A SYNTHESIS OF GEMINALLY FUNCTIONALIZED CYCLIC AMINOCARBOXLIC ACIDS BY DIELS-ALDER REACTION AND 1,3-DIPOLAR CYCLO-ADDITION USING α,β-DEHYDROALANINATES

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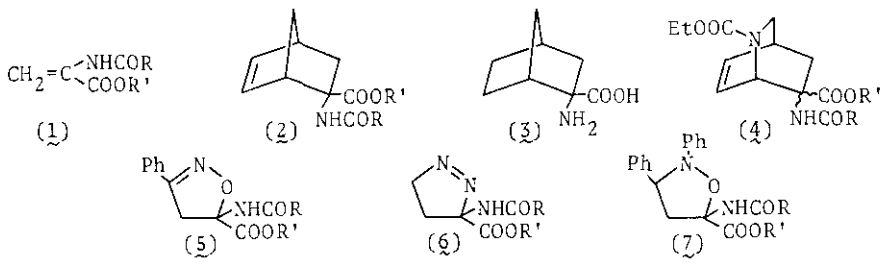
α,β-Dehydroalaninates are recognized to be intermediates of extensive value in both organic synthesis and biological transformations. The vast majority of the literature dealing with the chemistry of α,β-dehydroalaninates involves nucleophilic and electrophilic addition reactions to give β and α substituted amino acids, respectively. We now report that the Diels-Alder reaction and the 1,3-dipolar cycloaddition of N-acyl-α,β-dehydroalaninates (1) generally proceed with high stereoselectivity or regioselectivity, thus providing a viable method for the synthesis of geminally functionalized cycloaliphatic and hetrocyclic amino-carboxylic acids having interesting biological activities.[1)2)]



The Diels-Alder reaction of 1 with cyclopentadiene afforded the norbornene derivatives in good yields, in which the *exo*-ester isomer (2) formed predominantly; in the reaction of N-methoxycarbonyl-α,β-dehydroalaninate, the *exo* isomer formed exclusively. The adduct was converted into the biologically active 2-amino-norbornane-2-carboxylic acid (3). The reaction of 1 with N-ethoxycarbonyldihydro-pyridine led to the construction of the bicyclic derivative (4). The 1,3-dipolar cycloaddition of 1 with several 1,3-dipoles has been found to proceed regiospe-cifically to give the geminally functionalized heterocyclic aminocarboxylic acids (5,6,7) in good yields. Thus, regardless of the presence of acetamido group, the regiochemistry and the rate of reaction in the 1,3-dipolar cycloaddition using α,β-dehydroalaninate show striking similarity to those in the case of ethyl acrylate.

1) H. Horikawa, T. Nishitani, T. Iwasaki, Y. Mushika, I. Inoue, and M. Miyoshi, Tetrahedron Lett., 4101 (1980).
2) H. Horikawa, T. Nishitani, T. Iwasaki, and I. Inoue, Tetrahedron Lett., in press.