FROM SMALL PEPTIDES AND AMIDE MACROCYCLIC RINGS TO PHARMACOPHORES: PHOTOCATALYSIS IN HOFFMAN-LÖFFLER-FREYTAG RADICAL REARRANGEMENTS

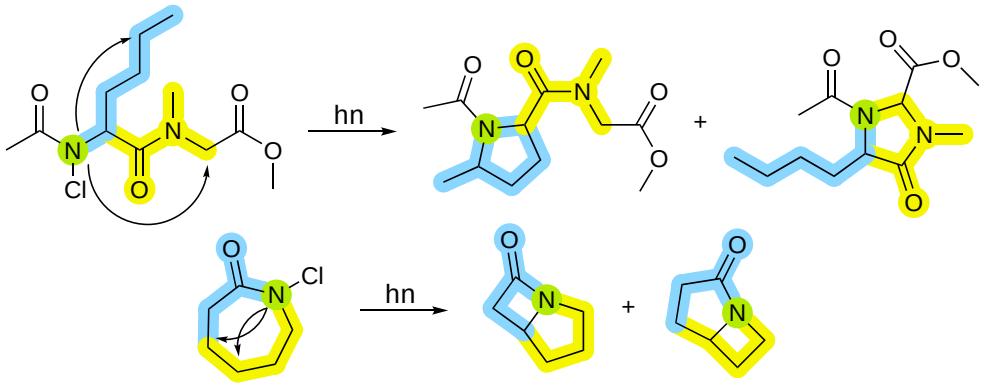
Gabrijel Zubčić[1], Kristina Pavić[1], Tomislav Portada[2], Jiangyang You[2], Erim Bešić[1], Valerije Vrček[1], Davor Šakić[1]

[1] University of Zagreb Faculty of Pharmacy and Biochemistry, Zagreb, Croatia
[2] Ruđer Bošković Institute, Zagreb, Croatia

e-mail: davor.sakic@pharma.unizg.hr

In medicinal chemistry and drug discovery, developing new methods for synthesizing complex organic molecules with specific structural motifs is essential. Late-stage functionalization techniques are particularly valuable, as they enable rapid modifications of parent compounds to produce a variety of drug candidates. Among these methods, the Hofmann-Löffler-Freytag (HLF) reaction is notable for its use of light-activated radical rearrangements to create complex structures.

This poster focuses on adapting the HLF reaction for converting small peptides and amide-containing macrocyclic compounds into scaffolds and pharmacophores, a process that enhances the synthesis toolkit for pharmaceutical development. This method not only facilitates the creation of drugs with improved efficacy and specificity but also demonstrates the utility of radical rearrangements under controlled conditions.



A significant part of our discussion will be dedicated to computational simulations that investigate the regioselectivity of HLF in small peptides towards ring formation in the backbone *vs*. in the sidechains, making them more stable to hydrolysis. Additionally, amide-linked macrocycles processed through the HLF reaction can form multiple bicyclic patterns, including bicyclic scaffolds present in many pharmaceuticals. These simulations are crucial for predicting reaction outcomes and optimizing conditions, thereby improving the efficiency and selectivity of this synthetic approach. By integrating computational insights with practical chemistry, we aim to refine the HLF reaction for more effective drug synthesis.

Keywords: photocatalysis, synthetic strategies, radical rearrangements

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