JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

pubs.acs.org/JACS

Reductive Elimination from Arylpalladium Cyanide Complexes

Jessica L. Klinkenberg and John F. Hartwig*,†

Department of Chemistry, University of Illinois, 600 South Mathews Avenue, Urbana, Illinois 61801, United States, and Department of Chemistry, University of California, Berkeley, California 94720, United States

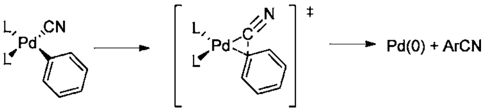
Supporting Information

ABSTRACT: We report the isolation and characterization of arylpalladium cyanide complexes that undergo reductive elimination to form arylnitriles. The rates of reductive elimination from a series of arylpalladium cyanide complexes reveal that the electronic effects on the reductive elimination from arylpalladium cyanide complexes are distinct from those on reductive reductive eliminations from arylpalladium alkoxo, amido, thiolate, and enolate complexes. Arylpalladium cyanide complexes containing aryl ligands with electron-donating substituents undergo reductive elimination of aromatic nitriles faster than complexes containing aryl ligands with electron-withdrawing substituents. In addition, the transition state for the reductive elimination of the aromatic nitrile is much different from that for reductive eliminations that occur from most other arylpalladium complexes. Computational studies indicate that the reductive elimination of an arylnitrile from Pd(II) occurs through a transition state more closely related in structure and electronic distribution to that for the insertion of CO into a palladium−aryl bond.

The palladium-catalyzed cyanation of aryl halides has become a common method for the synthesis of arylnitriles.[1] Since the first report by Takagi in 1973,[2] a large number of transition metal-catalyzed cyanations of aryl halides have been reported, and recently developed protocols occur under conditions suitable for commercial production.[1,3] Despite these advances, little information on the productive steps of the catalytic cycle has been reported. Grushin and co-workers observed anionic Pd(0) and Pd(II) cyanide complexes from displacement of the phosphine ligand with cyanide and showed that these complexes do not undergo the oxidative addition and reductive elimination steps proposed to occur during the catalytic cycle.[4] Subsequently, Beller and co-workers demonstrated the advantageous effect of diamines on the oxidative addition of aryl halides to $Pd(PPh_3)_4$ in the presence of excess cyanide ion and on the rate of transmetalation proposed to form an arylpalladium cyanide that undergoes reductive elimination. However, the arylpalladium cyanide complex was not observed.[5]

Thus, no reports have described the isolation of an arylpalladium cyanide complex or evaluated its propensity to undergo reductive elimination. Metal−cyanide linkages are well known to be thermodynamically stable,[6] and the facile formation of anionic Pd(II) cyanide complexes[4] underscores the fact that Pd forms strong bonds with cyanide ligands. However, the absence of an observed arylpalladium(II) cyanide complex suggests that such complexes could be unstable; they could degrade in the presence of excess cyanide to form anionic species, or the sp^2−sp carbon−carbon bond-forming reductive elimination to form arylnitriles could be fast. If arylpalladium cyanide complexes could be isolated and induced to undergo reductive elimination (Scheme 1), then one could gain information on the factors controlling the rates of this process. Moloy and Nolan proposed that reductive elimination of alkylnitriles occurs by a mechanism related to that for carbon monoxide insertion on the basis of relative rates that coincided with those for CO insertion into metal−alkyl bonds. An accelerating effect of Lewis acids on the reductive elimination further supported a mechanism related to insertion. However, coupling of a cyano ligand with an aryl group could occur by a process much different than that for coupling with an alkyl group, and elimination of an arylnitrile allows the electronic effects on this class of reductive elimination to be probed in the absence of steric effects.[7,8]

Scheme 1. Reductive Elimination of an Arylnitrile from a Proposed Arylpalladium Cyanide Complex



Here we report an isolated arylpalladium cyanide complex and reductive eliminations from this complex and its congeners to form aromatic nitriles. The experimental and computational data we report assess the relationships between this reductive elimination and related reductive eliminations from aryl Pd(II) complexes or migratory insertions of CO. The effects of the electronic properties of the aryl ligand on the rates and thermodynamics for reductive elimination to form arylnitriles contrast with those of reductive eliminations from Pd(II) to form other types of C−C bonds[9] or C−N,[10] C−O,[11] or C−S[12] bonds.[13] Instead, our data and computational studies imply that the transition state maps closely onto that for insertion of CO into a metal−aryl bond.

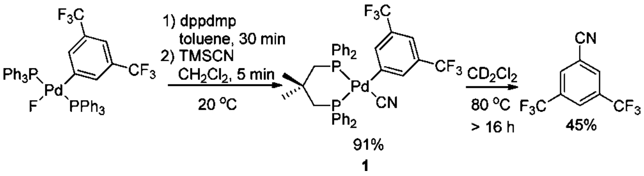
Our studies began with efforts to isolate a stable arylpalladium cyanide complex. A variety of bisphosphine-ligated *p*-tolylpalladium bromide complexes were treated with sources of cyanide. The reactions of *p*-tolylpalladium(II) bromide complexes containing 1,1′-bis(diphenylphosphino)-

Received: January 25, 2012
Published: February 21, 2012

ferrocene (DPPF) and 1,1′-bis(diisopropylphosphino)ferrocene (D^{i}PPF) with NBu_4CN at 20 °C led to complete conversion of the complexes, as determined by ^{31}P NMR spectroscopy. ^1H NMR analyses of the reaction mixtures indicated the formation of *p*-tolylnitrile in 89 and 98% yield, respectively, but the presumed arylpalladium cyanide complex was not observed directly. However, the Josiphos (CyPF-*t*-Bu)-ligated *p*-tolylpalladium bromide complex reacted with $NBu_4{}^{13}CN$ at −78 °C to form a new complex that was sufficiently stable to be characterized at −40 °C by ^1H and ^{31}P NMR spectroscopy. The two doublets of doublets in the ^{31}P NMR spectrum confirmed the binding of one labeled cyanide ligand to Pd (see Supporting Information for spectra). After the solution warmed to room temperature, *p*-tolylnitrile was formed in 88% yield.

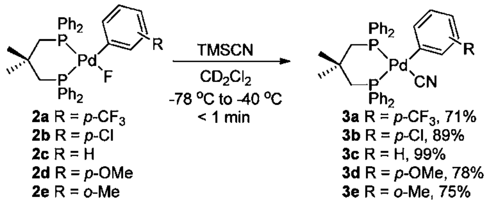
The arylpalladium cyanide complex (aryl = *p*-Cl-C_6H_4) containing the rigid bisphosphine ligand 1,3-bis(diphenylphosphino)-2,2-dimethylpropane (dppdmp) generated in situ from the reaction of (dppdmp)Pd(C_6H_4-*p*-Cl)(F) and TMSCN was even more stable. This complex persisted for hours at room temperature, as determined by ^{31}P NMR spectroscopy, whereas the complex containing the more electron-rich *p*-anisyl group was unstable at room temperature. Ultimately, we found that **1**, containing two trifluoromethyl groups on the Pd-bound aryl ligand, was stable enough to be isolated in 91% yield (Scheme 2). Complex **1** was characterized by ^1H and ^{31}P NMR and IR spectroscopy. This complex undergoes reductive elimination at elevated temperatures over an extended time; heating a solution of **1** at 80 °C for 16 h led to the conversion of >95% of **1** to form 3,5-trifluoromethylbenzonitrile in 45% yield, according to ^1H NMR spectroscopy (Scheme 2).[14]

Scheme 2. Synthesis and Reductive Elimination of Arylpalladium Cyanide Complex 1



These initial studies indicated that the arylpalladium cyanide complex containing an electron-poor aryl group is more stable toward reductive elimination than the analogous complex containing a more electron-rich aryl group. This relative reactivity contrasts with that for reductive eliminations to form C–C bonds from arylpalladium(II) and arylplatinum(II) complexes, which occur faster from complexes containing electron-withdrawing substituents on the aryl group than from analogous complexes containing electron-donating substituents.[9,13]

To investigate the effect of the electronic properties of the reacting aryl ligand quantitatively, a series of dppdmp-ligated arylpalladium cyanide complexes were prepared from fluoride complexes **2a–e**. Reaction of these fluoride complexes with TMSCN formed arylpalladium cyanide complexes **3a–e** (eq 2), which were characterized at low temperature by ^1H and ^{31}P NMR spectroscopy and at room temperature by IR spectroscopy in some cases. Only the 3,5-trifluoromethyl-substituted **1** described above was stable enough to be isolated.



(2)

Complexes **3a–e** underwent reductive elimination at 20 or 40 °C at convenient rates in *N*,*N*-dimethylformamide (DMF) and CD_2Cl_2 to form the corresponding arylnitrile products in 80–95% yield (Scheme 3 and Table 1). In DMF, the Pd(0) product was Pd(dppdmp)$_2$, which was isolated in 72% yield by heating **2a**, TMSCN, and dppdmp at 80 °C in DMF for 30 min. In CD_2Cl_2, the palladium product was (dppdmp)$PdCl_2$, which crystallized from the solution of **2e** and TMSCN (Scheme 3, **3e**) apparently, the Pd(0) product reacts with the CD_2Cl_2 solvent.

Scheme 3. Reductive Elimination from Arylpalladium Cyanide Complexes 3a–e

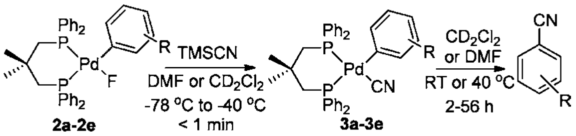


Table 1. Yields and Rates of Reductive Elimination from 3a–e

complex	R	k_{DCM} $(10^{-4}\ s^{-1})^a$	k_{DMF} $(10^{-4}\ s^{-1})^a$	yield (%)^b
3a	*p*-CF_3	0.23	–	81^g
3a	*p*-CF_3	1.8	0.73	94
3a	*p*-CF_3	3.2^{e,f}	3.6^f	81
3b	*p*-Cl	0.62^d	–	77^h
3b	*p*-Cl	6.7^e	1.3	98
3c	H	2.5^d	11	80
3d	*p*-OMe	7.4^c	21	94
3e	*o*-Me	5.9	22	93

[a] First-order rate constants determined by monitoring the decay of the cyanide complex by ^1H NMR spectroscopy (k_{DCM}, in CD_2Cl_2) or ^{31}P NMR spectroscopy (k_{DMF}, in DMF). [b] Yield of the arylnitrile for the reductive elimination step as determined by ^1H NMR spectroscopy (in CD_2Cl_2). [c] Average of three separate runs. [d] Average of two separate runs. [e] At 40 °C. [f] With 2 equiv of $B(C_6F_5)_3$. [g] Yield after 81% conversion of **3a**. [h] Yield after 87% conversion of **3b**.

The rate constants for reductive elimination were measured by monitoring the reaction by ^1H and ^{31}P NMR spectroscopy over a period of 2–56 h and are shown in Table 1. Indeed, complexes containing electron-withdrawing substituents on the aryl ligand (**3a,b**, Scheme 3) underwent reductive elimination more slowly than those containing an unsubstituted aryl ligand (**3c**) or an electron-donating substituent on the aryl ligand (**3d**) (Scheme 3), and a ρ value of −2.0 in CD_2Cl_2 and DMF was obtained from Hammett plots (see the Supporting Information). This trend in the electronic effects suggests that the aryl ligand acts as a nucleophile in the coupling with an electrophilic cyanide ligand. As a side note, **3e** containing an ortho-substituted tolyl ligand reacted more rapidly than the less congested arylpalladium cyanide complexes.

Prior reductive eliminations to form alkylnitriles from alkylpalladium cyanide complexes were accelerated by coordination of Lewis acids to the nitrogen of the cyanide ligand.[7] Reactions of **3a** with added $B(C_6F_5)_3$ at 40 °C were only 2–5 times as fast as those without added $B(C_6F_5)_3$, whereas the prior reactions of an alkylpalladium cyanide complex with added Lewis acids were 1−2 orders of magnitude faster than the reactions without an added Lewis acid. Although small, this effect of Lewis acid is consistent with a pathway in which the aryl group acts as a nucleophile and the cyanide ligand as an electrophile.

A series of computational studies was conducted to gain insight into the origin of the electronic effects on the reductive elimination of arylnitriles from arylpalladium(II) complexes. The ground-state and transition-state structures of three model PMe_3-ligated arylpalladium cyanide complexes were calculated, and the results of these calculations are shown in Figure 1. The reductive elimination of benzonitrile from the phenylpalladium cyanide complex containing two cis-disposed PMe_3 ligands was computed to have a barrier of 16.7 kcal/mol. The barrier to elimination from the complex containing the more electron-donating *p*-aminophenyl group (16.1 kcal/mol) was computed to be lower than that for elimination from the complex containing the more electron-poor *p*-trifluoromethylphenyl group (17.2 kcal/mol). These results agree with the experimental observation that reductive elimination from the more electron-rich arylpalladium cyanide complexes is faster than that from the more electron-poor analogues.

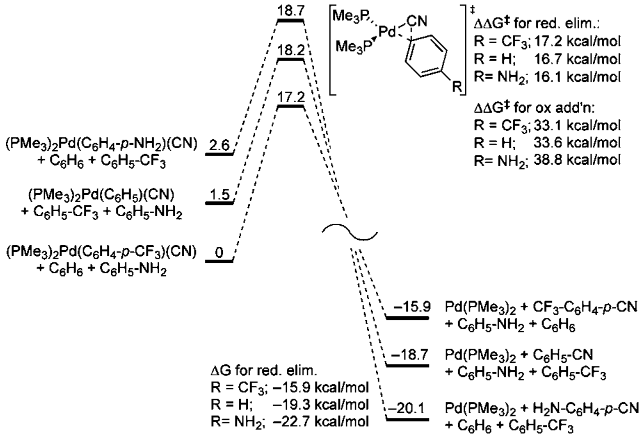


Figure 1. Ground-state, transition-state, and overall free energies in kcal/mol for PMe_3-ligated arylpalladium cyanide complexes undergoing reductive elimination of arylnitriles.

The effect of the electronic properties of the aryl group on the thermodynamic driving force for the reductive elimination was parallel to, but much larger, than that on the relative rate. Reductive elimination of the arylnitrile from *p*-aminobenzonitrile was computed to be more downhill ($\Delta G^{\ddagger} = -22.7$ kcal/mol) than reductive elimination to form benzonitrile ($\Delta G^{\ddagger} = -19.3$ kcal/mol), which in turn was predicted to be more downhill than reductive elimination of *p*-trifluoromethylbenzonitrile ($\Delta G^{\ddagger} = -15.9$ kcal/mol) (Figure 1). The large differences in the driving force arise from the contrasting electronic effects of the substituents on the arylpalladium cyanide and arylnitrile products. Electron-withdrawing substituents stabilize the arylpalladium species but destabilize the arylnitrile product.

This range of computed driving forces (6.8 kcal/mol) is much larger than the range of computed transition-state energies (1.5 kcal/mol). As a result, the barrier for reductive elimination is lower for complexes containing electron-donating substituents on the aryl ligand, but the barrier for the reverse oxidative addition is computed to be lower for complexes with electron-withdrawing substituents on the aryl ligand.

In contrast to this trend, the magnitude of the effect of the aryl substituent on the transition-state energy for reductive eliminations of arylamines, which occur faster from complexes containing more electron-poor Pd-bound aryl groups, was computed previously to be similar to the magnitude of the effect on the ground state energies (8.2 vs 8.9 kcal/mol, respectively).[15] These effects are similar because arylpalladium complexes and arylamines are both stabilized by electron-withdrawing substituents. Thus, we propose that the strong and opposite electronic effects of the substituents on the stabilities of the starting Pd complexes and the nitrile products causes the unusual electronic effect on the rate of reductive elimination of arylnitriles.[16]

A second contribution to the observed electronic effect could stem from the relationship between the reductive elimination of arylnitriles and insertion of CO into a metal−aryl bond. As noted in the introduction, the reductive elimination of alkylnitriles from a neopentylpalladium cyanide complex was suggested to be related to the insertion of CO.[8] Consistent with this proposed relationship, insertion of CO into a palladium−aryl bond is known to be faster for complexes containing electron-donating substituents on the aryl ligand,[17] and CO insertion into a M−C bond in which the hydrocarbyl ligand is more electron-donating is more thermodynamically favored than CO insertion into a M−C bond in which the hydrocarbyl ligand is more electron-withdrawing.[18]

Computational data provide a more precise view of the relationships between these two reactions. The computed ground-state structures of neutral PMe_3-ligated phenylpalladium(II)-cyanide and cationic PMe_3-ligated phenylpalladium(II)−CO complexes, as well as the transition states for reductive elimination of benzonitrile and insertion of CO into a palladium−phenyl bond, are overlaid in Figure 2.

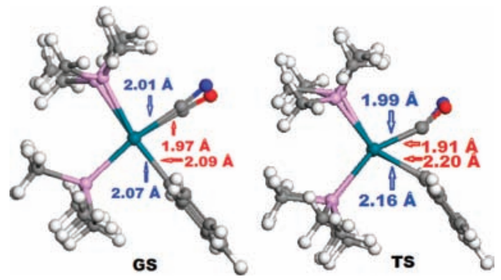


Figure 2. Computed structures of a PMe_3-ligated phenylpalladium cyanide complex (blue labels) and a PMe_3-ligated arylpalladium CO complex (red labels) in the ground state (GS) and transition state (TS) prior to reductive elimination of benzonitrile or insertion of CO. Atom colors: Pd, turquoise; P, pink; C, gray; N, blue; O, red; H, white.

The reaction coordinate for reductive elimination of aromatic nitriles resembles that for insertion of CO into a palladium−aryl bond. The C−N bond length in the ground-state cyanide complex and the C−O bond length in the ground-state carbonyl complex differ by only 0.03 Å. Likewise, the C−N and C−O bond lengths in the transition states differ by only 0.01 Å. The bond angles involving the CX (X = N, O) ligands and the phenyl ligand in the two complexes also change by a similar amount during the two reactions. The C−Pd−C angle changes from 85.7° in the ground state to 59.5° in the transition state (Δ = 26.2°) during reductive elimination of the arylnitrile, while the C−Pd−C angle changes from 81.8° to 54.8° (Δ = 27.0°) during insertion of CO into the palladium−aryl bond. The distortion from planarity reported for a related transition state involving oxidative addition of aromatic nitriles to Ni(0) was not observed for the second-row Pd system.[19]

The difference between a more synchronous coupling of two ligands and a more asynchronous migratory bond formation has been proposed to indicate distinct forms of concerted reductive elimination. Calhorda[20] reported extended Hückel theory calculations of the transition-state structures for C−C bond formation through these two pathways and proposed that that the more synchronous process involved lengthening of the two Pd−C bonds, while the "migratory reductive elimination" involved lengthening of the M−C bond of the migrating group and shortening of the Pd−C bond of the unsaturated ligand to which migration occurs. Data in more recent work by Morokuma and co-workers[21] revealed that the Pd−alkynyl bond distances were constant or shortened during reductive elimination to form an enyne or phenylacetylene (1.99 Å and 2.00 to 1.99 Å, respectively) from a vinyl- or arylpalladium acetylide complex, while the palladium−vinyl and palladium−aryl bonds lengthened (2.06 to 2.11 Å and 2.04 to 2.09 Å, respectively). For the reaction of the carbonyl and cyanide complexes depicted in Figure 2, the palladium−carbonyl bond shortens from 1.97 to 1.91 Å and the palladium−cyanide bond from 2.01 to 1.99 Å in going from the ground to the transition state, while the palladium−aryl bonds lengthen by 0.11 and 0.09 Å, respectively. These changes are consistent with a "migratory" reductive elimination.

In conclusion, a series of arylpalladium(II) cyanide complexes that undergo reductive elimination of arylnitriles have been characterized, and studies of these complexes by experimental and computational methods have provided insight into the mechanism of reductive elimination of arylnitriles. In contrast to the vast majority of reductive eliminations from arylpalladium(II) complexes, the reductive elimination of aromatic nitriles from arylpalladium(II) cyanide complexes is accelerated by electron-donating substituents on the aryl ligand. This result stems from the large electronic effect on the thermodynamic driving force for the reductive elimination of arylnitriles.[22] In addition, density functional theory calculations indicate that the transition-state structure for the reductive elimination from an arylpalladium cyanide complex is more similar to that for insertion of CO into a palladium−aryl bond than to the transition-state structure for reductive elimination to form alkylarenes. Future studies will seek to reveal the scope of this trend in transition-state structure and use this information to improve couplings of sp-hybridized groups.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

All experimental procedures and spectroscopic data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

jhartwig@berkeley.edu

Present Address

[†]Department of Chemistry, University of California Berkeley, 718 Latimer Hall, Berkeley, CA 94720.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Giang Vo for the synthesis of dppdmp and the characterization of complex **2b**. We thank the NIH (GM-58108) for support of this work and Johnson-Matthey for a gift of $PdCl_2$.

■ REFERENCES

(1) Sundermeier, M.; Zapf, A.; Beller, M. *Eur. J. Inorg. Chem.* **2003**, 3513.

(2) Takagi, K.; Okamoto, T.; Sakakibara, Y.; Oka, S. *Chem. Lett.* **1973**, 471.

(3) Ryberg, P. *Org. Process Res. Dev.* **2008**, *12*, 540. Torborg, C.; Beller, M. *Adv. Synth. Catal.* **2009**, *351*, 3027. Hatsuda, M.; Seki, M. *Tetrahedron* **2005**, *61*, 9908.

(4) Dobbs, K. D.; Marshall, W. J.; Grushin, V. V. *J. Am. Chem. Soc.* **2007**, *129*, 30. Erhardt, S.; Grushin, V. V.; Kilpatrick, A. H.; Macgregor, S. A.; Marshall, W. J.; Roe, D. C. *J. Am. Chem. Soc.* **2008**, *130*, 4828.

(5) Sundermeier, M.; Zapf, A.; Mutyala, S.; Baumann, W.; Sans, J.; Weiss, S.; Beller, M. *Chem.—Eur. J.* **2003**, *9*, 1828.

(6) Bryndza, H. E.; Domaille, P. J.; Tam, W.; Fong, L. K.; Paciello, R. A.; Bercaw, J. E. *Polyhedron* **1988**, *7*, 1441. Halpern, J.; Guastalla, G.; Bercaw, J. *Coord. Chem. Rev.* **1972**, *8*, 167. Chapman, K. W.; Chupas, P. J.; Kepert, C. *J. Am. Chem. Soc.* **2006**, *128*, 7009. Jones, L. H. S.; Basil, I. *Acc. Chem. Res.* **1976**, *9*, 123. Jones, L. H. *Inorg. Chem.* **1963**, *2*, 777.

(7) Huang, J.; Haar, C. M.; Nolan, S. P.; Marcone, J. E.; Moloy, K. G. *Organometallics* **1999**, *18*, 297.

(8) Marcone, J. E.; Moloy, K. G. *J. Am. Chem. Soc.* **1998**, *120*, 8527.

(9) Culkin, D. A.; Hartwig, J. F. *Organometallics* **2004**, *23*, 3398.

(10) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 8232.

(11) Mann, G.; Incarvito, C.; Rheingold, A. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 3224.

(12) Mann, G.; Baranano, D.; Hartwig, J. F.; Rheingold, A. L.; Guzei, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 9205. Alvaro, E.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 7858.

(13) Hartwig, J. F. *Inorg. Chem.* **2007**, *46*, 1936.

(14) 1,3-Trifluoromethylbenzene was the major side product.

(15) Hoi, K. H.; Çalimsiz, S.; Froese, R. D. J.; Hopkinson, A. C.; Organ, M. G. *Chem.—Eur. J.* **2011**, *17*, 3086.

(16) Consistent with the assertion that the properties of the cyano group lead to the observed electronic effect, Jones and co-workers reported an example of similar thermodynamic control over the electronic effects on the oxidative addition of arylnitriles by Ni(0). As we have predicted for these Pd complexes, arylnitriles with electron-donating substituents underwent slower oxidative addition to Ni(0), but data indicating faster reductive elimination from the arylnickel(II) cyanide species can be extracted from this study. See: Garcia, J. J.; Brunkan, N. M.; Jones, W. D. *J. Am. Chem. Soc.* **2002**, *124*, 9547.

(17) Garrou, P. E.; Heck, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 4115.

(18) Anderson, G. K.; Cross, R. J. *J. Chem. Soc., Dalton. Trans.* **1979**, 1246. Cross, R. J.; Gemmill, J. *J. Chem. Soc., Dalton Trans.* **1981**, 2317.

(19) Ateşin, T. A.; Li, T.; Lachaize, S.; García, J. J.; Jones, W. D. *Organometallics* **2008**, *27*, 3811.

(20) Calhorda, M. J.; Brown, J. M.; Cooley, N. A. *Organometallics* **1991**, *10*, 1431.

(21) Ananikov, V. P.; Musaev, D. G.; Morokuma, K. *Organometallics* **2005**, *24*, 715.

(22) This result also parallels the accelerating effect of electron-donating substituents on the aryl groups during reductive elimination from arylpalladium phosphonate complexes, although the origins of this effect were not determinined. See: Kohler, M. C.; Grimes, T. V.; Wang, X.; Cundari, T. R.; Stockland, R. A. *Organometallics* **2009**, *28*, 1193.