2.7.1 Research Highlights for the period 2017-2019

Homogeneous Catalysis and Reaction Design by Bill Morandi

ABSTRACT: During the period 2017-2019, the homogeneous catalysis and reaction design group has produced many research milestones in the area of amination, deoxygenation and catalytic reversible reactions. The short report below concisely describes some of these recent highlights.

The period from 2017 to 2019 has seen many exciting developments in the homogeneous catalysis and reaction design group. These results have culminated in an offer for a tenured Professorship for Bill Morandi at the ETH Zurich (Successor of Prof. Diederich). Two former group members (Zhong Lian and Xianjie Fang) have also secured prestigious independent professorships in China as a result of their work in the group.

Scientifically, the first area where the group has made considerable progress is the area of shuttle catalysis.[1] This concept was introduced previously by our group, and was significantly expanded through the development of a transfer hydrochlorocarbonylation reaction.[2] This previously unknown reaction allows for the direct synthesis of acid chlorides from simple alkynes and alkenes without using carbon monoxide. Importantly, this reaction was not possible using traditional carbonylation reactions, clearly highlighting the possibility to use the concept of shuttle catalysis to unlock new reactivity in organic synthesis.

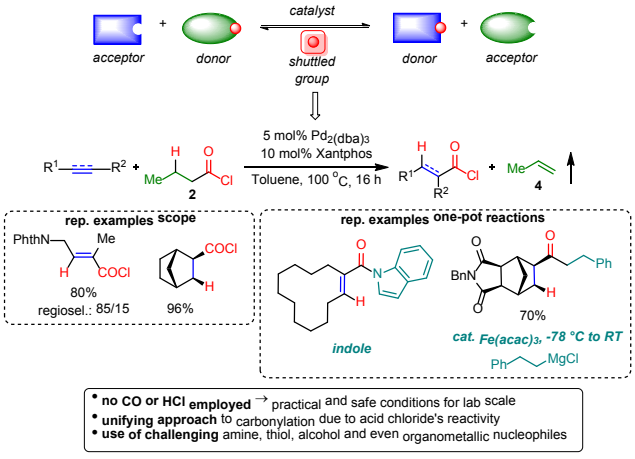

Figure 1: Catalytic transfer hydrochlorocarbonylation of alkynes and alkenes under Pd-catalysis.

Following up on our concept of shuttle catalysis, our group has moved towards the development of group exchange reactions which can be considered as single bond metathesis reactions. We have been able to develop a functional group metathesis reaction wherein two different functional groups are exchanged between two substrates.[3] In this process, a Pd catalyst mediates the exchange between an acid chloride and an iodide group. This metathesis reaction was used in the rapid preparation of acid chlorides and aryl iodides. Interestingly, mechanistic studies revealed that the Xantphos ligand acts as an aryl group shuttle that mediates the group transfer between the two substrates.

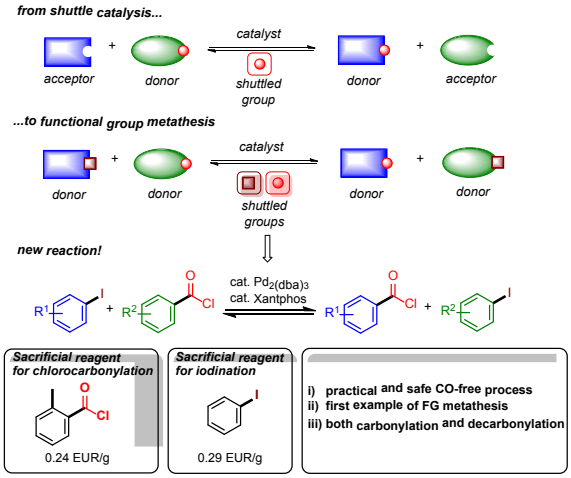

Figure 2: Catalytic functional group metathesis under Pd-catalysis.

A C–S bond metathesis has also been developed using a reversible transfer arylation strategy.[4] This reaction represents a new, complementary approach to traditional, kinetically controlled cross-coupling reactions. Using this reaction, libraries of bioactive compounds can readily be accessed and a commercial polymer (polyphenylene sulfide) could be depolymerized efficiently. More recently, the development of a Ni-based system allowed us to extend this reactivity to challenging macrocyclizations taking advantage of the self-correcting ability of this metathesis reaction. Overall, this reaction provides a new entry into the manipulation of aromatic thioethers which are key components of bioactive molecules and materials.

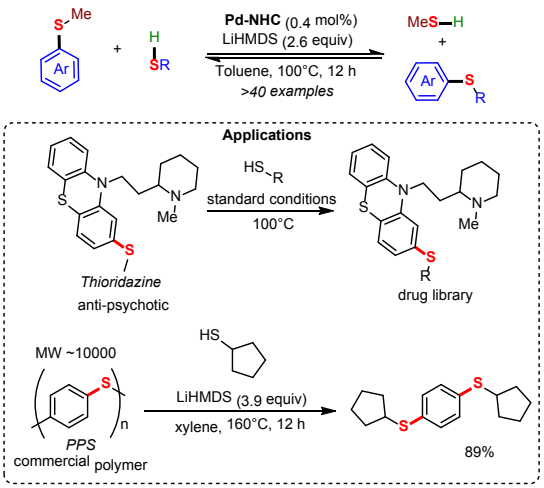

Figure 3: Catalytic C-S bond metathesis and synthetic applications.

This strategy could also be used to perform C–P bond metathesis for the synthesis of complex phosphorous containing heterocycles.[4] Using this strategy, a commonly encountered side reaction in catalytic cross-coupling, aryl group scrambling, could be turned into a new powerful method for the rapid discovery of novel phosphorous heterocycles for applications in catalysis or materials science.

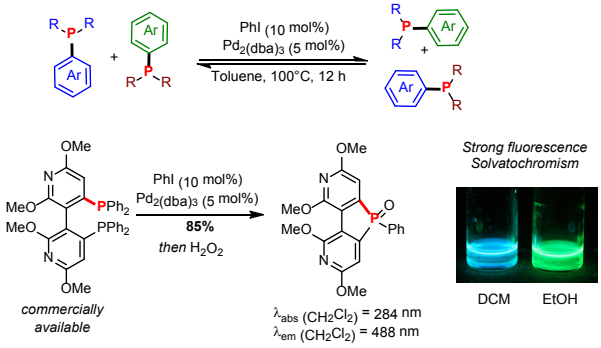

Figure 4: Catalytic C-P bond metathesis and synthetic applications.

The group has further been active in the catalytic amination of alkenes. One of the highlights was the discovery of an alkene aminochlorination reaction which exhibits an extremely broad substrate scope.[5] This reaction utilizes an inexpensive Fe catalyst and NaCl as the chloride source. Using this new transformation, many unprotected bioactive substrates could be aminated, boding well for the application of this reaction in medicinal and agrochemistry.

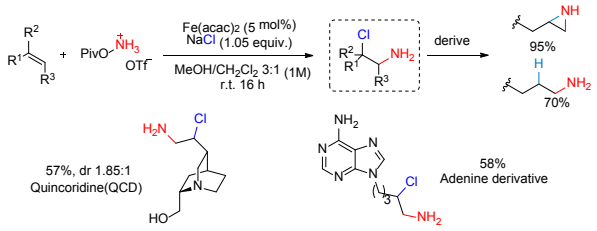

Figure 5: Fe-catalyzed aminochlorination of alkenes using an hydroxylamine-derived reagent and NaCl.

Finally, the group further explored the possibility of selectively defunctionalizing polyol derivatives. One of the highlights was a collaborative project with the Thiel group (MPI) where we developed an unusual example of reductive pinacol type rearrangement.[6] A salient feature of this work was the possibility to use completely unactivated diols which are traditionally unreactive in pinacol rearrangement. Experimental and theoretical studies have shed light on the underlying effects controlling this intriguing reactivity.

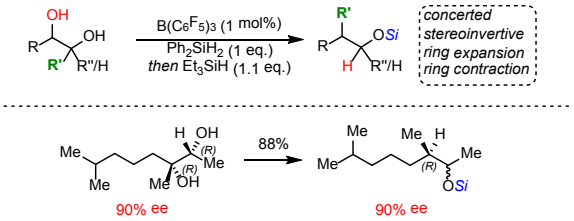

Figure 6: Boron-catalyzed reductive Pinacol-type rearrangement.

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