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Rationalization of the mechanism of *in situ* Pd(0) formation for cross-coupling reactions from novel unsymmetrical pincer palladacycles using DFT calculations

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ABSTRACT

Density functional theory (DFT) is used to determine the mechanism for Pd(0) generation from pincer palladacycle pre-catalysts. The elucidated mechanisms comprise two key steps, transmetallation and reductive elimination. It is found that the presence of a base in the pre-catalyst activation step serves to significantly lower the Gibbs free energy barrier of the transmetallation step and the Gibbs free energy of the overall pre-catalyst activation. The DFT results are used to rationalize the catalytic activity of a number of pincer palladacycles in the Suzuki-Miyaura coupling of sterically demanding and electronically deactivated aryl bromides with 2-tolylboronic acid. A strong correlation exists between the Gibbs free energy barrier of the transmetallation step and/or overall pre-catalyst activation energy and the percentage conversions of the Suzuki- Miyaura coupling in the presence of the novel pre-catalysts. The data presented suggest that the slow, controlled release of the “true, active catalyst,” Pd(0), from the pincer palladacycle pre-catalysts provides the optimum reaction conditions and may be achieved by a high transmetallation energy barrier or overall pre-catalyst activation energy or both.

1. Introduction

The numerous application of palladacycles [1] in catalysis [2–4] since the discovery of their catalytic activity by Hermann and Beller et al. [5,6], over the last two decades cannot be overemphasized. This has become a vibrant research area amongst academics and industrialists as evidenced by the plethora of scholarly articles and reviews [1–4] and an excellent book [7] now available. Of increasing significance is the employment of these species, especially the pincer-type palladacycles (in which a Pd-C bond is intramolecularly stabilized by two donor atoms in a YCY’ architecture, where C is the carbon of the Pd-C bond [8–11]) in the Suzuki-Miyaura [12,13] (SM) and Mizoroki-Heck [14] carbon-carbon (C-C) cross-coupling reactions which have emerged as highly important and facile routes to e.g., complex pharmaceuticals and industrially important starting materials [7]. Symmetrical palladacycles are attractive [1] due to their relative ease of synthesis as compared to unsymmetrical analogues. However, the latter offer the potential for fine tuning their reactivity and properties by adapting their ligand architectures [13].

Moreover, a number of reports in the literature assert that unsymmetrical pincer palladacycles often exhibit higher catalytic activity than their symmetrical counterparts [13,15,16]. In all cases, palladacycles, whether symmetrical, unsymmetrical pincers, or of the type C-Pd-Y, are thought to be pre-catalysts and, hence, precursors to Pd(0) [5,6,17–23] (Scheme 1 and 2).

In palladacycle chemistry, the well-studied key steps that occur during the SM reactions namely, transmetallation (TM) and reductive elimination (RE), have been studied via experimental [21] and theoretical (density functional theory, DFT) investigations [24].

Herein, we present a study of the pre-catalyst activation process for SM reactions involving palladacycles. The investigation starts with a thorough exploration of the formation of Pd(0) from symmetrical pincer palladacycles, YCY (**1**–**3**, Fig. 1) with and without base, and with and without solvent effects. This is extended to model unsymmetrical pincer YCY’ palladacycles (**4**–**6**, Fig. 1) to determine the effect of different donor ligand groups on the process. Based on the conclusions from these extensive studies on small and/or model systems, the formation mechanism of Pd(0)

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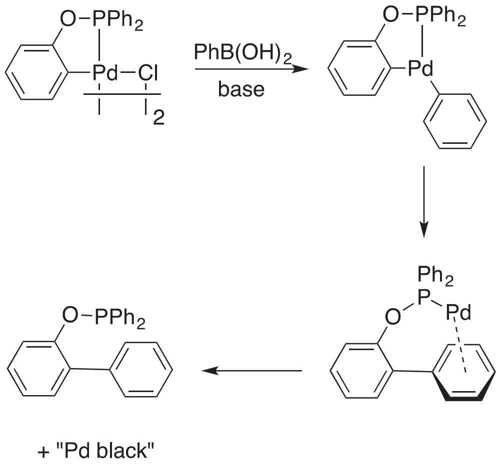


Scheme 1. Stabilization of Pd(0) in C-Pd-Y palladacycles.

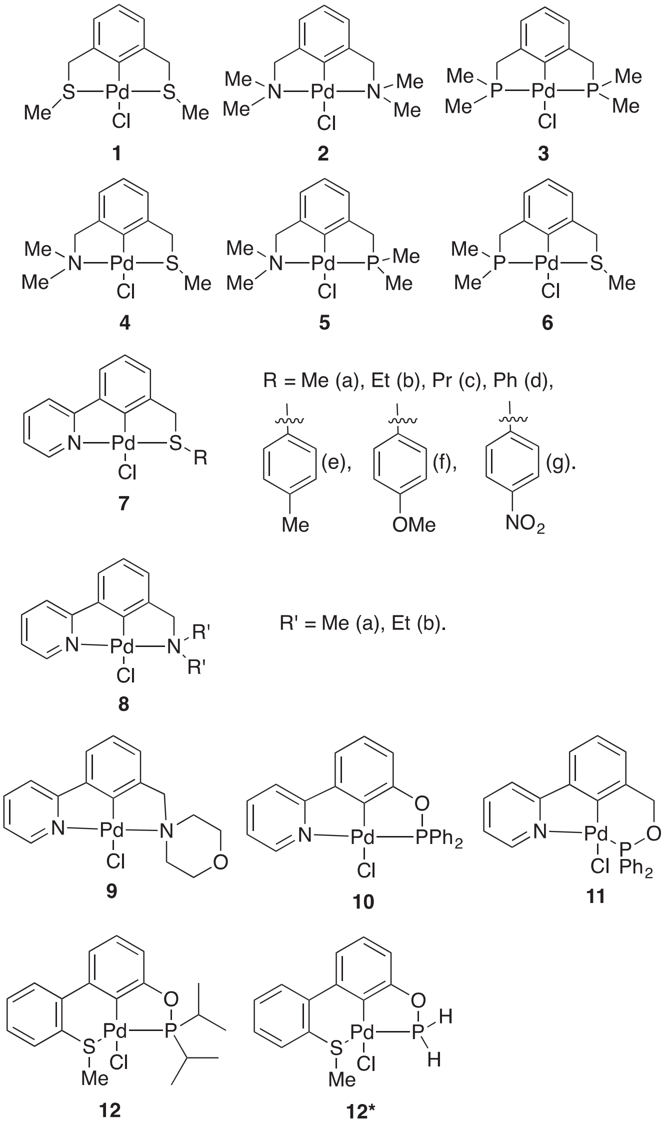


Fig. 1. Pincer palladacycles investigated in this study.

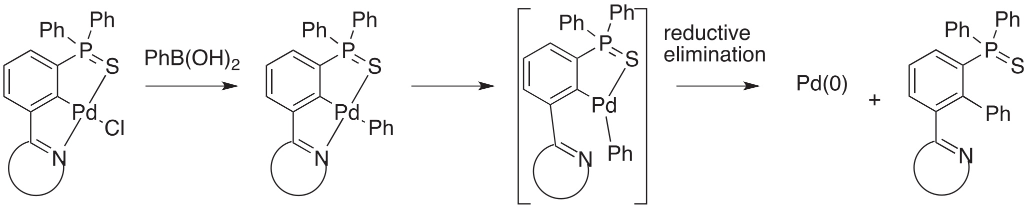
from recently synthesized YCY' pincer palladacycles (**7**–**12**, Fig. 1) will be explored. Finally, the results of these theoretical investigations will be used to rationalize catalytic testing of the newly-synthesized pincer palladacycles (**7**–**12**, Fig. 1) in the SM coupling of sterically demanding and electronically deactivated aryl bromides with phenylboronic acid. The synthesis has been reported for: **1** [25–27], **2** [28], **7a** [29], **7b-f** [30] and **8-11** [31].

2. Computational details

Calculations were performed using density functional theory as implemented in the GAUSSIAN 09 [32] package. All Pd complexes along the reaction pathway were considered in their singlet spin state. It was shown previously [9] that the geometric features of pincer palladacycles can be accurately reproduced by both PBE [33–35] and ωB97XD [36], and that the ωB97XD functional provides accurate energetics due to the inclusion of dispersion and long range corrections [37]. The detailed study of **1** - **6**, along with **7a**, was performed at the ωB97XD/6-311++G(2df,2p)[SDD]//PBE/6-31 + G(d,p)[SDD] level of theory, and investigation of the recently synthesized pincer palladacycles (**7a-g** - **12**) was performed at the ωB97XD/6-311++G(2df,2p)[SDD]//ωB97XD/6-31++G(d,p)[SDD] level of theory. Here the notation, 6-31 + G(d,p)[SDD] for example, implies all non-metal atoms were described by the standard basis set: 6-31 + G(d,p) in this case, and palladium was described by the relativistic effective core potential, SDD [38,39].

In each case, the minima and transition states on the potential energy surface (PES) were confirmed by the absence or presence of a single imaginary vibrational frequency mode, respectively [40] via frequency calculations performed at 298.15 K and 1 atm. The connectivity of the transition states to their adjacent minima was confirmed by eigenvector following calculations [41–43]. The Gibbs free energy corrections obtained at PBE/6-31 + G(d,p)[SDD] or ωB97XD/6-31++G(d,p)[SDD] level of theory were applied, unscaled, to the single point energy calculations using ωB97XD/6-311++G(2df,2p)[SDD].

Solvent effects were included using the polarizable continuum model (PCM) [44,45] with the continuous surface charge formalism of Scalmani and Frisch [46]. Solvent corrections were obtained for the gas-phase optimized geometries using the self-consistent reaction field (SCRF) with Universal Force Field (UFF) atomic radii at the ωB97XD/6-311++G(2df,2p)[SDD] level of theory. For **1-6** the non-polar solvents toluene ($\varepsilon = 2.374$), tetrahydrofuran ($\varepsilon = 7.426$)



Scheme 2. Formation of Pd(0) from unsymmetrical pincer palladacycles.