Pyrrolidine-2-carboxylic Acid (L-Proline)

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Introduction

Pyrrolidine-2-carboxylic acid commonly known as L-Proline (I) has shown, in recent times, excellent catalytic activity, in catalyzing a wide variety of reactions such as aldol,1,2 Mannich,3,4,10,12 Michael,6,7,9 in a highly enantioselective manner. These reactions have produced a variety of useful chiral materials for organic synthesis.

Most of the L-Proline (I) catalyzed reactions are believed to involve enamine (II) as key intermediate in its catalytic cycle (Scheme 1).

Abstracts

L-Proline (I) catalyzes the asymmetric aldol reaction between acetone and various aldehydes. In the case of hydroxy acetone, it gives anti-diols in excellent diastereo- and enantioselectivities.1,2

\[
\text{R} + \text{CHO} \xrightarrow{\text{I}, \text{DMSO}, \text{r.t.}} \text{OH} + \text{R} \\
X = \text{H}, \text{OH.} \quad \text{67-99% ee}
\]

L-Proline catalyzes the Michael reaction of ketones with nitro olefins to provide a variety of chiral Michael addition products.6,8

\[
\text{R} + \text{ArNO}_2 \xrightarrow{\text{I}, \text{DMSO}, \text{r.t.}} \text{Ar} + \text{NO}_2 \\
\text{23% ee}
\]
L-Proline catalyzes asymmetric the three component coupling involving Mannich reaction of acetone aldehydes and aryl amines to give β-amino ketones. In case of hydroxycetone it gives α-hydroxy β-amino ketones in good to excellent ee. This reaction complements the Sharpless asymmetric aminohydroxylation.3–5,10

L-Proline catalyzes Mannich type reaction of protected α-imino ethyl glyoxylate with a variety of ketones to provide functionalized α-amino acids in high enantioselectivities.11,12

L-Proline catalyzes α-amination of ketones by applying azodicarboxylate as nitrogen source to give chiral α-hydrazino, α-amino ketones, and alcohols.13

Recently, I has proved to be the best catalyst for asymmetric Robinson annulation.5

References