

The Synthesis of Purpurosamine B Derivatives

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(Received June 7, 1980)

Synopsis. Purpurosamine B and its 6-epimer have been found in antibiotic gentamicin C₂ 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-pyranoside²⁾ (**1**) gave a mixture of two diastereomers, methyl 2-acetamido-2,3,4,7-tetradecoxy-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**).

Experimental⁴⁾

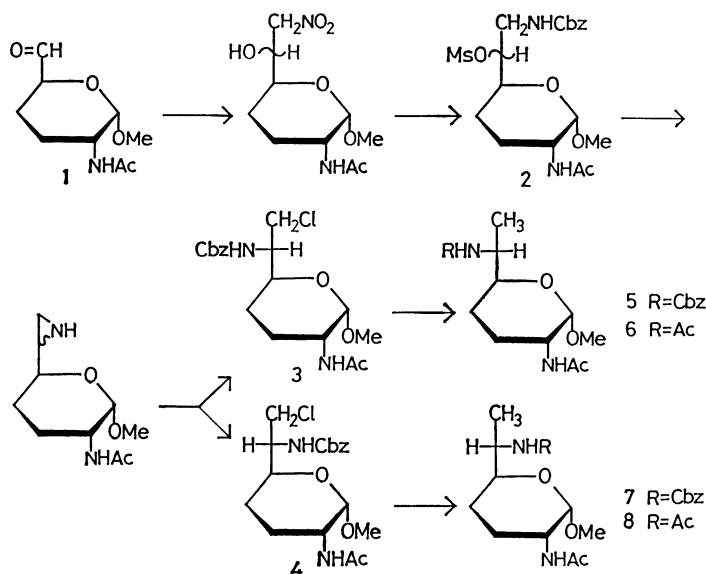
A Mixture of Methyl 2-Acetamido-7-(benzyloxycarbonylamino)-2,3,4,7-tetradecoxy-6-*O*-mesyl- α -D-ribo- and - β -L-lyxo-heptopyranosides (**2**). A 1.34-g portion of methyl 2-acetamido-2,3,4-trideoxy- α -D-erythro-hexodialdo-1,5-pyranoside²⁾ (**1**) was treated with nitromethane (0.62 ml) in the presence 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 paper²⁾ 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 C₁₉H₂₈N₂SO₈: 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 CHCl₃-



Scheme 1.

ether to give 139 mg (23%) of **3**: mp 196—197 °C; $[\alpha]_D^{20} + 76.7^\circ$ (c 0.43, CHCl_3); $^1\text{H NMR}$ (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 $\text{C}_{18}\text{H}_{25}\text{N}_2\text{ClO}_5$: 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; $[\alpha]_D^{20} + 59.3^\circ$ (c 1.03, CHCl_3); $^1\text{H NMR}$ (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 $\text{C}_{18}\text{H}_{25}\text{N}_2\text{ClO}_5$: 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; $[\alpha]_D^{20} + 98.4^\circ$ (c 0.95, CHCl_3); $^1\text{H NMR}$ (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 $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_5$: 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; $[\alpha]_D^{20} + 185.7^\circ$ (c 0.7, methanol); $^1\text{H NMR}$ ($\text{CDCl}_3\text{-CD}_3\text{OD}$) 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; $[\alpha]_D^{20} + 195^\circ$.

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; $[\alpha]_D^{20} + 55.6^\circ$ (c 0.99, CHCl_3); $^1\text{H NMR}$ (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 $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_5$: 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; $[\alpha]_D^{20} + 62.5^\circ$ (c 0.99, methanol). The $^1\text{H NMR}$ 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⁾