L-Proline and D-Proline (Chiral Amino Acid Catalysts)

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In the 21st century, the use of small organic molecules as chiral organocatalysts has become a powerful strategy and an attractive field in organic chemistry. Among the catalysts developed, L/D-proline and its derivatives catalyzed a wide range of reactions. L/D-Proline collectively has the application as catalysts in asymmetric Mannich reactions for chiral \( \beta \)-aminocarbonyls, aldheyde aldol reaction for the synthesis of erythro equivalents, domino Mannich–Aza-Michael reactions, Morita–Bayliss–Hillman reactions, Heck cross-coupling reactions, multicomponent reactions, in the synthesis of bioactive diketopiperazines, spirooxindoles and also in phosphodiester bond linkages to recognize DNA and RNAs and in bifunctional catalysts, it acts as co-catalyst. In addition, the application in the preparation of a wide variety of chiral catalysts like chiral MOFs, Barbas–List aldol catalysts, bile acid catalysts and has excellent use in autocatalysis strategy, to form the initial enantiorich isomers, which further autocatalyze the reactions. L/D-proline also served as building blocks in construction of chiral 3D architectures.

Table 1 Use of L-Proline and D-Proline (Chiral Amino Acid Catalysts)

<table>
<thead>
<tr>
<th>Reactions</th>
<th>Catalyst</th>
<th>Conditions</th>
<th>Yield</th>
<th>ee</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) One-pot synthesis of isoxazoline-N-oxides</td>
<td>L/D-proline</td>
<td>K2CO3, MeOH+</td>
<td>90%</td>
<td>86%</td>
</tr>
<tr>
<td>(B) Cross-aldol reaction</td>
<td>L/D-proline</td>
<td>HCOOH</td>
<td>87%</td>
<td>87%</td>
</tr>
</tbody>
</table>

Figure 1 General structures of L-proline and D-proline

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(C) In an enantioselective asymmetric hetero-Diels–Alder reaction of enones and aldehydes, the Zhao group used supramolecular bi-functional organocatalysts, which were synthesized by using L/D-proline and Cinchona alkaloids (quinidine thiourea), linked to each other through ionic hydrogen bonds for high stereoselectivity.

(D) L/D-Proline catalyze the asymmetric Morita–Baylis–Hillman (MBH) reaction in the presence of brucine-N-oxide as co-catalyst, through iminium intermediates. This dual catalytic system forms MBH products with opposite configuration with the respective L/D-proline and Cinchona alkaloids (quinidine thiourea), linked to each other through ionic hydrogen bonds for high stereoselectivity.

(E) Rawat et al. developed a novel L/D-proline catalyzed sequential a-amination–reductive cyclization of α-nitrohydroxy cinnamaldehydes for the construction of 3-substituted chiral tetrahydroquinolines (THQ) with good enantioselectivity, which were further applied in the total synthesis of bioactive (−)-sumanirole (96% ee) and (S)-903 (92% ee).

References