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Intramolecular Alkene Aminopalladation Reactions of (dppf)Pd(Ar)[N(Ar^1)(CH$_2$)$_3$CH=CH$_2$] Complexes. Insertion of Unactivated Alkenes into Pd−N Bonds

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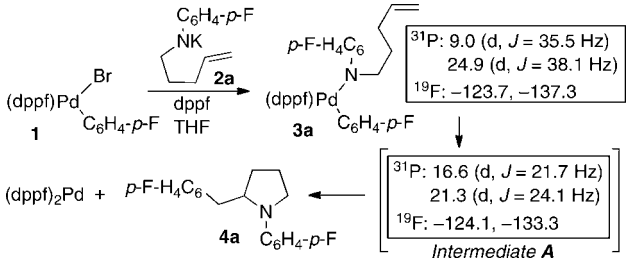
The prospect of effecting *syn*-migratory insertion of alkenes into palladium−nitrogen bonds has been of longstanding interest in organometallic chemistry. Studies on the viability of this transformation were a focal point of early work toward the development of late-metal catalyzed hydroamination reactions.[1,2] However, a number of experiments suggested that aminopalladation reactions of alkenes generally proceed through outer-sphere *anti*-addition pathways.[3] More recently, the *syn*-insertion of alkenes into Pd−N bonds has been implicated as a key step in many useful Pd-catalyzed reactions including alkene carboaminations,[4] diaminations,[5] oxidative aminations,[6] chloroaminations,[7] aminoacetoxylations,[8] and hetero-Heck transformations.[9,10] However, despite the considerable interest in these processes, the *syn*-migratory insertion of an alkene into the Pd−N bond of a well-characterized palladium amido complex has yet to be observed.[2,11,12]

Scheme 1



In this communication we describe the synthesis of (dppf)Pd(C$_6$H$_4$-*p*-F)[N(Ar^1)(CH$_2$)$_3$CH=CH$_2$] complexes **3**,[13] which are thought to be intermediates in Pd-catalyzed alkene carboamination reactions.[4] We illustrate that these complexes are transformed to 2-benzylpyrrolidines via migratory insertion of the alkene into the Pd−N bond, followed by reductive elimination of the resulting (dppf)palladium(aryl)(pyrrolidin-2-yl-methyl) complexes. These are the first examples of insertions of alkenes into Pd−N bonds of well-defined complexes.

Prior studies on the synthesis of L$_n$Pd(Ar)(NRR′) complexes suggested that the high reactivity of these species would preclude their isolation in most cases.[14] As such, the isolable (dppf)Pd(C$_6$H$_4$-*p*-F)(Br) complex **1** was prepared using previously described routes,[14,15] and the potassium anilide salt of *N*-(C$_6$H$_4$-*p*-F)-pent-4-enylamine (**2a**) was synthesized via deprotonation of the corresponding amine with KN(TMS)$_2$.[14] As shown in Scheme 1, a solution of **1** in THF or THF-d_8 was treated with **2a** (1.05 equiv) in the presence of 2-fluorotoluene as internal standard and dppf (2 equiv) as a trap for Pd(0). The conversion of **1** to **3a** was complete upon mixing, and the formation of amido complex **3a** was evident by the presence of a pair of doublets at 24.9 ppm (J_{PP} = 38.1 Hz) and 9.0 ppm (J_{PP} = 35.5 Hz) in the ^{31}P NMR spectrum, which are comparable to data previously reported for (dppf)Pd(Ar)[N(Ar^1)(R)] complexes.[14,16] New signals at −123.7 and −137.3 ppm were also observed in the ^{19}F NMR spectrum of **3a**.

Shortly after forming,[17] amido complex **3a** underwent reaction to generate a new intermediate complex (**A**), which exhibited ^{19}F NMR resonances at −124.1 and −133.3 ppm and ^{31}P NMR signals at 21.3 ppm (J_{PP} = 24.1 Hz) and 16.6 ppm (J_{PP} = 21.7 Hz). This intermediate was transformed to pyrrolidine **4a** and (dppf)$_2$Pd at a rate that appeared to be roughly comparable to that of its formation from **3a**. Overall, the conversion of **3a** to **4a** proceeded in 86% NMR yield in 45 min at 24 °C. No additional intermediates on the pathway from **3a** to **4a** were detected, and no side products resulting from β-hydride elimination were observed.

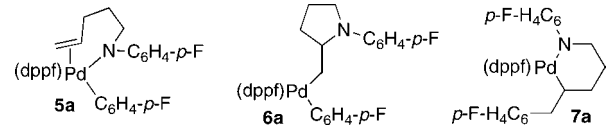
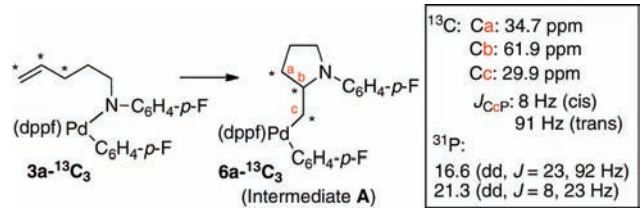


Figure 1. Possible structures of intermediate **A**.

As shown in Figure 1, it seemed most likely that intermediate **A** was either a five-coordinate alkene complex (**5a**) or an aryl(alkyl) palladium complex (**6a**). In addition, although Pd-catalyzed carboamination reactions have been shown to proceed through aminopalladation rather than carbopalladation pathways,[4] we sought to exclude the possible intermediacy of **7a** in the stoichiometric transformation. However, the data obtained in our initial experiments could not be used to assign the structure of **A**. For example, the ^{1}H NMR alkene signals of **3a** decreased as the reaction proceeded, but this region of the spectrum was sufficiently complicated that the presence of a new alkene containing intermediate (**5a**) could not be definitively confirmed or refuted. Similarly, the complicated ^{1}H NMR data also did not allow for differentiation of **6a** vs **7a**. We observed that (dppf)Pd(C$_6$H$_4$-*p*-F)[CH$_2$(cyclopentyl)] (**8**) generated *in situ* from **1** and (cyclopentyl)CH$_2$MgBr underwent C−C bond-forming reductive elimination in <5 min at rt,[18] which seemed to argue against the intermediacy of **6a**. However, the reductive elimination of **6a** could be significantly slowed relative to **8** due to the inductive electron-withdrawing effect of the nitrogen atom in **6a**.[19] Thus, the identity of intermediate **A** could not be ascertained without additional experimentation.

Scheme 2



To elucidate the structure of **A** we prepared and examined the reactivity of ^{13}C labeled amido complex **3a-^{13}C$_3$** (Scheme 2). Analysis of the reaction by ^{13}C and ^{31}P NMR indicated that intermediate **A** is

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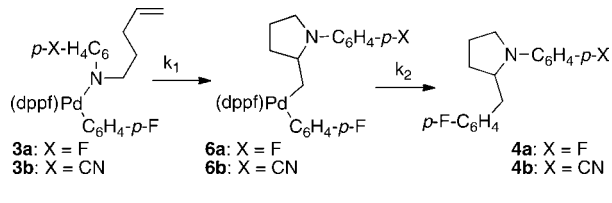
the aryl(alkyl)palladium complex **6a**. The chemical shifts of the labeled carbon atoms in **A** were not consistent with an alkene, and the chemical shift of C_b indicated it was located adjacent to a heteroatom. Thus, this data ruled out the possible intermediacy of **5a** and **7a**.[20] Moreover, the ^{31}P chemical shifts, coupling constants, and J_{CP} correlate well with data reported by Brown for (dppf)Pd(Ph)(Me).[18,21]

Having ascertained the structure of intermediate **A**, kinetic data were measured at 24 °C for the transformation of amido complex **3a** to pyrrolidine **4a** by way of intermediate **6a** (Scheme 3 and Figure 2). Rate constants were extracted for the consecutive first-order reactions (**3a** to **6a**, $k_1 = 1.74 \times 10^{-3}$ s^{-1}; **6a** to **4a**, $k_2 = 1.36 \times 10^{-3}$ s^{-1}), which occur with rates within 1 order of magnitude from each other.[22] The activation parameters for the conversion of related amido complex **3b** to **4b** were determined by Eyring plot analysis (25−60 °C)[23] and are similar for both steps of the transformation. For the conversion of **3b** to **6b** $\Delta H^{\ddagger} = 24.8 \pm 0.6$ kcal/mol, $\Delta S^{\ddagger} = 4.6 \pm 1.8$ eu. For the reductive elimination of **4b** from **6b** $\Delta H^{\ddagger} = 23.3 \pm 0.8$ kcal/mol, $\Delta S^{\ddagger} = 4.6 \pm 2.5$ eu. The reaction enthalpies are comparable to those observed for insertion of alkenes into late-metal−carbon bonds[24a−c] and for C−C bond-forming reductive elimination processes.[24d] The small entropy values are consistent with unimolecular transformations.[24]

Scheme 3



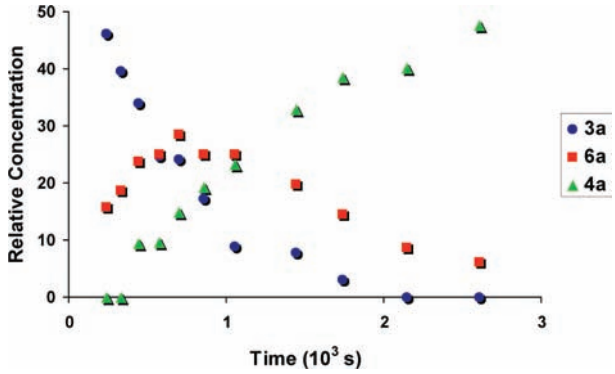
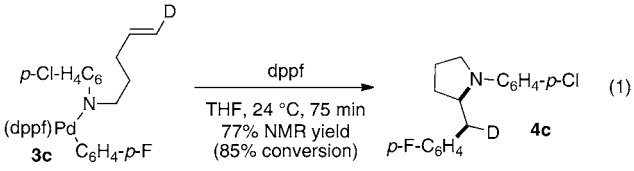


Figure 2. Kinetic plot for the conversion of **3a**→**6a**→**4a**.

The stereochemistry of the aminopalladation reaction was determined through reaction of deuterated amido complex **3c**. As shown in eq 1, this complex was cleanly transformed to pyrrolidine **4c** with net *syn*-addition of the aryl group and the N-atom across the C−C double bond. This supports a mechanism involving *syn*-migratory insertion of the alkene into the Pd−N bond, rather than amide dissociation, alkene coordination, and outer-sphere attack of the pendant nucleophile. This result is also consistent with the stereochemical outcome of Pd-catalyzed carboamination reactions between γ-aminoalkene derivatives and aryl bromides.[4]



(1)

In conclusion, we have described the first examples of intramolecular *syn*-migratory insertion reactions of alkenes into well-defined palladium(aryl)(amido) complexes. These reactions proceed with complete chemoselectivity for insertion into the Pd−N bond vs the Pd−C bond and provide observable (dppf)palladium(aryl)(pyrrolidin-2-yl-methyl) complexes. These results provide further support for postulated *syn*-aminopalladation mechanistic pathways in palladium-catalyzed alkene difunctionalization reactions.[4−10] Further studies on factors that influence the rates of these transformations are currently underway.

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Supporting Information Available: Experimental procedures, characterization data for all new compounds, copies of ^{1}H, ^{31}P, ^{19}F, and ^{13}C NMR spectra, and descriptions of stereochemical assignments. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Key data from ref 14 for (dppf)Pd(C_6H_4-*p*-CF_3)[N(Me)(C_6H_4-*p*-Me)]: ^{31}P NMR (−45 °C): δ 9.3 (br), 24.3 (d, $J = 38$ Hz).
(17) Detectable amounts of intermediate **A** were observed after 2 min at rt.
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(20) See the Supporting Information for a detailed description of the structural assignment of **6a** and the stereochemical assignment of **4c**.
(21) Key data from ref 18 for (dppf)Pd(Ph)(Me): ^{31}P NMR: δ 17.8 (d, $J = 23$ Hz), 21.3 (d, $J = 23$ Hz). ^{13}C NMR: J_{CP}: 9 Hz (*cis*), 97 Hz (*trans*).
(22) Neither excess phosphine ligand nor excess potassium *N*-arylamide had an effect on k_1 or k_2.
(23) The *N*-(C_6H_4-*p*-CN) derivative **3b** was employed for these studies as it reacted at a slower rate than **3a**, which simplified experimental setup and allowed for rates to be measured over a range of temperatures above rt.
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