluminum hydride reduction of **21** gave a new isomeric deoxy compound (**22**) which was not identical with either of the afore-mentioned deoxy compounds (**10** and **11**). Compound **22** was oxidized with DMSO and acetic anhydride or with chromium trioxide pyridine complex to give the 4-ketone (**18**). Based on these facts, compound **22** was determined to be methyl 2,6-dibenzyloxycarbonylamino-2,3,6-trideoxy-α-D-*xylo*-hexopyranoside, indicating that an attack of a hydride occurred at the 3-position of the D-*galacto*-epoxide (**21**).

## Experimental

Melting points (mp) are not corrected. Infrared (IR) spectra were recorded on a JASCO A-2 spectrometer, NMR spectra on a Hitachi-Perkin Elmer R-24 spectrometer, and mass spectra (MS) on a JEOL JMS-OlSG mass spectrometer. Optical rotations were measured on a Perkin-Elmer Model 141 automatic polarimeter in 1 dm tubes. Thin-layer chromatography (TLC) was performed on TLC-plates, Silica gel $F_{254}$ precoated, layer thickness 0.25 mm (E. Merck, AG) and spots were visualized by spraying with vanadic acid–sulfuric acid reagent or with an ethanolic solution of phosphomolybdic acid. For column chromatography on silica gel, Wakogel C-200 (Wako Pure Chemical Industries, Ltd., Osaka) was used. Solvents were removed by rotary flash evaporator at diminished pressures and usually at 35—50°.

**Methyl 6-Azido-2-benzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside** (**3**)——A stirred solution of 15.2 g of methyl 2-benzyloxycarbonylamino-2-deoxy-6-O-tosyl-α-D-glucopyranoside[4] (**2**) and 2.5 g of $NaN_3$ in 60 ml of DMSO was heated at 90—100° for 2 hr under $N_2$ atmosphere. The cooled mixture was diluted with $H_2O$ and extracted with $CHCl_3$. The extract was washed with $H_2O$, dried and evaporated *in vacuo*, leaving a crystalline mass which was recrystallized from EtOH–hexane to 8.68 g of **3**, mp 120°, fine needles, $[\alpha]_D^{20}$ +53.9° ($c$=0.38, $CHCl_3$). IR $\nu_{max}^{Nujol}$: 2100 $cm^{-1}$ (azide), no absorption of OTs. *Anal.* Calcd. for $C_{15}H_{20}O_6N_4 \cdot 1/2H_2O$: C, 50.49; H, 5.79; N, 15.70. Found: C, 50.46; H, 5.98; N, 15.57.

**Methyl 2,6-Dibenzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside** (**1**)——(i) To a stirred solution of 20.5 g of **3** in 450 ml of tetrahydrofuran was added portionwise 6.64 g of $LiAlH_4$ at 0° under $N_2$ atmosphere. After further stirring for 2 hr at 0°, aq. MeOH was added dropwise for decomposition of the excess reagent. The precipitates were filtered off and the filtrate was made basic with $Na_2CO_3$ (solid). To the solution was added dropwise 19.6 g of benzyloxycarbonyl chloride at 0° and the mixture was stirred for another 1 hr. Then, the mixture was diluted with ice-water and extracted with $CHCl_3$. The extract was washed with $H_2O$, dried and evaporated *in vacuo*, leaving a crystalline mass which was recrystallized from EtOH to 16.5 g of **1**, mp 172—174°, prisms, $[\alpha]_D^{20}$ +15.3° ($c$=0.36, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{28}O_8N_2$: C, 59.99; H, 6.13; N, 6.08. Found: C, 60.00; H, 6.15; N, 6.44.

ii) To a stirred mixture of 10 g of **3**, 100 ml of acetone, 25 ml of $H_2O$, and 30 g of zinc powder was added dropwise 10 ml of conc. HCl with cooling and vigorous stirring. After 30 min, the mixture was filtered and the filtrate was concentrated to half volume *in vacuo* then 25 ml of $H_2O$, 20 g of $Na_2CO_3$ (solid) and 15 g of benzyloxycarbonyl chloride was added successively with stirring. Stirring was continued for 3 hr and the resulting precipitates were extracted with $CHCl_3$. The extract was evaporated and recrystallized to 5.2 g of **1**.

**Tosylation of Methyl 2,6-Dibenzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside** (**1**)——To a stirred solution of 350 mg of **1** in 3 ml of pyridine was added in portions 296 mg of TsCl at room temperature and the mixture was allowed to stand overnight. After working up in the usual manner, the product was dissolved in $CHCl_3$ and was charged on a column of silica gel (10 g) packed with benzene. After washing with benzene, the column was eluted with AcOEt–benzene (1: 4, v/v). Evaporation of fast-running fractions gave a crystalline mixture (266 mg) which was recrystallized from EtOH to 45 mg of the 4-*p*-toluenesulfonate (**5**), needles, mp 170°, $[\alpha]_D^{21}$ +39.6° ($c$=2.6, $CHCl_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3460, 3400, 3270 (OH, NH), 1600, 1190, 1180 (OTs). NMR ($CDCl_3$) $\delta$ ppm: 2.41 (3H, s, $CH_3$ of tosyl), 3.25 (3H, s, $OCH_3$), 4.67 (1H, d, $J$=3 Hz, H-1). *Anal.* Calcd. for $C_{30}H_{34}O_{10}N_2S$: C, 58.62; H, 5.58; N, 4.56; S, 5.23. Found: C, 58.22; H, 5.66; N, 4.52; S, 5.37.

In succession, fractions obtained by further elution with the same solvent system were evaporated, leaving 100 mg of the pure 3-*p*-toluenesulfonate (**4**), mp 122°, prisms (from EtOH–hexane), $[\alpha]_D^{21}$ +42.1° ($c$=2.87, $CHCl_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3580 (OH), 3320 (NH), 1600, 1190, 1180 (OTs). NMR ($CDCl_3$) $\delta$ ppm: 2.37 (3H, s, $CH_3$ of tosyl), 3.28 (3H, s, $OCH_3$), 4.70 (1H, d, $J$=3 Hz, H-1). *Anal.* Calcd. for $C_{30}H_{34}O_{10}N_2S$: C, 58.62; H, 5.58; N, 4.56; S, 5.23. Found: C, 58.11; H, 5.52; N, 4.46; S, 5.09.

Further, the mother liquor left by recrystallization of these sulfonates was collected and evaporated. The residue (194 mg) was separated by preparative TLC (solvent system: AcOEt: benzene=2: 3, v/v, silica gel 2×200×200 mm), giving 34 mg of the 4-sulfonate (**5**) and 73 mg of the 3-sulfonate (**4**), along with 25 mg of the 3,4-disulfonate, powder (from hexane), mp 56—60°. The analytical sample of the 3,4-disulfonate was not obtained, but its NMR spectrum exhibited two kinds of methyl signals of the tosyl groups at $\delta$ 2.41 and 2.35.

**Methyl 4,6-O-Benzylidene-2-benzyloxycarbonylamino-2-deoxy-3-O-tosyl-α-D-glucopyranoside** (7)——To a solution of 3.1 g of methyl 4,6-O-benzylidene-2-benzyloxycarbonylamino-2-deoxy-α-D-glucopyranoside[8] (6) in 20 ml of pyridine was added 3.6 g of TsCl and the mixture was allowed to stand for 2 days at room temperature. Working up in the usual manner and recrystallization of the product (3.8 g) from EtOH gave 7, mp 119—121° (softening at 81°), $[\alpha]_D^{20}$ +5.9° ($c$=0.78, $CHCl_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1600, 1190, 1175 (OTs), NMR ($CDCl_3$) $\delta$ ppm: 2.23 (3H, s, $CH_3$ of tosyl), 3.37 (3H, s, $OCH_3$), 4.78 (1H, d, $J$=3.5 Hz, H-1). *Anal.* Calcd. for $C_{29}H_{31}O_9NS$: C, 61.14; H, 5.49; N, 2.46; S, 5.63. Found: C, 61.11; H, 5.53; N, 2.47; S, 5.58.

**Methyl 2-Benzyloxycarbonylamino-2-deoxy-3,6-di-O-tosyl-α-D-glucopyranoside** (8)——A mixture of 1.5 g of 7, 19 ml of AcOH, and 6 ml of $H_2O$ was warmed on a steam bath for 15 min, then, after cooling, diluted with 20 ml of $H_2O$ and evaporated *in vacuo* below 45°. The residue was dissolved in EtOH and hexane was added. The resulting amorphous product was tosylated with 0.7 g of TsCl in 6 ml of pyridine, giving 1.7 g of a crude 8, which was purified by silica gel chromatography (30 g of silica gel packed with $CHCl_3$, eluted with 1% MeOH–$CHCl_3$, v/v) to give 0.81 g of 8, amorphous powder, $[\alpha]_D^{20}$ +65.7° ($c$=0.77, $CHCl_3$). NMR ($CDCl_3$) $\delta$ ppm: 2.33 (3H, s, $CH_3$ of tosyl), 2.40 (3H, s, $CH_3$ of tosyl). *Anal.* Calcd. for $C_{29}H_{33}O_{11}NS_2$: C, 54.79; H, 5.23; N, 2.20; S, 10.09. Found: C, 54.62; H, 5.24; N, 2.44; S, 9.93.

**Methyl 2,6-Dibenzyloxycarbonylamino-2,6-dideoxy-3-O-tosyl-α-D-glucopyranoside** (4)——A mixture of 670 mg of 8, 100 mg of $NaN_3$, and 3 ml of DMSO was stirred at 110—120° for 1 hr under $N_2$ atmosphere. The cooled mixture was treated in the usual manner, giving 477 mg of a 6-azido-3-sulfonate (9) as a syrup. IR $\nu_{max}^{liq.}$ : 2100 $cm^{-1}$ (azide). NMR ($CDCl_3$) $\delta$: 2.30 ppm (3H, s, $CH_3$ of tosyl).

The 6-azide (9, 470 mg) thus obtained was dissolved in 3 ml of tetrahydrofuran and 100 mg of $LiAlH_4$ was added in portions with stirring and cooling. After 1.5 hr stirring, the mixture was worked up and was successively treated with 0.2 ml of benzyloxycarbonyl chloride as described earlier in the case of 3→1, affording 533 mg of a syrup which was purified by chromatography to give 301 mg of 4, mp 122°. The identification with the sample obtained before was carried out by infrared spectrometry, mixed mp and TLC.

**Sodium Borohydride Reduction of Methyl 2,6-Dibenzyloxycarbonylamino-2,6-dideoxy-3-O-tosyl-α-D-glucopyranoside** (4)——A mixture of 440 mg of 4, 60 mg of $NaBH_4$, and 4.4 ml of DMSO was stirred at 80° (bath temp.) for 1 hr under nitrogen atmosphere. After another 20 mg of $NaBH_4$ was added, the reaction was continued for 4 hr. The cooled mixture was diluted with $H_2O$ and the excess hydride was decomposed with AcOH. The mixture was extracted with $CHCl_3$ and the extract was washed with $H_2O$, dried and evaporated *in vacuo*. The residue was charged on a silica gel plate for preparative TLC (2×200×200 mm) and developed with AcOEt–benzene (1: 1, v/v). After extraction of each component with MeOH–$CHCl_3$ (3: 7, v/v) in the usual manner and evaporation of the solvent, 74 mg of the crude unchanged material (4) (fastest-moving), 20 mg of methyl 2,6-dibenzyloxycarbonylamino-2,3,6-trideoxy-α-D-*ribo*-hexopyranoside (10), mp 167—170°, needles, and 94 mg of the 2,4,6-trideoxy isomer (11), amorphous powder, $[\alpha]_D^{20}$ +41.8° ($c$=0.8, $CHCl_3$) (slowest-moving), were obtained. NMR ($CDCl_3$) $\delta$ ppm for 10: 1.2—2.3 (2H, m, $-CH_2-$), 3.20 (3H, s, $OCH_3$), 4.45 (1H, d, $J$=4 Hz, H-1); for 11: 1.3—2.0 (2H, m, $-CH_2-$), 3.25 (3H, s, $OCH_3$). Mass Spectrum $m/e$ for 10 and 11: 413 ($M^+-OCH_3$), 412 ($M^+-HOCH_3$). *Anal.* Calcd. for 10 as $C_{23}H_{28}O_7N_2$: C, 62.15; H, 6.35; N, 6.30; Found for 10: C, 61.70; H, 6.04; N, 6.43; Calcd. for 11 as $C_{23}H_{28}O_7N_2 \cdot 1/2H_2O$: C, 60.92; H, 6.45; N, 6.18; Found for 11: C, 61.06; H, 6.39; N, 6.27.

Acetylation of 10 and 11 with a mixture of $Ac_2O$ and pyridine gave the acetate of 10, mp 156—158°, needles (from EtOH) and the acetate of 11, amorphous, respectively. IR $\nu_{max}$ $cm^{-1}$: for the acetate of 10 (Nujol): 3350 (NH), 1740 (OAc), 1710, 1680, 1530 (NHCOO); for the acetate of 11 (liq.): 1740 (shoulder, OAc), 1720, 1520 (NHCOO). NMR ($CDCl_3$) $\delta$ ppm for the acetate of 10: 1.92 (3H, s, $CH_3CO$); for the acetate of 11: 2.00 (3H, s, $CH_3CO$), 3.26 (3H, s, $OCH_3$), 1.3—2.0 (2H, m, $-CH_2-$). Mass Spectrum $m/e$ for the acetate of 10: 486 ($M^+$), 455 ($M^+-OCH_3$), 454 ($M^+-H\,OCH_3$); for the acetate of 11: 486 ($M^+$), 455 ($M^+-OCH_3$), 426 ($M^+-CH_3COOH$), 395 ($M^+-OCH_3-CH_3COOH$). *Anal.* Calcd. for the acetate of 10 as $C_{25}H_{30}O_8N_2$: C, 61.72; H, 6.22; N, 5.76. Found: C, 61.31; H, 6.10; N, 5.78.

**Methyl 4,6-O-Benzylidene-2-deoxy-2-methoxycarbonylamino-3-O-tosyl-α-D-glucopyranoside** (13)——A mixture of 10 g of methyl 2-deoxy-2-methoxycarbonylamino-α-D-glucopyranoside (12), 50 g of benzaldehyde, and 20 g of $ZnCl_2$ (anhyd.) was stirred at room temperature for 2 hr. Then, after 100 ml of $H_2O$ was added to the reaction mixture, the resulting crystals were washed with petroleum ether several times and recrystallized from EtOH to give 17 g of needles, mp 201—202°. Further recrystallization afforded silky needles, mp 214—215°, $[\alpha]_D^{21}$ +44.2° ($c$=1.4, $CHCl_3$). *Anal.* Calcd. for $C_{16}H_{21}O_7N$: C, 56.63; H, 6.24; N, 4.13. Found: C, 56.69; H, 6.10; N, 4.11.

A solution of 1.9 g of the benzylidene derivative and 6.4 g of TsCl in 11 ml of pyridine was allowed to stand at room temperature overnight. Working up in the usual manner, 2.4 g of 13 was obtained as powder. The analytical sample was obtained by recrystallization from EtOH, needles, mp 164—166°, $[\alpha]_D^{21}$ −4.8° ($c$=3.1, $CHCl_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1600, 1190, 1175 (OTs). NMR ($CDCl_3$) $\delta$ ppm: 2.23 (3H, s, $CH_3$ of tosyl), 3.38 (3H, s, $OCH_3$), 3.65 (3H, s, $CH_3OCO-$), 4.76 (1H, d, $J$=4 Hz, H-1), 5.43 (1H, s, $=C\underline{H}-C_6H_5$), 7.28 (5H, s, $-C_6H_5$), 6.93, 7.16 (2H each, d, $J$=9 Hz, $C_6\underline{H}_4$ to tosyl). *Anal.* Calcd. for $C_{23}H_{27}O_9NS$: C, 55.97; H, 5.52; N, 2.84; S, 6.50. Found: C, 56.11; H, 5.48; N, 2.82; S, 6.19.

**Methyl 2-Deoxy-2-methoxycarbonylamino-3-O-tosyl-α-D-glucopyranoside** (14)——A mixture of 19 g of 13, 90 ml of AcOH, and 72 ml of $H_2O$ was warmed on a steam bath for 5 min and evaporated *in vacuo*

to dryness. The residue was dissolved in $CHCl_3$ and the solution was washed with aq. $NaHCO_3$ and successively with $H_2O$, and dried. Evaporation of the solvent left a syrup, which on washing with hexane gave 15 g of **14**, as a thick syrup. The analytical sample was obtained by chromatography over silica gel using 3% (v/v) MeOH–$CHCl_3$ as eluant. NMR ($CDCl_3$) $\delta$ ppm: 2.40 (3H, s, $CH_3$ of Ts), 3.34 (3H, s, $OCH_3$), 3.55 (3H, s, $-COOCH_3$), 4.21 (1H, d, $J=4$ Hz, H-1), 7.25, 7.78 (2H each, d, $J=9$ Hz, $C_6\underline{H}_4$ of Ts). *Anal.* Calcd. for $C_{16}H_{23}O_9NS\cdot 1/2H_2O$: C, 46.36; H, 5.84; N, 3.38; S, 7.74. Found: C, 46.57; H, 5.49; N, 3.11; S, 7.54.

**Methyl 2,3-Dideoxy-2-methoxycarbonylamino-α-D-*ribo*-hexopyranoside (16)**——A stirred mixture of 14.5 g of **14**, 4.5 g of NaI, and 75 ml of DMF was heated at 90—100° overnight. The cooled reaction mixture was diluted with $H_2O$ and, after addition of 50 g of lead acetate (solid), was shaken. After filtration, the aqueous solution was evaporated *in vacuo* and residue was extracted with boiling $CHCl_3$. The extract was dried and evaporated to give 3.25 g of the crude 3-iodide (**14**) which was recrystallized from MeOH–ether to give fine needles, mp 188—189°. *Anal.* Calcd. for $C_9H_{16}O_6NI$: C, 29.93; H, 4.47; N, 3.88; I, 35.14. Found: C, 29.80; H, 4.49; N, 3.85; I, 35.11.

A solution of 3.2 g of **15** and 47 mg of KOH in 100 ml of EtOH was stirred over 23.5 ml of Raney nickel under $H_2$ atmosphere at room temperature and 1 atm for 2 hr. The catalyst was filtered and washed with EtOH. The combined washings and filtrate were evaporated and the residue was extracted with $CHCl_3$ several times. The extract was evaporated and was recrystallized from MeOH–ether to give 1.2 g of **16**, needles, mp 170—171°, $[\alpha]_D^{22}$ +98.5° ($c=3.0$, $H_2O$). Mass Spectrum *m/e*: 204 ($M^+-OCH_3$). *Anal.* Calcd. for $C_9H_{17}O_6N$: C, 45.95; H, 7.28; N, 5.96. Found: C, 45.81; H, 7.30; N, 5.91.

A solution of methyl 2,3-dideoxy-4,6-O-isopropylidene-2-methoxycarbonylamino-α-D-*ribo*-hexopyranoside[1] in 80% aq. AcOH was heated on a steam bath for 30 min. Evaporation of the solvent *in vacuo* gave solid of **16** which was recrystallized and identified with the sample obtained as above by mixed mp, infrared spectrometry and TLC.

**Methyl 2,6-Dibenzyloxycarbonylamino-2,3,6-trideoxy-α-D-*ribo*-hexopyranoside (10)**——To an ice-cold solution of 1.2 g of **16** in 13 ml of pyridine was added dropwise a solution of 680 mg of TsCl in 2 ml of pyridine with stirring and the mixture was allowed to stand overnight in a refrigerator. Working up in the usual manner, the product was recrystallized from EtOH to give 1.46 g of the 6-*p*-toluenesulfonate, powder-like crystals, mp 138°, $[\alpha]_D^{19}$ +102° ($c=0.7$, $CHCl_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1190, 1170 (OTs). *Anal.* Calcd. for $C_{16}H_{22}O_8NS$: C, 49.40; H, 5.71; N, 3.61; S, 8.26. Found: C, 49.54; H, 5.89; N, 3.68; S, 8.53.

A stirred solution of 1.46 g of the 6-*p*-toluenesulfonate thus obtained and 730 mg of $NaN_3$ in 37 ml of DMSO was heated at 90—100° in an atmosphere of $N_2$ for 2 hr, and was diluted with cold $CHCl_3$. The solution was washed with aq. sat. NaCl, dried, and evaporated, leaving 0.8 g of the crude 6-azide which was recrystallized from EtOH–hexane to give needles, mp 115°, $[\alpha]_D^{22}$ +34.1° ($c=3.0$, $CHCl_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 2100 ($N_3$), no absorption due to OTs. *Anal.* Calcd. for $C_9H_{16}O_5N_4$: C, 41.53; H, 6.20; N, 21.53. Found: C, 42.63; H, 6.34; N, 20.77.

Through a stirred mixture of 496 mg of the 6-azide, 10 ml of MeOH, 5 ml of $H_2O$, and 300 mg of 10% Pd-C was bubbled hydrogen at room temperature for 30 min and filtered. After addition of 2 g of $Ba(OH)_2$ (solid), the mixture was refluxed for 4 hr and the cooled mixture was filtered. Benzyloxycarbonyl chloride (5 ml) was added to the cooled filtrate with stirring and the mixture was stirred for 2 hr at room temperature. The resulting crystalline mass was collected by decantation, washed with $H_2O$ and dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with aq. $NaHCO_3$ and with $H_2O$, dried and evaporated. The residue was triturated with ether and recrystallized from EtOH to give 70 mg of **10**, needles, mp 169—170°, $[\alpha]_D^{21}$ +2.9° ($c=3$, $CHCl_3$), which was identical with the sample obtained by $NaBH_4$ reduction of **4** as described earlier.

**Methyl 2,6-Dibenzyloxycarbonylamino-2,4,6-trideoxy-α-D-*erythro*-hexopyranosid-3-ulose (17)**——A solution of 40 mg of **11** in a mixture of 0.5 ml of $Ac_2O$ and 0.5 ml of DMSO was allowed to stand overnight at room temperature. The reaction mixture was diluted with $H_2O$ and the resulting precipitates were collected and dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with $H_2O$, dried and evaporated to give 38 mg of **17** as chromatographically homogeneous amorphous powder. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3300 (NH), 1730 (C=O), 1700, 1540 (NHCOO). Mass Spectrum *m/e*: 442 ($M^+$), 411 ($M^+-OCH_3$). *Anal.* Calcd. for $C_{23}H_{26}O_7N_2$: C, 62.43; H, 5.92; N, 6.33. Found: C, 62.45; H, 5.98; N, 6.19.

**Methyl 2,6-Dibenzyloxycarbonylamino-2,3,6-trideoxy-α-D-*erythro*-hexopyranosid-4-ulose (18)**——A solution of 100 mg of **10** in a mixture of 0.5 ml of $Ac_2O$ and 0.5 ml of DMSO was allowed to stand overnight at room temperature. Water was added to the solution to precipitate crystals, which revealed two spots on TLC (benzene–AcOEt, 1:1, v/v). The crude crystals were chromatographed on preparative TLC (silica gel, 2×200×200 mm) with benzene–AcOEt (1:1, v/v). Extraction with $CHCl_3$–MeOH (1:1, v/v) followed by evaporation of the solvent gave 56 mg of **18** (slower-moving component), mp 157—158° (from EtOH). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3350 (NH), 1730 (C=O), 1690, 1530 (NHCOO). Mass Spectrum *m/e*: 442 ($M^+$), 443 ($M^++1$). *Anal.* Calcd. for $C_{23}H_{26}O_7N_2$: C, 62.43; H, 5.92; N, 6.33. Found: C, 62.45; H, 5.98; N, 6.19.

As a by-product, 20 mg of the 4-O-(methylthio)methyl derivative (faster-moving) was isolated and recrystallized from EtOH to needles, mp 153—154°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3350 (NH), 1690, 1540 (NHCFO). Mass Spectrum *m/e*: 504 ($M^+$), 505 ($M^++1$) (Calcd. for $C_{25}H_{32}O_7N_2S$: 504).

**Methyl 3,4-Anhydro-2,6-dibenzyloxycarbonylamino-2,6-dideoxy-α-D-allopyranoside (19)**——To a solution of 1 g of **4** in 15 ml of MeOH was added 0.9 ml of 2N NaOMe in MeOH and the mixture was allowed to stand

for 2 days at room temperature. Then, the mixture was diluted with $H_2O$ and extracted with $CHCl_3$. The extract was dried and evaporated and the residue was triturated with hexane–ether and recrystallized from EtOH, giving 0.6 g of **19**, fine needles, mp 134—136°, $[\alpha]_D^{20}$ −9.6° ($c$=1.8, $CHCl_3$). NMR ($CDCl_3$) $\delta$ ppm: 4.60 (1H, d, $J_{1,2}$=5.5 Hz, H-1), 3.99 (1H, t, $J_{2,3}$=5.5 Hz, H-2), 4.3—3.9 (1H, m, H-5), 3.64—3.27 (2H, q, $J_{3,4}$=5.5 Hz, H-3,4), ~3.25 (2H, H-6,6'), 3.24 (3H, s, $OCH_3$). *Anal.* Calcd. for $C_{23}H_{26}O_7N_2$: C, 62.43; H, 5.92; N, 6.33. Found: C, 61.95; H, 5.79; N, 6.33.

**Methyl 2,6-Dibenzyloxycarbonylamino-2,4,6-trideoxy-α-D-*ribo*-hexopyranoside (11)**——i) A mixture of 220 mg of **19**, 300 mg of NaI, 17 mg of anhyd. NaOAc, 0.32 ml of AcOH, and 3 ml of acetone was refluxed for 3 hr, then diluted with $CHCl_3$ and washed with $H_2O$. The organic layer was dried and evaporated, leaving 242 mg of the iodohydrin (**20**) which revealed one spot on TLC.

The iodohydrin (**20**) (180 mg) thus obtained was dissolved in 5 ml of EtOH and 1 ml of Raney nickel in EtOH and an excess amount of triethylamine was added. The mixture was shaken under $H_2$ (2.5 kg/cm²) for 2 hr at room temperature, filtered, and evaporated *in vacuo* to dryness. The residue was dissolved in $CHCl_3$ and washed with $H_2O$, dried and evaporated, leaving 77 mg of **11** which was identical with the sample obtained before.

ii) To an ice-cold solution of 500 mg of **19** in 30 ml of tetrahydrofurane, 120 mg of $LiAlH_4$ was added with stirring. After having been stirred in an ice-bath for 2.5 hr, the mixture was diluted with 100 mg of $CHCl_3$ and with aq. MeOH for decomposition of the excess reagent. A fter filtration, the mixture was washed with aq. NaCl, dried and evaporated to leave 415 mg of an amorphous residue which was chromatographed on preparative TLC (silica gel, 2×200×200 mm, AcOEt–benzene, 1: 1, v/v). Thus, 138 mg of **11** was obtained as amorphous solid.

**Methyl 3,4-Anhydro-2,6-dibenzyloxycarbonylamino-2,6-dideoxy-α-D-galactopyranoside (21)**——i) A mixture of 307 mg of **5**, 57 mg of $NaBH_4$ and 3 ml of DMSO was stirred at 70° for 2.5 hr under $N_2$ atmosphere. The cooled mixture was worked up as before, giving a crystalline mass which was recrystallized from EtOH to give 140 mg of **21**, needles, mp 165°, $[\alpha]_D^{21}$ +33.3° ($c$=2.46, $CHCl_3$). NMR ($CDCl_3$) $\delta$ ppm; 4.55 (1H, d, $J$=5 Hz, H-1), 4.2—3.7 (2H, m, H-2,5), 3.30 (3H, s, $OCH_3$), 3.10 (2H, s, H-6,6'), 3.6—3.2 (2H, m, H-3,4). *Anal.* Calcd. for $C_{23}H_{26}O_7N_2$: C, 62.43; H, 5.92; N, 6.33. Found: C, 62.37; H, 5.82; N, 6.15.

ii) To a solution of 1.4 g of **5** in 35 ml of MeOH containing 1 ml of $CHCl_3$ was added 1.8 ml of 2N $NaOCH_3$ in MeOH and the mixture was stirred at room temperature for 1 hr. The resultant crystals were collected and recrystallized from EtOH to give 1.04 g of **21**.

**Methyl 2,6-Dibenzyloxycarbonylamino-2,3,6-trideoxy-α-D-*xylo*-hexopyranoside (22)**——To an ice-cold solution of 2.0 g of **21** in 30 ml of tetrahydrofurane, 1.0 g of $LiAlH_4$ was added with stirring. After stirring for 2 hr with cooling, the mixture was diluted with $CHCl_3$, then with aq. MeOH for decomposition of the reagent, and filtered. The filtrate was worked up as before and the product (1.5 g) was chromatographed over silica gel (44 g in benzene) with AcOEt–benzene (1: 9 and 3: 17, v/v), giving 200 mg of **22**, 470 mg of crude **22**, and 63 mg of an unidentified product which gave a positive ninhydrin test. The pure sample of **22** has mp 192—193°, $[\alpha]_D^{21}$ +61.2° ($c$=2.3, $CHCl_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3500 (OH), 3320 (NH), 1680, 1880, 1540 (NHCOO).

Acetylation of 50 mg of **22** with a mixture of 0.25 ml of pyridine and 0.25 ml of $Ac_2O$ gave the acetate of **22**, granules, mp 173—175° (from EtOH–hexane). NMR ($CDCl_3$) $\delta$ ppm: 2.10 (3H, s, $OCOCH_3$). IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3350 (NH), 1730 (OAc), 1690, 1680, 1540 (NHCOO). Mass Spectrum $m/e$: 486 ($M^+$), 455 ($M^+-OCH_3$), 454 ($M^+-HOCH_3$.) *Anal.* Calcd. for $C_{25}H_{30}O_8N_2$: C, 61.72; H, 6.22; N, 5.76. Found: C, 61.55; H, 6.28; N, 5.79.

**Oxidation of Methyl 2,6-Dibenzyloxycarbonylamino-2,3,6-trideoxy-α-D-*xylo*-hexopyranoside (22)**——i) A solution of 60 mg of **22** in 0.4 ml of DMSO and 0.4 ml of $Ac_2O$ was allowed to stand overnight at room temperature. Working up in the usual manner gave 70 mg of a crystalline mixture which revealed two spots on TLC. The preparative TLC on silica gel (2×100×200 mm, AcOEt–benzene, 1: 1, v/v) gave 12 mg of a 4-O-(methylthio)methyl derivative (faster-moving, mp 180—185°; $\delta$ 2.06 ppm in $CDCl_3$, $SCH_3$; Mass Spectrum $m/e$: 504, $M^+$) and 35 mg of **18** which was identified with the sample obtained before by mixed mp and infrared spectrometry.

ii) To an ice-cold, stirred mixture of 150 mg of $CrO_3$ and 5.5 ml of pyridine, 42 mg of **22** was added. Stirring was continued overnight at room temperature and the mixture was diluted with AcOEt. The resulting precipitates were filtered off and the filtrate was evaporated *in vacuo*. The residue was extracted with AcOEt and the extract was evaporated to dryness, leaving 30 mg of **18** which was recrystallized from EtOH.