

1. Publishable summary

Over the past few decades, Bergman, Hartwig, Davies, and many others have demonstrated that the selective and efficient functionalization of non-activated C(sp³)-H bonds of simple aliphatic substrates can be achieved through diverse metal-catalyzed reactions.^[1] However, achieving catalyst-controlled selective C(sp³)-H bond functionalization of more complex substrates such as alpha-amino acids remains a challenging task. In this regard, within this project, we aimed at studying the *catalytic functionalization of inert C(sp³)-H bonds assisted by sulfur-tethered directing groups* paying particular attention to the *straightforward chemical modification of amino acids and peptides*.

Amino acids are versatile chiral building blocks in total synthesis and ligand design.^[2] However, the limited number of amino acids genetically encoded is rather limited and therefore there is a need for new methodologies to achieve their straightforward chemical modification.

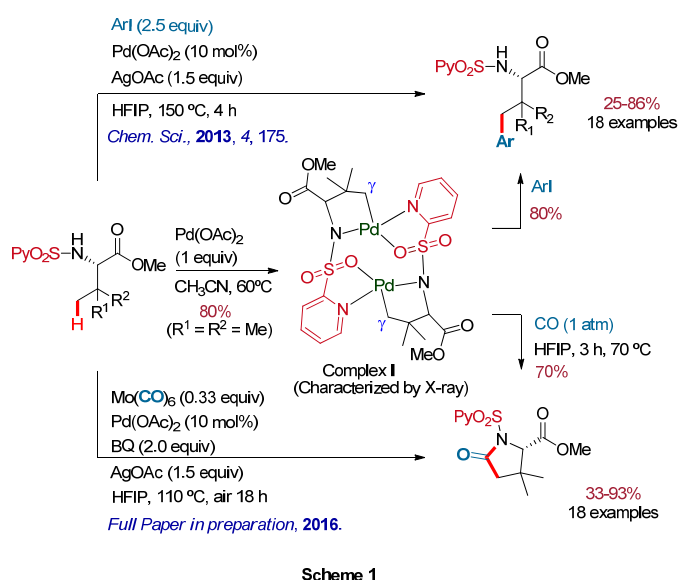
The most relevant results are presented in Scheme 1. We have developed an efficient protocol to perform the remote palladium-catalyzed gamma-C(sp³) C-H arylation of *N*-(2-pyridyl)sulfonyl amino acid derivatives (**Phase I: Chem. Sci., 2013, 4, 175**);^[3] as well as a selective gamma-C(sp³)-H carbonylation of *N*-(2-pyridyl)sulfonyl (*N*-SO₂Py)-protected amines by using palladium-catalysis and Mo(CO)₆ as carbonyl source (**Phase II: Full Paper in preparation, 2016**).^[4] Both functionalization processes have been applied to the post-synthetic modification of small peptides as a means of optimizing their molecular function or discovering new biologically active candidates.^[5] This extension to the late-stage

functionalization of more complex molecules not only adds more weight to the functional group tolerance of the methods, but also illustrates the capacity of the bidentate *N*-SO₂Py directing group to act in the presence of other coordinating elements. The ability to induce site-specific reactivity on a given molecule at otherwise unreactive sites in complex settings has tremendous significance to the field of complex molecule synthesis.

In any case, general aspects of each type of C-H functionalization, including remaining challenges as well as mechanistic details, have been explored.

Bibliography

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