CHEMOSELECTIVE ACTIVATION OF AMIDE CARBONYLS TOWARDS NUCLEOPHILIC REAGENTS

Bartłomiej FURMAN[1]*

[1]*Institute of Organic Chemistry PAS, Kasprzaka 44/52, 01-224, Warsaw*

* *furbar@icho.edu.pl*

Amides represent an important class of compounds in chemistry, chemical biology and pharmaceutical industry. Their broad utility in many fields is closely tied to the structure of the amide moiety which endows these compounds with unique features. The low reactivity of amide carbonyls towards nucleophiles is a major obstacle to their further functionalization. Selective activation of amides and lactams enables access to novel reactivity pathways and opens up intriguing perspectives in synthesis.

Recently, we have demonstrated that upon treatment with $Cp_2Zr(H)Cl$ (Schwartz's reagent), five- and six-membered lactams, including sugar- and hydroxy acid-derived lactams,[1] can be easily converted into imines under mild conditions. In addition, as was also shown, in situ generated cyclic imines can be directly subjected to further reactions with nucleophilic reagents such as allyltributylstannane,[1b] Grignard reagents,[1b] enolates[1b] or Danishefsky's diene[1a] to afford α-functionalized pyrrolidines, piperidines and polyhydroxylated pyrrolidine peptidomimetic[1c] scaffolds in a one-pot manner. The key advantage of the presented approach is the simplicity and convenience of generation of sugar-derived imines from readily available starting materials: sugar-derived lactams. The use of sugar-derived lactams as cyclic imine precursors is crucial to the efficiency of the described synthetic method. These compounds are more readily prepared, handled, and stored than the alternative precursors of cyclic imines such as nitrones, *N*-chloroamines or azido aldehydes. In the second part of the lecture a method for preparing 2,3-disubstituted indoles from commercially available isatins will be briefly presented.[2]

Acknowledgements

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References:

[1] (a) P. Szcześniak, S. Stecko, E. Maziarz, O. Staszewska-Krajewska, B. Furman, J. Org. Chem. 79 (2014) 10487, (b) P. Szcześniak, S. Stecko, O. Staszewska-Krajewska, B. Furman, Tetrahedron 70 (2014) 1880, (c) P. Szcześniak, S. Stecko, E. Maziarz, B. Furman, J. Org. Chem. 80 (2015) 3621–3633.

[2] A. Ulikowski, B. Furman, Org. Lett. 18 (2016) 149.

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