ASYMMETRIC SYNTHESIS OF β-LACTAM ANTIBIOTICS

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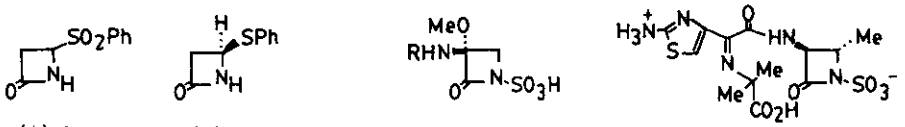
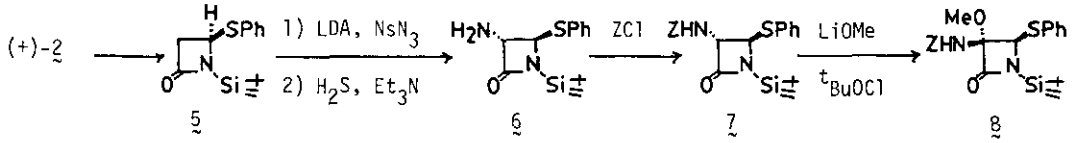
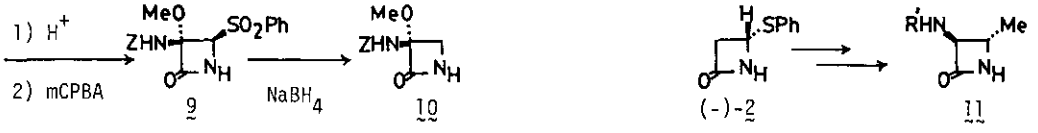
As a part of our synthetic studies toward the β-lactam antibiotics, we have pursued the total synthesis of (+)-thienamycin from (+)-4-phenylthio-2-azetidinone ((+)-2) prepared by utilizing the asymmetric introduction of thiophenol to (±)-4-phenylsulfonyl-2-azetidinone ((±)-1) in the presence of cinchonidine. In this presentation, at first, the detail of the asymmetric synthesis of (+)-2 and its conversion to (+)-thienamycin are presented.

In the second, the synthesis of the key synthetic intermediate (10) for optically active sulfazecin (3) is presented. Namely, the protected azetidinone (5) derived from (+)-2 was converted to the amine (6) by azidation (2-naphthalenesulfonyl azide) and reduction (H_2S), which was transformed to the benzyloxycarbonyl derivative (7) by the standard method. The introduction of a methoxy group to 7 was carried out by reaction with t-BuOCl and methanolic LiOMe in CH_2Cl_2. Since the desulfurization of 8 catalyzed by Raney-Nickel did not give any desired product, 8 was converted to the sulfone (9), which could be converted to the key intermediate (10) for sulfazecin by reductive removal of the sulfonyl group with $NaBH_4$ in THF.

The synthesis of the key intermediate (11) for the synthesis of SQ26776 (4) was also attempted by employing the enantiomeric isomer (-)-2 obtainable from the similar asymmetric introduction of thiophenol.







Ns=2-naphthalenesulfonyl, Z=-$COOCH_2Ph$

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