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# Aminosugars. XX. Synthesis of Some Derivatives of 2-Acetamido-2-deoxy-D-mannose[1]

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Preparation of 2-acetamido-2-deoxy-D-mannose (**2**) by epimerization of the corresponding D-glucose was improved by addition of $Ni^{2+}$ ion to the equilibration system, and several derivatives of **2** were synthesized. *N*-glycosides were obtained by using ammonium chloride as a catalyst, and *p*-nitrophenyl glycoside by a fusion method. The composition of four isomers in benzylglycosidation of **2** was determined to be 66% α-pyranoside (**6**), 11% β-pyranoside, 16% α-furanoside (**5**) and 7% β-furanoside. Benzylidenation of **6** gave the corresponding 4,6-*O*-benzylidene derivative which was converted into the 3-*O*-acetate (**8**) by acetylation, and to the corresponding 2-amino-2-deoxy derivative by treatment with ethanolic potassium hydroxide. Oxidation of **6** with oxygen in the presence of platinum-charcoal and following esterification gave the corresponding methyl uronate which was derived to the di-*O*-acetate (**11**). Periodate oxidation and the following hydrogenation of **5** gave benzyl 2-acetamido-2-deoxy-α-D-lyxofuranoside which was then derived to di-*O*-acetate (**13**). Nitromethane condensation of **2** in barium hydroxide solution gave one isomeric 1-*C*-nitro-1-deoxy-D-heptitol which was converted into methyl 3-acetamido-3-deoxy-D-*glycero*-D-*galacto*-α-heptopyranoside (**18**). First-order analyses of NMR spectra of **8**, **11**, **13**, and tetra-*O*-acetate of **18** are described.

Of the 2-aminosugars found in nature 2-amino-2-deoxy-D-glucose and -D-galactose derivatives have been extensively studied.[2] However, the corresponding D-mannose derivatives have been scarcely investigated at all due to difficulty of availability from both natural and synthetic resources. In addition, 2-acetamido-2-deoxy-D-mannose (**2**) is known to be a component of *N*-acetyl-neuraminic acid,[3] and the corresponding uronic acid was recently found in polysaccharides of bacterial cell walls.[4-6] The authors studied an improved preparation of **2** by the epimerization of 2-acetamido-2-deoxy-D-glucose (**1**), and have synthesized several derivatives.

## Results and Discussion

The epimerization of **1** in alkaline mediums such as sodium or ammonium hydroxide solution has been examined,[7-9] but, the formation of **2** at the pseudo-equilibrium did not exceed *ca.* 15%. Considering the yield would increase if the equilibrium was shifted toward **2** by a complex formation with metallic ions, we examined their effect on the epimerization of **1** in ammonium hydroxide solution by PPC. Ions such as $Mg^{2+}$, $Cu^{2+}$, $Cr_2O_7^{2-}$, $Ca^{2+}$, $Zn^{2+}$, or $Ba^{2+}$ decreased and $MoO_4^{2-}$, $Ni^{2+}$, $Mn^{2+}$, $Fe^{3+}$, $Co^{2+}$, or $Pb^{2+}$ ion increased the formation of **2**. Effects of the latter were studied in detail by glc. The results given in Fig. 1 indicate that the addition of nickel ion increased markedly the yield of **2** up to 25%. Though the mechanism is not yet clear, it is obvious that the coexistence of metallic ion change more or less the equilibration between **1** and **2**. From the equilibration mixture, **2** was isolated by an improved method of Carlo *et al.*[10]

As derivatives of **2**, some *N*-glycosides were first prepared in the usual way.[11] When ethanol solution of **2** and aromatic amines (aniline, *o*-toluidine, *m*- and *p*-nitroaniline, and α- and β-naphthylamine) were refluxed

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[3] D. J. Comb and S. Roseman, *J. Amer. Chem. Soc.*, **80**, 497 (1958).

[4] H. R. Perkins, *Biochem. J.*, **83**, 5 (1962).

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[7] S. Roseman and C. T. Spivak, *J. Amer. Chem. Soc.*, **81**, 2403 (1959).

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TABLE 1. PHYSICAL CONSTANTS OF *N*-ARYL 2-ACETAMIDO-2-DEOXY-*β*-D-MANNOPYRANOSIDES (**3**).

| | R | Mp (°C) | Yield (%) | $[\alpha]_D^{23}$ (*c* methanol) | Formula | Analysis (%) Calcd C | H | N | Found C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **3a** | Phenyl | 154—155 | 62 | −163 (1.05) | $C_{14}H_{20}N_2O_5$ | 56.74 | 6.80 | 9.45 | 55.98 | 6.57 | 9.52 |
| **3b** | *o*-Tolyl | 172—173 | 56.6 | −182 (1.10) | $C_{15}H_{22}N_2O_5$ | 58.05 | 7.15 | 9.03 | 57.93 | 7.30 | 9.05 |
| **3c** | *m*-Nitrophenyl | 161—162 | 28.4 | −196 (0.84) | $C_{14}H_{19}N_3O_7H_2O$ | 46.79 | 5.91 | 11.69 | 47.10 | 5.72 | 11.51 |
| **3d** | *p*-Nitrophenyl | 188—189 | 38.2 | −220 (1.04) | $C_{14}H_{19}N_3O_7 1/3H_2O$ | 48.41 | 5.71 | 12.10 | 48.56 | 5.61 | 11.76 |
| **3e** | *β*-Naphthyl | 146—147 | 2.6 | −179 (0.95) | $C_{18}H_{22}N_2O_5 1/2H_2O$ | 60.82 | 6.83 | 7.88 | 60.81 | 6.57 | 7.78 |
| **3f** | *α*-Naphthyl | 164—165 | 8 | −154 (0.74) | $C_{18}H_{22}N_2O_5 1/3H_2O$ | 61.35 | 6.58 | 7.95 | 61.52 | 6.41 | 7.93 |

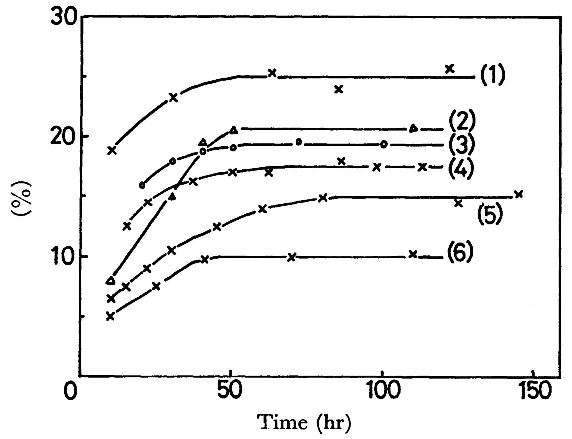

Fig. 1. Effect of metallic salt on the formation of **2** by epimerization of **1**.
(1): $NiCO_3 \cdot Ni(OH)_2$, (2): $Fe_2(SO_4)_3$, (3): $Co(OAc)_2$, (4): $(NH_4)_2MoO_4$, (5): Without metallic salt. (6): $MnSO_4$

in the presence of ammonium chloride as a catalyst, the corresponding *N*-glycosides (**3a**—**f**) were obtained as crystals. However, in the cases of *o*-nitroaniline, 2,4-dinitroaniline and diphenylamine, the starting materials were recovered. Anomeric configuration of **3a**—**f** was deduced to be *β* from their negative optical rotations. Their physical constants are summarized in Table 1. *p*-Nitrophenyl glycoside (**4**) of **2** was newly prepared from the corresponding *N*,*O*-pentaacetate by a fusion method[12] in 20.8% yield.

On the other hand, in the benzylglycosidation of **2** in the presence of boron trifluoride and hydrogen chloride carried out by Plimmer *et al.*,[13] only the corresponding α-furanoside (**5**) was isolated as the tri-*O*-acetate in a low yield after acetylation of the products. We repeated the experiment and proved the composition of the corresponding α-pyranoside, *β*-pyranoside, α-furanoside, and *β*-furanoside in the product to be 66%, 11%, 16%, and 7%, respectively. After benzylglycosidation, the reaction mixture was poured into water and extracted with ether. Concentration of the aqueous solution gave crystalline benzyl 2-acetamido-2-deoxy-α-D-mannopyranoside (**6**) in 31.7% yield, which was identical with that derived *via* 4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyrano)-2-methyl-$\Delta^2$-oxazoline.[14] The ether extracts were re-extracted with water. Evaporation of the resulting solution gave **5** in 0.5% yield. In order to elucidate the ratio of the four isomers, sirups A and B obtained from the mother liquors of **6** and **5**, respectively, were examined by glc. Sirups A and B showed four and three peaks, respectively, in the ratio given in Fig. 2, and peaks a and d were identified with **6** and **5**, respectively. The other two peaks b and c were deduced to be *β*-pyranoside and *β*-furanoside, respectively, from their retention times. The ratio of the four isomers of benzyl glycoside mentioned above was calculated from the yields of **5** and **6**, the area ratio of each peak and the amount of sirup A and B. The results are consistent with the fact that Gross *et al.*[15] isolated ethyl 2-acetamido-2-deoxy-α-D-mannopyranoside from the glycosidation mixture by column chromatography in 62% yield.

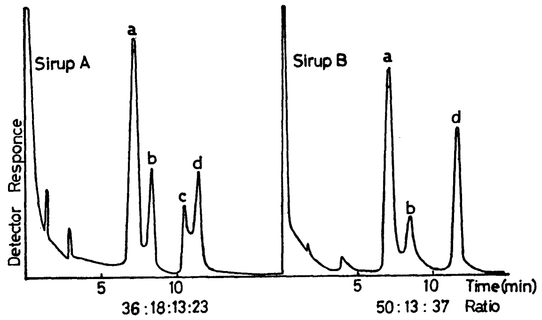

Fig. 2. Gas chromatogram of sirup A and sirup B.
(Column: 1.5% OV-17 on Chromosorb G, 2m×4mm; carrier gas: $N_2$, 60 m*l*/min; temperature: 235°C).

Benzylidenation of **6** gave benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranoside (**7**), whose structure was ascertained by the NMR spectrum of its 3-*O*-acetyl derivative (**8**). *N*-Deacetylation of **7** with potassium hydroxide in ethanol gave benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranoside (**9**). Catalytic oxidation of **6** with oxygen in the presence of platinum-charcoal gave benzyl 2-acetamido-2-deoxy-α-D-mannopyranosiduronic acid (**10**), whose structure was ascertained by the NMR spectrum of the corresponding methyl 3,4-di-*O*-acetyl-uronate (**11**). In addition, **5** was converted into benzyl 2-acetamido-2-

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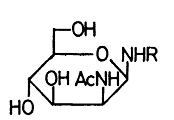
[12] M. L. Wolfrom, P. Chakravarty, and D. Horton, *J. Org. Chem.*, **30**, 2728 (1965).

[13] J. R. Plimmer, N. Pravdic, and H. G. Fletcher Jr., *ibid.*, **32**, 1982 (1967).

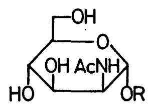
[14] N. Pravdic, T. D. Inch, and H. G. Fletcher Jr., *ibid.*, **32**, 1815 (1967).

[15] P. H. Gross, K. Brendel, and H. K. Zimmerman Jr., *Ann. Chem.*, **691**, 198 (1966).

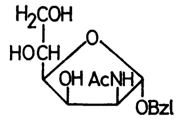
deoxy-α-D-lyxofuranoside (**12**) by periodate oxidation and the succeeding reduction with sodium borohydride. The NMR spectrum of its 3,5-di-*O*-acetyl derivative (**13**) was completely in line with its structure.



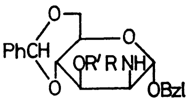
**3 a**: R=phenyl
**b**: R=*o*-tolyl
**c**: R=*m*-nitrophenyl
**d**: R=*p*-nitrophenyl
**e**: R=α-naphthyl
**f**: R=β-naphthyl



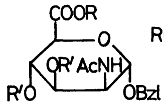
**4** R=*p*-nitrophenyl
**6** R=benzyl



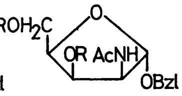
**5**



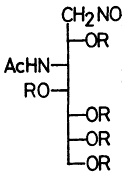
**7** R=H, R'=Ac
**8** R=R'=Ac
**9** R=R'=H



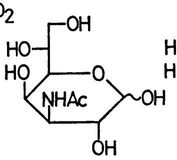
**10** R=R'=H
**11** R=$CH_3$
R'=Ac



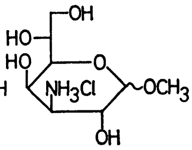
**12** R=H
**13** R=Ac



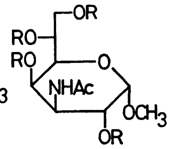
**14** R=H
**15** R=Ac



**16**



**17**



**18** R=H
**19** R=Ac

In a previous paper, one of the authors (J. Y.) reported that nitromethane condensation of D-glucose was accomplished only in water in the presence of barium hydroxide as a catalyst, but not that of **1**.[16] However, 1-*C*-nitro-1-deoxy derivative (**14**) from **2** was easily obtained under the same conditions, which gave the corresponding tetra-*O*-acetate (**15**). The configuration at *C*-2 of **14** was determined by conversion into the corresponding 3-acetamido-3-deoxy-D-heptose (**16**) by the Nef reaction, which was nearly the same as 3-acetamido-3-deoxy-D-*glycero*-D-*galacto*-heptose synthesized by the cyanohydrin method.[9] Methyl-glycosidation of **16** with 3% methanolic hydrogen chloride was accompanied by de-*N*-acetylation to give the corresponding methyl α,β-glycoside hydrochloride (**17**). *N*-Acetylation and per-acetylation of **17** gave pure *N*-acetate (**18**)[9] and *N*,*O*-pentaacetate (**19**) of the corresponding methyl α-D-glycoside, respectively. The configuration of **19** was proved to be methyl 3-acetamido-3-deoxy-D-*glycero*-D-*galacto*-α-heptopyranoside by the analysis of NMR spectrum (Fig. 3). The irradiation of NH or $H_4$ caused $H_3$ proton signals to change from an octet to a quartet. However, no change of $H_5$ proton signals indicates that $J_{4,5}$ is nearly zero. Moreover, irradiation of $H_7$ caused $H_{7'}$ proton signals to collapse to a doublet and changed the appearance of $H_2$ and $H_6$ proton signals. Assignments of $H_2$ and $H_6$ protons were also supported by the fact that their tickling caused $H_7$ and $H_{7'}$ proton signals to collapse to a doublet, and $H_5$ to a singlet. It would be rational that proton signals attached to carbons having secondary acetoxyl groups appear in lower magnetic field than that of others. NMR parameters of **8**, **11**, **13**, and **19** are summarized in Table 2. We see that coupling constants of ring protons in **8** and **11** present the characteristics of the configuration of α-D-mannopyranoside. The same value for $J_{2,3}$ and $J_{3,4}$ in **13** indicates that it exists in a twist conformation in which $C_2$ and $C_3$ atoms are displaced in the opposite sense to the plane of the other ring atoms.[17,18] Similarly, the value for $J_{2,3}$ of **19** is consistent with the di-axial relationship of the D-*glycero*-D-*galacto*-heptopyranoside configuration. It should be noted that distortion of the pyranoside-ring in **19** is suggested by the values for $J_{4,5}$ and $J_{1,2}$.

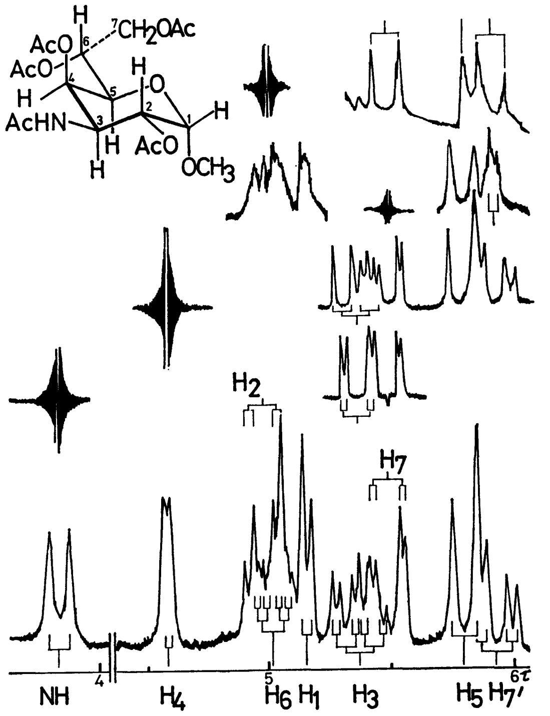


Fig. 3. NMR spectrum of methyl 3-acetamido-3-deoxy-2,4,6,7-tetra-*O*-acetyl-D-*glycero*-D-*galacto*-α-heptopyranoside (100 MHz, $CDCl_3$).

## Experimental

The melting points were determined on a sulfuric acid bath and uncorrected. Optical rotations were measured in 0.5 or 0.2-dm tubes with a Carl Zeiss Photoelectric Polarimeter. NMR spectra were recorded at 100 MHz with a JNM 4H-100 Spectrometer, with tetramethylsilane as an internal standard. Glc was carried out with a Shimadzu 4-A Chromatograph using a flame ionization detector. IR spectra were recorded with a Hitachi Model EPI-GS Spectrophotometer. Chemical shifts and coupling constants were recorded in τ and Hz scales, and IR frequencies in $cm^{-1}$.

*Examination of the Effect of Metallic Ions on the Epimerization of 2-Acetamido-2-deoxy-D-glucose (1). (i) Paper Chromatography*: An aqueous solution of **1** (10 mg) and one of the metallic salts (5 mg) described below was adjusted with

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16) J. Yoshimura and H. Ando, *Nippon Kagaku Zasshi*, **85**, 138 (1964).

17) L. D. Hall, *Chem. Ind.* (London), **1963**, 950.

18) H. Ando and J, Yoshimura, This Bulletin, **43**, 2966 (1970).

TABLE 2. CHEMICAL SHIFTS AND COUPLING CONSTANTS OF RING PROTONS OF COMPOUNDS **8**, **11**, **13**, AND **19**[a)]

| Compound | $H_1$ | $H_2$ | $H_3$ | $H_4$ | $H_5$ | $H_6$ | Other protons |
|---|---|---|---|---|---|---|---|
| **8** | 4.86(d)<br>$J_{1,2}=1.0$ | 4.62(oct)<br>$J_{2,3}=6.5$ | 4.10(q)<br>$J_{3,4}=10$ | 5.55(t)<br>$J_{4,5}=10$ | 5.69(sex)<br>$J_{5,6'}=11$<br>$J_{5,6}=4.5$ | 6.43(t)<br>5.72(q)<br>$J_{6,6'}=11$ | 1.07(NH: d, $J_{NH,H_2}=9.5$), 2.65(Ph), 4.35 (methine), 5.23 and 5.43 ($CH_2$: ABq, $J=12$), 7.85(OAc), 7.98(NAc) |
| **11** | 5.07(d)<br>$J_{1,2}=2.0$ | 5.30(m)<br>$J_{2,3}=4.5$ | 4.60(q)<br>$J_{3,4}=10$ | 4.75(q)<br>$J_{4,5}=10$ | 5.67(d)<br>— | —<br>— | 2.66(Ph), 3.64(NH: d, $J_{NH,H_2}=8.8$), 5.26 and 5.44 ($CH_2$: ABq, $J=12$), 6.27($OCH_3$), 7.99(OAc), 8.03(NAc) |
| **13** | 4.96(d)<br>$J_{1,2}=2.5$ | 5.27(sep)<br>$J_{2,3}=5.5$ | 4.41(t)<br>$J_{3,4}=5.5$ | 5.54(q)[b)]<br>$J_{4,5}=4.4$<br>$J_{4,5'}=6.1$ | 5.78[b)]<br>— | —<br>— | 2.70(Ph), 3.61(NH: d, $J_{NH,H_2}=8.8$), 5.29 and 5.49 ($CH_3$: ABq, $J=12$), 7.92 and 7.94 (OAc), 8.03(NAc) |
| **19** | 5.15(d)<br>$J_{1,2}=3.5$ | 4.98(q)<br>$J_{2,3}=11$ | 5.37(sep)<br>$J_{3,4}=2.9$ | 4.58(d)<br>$J_{4,5}=0.5$ | 5.80(d)<br>$J_{5,6}=9.4$ | 5.01(oct)<br>$J_{6,7'}=3.9$<br>$J_{6,7}=2.1$ | 3.83(NH: d, $J_{NH,H2}=8.1$), 5.48 and 5.93 ($H_{7,7'}$: $J_{7,7'}=12.2$), 6.60(OMe), 7.85, 7.88, 8.02,and 8.13 (NAc and 4×OAc) |

a) Compound **8** was measured in pyridine-$d_5$ and the others in chloroform-$d_1$.
b) The peaks of $H_4$, $H_5$, and $H_5$ were analyzed as an $AB_2$ system.

ammonia (*ca.* 1 m*l*) to pH 11, allowed to stand at room temperature for 24 hr, and examined by ppc with a borated paper of Tokyo Filter Paper No. 50A and 1-butanol–pyridine–water (6:4:3, v/v) as a developing solvent. $R_f$ values of **1** and 2-acetamido-2-deoxy-D-mannose were 0.58 and 0.16, respectively, and the amounts of both compounds were roughly estimated by visual comparison of both spots developed with aniline hydrogen phthalate. Metallic salts such as nickel carbonate, ferric sulfate, lead acetate, manganese sulfate, cobalt sulfate, and ammonium molybdate (Group A) increased, and barium hydroxide, magnesium acetate, cupric acetate, calcium acetate, zinc chloride, and potassium dichromate (Group B) decreased the formation of **2**.

*(ii) Gas-Liquid Chromatography*: A solution of a metallic salt (0.5 g) of group A, **1** (5.0 g), and concentrated aqueous ammonia (0.4 m*l*) in water (15 m*l*) was allowed to stand at room temperature. An aliquot (0.2 m*l*) of the reaction mixture was evaporated to dryness at suitable intervals, and the residue was subjected to gas-liquid chromatography after trimethylsilylation. The yield of **2** was calculated from the ratio of peak areas of **1** and **2**. The retention times of **1** and **2** were 9.2 and 5 min, respectively, under the following conditions. Column: 1.5% OV-17 on Chromosorb G, 3 m×3 mm. Carrier gas: $N_2$, 1.12 kg/cm². Temp.: 165°C.

*Preparation of 2-Acetamido-2-deoxy-*D*-mannose (2).* A solution of **1** (500 g) and nickel carbonate (25 g) in water (1.5 *l*) was adjusted to pH 11 with concentrated ammonia (*ca.* 15 m*l*), allowed to stand at room temperature for 3 days under nitrogen atmosphere, and then neutralized by addition of dry ice. Nickel ions were removed from the reaction mixture as sulfide, and the aqueous solution was evaporated. Unchanged **1** deposited during the course of the concentration was recovered by filtration. The sirup remained was dried on phosphorus pentoxide, extracted several times with hot ethanol (each 150 m*l*), and the combined extracts were evaporated after filtration of **1** precipitated. The residual sirup was crystallized from aqueous ethanol (50%)–acetone, and recrystallized from water–acetone. Yield, 100 g (20%); mp 124—126°C (lit,[10)] mp 127—128°C).

N-*Aryl 2-Acetamido-2-deoxy-β-*D*-mannopyranosyl Amines (3a—f).* A solution of **2** (200 mg), an amine (4 molar equivalent), and ammonium chloride (4 mg) in absolute ethanol (6 m*l*) was refluxed for 1 hr. Partial evaporation of ethanol (4 or 5 m*l*) and addition of ether gave crystals. *N*-Glycosides were recrystallized from ethanol–ether. The results are shown in Table 1. The compounds show characteristic IR absorptions of an amide and aromatics, respectively.

p-*Nitrophenyl 2-Acetamido-2-deoxy-α-*D*-mannopyranoside (4).* Acetylation of **2** with a mixture of acetic anhydride and pyridine gave 2-acetamido-2-deoxy-1,3,4,6-tetra-*O*-acetyl-*β*-D-mannopyranose[12)] in 53% yield. To a fused mixture of this acetate (200 mg, 0.51 mmol) and *p*-nitrophenol (287 mg, 2.1 mmol) was added a mixture of acetic acid and acetic anhydride (1 m*l*; 19: 1 v/v) containing *p*-toluenesulfonic acid (4 mg), and heated for 75 min at 120—125°C, with continuous evacuation by a water pump to remove acetic acid. A chloroform solution of the reaction mixture was then washed with water, N-sodium hydroxide, and again water, and concentrated to a sirup. To a solution of the dried sirup in absolute methanol was added metallic sodium (10 mg) under cooling and the reaction mixture was allowed to stand for 2 hr at room temperature, neutralized with Amberlite IR-120 ($H^+$), and concentrated to a sirup crystallized from ethyl acetate. Yield, 40 mg (20.8%); mp 101—102.5°C; $[\alpha]_D^{23}$ +65.4° (*c* 1.0, methanol). IR: 1640 and 1540 (NHAc), 1590 and 1505 (phenyl), and 1500 ($NO_2$).

Found: C, 48.26; H, 5.53; N, 7.92%. Calcd for $C_{14}H_{18}N_2O_8 \cdot 1/3H_2O$: C, 48.28; H, 5.40; N, 8.04%.

*Benzylglycosidation of 2-Acetamido-2-deoxy-α-*D*-mannose.* An admixture of **2** (100 g, 0.42 mol), distilled benzyl alcohol (920 m*l*) and boron trifluoride etherate (10 m*l*) was heated at 100—105°C for 1 hr under stirring and the reaction was continued for 1 hr after the addition of hydrochloric acid (5 g). The reaction mixture was evaporated *in vacuo* to give a sirup, which was dissolved in water and extracted with ether to remove benzyl alcohol. The water layer was passed through a column of Amberlite IRA-410 ($OH^-$), decolorized and concentrated to a loose sirup from which benzyl 2-acetamido-2-deoxy-α-D-mannopyranoside (**6**) was deposited. **6** was recrystallized from water; yield, 40.3 g (31%); mp 76—79°C; $[\alpha]_D^{23}$+97.5° (*c* 0.6, chloroform), (lit,[14)] mp 73—78°C; $[\alpha]_D^{20}$+97.3°). IR: 1630 and 1560 (NHAc).

Found: C, 57.99; H, 7.10; N, 4.50%. Calcd for $C_{15}H_{21}NO_6$: C, 57.86; H, 6.80; N, 4.50%.

When **6** could not be obtained as crystals, benzylidenation of a part of the dried sirup easily gave benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranoside (**7**) as crystals in *ca.* 30% yield, and hydrolysis of **7** with 60—70% aqueous acetic acid gave **6** as crystals available for seeding.

The ether extract was re-extracted with water, and the water solution was neutralized with Amberlite IRA-410 and concentrated to a sirup, which was crystallized from methanol–*n*-hexane to give benzyl 2-acetamido-2-deoxy-α-D-mannofuranoside (**5**) as crystals. Yield, 0.65 g (0.5%); mp 167—168°C; $[\alpha]^{23}_{D}+134.7°$ (*c* 0.5, methanol), (lit,[13] mp 172—173°C, $[\alpha]^{20}_{D}+132°$). IR: 1620 and 1560 (NHAc).

Found: C, 58.07; H, 6.91; N, 4.46%. Calcd for $C_{15}H_{21}NO_6$: C, 57.86; H, 6.80; N, 4.50%.

A pure sample of **5** also could be obtained by the purification of crude products *via* 5,6-*O*-isopropylidenation and de-5,6-*O*-isopropylidenation, but the isopropylidene derivative could not be crystallized.

The results of the analysis of sirup obtained from the mother liquor of **5** and **6** by glc are given in Fig. 2.

*Benzyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-α-*D*-mannopyranoside (7).* A mixture of **6** (10 g, 32 mmol), benzaldehyde (100 m*l*) and zinc chloride (21 g) was shaken for one day at room temperature, and then poured into ice–water (200 m*l*). The resulting mixture was allowed to stand for 2 hr under occasional stirring, and the water layer was decanted off. An oily liquid which remained was triturated three times with petroleum ether to give a powder, which was washed with ether and crystallized from methanol. Yield, 9.0 g (70%); mp 210—211.5°C; $[\alpha]^{23}_{D}+45.6°$ (*c* 0.8, methanol). IR: 3350 (NH), 1640 and 1520 (NHAc).

Found: C, 66.34; H, 6.42; N, 3.65%. Calcd for $C_{22}H_{25}NO_6$: C, 66.15; H, 6.31; N, 3.51%.

*Benzyl 2-Acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-*D*-mannopyranoside (8).* A sample of **7** (200 mg, 0.5 mmol) was acetylated with acetic anhydride (2 m*l*, 20 mmol) and pyridine (2 m*l*) in the usual way to give **8** quantitatively; mp 221—222°C; $[\alpha]^{23}_{D}+61.4°$ (*c* 1.0, methanol). IR: 3375 (NH), 1715 (OAc), 1670 and 1515 (NHAc).

Found: C, 65.17; H, 6.03; N, 3.26%. Calcd for $C_{24}H_{27}NO_7$: C, 65.29; H, 6.16; N, 3.17%.

*Benzyl 2-Amino-4,6-*O*-benzylidene-2-deoxy-α-*D*-mannopyranoside (9).* A solution of **7** (14.6 g) and potassium hydroxide (39 g) in ethanol (150 m*l*) was refluxed for 16 hr, and then poured into ice-water. The resulting precipitate was filtered, washed with water and recrystallized from ethanol–petroleum ether to give crystals in 78% (10.1 g) yield. Mp 133—134°C; $[\alpha]^{23}_{D}+64.7°$ (*c* 0.6, methanol). IR: 3375, 3310, 1570 ($NH_2$); NMR ($CDCl_3$): 2.69 (phenyl), 4.52 (methine), 5.24 ($H_1$; s), 5.35 and 5.56 ($-CH_2-$; ABq, $J=11.8$), 6.78 ($H_2$; d, $J_{2,3}=4.9$), 5.48 ($H_3$; q, $J_{3,4}=8.5$), 7.78 (OH and $NH_2$).

Found: C, 67.21; H, 6.84; N, 4.12%. Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92%.

*Benzyl 2-Acetamido-2-deoxy-α-*D*-mannopyranosiduronic Acid (10).* A suspension of **6** (30 g, 96 mmol) and platinum-charcoal (10%, 20 g) in water (600 m*l*) was stirred on a bath at 89—93°C with bubbling of oxygen gas. The pH of the reaction mixture was occasionally adjusted to 7.0—7.8 by the addition of sodium bicarbonate solution, and over oxidation was controlled by the addition of *sec*-butanol. The reaction was followed by tlch wit 1-butanol–water–acetic acid (4:5:1, upper phase), and stopped when a spot of the starting material disappeared. The undissolved materials were then filtered off, and the filtrate was treated with Amberlite IR-120 ($H^+$) to remove sodium ions, decolorized and concentrated to give a solid which was crystallized from water; yield, 16.0 g (51%), mp 197°C (decomp.), $[\alpha]^{23}_{D}+52.6°$ (*c* 0.5, water). IR: 1705 (COOH), 1615 and 1540 (NHAc).

Found: C, 55.67; H, 5.85; N, 4.25%. Calcd for $C_{15}H_{19}NO_7$: C, 55.38; H, 5.89; N, 4.31%.

*Methyl (Benzyl 2-Acetamido-3,4-di-*O*-acetyl-α-*D*-mannopyranoside)uronate (11).* To a solution of ***10*** (1.0 g, 3.1 mmol) in methanol (70 m*l*) was added diazomethane (*ca.* 1.1 g, 26 mmol) in ether (15 m*l*) under ice-cooling, and the reaction mixture was allowed to stand for 1 hr at room temperature, and then evaporated to give a sirup which showed two spots on a tlc. An aqueous solution of the sirup was extracted with ether to remove impurities, and concentrated. The resulting sirup was dried and acetylated by the usual method to give **11** as a sirup. Yield, 0.85 g (65%); $[\alpha]^{22}_{D}+77.3°$ (*c* 0.8, methanol). IR: 3280 (NH), 1750 (OAc), 1650 and 1540 (NHAc).

Found: C, 57.20; H, 6.49; N, 3.02%. Calcd for $C_{20}H_{25}NO_9$: C, 56.73; H, 5.95; N, 3.31%.

*Benzyl 2-Acetamido-2-deoxy-α-*D*-lyxofuranoside (12).* To a solution of **5** (1.0 g, 3.2 mmol) in water (16 m*l*) was added sodium metaperiodate (0.76 g, 3.5 mmol) in water (10 m*l*), and the reaction mixture was allowed to stand for 1 hr at room temperature and then sodium borohydride (0.21 g, 5.5 mmol) in water (5 m*l*) was added dropwise under stirring. The resulting solution was deionized with Amberlite IR-120B and IRA-410 and concentrated. The sirup obtained was decolorized in methanol. Evaporation of methanol gave crystals which was recrystallized from methanol–petroleum ether. Yield, 0.8 g (90%); mp 127—128°C; $[\alpha]^{23}_{D}+76.7°$ (*c* 0.26, methanol); IR: 1635 and 1540 (NHAc).

Found: C, 59.39; H, 6.74; N, 4.94%. Calcd for $C_{14}H_{19}NO_5$: C, 59.77; H, 6.81; N, 4.98%.

*Benzyl 2-Acetamido-3,5-di-*O*-acetyl-2-deoxy-α-*D*-lyxofuranoside (13).* Acetylation of **12** (99 mg, 0.35 mmol) with acetic anhydride (1 m*l*, 10 mmol) and pyridine (1 m*l*) gave **13** in 78.6% (102 mg) yield. The substance was recrystallized from ether; mp 122—124°C; $[\alpha]^{21}_{D}+99.8°$ (*c* 0.6, methanol); IR: 3280 (NH), 1750 (OAc), 1650 and 1540 (NHAc).

Found: C, 59.39; H, 6.35; N, 3.79%. Calcd for $C_{18}H_{23}NO_7$: C, 59.18; H, 6.33; N, 3.83%.

*3-Acetamido-1,3-dideoxy-1-*C*-nitro-*D-glycero-D-galacto-*heptitol (14).* To a mixed solution of **2** (40 g, 167 mmol) in water (80 m*l*) and nitromethane (100 m*l*, 1.85 mol) was added barium hydroxide octahydrate (112 g, 356 mmol) under cooling and stirring. The reaction mixture was stirred for 1 hr at 40—45°C. Ethanol (120 m*l*) was then added to precipitate barium salts. The mixture was allowed to stand overnight in a refrigerator, and the supernatant layer was decanted off, from which **2** was recovered (11.6 g, 29%). The precipitate was dissolved in 2N-acetic acid, and barium ions were immediately removed by addition of 2N-sulfuric acid and filtration. The filtrate was concentrated to give **15** as crystals. When **15** could not be obtained as crystals, the sirup was dissolved in water (50 m*l*) and impurities were extracted with ethyl acetate. The solution was then concentrated again to give **15** as crystals. The product was recrystallized from water–ethanol; yield, 8.4 g (26%); mp 213—214°C (decomp.); $[\alpha]^{23}_{D}-50.1°$ (*c* 1.2, water). IR: 1620 and 1550 (NHAc), 1520 ($NO_2$).

Found: C, 38.02; H, 6.24; N, 10.20%. Calcd for $C_9H_{18}N_2O_8$: C, 38.30; H, 6.43; N, 9.93%.

*3-Acetamido-2,4,6,7-tetra-*O*-acetyl-1-*C*-nitro-1,3-dideoxy-*D-glycero-D-galacto-*heptitol (12).* To a suspension of **14** (100 mg, 0.36 mmol) in acetic anhydride (2 m*l*, 19 mmol) was added one drop of concentrated sulfuric acid. The mixture was allowed to stand overnight at room temperature, poured into ice-water (30 m*l*) and extracted with chloroform. The extract was washed with water thorougly and concentrated to give crystals quantitatively, which were recrystallized from ethanol–ether; mp 131—132°C; $[\alpha]_D^{23}-13.7°$ (*c* 1.04, methanol). IR: 1745 (OAc), 1650 and 1550 (NHAc), 1520 and 1365 ($NO_2$).

Found: C, 45.98; H, 5.80; N, 5.68%. Calcd for $C_{19}H_{28}N_2O_{13}$: C, 46.35; H, 5.73; N, 5.69%.

*3-Acetamido-3-deoxy-*D-glycero-D-galacto-*heptose (16).* A solution of **14** (4.0 g, 14.2 mmol) in 2N-sodium hydroxide (50 m*l*) was added dropwise to 14.4N-sulfuric acid (100 m*l*) at a temperature controlled under 2°C. Ice–water (250 m*l*) was poured into the reaction mixture in order to prevent temperature rise. Barium carbonate (284 g) was added to remove sulfate ions, and the mixture was stirred for 6 hr. After the precipitate was filtered off, the filtrate was treated with Amberlite IR-120 ($H^+$), concentrated to give a residue which was crystallized and recrystallized from water–ethanol. Yield, 3.07 g (86%); mp 215—216°C (decomp.); $[\alpha]_D^{23}+162°$ (5 min), +116° (24 hr), (*c* 0.48, water), (lit,[9] mp 223—225°C, $[\alpha]_D+150° \rightarrow +110°$). IR: 1605 and 1555 (NHAc).

Found: C, 42.74; H, 6.81; N, 5.53%. Calcd for $C_9H_{17}NO_7$: C, 43.02; H, 6.82; N, 5.58%.

*Methyl 3-Amino-3-deoxy-*D-glycero-D-galacto-*α,β-heptopyranoside Hydrochloride (17).* A suspension of dried **16** (1.5 g, 48 mmol) and Drierite (1 g) in methanol (46 m*l*) containing hydrochloric acid (3%) was refluxed for 50 hr, and filtered and the filtrate was evaporated. Hydrochloric acid was completely removed by evaporation three times of a methanol solution of the residue and the residue was crystallized from methanol–ethyl acetate. Yield, 0.90 g (55.8%); mp 212°C (decomp.); $[\alpha]_D^{22}+126°$ (*c* 0.5, water). IR: 1605 and 1520 ($NH_3^+$).

Found: C, 36.71; H, 7.01; N, 5.62%. Calcd for $C_8H_{17}NO_6 \cdot HCl$: C, 37.00; H, 6.99; N, 5.39%.

*Methyl3-Acetamido-3-deoxy-*D-glycero-D-galacto-*α-heptopyranoside (18).* To a solution of **17** (330 mg, 1.27 mmol) in methanol (30 m*l*) containing 31 mg (1.35 mmol) of sodium metal was added acetic anhydride (0.14 m*l*) under stirring. After standing for 1 hr at room temperature, the reaction mixture was treated with silver carbonate (0.3 g) and filtered. The filtrate was deionized with Amberlite IR-120B ($H^+$), and evaporated to give crystals (326 mg, 97%), which were recrystallized from methanol–ethyl acetate–petroleum ether. Yield, 200 mg (60%): mp 224°C (decomp.); $[\alpha]_D^{22}+203°$ (*c* 0.5, water), (lit,[9] mp 233—236°C, $[\alpha]_D^{23}+207°$). IR: 3300 (NH), 1640 and 1550 (NHAc).

Found: C, 45.55; H, 7.33; N, 5.56%. Calcd for $C_{10}H_{19}NO_7$: C, 45.28; H, 7.22; N, 5.28%.

*Methyl 3-Acetamido-3-deoxy-2,4,6,7-tetra-*O*-acetyl-*D-glycero-D-galacto-*α-heptopyranoside (19).* Acetylation of **17** by the usual method gave the corresponding tetraacetate which was recrystallized from ether, in 53.8% yield. Mp 184—186°C; $[\alpha]_D^{21}+172°$ (*c* 1.01, methanol). IR: 3350 (NH), 1740 (OAc), 1660 and 1535 (NHAc).

Found: C, 49.61; H, 6.34; N, 3.00%. Calcd for $C_{18}H_{27}NO_{11}$: C, 49.88; H, 6.28; N, 3.23%.

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