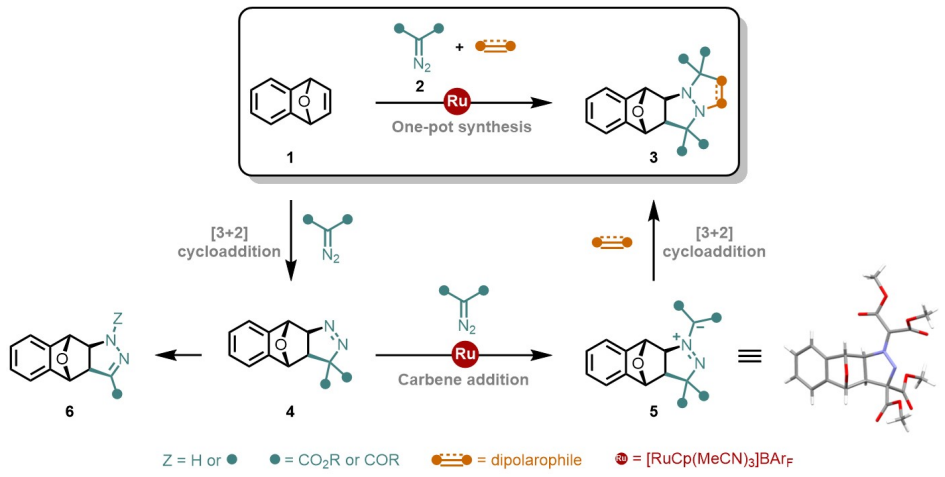
CpRu-Catalyzed Multicomponent Synthesis of Polyheterocycles Pyrazolidines Through Cycloadditions and Metal-Carbene Addition

C. Montagnon[1], J. Bultel[1], C. Besnard[1], J. Lacour[1]*

[1]Department of Organic Chemistry and Laboratory of Crystallography, University of Geneva, Switzerland

Cyclopentadienyl-Ruthenium (II) complexes are known to efficiently promote the decomposition of diazo malonates and α-diazo-β-ketoesters to generate *Fischer*-type carbenes. These electrophilic intermediates form ylides in presence of various *Lewis* bases, such as cyclic ethers,[1] ketones,[2] and lactams,[3] among others. Subsequently, the reactive zwitterions can undergo different rearrangement or insertion reactions to obtain different classes of functionalized heterocycles.

Based on previous reactivities developed in our lab with oxonium[1] and ammonium[4] ylides, and in divergence with recently reported studies using 2,2,2-trifluorodiazoethane,[5] the reactivity of bicyclic ether **1** and diazomalonate **2** under ruthenium (II) catalysis was investigated. Herein, a fully-diastereoselective one-step synthesis of diaza polycyclic compounds **3** *via a* series of cascade reactions is obtained. More interestingly, this reaction can also be done stepwise, and each intermediate **4** and **5** can be isolated in high yields. Moreover, ylides **5** showed unusual stability, as they can be stored at room temperature under air conditions and can further react with various dipolarophiles to access symmetrical on non-symmetrical polycyclic pyrazolidines. In addition, the cycloadduct **4** can undergo rearrangements such as a 1,3-ester shift or a decarboxylation to afford corresponding pyrazolines scaffolds **6**. We thus report a direct methodology to access valuable N−N bond-containing heterocycles, which are presented in many natural products and bioactive molecules.[6]



[1] Léo Egger, Laure Guénée, Thomas Bürgi, Jérôme Lacour, *Adv. Synth. Catal.,* **2017**, 359, 2918-2923. [2] Júlia Viñas-Lóbez, Guillaume Levitre, Adiran De Aguirre, Céline Besnard, Amalia I. Poblador-Bahamonde, Jérôme Lacour, *ACS Org. Inorg. Au,* **2021**, 1, 11-17. [3] Romain Pertschi, Elodie Brun, Adiran De Aguirre, Laure Guénée, Amalia I. Poblador-Bahamonde, Jérome Lacour, *Helv. Chim. Acta,* **2021**, 104, e2100122. [4] Alejandro Guarnieri-Ibáñez, Adiran De Aguirre, Céline Besnard, Amalia I. Poblador Bahamonde, Jérôme Lacour, *Chem. Sci.,* **2021**, 12, 1479-1485. [5] Tingting Cao, Zhen Yang, Yunfang Sun, Nannan Zhao, Shan Lu, Jing Zhang, Lei Wang, *Eur. J. Org. Chem.,* **2021**, 2021, 2950-2954. [6] (a) Lachlan M. Blair, Jonathan Sperry, *J. Nat. Prod.,* **2013**, 76, 794-812; (b) Jimi M. Alex, Raj Kumar, *J. Enzyme Inhib. Med. Chem.,* **2014**, 29, 427-442.