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Dissertation Defense

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Location: SRB, 139

Sustainable Nanocatalysis in Water for C–C and C–N Cross-Couplings

Abstract

Nature's way of making complex molecules has inspired synthetic chemists to design efficient and environmentally responsible retro-synthetic pathways. Along these lines, chemistry in water, especially micellar catalysis, has gained popularity in the last two decades.¹ Direct adoption of this technology by numerous pharmaceutical industries has demonstrated its scalability resulting in reduced process cost, waste generation, and other improved economic/environmental parameters.^{2,3} Despite these advancements, fundamental understanding of micellar catalysis is currently lacking. Therefore, we provide mechanistic insights into micellar catalysis in the context of palladium (Pd)-catalyzed cross-coupling reactions.

For efficient micellar Pd-catalysis, our laboratory has reported a novel proline-based amphiphile PS-750-M (*now commercially available by Sigma-Aldrich, catalog # 911178 and 911151*).^{4,5} In this amphiphile, the presence of tertiary amide functional group within the linker region provides significant polarity to the micellar inner-core, enabling the accommodation of polar substrates and reactive intermediates. This unique structural advantage has been exploited for the development of various valued transformations in the context of nanocatalysis, cross-couplings, amide couplings, hydrogenations, oxidations/reductions, etc.⁵ Utilizing the same amphiphile, the dissertation work focuses on fundamental understanding, industrial applications, and advancements of micellar catalysis.

First part of the dissertation work describes the development of a novel bimetallic heterogeneous Pd/copper (Cu) catalyst for challenging cross-couplings of primary and secondary amines with (hetero)aryl halides.⁶ The structure, morphology, and stability of this charcoal immobilized phosphine bound Pd/Cu catalyst were extensively studied using various state-of-the-art techniques. The heterogeneous nature of the catalyst imparts recyclability as verified by Scott's method⁸ and reduces the metal leaching. Likewise, a bimetallic Pd/Cu nanocatalyst was developed to promote the selective C–N bond-forming reaction between nitro(hetero)arenes and (hetero)aryl(pseudo)halides under mild micellar domino reductive-coupling conditions. This was achieved by suppressing the detrimental dehalogenation pathway.

Next, the reactivity of carbanion-type intermediates was explored under aqueous micellar conditions to enable Pd-catalyzed α -arylation of arylacetonitriles as well as carboxylation of aryl halides.⁸ The shielding effect imparted by the nano-micelles of PS-750-M plays a crucial role in determining the lifetime of the reactive intermediates under aqueous conditions. With fine-tuning of the Pd nanocatalysts, desired reactions were achieved with a broad substrate scope and scalability. Detailed mechanistic investigations using ³¹P NMR spectroscopy support the intermediacy of carbanion.

Finally, the structural features of the amphiphile PS-750-M were harnessed for the ligand-free Pd nanocatalysis under aqueous conditions.^{9,10} Here, the ester and amide carbonyls of the surfactant molecule bind to the Pd nanoparticles and promote oxidative-Heck couplings, Suzuki-Miyaura couplings of *water-sensitive acid chlorides*. Spectroscopic tools, such as ¹³C NMR, IR, and SERS, were used to verify the binding of Pd with amphiphile.

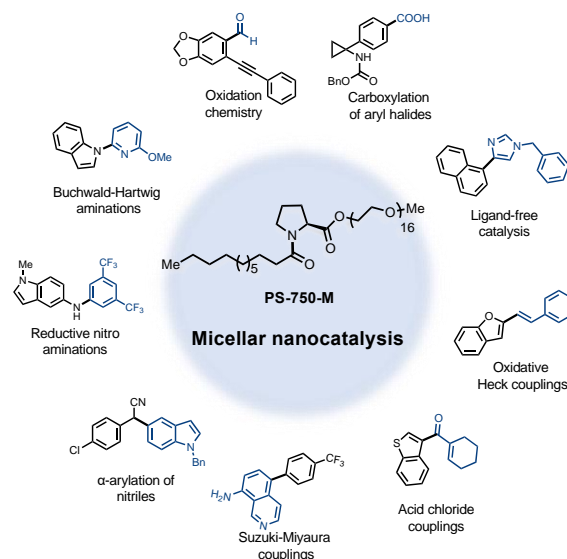


Figure 1. Overview of PS-750-M mediated micellar catalysis.

References

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