BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 3619—3624 (1972)

Studies on Aminosugars. XXXI. Synthesis of 3,4-Dideoxy-3-enosides and the Corresponding 3,4-Dideoxysugars[1)]

Sumio UMEZAWA, Yasushi OKAZAKI, and Tsutomu TSUCHIYA

Department of Applied Chemistry, Faculty of Engineering, Keio University, Hiyoshi-cho, Kohoku-ku, Yokohama

(Received May 11, 1972)

As model experiments to prepare unsaturated and deoxy variants of complex aminoglycosidic antibiotics, methyl 3,4-dideoxy-α-D-*erythro*-hexopyranoside (**8**) and methyl 2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hexopyranoside (**15**) have been synthesized through the corresponding 3,4-unsaturated glycosides (**6**, **12**), which were prepared from the corresponding 3,4-di-*O*-mesyl derivatives (**5**, **11**) by treatment with sodium iodide and zinc dust in high yields. These are rare examples of 3,4-dideoxy and 3,4-unsaturated sugars.

Unsaturated sugars are drawing attention in recent years from biological point of view. However, 3,4-unsaturated sugars were rarely reported. Recently, we described the synthesis of 3′,4′-dideoxykanamycin B[2)] which is active against drug-resistant bacteria, by utilizing a 3,4-unsaturated intermediate. The present synthesis was undertaken as a fundamental experiment to see if a practical method could be worked out for converting aminoglycosidic antibiotics into their unsaturated and dehydroxylated derivatives.

Cyclic sugars having one double bond and no substituents on the unsaturated carbons can be classified into four groups, namely, 1,2- (glycals), 2,3-, 3,4- (in pyranoses) and 5,6-double bonded (in furanoses) sugars. Among them, glycals are most popular and 2,3-dideoxy-2-enoses are prepared mostly by the double bond migration of glycals. Terminal 5-enoses are also prepared fairly easily from mother sugars by applying the methods adopted to open-chain sugars. In order to introduce 2,3-unsaturation into cyclic sugars 2,3-epoxide,[3)] 2,3-episulfide,[4)] 2,3-epimine,[5)] 2,3-iodotosylates,[6)] azidotosylate,[7)] 2,3-iodoacetates,[8)] 2,3-iodohydrin,[9)] 2,3-carbonate,[10)] 2,3-thionocarbonate,[11)] 2,3-disulfonates[11)] and compounds having a deoxy group at 2 or 3 position[12)] are utilized as an intermediate.

1) A part of this paper was read by S. Umezawa at New Natural Product Syntheses, the 23rd International Congress of Pure and Applied Chemistry at Boston, U. S. A., July 28, 1971. Short communication: S. Umezawa, T. Tsuchiya, and Y. Okazaki, This Bulletin, **44**, 3494 (1971).

2) H. Umezawa, S. Umezawa, T. Tsuchiya, and Y. Okazaki, *J. Antibiot.* (Tokyo), **24**, 485 (1971).

3) D. Horton and W. N. Turner, *Tetrahedron Lett.*, **1964**, 2531.

4) J. E. Christensen and L. Goodman, *J. Amer. Chem. Soc.*, **83**, 3827 (1961).

5) R. D. Guthrie and D. King, *Carbohyd. Res.*, **3**, 128 (1966).

6) F. H. Newth, *J. Chem. Soc.*, **1956**, 471; R. U. Lemieux, E. Fraga, and K. A. Watanabe, *Can. J. Chem.*, **46**, 61 (1968).

7) R. D. Guthrie, R. D. Well, and G. J. Williams, *Carbohyd. Res.*, **10**, 172 (1969).

8) A. Rosenthal and J. N. C. Whyte, *Can. J. Chem.*, **46**, 2245 (1968).

9) S. Hanessian and N. R. Plessas, *J. Org. Chem.*, **34**, 2163 (1969).

10) A. Klemer and G. Mersmann, *Carbohyd. Res.*, **12**, 219 (1970).

11) E. Albano, D. Horton, and T. Tsuchiya, *ibid*, **2**, 349 (1966).

12) H. R. Bolliger and D. A. Prins, *Helv. Chim. Acta*, **29**, 1061 (1946); R. J. Ferrier, *J. Chem. Soc.*, **1964**, 5443.

As for the examples of 3,4-unsaturated sugars, Bock and Pedersen[13] prepared a 3,4-dideoxy-3-enopyranoside by reduction of the corresponding 3,4-dideoxy-3-eno-2-keto precursor which was prepared by double bond migration of a glycal. Ferrier and Vethaviyaser[14] prepared 3,4-dideoxy-3-enopyranosides by 1,3-azido or 1,3-thiocyano migration of the corresponding 2,3-unsaturated precursors. Hains[15] prepared benzyl 2-*O*-benzyl-3,4-dideoxy-3-eno-α-D-*glycero*-pentoside from benzyl 2-*O*-benzyl-β-L-arabinopyranoside 3,4-thionocarbonate by utilizing Corey-Winter method.[16] In this paper, we wish to describe the syntheses of the 2,6-di-*O*-benzoyl derivative (**6**) of methyl 3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside, methyl 2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hex-3-enopyranoside (**13**) and their hydrogenation products, namely, methyl 3,4-dideoxy-α-D-*erythro*-hexopyranoside (**8**) and methyl 2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hexopyranoside (**15**).

We intended to prepare some unsaturated and deoxy derivatives of 2,6-diamino-2,6-dideoxy-D-glycose because an appreciable number of useful antibiotics (kanamycin B,[17] neomycin B, C, vistamycin, butyrosin A, B *etc.*) contain the sugar as one of their constituents. Since the deoxy derivatives of aminosugars are rarely known, we initiated the synthesis of an unsaturated derivative of methyl α-D-galactopyranoside (**1**) as a model experiment, taking into consideration the presence of 3,4-*cis*-diol group in it.

Methyl 3,4-*O*-isopropylidene-α-D-galactopyranoside (**2**) prepared from **1** in a high yield was benzoylated and the isopropylidene group of the di-*O*-benzoyl derivative (**3**) was removed by 75% acetic acid to yield methyl 2,6-di-*O*-benzoyl-α-D-galactopyranoside (**4**) quantitatively.

Tipson-Cohen method,[18] which utilized vicinal disulfonic ester groups for making an unsaturated bond was then applied to this product, because the method had been proved to be applicable to cyclic sugars having *trans*-diequatorial sulfonyloxy groups by Horton *et al.*[11] Mesylation of **4**, giving a di-*O*-mesyl derivative (**5**) was followed by treatment with sodium iodide and zinc dust at 130—150°C for 1.5 hr in DMF to give a 3,4-unsaturated derivative, namely, methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (**6**) in a yield of 93%, syrup, $[\alpha]_D^{22}$ −17.3° (*c* 1, chloroform). The high yield is noteworthy in contrast with that (~50%) from[11] methyl 4,6-*O*-benzylidene-2,3-di-*O*-sulfonyl-α-D-glucopyranosides, and may suggest that the initial nucleophilic attack of iodide ion might occur at C-4 of **5** much more easily[19] than that at C-3 or C-2 of the above-mentioned sugar

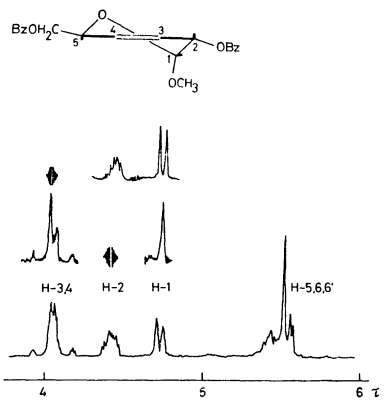

Fig. 1. The NMR spectrum of **6** in $CDCl_3$ at 100 MHz.

derivatives, though details of the mechanism of the reaction remain equivocal. The structure of **6**, was confirmed by the NMR spectrum (Fig. 1); Irradiation of a multiplet at τ 4.42 caused the H-1 doublet (τ 4.73, J~4 Hz) to collapse to a singlet, and consequently it was assigned to H-2. At the same time, 2-proton deformed AB quartet centered at τ 4.06 was assigned to double bond protons at C-3 and 4; the τ-value and the signal pattern ($J_{3,4}$~11 Hz) agreed with the structure. Irradiation of H-3,4 caused H-2 multiplet to collapse to a quartet ($J_{1,2}$ 4 Hz and ~2.5 Hz), the latter coupling being assigned to $J_{2,5}$. The magnitude of this homoallylic coupling[20] showed that H-2 and 5 stand nearly axially to the plane including the C_2–C_3=C_4–C_5 bond and the result shows that **6** is a derivative having 3,4-unsaturated α-D-*erythro* structure in the half-chair conformation. The conformation is reasonable also in view of anomeric effect.

Compound **6** was hydrogenated in an usual manner to give a 3,4-dideoxy derivative (**7**).[21] In its NMR spectrum, a 4-proton multiplet appeared at τ 7.6—8.5, indicating the presence of a ethylene protons. Removal of the protecting groups from **7** gave methyl 3,4-dideoxy-α-D-*erythro*-hexopyranoside (**8**), $[\alpha]_D^{22}$ +126° (*c* 1.1, water)

Next, an analogous sequence of reactions were applied to methyl 2,6-dideoxy-2,6-dimethoxycarbonylamino-α-D-glucopyranoside (**10**) which was prepared by methanolysis of tetra-*N*-methoxycarbonylneamine (**9**), and the di-*O*-mesyl derivative (**11**) of **10** was treated likewise as described in the preparation of **6**. Treatment of **11** with sodium iodide and zinc dust in DMF at 98°C for 3 hr gave the 3,4-unsaturated derivative (**12**), $[\alpha]_D^{20}$ −35° (*c* 0.7, methanol), in a yield of 90%. Since **11** has vicinally situated *trans*-diequatorial sulfonic ester groups, this reaction will be the first example that *trans*-diequatorial sulfonic ester groups went to unsaturation smoothly in a high yield. The smooth reaction will in part be attributable to the presence of a C-4 sulfonyloxy group, which is suscep-

13) K. Bock and C. Pedersen, *Tetrahedron Lett.*, **1969**, 2983.
14) R. J. Ferrier and N. Vethaviyaser, *J. Chem. Soc., C*, **1971**, 1907.
15) A. H. Haines, *Carbohyd. Res.*, **1**, 214 (1965).
16) E. J. Corey and R. A. E. Winter, *J. Amer. Chem. Soc.*, **85**, 2677 (1963).
17) H. Umezawa, M. Ueda, K. Maeda, K. Yagishita, S. Kondo, Y. Okami, R. Utahara, Y. Osato, K. Nitta, and T. Takeuchi, *J. Antibiot.* (Tokyo), *Ser. A*, **10**, 188 (1957); T. Ito, M. Nishio, and H. Ogawa, *ibid*, **17**, 189 (1964).
18) R. S. Tipson and A. Cohen, *Carbohyd. Res.*, **1**, 338 (1965).
19) A. C. Richardson, *ibid.*, **10**, 395 (1969).
20) L. M. Jackman and S. Sternhell, "Application of NMR spectroscopy in organic chemistry," 2nd edition, Pergamon Press (1969), p. 325.
21) This compound (**7**) has recently been synthesized by a different way: K. Bock and C. Pedersen, *Acta Chem. Scand.*, **25**, 1021 (1971).

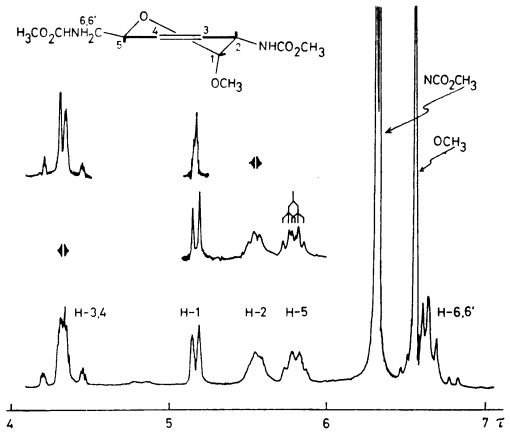

Fig. 2. The NMR spectrum of **12** in $CDCl_3$-D_2O at 100 MHz.

tible to an attack by a nucleophilic reagent, but neighboring group assistance by methoxycarbonylamino groups at C-2 and 6 should also be considered. The structure of **12** was confirmed by its NMR spectrum (Fig. 2) and double irradiation experiments (see Experimental). The coupling constants $J_{1,2}$ 4.2 Hz, $J_{3,4}$ 11 Hz, $J_{2,5}$~4 Hz (homoallylic), $J_{5,6}$ 5.3 Hz and $J_{5,6'}$ 4 Hz were confirmed. Small couplings ($J<1$ Hz) were also observed between H-3,4 and H-1, between H-3,4 and H-2, and between H-3,4 and H-5. These values indicated that **12** is in a half-chair conformation as depicted in Fig. 2.

Removal of the protecting groups from **12** gave the desired 3,4-unsaturated glycoside (**13**) as needles of monosulfate hemihydrate, $[\alpha]_D^{22}+26°$ (*c* 1, water). The NMR experiments of **13** (Fig. 3) again showed the coupling constants, $J_{1,2}$ 4.2 Hz, $J_{3,4}$ 11 Hz, $J_{2,5}$ 3.5 Hz, $J_{5,6}$ 6 Hz and $J_{5,6'}$ 4 Hz, being consistent with the half-chair conformation.

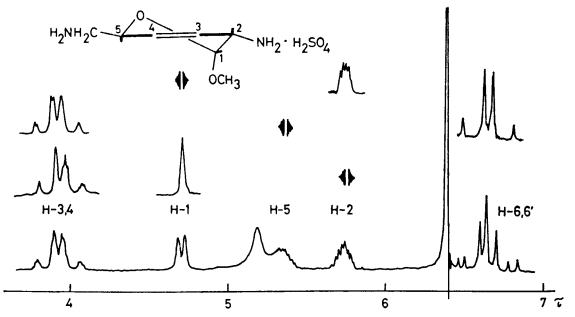

Fig. 3. The NMR spectrum of **13** in D_2O at 100 MHz.

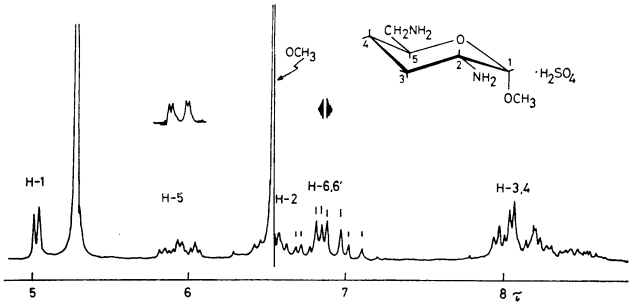

Fig. 4. The NMR spectrum of **15** in D_2O at 100 MHz.

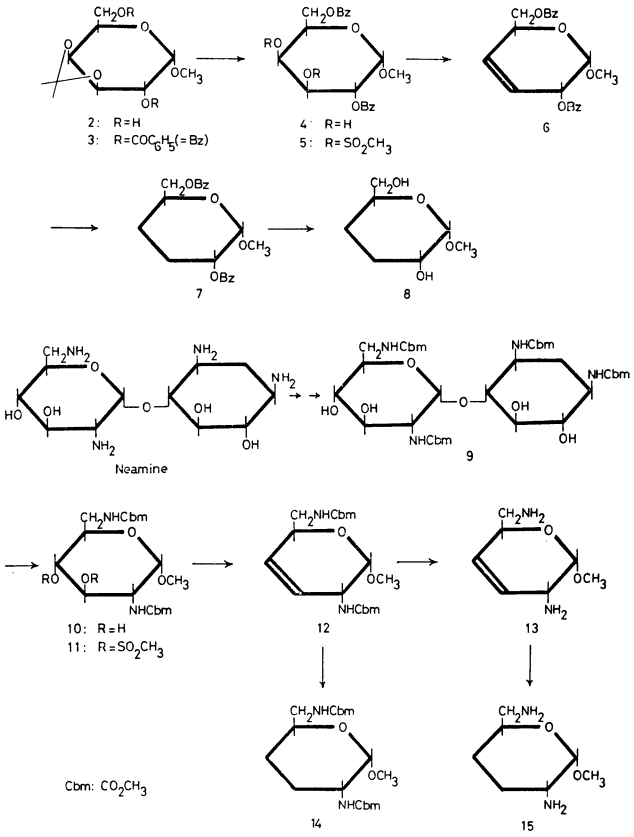

Chart 1.

Hydrogenation of **12** gave a tetradeoxy derivative (**14**), $[\alpha]_D^{19}+126°$ (*c* 0.7, methanol). Removal of the protecting groups then gave the 3,4-saturated glycoside (**15**) as needles of monosulfate hydrate, $[\alpha]_D^{22}+128°$ (*c* 1, water). The NMR spectrum was shown in Fig. 4.

Experimental

The NMR spectra were measured with a Varian A-60D or a Varian HA-100(at 100 MHz) spectrometer. Tetramethylsilane (for the solution of deuteriochloroform) and sodium 4,4-dimethyl-4-silapentane-1-sulfonate (for the solution of deuterium oxide) were used as the internal standards. Thin layer chromatography (tlc) was carried out on microscope slides coated with silica gel, and the spots were visualized with sulfuric acid.

*Methyl α-D-Galactopyranoside (**1**).* A suspension of D-galactose (5 g) in 4% hydrogen chloride in methanol (200 m*l*) was refluxed for 7 hr. Tlc (chloroform-methanol 5 : 2) of the reaction mixture showed that the starting material (R_f 0.30) disappeared and methyl α-D-galactofuranoside (R_f 0.63) and methyl α and β-D-galactopyranosides (R_f 0.47) appeared. Basic lead carbonate (30 g) was added and, after vigorous stirring, the suspension was centrifuged. The supernatant layer was evaporated to give a syrup (6 g). The syrup (22 g) was passed through a short column of Dowex 1×2 (OH form, 80 m*l*) with aid of water and the fraction containing galactopyranosides were evaporated. The resultant syrup (18.5 g) was dissolved in water and ethanol (12 m*l*) was added to cause crystallization of **1**, 7.15 g, mp ~97°C (not sharp), $[\alpha]_D^{20}+180°$ (*c* 1, water) (lit,[22] 111—

22) D. F. Mowery, Jr. and G. R. Ferrante, *J. Amer. Chem. Soc.*, **76**, 4103 (1954).

115°C, $[\alpha]_D^{20}+178°$). From the mother liquor another crop (2.73 g) was obtained. Total yield was 46%.

Found: C, 39.85; H, 7.90%. Calcd for $C_7H_{14}O_6 \cdot H_2O$· C, 39.62; H, 7.60%.

*Methyl 3,4-O-Isopropylidene-α-D-galactopyranoside (**2**).* Compound **1** was treated likewise as described by Buchanan and Saunders[23] and the crude product was extracted with ethyl acetate instead of acetone.[23] The solution was evaporated to give a syrup, which was chromatographed on a column of silica gel with ethyl acetate. From the earlier eluate, **2** was obtained in a yield of 64% (lit,[23] 47%), mp 103—105°C, $[\alpha]_D^{20}+163°$ (*c* 1.8, water) (lit,[23] 103—104°C, $[\alpha]_D^{22}+161°$ in chloroform). From the late eluate the 4,6-*O*-isopropylidene derivative was obtained in a yield of 17%.

*Methyl 2,6-Di-O-benzoyl-3,4-O-isopropylidene-α-D-galactopyranoside (**3**).* To a solution of **2** (3.0 g) in dry pyridine (60 m*l*), benzoyl chloride (4.5 m*l*) was added and the solution was allowed to stand for 30 min. After addition of water (0.8 m*l*), the solution was concentrated to approximately 10 m*l*, and to the concentrate, chloroform (200 m*l*) was added. After stirring, the organic layer was washed successively with potassium hydrogen sulfate solution, sodium hydrogen carbonate solution and water, dried over sodium sulfate and evaporated to give a syrup, 5.5 g (97%), $[\alpha]_D^{21}+134°$ (*c* 2.3, methanol); IR: 1725, 1260, 1110, 1070; 1043, 1023, 1010 (w), 995, 958 (w), 915, 865, 840, 800, 773 (w), 708 (s) cm^{-1}.

Found: 65.02; H, 6.11%. Calcd for $C_{24}H_{26}O_8$: C, 65.14; H, 5.92%.

NMR (in $CDCl_3$): τ 8.62 and 8.41 (both 3H singlets, isopropylidene), 6.60 (3H s, OCH_3), 5.2—5.7 (5H m), 4.92 (1H d, J 3.5 Hz, H-1), 4.75 (1H q, J 3.5 and 7.3 Hz, H-2), 2.3—2.7 (6H) and 1.75—2.0 (4H)(each multiplet, typical for benzoyl protons); $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 7.3 Hz.

*Methyl 2,6-Di-O-benzoyl-α-D-galactopyranoside (**4**).* A solution of **3** (1.19 g) in 75% aqueous acetic acid (10 m*l*) was heated at 90°C for 15 min. The solution was evaporated and coevaporated with toluene to give a syrup. The syrup was dissolved in ethyl acetate and the solution was washed with sodium hydrogen carbonate solution and water, dried over sodium sulfate and evaporated to give a syrup, 1.05 g (97%), which crystallized on seeding. Recrystallization was carried out from methyl ethyl ketone-petroleum ether, mp 125—127°C, $[\alpha]_D^{22}+107°$ (*c* 1, chloroform); IR (KBr): 1720, 1275, 1115, 1095; 1040, 1023, 1010 (w), 995 (w), 970, 935 (w), 915, 890, 840 (w), 800, 780, 707 (s) cm^{-1}.

Found: C, 62.92; H, 5.65%. Calcd for $C_{21}H_{22}O_8$: C, 62.68; H, 5.51%.

*Methyl 2,6-Di-O-benzoyl-3,4-di-O-mesyl-α-D-galactopyranoside (**5**).* A solution of **4** (3.09 g) and methanesulfonyl chloride (2.7 g) in pyridine (78 m*l*) was allowed to stand at room temperature overnight. On tlc with benzene-ethyl acetate (10 : 1), **4**, (R_f 0.04) and initially appeared mono-*O*-mesyl derivative (R_f 0.15) disappeared and **5** (R_f 0.40) appeared as the final product. Water (0.8 m*l*) was added and the solution was evaporated to give a syrup, which was dissolved in chloroform. The solution was washed with sodium hydrogen carbonate solution and with water, dried over sodium sulfate and evaporated to give a thick syrup, 4.21 g (98%), $[\alpha]_D^{25}+136°$ (*c* 1.3, chloroform); IR (KBr): 1725, 1360 (ν_{as} SO_2), 1270, 1175, (ν_s SO_2), 1110; 1025, 965, 930 (sh), 915 (s), 850 (s), 805, 777, 760, 710 (s).

Found: C, 49.41; H, 4.84; S, 11.43%. Calcd for $C_{23}H_{26}O_{12}S_2$: C, 49.45; H, 4.69; S, 11.48%.

NMR (in $CDCl_3$): τ 6.93 and 6.76 (both 3H singlets, SO_2CH_3), 6.57 (3H s, OCH_3), 5.2—5.75 (3H m), 4.67—4.80 (1H m), 4.55 (3H, singlet-like pattern, width at half-height was 3.5 Hz); 2.3—2.7 (6H) and 1.7—1.95 (4H) (benzoyl protons).

*Methyl 2,6-Di-O-benzoyl-3,4-dideoxy-α-D-erythro-hex-3-enopyranoside (**6**).* To a solution of **5** (2.07 g) in dry DMF (40 m*l*, dried over CaH_2), dry sodium iodide (10 g) and zinc dust (4 g) were added and the mixture was heated in an oil bath (130—150°C) with vigorous stirring for 1.5 hr. Hot chloroform was added and the mixture was filtered while hot and the solution was evaporated *in vacuo* with subsequent coevaporation with toluene. The residue obtained was extracted with chloroform and the solution was washed successively with water, sodium thiosulfate solution and with water again, dried over sodium sulfate and evaporated to give a syrup, 1.27 g (93%). On tlc with benzene-ethyl acetate (10 : 1), the syrup showed a single spot (R_f 0.66). The syrup was distilled under vacuum (0.0005 mm) on an oil bath (180—190°C) to give a liquid, $[\alpha]_D^{22}-17.3°$ (*c* 1, chloroform); IR: 1725; no peaks in 1610—1700; 1265, 1100, 707 cm^{-1}.

Found: C, 68.36; H, 5.72%. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47%.

NMR (in $CDCl_3$ at 100 MHz)(Fig. 1): τ 6.25 (3H s, OCH_3), 5.35—5.6 (3H m, H-5,6,6'), 4.73 (1H d with small splittings, $J\sim4$ Hz, H-1), 4.42 (1H m, H-2); 4.06 (2H multiplet, which is a deformed AB quartet ($J_{AB}\sim11$ Hz), H-3,4); 2.35—2.70 (6H m.) and 1.85—2.0 (4H m) (benzoyl protons).

*Methyl 2,6-Di-O-benzoyl-3,4-dideoxy-α-D-erythro-hexopyranoside (**7**).* A solution of **6** (1.36 g) in methanol (5 m*l*) was hydrogenated with palladium black and hydrogen under pressure (50 lbs/sq. inch) at room temperature for 5 hr. The reaction mixture was filtered and the solution was evaporated to give syrup, 1.22 g (88%), which crystallized on standing. This was recrystallized from ethanol, mp 70—71°C, $[\alpha]_D^{22}+56.7°$ (*c* 1, chloroform); IR (KBr): 1720, 1715, 1270, 1095; 1038, 1025, 1010, 995, 955, 900, 875, 860, 705 (s), 680 cm^{-1}.

Found: C, 68.34; H, 6.13%. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99%.

NMR (in $CDCl_3$): τ 7.6—8.6 (4H m, H-3,3', 4,4'), 6.54 (3H s, OCH_3), 5.5—6.0 (3H m, H-5,6,6'), 4.7—5.1 (2H m, H-1 and 2), 2.3—2.7 (6H) and 1.75—2.05 (4H) (benzoyl protons).

*Methyl 3,4-Dideoxy-α-D-erythro-hexopyranoside (**8**).* To a solution of **7** (4.73 g) in methanol (40 m*l*), 3 M sodium methoxide in methanol (1.4 m*l*) was added and the solution was allowed to stand for 10 min. After addition of a small amount of Amberlite IR-120 (H^+ form), the solution was filtered and evaporated to give a syrup. The aqueous solution (500 m*l*) of the syrup was shaken with a small amount of ether and the aqueous layer separated was evaporated to give a syrup, 1.84 g (89%), $[\alpha]_D^{22}+126°$ (*c* 1.1, water); IR (KBr): 1450, 1050 (s), 985 (sh), 963, 925, 900, 845, 785 (w) cm^{-1}.

NMR (in D_2O): τ 7.9—8.6 (4H m, H-3,3',4,4'), 6.53 (3H s, OCH_3), 6.05—6.5 (4H m., H-2,5,6,6'), 5.29 (1H d, $J_{1,2}$ 3.5 Hz, H-1).

*Methyl 2,6-Dideoxy-2,6-dimethoxycarbonylamino-α-D-glucopyranoside (**10**).* To a mixture of neamine tetrahydrochloride[24] (1.02 g) and basic lead carbonate (7 g) in aqueous acetone (1 : 1, 20 m*l*), methoxycarbonyl chloride (1.01 g) was added dropwise with stirring at room temperature, and stirring was continued for 3 hr. Tlc (ethyl acetate-methanol 5 : 1) of

23) J. G. Buchanan and R. M. Saunders, *J. Chem. Soc.*, **1964**, 1796.

24) K. Tatsuta, E. Kitazawa, and S. Umezawa, This Bulletin, **40**, 2371 (1967).

the reaction mixture showed that neamine (R_f 0) disappeared and the tetra-*N*-methoxycarbonyl derivative (**9**, R_f 0.45) appeared. The reaction mixture was filtered, and the mass separated was washed with hot water several times. Filtrate and the washings were combined and concentrated to a small volume. Dowex 1×2 (OH form) resin (1.5 m*l*) was added and the mixture was shaken for a while whereupon some precipitates were liberated. The mixture was filtered and the solution was evaporated and then coevaporated with benzene to give a solid (1.07 g)[25], which still contained some inorganic salts. The crude **9** (4 g) obtained above was suspended in 8% hydrogen chloride in methanol (80 m*l*) and the mixture was refluxed for 40 hr. Tlc (ethyl acetate–ethanol 8 : 1) of the resulting solution showed three spots of R_f 0.56 (**10**), 0.40 (β-anomer of **10** ?) and 0.09 (probably *N,N'*-dimethoxycarbonyl-2-deoxystreptamine; the color appeared on strong heating after spraying sulfuric acid; when the crude isolated product was treated with hot basic solution, the product liberated 2-deoxystreptamine). The pale-brown solution was neutralized with anhydrous sodium carbonate (13.5 g) under stirring and the inorganic salts precipitated were removed by centrifuging. The supernatant layer was evaporated and coevaporated with toluene and the residue obtained was extracted with *p*-dioxane (30 m*l*×3). The solution, which contained **10** and a small amount of 2-deoxystreptamine derivative described above but was free from inorganic salts, was evaporated. The methanol solution (10 m*l*) of the residue (2.3 g) was charged on a short column of alumina (50 g, Woelm acidic) and developed with ethyl acetate–methanol (1 : 1). The eluate containing **10** was evaporated to give a solid (1.54 g), which was proved to contain only a slight amount of the 2-deoxystreptamine derivative. The solid was then recrystallized from methanol to give **10** (0.79 g). The mother liquor, after evaporation, was chromatographed with methanol on a column of Dowex 1×2 (OH form, 100 m*l*), pretreated with methanol. Compound **10**, the 2-deoxystreptamine derivative (R_f 0.09) and a by-product (R_f 0.40) were eluted in this order. The fraction containing **10** was evaporated to give a solid (0.37 g). Total yield of **10** was 1.16 g (52%). The combined product was finally recrystallized from a hot mixture of methanol–acetone (1 : 4), mp 175—177°C, $[\alpha]_D^{21}$ +108° (*c* 0.7, water); IR (KBr): 1690 (s, broad), 1550, 1440, 1290, 1275, 1060; 978, 947, 925 (w), 900 (w), 835 (w), 785, 770 (w), 760 (w), 710 cm^{-1}.

Found: C, 42.60; H, 6.76; N, 8.88%. Calcd for $C_{11}H_{20}N_2O_8$: C, 42.86; H, 6.54; N, 9.09%.

NMR (in D_2O): τ 6.63 (3H s, OCH_3), 6.31 (6H s, $NHCO_2C\underline{H}_3$), 6.2—7.2 (6H), 5.23 (1H d, $J_{1,2}$ 2.3 Hz, H-1).

The fraction containing the product of R_f 0.40 was evaporated to give a solid (125 mg), $[\alpha]_D^{21}$ −9.8° (*c* 0.7, water).

*Methyl 2,6-Dideoxy-3,4-di-*O*-mesyl-2,6-dimethoxycarbonylamino-*α*-*D*-glucopyranoside (**11**).* To a solution of **10** (615 mg) in pyridine (12 m*l*), methanesulfonyl chloride (600 mg) was added and the solution was allowed to stand overnight. Tlc (benzene–ethyl acetate 1 : 3) showed that **10** (R_f 0.14) and a monomesyl derivative (R_f 0.47), which appeared in an early stage, disappeared, and **11** (R_f 0.59) appeared as the final product. Similar treatment of the solution with that described in the preparation of **5** gave a solid, 840 mg (92%), which was recrystallized from ethanol, mp 193—195 °C, $[\alpha]_D^{23}$ +94° (*c* 1.5, chloroform); IR (KBr): 1710 (sharp), 1545, 1355 (ν_{as} SO_2), 1277, 1175 (ν_s SO_2); 1055, 1030, 975, 965, 930, 908, 852, 842, 820, 777, 755, 722 cm^{-1}.

25) This experiment was performed by Yasushi Takagi of our laboratory.

Found: C, 33.84; H, 5.03; N, 6.04; S, 13.99%, Calcd for $C_{13}H_{24}N_2O_{12}S_2$: C, 33.62; H, 5.21; N, 6.03; S, 13.81%.

NMR (in $CDCl_3$): τ 6.90 and 6.77 (both 3H singlets, SO_2CH_3), 6.59 (3H s, OCH_3), 6.29 (6H s, $NHCO_2C\underline{H}_3$), 5.36 and 5.06 (both 1H triplets, J 9 Hz, H-3 and 4), 5.22 (1H d, $J_{1,2}$ 3.2 Hz, H-1); $J_{2,3}=J_{3,4}=J_{4,5}$ 9 Hz.

*Methyl 2,3,4,6-Tetradeoxy-2,6-dimethoxycarbonylamino-*α*-*D*-erythro-hex-3-enopyranoside (**12**).* To a solution of **11** (503 mg) in dry DMF (10 m*l*), dry sodium iodide (5.5 g) and zinc dust (2.5 g) were added and the mixture was heated in an oil bath (98±1°C) for 3 hr with vigorous stirring. On tlc with benzene–ethyl acetate (1 : 2), **11** (R_f 0.39) disappeared and a product (R_f 0.52) appeared. Hot chloroform (60 m*l*) was added and the reaction mixture was filtered. The solution was washed successively with water (60 m*l*), saturated sodium thiosulfate solution (30 m*l*) and with water (60 m*l*×2), dried over sodium sulfate and evaporated to give a syrup, 268 mg (90%), which crystallized on standing and recrystallized from ethanol, mp 157—159°C, $[\alpha]_D^{20}$ −35° (*c* 0.7, methanol); IR (KBr): 1695, 1540, 1250, 1105, 1055, 1008; 955 (w), 942, 915, 843, 803, 784, 733, 700 cm^{-1}.

Found: C, 48.20; H, 6.43; N, 10.02%. Calcd for $C_{11}H_{18}N_2O_6$: C, 48.17; H, 6.61; N, 10.21%.

NMR: To a solution of **12** in deuteriochloroform, deuterium oxide was added and, after storage for one day, the solution was measured at 100 MHz (Fig. 2): τ 6.69 (1H q, *J* 5.3 and 14 Hz, H-6), 6.59 (1H q, *J* 4 and 14 Hz, H-6′), 5.80 (1H incomplete quartet, H-5), 5.55 (1H m, H-2), 5.17 (1H d, H-1), 4.17—4.48 (2H m, H-3,4).

Irradiation at τ 4.32 (H-3,4) caused the H-5 multiplet to become double triplets (*J* 4, 4 and 5.3 Hz), the H-2 multiplet to become an incomplete triplet (*J*∼4 Hz) and H-1 doublet to become a sharp doublet (*J* 4.2 Hz). Irradiation at τ 5.55 (H-2) caused the H-1 doublet to collapse to a singlet and H-3,4 multiplet to collapse to an AB quartet (J_{AB} 11 Hz); as for the AB quartet, the pair in the lower field became more sharpened than that in the higher field. Irradiation at τ 5.80 (H-5) caused the H-6,6′ octet to collapse to an AB quartet (*J* 4 Hz).

*Methyl 2,6-Diamino-2,3,4,6-tetradeoxy-*α*-*D*-erythro-hex-3-enopyranoside (**13**).* To a solution of **12** (179 mg) in aqueous methanol (5 : 1, 3 m*l*), barium hydroxide octahydrate (600 mg) was added and the mixture was refluxed for 4 hr. On tlc with *n*-butanol–pyridine–water–acetic acid (6 : 4 : 3 : 1), the reaction mixture showed two spots of R_f 0.25 and 0.69 (very weak). Carbon dioxide was introduced and the resulting precipitates were removed by centrifuging. The supernatant layer was evaporated to give a residue, which was neutralized with 1 N sulfuric acid and after treatment with charcoal, the mixture (pH∼3) was concentrated to approximately 0.5 m*l*. Addition of acetone gave needles, 146 mg (85% as **13** sulfate hemihydrate), mp: gradually decomposed over than 180°C, $[\alpha]_D^{22}$ +26° (*c* 1, water).

Found: C, 31.96; H, 6.63; N, 9.94; S, 11.84%. Calcd for $C_7H_{14}N_2O_2\cdot H_2SO_4\cdot 1/2H_2O$: C, 31.69; H, 6.46; N, 10.56; S, 12.09%.

NMR (in D_2O at 100 MHz)(Fig. 3): τ 6.69 (1H q, *J* 6 and 14 Hz, H-6), 6.61 (1H q, *J* 4 and 14 Hz, H-6′), 5.74 (1H m, H-2), 5.35 (1H m, H-5), 4.70 (1H d, *J* 4.2 Hz, H-1), 3.92 (2H m, H-3,4).

Irradiation of H-1 caused the H-2 multiplet to collapse to a quartet (*J*∼1.5 and 3.5 Hz).

*Methyl 2,3,4,6-Tetradeoxy-2,6-dimethoxycarbonylamino-*α*-*D*-erythro-hexopyranoside (**14**).* A solution of **12** (416 mg) in aqueous methanol (1 : 4, 5 m*l*) was hydrogenated with palladium black and hydrogen under pressure (50 lbs/sq. inch) at 35°C overnight. On tlc with benzene–ethyl acetate (1 : 2),

both the starting material (**12**) and the product (**14**) gave the same R_f-value (0.52), however, they were distinguished each other by their coloration with anisaldehyde-sulfuric acid[26]: **12** colored orange initially and then turned brown after 1 hr and **14** colored blueviolet to yellow (after 1 hr). The mixture was filtered and evaporated to give a thick syrup, 400 mg (95%), $[\alpha]_D^{19}+126°$ (*c* 0.7, methanol); IR (KBr): 1700, 1540, 1275, 1260; 1050, 1027, 1020, 980, 948, 915, 890 (w), 784, 715 (w) cm^{-1}.

Found: C, 48.10; H, 7.42; N, 10.21%, Calcd for $C_{11}H_{20}N_2O_6$: C, 47.82; H, 7.30; N, 10.14%.

NMR (in $CDCl_3$): τ 8.0—8.6 (4H m, H-3,3',4,4'), 6.62 (3H s, OCH_3),6.31 (6H s, $NHCO_2C\underline{H}_3$), 5.35 (1H d, $J_{1,2}$ 3.5 Hz, H-1).

*Methyl 2,6-Diamino-2,3,4,6-tetradeoxy-α-*D*-*erythro*-hexopyranoside (**15**).* To a solution of **14** (414 mg) in aqueous methanol (5 : 1, 6 m*l*), barium hydroxide octahydrate (1.2 g) was added and the mixture was refluxed under stirring for 3 hr. Carbon dioxide was introduced and the mixture was treated as described in the preparation of **13** to give **15**, needles, 288 mg (94% as sulfate monohydrate). Mp: gradually decomposed over than 180°C (slightly changed at ~135°C), $[\alpha]_D^{22}+128°$ (*c* 1, water).

Found: C, 30.45; H, 7.04; N, 9.85; S, 11.62%. Calcd for $C_7H_{16}N_2O_2\cdot H_2SO_4\cdot H_2O$: C, 30.43: H, 7.30; N, 10.14; S, 11.60%.

NMR (in D_2O at 100 MHz)(Fig. 4): τ 7.9—8.7 (4H m, H-3,3',4,4'); 6.96 (1H q, *J* 8.7 and 13.5 Hz, H-6) and 6.80 (1H q, *J* 3.5 and 13.5 Hz, H-6'); these signals formed the AB part of an ABX system; 6.53 (3H s, OCH_3), 6.52 (1H m, H-2), 5.94 (1H m, H-5), 5.03 (1H d, *J* 3.3 Hz, H-1).

Irradiation at τ 6.52 (H-2) caused the H-1 doublet to collapse to a singlet and the multiplet at τ 7.9—8.7 to change. Irradiation at τ 6.87 caused the H-5 multiplet to collapse to a quartet (*J* 2 and 10.5 Hz); $J_{1,2}$ 3.3 Hz, $J_{4ax,5}$ 10.5 Hz, $J_{4eq,5}$ 2 Hz, $J_{5,6}$ 8.7 Hz, $J_{5,6'}$ 3.5 Hz, $J_{6,6'}$ 13.5 Hz.

The authors wish to thank Dr. Hiroshi Naganawa of the Institute of Microbial Chemistry for carrying out decouplings in the NMR spectra and to Mr. Saburo Nakada for the elemental analysis.

26) E. Stahl and U. Kaltenbach, *J. Chromatogr.*, **5**, 351 (1961).