SYNTHESIS OF β-LACTAMS WITH THIENAMYCIN-TYPE SIDECHAIN

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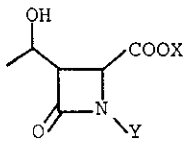
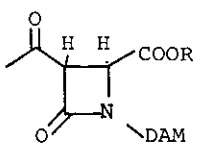
It has been well-known that 3-(1-hydroxyethyl)-2-azetidinone(1) is a potential intermediate for the synthesis of carbapenem and penem derivatives such as thienamycin and its penem analog.



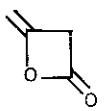
(1)

We describe here a simple and effective synthesis of azetidinone(1) via 3-acetyl-2-azetidinone derivatives. The preparation of 3-acetyl-2-azetidinones(2) was successfully accomplished by the cycloaddition reaction between diketene(3) and imine(4) in the presence of imidazole catalyst. It was found that this cycloaddition afforded predominantly the trans isomer(2) in excellent yield and the 3S,4S-azetidinone(2, R = ℓ-(-)-menthyl), which has the desired configuration for thienamycin, was obtained as a main product in the case of the cycloaddition between (3) and (4, R = ℓ-(-)-menthyl). The compounds(2) could be converted to the corresponding 1-hydroxyethyl derivatives(5) by reduction of the acetyl group.

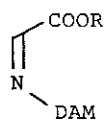
The efficient transformation of (5) into 4-acetoxy-3-(1-hydroxyethyl)-2-azetidinone(6) will also be presented.



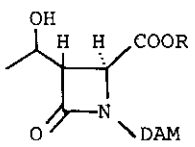
(2)



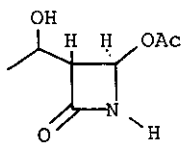
(3)



(4)



(5)



(6)

DAM = di-p-anisylmethyl