

Reductive Elimination of Alkylamines and Ethers: Reactions of Bisphosphine-Ligated Palladium(II) Complexes

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Compounds containing the amine functionality have applications that include pharmaceuticals, insecticides, lubricants, dyes, and ligands for metal ions. Linear alkylamines are currently prepared by one of three possible reactions: nucleophilic alkylation, hydroformylation and reductive amination, or hydrocyanation of an olefin and reduction of the corresponding nitrile. Amine alkylation is not practiced on an industrial scale because processing the halide waste is not economical; hydroformylation and hydrocyanation are not practiced on a laboratory scale due to the high pressure and the toxicity of the required reactants. Hydroformylation and hydrocyanation involve the addition of a carbon atom to the alkyl chain, and the number of carbons on the alkyl chain can influence the physical properties of the alkylamine.¹

One possible solution to this problem is to convert the olefin directly to an alkylamine without the intervening aldehyde or nitrile intermediates by a process called hydroamination. One of the major issues with current hydroamination methods is the balance between linear (“anti-Markovnikov”) and internal (“Markovnikov”) products.^{2, 3} The linear product is more industrially desirable, whereas modern hydroamination methods yield the internal product. The development of a catalyst to provide the linear product was listed as one of the “Top Ten Challenges” in 1993 and remains an unsolved problem.⁴ The C-N bond-forming reaction for a proposed hydroamination reaction involves reductive elimination from an alkyl amido complex, yet this elementary reaction is uncommon from isolated complexes (Figure 1).

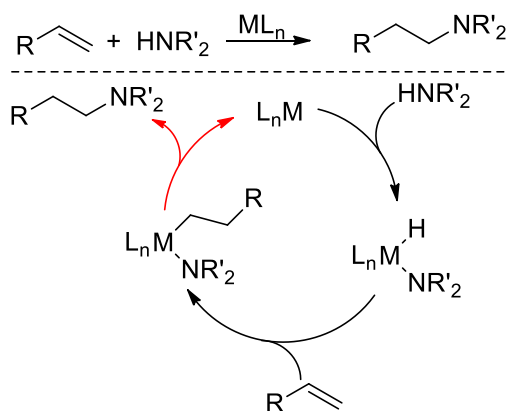


Figure 1. Proposed catalytic cycle for the formation of linear alkylamines.

Thus far, only high-valent $Pt(IV)$ ⁵ or $Ni(III)$ ^{6, 7} complexes have been demonstrated to undergo $C(sp^3)-N$ reductive elimination. We show that reductive elimination to form a $C(sp^3)-N$ bond from benzylpalladium(II) amido complexes occurs, and we provide experimental evidence that the C-N bond-forming reaction occurs by an ionic mechanism.⁸ The stereochemical outcome

of the reaction indicates an ionic pathway, but the process lacks many of the effects of electronic and solvent perturbations that typically signal an ionic intermediate (Figure 2).

We also report thermal reductive elimination from benzylpalladium(II) aryloxy complexes to form a C(sp³)-O bond, and a series of experiments provide insight into the mechanism of the C-O bond-forming reaction.⁹ In short, our data show that the mechanism of this reaction is more akin to reductive eliminations to form C(sp³)-N bonds from palladium(II) than those that form C(sp²)-O bonds from palladium(II) or any type of C-O or C-N bond from higher-valent metal centers. However, our data indicate that substantial differences exist between reductive eliminations to form the C(sp³) bonds in ethers and amines from palladium(II) (Figure 2).

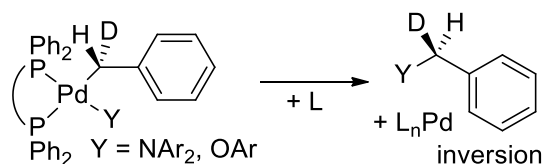


Figure 2. Benzylpalladium complexes react by an ionic mechanism.

Finally, we attempted to synthesize and isolate alkylpalladium(II) amido complexes to study the C-N reductive elimination reaction from complexes other than benzylpalladium species. We investigated neopentylpalladium amido complexes and observed reductive elimination in low yield to form the alkylamine product (Figure 3). Complexes with other hydrocarbyl ligands were investigated, but these complexes did not provide any of the C-N reductive elimination product. We also investigated azametallacyclic complexes and observed reductive elimination from norbornylpalladium complexes, although the yield of the indoline product was low. Reductive elimination from the neopentylpalladium and metallacyclic palladium complexes is proposed to occur by a concerted reductive elimination mechanism. Our final investigation focused on non-metallacyclic norbornylpalladium complexes, but once again, the yield of the C-N reductive elimination product was low (Figure 3). By examining the stereochemical configuration of the products from reductive elimination, it appears that both a concerted and ionic mechanism may be operative. Although the yields of the alkylamine products are low in each case, these are the first reductive eliminations to form alkylamines from low-valent alkylmetal amido complexes without the addition of an oxidant.

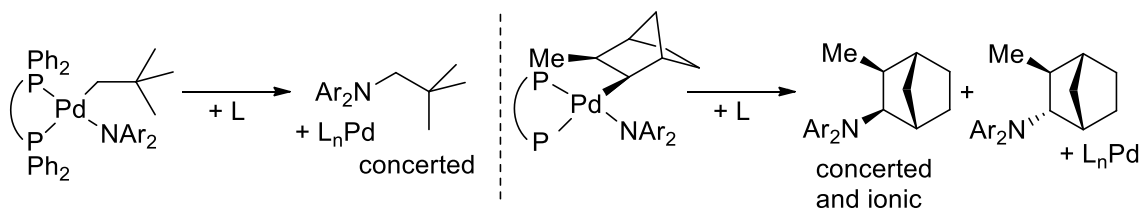


Figure 3. Proposed mechanisms for reductive elimination from alkylpalladium complexes.

The data collected demonstrate that C(sp³)-N reductive elimination from purely alkyl Pd(II) complexes can occur, albeit in low yield. We propose a concerted mechanism for the C(sp³)-N

reductive elimination reaction for neopentylpalladium and metallacyclic palladium complexes. In contrast, we propose an ionic mechanism for the C(sp³)-N bond-forming reductive elimination for benzyl palladium and potentially for some norbornylpalladium complexes. It is apparent from these data that C(sp³)-N reductive elimination from purely alkyl Pd(II) complexes can occur, but this reaction is challenging to achieve in high yield.

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