The Synthesis of Purpurosamine B Derivatives

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Synopsis. Purpurosamine B and its 6-epimer have been found in antibiotic gentamicin C_2 and fortimicin A respectively. Methyl 2,6-di-*N*-acetyl-α-purpurosaminide B and its corresponding 6-epimer have been synthesized from methyl 2-acetamido-2,3,4-trideoxy-α-D-*erythro*-hexodialdo-1,5-pyranoside.

In a continuation of preceding papers,[1,2] the synthesis of methyl 2,6-di-*N*-acetyl-α-purpurosaminide B (**6**) and its 6-epimer (**8**) will be described in the present paper. The nitromethane addition of methyl 2-acetamido-2,3,4-trideoxy-α-D-*erythro*-hexodialdo-1,5-pyranoside[2] (**1**) gave a mixture of two diastereomers, methyl 2-acetamido-2,3,4,7-tetradeoxy-7-nitro-α-D-*ribo*- and -β-L-*lyxo*-heptopyranosides, in a yield of 49%. The catalytic hydrogenation of the mixture, followed by treatment with benzyloxycarbonyl chloride in pyridine afforded 7-benzyloxycarbonylamino derivatives in a yield of 69%. The mesylation of the derivatives gave a mixture of 6-*O*-mesyl derivatives (**2**) in a yield of 89%.

Compound **2** was converted to aziridine derivatives by treatment with sodium isopropoxide. When the derivatives reacted with benzyloxycarbonyl chloride in dioxane and subsequently treated with HCl in dioxane, methyl 2-acetamido-6-(benzyloxycarbonylamino)-7-chloro-2,3,4,6,7-pentadeoxy-α-D-*ribo*-heptopyranoside (**3**) and the corresponding β-L-*lyxo* derivative (**4**) were obtained in 23 and 35% yields respectively.

The dehalogenation of **3** with tributylstannane gave methyl 2-acetamido-6-(benzyloxycarbonylamino)-2,3,4,6,7-pentadeoxy-α-D-*ribo*-heptopyranoside (**5**) in a yield of 84%; this was then converted to methyl 2,6-di-*N*-acetyl-α-purpurosaminide B (**6**), which was found to be identical with an authentic sample.[3]

Analogous reaction sequences of **4** gave methyl 2,6-di-*N*-acetyl-6-*epi*-α-purpurosaminide B (**8**).

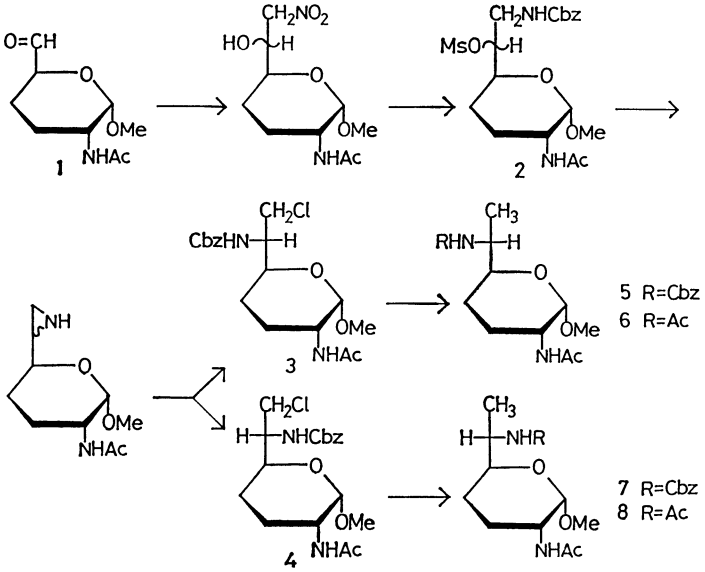
Experimental[4]

A Mixture of Methyl 2-Acetamido-7-(benzyloxycarbonylamino)-2,3,4,7-tetradeoxy-6-O-mesyl-α-D-ribo- and -β-L-lyxo-heptopyranosides (2). A 1.34-g portion of methyl 2-acetamido-2,3,4-trideoxy-α-D-*erythro*-hexodialdo-1,5-pyranoside[2] (**1**) was treated with nitromethane (0.62 ml) in the presence of sodium methoxide at an ambient temperature for 40 h, as has been described in the preceding paper,[2] without recrystallization, to give 845 mg (49%) of a mixture of the two diastereomers.

The product was catalytically hydrogenated and subsequently treated with benzyloxycarbonyl chloride to give 805 mg (69%) of 7-*N*-benzyloxycarbonyl derivatives. The derivatives were mesylated analogously to the method described in the preceding paper[2] to give 872 mg (89%) of **2**: mp 123—126 °C.

Found: C, 51.25; H, 6.27; N, 6.34; S, 6.90%. Calcd for $C_{19}H_{28}N_2SO_8$: C, 51.34; H, 6.35; N, 6.30; S, 7.21%.

Methyl 2-Acetamido-6-(benzyloxycarbonylamino)-7-chloro-2,3,4,6,7-pentadeoxy-α-D-ribo-heptopyranoside (3) and -β-L-lyxo-heptopyranoside (4). To a solution of sodium isopropoxide (0.11 g of Na in 10 ml of isopropyl alcohol) in dioxane (5 ml), **2** (780 mg) was added, and the mixture was heated under reflux for 2 h. The solution was then concentrated, and benzyloxycarbonyl chloride (1.4 ml of 30% toluene solution) was added to a solution of the residue in dioxane (10 ml). After 3 h, dioxane (5 ml) containing 3% HCl was added to the mixture. After 1 h, the mixture was neutralized with Amberlite IRA-400(OH^-) and concentrated. The residue was purified on a silica-gel column using 3:2 (v/v) 2-butanone–toluene. Fractions homogeneous on TLC (R_f 0.43) in the same solvent were combined and concentrated. The residue was recrystallized from $CHCl_3$–



Scheme 1.

ether to give 139 mg (23%) of **3**: mp 196—197 °C; $[\alpha]_D^{20}$ +76.7° (*c* 0.43, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.98 (s, 3, NAc), 3.42 (s, 3, OCH_3), 4.59 (d, 1, J=3.4 Hz, H-1), 5.78 (d, 1, J=8.5 Hz, NH-2).

Found: C, 56.36; H, 6.47; N, 7.18; Cl, 9.00%. Calcd for $C_{18}H_{25}N_2ClO_5$: C, 56.17; H, 6.55; N, 7.28; Cl, 9.21%.

Fractions homogeneous on TLC (R_f 0.46) were combined and concentrated, and the residue was recrystallized from ether to give 211 mg (35%) of **4**: mp 145—146 °C; $[\alpha]_D^{20}$ +59.3° (*c* 1.03, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.97 (s, 3, NAc), 3.40 (s, 3, OCH_3), 4.59 (d, 1, J=3.4 Hz, H-1), 5.66 (d, 1, J=10 Hz, NH-2).

Found: C, 55.90; H, 6.50; N, 7.47; Cl, 9.45%. Calcd for $C_{18}H_{25}N_2ClO_5$: C, 56.17; H, 6.55; N, 7.28; Cl, 9.21%.

*Methyl 2-Acetamido-6-(benzyloxycarbonylamino)-2,3,4,6,7-pentadeoxy-α-*D-ribo-*heptopyranoside (**5**).* To a solution of **3** (74 mg) in dioxane (5 ml), tributylstannane (1.0 ml) and a small amount of α,α′-azobisisobutyronitrile were added under a N_2 atmosphere. After 7 h at 80 °C, the mixture was concentrated and the residue was purified on a silica-gel column using 3:2 (v/v) 2-butanone–toluene to give 56 mg (84%) of **5**: mp 195—196 °C; $[\alpha]_D^{20}$ +98.4° (*c* 0.95, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.97 (s, 3, NAc), 3.31 (s, 3, OCH_3), 4.59 (d, 1, J=3.2 Hz, H-1), 5.00 (d, 1, NH-6), 5.68 (d, 1, J=10 Hz, NH-2).

Found: C, 61.53; H, 7.42; N, 7.93%. Calcd for $C_{18}H_{26}N_2O_5$: C, 61.69; H, 7.48; N, 8.00%.

*Methyl 2,6-Diacetamido-2,3,4,6,7-pentadeoxy-α-*D-ribo-*heptopyranoside (Methyl 2,6-Di-*N*-acetyl-α-purpurosaminide B) (**6**).* Compound **5** (48 mg) was hydrogenated in methanol (10 ml) in the presence of Pd black under a H_2 atmosphere for 48 h. The product was acetylated with acetic anhydride in methanol to give 24 mg (69%) of **6**: mp 261—262 °C; $[\alpha]_D^{20}$ +185.7° (*c* 0.7, methanol); ^1H NMR ($CDCl_3$–CD_3OD) δ 1.15 (d, 3, J=6.7 Hz, CH_3), 1.99 (s, 6, 2 NAc), 3.41 (s, 3, OCH_3), 4.67 (d, 1, J=3.1 Hz, H-1). The IR spectrum of **6** was superimposable on that of an authentic sample.[3] (Found: C, 55.71; H, 8.44; N, 10.76%). Lit,:[3] mp 261—262 °C; $[\alpha]_D^{20}$ +195°.

*Methyl 2-Acetamido-6-(benzyloxycarbonylamino)-2,3,4,6,7-pentadeoxy-β-*L-lyxo-*heptopyranoside (**7**).* Compound **4** (100 mg) was treated with tributylstannane (0.5 ml) as has been described above to give 82 mg (90%) of **7**: mp 163—164 °C; $[\alpha]_D^{20}$ +55.6° (*c* 0.99, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.21 (d, 3, J=6.7 Hz, CH_3), 1.96 (s, 3, NAc), 3.36 (s, 3, OCH_3), 4.59 (d, 1, J=3.2 Hz, H-1), 5.00 (d, 1, NH-6), 5.64 (d, 1, J=9.0 Hz, NH-2).

Found: C, 61.83; H, 7.35; N, 7.94%. Calcd for $C_{18}H_{26}N_2O_5$: C, 61.69; H, 7.48; N, 8.00%.

*Methyl 2,6-Diacetamido-2,3,4,6,7-pentadeoxy-β-*L-lyxo-*heptopyranoside (Methyl 2,6-Di-*N*-acetyl-6-epi-α-purpurosaminide B) (**8**).* Compound **7** (50 mg) was hydrogenated and subsequently acetylated as has been described above to give 33 mg (88%) of **8**: mp 212—213 °C; $[\alpha]_D^{20}$ +62.5° (*c* 0.99, methanol). The ^1H NMR and IR spectra of **8** were superimposable on those of an authentic sample.[2]

References

1) T. Suami, Y. Honda, and T. Kato, *Chem. Lett.*, **1978**, 1125.

2) T. Suami, Y. Honda, T. Kato, M. Masu, and K. Matsuzawa, *Bull. Chem. Soc. Jpn.*, **53**, 1372 (1980).

3) The identification of methyl 2,6-di-*N*-acetyl-α-purpurosaminide B has been performed by Dr. P. J. L. Daniels, Research Division, Schering Plough Co., Bloomfield, N. J., 07003, U. S. A., to whom the authors' thanks are due.

4) The general methods used in the present work have been described in the preceding paper.[2]