Synthesis of α-Quaternary Pyrrolidines by Ru and Cu-Catalyzed Condensation of α-Diazo-β-Ketoesters and γ-Lactams and Efficient Access to 9-Membered-fused Pyrazoles

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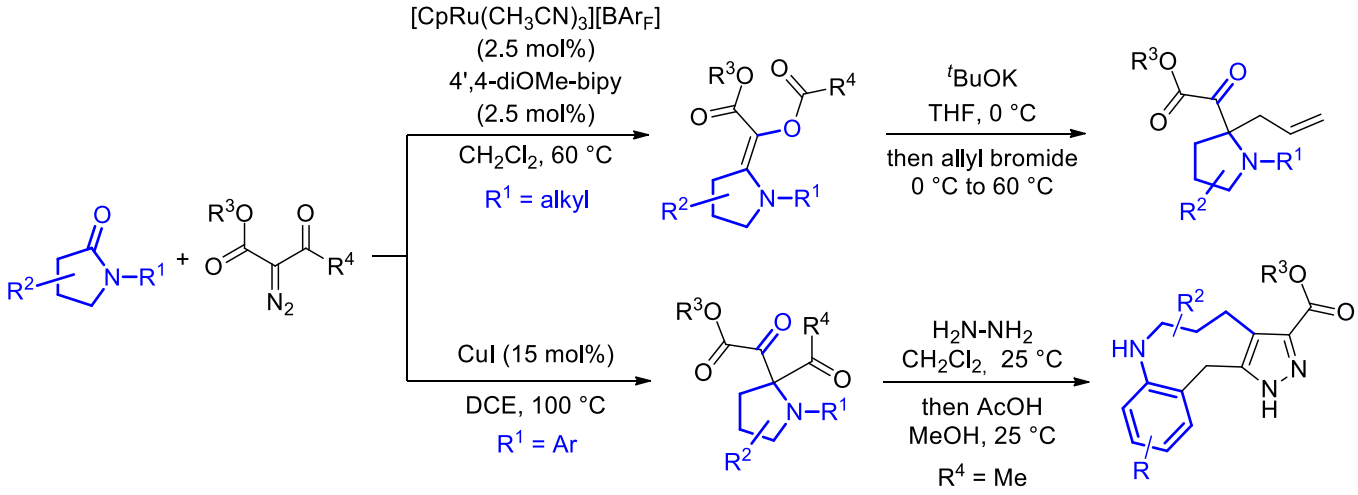
Building and increasing molecular complexity in a few synthetic steps is a challenge in heterocyclic chemistry. Many transition metal complexes - including ruthenium, rhodium and copper catalysts - have been shown to promote diazo decompositions and subsequent reactions with various Lewis basic substrates, allowing the straightforward access to several types of heterocycles.[1]

In the particular case of α-diazo-β-ketoesters and γ-lactams as substrates, Ru and Cu catalysts exhibit complementary reactivities. Indeed, when reacted with *N*-aryl-γ-lactams, CuI promotes the formation of *N*-aryl-pyrrolidines carrying α-quaternary centers through a [1,2]-acyl migration on the carbon,[2] whereas Ru reacts with *N*-alkyl-pyrrolidinones to afford unsaturated pyrrolidines via a [1,2]-Brook-like rearrangement of the acyl group. The obtained products can then be transformed into highly substituted α-quaternary pyrrolidines through a one-pot O-alkylation/[3,3] sigmatropic rearrangement sequence.

In addition, using a combination of hydrazine and an acid source, *N*-aryl pyrrolidines are efficiently transformed into novel pyrazolo[3,4-e]azonines motifs in very high yield via a two-steps one-pot process. A mild Aza-Claisen rearrangement drives the concomitant formation of the pyrazole and the azonane core, affording substructures which might reveal as potential biologically relevant products.



[1] (a) Achard T., Tortoreto C., Poblador-Bahamonde A. I., Guénée L., Bürgi T., Lacour J., *Angew. Chem. Int. Ed.* **2014**, *53*, 6140; (b) Tortoreto C., Achard T., Egger L., Guénée L., Lacour J., *Org. Lett.* **2016**, *18*, 240 ; (c) Egger L., Guénée L., Bürgi T., Lacour J., *Adv. Synth. Catal.* **2017**, *359*, 2918.
[2] S. Goudedranche, C. Besnard, L. Egger, J. Lacour, *Angew. Chem. Int. Ed.* **2016**, *55*, 13775.