ASYMMETRIC SYNTHESIS OF (+)-THIENAMYCIN

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In the extension of our synthetic studies on β-lactam antibiotics having carbapenem and carbacephem skeletons, we have pursued several interesting transformation of the versatile synthetic intermediate, dl-4-propargylazetidin-2-one (I), obtainable easily from 4-phenylsulfonylazetidin-2-one.[1] In the first part of this presentation, the transformation of dl-I to the intermediate (IV) for thienamycin synthesis, which has been achieved by employing an extremely mild method developed for the conversion of propiolic esters (III) to β-keto esters (IV), is presented.

In the second, the studies directed toward the asymmetric synthesis of (+)-thienamycin (VII) are presented. Optically active 4-phenylthioazetidin-2-one (V) could be prepared by the reaction of 4-acetoxyazetidin-2-one with thiophenol (5 equiv) in the presence of cinchonidine (2 equiv) in benzene (80% chemical yield, 45% optical yield). Simple recrystallization of the product from ether-petr. ether gave the optically pure V (ca.20%). The optically inactive V recovered from the mother liquor could be again converted to the optically pure V by using the same reaction procedure after oxidizing the optically inactive V to the sulfone (90% chemical yield, 50% optical yield).

The optically pure V thus obtained was transformed to the synthetic intermediate (II) for the synthesis of the optically active thienamycin (VII) by the route described below.

Further conversion of the optically pure II to (+)-thienamycin will be discussed.

1) Tetrahedron Lett., 22, 4819 (1981); ibid., 23, 2875 (1982).