

BIOMINETIC SYNTHESIS OF  $\beta$ -AMINO-4-AMINO-6-CARBOXY-5-METHYL-  
2-PYRIMIDINEPROPIONIC ACID DERIVATIVESKazuo Achiwa and Sigeaki SasakiFaculty of Pharmaceutical Sciences, University of Tokyo,Bunkyo-ku, Tokyo 113, Japan

Biomimetic synthesis of  $\beta$ -amino-4-amino-6-carboxy-5-methyl-2-pyrimidinepropionic acid derivative (1), a biologically important part of Bleomycins, one of effective antitumor antibiotics, was described.

From the consideration on the speculation that the  $\beta$ -amino acid (1) may be derived from N- $\alpha$ -aspartyl- $\beta$ -methylasparagine, a dipeptide, by dehydration, amination, and dehydrogenation, We selected 4-amino-3-t-butoxycarbonyl-4-methylisoxazole (2) as the starting material.

Reaction of 2 with N-benzyloxycarbonylaspartic acid  $\beta$ -methyl ester  $\alpha$ -chloride gave the corresponding 4-acylamino-3-t-butoxycarbonyl-4-methylisoxazole (3) in the optically active form. Successive hydrogenation of 3 in ethyl acetate-acetic acid (5%) afforded the  $\beta$ -N-t-benzyloxycarbonyl-6-t-butoxycarbonyl-4-hydroxy-5-methyl-2-pyrimidinepropionic acid methyl ester (4). Further treatment of 4 with  $\text{SOCl}_2$ -DMF and lig.  $\text{NH}_3$  gave  $\beta$ -N-benzyloxycarbonylamino-6-t-butoxycarbonyl-4-amino-5-methyl-2-pyrimidinepropionic acid amide (5). Unfortunately, the optical activity of 4 and 5 was lost perhaps in the stage of the formation of pyrimidine ring.

Further investigations along this line are actively under way.