SYNTHESIS OF THIENAMYCIN AND 2-ALKYLTHIOMETHYL-CARBAPENEM (2-HOMO-THIENAMYCIN) ANALOGUES FROM 6-AMINOPENICILLANIC ACID

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In view of growing interests in thienamycin due to its strong antimicrobial activity, 2-alkylthiomethyl-carbapenem derivatives(2-homo-thienamycin)(8) have been the object of our synthesis since its activity is expected to be excellent judging from the analogy of mechanism of a reaction of 3-thiomethyl-cephalosporins with an enzyme(Fig. 1).

6-Aminopenicillanic acid(6-APA)(1) was converted to the known methyl 6α-bromo-penicillanate-1,1-dioxide(2), which was successively treated with DBU in THF, trifluoroacetic acid and p-benzoquinone to afford the ring opened sulfone(3a). After dimethylation, the dimethoxybenzenesulfonyl derivative(3b) was reacted with lithium dibutylcopper and acetaldehyde to give the hydroxyethyl compound (4), in which the configuration of the hydroxyl part was mainly S. After conversion of (4) to (5), the allyl derivative(6) was obtained by treatment of (5) with allylmagnesium chloride. The resulting 4-allyl-azetidinone(6) was transformed into thienamycin(7) and 2-homo-thienamycin(8) in several steps. Microbiological activities of (8) will be briefly discussed.

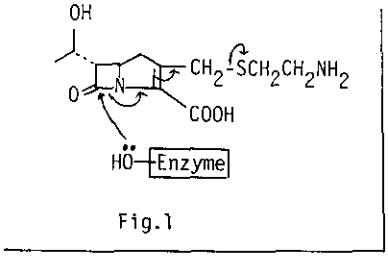

Fig.1