SYNTHETIC STUDY OF CARBAPENEMS UTILIZING D-GLUCOSAMINE

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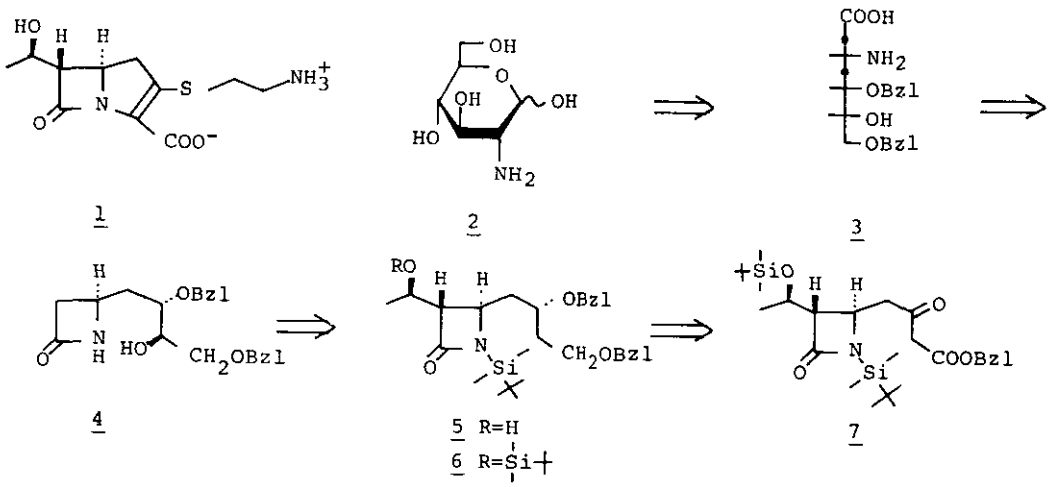
Thienamycin (1) and related naturally occurring carbapenems are new-generation β-lactam antibiotics which are endowed with unique structures and unusually potent antibacterial activity.

We wish to report the stereocontrolled total synthesis of (+)-1 via the Merck's intermediate (7) starting with commercially available D-glucosamine. D-Glucosamine (2) was transformed into the homologated β-amino acid (3) in 14 steps, which was cyclized with Ph_3P-$(PyS)_2$ to give the β-lactam (4). Protection of NH and removal of the hydroxyl group of 4 followed by condensation with acetaldehyde gave the diastereoisomer (5) as the major product. After O-silylation, the resulting 6 was debenzylated and a diol obtained was regioselectively oxidized by Pt-catalyzed autoxidation to give a hydroxy acid, which was converted, in 2 steps, to the known key intermediate (7) for the synthesis of (+)-thienamycin (1)[1].

An alternative construction of carbapenems from the amino acid (3) will also be discussed.



1) S.Karady, J.S.Amato,R.A.Reaman, and L.M.Weinstock, J. Am. Chem. Soc., 103, 6765(1981).