1. Peptidic Catalysts of the H-Pro-Pro-Xaa Type – Substrate Scope, Reaction Mechanism & Conformational Analysis

Peptides are among the most reactive and stereoselective 2° amine catalysts... 

Reaction Mechanism and peptide conformation studied in depth...

Ground state

Enamine

H-Pro-Pro-Xaa type catalysts are excellent model systems to derive design principles to improve peptidic & 2° amine catalysts

2. Optimization of Peptidic Catalysts

About 75% of all peptidic catalysts contain at least one proline residue...

Design principle: High population of trans amide: high reactivity, chemoselectivity & stereoselectivity

Tools: 

- Ring size analogues of Pro
- γ-substituted Pro derivatives

Applications:

- Low catalyst loading
- Solvent-free conditions

High stereoselectivity

3. Optimization of 2° Amine Catalysts

The enamine intermediate is involved in the rate- and stereodetermining step...

Design principle: High population of endo pyramidalized enamine: high reactivity & stereoselectivity

Tools: Bigenic Pro derivatives

Application: Access to γ-nitroaldehydes bearing N-heterocycles

4. Reversal of the Diastereoselectivity

More than 100 organocatalysts are known that form syn-configured γ-nitroaldehydes but no general access to anti-configured products is known...

Design principle: α-cis enamine leads to anti-configured product

Tools: 4.4-nitroaldolized Pro derivatives

Application: Access to anti-configured γ-nitroaldehydes

5. Conclusion

Conformational tuning of organocatalysts enables both, improved catalytic performance and emergence of new reactivity.

Thanks!