

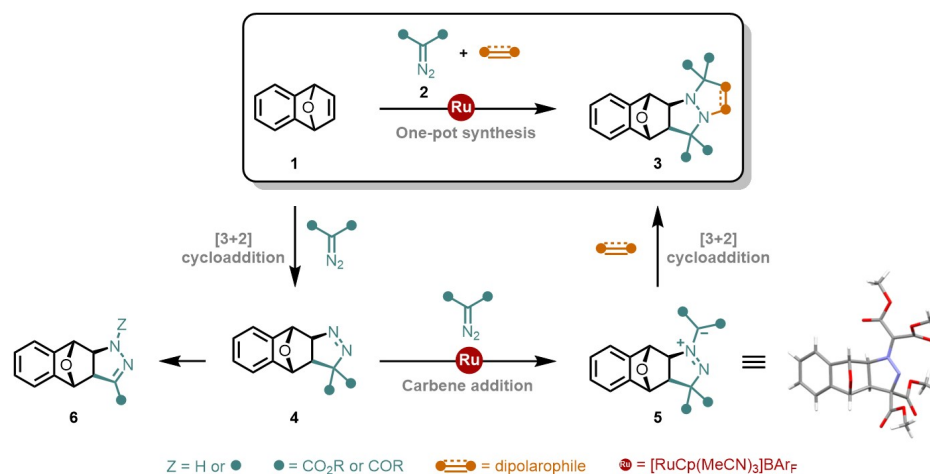
## CpRu-Catalyzed Multicomponent Synthesis of Polyheterocycles Pyrazolidines Through Cycloadditions and Metal-Carbene Addition

C. Montagnon<sup>1</sup>, J. Bultel<sup>1</sup>, C. Besnard<sup>1</sup>, J. Lacour<sup>1\*</sup>

<sup>1</sup>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  $\alpha$ -diazo- $\beta$ -ketoesters to generate Fischer-type carbenes. These electrophilic intermediates form ylides in presence of various Lewis bases, such as cyclic ethers,<sup>[1]</sup> ketones,<sup>[2]</sup> and lactams,<sup>[3]</sup> 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<sup>[1]</sup> and ammonium<sup>[4]</sup> ylides, and in divergence with recently reported studies using 2,2,2-trifluorodiaoethane,<sup>[5]</sup> 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 or 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.<sup>[6]</sup>



- [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, Jérôme 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**, 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.