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NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 50.[1] A STEREOSELECTIVE SYNTHESIS OF A DERIVATIVE OF L-VANCOSAMINE, A CARBOHYDRATE COMPONENT OF THE ANTIBIOTICS VANCOMYCIN AND SPORAVIRIDIN[2]

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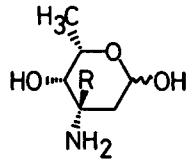
A derivative of L-vancosamine, a carbohydrate component of the antibiotics vancomycin and sporaviridin, has been prepared from L-lactic acid in a highly stereoselective manner.

In our preceding paper we have reported[1] a highly efficient stereoselective synthesis of L-daunosamine (**1**, 3-amino-2,3,6-trideoxy-L-lyxo-hexose) from L-lactic acid through direct C-acylation using diphenyl phosphorazidate (DPPA, $(PhO)_2P(O)N_3$). Using the same methodology to this daunosamine synthesis, we have now succeeded a stereoselective synthesis of a derivative of L-vancosamine[3,4,5] (**2**, 3-amino-2,3,6-trideoxy-3-C-methyl-L-lyxo-hexose), which is a carbohydrate component of the antibiotics vancomycin[6] and sporaviridin.[7]

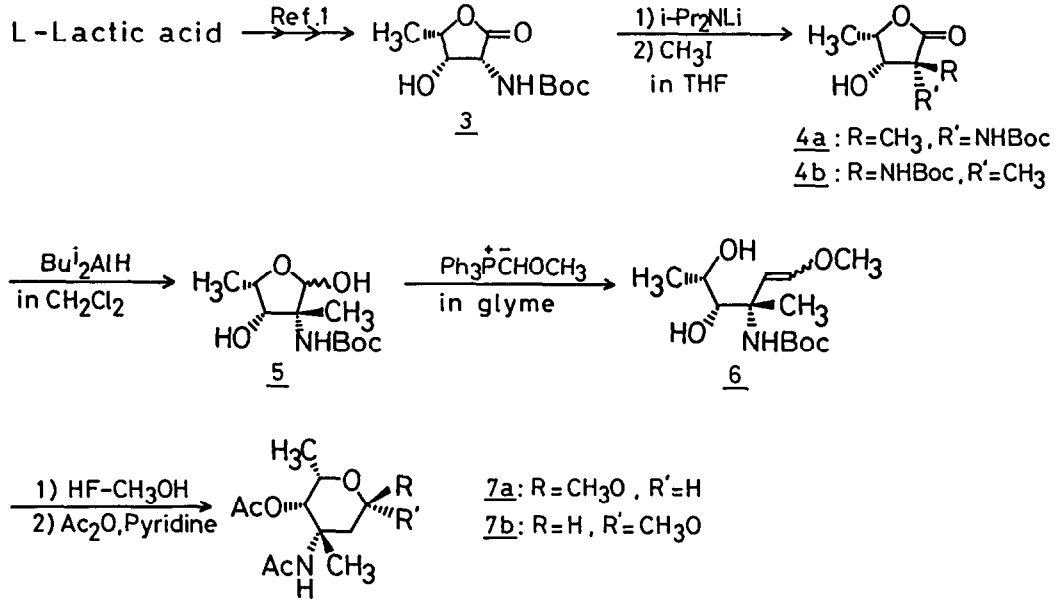


1, R = H L-Daunosamine

2, R = CH_3 L-Vancosamine

L-Lactic acid was efficiently converted[1] to 2-tert-butoxycarbonylamino-2,5-dideoxy-L-lyxono-1,4-lactone (**3**), which was lithiated with lithium diisopropylamide (3.3 equiv) in tetrahydrofuran (-73 ∿ -74°C, 40min; under argon) and treated with methyl iodide (1.2 equiv) (-73°C, 2hr; -50 ∿ -60°C, 4hr) to give an epimeric mixture of the C-methylated lactones **4a** and **4b**, a colorless oil, $[\alpha]_D^{21}$ -59.8° (c=0.73, MeOH),[8] in 67% yield. Their ratio was determined by the gas chromatographic analysis[9] to be 96:4. Definitely, the methylation preferentially occurs from the less hindered side of the molecule **3**. Reduction of **4** with diisobutylaluminum hydride in CH_2Cl_2 (-73°C, 1.5hr; under argon) and purification of the crude product on a silica gel column afforded the pure lactol **5** as a colorless oil, $[\alpha]_D^{21}$ -11.7° (equil., c=0.59, MeOH), in 73% yield. The Wittig reaction of the lactol with an excess (5 equiv) of methoxymethylenetriphenylphosphorane[1] in glyme (-5 ∿ -10°C, 30min; room temp., 1hr; under argon) afforded the methyl enol ether **6** as a colorless oil in 56% yield. The enol ether **6** was unexpectedly labile, and failed to give the vancosamine skeleton under various acidic conditions including 20% hydrochloric acid-tetrahydrofuran, which was found to be suitable for

the construction of L-daunosamine (1) from the demethylated analog of 6.[1] After various trials, we finally found that hydrofluoric acid was suitable to cyclize 6. Thus, treatment of 6 with 46% hydrofluoric acid-methanol (room temp., 18hr), neutralization with triethylamine, then acetylation with acetic anhydride in pyridine (room temp., 15hr) afforded an anomeric mixture of methyl N,O-diacetyl-L-vancosaminides (7a: mp 163-165°C, $[\alpha]_D^{26}$ -210° (c=0.1, MeOH), and 7b: mp 115-119°C). Both synthetic vancosamine derivatives were completely identical with samples derived from sporaviridin by IR, ^{1}H- and ^{13}C-NMR spectral comparisons.



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References and Notes

1) For Part 49, see Y. Hamada, A. Kawai, and T. Shioiri, *Tetrahedron Lett.*, submitted (the preceding paper).
2) Presented in part at the 104th Annual Meeting of Pharmaceutical Society of Japan, Sendai, March, 1984, *Abstracts* p. 215.
3) For the structure, see a) W. D. Weringa, D. H. Williams, J. Feeney, J. P. Brown, and R. W. King, *J. Chem. Soc. Perkin I* , 443 (1972); b) A. W. Johnson, R. M. Smith, and R. D. Guthrie, *J. Chem. Soc. Perkin I*, 2153 (1972).
4) For the synthesis, see a) T. T. Thang, F. Winternitz, A. Olesker, A. Lagrange, and G. Lukacs, *J. Chem. Soc. Chem. Commun.*, 153 (1979); b) I. Dyong and H. Friege, *Chem. Ber.*, 112, 3273 (1979); c) H. I. Ahmad, J. S. Brimacombe, A. S. Mengech, and L. C. N. Tucker, *Carbohydr. Res.*, 93, 288 (1981); d) G. Fronza, C. Fuganti, P. Grasselli, and G. Pedrocchi-Fantoni, *Tetrahedron Lett.*, 22, 5073 (1981).
5) Before the chiral synthesis, the synthesis of the racemic derivative has been efficiently carried out by the same reaction sequence.
6) Merck Index, Tenth Edition, Merck & Co., Inc., 1983, 9731
7) K.-I. Harada, S. Ito, and M. Suzuki, *Chem. Pharm. Bull.*, 30, 4288 (1982).
8) All of the products gave satisfactory elemental and spectral analysis.
9) Gas chromatographic analysis was carried out by the use of 2% silicone AN-600 column, 1m, flow rate 50ml/min, 80°C → 300°C: Retention time; 4a, 7.66min; 4b, 6.06min.

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