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Transforms Enabled by Copper Photocatalysis

Olefin Functionalization

Copper has served a rich history in organic synthesis through a plethora of reactivities such as Lewis-acid catalysis, cross-coupling, and conjugate additions. Despite the prevalence of these reactivity modes, copper's photocatalytic counterpart would remain obscured in history even through McMillin's seminal discovery of the first photoexcited copper complex in 1977 and Sauvage's optimized complex
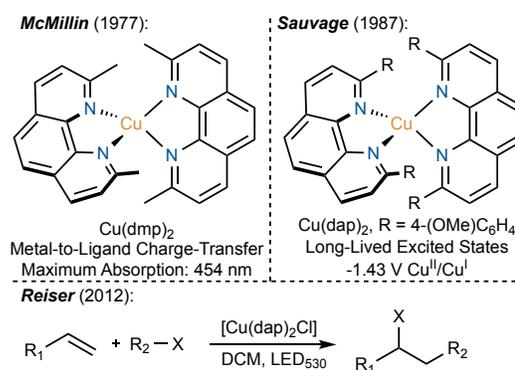

Figure 1. Complex Optimization and Application

for reductive homo-coupling of benzylic arenes in 1987.[1,2] Three decades later in 2012, Reiser engaged in the resurgence of copper photocatalysis through a preliminary communication on the carbohalogenation of olefins (Figure 1).[3] This reactivity provided a foundation for the functionalization of olefins with a variety of reagent classes. Further evolution from these advancements includes employment of more intricate partners and the incorporation of enantioinduction.

Cross-Coupling

As Reiser began to explore the functionalization of olefins, there was concurrent seminal efforts from the Sanford group which reported the trifluoromethylation of boronic acids through a traditional photocatalytic system employing copper (Figure 2).[4] Expansion of the copper metallophotocatalysis regime then turned towards more challenging bond formations as seen through the cross-dehydrogenative coupling of tetrahydroisoquinolines with alkynes. In addition to

Figure 2. Advancements in Cross-Coupling

these findings, alternative reaction pathways of a copper photoinduced systems allowed for the enantioconvergent N-alkylation of amines through mild conditions.[5] These new mechanistic
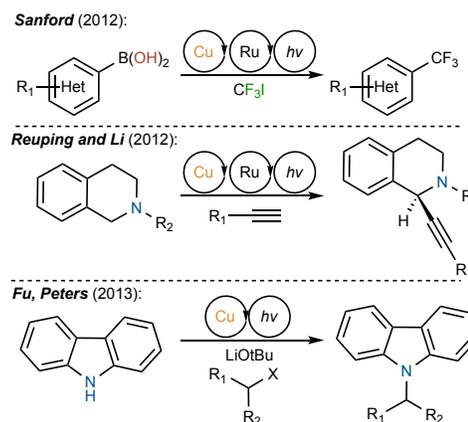
paradigms which proceed through radical pathways have since evolved into general systems transforming common building blocks such as alkyl halides and enabling their transformation to either trifluoromethylated or aminated derivatives.

Decarboxylative Functionalization

A common limitation of the recently released methods employing copper photocatalysis is the pre-requisite for a site-selective functional group to serve as the radical source. Coincidentally, in the last decade, redox-active esters have demonstrated their facile ability to generate radical precursors. The merging of both reactivity manifolds has resulted in the over-writing of the previous limitations of copper photocatalysis and now enables a diverse scope in reactivity. An initial report disclosed the decarboxylative difluoroacetylation of conjugated carboxylic acids.[6] Although this report did not detail a complex transformation, it would soon be followed by continuous developments in carbon-heteroatom bond

Figure 3. Decarboxylative Methods

formation and ultimately the construction of carbon-carbon bonds.[7,8] Considering these discoveries, new transforms are also emerging with an entirely new perspective in the form of introducing carbon-carbon π bonds.[9]

In a span of ten years, copper catalysis is now expanding the arsenal of synthetic chemists through the development of its photocatalytic counterpart. Initial reports have led to the solution to long-standing problems in olefin functionalization, carbon bond formation with a variety of partners, and decarboxylative processes are enabling novel unanticipated transforms. Further developments in the scopes and mechanistic investigations of these processes will enable chemical practitioners to rationally design novel reactivity by simply choosing the catalytic regime necessary.

References:

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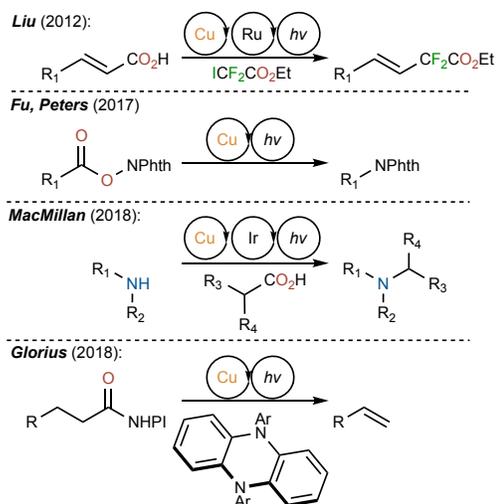[7] Fu, G. *J. Am. Chem. Soc.* **2017**, 139, 12153.   [8] MacMillan, D. *Nature*, **559**, 83.   [9] Glorius, F. *ACS Catal.* **2018**, 8, 1715.