Design and development of proline-based autocatalytic system

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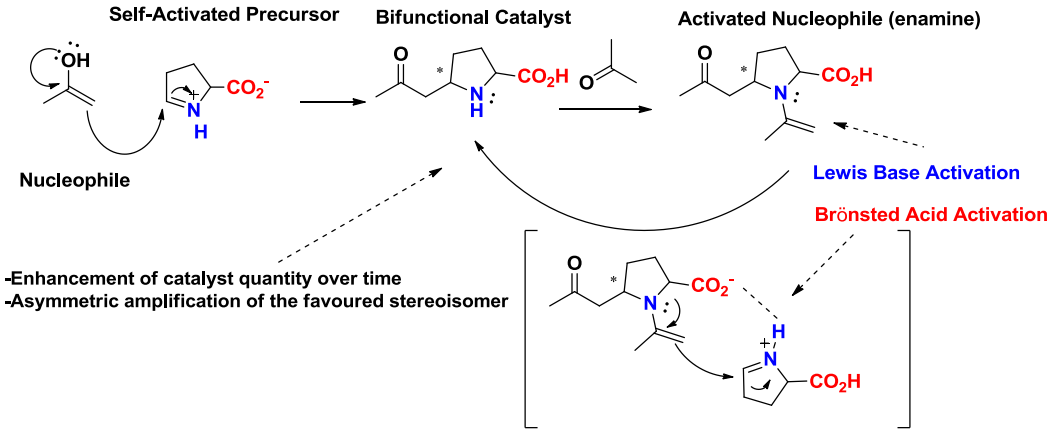
Replication and homochirality of biomolecules (*L*-amino acids and *D*-sugars) are crucial features of living systems.[1] Autocatalytic reactions are at the basis of the mechanism of these processes.[2] The aim of our research is to develop a general methodology for asymmetric autocatalytic synthesis based on the following concept: *the synthetic route to the autocatalytic molecule must involve one step process in which two different catalytic functions are created and preserved in the final molecule, making it catalytically active towards its own precursors*. Here we present an autocatalytic system based on Δ^1-pyrroline-5-carboxylate.



This unsaturated proline is expected to react with acetone, in a Mannich type reaction, to form a bifunctional, chiral catalyst. The catalyst will be able to activate the acetone by formation of an enamine (Lewis base activation), which will react with the pyrroline to provide more product/catalyst. Of the four synthetic strategies, which have been carried out to develop the precursor in its neutral form, the one relying on a solid phase Staudinger aza-Wittig key-step[3] has provided promising results. Once optimized, this route will deliver, in five steps, Δ^1-pyrroline-5-carboxylate to be tested as autocatalyst. Recent progress will be reported.

[1] L. E. Orgel *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 12503.
[2] a) K. Soai and T. Kawasaki *Chirality* **2006**, *18*, 469; b) M. Mauksch , S. B. Tsogoeva, S. Wei, I. M. Martynova *Chirality* **2007**, *19*, 816.
[3] Kiessling et *al. Org. Lett* **2012**, *14*, 1378.