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Abstract

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The Synthesis of (2R,5R)-2-Amino-5-Hydroxyhexanoic Acid by Intermolecular Cycloaddition

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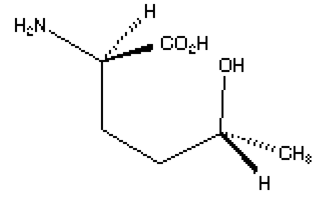

(2R, 5R)-2-Amino-5-hydroxyhexanoic Acid

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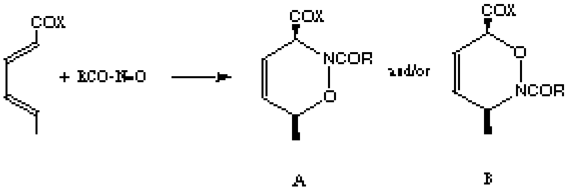
Introduction

The enantioselective synthesis of alpha amino acids which contain an additional chiral center at a remote position presents an important and complex synthetic problem. We have previously described the employment of a hetero Diels-Alder reaction for this purpose.[1] In this project this methodology was notably extended, as demonstrated by the short synthesis of (2R,5R)-2-amino-4-hydroxyhexanoic acid.

The key step in the synthesis is the Diels-Alder reaction of a sorbic acid derivative with an acyl nitroso compound (equation 1).



Equation 1

The use of this reaction in this case, was dependent on two requirements. First, chirality had to be induced. Second, the usual regioselectivity which leads to product B has to be reversed to form product A.[2] Both goals were achieved by connecting the diene and the dienophile through an L-proline moiety. The bridging proline served both as a chiral auxiliary and at the same time, enforced the proper regioselectivity.

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Comments

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