

A CHIRAL SYNTHESIS OF CARBAPENEM ANTIBIOTICS FROM PENICILLINS

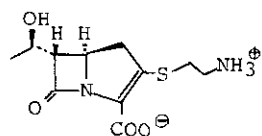
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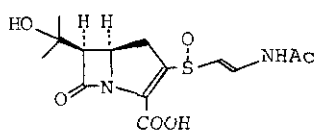
A chiral synthetic method for carbapenem antibiotics from penicillin 3 will be described. A key feature in this synthetic approach is that the amino group in 3 serves as a controlling handle for the stereoselective introduction of two alkyl groups into the C<sub>3</sub>- and C<sub>4</sub>- positions of the azetidinone rings (4 → 5 and 8 → 9).

The allylazetidinone 5, obtained stereospecifically by a AgBF<sub>4</sub>-catalyzed reaction of the chloride 4 with allyltrimethylsilane (M. Aratani, K. Sawada and M. Hashimoto, Tetrahedron Lett., 23, 3921 (1982)), was converted to 6. Aldol reaction and alkylation of the dianion derived from 6 with electrophiles gave stereo- and chemo-selectively the trans-alkylated products 7, one of which was converted into the known intermediate 10 for the synthesis of (+)-thienamycin 1.

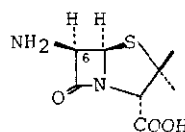
To synthesize the cis-substituted carpetimycin 2, 5 was transformed into the bicyclic isonitrile 8. Aldol reaction of 8 with acetone followed by stereoselective triphenyltin hydride reduction of the isonitrile group gave 9. The acid 11 derived from 9 was converted to carpetimycin 2 analogs.



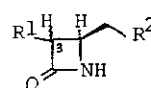
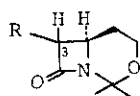
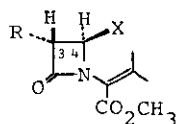
1 thienamycin



2 carpetimycin A



3



4 : R=Ft, X=Cl

8 : R=CN

10 : R<sup>1</sup>=MeCH(OZ)-, 3β-H

5 : R=Ft, X=CH<sub>2</sub>CH=CH<sub>2</sub>

9 : R=Me<sub>2</sub>C(OH)-, 3α-H

R<sup>2</sup>= -CH(OMe)<sub>3</sub>

6 : R=H, X=CH<sub>2</sub>CH=CH<sub>2</sub>

11 : R<sup>1</sup>=Me<sub>2</sub>C(OZ)-, 3α-H

7 : R=Me, Et, MeCH(OH)-, Me<sub>2</sub>C(OH)-  
X=CH<sub>2</sub>CH=CH<sub>2</sub>

R<sup>2</sup>= -COOH