Cγ-SUBSTITUENTS AS TOOLS TO INFLUENCE THE REACTIVITY AND STEREOSELECTIVITY OF PROLINE BASED CATALYSTS

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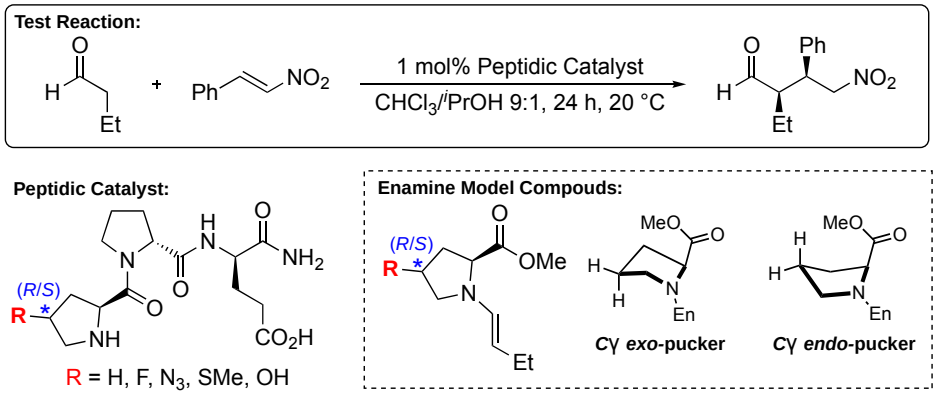
Tripeptides of the H-Pro-Pro-Xaa type are highly reactive and stereoselective catalysts for asymmetric aldol reactions and conjugate addition reactions of carbonyl compounds to nitroolefins, dicyanoolefins and unprotected maleimide [1]. For example, as little as 0.1 mol% H-DPro-Pro-Glu-NH_2 suffices to catalyze conjugate addition reactions of aldehydes to nitroolefins in high yields and excellent stereoselectivities [2]. Mechanistic studies showed, that the catalytic cycle proceeds *via* an enamine intermediate, which takes part in the rate- and stereodetermining C–C-bond formation step [3]. We envisioned that the enamine reactivity and stereoselectivity can be influenced by changing the conformation of the *N*-terminal proline. We introduced substituents at the Cγ-position of the proline ring, which are known to favor different ring puckers [4]. We used the conjugate addition reaction of butanal to nitrostyrene as testing ground to analyze the performance of the Cγ-substituted catalysts by *in situ* IR- and NMR-spectroscopic experiments. We complemented our findings by studies on enamine model compounds, which were derived from Cγ-substituted proline methyl esters. Our investigations provided insight into the effect of different ring puckers on the reactivity and stereoselectivity of proline derived catalysts.



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