

Prolinamides as Asymmetric Organocatalysts

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6.1 Aldol Reaction

6.1.1 Prolinamides as Organocatalysts in Aldol Reactions

Organocatalysed aldol reaction¹ has been extensively studied after being rediscovered in 2000 when List *et al.* developed the first proline-catalysed asymmetric direct intermolecular reaction.² The aldol process is defined as the reaction of two carbonyl compounds to produce β -hydroxy carbonyl derivatives, and many combinations of starting compounds could be envisaged, but the most studied are summarised in Scheme 6.1.

The simplest reaction occurs by using acetone as donor and nonenolisable aldehyde (eqn. (1) in Scheme 6.1), because a single regio- and diastereoisomer is obtained. The reaction of symmetrically substituted cyclic or acyclic ketones only yields one regioisomer, but a mixture of diastereoisomers could be formed (eqn. (2)), whereas mixtures of regio- and diastereoisomers can be obtained by reaction of unsymmetrically substituted ketones and aldehydes (eqn. (3)).

The use of two different ketones in aldol reactions has been also studied although, as a general trend, an activated acceptor such as α -ketoesters,