The Ligand: An Overlooked Element in Sustainable Catalysis

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Abstract. Ligands are crucial for catalysis, but their synthesis and purification generate waste, consume energy and resources, and may release toxins. Therefore, it's important to mitigate their impact on sustainability and waste generation by carefully designing the processes that involve very low ligand loading or are ligand-free.

Critical Components of Catalysis. Solvent, metal, and ligand are the fundamental components of sustainable catalysis (Figure 1A). Sustainable solvents help reduce the use of hazardous organic solvents, which can contribute to pollution and health hazards. Water is a sustainable and green solvent due to its abundance, non-toxicity, and recyclability. Many processes that use water as a solvent require lower temperatures and pressures than alternative solvents, resulting in energy savings and reduced carbon emissions [1]. However, water has limitations, such as corroding certain materials and inefficiently dissolving non-polar substances. Micellar catalysis has emerged as a promising technology that overcomes some limitations and enables catalysis in aqueous environments. The designer surfactants leading to micelles act as dynamic nanoreactors to achieve catalysis in water. Although it has numerous benefits, this technique has limitations, including the need for ligands on metals and solvents for product extraction [2]. Despite this, micellar catalysis has demonstrated remarkable potential in addressing challenges associated with conventional catalytic methods.

The earth-abundant metal catalysis is vital in advancing sustainability by offering cost-effective, accessible, and environment-friendly solutions across various industries. Earth-abundant metals such as iron, copper, nickel, cobalt, and manganese are more widely available and less costly than precious metals like platinum, palladium (Pd), and gold [3]. However, when precious metals are used in low loading without expensive ligands and toxic solvents, in a holistic sense, it may lead to sustainable catalysis. However, when used with costly ligands in high loading, regardless of earth-abundant metals, the catalysis impact diminishes as toxic solvents and often expensive metals may be required for ligand synthesis. Thus, the ligand is the second most crucial element in catalysis after solvents.

Ligands in Palladium Catalysis. Unfortunately, the ligand is an often overlooked element in sustainable catalysis. In catalysis, ligands play a fundamental role in modulating the reactivity and selectivity of metal catalysts (Figure 1B). By carefully selecting ligands, chemists design catalysts with improved activity, selectivity, and stability, thus enhancing the efficiency and sustainability of catalytic processes. In addition to their role in traditional homogeneous catalysis, ligands also play a crucial role in heterogeneous catalysis by functionalizing and stabilizing catalytic surfaces and may, therefore, improve their activity and selectivity. By designing ligands that selectively bind to specific sites on the catalyst surface, the efficiency of heterogeneous catalytic reactions can be enhanced while minimizing undesired side reactions. Likewise, the role of ligands in earth-abundant metal catalysis is critical and multifaceted, influencing the catalyst's activity, selectivity, and stability. Thus, the ligand represents a cornerstone in sustainable catalysis, and their environmental impact cannot be ignored.

Using no ligands or very low ligand loadings is the optimal choice for catalysis. Micelles can serve as ligands and vesicles to accommodate the metal, leading to ligand-free or low metal-loading catalysis. Lipshutz was the first to report using low-level ligand-loading Pd catalysis in water [4]. By forming a complex of highly lipophilic HandaPhos ligand with Pd in a 1:1 ratio, a micelle-soluble complex was created (Figure 1C). This enabled Suzuki-Miyaura couplings in water with <1000 ppm Pd. The presence of optimal lipophilicity and sterically bulky groups in the ligand allowed for efficient micellar catalysis. The theoretical investigation showed that while the formation of di-ligated complexes of HandaPhos is endothermic by +66kJ/mol for HandaPhos, it is exothermic by -62kJ/mol for XPhos, suggesting the need for only one HandaPhos molecule per Pd. Later, Senanayke and co-workers reported using the BIDIME ligand in Triton X micelles to achieve Suzuki-Miyaura couplings with 500-2000 ppm Pd [5]. However, the synthesis of BIDIME and HandaPhos ligands is resource intensive. Lipshutz has also reported less resource-intensive Fe ppm Pd technology for efficient cross-couplings at the ppm level of Pd [6]. Nevertheless, ligands are still necessary to accomplish such chemistry (Figure 1D).

Ligand-Free Palladium Catalysis. Although ligand-free Pd catalysis has existed for over two decades [7,8], it is difficult to determine its practicality when applied to complex substrates (Figure 2A). Previously, organic solvents or an aqueous environment above the boiling point of water were required [9]. However, in a recent collaboration with Takeda Pharmaceuticals, Handa, Leahy, and co-workers reported ligand-free cross-couplings of (hetero)aryl halides and water-sensitive acid chlorides with (hetero)arylboronic acids in water [10]. The report revealed the nature of the catalysts, which was the in-situ formation of ultrasmall nanoparticles of Pd(0) encapsulated by the micelles of PS-750-M (Figure 2B). The ^{13}C nuclear magnetic resonance (NMR), infrared, and surface-enhanced Raman spectroscopy provided evidence for this. The formation of ultrasmall nanoparticles of Pd in its zero oxidation state was supported by high-resolution transmission electron microscopy imaging and X-ray photoelectron spectroscopy. The micelles charged with Pd(0) showed ^{13}C signals at 183.4-180.3 ppm, while the Pd-free micelles displayed such signals at 175.5-173.6 ppm. These signals arise from the metal-bound and unbound carbonyl groups of PS-750-M.

Ligand-Free Iridium Catalysis. Recycling a metal catalyst and not requiring a ligand makes catalysis sustainable. Recently, Handa and Gallou reported an example of this with the selective aromatic ring hydrogenation of phosphine oxide scaffolds using ligand-free ultrasmall nanoparticles of iridium(0) [11]. The in-situ generated nanoparticles catalyzed the site-selective hydrogenation of aromatic rings, synthesizing important ligand-like structures (Figure 2C). The presence of hydride and solvent-nanoparticle-substrate interaction was responsible for the catalytic selectivity. Although the catalyst is recyclable and ligand-free, the downside of this technology is the requirement of high hydrogen pressure and the use of hexafluoroisopropanol as solvent.

Impact of Ni versus Pd Catalysis on Climate Change—A Case Study. Luescher, Lipshutz and Gallou compared the sustainability of Pd vs. Ni catalysis by calculating the amount of CO_2 generated from the specified catalytic processes [12]. They found that the amount of metal loading used is inconsequential in terms of the affect on sustainability (Figure 2D). The study included a comparison of the environmental indicators for producing 1 kg of virgin Pd and Ni from freshly mined ore. While Ni was found to be more sustainable in this respect. The case study looking at several additional factors associated with conducting Ni-catalyzed Suzuki couplings in organic solvents versus the same reaction catalyzed by Fe ppm Pd in water showed that the latter is far more favorable in terms of the impact on climate change. The calculations indicated that such a Ni-catalyzed reaction generates 2326 kg CO_2 per kg of desired product, while 1554 kg CO_2 are produced for the same transformation when Fe ppm Pd catalysis is employed in water. In both studies, ligands play a crucial role in the outcome from each reaction. The study showcased that consideration of cost for earth-abundant metals versus precious metals alone is not enough to determine if a process is sustainable.

Concluding Remarks. The importance of ligand-enabled and ligand-free sustainable catalysis cannot be overstated in the context of green chemistry and sustainable development. Ligands play a crucial role in enhancing catalytic efficiency, selectivity, and stability, while ligand-free systems offer simplicity and cost-effectiveness. When developing earth-abundant metal catalysis, factors focused on metal loading, type of ligand used, and the choice of reaction medium cannot be overlooked in evaluating overall sustainability. Although ligand-free catalysis is not applicable to all transformations, it is important to embrace new innovative catalytic strategies to advance scientific frontiers, which is imperative for fostering a more sustainable future for generations to come.

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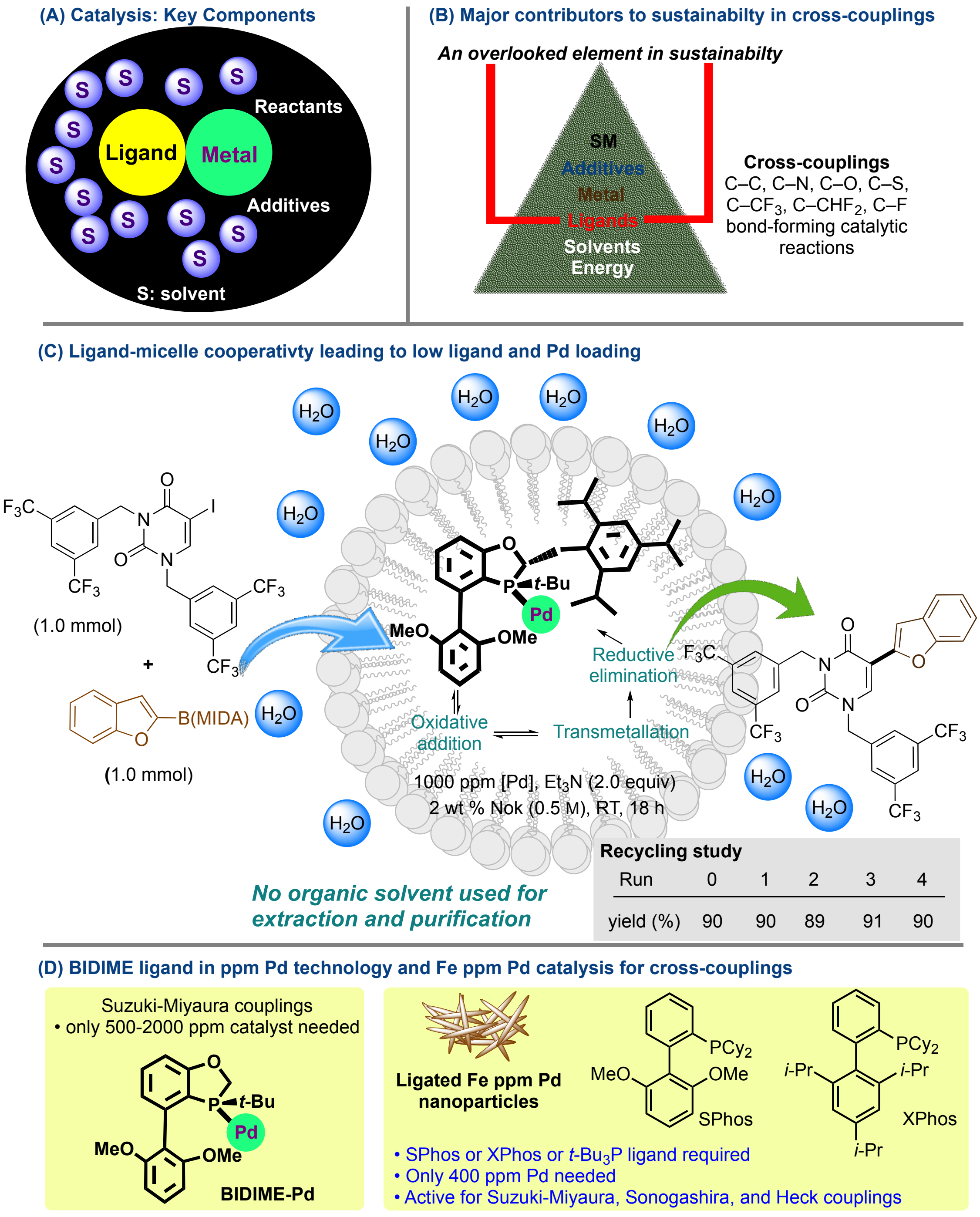

Figure 1. Ligands in Sustainable Catalysis. (A) Significant components in catalytic events; (B) factors impacting sustainability in cross-couplings; (C) HandaPhos ligand- and micelle-enabled Suzuki-Miyaura couplings with ppm Pd in water [4]; (D) BIDIME and nanoparticle technology for cross-couplings with ppm levels of Pd [5] and Fe ppm Pd technology [6].

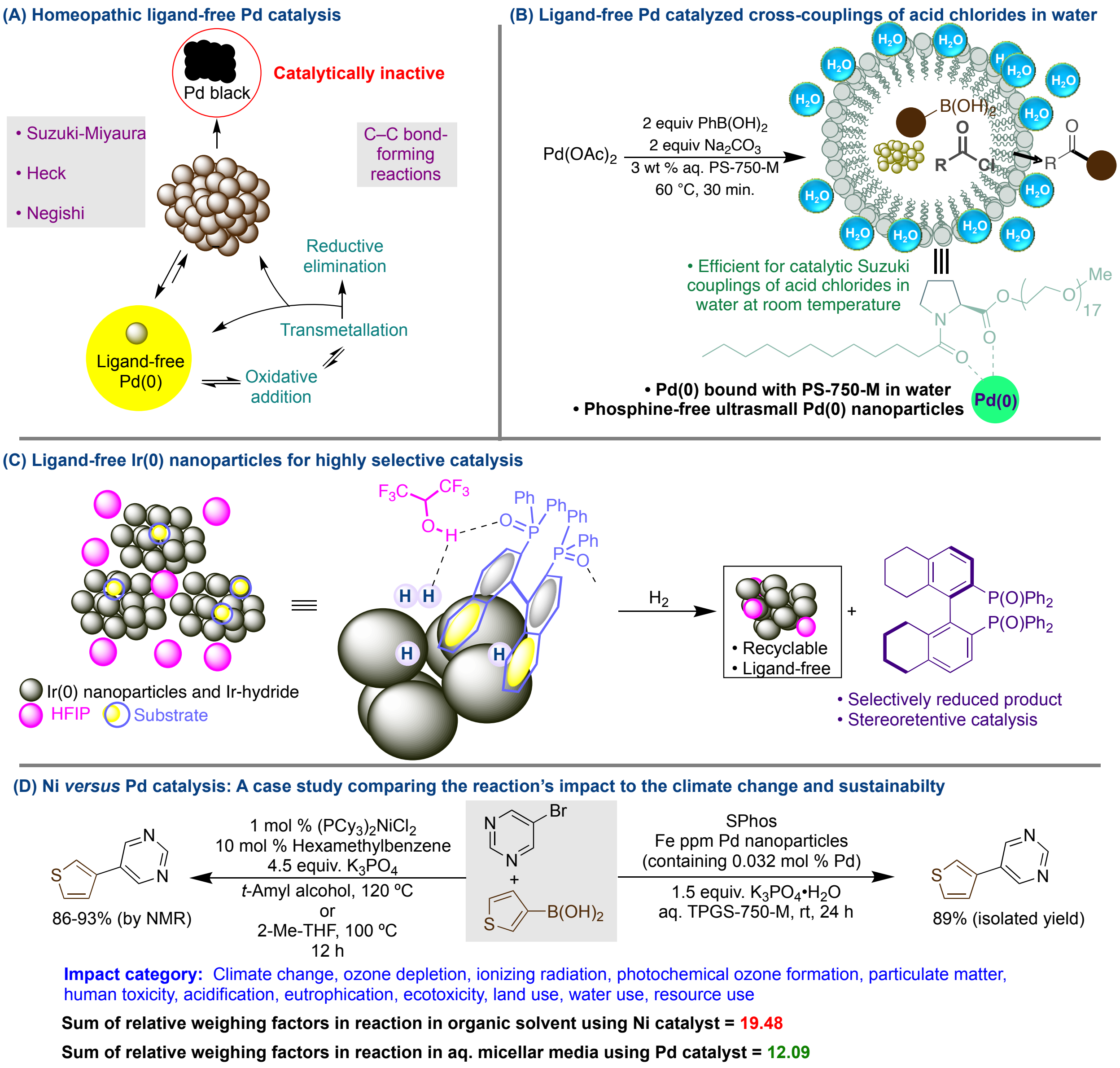

Figure 2. Ligand-Free Catalysis. (A) Seminal ligand-free Pd catalysis [7,8]; (B) micellar catalysis on challenging reactions and substrates [10]; (C) sustainable Ir(0) catalysis [11]; (D) a case study on Ni versus Pd catalysis for sustainability [12].