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A Highly Active Palladium Catalyst for Intermolecular Hydroamination. Factors that Control Reactivity and Additions of Functionalized Anilines to Dienes and Vinylarenes

Adam M. Johns, Masaru Utsunomiya, Christopher D. Incarvito, and John F. Hartwig*

Contribution from the Department of Chemistry, Yale University, P.O. Box 208107, New Haven, Connecticut 06520-8107

Received August 31, 2005; E-mail: John.Hartwig@yale.edu

Abstract: We report a catalyst for intermolecular hydroamination of vinylarenes that is substantially more active for this process than catalysts published previously. With this more reactive catalyst, we demonstrate that additions of amines to vinylarenes and dienes occur in the presence of potentially reactive functional groups, such as ketones with enolizable hydrogens, free alcohols, free carboxylic acids, free amides, nitriles, and esters. The catalyst for these reactions is generated from $[Pd(\eta^3\text{-allyl})Cl]_2$ (with or without added AgOTf) or $[Pd(CH_3CN)_4](BF_4)_2$ and Xantphos (9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene), which generates complexes with large P−Pd−P bite angles. Studies on the rate of the C−N bond-forming step that occurs by attack of amine on an η^3-phenethyl and an η^3-allyl complex were conducted to determine the effect of the bite angle on the rate of this nucleophilic attack. Studies on model η^3-benzyl complexes containing various bisphosphines showed that the nucleophilic attack was faster for complexes containing larger P−Pd−P bite angles. Studies of substituted unsymmetrical and unsubstituted symmetrical model η^3-allyl complexes showed that nucleophilic attack on complexes ligated by Xantphos was faster than on complexes bearing ligands with smaller bite angles and that nucleophilic attack on unsymmetrical allyl complexes with larger bite angle ligands was faster than on unsymmetrical allyl complexes with smaller bite angle ligands. However, monitoring of catalytic reactions of dienes by ^{31}P NMR spectroscopy showed that the concentration of active catalyst was the major factor that controlled rates for reactions of symmetrical dienes catalyzed by complexes of phosphines with smaller bite angles. The identity of the counterion also affected the rate of attack: reactions of allylpalladium complexes with chloride counterion occurred faster than reactions of allylpalladium complexes with triflate or tetrafluoroborate counterion. As is often observed, the dynamics of the allyl and benzyl complexes also depended on the identity of the counterion.

Introduction

Catalytic intermolecular hydroamination of olefins remains a challenging transformation.[1−3] To date, complexes of lanthanides,[4] group IV transition metals,[5] and late transition metals[6−11] have been shown to catalyze the intermolecular addition of amine N−H bonds across vinylarenes and allenes. Recently, reports of intramolecular hydroaminations of alkenes have also appeared.[1,12−20] Although the lanthanide catalysts have displayed higher reactivity toward olefins than late transition metals, catalysts based on late transition metals are likely to be more tolerant of polar functional groups in the reagents and to be amenable to assembly in air. Thus, if the activities of late metal catalysts for additions of amines to olefins could be increased, such that they rival those of early metal catalysts, then the current advantages of both classes of catalyst could be gained.

Because an amino group is harder than some functional groups yet softer than others, it is not clear which functional groups will be compatible with catalytic hydroamination.

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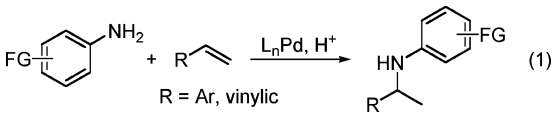
Although scattered hydroaminations in the presence of certain functional groups have been reported,[4,21,22] no study of the compatibility of catalysts for hydroamination with substrates bearing functional groups that often interfere with catalytic reactions, such as alcohols, carboxylic acids, esters, amides, enolizable keto groups, and nitriles, has been conducted with any metal. Therefore, we have begun to assess whether late-metal complexes can catalyze the additions of N−H bonds in the presence of a variety of accompanying functional groups (eq 1).



(1)

In combination with this work, we have been conducting studies to improve the rates of the catalytic hydroamination to expand reaction scope. Increasing the rate of the desired addition of the amine across an olefin would likely decrease formation of products from side reactions and reduce deactivation of the catalyst. Previous work on the mechanism of the palladium-catalyzed hydroamination of vinylarenes showed that the C−N bond in the amine product is formed by nucleophilic attack of the aryl or aliphatic amine on an η^3-phenethyl complex and that this step can be turnover limiting.[9,23] Thus, the activity of the catalyst is likely to be improved by finding a means to accelerate nucleophilic attack on the η^3-phenethyl complex. Although nucleophilic attack on allyl groups is a classic organometallic transformation, the factors that affect the rate of attack on η^3-benzyl groups are not well understood. Even studies that directly measure the rate of nucleophilic attack on allyl groups as a function of the ancillary ligand are not well documented.[24−26]

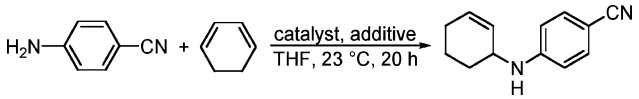
We report studies that increase the activity of the catalyst for the hydroamination of vinylarenes and dienes, that assess the ability of this catalyst to add amines to olefins in the presence of several types of typically reactive polar functionalities, and that probe the origin of the increased activity of the catalyst. We show that the combination of the wide bite-angle bisphosphine Xantphos and certain palladium precursors is highly active for the hydroamination of vinylarenes and 1,3-dienes. This combination of catalyst precursor and ligand catalyzes hydroaminations in the presence of alcohol, carboxylic acid, amide, ester, enolizable keto, and nitrile functional groups, and our data imply that the increased activity of this catalyst for the hydroamination of vinylarenes originates from the effect of bite angle on the rate of nucleophilic attack on the coordinated η^3-phenethyl ligand.

Results and Discussion

1. Effect of Catalyst Components on Rate. a. Effect of Ligands and Catalyst Precursor. Our studies toward catalysts with improved activity and high functional group tolerance were initiated by conducting reactions with the weakly nucleophilic *p*-cyanoaniline. Because the palladium-catalyzed addition of arylamines to vinylarenes and dienes occurs faster with amines that are more nucleophilic, reactions of this arylamine would single out the most reactive catalysts. The hydroaminations of dienes with this amine in the presence of previous catalysts occurred in low yield: the reaction of *p*-cyanoaniline with 1,3-cyclohexadiene catalyzed by $Pd(PPh_3)_4$ and 10% added trifluoroacetic acid formed only 22% of the addition product after 20 h at 23 °C. The hydroaminations of vinylarenes with this amine in the presence of previous catalysts also occurred in low yield: the reaction of *p*-cyanoaniline with styrene catalyzed by $Pd(PPh_3)_4$ and 5% added triflic acid or by $(DPPF)Pd(OTf)_2$, both of which catalyze the addition of aniline to styrene,[8] formed less than 15% of the product from addition of *p*-cyanoaniline after 20 h at 100 °C.

A series of reactions of *p*-cyanoaniline with 1,3-cyclohexadiene catalyzed by palladium complexes of bidentate ligands are summarized in Table 1. These reactions showed that complexes of Xantphos (Figure 1), which contain a wide P−Pd−P bite angle, are substantially more active as catalysts for the addition of aromatic amines to dienes than are complexes

Table 1. Effect of Catalyst Components and Acid on the Hydroamination of 1,3-Cyclohexadiene with 4-Aminobenzonitrile[a]



entry	Pd precursor	ligand	additive	yield[b]
1	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	2% Xantphos	-	99
2	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	2% Xantphos	2% AgOTF	3
3	2% [(Xantphos)Pd-(η^3-allyl)]OTf	-	-	2
4	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	2% Xantphos	10% HCl	87
5	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	2% DPEphos	-	7
6	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	2% DPPF	-	2
7	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	2% BINAP	-	0
8	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	2% DPPPent	-	0
9	1% $[Pd(\eta^3\text{-allyl})Cl]_2$	4% PPh_3	-	0
10	2% $Pd(PPh_3)_4$	-	10% TFA	22
11[c]	2% $Pd(PPh_3)_4$	-	10% TFA	11
12	-	-	10% TfOH	0
13	-	-	10% HBF_4[d]	0
14	-	-	10% HCl[e]	0

[a] Reaction conditions: 0.5 mmol of 4-aminobenzonitrile, 1.0 mmol of 1,3-cyclohexadiene, 1.0 mL of THF, 20 h at 23 °C. [b] GC yields, in percent. [c] Toluene was used in the place of THF. [d] 54 wt % in diethyl ether. [e] 1.0 M in diethyl ether. Ligand abbreviations: Xantphos = 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene, DPEphos = bis(2-diphenylphosphinophenyl)ether, DPPF = 1,1′-bis(diphenylphosphino)ferrocene, Binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, DPPPent = 1,5-bis(diphenylphosphino)pentane.

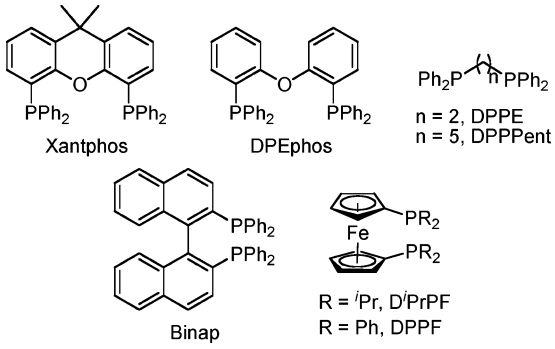


Figure 1. Structures of the ligands used in experiments summarized in Tables 1 and 2.

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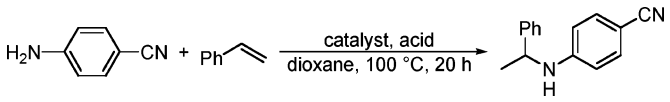
Table 2. Effect of Catalyst Components and Acid on the Hydroamination of Styrene with 4-Aminobenzonitrile[a]



entry	Pd precursor	ligand	acid	yield[b]
1	2% (Xantphos)Pd(OTf)$_2$	-	-	81 (93)
2	2% (Xantphos)PdCl$_2$	-	-	0
3	2% (DPPF)Pd(OTf)$_2$	-	-	7 (13)
4	2% [(Xantphos)Pd(CH$_3$CN)$_2$](OTf)$_2$	-	-	76 (91)
5	2% (DPPF)Pd(CH$_3$CN)$_2$(OTf)$_2$	-	-	9 (16)
6	2% Pd(TFA)$_2$	3% Xantphos	5% TfOH	66
7	2% Pd(TFA)$_2$	2% DPPPent	20% TfOH	11
8	2% Pd(TFA)$_2$	3% BINAP	5% TfOH	2
9	2% Pd(TFA)$_2$	3% DPEphos	5% TfOH	10
10	2% Pd(TFA)$_2$	3% D^{i}PrPF	20% TfOH	0
11	2% Pd(PPh$_3$)$_4$	-	5% TfOH	2
12	2% [Pd(COD)(η^3-allyl)]OTf	2% Xantphos	-	86 (36)
13	2% [Pd(COD)(η^3-allyl)]OTf	2% DPPF	-	2 (13)
14	2% [Pd(COD)(η^3-allyl)]OTf	2% DPEphos	-	3 (14)
15	2% [Pd(COD)(η^3-allyl)]OTf	2% BINAP	-	0 (16)
16	2% [Pd(COD)(η^3-allyl)]OTf	2% DPPPent	-	2 (10)
17	2% [Pd(COD)(η^3-allyl)]OTf	2% DPPE	-	0 (9)
18	-	-	10% TfOH	0
19	-	-	10% HBF$_4$[c]	0

[a] Reaction conditions: 0.5 mmol of 4-aminobenzonitrile, 1.0 mmol of styrene, 0.5 mL of dioxane, 20 h at 100 °C. [b] GC yields, in percent. Values in parentheses were obtained by conducting the reaction in the presence of 10 mol % TfOH. [c] 54 wt % in diethyl ether. Ligand abbreviations: Xantphos = 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene, DPPPent = 1,5-bis(diphenylphosphino)pentane, Binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, DPEphos = bis(2-diphenylphosphinophenyl)ether, D^{i}PrPF = 1,1′-bis(di-*i*-propylphosphino)ferrocene, DPPF = 1,1′-bis(diphenylphosphino)ferrocene, DPPPent = 1,5-bis(diphenylphosphino)pentane, DPPE = 1,2-bis(diphenylphosphino)ethane.

of related bisphosphines that are less rigid, such as 2,2′-bis-(diphenylphosphino)biphenyl ether, or that have smaller bite angles, such as BINAP and DPPF. A comparison of the reactions with and without AgOTf to abstract chloride from the catalyst shows that the reactions containing chloride occurred in higher yields. Reactions initiated with the isolated allylpalladium triflate complex (Table 1, entry 3) occurred in yields that were similar to those catalyzed by the species generated in situ from the combination of allylpalladium chloride and AgOTf.

Table 2 summarizes reactions of *p*-cyanoaniline with styrene catalyzed by palladium complexes of bidentate ligands in the presence and absence of triflic acid. The results also show that complexes of Xantphos are more reactive than those of the other ligands. This increased reactivity was observed with a series of palladium precursors. Reactions starting from (chelate)Pd(OTf)$_2$ complexes, from Pd(TFA)$_2$, ligand and added acid, or from [Pd(COD)(η^3-allyl)]OTf were faster when Xantphos was used as ligand than when the other bisphosphines were used as ligand. In contrast to the hydroamination of dienes, the hydroamination of vinylarenes was much faster when chloride was absent from the reaction system.

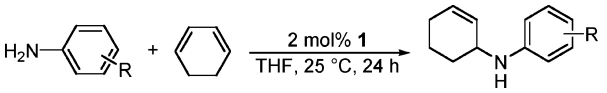
The consistency of the reaction yields with Xantphos as ligand depended on the catalyst precursor. Reaction of 1,3-cyclohexadiene and anilines conducted with isolated (Xantphos)Pd(η^3-allyl)Cl (**1**) reproducibly occurred in high yield, whereas reactions catalyzed by the combination of Xantphos and [Pd(η^3-allyl)Cl]$_2$ were more variable, even with the same substrate combination. Likewise, reactions of styrene and anilines conducted with (Xantphos)Pd(η^3-allyl)OTf (**2**), generated from **1** and AgOTf, as catalyst occurred in high yields more consistently than did reactions conducted with (Xantphos)Pd(OTf)$_2$ as catalyst.

b. Effect of Acid. One could envision that the reactions would be simpler to conduct and could be more compatible with certain functionality if they were conducted in the absence of any acid cocatalyst. However, the reactions catalyzed by several of the combinations of palladium precursor and ligand occurred in higher yields in the presence of acid, and others occurred in higher yields in the absence of added acid. Thus, the precise effect of acid on the rates and yields is difficult to ascertain without a determination of the turnover-limiting step in each case.[27]

Several trends could be drawn, however. For example, previously published reactions catalyzed by complexes of DPPF, BINAP, and PPh$_3$ were slow in the absence of added acid cocatalyst, unless the isolated bis-triflate complexes were used as precursor.[8] Yet, reactions of complexes of Xantphos generated in situ occurred at acceptable rates in the absence of added acid. For example, the complex formed in situ from [Pd(COD)(η^3-allyl)]OTf and Xantphos catalyzed the addition of *p*-cyanoaniline to styrene in 86% yield without added TfOH (Table 2, entry 12). The same reaction occurred to lower conversions in the presence of added triflic acid. Likewise, this slower rate in the presence of acid contrasts with the effect of acid on the reactions with most catalyst and substrate combinations and could result, in this case, from an interaction of the acid cocatalyst with the free bidentate ligand because displacement of COD from this precursor is likely to be slower than coordination of bisphosphine to Pd(TFA)$_2$. The hydroamination of 1,3-cyclohexadiene with aniline catalyzed by the combination of Xantphos and

(27) (a) Acid-catalyzed hydroaminations in the absence of metal have been reported,[27b,c] but control studies conducted on the addition of *p*-cyanoaniline to cyclohexadiene and styrene (Table 1, entries 12−14 and Table 2, entries 18 and 19) showed that acid alone does not catalyze the hydroamination. Further, the acid-catalyzed reactions of anilines to vinylarenes[27b] are slower than the palladium-catalyzed reactions of this work and give a mixture of products from addition of N−H and C−H bonds across the vinylarene. The acid-catalyzed reactions of dienes occur to low conversion. (b) Anderson, L. L. A., J.; Bergman, R. G. *J. Am. Chem. Soc.* **2005**, *127*, 14542−14543. (c) Schlummer, B.; Hartwig, J. F. *Org. Lett.* **2002**, *4*, 1471−1474.

Table 3. Palladium Catalyzed Hydroamination of 1,3-Cyclohexadiene with Bifunctional Aromatic Amines[a]



entry	amine	yield[b]	entry	amine	yield[b]
1	R = 3-NO_2	96	8[d]	R = 2-CN	98
2[c]	R = 4-NO_2	99	9	R = 3-CN	99
3	R = 3-COOH	81	10	R = 4-CN	97
4	R = 3-$COCH_3$	93	11	R = 2-CO_2Et	88
5	R = 4-$COCH_3$	99	12	R = 3-CO_2Et	82
6	R = 2-SMe	98	13	R = 4-CO_2Et	95
7	R = 4-SMe	99	14[d]	R = 2-OH	57

[a] Reaction conditions: 1.0 mmol of amine, 2.0 mmol of 1,3-cyclohexadiene, 2.0 mL of THF. [b] Isolated yield (average of two runs), in percent. [c] 50 °C. [d] 4.0 mmol of diene, 1.0 mL of THF, 50 °C.

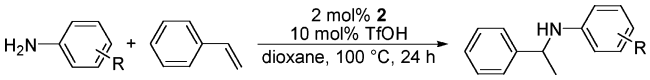
allylpalladium chloride dimer in the presence of HCl as acid cocatalyst occurred in a lower yield than the same hydroamination in the absence of the acid cocatalyst (Table 1, entry 4). In contrast to these reactions that were retarded by acid, the hydroaminations of styrene with aniline catalyzed by either (Xantphos)Pd(OTf)$_2$ or [(Xantphos)Pd(CH$_3$CN)$_2$](OTf)$_2$ (Table 2, entries 1 and 4) occurred in higher yields in the presence of an acid cocatalyst than they did in the absence of an acid cocatalyst.

c. Hydroamination of Dienes and Vinylarenes with Anilines Bearing Polar and Protic Functional Groups. The reactions of 1,3-cyclohexadiene with a series of anilines containing diverse functionalities are summarized in Table 3. In general, reactions of a 2:1 ratio of diene to amine in the presence of 2 mol % catalyst afforded good to excellent yields of the desired allylic amine after 24 h at room temperature. A few of the reactions conducted with anilines containing electron-withdrawing substituents (Table 3, entries 2, 8, and 14) required slightly higher temperatures to occur to completion, but even the reactions of anilines with the strongly electron-withdrawing nitro group occurred to completion. Reactions of anilines with functionality in the ortho position occurred to completion if the ratio of diene to amine and the overall concentration were increased.

Most striking, the results in Table 3 show that reactions occurred selectively at the amine N−H bond over many other types of functional groups and without poisoning of the catalyst. The reactions occurred selectively at the amine N−H bond over the carboxylic acid or phenolic O−H bonds; the catalyst was not poisoned by formation of palladium carboxylates or phenoxides. The reaction also occurred with anilines bearing enolizable hydrogens without the interference of palladium enolate complexes. Anilines with other groups that could coordinate to palladium, such as a thioether in the ortho-position or cyano groups in ortho-, meta-, or para-positions, all reacted in high yields. Finally, reactions of anilines with pendant esters occurred without generating the corresponding amide or metal amidate complex.

Table 4 summarizes reactions of anilines with styrene. Again, a 2:1 ratio of olefin to amine with 2 mol % catalyst and 10 mol % acid cocatalyst led to addition of the arylamine. These reactions afforded moderate to excellent yields of the Markovnikov addition product after 24 h at 100 °C. The scope of these reactions and the compatibility with auxiliary functional groups was even superior to that of the reactions of anilines with 1,3-cyclohexadiene. In addition to reactions of the anilines

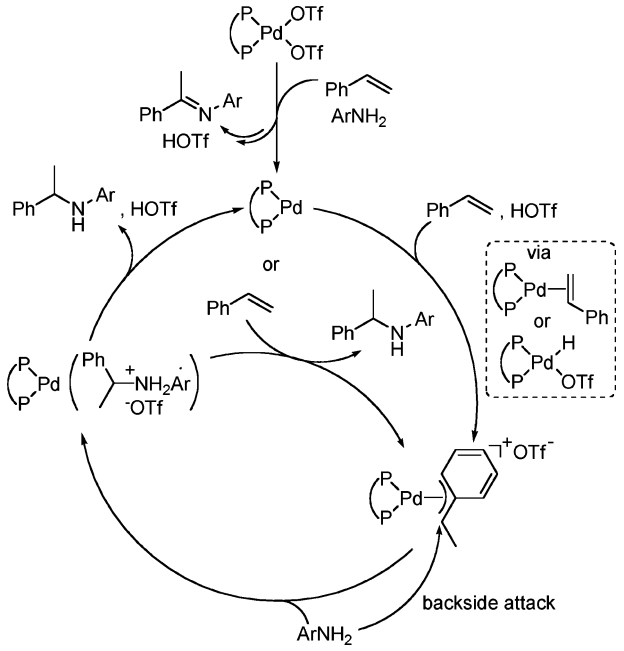
Table 4. Palladium Catalyzed Hydroamination of Styrene with Bifunctional Aromatic Amines[a]



entry	amine	yield[b]	entry	amine	yield[b]
1	R = 2-OH	80	8	R = C-CN	71
2	R = 4-CH_2CH_2OH	89	9	R = 3-CN	90
3	R = 3-COOH	92	10	R = 4-CN	72
4[c]	R = 3-$COCH_3$	81	11	R = 2-CO_2Et	99
5	R = 4-$COCH_3$	71	12	R = 3-CO_2Et	92
6	R = 2-SMe	59	13[d]	R = 4-CO_2Et	89
7[d]	R = 4-SMe	88	14[d]	R = 3-$NHCOCH_3$	91
			15[d]	R = 4-$CONH_2$	86

[a] Reaction conditions: 1.0 mmol of amine, 2.0 mmol of styrene, 1.0 mL of dioxane. [b] Isolated yield (average of two runs), in percent. [c] Reaction catalyzed by 2 mol % Xantphos, and 2 mol % [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$. [d] Reaction run without TfOH cocatalyst.

Scheme 1. Proposed Mechanisms for the Hydroamination of Vinylarenes



shown in Table 3, the reaction of an aromatic amine with a pendant primary alcohol with styrene occurred in high yield (Table 4, entry 2). Moreover, addition of the N−H bond of an aniline derivative containing an *N*-aryl amide (Table 4, entry 14) or a primary amide (Table 4, entry 15) occurred in high yield.[28] In keeping with the mechanism for these hydroaminations of vinylarenes and dienes (vide infra), hydroaminations of alkenes under analogous conditions do not occur.

2. Mechanistic Studies of Hydroamination. Origin of the Difference in Reactivity of Bisphosphine-Ligated Catalysts. a. Synthesis and Dynamic Studies of η^3-Phenethyl and η^3-Benzyl Complexes. Previous mechanistic work on vinylarene hydroamination suggested that this hydroamination occurs by one of the two pathways in Scheme 1. Further, these data indicated that an η^3-arylethyl complex was the catalyst resting state and that nucleophilic attack on this intermediate to form the C−N bond in the product was turnover limiting.[23] The effect of ligand structure on the rate of additions of amines to η^3-

(28) Results of ongoing studies on the additions of aliphatic amines to dienes and vinylarenes will be published in due course

Scheme 2. Synthesis of Benzylpalladium Complexes **4**−**10**

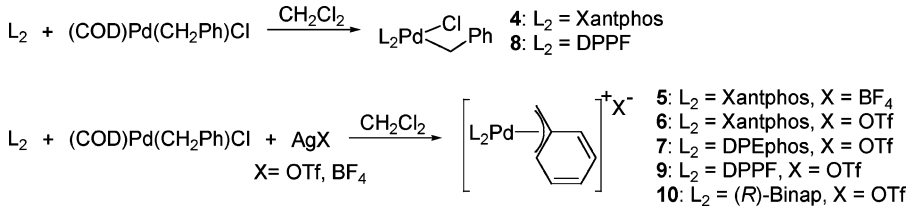
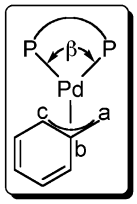
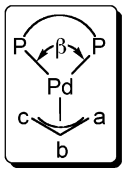


Table 5. Comparison of Pd−C and P−Pd−P Angles of Benzyl Complexes **6**, **7**, and **9** and Allyl Complexes **1** and **12**

Complex	β (°)	Pd-C_a	Pd-C_b	Pd-C_c
[(Xantphos)Pd(η^3-benzyl)]OTf (**6**)	108.11(5) 107.45(2)	2.085(6) 2.095(6)	2.238(5) 2.239(5)	2.686(6) 2.584(6)
[(DPEphos)Pd(η^3-benzyl)]OTf (**7**)	104.08(4)	2.102(4)	2.275(3)	2.408(4)
[(DPPF)Pd(η^3-benzyl)]OTf (**9**)	101.95(4) 102.19(5)	2.093(4) 2.110(4)	2.251(3) 2.240(4)	2.418(4) 2.374(4)



Complex	β (°)	Pd-C_a	Pd-C_b	Pd-C_c
[(Xantphos)Pd(η^3-allyl)]Cl (**1**)	107.83(4)	2.178(4)	2.160(4)	2.179(4)
[(DPPF)Pd(η^3-allyl)]Cl (**12**)	100.73(4)	2.180(3)	2.175(3)	2.177(3)



phenethyl and η^3-allyl complexes and the effect of the differences in rate of this elementary reaction on the catalytic process were ambiguous because the rates of palladium-catalyzed allylic alkylations with malonate nucleophiles, which occur through analogous allyl complexes, were slower when catalyzed by palladium complexes of Xantphos than those when catalyzed by palladium complexes of DPPF or DPEphos.[29] To determine if the increase in rate of hydroamination with complexes of Xantphos was due to an increase in the rate of nucleophilic attack on the η^3-arylethyl ligand, we prepared η^3-benzyl complexes ligated by Xantphos, DPEphos, DPPF, and (*R*)-BINAP, as well as η^3-allyl complexes ligated by a Xantphos, DPEphos, DPPF, (*R*)-BINAP, and DPPE.

We first sought to prepare η^3-phenethyl complexes ligated by Xantphos and DPPF by combining CpPd(η^3-allyl) with the desired ligand in an excess of styrene[30] and adding anilinium triflate to the resulting styrene complex. The reaction of CpPd(η^3-allyl) with Xantphos or DPPF in an excess of styrene formed the corresponding η^2-styrene complexes in quantitative yields if a 50-fold excess of styrene was used. We were unable to isolate these complexes but were able to characterize them in solution (see Supporting Information). To obtain spectral data on these olefin complexes in the absence of the large excess of styrene, we prepared complexes of electron poor vinylarenes because they could be prepared with low ratios of olefin to metal. The Xantphos and DPPF η^2-vinylarene complexes of 3-trifluoromethylstryene were generated quantitatively in solution with only 1 equiv of vinylarene.

The ^{31}P NMR spectra of the series of vinylarene complexes varied. The ^{31}P NMR spectra of [(DPPF)Pd(η^2-styrene)] consisted of a pair of broad singlets at 17.7 and 15.1 ppm, the spectra of [(DPPF)Pd(η^2-3-trifluoromethylstyrene)] consisted of a pair of doublets (δ 19.0, 15.6 ppm, J_{PP} = 17.9 Hz), the spectra of [(Xantphos)Pd(η^2-styrene)] consisted of one broad singlet at 9.86 ppm, and the spectra of [(Xantphos)Pd(η^2-3-trifluoromethylstyrene)] consisted of a pair of broad singlets at 11.9 and 8.12 ppm (Figure S3). These data suggest that rotation about the metal−alkene bond, exchange with free vinylarene, or partial dissociation of the bisphosphine ligand occur at rates that depend on the bisphosphine bite angle and vinylarene electronics.

Treatment of the styrene complex ligated by DPPF with anilinium triflate gave a mixture of the syn and anti η^3-phenethyl complexes (3:1),[31] which was recrystallized to yield [(DPPF)Pd(η^3-phenethyl)]OTf (**3**) as a single isomer. This observation suggests that the formation of an η^3-phenethyl complex is more likely to occur by addition of acid to a vinylarene complex than by the reversed order of addition of a vinylarene to a cationic palladium hydride generated by protonation of a palladium(0) complex. The ^{31}P NMR spectra of the major isomer consisted of a pair of doublets (δ 33.62, 22.90 J_{PP} = 54.3 Hz). In contrast, addition of anilinium triflate to the styrene complex ligated by Xantphos did not form an η^3-phenethyl complex that was stable enough to isolate. Free styrene and zerovalent palladium complexes were among the products that were generated by the protonation of the η^2-styrene complex ligated by Xantphos.

In lieu of a set of η^3-phenethyl complexes with varied phosphine ligands, we prepared a set of more stable η^3-benzyl complexes ligated by Xantphos, DPEPhos, DPPF, and (*R*)-BINAP. [(Xantphos)Pd(η^3-benzyl)]Cl (**4**), [(Xantphos)Pd(η^3-benzyl)]BF_4 (**5**), [(Xantphos)Pd(η^3-benzyl)]OTf (**6**), [(DPEphos)-Pd(η^3-benzyl)]OTf (**7**), [(DPPF)Pd(benzyl)Cl] (**8**), [(DPPF)Pd(η^3-benzyl)]OTf (**9**), and [(R−BINAP)Pd(η^3-benzyl)]OTf (**10**) were prepared by the addition of the bisphosphine and, when appropriate, either AgOTf or $AgBF_4$ to (COD)Pd(CH_2Ph)Cl (Scheme 2). These complexes were characterized by ^{1}H, ^{31}P,

(29) The Xantphos complexes, however, showed unusual regioselectivity for attack at the more substituted carbon of an unsymmetrical allyl substrate. See: van Haaren, R. J.; Goubitz, K.; Fraanje, J.; van Strijdonck, G. P. F.; Oevering, H.; Coussens, B.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Inorg. Chem.* **2001**, *40*, 3363−3372.

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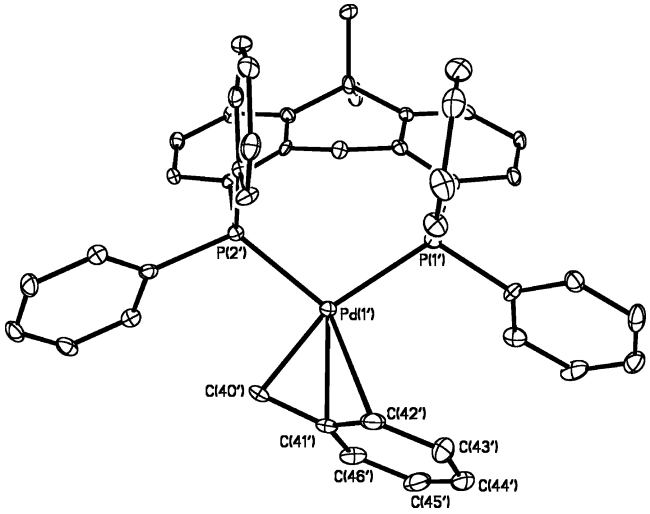


Figure 2. ORTEP plot of one of the two independent molecules of [(Xantphos)Pd(η^3-benzyl)]OTf (**6**) at 30% probability level (hydrogen atoms and triflate counterion omitted for clarity). Selected bond lengths and angle: Pd1−C40 = 2.085(6) Å; Pd1−C41 = 2.238(5) Å; Pd1−C46 = 2.686 Å; Pd1−C42 = 2.986 Å; Pd1−P1 = 2.4031(17) Å; Pd1−P2 = 2.3036(16) Å; P2−Pd1−P1 = 108.11(5)°. Selected bond lengths and angle for the second independent molecule: Pd1′−C40′ = 2.095(6) Å; Pd1′−C41′ = 2.239(5) Å; Pd1′−C46′ = 3.091 Å; Pd1′−C42′ = 2.584(6) Å; Pd1′−P1′ = 2.4057(16) Å; Pd1′−P2′ = 2.3095(15) Å; P2′−Pd1′−P1′ = 107.45(2)°.

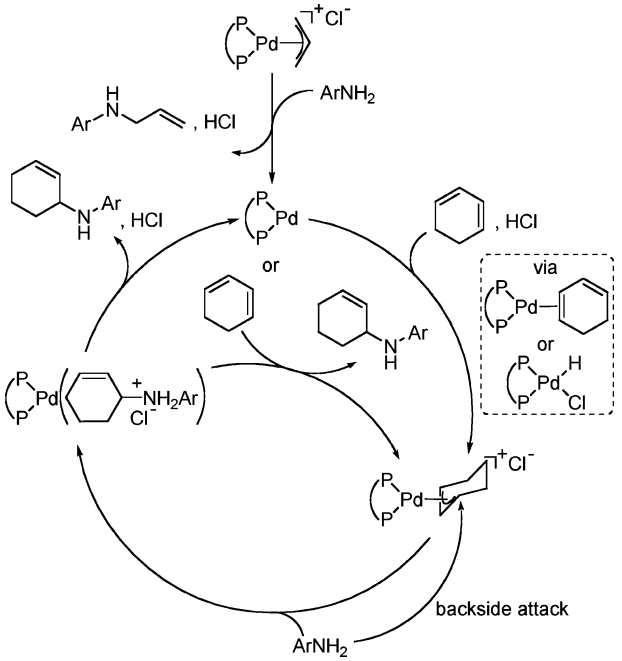
^{13}C NMR spectroscopy and elemental analysis. The ^{31}P NMR spectrum of DPPF-ligated **9** consisted of a typical pair of doublets. However, the ^{31}P NMR spectrum of Xantphos complexes **4**−**6** at room temperature consisted of a single resonance at 12.9, 11.1, and 13.3 ppm, respectively.

The ^{1}H and ^{31}P NMR spectra of [(Xantphos)Pd(η^3-benzyl)]-OTf (**6**) were temperature dependent (Figures S1 and S2). The singlet ^{31}P NMR resonance of triflate **6** was resolved into two doublets at lower temperatures, with a coalescence temperature of approximately −25 °C. A single resonance for the two benzylic protons was observed at room temperature. This signal broadened, but was not fully resolved, at −80 °C. Therefore, a rapid η^3-to-η^1 interconversion occurs at low temperature, but exchange between T-shaped geometries via Y-shaped intermediates is slow on the NMR time scale below −25 °C.

X-ray diffraction studies were conducted on the benzylpalladium complexes [(Xantphos)Pd(η^3-benzyl)]OTf (**6**), [(DPEphos)Pd(η^3-benzyl)]OTf (**7**), and [(DPPF)Pd(η^3-benzyl)]OTf (**9**). Table 5 provides a comparison of distances between the metal and the three carbons of the benzyl group bound to the metal and the P−Pd−P bite angles for these three benzyl complexes, as well as related data on two allyl complexes described in a later section. The triflate counterion in each of the benzyl complexes was far from bonding to the metal. Although the Pd−O distance varied a large amount in the various structures, the shortest distance was a long 3.28 Å.

[(Xantphos)Pd(η^3-benzyl)]OTf (**6**) (Figure 2) crystallized as two chemically equivalent but crystallographically independent molecules with η^3-benzyl ligands. The bond distance to the benzylic carbon (2.085(6) and 2.095(6) Å) was much shorter than the distance to the ipso carbon (2.238(5) and 2.239(5) Å) or the distance to the closer of the ortho carbons (2.686 and 2.584(6) Å). The bite angles in these two crystallographically independent molecules were 108.11(5)° and 107.45(2)°.

Scheme 3. Proposed Mechanisms for the Hydroamination of 1,3-Dienes



These crystallographic data for **6** can be compared to those for DPEphos-ligated benzyl complex **7** (Figure S6) and DPPF-ligated benzyl complex **9** (Figure S7, S8). As shown in Table 5, the Pd−C distances in DPEphos-ligated **7** and DPPF-ligated **9** were similar to those in Xantphos complex **6**. The bite angle in **7** was found to be 3.4°−4.1° smaller than that in **6**, and the bite angle in **9** was found to be 5.4°−6.1° smaller than that in **6**. The bite angle of **7**, 104.08(4)°, was similar to that of the previously characterized palladium complexes ligated by DPEphos.[29,32−34]

b. Synthesis and Dynamic Studies of η^3-Allyl Complexes. Scheme 3 shows how η^3-allyl complexes are likely to be intermediates in the hydroamination of conjugated dienes, just as the η^3-phenethyl complexes appear to be intermediates in the hydroamination of vinylarenes.[23] The allyl-palladium chloride complexes [(Xantphos)Pd(η^3-allyl)]Cl (**1**), [(DPEphos)Pd-(η^3-allyl)]Cl (**11**), [(DPPF)Pd(η^3-allyl)]Cl[35] (**12**), [((*R*)-BINAP)-Pd(η^3-allyl)]Cl (**13**), and [(DPPE)Pd(η^3-allyl)]Cl[36] (**14**) were prepared by the addition of 2 equiv of the appropriate bisphosphine to [Pd(η^3-allyl)Cl]$_2$. [(Xantphos)Pd(η^3-allyl)]BF$_4$ (**15**), [(Xantphos)Pd(η^3-allyl)]OTf (**2**), [((*R*)-BINAP)Pd(η^3-allyl)]BF$_4$ (**16**), and [((*R*)-BINAP)Pd(η^3-allyl)]OTf[37] (**17**) were prepared by addition of the appropriate bisphosphine to [Pd(η^3-allyl)-Cl]$_2$, followed by 2 equiv of the corresponding silver salt. Each of these complexes was characterized by ^{1}H, ^{31}P, ^{13}C NMR spectroscopy and elemental analysis.

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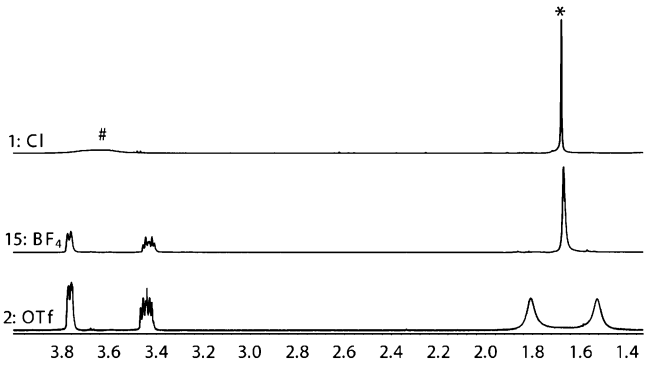

Figure 3. 500 MHz ^{1}H NMR spectra of (Xantphos)Pd(η^3-allyl)X at 22 °C in CD_2Cl_2 (top, X = Cl; middle, X=BF_4; bottom, X=OTf). # and * designate the terminal allyl protons and dimethyl backbone of Xantphos, respectively.

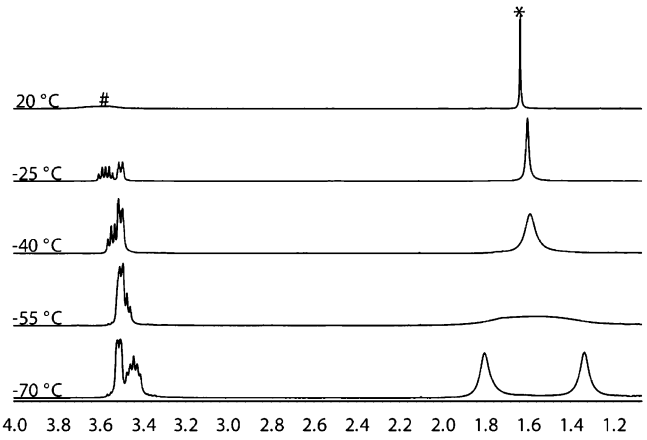

Figure 4. 400 MHz ^{1}H NMR spectra of (Xantphos)Pd(η^3-allyl)Cl (**1**) at various temperatures in CD_2Cl_2. # and * designate the terminal allyl protons and dimethyl backbone of Xantphos, respectively.

The ^{1}H NMR spectra of Xantphos-ligated complexes **1**, **2**, and **15** with chloride, OTf, and BF_4 counterions were distinct (Figure 3). The terminal protons syn and anti to the central proton of the allyl group in chloride complex **1** interconverted on the NMR time scale at room temperature. They were resolved at −25 °C (Figure 4). The terminal allyl protons of complexes **15** and **2** containing the less-coordinating BF_4 and OTf counterions interconverted more slowly. Signals corresponding to the syn and anti protons of the allyl termini of both complexes were resolved at room temperature. The interconversion of two terminal allyl protons likely occurs by the common η^3-η^1-η^3 mechanism.[38] If so, then the more coordinating chloride counterion appears to promote the η^3- η^1- η^3 process.[39]

The dynamics of the backbone methyl groups also varied with the counterion. A single resonance corresponding to the backbone methyl groups of the Xantphos ligand in **1** and **15** was observed at room temperature, whereas two distinct, broad resonances corresponding to these methyl groups in complex **2** were observed at room temperature. The methyl groups of the Xantphos backbone of **1** coalesced at −55 °C (Figure 4), while the resonances corresponding to the methyl groups of the Xantphos backbone of **15** coalesced at −18 °C. The difference between the rates of interconversion of the syn and anti protons of the allyl group and the two backbone methyl groups of the ligand bearing different counterions is surprisingly large. The backbone methyl groups can interconvert by reversible dissociation of one-half of the bidentate ligand[40] or pseudorotation via a pentacoordinate palladium complex formed by coordination of the counterion.[41]

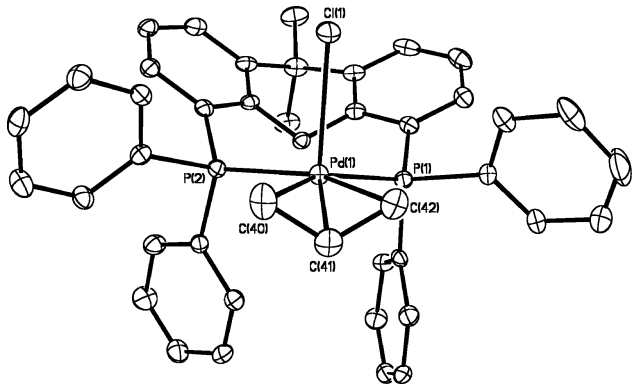

Figure 5. ORTEP plot of (Xantphos)Pd(η^3-allyl)Cl (**1**) at 30% probability level (hydrogen atoms and cocrystallized benzene omitted for clarity). Selected distances and angle: Pd1−C40 = 2.178(4) Å; Pd1−C41 = 2.160(4) Å; Pd1−C42 = 2.179(4) Å; Pd1−P1 = 2.3623(10) Å; Pd1−P2 = 2.3502(11) Å; Pd1−Cl1 = 2.7694(10) Å; P2−Pd1−P1 = 107.83(4)°.

X-ray diffraction studies were conducted on Xantphos complex **1** (Figure 5) and DPPF complex **12** (Figure S9). Data on the M−C distances and P−Pd−P angles are included in Table 5. These studies showed that the bite angles were 108° and 101°, respectively. These angles are indistinguishable from those angles found in the η^3-benzyl complexes. In contrast to most η^3-allyl complexes of palladium, Xantphos complex **1** displayed a geometry that can be best described as distorted square pyramidal with two sites of the equatorial plane occupied by the η^3-allyl ligand and the axial site occupied by a weakly bound chloride. The metal−chloride distance was long (2.77 Å), but within the sum of the van der Waals radii for palladium and chloride.[42] The structure of DPPF-complex **12** indicated a weaker Pd−Cl interaction or the lack of an interaction. The Pd−Cl distance in this complex was 3.16 Å. Although five-coordinate, 18-electron complexes of palladium are precedented, they are rare.[20,43−49] Only a few examples of (chelate)M(η^3-allyl)X complexes in which X is a coordinated halide have been structurally characterized,[50−55] and only one of these contains palladium as the central atom.[55]

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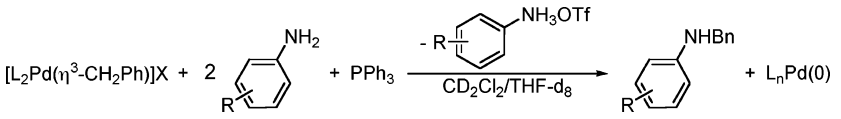
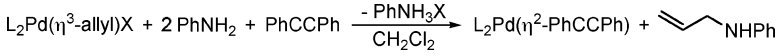
Table 6. Nucleophilic Attack of Anilines on [(L_2)Pd(η^3-CH_2Ph)]OTf[a]



entry	complex	X	L_2	bite angle (deg)	amine	$t_{1/2}$ (min)	k_{obs} (s^{-1}) × 10^4
1	**6**	OTf	Xantphos	108.11(5), 107.45(5)[b]	R = H	26.3	4.40
2					R = 3-CN	41.1	2.81
3					R = 4-CN	34.6	3.34
4	**5**	BF_4			R = H	12.7	9.11
5	**7**	OTf	DPEphos	104.08(4)[b]	R = H	54.1	2.13
6	**9**	OTf	DPPF	102.19(5), 101.95(4)[b]	R = H	328	0.352
7		OTf			R = 3-CN	610	0.19
8		OTf			R = 4-CN	630	0.18
9	**10**	OTf	(*R*)-Binap	95.97(4)[c]	R = H	544	0.212

[a] Reaction conditions: 0.014 M Pd complex, 0.070 M amine, 0.014 M PPh_3, 9.0 mM 1,3,5-trimethylbenzene (internal standard) in 0.2 mL of CD_2Cl_2 and 0.6 mL of THF-d_8 at 60 °C. [b] Values taken from crystal structures. For complexes ligated by Xantphos and DPPF, two independent molecules were present in the unit cell. [c] The bite angle for [((*R*)-BINAP)Pd(η^3-allyl)]OTf[37] was used.

Table 7. Nucleophilic Attack of Anilines on [(L_2)Pd(η^3-allyl)]X[a]



entry	complex	L_2	X	bite angle (deg)	$t_{1/2}$ (min)	k_{obs} (s^{-1}) × 10^4
1	**1**	Xantphos	Cl	107.83(4)[b]	38.8	2.98
2	**15**	Xantphos	BF_4	108.11(7)[c]	143	0.807
3	**2**	Xantphos	OTf	108.11(7)[c]	185	0.625
4	**11**	DPEphos	Cl	104.08(4)[b]	55.4	2.08
5	**12**	DPPF	Cl	100.73(4)[b]	100[e]	0.96
6	**13**	(*R*)-Binap	Cl	95.97(4)[d]	58.4	1.98
7	**14**	DPPE	Cl	85[c]	57.8	2.00

[a] Reaction conditions: 0.029 M Pd complex, 2.9 M amine, 0.44 M diphenylacetylene, PPh_3 (external standard) in 0.5 mL of CH_2Cl_2 at 45 °C. [b] Values taken from crystal structures. For entry 4 the value from [(DPEphos)Pd(η^3-CH_2Ph)]OTf was used. [c] Values obtained from ref 33. [d] Reference 37. [e] ±20 min.

c. Relative Rates of Reactions of Arylamines with η^3-Benzyl, η^3-Allyl, and η^3-1,1-Dimethylallyl Complexes Ligated by Bisphosphines. The reactions of arylamines with bisphosphine-ligated, benzyl complexes **4**−**10** were monitored by ^{1}H NMR spectroscopy at 60 °C in a mixture of CD_2Cl_2 and THF-d_8. Triphenylphosphine was added to each reaction to trap the palladium(0) product. In the presence of PPh_3, the observed palladium(0) products are Pd(bisphosphine)$_2$ and Pd(PPh_3)$_4$. The rate of nucleophilic attack was unaffected by the concentration of added phosphine; reactions with 5 and 10 equiv of added PPh_3 occurred with indistinguishable rate constants.

Table 6 summarizes the half-lives and rate constants for the reactions of benzylpalladium complexes **5**−**7**, **9**, and **10** with aniline and the reactions of benzylpalladium complexes **6** and **9** with 3-aminobenzonitrile and 4-aminobenzonitrile, to form the corresponding *N*-benzylarylamines. Most striking, these data show that an increase in bite angle from 102° to 108° leads to an increase in the rate of nucleophilic attack by an order of magnitude. In addition, these data show that nucleophilic attack by aniline is 1.3 to 1.9 times faster than attack by the less electron-rich 3- and 4-aminobenzonitriles.

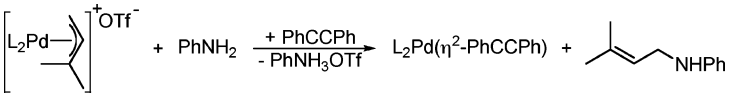
The reaction of [(Xantphos)Pd(η^3-benzyl)]BF_4 (**5**) with aniline (Table 6, entry 4) revealed a significant effect of the counterion on the rate of the nucleophilic attack. The rate of the reaction of the aniline with BF_4 complex **5** was 2 times greater than that of the analogous reaction with triflate **7** (Table 3, entry 1). This result was surprising because the triflate and tetrafluoroborate counterions are not bound to the metal and would not be expected to affect the geometry or electrophilicity of the metal center. These results were used to further improve the catalyst, as will be subsequently described. More expected, the chloride complex **4**, which would be anticipated to contain an η^1-benzyl group and coordinated chloride,[46] did not react with arylamines to form the *N*-benzylaniline product.[56]

Table 7 summarizes the half-lives and rate constants for the reactions of allylpalladium complexes **1**, **2**, and **11**−**15** with aniline. The rates of reaction of 0.029 M allylpalladium complexes in CH_2Cl_2 with 100 equiv of aniline at 45 °C to form *N*-allylaniline were measured by ^{31}P NMR spectroscopy. These reactions were conducted with added diphenylacetylene to trap the palladium(0) product; reactions of allylpalladium complexes containing chloride counterions in the presence of added triphenylphosphine to trap the palladium(0) formed a mixture of uncharacterized products. The rate of nucleophilic attack was not affected by the concentration of added diphenylacetylene; reactions with 5 and 10 equiv of added diphenylacetylene occurred with indistinguishable rate constants. Unlike the correlation of the rate of nucleophilic attack to the bite angle observed for benzylpalladium complexes, no simple trend in the rate of nucleophilic attack on the ancillary ligand bite angle was observed. The Xantphos complex, which contains the largest bite angle (108°), did undergo nucleophilic attack by aniline faster than the allyl complexes of the other ligands. However, nucleophilic attack by aniline on the complexes

(55) Hansson, S.; Norrby, P. O.; Sjogren, M. P. T.; Akermark, B.; Cucciolito, M. E.; Giordano, F.; Vitagliano, A. *Organometallics* **1993**, *12*, 4940−4948.

(56) Preparation and crystallographic characterization of [(Xantphos)Pd(η^3-benzyl)Br] (**18**) show an η^3 coordination mode for the benzyl ligand with the bromide coordinated in the apical position. See Supporting Information.

Table 8. Nucleophilic Attack of Aniline on [(L_2)Pd(η^3-1,1-dimethylallyl)]OTf[a]



entry	complex	equiv $PhNH_2$	T (°C)	L_2	$t_{1/2}$ (min)	k_{obs} (s^{-1}) × 10^4
1	19	5	45	Xantphos	86.4	1.3
2		15	45	DPEphos	32.0	3.6
3	20	15	45	DPEphos	840	0.14
4		200	45		19.3	6.0
5	21	15	45	DPPF	<10% conv @12 h	
6		200	45		250	0.46
7[b]		200	75		58	2.0
8[b]	22	200	75	(*R*)-Binap	28.8% conv @1 h	

[a] Reaction conditions: 0.039 M Pd complex, 0.44 M diphenylacetylene, PPh_3 (external standard) in 0.5 mL of CH_2Cl_2 with 5, 15, or 200 equiv of $PhNH_2$ at 45 or 75 °C. [b] Reaction run in 1,2-dichloroethane.

containing smaller bite angles than the Xantphos complex and more flexible ligand backbones occurred with similar rates. The allylpalladium complex ligated by DPPF reacted more slowly than the other allylpalladium complexes, but the rate constants were difficult to reproduce, and the value presented for reaction of this complex (Table 7, entry 5) has significant error.

Like the rates of reactions of the η^3-benzyl complexes, the rates of reactions of the allyl complexes were significantly affected by the identity of the counterion. One might expect that the complex with the less coordinating anion would be more electrophilic, but Xantphos-ligated allyl complexes **2** and **15** containing triflate and tetrafluoroborate counterions reacted significantly slower than the analogous complex **1** containing a more coordinating chloride ion. Although unexpected, this trend for the rates of nucleophilic attack on the allyl complexes qualitatively paralleled that for the rates of nucleophilic attack on the Xantphos-ligated benzylpalladium complexes with tetrafluoroborate and triflate counterions. Moreover, this trend is consistent with the yields of the hydroaminations of dienes catalyzed by complexes with these counterions. The yield of allylamine from diene hydroamination catalyzed by the combination of Xantphos and [Pd(η^3-allyl)Cl]$_2$ was higher than the yield from the hydroamination conducted in the presence of AgOTF (Table 1, entries 1 and 2).

The difference between the smooth, positive correlation between bite angle and rate of nucleophilic attack on the benzylpalladium complexes and lack of an overarching correlation between bite angle and rate of nucleophilic attack on the symmetrical allyl complexes led us to conduct experiments to determine whether the difference resulted from inherent electronic properties of an η^3-benzyl group and an η^3-allyl group or from the symmetries of an η^3-benzyl and a symmetric, unsubstituted η^3-allyl ligand. To distinguish between these possibilities, we prepared a series of 1,1-dimethylallylpalladium complexes bearing bisphosphines with different bite angles. [(Xantphos)Pd(η^3-1,1-dimethylallyl)]OTf (**19**),[29] [(DPEphos)-Pd(η^3-1,1-dimethylallyl)]OTf (**20**),[29] [(DPPF)Pd(η^3-1,1-dimethylallyl)]OTf (**21**), and [((*R*)-Binap)Pd(η^3-1,1-dimethylallyl)]-OTf (**22**) were prepared by the addition of 2 equiv of the appropriate bisphosphine and 2 equiv of AgOTf to [Pd(η^3-1,1-dimethylallyl)Cl]$_2$.

The rates of reaction of 0.039 M of each of the 1,1-dimethylallylpalladium complexes with varying amounts of aniline in CH_2Cl_2 or 1,2-dichloroethane at 45 °C or 75 °C, respectively, were measured by ^{31}P NMR spectroscopy (Table 8). These reactions, like the reaction of the parent allyl complexes, were conducted with added diphenylacetylene to trap the palladium(0) product. The reaction of aniline with each of these complexes formed *N*-(3-methylbut-2-enyl)aniline from attack at the unsubstituted terminus of the allyl group. Similar to the correlation between bite angle and rate of attack on benzylpalladium complexes, a clear positive correlation was observed between the ligand bite angle and rate of attack of aniline on 1,1-dimethylallylpalladium complexes. The effect of bite angle on the rate of nucleophilic attack on the unsymmetrical η^3-allyl complexes was even greater than that for nucleophilic attack on the η^3-benzyl complexes. Complexes of Xantphos and DPEphos (Table 8, entries 2 and 3), which have an approximately 4° difference in bite angle, and complexes of DPEphos and DPPF (Table 8, entries 4 and 6), which have an approximately 3° difference in bite angle, displayed an order of magnitude difference in the rate of nucleophilic attack. This larger dependence was observed, even though there is no significant difference in the bite angles of η^3-benzyl and η^3-1,1-dimethylallyl complexes of the same bisphosphine (ref 29 and vide supra).

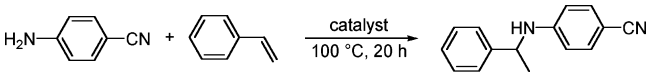
Thus, the correlation between the rate of attack and ligand bite angle appears to arise when the η^3-ligand is substituted unsymmetrically. The origin of the dependence of the correlation between rate of attack and bite angle on the substitution pattern of the η^3-ligand may result from differences in the ground-state structures of the unsymmetrical and symmetrical ligands. X-ray diffraction showed that the difference between the M−C distances in the benzyl complex increased with increasing bite angle, while the two M−C distances were naturally indistinguishable in the complexes containing the symmetrical, unsubstituted allyl ligand. This greater dissymmetry of the binding of the unsymmetrical η^3-benzyl ligand, and the presumed greater dissymmetry of the binding of the 1,1-disubstituted allyl ligand, with increasing size of the bite angle is likely to make one end of the allyl group more electrophilic than the other and thereby increase the rate of nucleophilic attack.

d. Identification of the Turnover-Limiting Step.[28] To determine if the effects of ligand and counterion translated to differences in rates of the overall catalytic process, we conducted experiments to determine the resting state of the catalyst and the turnover-limiting step with several catalysts and substrate combinations. Additions of aniline to styrene catalyzed by isolated [(DPPF)Pd(η^3-benzyl)]OTf (**9**) and [(Xantphos)Pd(η^3-benzyl)]OTf (**6**) and additions of aniline to 1,3-cyclohexadiene

catalyzed by [(Xantphos)Pd(η^3-allyl)Cl] (**1**) were monitored by ^{31}P NMR spectroscopy. In agreement with previous work,[9,23] the [(DPPF)Pd(η^3-phenethyl)]OTf (**3**) complex was the major palladium complex in the reaction of styrene with aniline containing HOTf as cocatalyst. These data indicate that attack of amine on the η^3-phenethyl ligand is the turnover-limiting step of the catalytic cycle when DPPF is used as ligand. Unfortunately, the ^{31}P NMR spectrum of the reaction of aniline with styrene catalyzed by [(Xantphos)Pd(η^3-benzyl)]OTf (**6**) contained many resonances that could not be assigned to specific complexes at this time. However, ^{31}P NMR spectroscopic monitoring of the addition of aniline to 1,3-cyclohexadiene catalyzed by [(Xantphos)Pd(η^3-allyl)]Cl (**1**) showed that [(Xantphos)Pd(η^3-cyclohexenyl)]Cl (**23**) was the major intermediate in solution. This observation implies that nucleophilic attack of amine on the allyl complex is turnover limiting. Thus, the faster rate of stoichiometric addition of aniline to the allyl complexes ligated by Xantphos than that of addition to the allyl complexes ligated by other bisphosphines accounts for at least a portion of the faster rate of catalytic hydroamination of dienes when Xantphos is used as ligand. The identity of the cyclohexenyl complex **23** was confirmed by independent synthesis from [Pd(η^3-cyclohexenyl)Cl]$_2$[57] and 2 equiv of Xantphos per dimer.

e. Relationship between the Rate of Stoichiometric Nucleophilic Attack on η^3-Allyl Complexes and the Rate of Catalytic Hydroamination of 1,3-Dienes. To determine the origin of the difference in rates of hydroamination of dienes with the different precatalysts, the reactions of aniline with 1,3-cyclohexadiene initiated with [(Xantphos)Pd(η^3-allyl)]Cl (**1**), [(DPPF)Pd(η^3-allyl)]Cl (**12**), and [((*R*)-BINAP)Pd(η^3-allyl)]Cl (**13**) as precatalysts were monitored by ^{31}P NMR spectroscopy. The major palladium complexes in each reaction were precatalyst and [(bisphosphine)Pd(η^3-cyclohexenyl)]Cl. However, the concentration of [(bisphosphine)Pd(η^3-cyclohexenyl)]Cl was lower for complexes with smaller bite angles. Complementing these changes in the concentration of the allyl complex, the concentration of catalytically inactive [(bisphosphine)PdCl$_2$][58] was greater in reactions catalyzed by complexes containing bisphosphines with smaller bite angles. The origin of the relationship between bisphosphine bite angle and concentration of (bisphosphine)PdCl$_2$ is unclear. However, the decomposition of bisphosphine allylpalladium complexes bearing halide counterions has previously been shown to form (bisphosphine)-PdCl$_2$.[59] These data provide a second reason that the hydroamination of dienes varies with ligand, besides faster attack of the amine on the allyl group of Xantphos **1**. Considering that the rate of nucleophilic attack on the symmetric allyl complexes ligated by DPPF and BINAP was relatively insensitive to the bite angle (vide supra) but that the concentration of the DPPF-ligated allyl complex was higher, we propose that the differences in rates of the hydroamination of dienes by DPPF and BINAP complexes are due to the differences in concentrations of the allyl complexes, and not due to a difference in the rate of nucleophilic attack on the allyl intermediate. Moreover, we propose that the faster hydroaminations of dienes catalyzed by Xantphos complexes of palladium result from a sum of the faster rate of nucleophilic attack on the allyl ligand and a higher concentration of the allyl intermediate.

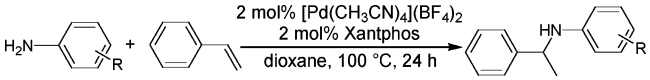
Table 9. Effect of Catalyst Components on the Hydroamination of Styrene with 4-Aminobenzonitrile[a]



entry	catalyst	yield[b]
1	2% [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ + 2% Xantphos	96
2	2% [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ + 2% DPPF	11
3	2% [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ + 2% DPEPhos	14
4	2% [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ + 2% BINAP	3
5	2% [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ + 2% DPPPent	6
6	2% [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ + 2% DPPE	0

[a] Reaction conditions: 0.5 mmol of 4-aminobenzonitrile, 1.0 mmol of styrene, 0.5 mL of dioxane. [b] GC yields, in percent.

Table 10. [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$/Xantphos Catalyzed Hydroamination of Styrene with Bifunctional Aromatic Amines[a]



entry	amine	yield[b]
1	R = 3-COCH$_3$	83 (81)
2	R = 2-SMe	56
3	R = 4-SMe	88 (84)
4	R = 2-CN	65
5	R = 4-CN	65

[a] Reaction conditions: 1.0 mmol of amine, 2.0 mmol of styrene, 1.0 mL of dioxane. [b] GC yields, in percent. Values in parentheses are isolated yields (average of two runs), in percent.

3. Further Catalyst Improvements. Reactions Catalyzed by Bisphosphine and [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$. To determine if the faster rate of nucleophilic attack of arylamine on [(Xantphos)Pd(η^3-benzyl)]BF$_4$ (**5**) vs [(Xantphos)Pd(η^3-benzyl)]OTf (**6**) translates into a faster catalytic reaction, *p*-cyanoaniline was allowed to react with styrene in the presence of a catalyst generated in situ from [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ and Xantphos (Table 9). Indeed, the reaction catalyzed by the combination of Xantphos and [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ (Table 9, entry 1) occurred in higher yield than the reaction catalyzed by the analogous triflate complex [(Xantphos)Pd(CH$_3$CN)$_2$](OTf)$_2$ (Table 2, entry 4).

The combination of Xantphos and [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ was also evaluated for the reactions of Table 4 that occurred in moderate yields with 2 mol % (Xantphos)Pd(η^3-allyl)OTf and 10 mol % TfOH as catalyst. Indeed, the reaction of 1-(3-aminophenyl)ethanone with styrene occurred in higher yield (Table 10, entry 1) with Xantphos and [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ as catalyst, instead of (Xantphos)Pd(η^3-allyl)OTf as catalyst. However, not all reactions catalyzed by the complex generated from [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ occurred in higher yield than those catalyzed by (Xantphos)Pd(η^3-allyl)OTf. For example, reactions of styrene with anilines bearing thiomethyl or nitrile functionalities occurred in similar yields with the two catalysts (Table 10, entries 2−5), but the rate of the reactions catalyzed by the combination of Xantphos and [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$ were faster, and the catalyst can be assembled in situ. Consistent with our results that showed faster attack of the arylamine on the allyl

(57) Stoichiometric rate data for the nucleophilic addition of arylamines to benzylpalladium and allylpalladium complexes were obtained at different temperatures and concentrations than those of the catalytic reaction. However, a qualitative comparison of the rates of stoichiometric additions and catalytic transformations shows that they occur on similar time scales.
(58) Trost, B. M.; Strege, P. E.; Weber, L.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3407−15.
(59) XantphosPdCl$_2$ (**24**) was independently prepared and characterized by ^{1}H, ^{13}C, ^{31}P NMR spectroscopy and X-ray diffraction.

palladium chloride complexes than on the allyl palladium complexes with a tetrafluoroborate counterion, reactions of dienes catalyzed by the combination of Xantphos and [Pd(η^3-allyl)Cl]$_2$ occurred in higher yields than reactions catalyzed by the combination of Xantphos and [Pd(CH$_3$CN)$_4$](BF$_4$)$_2$.

Conclusions

Highly active late transition metal catalysts for hydroaminations are needed to accomplish olefin hydroamination in a synthetically valuable fashion. Although much progress must be made to develop transition metal-catalyzed hydroamination, we have demonstrated that improved catalysts for additions of arylamines to vinylarenes and dienes can be developed and that these improved catalysts can tolerate the types of functionality commonly found in natural products and pharmaceutically active materials. This work has shown that palladium complexes of Xantphos are much more reactive catalysts for the hydroamination of dienes and vinylarenes than catalysts reported previously for this reaction. These reactions occur selectively to add the amine N−H bond of arylamines to vinylarenes in the presence of nitrile, nitro, ester, amide, carboxylic acid, phenolic hydroxyl, hydroxyalkyl, and enolizable keto groups.

In addition to demonstrating increased activity and high functional group tolerance from catalysts with Xantphos as ligand, we have revealed some of the factors that control the rates of the catalytic reactions and the rate of the C−N bond-forming step. By monitoring the reactions of isolated bisphosphine-ligated allyl- and benzylpalladium complexes with amines, we demonstrated a correlation between bite angle and rate of nucleophilic attack on η^3-benzyl complexes and unsymmetrical η^3-allyl complexes. We also showed that the population of active catalyst in the hydroaminations of dienes depends on the bite angle of the ligand and that the concentration of the allylpalladium complex may be the major factor that influences the rate of the catalytic hydroamination of symmetrical dienes. Finally, while the origin of the differences in the rate of attack as a function of counterion remain to be delineated, we have shown that the rate of attack is affected significantly by the counterion, even when it is not directly coordinated to the metal.

Experimental Procedures

General Experimental Procedure and Reagent Availability. All manipulations were carried out under an inert atmosphere using a nitrogen-filled glovebox or standard Schlenk techniques. All glassware was oven or flame dried immediately prior to use. THF and diethyl ether were obtained as HPLC grade without inhibitors; benzene, toluene, dichloromethane, and pentane were obtained as ACS reagent grade. THF, diethyl ether, benzene, toluene, dichloromethane, and pentane were degassed by purging with nitrogen for 45 min and dried with a solvent purification system containing a 1 m column containing activated alumina. All reagents were obtained from commercial sources and used without further purification. ^{1}H NMR spectra were obtained at 400 or 500 MHz and recorded relative to residual protio-solvent. ^{13}C NMR spectra were obtained at 101 or 126 MHz, and chemical shifts were recorded relative to the solvent resonance. ^{31}P NMR spectra were obtained at 122, 162, or 202 MHz, and chemical shifts are reported relative to 85% H$_3$PO$_4$. [Pd(η^3-allyl)Cl]$_2$[61] and [Pd(η^3-1,1-dimethylallyl)Cl]$_2$[62] were prepared using the reported procedures. (COD)Pd(CH$_2$Ph)Cl[63] was prepared via an alternate procedure to that found in the literature.

General Procedure for the Preparation of [(Bisphosphine)Pd(η^3-allyl)]Cl. Into a 50 mL round-bottom flask equipped with a magnetic stirbar was placed [Pd(η^3-allyl)Cl]$_2$ (200 mg, 0.547 mmol). Into a second 50 mL round-bottom flask equipped with a magnetic stirbar was placed 2 equiv of bisphosphine (1.09 mmol). Benzene (15 mL) was added to each flask, and the resulting solutions stirred for 10 min at 50 °C to ensure complete dissolution. The solutions were subsequently combined. After stirring for 30 min at 50 °C, the resulting solution/suspension was allowed to cool to room temperature. Complexes that precipitated were isolated by filtration in air and were washed 2 times with 50 mL of Et$_2$O and dried in vacuo. Complexes that were soluble in benzene were isolated by removing all volatiles and recystallizing the residue from dichloromethane and Et$_2$O or pentane. The resulting crystals were isolated from the supernatant, washed with 2 × 10 mL of Et$_2$O or pentane, and dried in vacuo.

General Procedure for the Preparation of [(Bisphosphine)Pd(η^3-allyl)]X (X = BF$_4$ or OTF). Into a 20 mL scintillation vial equipped with a magnetic stirbar was placed [Pd(η^3-allyl)Cl]$_2$ (29.4 mg, 0.0804 mmol) and 2 equiv of bisphosphine (0.161 mmol). Dichloromethane (4 mL) was added, and the solution was stirred for 10 min. The appropriate silver salt (2 equiv, 0.161 mmol) was added to the stirring solution, and the resulting suspension was stirred for 30 min. Filtration through Celite yielded a clear solution, which was concentrated to 1 mL under reduced pressure, layered with Et$_2$O or pentane, and cooled at −35 °C for 12 h. The resulting crystals were washed 2 times with 3 mL of Et$_2$O or pentane and dried in vacuo.

General Procedure for the Preparation of [(Bisphosphine)Pd(benzyl)Cl]. Into a 20 mL scintillation vial equipped with a magnetic stirbar was placed (COD)Pd(CH$_2$Ph)Cl (50.0 mg, 0.147 mmol) and 1 equiv of bisphosphine (0.147 mmol). Dichloromethane (4 mL) was added, and the solution was stirred for 10 min. Filtration through Celite yielded a clear solution, which was concentrated to 1 mL under reduced pressure, layered with pentane, and cooled at −35 °C. The resulting crystals were isolated from the supernatant, washed with 2 × 5 mL of pentane, and dried in vacuo.

General Procedure for the Preparation of [(Bisphosphine)Pd(η^3-benzyl)]X (X = BF$_4$ or OTF). Into a 20 mL scintillation vial equipped with a magnetic stirbar was placed (COD)Pd(CH$_2$Ph)Cl (50.0 mg, 0.147 mmol) and 1 equiv of bisphosphine (0.147 mmol). Dichloromethane (5 mL) was added, and the solution was stirred for 10 min. The appropriate silver salt (1 equiv, 0.147 mmol) was added to the stirring solution, and the resulting suspension was stirred for 10 min. Filtration through Celite yielded a clear solution, which was concentrated to 1 mL under reduced pressure, layered with Et$_2$O or pentane, and cooled to −35 °C. The resulting crystals were isolated from the supernatant, washed with 2 × 5 mL of Et$_2$O or pentane, and dried in vacuo.

General Procedure for the Preparation of [(Bisphosphine)Pd(η^3-1,1-dimethylallyl)]OTf. Into a 20 mL scintillation vial equipped with a magnetic stirbar was placed [Pd(η^3-1,1-dimethylallyl)Cl]$_2$ (40.0 mg, 0.0948 mmol) and 2 equiv of bisphosphine (0.190 mmol). Dichloromethane (5 mL) was added, and the solution was stirred for 10 min. Silver trifluoromethanesulfonate (2 equiv, 48.7 mg, 0.190 mmol) was added to the stirring solution, and the resulting suspension was stirred for 30 min. Filtration through Celite yielded a clear solution, which was concentrated to 1 mL under reduced pressure, layered with Et$_2$O or pentane, and cooled at −35 °C for 12 h. The resulting precipitate was washed 2 times with 3 mL of Et$_2$O or pentane and dried in vacuo.

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(62) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033−46.
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General Procedure for the Hydroamination of 1,3-Cyclohexadiene with Functionalized Anilines (Table 3). In a drybox, XantphosPd(η^3-allyl)Cl (**1**) (15.2 mg, 2.00×10^{-2} mmol), 1,3-cyclohexadiene (191 μL, 2.00 mmol), and the aniline (1.00 mmol) were placed into a small vial, dissolved in 2.00 mL of tetrahydrofuran, and sealed with a cap containing a PTFE septum. The reaction mixture was stirred at 25 °C for 24 h. Upon completion, the reaction mixture was directly adsorbed onto silica gel and purified by flash column chromatography.

General Procedure for the Hydroamination of Styrene with Functionalized Anilines (Table 4). In a drybox, XantphosPd(η^3-allyl)-OTf (**2**) (17.5 mg, 2.00×10^{-2} mmol), styrene (229 μL, 2.00 mmol), and the aniline (1.00 mmol) were placed into a small vial, dissolved in 1.00 mL of 1,4-dioxane, and sealed with a cap containing a PTFE septum. The reaction mixture was stirred at 100 °C for 12 h. Upon completion, the reaction mixture was directly adsorbed onto silica gel and purified by flash column chromatography.

Determination of the Rate Constants (k_{obs}) for the Nucleophilic Attack of Aniline and Substituted Anilines on Benzylpalladium Complexes. Benzylpalladium complexes (**4**−**10**) (0.0108 mmol), PPh_3 (0.0108 mmol), and 1,3,5-trimethylbenzene (0.00719 mmol, internal standard) were dissolved in a mixture of CD_2Cl_2 and THF-d_8 (0.2 mL: 0.4 mL), and the solution was transferred to a screw-capped NMR tube. The arylamines (0.054 mmol) in 0.2 mL THF-d_8 were added by syringe into the NMR tube immediately before the tube was placed in a probe at the appropriate temperature. Decay of the CH_2Ph resonance was monitored by ^{1}H NMR spectroscopy over at least three half-lives with an automated data collection program. Kinetic data were fit to the expression $y = m_1 + m_2 \exp^{-kt}$, in which k is the first-order rate constant k_{obs}.

Determination of the Rate Constants (k_{obs}) for the Nucleophilic Attack of Aniline and Substituted Anilines on Allylpalladium Complexes. Allylpalladium complexes (**1, 2, 11**−**15**) (0.0197 mmol), diphenylacetylene (0.296 mmol), and a capillary containing PPh_3 in tetrahydrofuran were loaded into a screw-capped NMR tube, followed by 0.50 mL of CH_2Cl_2. Aniline (1.98 mmol) was added by syringe into the NMR tube immediately before it was placed in a probe at the appropriate temperature. Decay of the allylpalladium complexes was monitored by ^{31}P NMR spectroscopy over at least three half-lives with an automated data collection program. Kinetic data were fit to the expression $y = m_1 + m_2 \exp^{-kt}$, in which k is the first-order rate constant k_{obs}.

Determination of the Rate Constants (k_{obs}) for the Nucleophilic Attack of Aniline on 1,1-Dimethylallylpalladium Complexes. 1,1-Dimethylallylpalladium complexes (**19**−**22**) (0.0197 mmol), diphenylacetylene (0.296 mmol), and a capillary containing PPh_3 in tetrahydrofuran were loaded into a screw-capped NMR tube, followed by 0.50 or 0.17 mL of CH_2Cl_2. Aniline (0.295 or 3.95 mmol) was added by syringe into the NMR tube immediately before it was placed in a probe at the appropriate temperature. Decay of the 1,1-dimethylallylpalladium complexes was monitored by ^{31}P NMR spectroscopy over at least three half-lives with an automated data collection program. Kinetic data were fit to the expression $y = m_1 + m_2 \exp^{-kt}$, in which k is the first-order rate constant k_{obs}.

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Supporting Information Available: Spectroscopic and analytical data of new compounds, information on procedures, and details of crystal structure analysis of complexes **1**, **6**, **7**, **9**, **12**, **18**, and **24** (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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