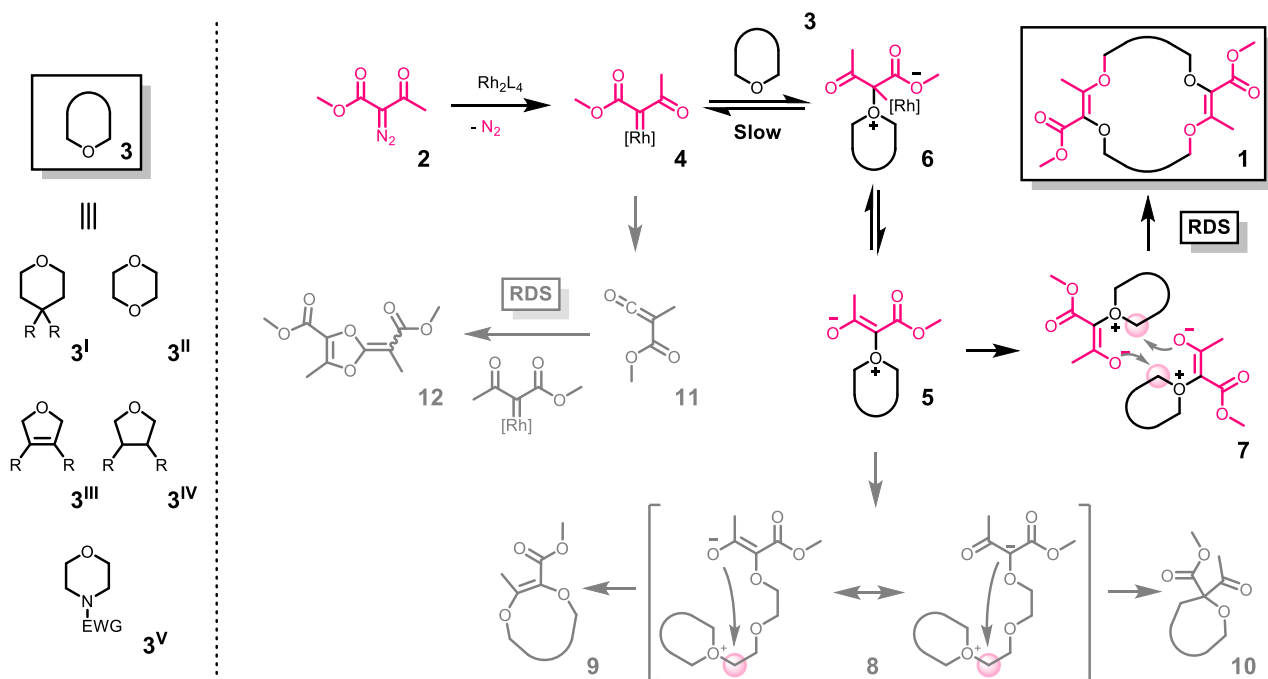


Impact of Diazo Concentration on Oxonium Ylide Based [3+n+3+n] Macrocyclizations

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Previously, our group reported the synthesis of polyether macrocycles **1** by [3+n+3+n] condensations of α -diazo- β -ketoesters **2** and cyclic ethers **3** under dirhodium catalysis. ^[1,2] Usually, this reaction yields corresponding macrocycles up to 78% isolated yield, starting with 6 equivalents of heterocycles of type **3^{II}**; such an excess in reactant becomes a drawback when **3** is not a regular commodity or a volatile heterocycle. A new method is now developed to lower the stoichiometry in cyclic ether. In fact, slow addition of diazo substrate can significantly increase the yield of the targeted macrocycle, providing a twofold increase for EWG-substituted morpholines **3^V**. Such result could be rationalised by mechanistic considerations involving an equilibrium between the metallocarbene **4** and the metal free oxonium ylide **5**. During the presentation, care will be taken to present the multiple parameters that need to be considered for yield improvement. Further studies to extend the range of accessible macrocycles are pursued to design novel and selective chemosensors for a wide variety of ionic atoms and molecules. ^[3]



[1] M. Vishe, R. Hrdina, L. Guénée, C. Besnard, J. Lacour, *Adv. Synth. Catal.*, **2013**, 355, 3161– 3169.

[2] A. Homberg, D. Poggiali, M. Vishe, C. Besnard, L. Guénée, J. Lacour, *Org. Lett.*, **2019**, 21 (3), 687-691

[3] M. Vishe, T. Lathion, S. Pascal, O. Yushchenko, A. Homberg, E. Brun, E. Vauthey, C. Piguet, J. Lacour *Helv. Chim. Acta*, **2018**, 101, e1700265