

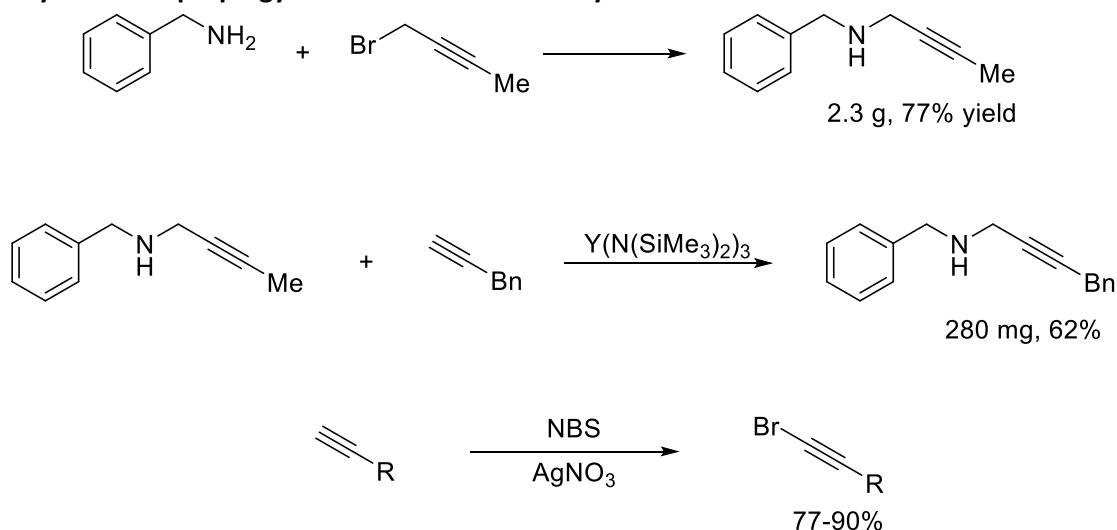
Palladium Catalysis for the Incorporation of Carbon Dioxide in Important Building Blocks

Supervisor: Phillip Greenwood (Phillip.greenwood@epfl.ch)

Aim: Synthesis and utilization of Propargylic amines and bromoalkynes for use in palladium-catalysed oxyalkylation using carbon dioxide as a tether.

General Background: The development of new catalytic reactions for accessing value-added building blocks for synthetic and medicinal chemistry is one of the most important fields of fundamental research in chemistry. Multi-component reactions using simple building blocks such as alkenes, alkynes or carbon dioxides are particularly important for a fast increase in molecular complexity. In this project, you will learn how to synthesize simple organic starting materials, and how to set up, analyse and optimize new catalytic processes.

Part 1: Synthesis of propargylic amines and bromo alkynes

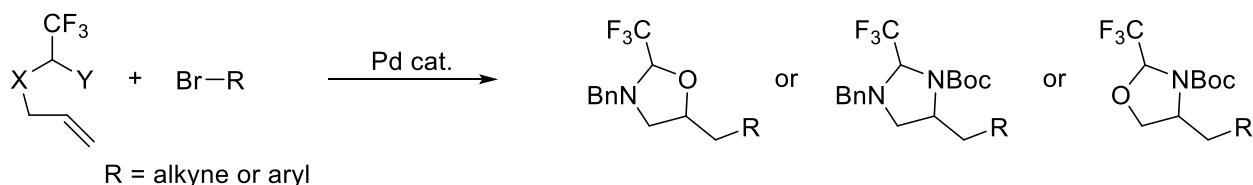


The goal of the first part of the project will be the synthesis of known propargylic amines and bromoalkynes. These organic substrates will be then examined in catalytic reactions in the second part of the project.

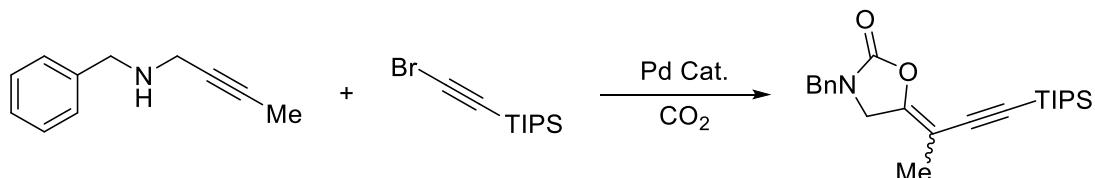
Part 2. Preliminary reactions towards the optimisation of a palladium catalysed transformation of propargylic amines using CO₂ derived tether.

The palladium-catalyzed functionalization of alkenes and alkynes is an important field of research, as these compounds are either bulk chemicals obtained from petroleum or easily synthesized. Nevertheless, it is very challenging to introduce functional groups onto carbon-carbon multiple bonds bonds, due to their low reactivity on one side, and the difficulty in controlling the regioselectivity on the other side. A classical solution is the use of tethers/linkers, between substrates and reagents, which allow enhanced reactivity and high selectivity. Nevertheless, multi-step procedures are usually needed to introduce or remove tethers.

In our group, we have developed more efficient palladium catalysed reactions using simple tethers derived from trifluoroacetaldehyde, which can be installed in situ and easily removed. The carboetherification and carboamination of allylic amines and the carboamination of allylic alcohols were subsequently developed. The products of these reactions can be transformed into vicinal diamines and aminoalcohols, which are highly abundant and useful moieties found in natural compounds and pharmaceuticals.



Further effort is underway to develop this chemistry for use on propargylic substrates. During the course of this work, an intriguing side reaction was observed in present of carbonate bases: the direct incorporation of carbon dioxide to form an oxazolidinone product. This is interesting, as carbon dioxide is certainly one of the cheapest C1 source and its incorporation in organic substrates as a tether therefore highly attractive. The goal of this project is to optimize these preliminary results to develop a synthetically useful process.



During this project, you will experience a number of techniques that are integral to research in organic chemistry, which includes performing air and moisture sensitive reactions, the use of a glove box, the use of metal catalysts and organic transformations from the mg to the g scale, requiring synthesis, purification and characterization.

- 1) U. Orcel and J. Waser; *Angew. Chem. Int. Ed.* **2015**, *54*, 5250 –5254
- 2) U. Orcel and J. Waser; *Angew. Chem. Int. Ed.* **2016**, *55*, 12881 –12885
- 3) B. Muriel, U. Orcel, J. Waser; *Org. Lett.* **2017**, *19*, 3548–3551