Synthesis of α-Trifluoromethylated Amino Acids using an Umpolung Strategy

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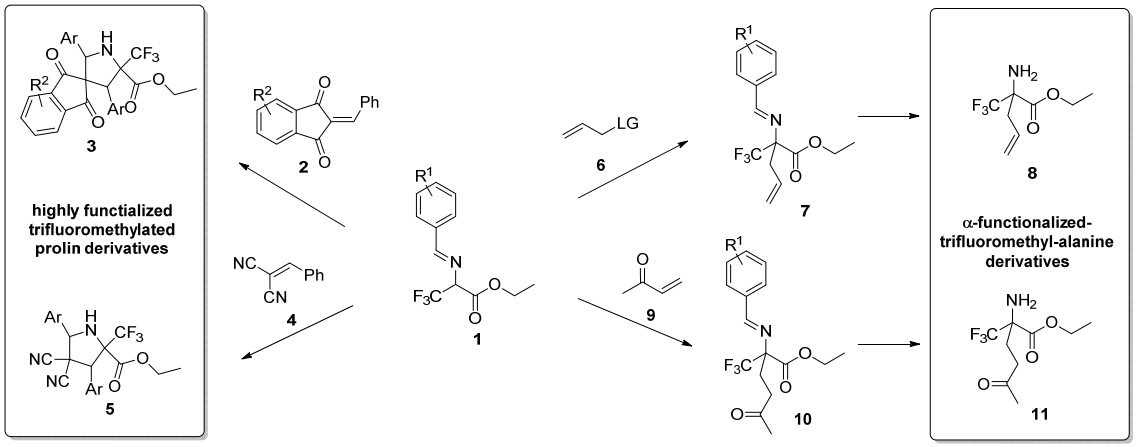
Umpolung reactions are used to create a whole new reactivity by reversing the polarity of common organic functionalization like carbonyls. There are a lot of examples for umpolung reactions of carbonyls as an acyl anion equivalent. The umpolung with imines is less frequently described. The first time imines were considered for this kind of reactions, was in 2004 by the group of S. A. Miller [1]. One of the first highly enantioselective example was published in the year 2015 by Li Deng et.al. in Nature [2].

To expand the use of this methodology this work presents an imine **1** which enables the access of different trifluoromethylated amino acids. The first syntheses of imine **1** was accomplished in 2003 by the group of V. A. Soloshonok [3]. Since then, no publication showed reactions with imine **1** as substrate for umpolung reactions. We herein report the synthesis of different trifluoromethalated amino acids starting from ethyl-3,3,3-trifluoropyruvate. With this strategy it is possible to address highly substituted proline derivatives or α-substituted trifluoro-alanine derivatives.



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[1] B. Jesse, E. Reich, A. K. Justice, B. T. Bechstead, J. H. Reibenspies, S. A. Miller, *J. Org. Chem.* (**2004**), 69, 1357.

[2] Y. Wu, L. Hu, Z. Li, L. Deng, *Nature* (**2015**), 523, 445.

[3] H. Ohkura, D. O. Berasov, V. A. Soloshonok, *Tetrahedron* (**2003**), 59, 1647.