Pd-catalyzed cycloaddition of bicyclic aziridine with isocyanates

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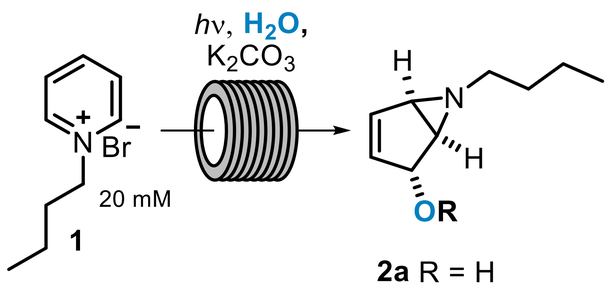
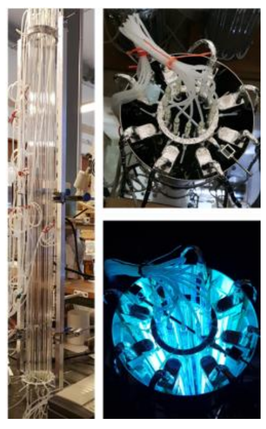
Introduction

Nitrogen-containing heterocycles are very common structures in both synthetic and natural products and they can have several applications in the pharmaceutical industry, since they contain a wide spectrum of biological activities. One example of these molecules is Imidazolidinones, which have shown activity against leukemia, lung cancer and metabolic disorders[1]. These cyclic urea frameworks can be obtained through transition-metal-catalyzed intermolecular cycloaddition using an aziridine moiety as starting material. These reactions often provide effective one-step procedures that result in heterocyclic derivatives, that are challenging to access through conventional approaches[2,3]. In this study, is presented the reaction between an acetyl bicyclic aziridine and several isocyanates, in the presence of Pd(0)-catalyst. The reactions proceed through ring opening of the aziridine moiety, with the formation of the π-allylpalladium complex, followed by cyclization *via* nucleophilic addition of nitrogen to the isocyanate, affording regioselectively imidazolidinones.

Previous work

Photochemical Synthesis of Aziridine



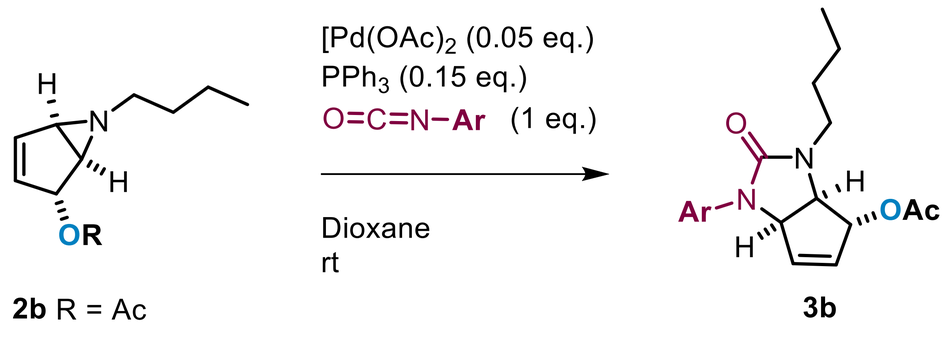


Synthesis of bicyclic aziridine **2a** from pyridinium salt **1** under continuous-flow using a home-made UV-reactor [4,5]

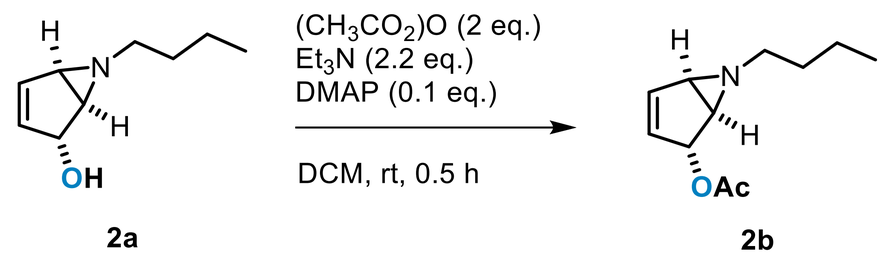
(A) 12 assembled parallel quartz tube reactor; (B) Top-view reactors; (C) Top-view reactors under photochemical irradiation [4,5].

This work

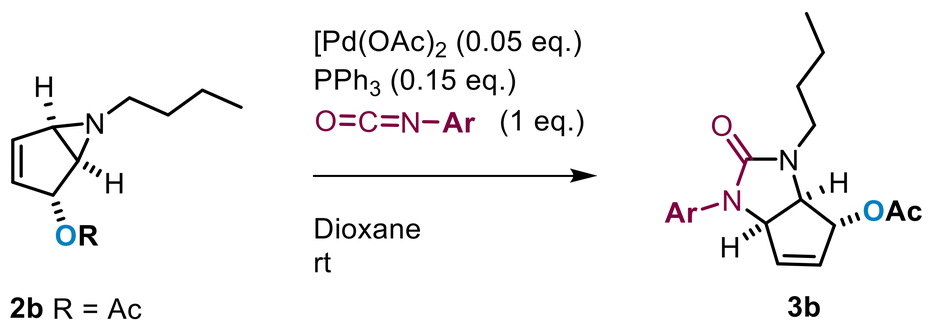
Pd-catalyzed cycloaddition of bicyclic aziridine

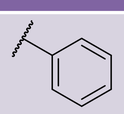
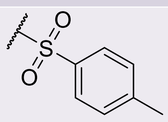
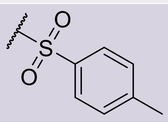


Synthesis of acetyl bicyclic aziridine 2b

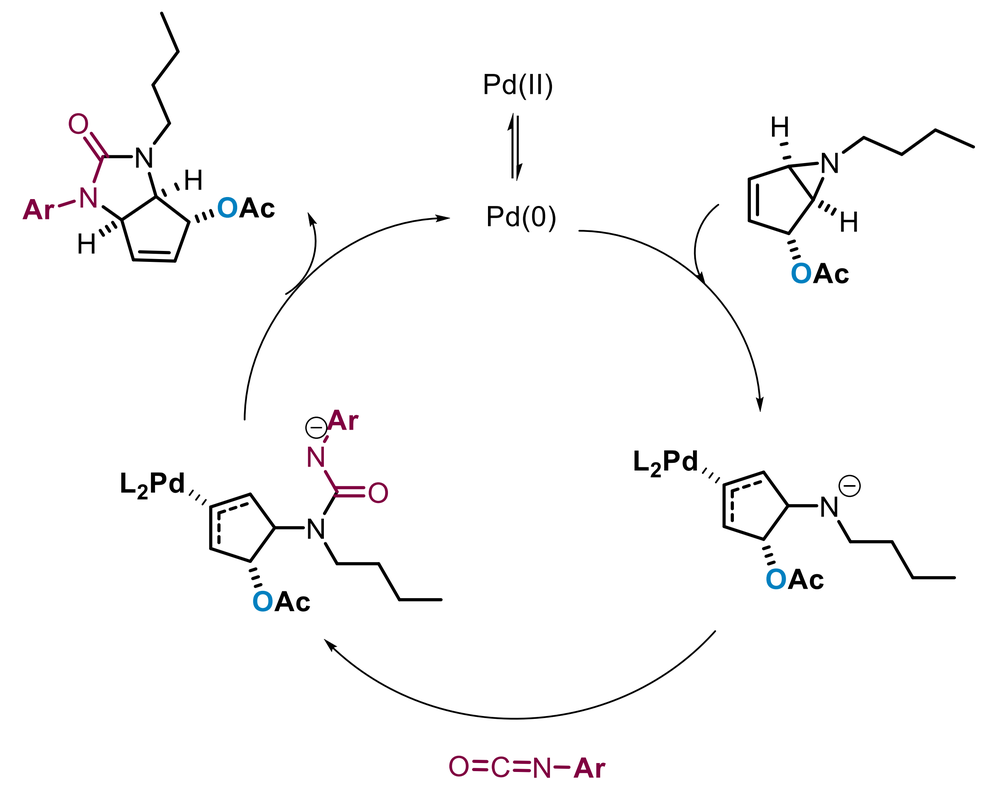


Reaction Scope



Entry	Ar	Reaction Time (h)	Yield (%)
1		1	75
2		1	13
3		2	61

Reaction Mechanism



References

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Acknowledgements

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