Zn(II)-CATALYZED [3+2] AND [4+2] ANNULATION OF INDOLES WITH AZOALKENES: DIVERGENT SYNTHESIS OF POLYCYCLIC INDOLINES

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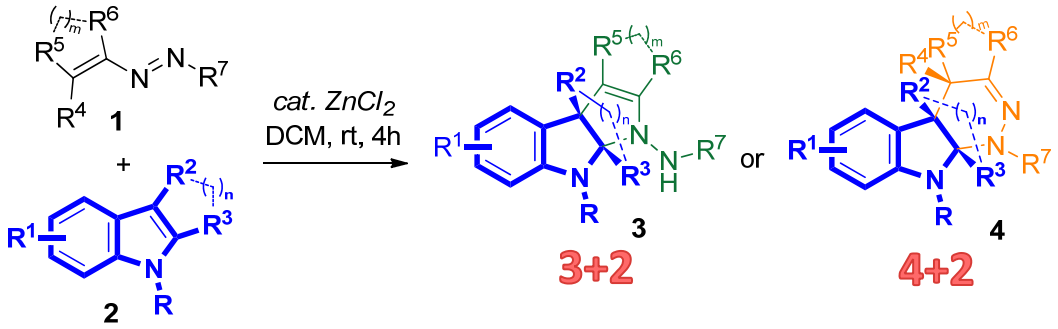
Despite recent advances, robust strategies for producing libraries of chemical compounds that have a structural connection with biologically active natural-like molecules, especially around privileged structures, are still significant and needed. The indoline substructure,[1] particularly that C2,C3-fused, is ubiquitously present in many naturally alkaloids, such as vindoline, strychnine, (–)-physostigmine, communesin F, physvenine, gliocladin B and (+)-aspidospermidine. Thus, their structural complexity and diversity, as well as promising bioactivities, make polycyclic indolines a particularly important target to inspire methodology development. Although a large number of metodologies have been designed for the construction of such appealing frameworks, only limited reports in the literature describe the synthesis of indoline fused heterocycles such as C2,C3-fused indoline-dihydropyrroles 3 and –tetrahydropiridazines 4. Fascinated by the synthetic potential of azoalkenes,[2] we herein report a Zn(II)-catalyzed divergent synthesis of polycyclic indolines through formal [3+2] and [4+2] annulations of azo-olefins 1 with indoles 2. Taking advantage of the reciprocal reactivity/nature of substituents of the reagents, the same couple of reagents selectively furnished different types of highly functionalyzed poly-azaheterocycles embedding the indolinic skeleton as common privileged substructure (Scheme 1).



Scheme 1

[1] For reviews, see: a) Silva, T. S.; Rodrigues Jr., M. T.; Santos, H.; Zeoly, L. A.; Almeida, W. P.; Barcelos, R. C.; Gomes, R. C.; Fernandes, F. S.; Coelho, F. *Tetrahedron*, 2019, *75*, 2063. b) Liu, D.; Zhao, G.; Xiang, L. *Eur. J. Org. Chem.*, 2010, 3975.

[2] For reviews, see: a) Attanasi, O. A.; De Crescentini, L.; Favi, G.; Filippone, P.; Mantellini, F.; Perrulli, F. R.; Santeusanio, S. *Eur. J. Org. Chem.*, 2009, 3109. b) Lopes, S. M. M.; Cardoso, A. L.; Lemos, A.; Pinho e Melo; T. M. V. D. J. *Chem. Rev.*, 2018, *118*, 11324. For excellent papers, see: c) Qi, L.-W.; Mao, J.-H.; Zhang, J.; Tan, B. *Nat. Chem.*, 2018, *10*, 58. d) Tong, M.-C.; Chen, X. C.; Li, J.; Huang, R.; Tao, H.; Wang, C.-J. *Angew. Chem. Int. Ed.*, 2014, *53*, 4680.