

## Reductive Elimination in High-Valent Palladium Catalysis

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November 6, 2018

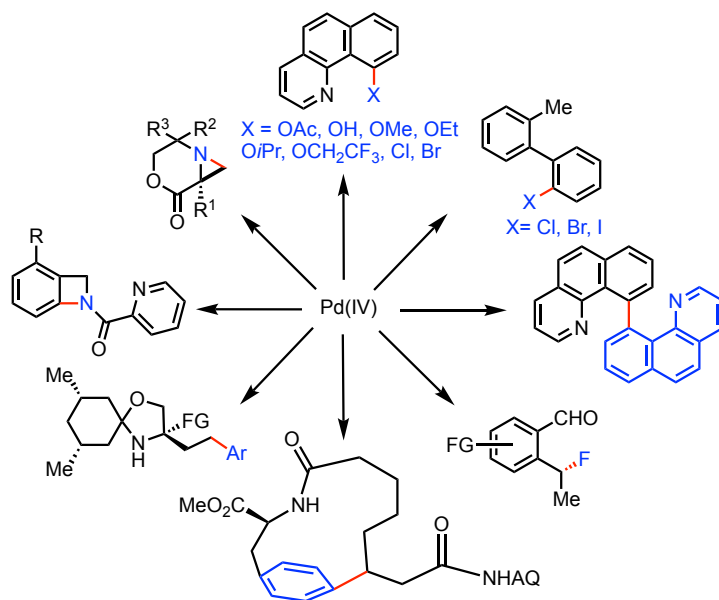
### Early Application and Mechanistic Studies of High-Valent Palladium Complexes

High-valent palladium catalysis has emerged as a valuable technology, enabling what would be kinetically slow and thermodynamically disfavored<sup>1</sup> reductive eliminations for Pd(II) species and enabling directed C—H activation at either the Pd(II) or Pd(IV) oxidation state within a Pd(II)/Pd(IV) or Pd(II)/Pd(III) catalytic cycle. High-valent palladium complexes have been known to exist for decades, but only over the last twenty years have they emerged as a synthetically useful technology.<sup>2</sup> Pioneering work using this technology to form C—C, C—O, C—N, and C—X bonds has been championed by Sanford and coworkers since the early 2000s.<sup>3</sup> Sanford's work in this field has focused largely on catalyst development and mechanism elucidation in C—H activation reactions, particularly for the steps of C—H activation and reductive elimination. The strongest evidence for Pd(IV)-mediated mechanisms is the stoichiometric generation, isolation, and characterization of various Pd(IV) species involved in catalytic cycles of interest by X-ray crystallography and NMR spectroscopy. Additionally, their catalytic competence was shown. Simultaneously, the research groups of Yu and Ritter began expanding the scope of competent reductive elimination partners and developing mechanistic probes of other related C—H activation/reductive elimination processes respectively.<sup>4,5</sup> Ritter determined that bimetallic Pd(III) complexes are formed in some reactions, sparking a debate on the nature of high-valent palladium species present in reactions. The understanding gained through these publications, which culminated in a coauthored publication between Ritter and Sanford connecting bimetallic Pd(III) and mononuclear Pd(IV) that provides evidence that bimetallic Pd(III) dimers can disproportionate

into mononuclear Pd(II) and Pd(IV) species, has enabled the application of Pd(IV) catalysis to new chemical challenges.<sup>6</sup>

### Selected Recent Applications of High-Valent Palladium Catalysis

Pioneering studies on the mechanism of C—C, C—X, and C—O bond forming reactions through C—H activation has enabled new methods that synthesize challenging organic motifs (Figure 1). These include the synthesis of highly strained nitrogen heterocycles<sup>7,8</sup> that are largely inaccessible by other routes, enantioselectively fluorinated benzaldehyde derivatives,<sup>9</sup> functionalized nitrogen ketals capable of being deprotected to give amino alcohols,<sup>10</sup> and biologically active, macrocyclic tripeptides, including strained cyclophanes.<sup>11</sup>



**Figure 1.** Applications of High-Valent Palladium Catalysis

### Summary

High-valent palladium catalysis has become extremely useful in enabling a variety of chemical transformations, particularly those plagued by challenging means.

### References

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