Systematic Variation of Bidentate Ligands Used in Aryl Halide Amination. Unexpected Effects of Steric, Electronic, and Geometric Perturbations

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Abstract: This paper presents effects of varying bidentate phosphine steric properties, electronic properties, and bite angle on product ratios in the amination of aryl bromides. Comparisons of the ratios of amine products to dehydrohalogenation products showed that catalysts containing electron rich, modestly hindered phosphines with small bite angles (∼90°) gave the best selectivities. Surprisingly, the arene side product formed from reaction of alkylamines deuterated in the N−H position or deuterated in the position α to the nitrogen showed low levels of deuterium incorporation in many examples. Steric properties and ligand bite angle had the greatest impact on the selectivity for monoarylation versus diarylation of primary amines; ligands with small bite angles gave higher monoarylation-to-diarylation ratios, as did ligands with increased steric bulk. Electron poor or sterically hindered bidentate phosphines reduced the amount of product resulting from aryl exchange of electron rich palladium-bound arenes with those of aryl groups on the phosphine ligands.

Introduction

The use of chelating phosphine ligands has greatly improved the palladium-catalyzed chemistry that forms arylamines from aryl halides or aryl triflates.[1−3] This development is synthetically important because aromatic amines are fundamental building blocks in natural products and organic materials,[4−6] but classical methods to prepare mixed alkylarylamines can be tedious, and nucleophilic aromatic substitution of aryl halides is limited to strongly electron deficient aryl halides or high-temperature processes involving ill−defined copper reagents.[7,8]

Originally, palladium complexes containing the labile, sterically encumbered, monodentate triarylphosphine ligands such as P(*o*-tolyl)$_3$ were the only catalysts for the intermolecular amination chemistry involving amines in the presence of tin amides.[9−12] Kinetic studies, along with investigations of the ligand steric effects on selectivity, showed that P(*o*-tolyl)$_3$ was unusually effective because each intermediate in the catalytic cycle was a highly unsaturated, monophosphine complex and because the selectivity for amination over reduction was enhanced by steric bulk.[11,13] It was, therefore, remarkable when a very different class of phosphine ligand, tightly bound chelating phosphines such as DPPF (1,1′-bis(diphenylphosphino)-ferrocene and BINAP (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl), were found to be more effective than P(*o*-tolyl)$_3$ in the amination chemistry for many amine and aromatic substrates.[2,3]

A chelating ligand possesses three major characteristics: electron-donating ability, steric properties, and the P−M−P angle often called "bite angle". The effect of these three properties on the selectivity in hydroformylations,[14−16] carbon dioxide hydrogenation,[17] and alkyne hydrosilylation[18,19] has been investigated over the years. However, chelating phosphines are often used in cross coupling chemistry, and few systematic studies have been conducted to reveal how all three factors affect this palladium- and nickel-catalyzed chemistry. Most of the focus has been placed upon the effect of the bite angle,[20] or on electronic and steric properties of monodentate phosphines.[21]

In rough terms, chelation inhibits β-hydrogen elimination of alkyl groups,[22,23] and a similar effect appears to control the selectivity of amido complexes that are intermediates in the

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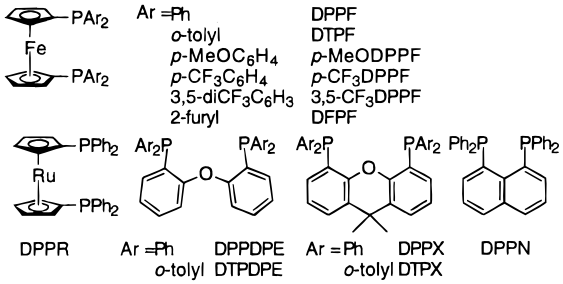


Figure 1. Structures of the bidentate phosphine ligands.

amination chemistry. We have recently shown that β-hydrogen elimination from amido complexes occurs from a 14-electron, three-coordinate intermediate.[24] In contrast, C−N bond-forming reductive elimination of amines from square planar Pd(II) complexes can occur from either a four- or three-coordinate intermediate.[25] Thus, chelating ligands provide enhanced selectivity for reductive elimination over β-hydrogen elimination in the amination chemistry.

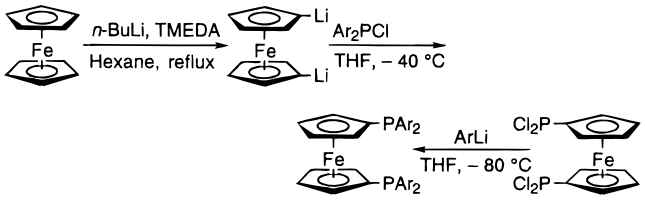
However, not all chelating ligands are equally effective, and no systematic studies have revealed why one ligand is more effective than another in the aryl halide amination chemistry. One might expect that more hindered chelating ligands would combine the benefits of the hindered P(*o*-tolyl)$_3$ with the benefits of chelation. One might also expect that electron poor ligands would enhance the formation of amination products, since reductive elimination is accelerated by reducing the electron density at the metal center.[26] Finally, reductive elimination is typically faster for complexes with chelating ligands containing large bite angles than it is for complexes with small bite angles.[20] Thus, one might expect that increasing the size of the bite angle created by the chelating phosphine would increase the yields of amination product.

We have tested these hypotheses in a systematic fashion by varying DPPF (1,1′-bis(diphenylphosphino)ferrocene). We have chosen to use this ligand as a parent structure because it is effective in the amination chemistry, it is simple to modify, and it has been used in many other transition-metal-catalyzed reactions. We have prepared ligands that are more hindered, more electron poor, or more electron rich than DPPF. We have also prepared bis(diarylphosphino) ligands that produce palladium complexes with both larger and smaller bite angles. The results from these studies are unexpected, and show that the rate for reductive elimination should not be the dominant consideration when ligands for the next generation amination catalysts are designed.

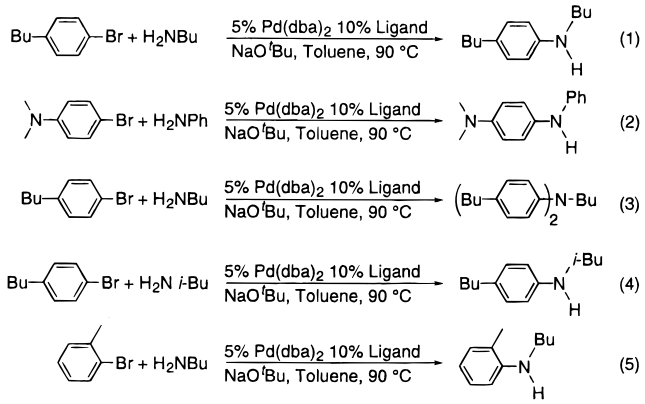
Results

1. Ligand Preparation. The ligands employed in this study are shown in Figure 1, along with their abbreviations. Typically, the ligands were prepared in multigram quantities by dilithiation of the backbone (Cp_2M, diaryl ether, or bromonaphthalene) followed by quenching with a chlorodiarylphosphine (Scheme 1).[14,27,28] Alternatively, some of these ligands were prepared in small quantities by addition of aryllithium or aryl Grignard reagents to bis(dichlorophosphino)ferrocene (Scheme 1).[29]

Scheme 1. General Procedure for Ligand Synthesis



Scheme 2. Model Reactions Studied



2. Selection of Model Reactions and Methods for Analysis. We chose the amination reactions in Scheme 2 for our studies because these reactions produced mixed secondary amines in modest yields and would, therefore, reveal both beneficial and detrimental effects of ligand steric and electronic perturbations. The reaction between (4-bromobutyl)benzene and *n*-butylamine and the reaction between (4-bromobutyl)benzene and isobutylamine occurred in yields between 55% and 65% for the parent DPPF ligand. The reaction between 4-bromo-*N*,*N*-dimethylaniline and aniline occurred in 75% yield when the parent DPPF was used as ligand. Thus, these three reactions were used for our studies on how ligand properties affect aminations of aryl halides using both primary alkylamines and primary arylamines.

The reactions were conducted using a combination of 5 mol % Pd(dba)$_2$ and 2 equiv of the chelating ligand. However, similar results were obtained with two other catalyst precursors, Pd(OAc)$_2$ and Pd[P(*o*-tolyl)$_3$]$_2$. In addition to the major amination product, competing products were arene, resulting from dehydrohalogenation of the aryl halide, and diarylalkylamine (or triarylamine in the case of aminations involving aniline) resulting from diarylation of the primary amine. Reactions involving 4-bromo-*N*,*N*-dimethylaniline also showed products from aryl group exchange between the phosphine and aryl halide. The relative amounts of the reaction products were assessed by gas chromatography, correcting for response factors obtained from isolated materials. Arylamine products were also isolated in selected cases to ensure that the GC values accurately corresponded to product distributions in larger scale reactions.

3. Results from Varying Ligand Steric, Electronic, and Geometric Properties. 3.a. Effect of Steric Perturbations. The results in Tables 1 and 2 show the effect of varying the steric bulk of the phosphine ligands on reaction 1 in Scheme 2. A comparison of DPPF and the *o*-tolyl version DTPF showed that the amount of arene product increased by roughly 8-fold with this increase in ligand size. Similar comparisons of phenyl- and *o*-tolylphosphine ligands based on diaryl ether backbones

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Table 1. Steric Effects on Reaction 1 in Scheme 2 To Give BuC_6H_5 **1**, *p*-BuC_6H_4NHBu **2**, and (*p*-$BuC_6H_4)_2NBu$ **3**

ligand	% **1**[a]	% **2**[a]	% **3**[a]
DPPF	4.4 ± 0.2	52 ± 2.5 (46)	22 ±1.0
DTPF	34 ± 1.0	36 ± 2.0	5.8 ± 0.4
DPPDPE	40 ± 2.5	11 ± 1.5	3.6 ± 0.9
DTPDPE	46 ± 8.0	25 ± 5.0	2.0 ± 0.7
DPPX	24 ± 1.2	47 ± 3.0	7.0 ± 1.4
DTPX	22 ± 1.5	35 ± 4.0	7.6 ± 1.8

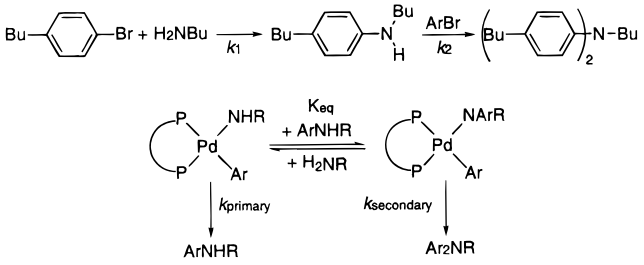
[a] Yields are based on the average of two or more runs. Yields in parentheses are isolated yields.

Table 2. Steric Effects on Aryl Migration for Reaction 2 in Scheme 2 To Give Me_2NPh **4**, $Me_2NC_6H_4NHPh$ **5**, and a Diarylamine

ligand	% **4**[a]	% **5**[a]	**5**:Ph_2NH[b]
DPPF	0 ± 0.2	69 ± 6.2 (75)	45 ± 14
DTPF	0.4 ± 0.4	78 ± 7.3	89 ± 9.6
DPPDPE[c])	0.4 ± 0.4	26 ± 6.1	21 ± 8.4
DTPDPE	1.7 ± 0.3	76 ± 5.9	150[d]
DPPX	0 ± 0.2	70 ± 1.1	4.9 ± 0.5
DTPX	0.5 ± 0.3	62 ± 4.1	3.9 ± 0.3

[a] Yields are based on the average of two or more runs. Yields in parentheses are isolated yields. [b] The migration product is a tolylphenylamine when *o*-tolylphosphine derivatives were used. [c] Reactions only went to 60% and 55% completion. [d] Diarylation product was less than the GC observation limits.

Scheme 3. Equilibrium and Rate Constants Involved in the Relative Rates for Mono- and Diarylation of Primary Amines



again showed no enhancement of the amine:arene ratio upon increasing the ligand steric properties, although the amine:arene ratio was not altered substantially in these cases.

Selectivity for arylation of the primary alkylamine over arylation of the alkylarylamine product must rely on the product's increased size and/or its decreased basicity. Equilibrium between the palladium amido complexes as well as the relative rates of reductive elimination for the primary and secondary amido complexes will determine the monoarylation vs diarylation products (Scheme 3). Steric effects are important, as ligand size was found to have a pronounced effect on the selectivity for the formation of monoarylamine product over diarylamine product (Tables 1 and 7). A comparison between DPPF and DTPF showed almost a 3-fold increase in the selectivity for formation of secondary alkylarylamine over tertiary diarylamine when DTPF was used as ligand along with 1.2 equiv of *n*-butylamine. Similar effects on selectivity were observed when diphenylphosphino- and di-*o*-tolylphosphino-substituted diphenyl ether ligands were employed.

In addition to evaluating ligand steric effects on the amination of electron neutral aryl bromides with primary alkylamines, we examined the impact of varying ligand steric properties on the amination of the electron rich aryl halide 4-bromo-*N*,*N*-dimethylaniline with aniline (reaction 2 in Scheme 2, Table 2). Electron rich aryl bromides often exchange with the aryl groups on the phosphine during catalytic and stoichiometric reactions

Table 3. Electronic Effects on Reactions 1 and 4 in Scheme 2 To Give BuC_6H_5 **1**, *p*-BuC_6H_4NHBu **2** or **6**, and (*p*-$BuC_6H_4)_2NBu$ **3** or **7**

ligand	amine	% **1**[a]	% **2** or **6**[a]	**2**:**3** or **6**:**7**[b]
p-MeODPPF	*n*-butyl	4.0 ± 0.6	55 ± 1.0	2.6 ± 0.1
p-MeODPPF	isobutyl	9.1 ± 0.8	68 ± 1.5	150[c]
DPPF	*n*-butyl	4.4 ± 0.2	52 ± 2.5 (46)	2.4 ± 0.1
DPPF	isobutyl	9.2 ± 1.5	69 ± 1.0 (42)	15 ± 1.8
p-CF_3DPPF	*n*-butyl	5.5 ± 0.5	53 ± 0.5	2.9 ± 0.1
p-CF_3DPPF	isobutyl	17 ± 1.5	49 ± 1.0	25 ± 8.1
3,5-CF_3DPPF	*n*-butyl	14 ± 2.5	49 ± 5.0	8.8 ± 0.2
DFPF	*n*-butyl	16 ± 1.5	40 ± 1.5	14 ± 3.0

[a] Yields are based on the average of two or more runs. Yields in parentheses are isolated yields. [b] Ratio of monoarylation to diarylation product. [c] Diarylation product was less than the GC observation limits.

by known aryl group exchange processes. Palladium-bound electron rich aryl groups are known to be particularly susceptible to these exchange processes.[30−32] In the case of the diphenylphosphino ligands, diphenylamine would be the diarylamine product resulting from rearrangement prior to amine formation. In the case of the di-*o*-tolylphosphino ligands, (*o*-tolylphenyl)-amine would be the product from rearrangement.

Consistent with previous data on palladium-catalyzed Heck reactions,[33] we found that an increase in steric bulk of the phosphine aryl group led to a significant reduction in the amount of amine product that results from prior aryl group migration in reactions catalyzed by complexes containing DPPF and DTPF. A similar effect of steric properties on aryl group rearrangements was observed for reactions catalyzed by DPPDPE and DTPDPE. However, no significant difference in the amount of rearrangement was observed for reactions catalyzed by the two types of ligands based on a xanthene backbone.

3.b. Effects of Perturbing Ligand Aryl Group Electronic Properties. The influence of phosphine aryl group electronic properties was evaluated by employing ligands that contained electron-donating and electron-withdrawing groups on the phosphine aromatic rings. As stated in the Introduction, one would expect that electron poor phosphines would accelerate the rate of reductive elimination and increase the amine:arene ratio. The effect of perturbing the phosphine aryl group electronic properties was small, but the observed effect contradicted our expectation that was based on conventional principles.

The reaction of *n*-butylamine with (4-bromobutyl)benzene was conducted with a combination of $Pd(dba)_2$ and several modified DPPF ligands. The results of experiments conducted with these modified ligands are provided in Table 3. Reactions conducted with the ligands 3,5-CF_3DPPF and DFPF, which would be less electron rich than DPPF, showed an increase in arene formation. Altering the phosphine-bound aromatic ring with a single substituent gave less substantial variation in the ratios of amination to reduction products. However, reactions involving *p*-CF_3-modified DPPF did give a slight increase in the amount of arene product relative to reactions with DPPF, while reactions conducted with the more electron rich *p*-MeO-modified DPPF ligand gave slightly decreased amounts of arene product.

The effect of reducing the phosphine aryl group electron density had a larger effect on the reactions of isobutylamine

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Table 4. Electronic Effects on Aryl Migration for Reaction 2 in Scheme 2 To Give Me_2NPh **4**, $Me_2NC_6H_4NHPh$ **5**, and a Diarylamine

ligand	% **4**[a]	% **5**[a]	**5**:ArPhNH[b]
p-MeODPPF	0.9 ± 0.9	71 ± 5.7	21 ± 6.5
DPPF	0 ± 0.2	69 ± 6.2 (75)	45 ± 14
p-CF_3DPPF	2.0 ± 1.0	74 ± 3.1	88[c]
3,5-CF_3DPPF	0 ± 0.2	67 ± 2.0	27 ± 4.0
DFPF	2.3 ± 0.4	65 ± 2.3	150[c]

[a] Yields are based on the average of two or more runs. Yields in parentheses are isolated yields. [b] Aryl group is that of the phosphine ligand. [c] These examples had at least one trial where the migration product was less than GC observation limits.

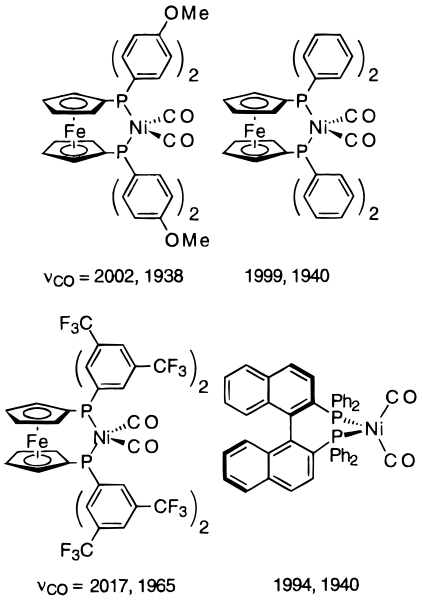

Figure 2. Changes in CO stretching frequency as a function of the phosphine aryl group and backbone.

(Table 3). For the reactions involving isobutylamine *p*-CF_3-DPPF gave a substantially increased amount of arene relative to the amount of arene in reactions involving DPPF and *p*-MeODPPF. This set of results from perturbing the aryl group electronic properties shows that electron poor ligands do not provide enhanced rates for reductive elimination relative to competing processes that form arene.

No trends were observed in monoarylation to diarylation selectivities as the electronics were perturbed. However, reactions involving the 3,5-CF_3DPPF ligand with butylamine or *p*-MeODPPF with isobutylamine did show significant differences relative to DPPF. Aryl exchange processes were affected by the electronic properties of the phosphine aryl group. During the coupling of the electron rich aryl bromide 4-bromo-*N*,*N*-dimethylaniline with aniline, reactions involving the electron poor and electron neutral DPPF derivatives gave less amine resulting from prior aryl group migration than did reactions involving the more electron rich *p*-MeODPPF (Table 4).

To understand the extent to which the CF_3 and OMe groups altered the electron density at the metal center and to determine potential electronic affects of changing the backbone from ferrocenyl to binaphthyl, we prepared carbonyl complexes containing the different ligands to evaluate changes in ν_{CO}. Figure 2 shows the ν_{CO} values for four Ni(0) complexes that were prepared by reaction of the modified DPPF ligands with $[Ni(CO)_2(PPh_3)_2]$. The electronic properties of monodentate ligands have been evaluated previously using IR data on $[Ni(CO)_3L]$ complexes.[34] Less change in ν_{CO} was observed for the DPPF ligands than might be expected on the basis of changes in ν_{CO} that resulted from variations in the aryl groups of monodentate triarylphosphine ligands. For comparison, previous changes in para substituents from Ph to *p*-$CF_3C_6H_4$[35] or from Ph to *p*-$MeOC_6H_4$[36] on Vaska's complex $[Ir(PPh_3)_2(CO)Cl]$, which contains two phosphine ligands, led to changes in ν_{CO} of roughly 10 wavenumbers. Further, these changes led to differences in oxidative addition reaction rates that varied by 2−3 orders of magnitude for MeI addition and an order of magnitude for H_2 addition.[35]

Table 5. Effect of the Bite Angle on Reaction 1 in Scheme 2 To Give BuC_6H_5 **1**, *p*-BuC_6H_4NHBu **2**, and $(p\text{-}BuC_6H_4)_2NBu$ **3**

ligand	bite angle (deg)	% **1**[a]	% **2**[a]	% **3**[a]
DPPN	82[b]	1.4 ± 1.0	78 ± 3.8	5.7 ± 0.7
BINAP	92.7,[c] 85[b]	0.9 ± 0.2	91 ± 2.0 (75)	3.0 ± 0.3
DPPF	99.0[c]	4.4 ± 0.2	52 ± 2.5 (46)	22 ± 1.0
DPPR	101[c]	36 ± 2.0	12 ± 1.0	5.2 ± 3.4
DPPDPE	101[b]	40 ± 2.5	11 ± 1.0	3.6 ± 0.9
DPPX	109[b]	24 ± 1.8	47 ± 3.0	7.0 ± 1.4

[a] Yields are based on the average of two or more runs. Yields in parentheses are averaged isolated yields. [b] Calculated values for the natural bite angle; see refs 15 and 38. [c] Values from crystallographic structure determination of the palladium dichloride complexes; see refs 22 and 39−41.

Our data for the DPPF ligands show that substantial changes in electron density can be detected by ν_{CO} for the di-CF_3 ligand, but only small changes were observed for the OMe-substituted ligand. Thus, these ligands perturb the electron density at the metal much less than do analogous monodentate ligands, and the resulting differences in selectivity will, therefore, be subtle. These data also demonstrate that the electronic donating abilities of BINAP and DPPF are more similar than one might expect, and that differences in selectivity between DPPF and BINAP most likely arise from structural, rather than electronic, differences.

3.c. Effect of Altering the Ligand Bite Angle. As noted in the Introduction, reductive elimination rates are typically accelerated by increased bite angle. In contrast to this established trend, the yields of arylamine were generally higher for reactions involving ligands with small bite angles (Table 5). The xanthene-based ligand gave more amination product than DPPR or the diphenyl ether based-ligand DPPDPE, but this difference is more likely to originate in the preorganized structure of this ligand relative to the flexible DPPDPE. A correlation between ligand bite angles and the amount of reduction product clearly showed that reducing the size of the bite angle led to decreasing amounts of reduction products, particularly for preorganized bidentate ligands such as BINAP and the naphthalene-based ligand DPPN.[37−41]

Reducing the size of the bite angle also led to increased selectivity for monoarylation over diarylation products. For the

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Table 6. Product Ratios for Diarylation Reaction 3 in Scheme 2 To Give BuC_6H_5 **1**, *p*-BuC_6H_4NHBu **2**, and (*p*-$BuC_6H_4)_2NBu$ **3**

ligand	% **1**[a]	% **2**[a]	% **3**[a]
DPPN	3.3 ± 0.1	4.3 ± 0.4	49 ± 0.6
BINAP	17 ± 4.0	8.7 ± 1.3	39 ± 11
DPPF	3.9 ± 0.8	3.1 ± 1.0	106 ± 8.0 (85)
DTPF	27 ± 1.0	17 ± 1.0	24 ± 4.0
DPPDPE	38 ± 1.0	2.1 ± 2.1	7.5 ± 3.6
DPPX	15 ± 1.5	5.4 ± 0.8	63 ± 11
p-MeODPPF	3.7 ± 2.3	5.0 ± 0.6	97 ± 8.5
p-CF_3DPPF	3.8 ± 0.5	1.9 ± 1.9	106 ± 15

[a] Yields are based on the average of two or more runs. Yields in parentheses are isolated yields.

Table 7. Effect of Amine Sterics: Product Ratios for Reaction 4 of Scheme 2 To Give BuC_6H_5 **1**, *p*-BuC_6H_4NH-*i*-Bu **6**, (*p*-$BuC_6H_4)_2$-N*i*-Bu **7**

ligand	% **1**[a]	% **6**[a]	**6** : **7**[a]
DPPN	1.5 ± 0.2	83 ± 0.9	48 ± 14
BINAP	1.0 ± 0.2	91 ± 0.5	150[b]
DPPF	9.2 ± 1.5	69 ± 1.0 (42)	15 ± 1.8
DTPF	34 ± 0.3	39 ± 1.0	80[b]
DPPDPE	46 ± 0.9	6.5 ± 0.6	2.8 ± 0.3
DPPX	33 ± 0.4	40 ± 0.5	9.8 ± 1.7

[a] Yields are based on the average of two or more runs. Yields in parentheses are isolated yields. [b] These examples had at least one trial where the diarylation product was less than the GC observation limits.

aminations involving *n*-butylamine, the ratio of monoarylation to diarylation product was highest for BINAP and DPPN. As this result would predict, ligands with large bite angles such as DPPF were superior for the one-pot formation of diarylated amine by reaction of *n*-butylamine with 2 equiv of aryl bromide (reaction 3 in Scheme 2, Table 6). It appears that DPPF has a large enough bite angle to accommodate the formation of tertiary amine. Yet, the reaction does not suffer from producing large amounts of reduction product as has been observed with the ligands that possess larger bite angles.

For the reaction of aniline with 4-bromo-*N*,*N*-dimethylaniline, no trend was observed between the bite angle and the amount of product resulting from aryl migration.

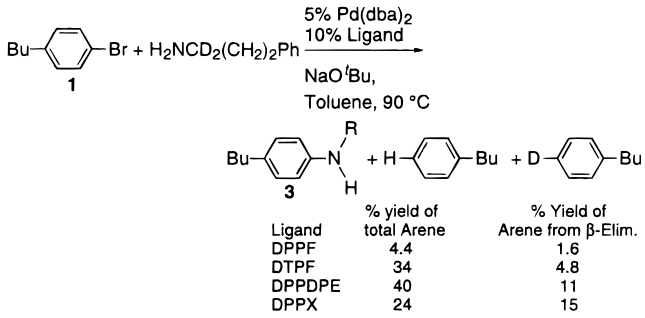
4. Effect of Substrate Steric Properties. It was not clear whether increasing the size of the amine would hinder formation of the geometry required for β-hydrogen elimination while accelerating the reductive elimination process, as was seen for reactions involving P(*o*-tolyl)$_3$,[42] or whether increased size of the amide would facilitate β-hydrogen elimination. In fact, the opposite effect of that detected previously for P(*o*-tolyl)$_3$ was observed with the catalysts containing chelating phosphines. A modest increase in the size of the amine led to an increase in the amount of arene, rather than arylamine, product.

Reactions with isobutylamine (reaction 4 in Scheme 2 and Table 7) catalyzed by Pd−DPPF gave a 2-fold increase in the amount of arene product relative to analogous reactions with *n*-butylamine. A larger increase in arene product was observed when DTPF was used as ligand. Perhaps more predictably, increasing the size of the amine substrate led to substantial improvement in the ratio of monoarylation to diarylation products for reactions involving both DPPF and DTPF. In fact, only trace amounts of diarylation product were ever observed in runs involving DTPF.

In contrast to increased amounts of arene that accompanied increasing size of the amine, substantially decreased amounts of arene were observed from reactions involving more hindered

(42) Hartwig, J. F.; Richards, S.; Barañano, D.; Paul, F. *J. Am. Chem. Soc.* **1996**, *118*, 3626−3633.

Scheme 4. Amount of Arene Formed from β-Hydrogen Elimination vs Arene from Competing Reactions



aryl halides. The reaction of 2-bromotoluene with *n*-butylamine gave the monoarylation product in 99% yield for BINAP, 96% yield for DPPF, 77% yield for DTPF, 50% yield for DPPDPE, 89% yield for DPPX, and 96% yield (±1.0%) for *p*-MeODPPF by GC. The product was isolated in 92% yield using DPPF. These yields are substantially increased over those for reactions of *n*-butylamine with (4-bromobutyl)benzene. No diarylation products were seen in any of these reactions.

5. Labeling Experiments. The unexpected effects of ligand properties on amine:arene ratios led us to evaluate whether the arene was actually formed from competing β-hydride elimination. Amination reactions between (1,1-dideuterio-3-phenylpropyl)amine and (4-bromobutyl)benzene were, therefore, conducted (Scheme 4). Butylbenzene formed from these reactions was then analyzed by mass spectrometry to determine the percent deuterium incorporation. The reactions were carried out under the same conditions as the coupling for butylamine with (4-bromobutyl)benzene. The reaction of (1,1-dideuterio-3-phenylpropyl)amine with (4-bromobutyl)benzene was conducted using 10 mol % DPPF, DTPF, DPPDPE, and DPPX with 5 mol % Pd(dba)$_2$ or Pd[P(*o*-tolyl)$_3$]$_2$. Results from GC/MS for reactions using Pd(dba)$_2$ as precursor showed only 37% deuterium incorporation into the arene for reactions involving DPPF, 14% for those involving DTPF, 27% for those with DPPDPE, and 64% for those with DPPX. These numbers increased slightly to 49%, 22%, 52%, and 73%, respectively, when Pd[P(*o*-tolyl)$_3$]$_2$ was used as the catalyst precursor (errors estimated at ±5.0%). Little or no hydrodehalogenation product occurred from chemistry involving the amine N−H position. Reaction of *N*,*N*-dideuterio-(3-phenylpropyl)amine and (4-bromobutyl)benzene catalyzed by Pd(dba)$_2$ and any of the four ligands showed little or no deuterated arene. Reactions conducted with protiated substrates in toluene-d_8 solvent also showed no deuterium incorporation.

Because the imines that would be produced in reactions involving primary alkylamines are unstable, it is difficult to assess the mass balance of aminations using these substrates. Further, we were concerned that a simple β-hydrogen elimination and subsequent reductive elimination would appear to be more complex because proton-transfer processes involving a palladium hydride intermediate may occur and reduce the percent deuterium incorporation. Thus, we conducted reactions with HNPh(CD$_2$Ph) that would produce a stable imine. In this case we observed an amount of deuterated arene that matched the amount of imine within experimental error. This result demonstrates that deuterium is not being lost by proton transfers involving a hydride intermediate. However, a substantial amount of undeuterated arene was again observed, and there was not enough imine byproduct to account for this arene. Thus, there are pathways other than β-hydrogen elimination and reductive elimination of arene that lead to dehydrohalogenation

of the aryl halide, and these pathways are most important with substrates containing unactivated hydrogens α to the nitrogen. The source of the proton in the arene product is not clear, but it is evident that much of the arene is formed by a process more complex than expected.

Discussion

At the outset of this study, our expectation and that of others[43] based on knowledge of the relationship between the properties of a metal complex and rates for reductive elimination and β-hydrogen elimination was an enhancement in the amount of amination product vs reduction product with sterically hindered and electron poor bidentate phosphine ligands. The experimental results of this study have shown the logic behind this prediction to be flawed at two levels. First, the majority of the arene in reactions of DPPF and DTPF is not formed by β-hydrogen elimination. Second, the amount of arene that *is* formed from β-hydrogen elimination increases with increasing size of the bidentate phosphine ligand and with increasing size of the bite angle. A modest increase in arene is formed by catalysts with the more weakly donating ligands. Thus, the effect of ligand properties on the amount of arene formed by β-hydrogen elimination is the opposite of the simple effects one would expect from previous studies on the chemistry of alkyl groups. The details of the steric, electronic, and bite angle properties and their effects on the reaction selectivities are discussed in the subsequent sections.

Effects of Perturbing Ligand Aryl Group Steric Properties. Increased steric bulk in either the ligands or the amine substrates caused an increase in the amount of reduction product. First, an increase in size of the rigid, bidentate phosphine ligand DPPF created by incorporating *o*-tolyl groups led to a dramatic increase in the amount of arene formed by reactions other than β-hydrogen elimination. Second, the amount of arene formed by β-hydrogen elimination increased rather than decreased, albeit less dramatically.

Apparently the steric properties of the ligand had two effects on the catalyst selectivity. First, increased steric effects accelerated a dehydrohalogenation process that competes with the amination and more standard dehydrohalogenation by β-hydrogen elimination. Second, the increasing size of the ligand had a greater effect on the rate of β-hydrogen elimination than on the rate of reductive elimination. The second result may occur because of partial dissociation of the bidentate phosphine, providing a three-coordinate palladium amide aryl complex that can readily undergo β-elimination. The steric effects are not simple, however, since reactions of the sterically hindered substrate 2-bromotoluene catalyzed by unmodified DPPF gave little reduction. One might expect the increased steric bulk of the palladium-bound aryl group to also favor formation of a three-coordinate palladium species.

Increasing the size of the phosphine ligands gave better monoarylation to diarylation selectivities. This effect is more simple to rationalize. Clearly, reaction of a sterically hindered complex with the larger secondary alkylarylamines is less favorable than reaction with the corresponding primary amine. These results also suggest that the higher reactivity of the primary amines in the amination process is largely due to steric effects.

Aryl group migration was also reduced when DTPF or DTPDPE was employed instead of DPPF or DPPDPE, respectively. Steric effects on aryl group exchange reactions were noted many years ago by Heck.[33] These aryl exchanges have been studied more thoroughly recently.[30−32]

Effects of Perturbing Ligand Aryl Group Electronic Properties. In contrast to the expectations that ligand electronic properties would effect the selectivity of the amination reactions by accelerating reductive elimination, little effect was observed. Further, the small trend that was observed was in the opposite direction of what one would expect. The small difference in selectivity resulting from variation of the aryl group electronic properties is explained by a weak transmission of the aryl group electronic properties to the metal center. The small differences in ν_{CO} values for the $L_2Ni(CO)_2$ complexes suggest that the metal center's electronic properties are less affected by variation in the chelating ligand aryl groups than they are by monodentate triarylphosphine ligands. Although we cannot explain precisely the unexpected observation that decreasing electron density at the metal center increases the amount of arene, the labeling study shows that most of the arene does not arise from β-hydrogen elimination. It should not be surprising, therefore, that the observed trends deviate from those predicted by trends in reaction rates for reductive elimination and β-hydrogen elimination. In fact, the dehydrohalogenation may occur during the aryl halide addition step or during formation of the palladium amido complex, rather than after the palladium amide is generated.

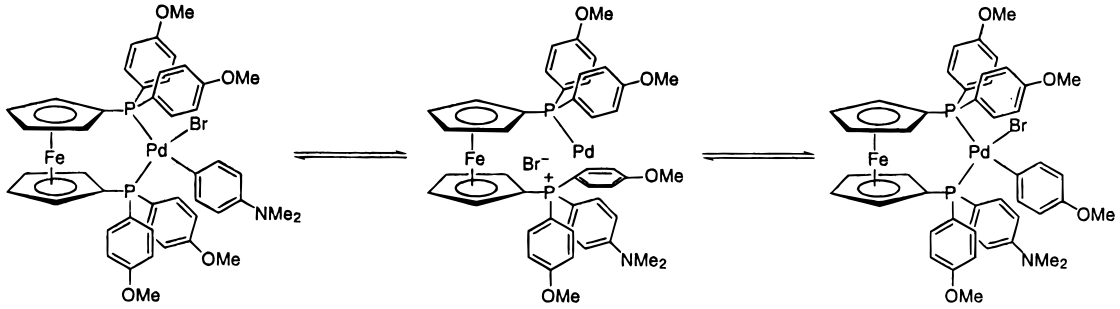
The basicity of the phosphine ligands also did not have a pronounced influence on the monoarylation to diarylation selectivities of primary amines. This result is consistent with the conclusion drawn above that steric effects are the dominant factor that control mono- vs diarylation of primary amines.

The phosphine electronic properties did have significant influence on the degree of aryl migration observed during the coupling of the electron rich aryl bromide 4-bromo-*N*,*N*-dimethylaniline with aniline (Scheme 2). Strongly electron donating phosphines gave larger amounts of rearranged product than did less donating ligands (Table 4). The equilibrium constant in these aryl exchange processes favors the placement of more electron rich aryl groups onto the phosphorus and the more electron poor aryl groups on the metal, but the exchange is more facile when electron rich aryl groups are on the starting phosphines.[30−32] It has been proposed that electron poor phosphines undergo reductive elimination with the aryl group to form phosphonium salts less readily than electron rich phosphines (Scheme 5),[31] making the aryl exchange process slower for electron poor phosphines compared to electron rich phosphines.

Effects of Altering the Ligand Bite Angle. Increasing ligand bite angle gave decreased ratios of amine to arene products, exactly the opposite result that would be expected considering the known effects of the bite angle on reductive elimination rates. This result can be explained by two factors. Again, much of the arene does not result from competing β-hydrogen elimination and reductive elimination, and so electronic effects on the rates for reaction of the amido complexes may not be important. Instead, electronic effects on the oxidative addition of aryl halide or formation of the amido complexes are likely to be more important. Second, the phosphines that provide larger bite angles can partially dissociate more readily than those with bite angles near 90°, generating three-coordinate intermediates that can undergo β-hydrogen elimination. Since a greater proportion of the arene results from β-hydrogen elimination during reactions involving phosphines that provide large bite angles than those involving phosphines that create small bite angles, it is likely that partial phosphine

(43) Marcoux, J.-F.; Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1568−1569.

Scheme 5. Previously Proposed Pathway for Aryl Group Exchange



dissociation does occur with these ligands. Thus, the increase in rates for β-hydrogen elimination and competing dehydrohalogenation processes is greater than the increase in rate for reductive elimination as a result of increasing the ligand bite angle.

Surprisingly, the monoarylation to diarylation selectivities were highest for ligands with small bite angles. We do not have a firm explanation for this result. However, this empirical observation may be useful for future ligand development. Further, this effect is useful in selecting a ligand for diarylation of primary amines.[44] Because the ligands that generate small bite angles are selective for monoarylation, they give lower yields for diarylations than do the ligands that create medium-sized bite angles. The ligands with larger bite angles (>95°) seem to accommodate more readily the secondary arylamine substrates than do those with smaller bite angles, but too large a bite angle leads to an increase in the amount of arene. Thus, $Pd(dba)_2$/DPPF is a good compromise in ligand properties for diarylation of primary amines.

There was a poor correlation between bite angle and the amount of observed rearrangement product for reaction of the electron rich arene 4-bromo-*N*,*N*-dimethylaniline with aniline. However, it was clear that BINAP, typically a ligand that gives clean reaction products, was one of the worst ligands of those tested and gave many different side products in addition to diphenylamine formed after aryl group exchange.

In many cases, an alteration of the ligand bite angle requires a change in the structure of the ligand backbone, which may lead to potential electronic perturbations. The use of nickel(0) dicarbonyl complexes to determine the electronic differences between binaphthyl and ferrocene as backbone in an admittedly crude fashion showed that the backbone did not substantially change the metal electronic properties. The two ν_{CO} values for the nickel complexes containing DPPF and BINAP varied by 5 and 0 cm^{-1}, while the ν_{CO} values varied by 15 and 27 cm^{-1} when the aryl substituent was varied from *p*-$MeOC_6H_4$ to 3,5-$CF_3C_6H_3$. Thus, the influence of changing the ligand backbone from binaphthyl to ferrocene on the metal electronic properties appeared to be minimal.

Effects of Substrate Steric Properties. Monoarylation to diarylation selectivities are higher for branched, primary aliphatic amine substrates. A small change in the amine steric properties, *n*-butylamine versus isobutylamine, produced an approximately 6-fold increase in monoarylation to diarylation selectivity for reactions conducted with a combination of $Pd(dba)_2$ and DPPF. Of course, the use of excess amine also led to improved product ratios. Reaction of 12 equiv of *n*-butylamine with (4-bromobutyl)benzene gave a monoaryl:diaryl product ratio that improved by a factor of 9, and gave the monoarylamine in 67% yield as determined by GC analysis.

Ortho substituents on the aryl bromide gave a large increase in yields mostly because diarylation is inhibited, but also because aryl halide reduction is minimized. For reactions catalyzed by a combination of $Pd(dba)_2$ and DPPF, the yield of monoarylated amine from reaction with *o*-methylbromobenzene was high. Although the reduced product toluene could not be detected by GC techniques, the high yield requires that little reduction occurred.

Experimental Section

Unless otherwise specified, all reagents were purchased from commercial suppliers and used without further purification. THF and toluene were distilled from sodium−benzophenone ketyl under nitrogen. The following phosphine ligands were prepared according to literature procedures: DPPR,[45] DPPDPE,[46] DPPX,[27,46] *p*-MeO-DPPF,[47,48] *p*-CF_3-DPPF,[14] DPPN.[49,50]

Reactions were set up in an inert atmosphere glovebox. Amines were added by syringe without degassing. ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were obtained on a GE QE 300 MHz, GE Ω 300 MHz, or Brucker AM500 MHz Fourier transform spectrometer. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded relative to residual protiated solvent; a positive value of the chemical shift denotes a resonance downfield from TMS. $^{31}P\{^1H\}$ NMR spectra were recorded relative to 85% H_3PO_4; a positive value of the chemical shift denotes a resonance downfield from H_3PO_4. Samples for elemental analysis were submitted to Robertson Microlit Labs, Inc., Madison, NJ 07940. Samples for mass spectrum analysis were submitted to The University of Illinois at Champaign-Urbana, School of Chemical Sciences. GC analyses were conducted on a Hewlett-Packard 5890 instrument connected to a 3395 integrator.

1,1′-Bis[bis(2-methylphenyl)phosphino]ferrocene.[28,51] Ferrocene (2.280 g, 12.26 mmol) was mixed with 2.1 equiv of *n*-butyllithium (2.66 M in hexanes, 9.68 mL, 25.74 mmol), 2.1 equiv of TMEDA (3.88 mL, 25.74 mmol), and hexane (50 mL) in an oven-dried flask fitted with a condenser, an addition funnel, and a N_2 inlet. The reaction was heated to reflux for 5 h before being cooled to −40 °C. A solution of bis(2-methylphenyl)chlorophosphine[52] (6.400 g, 25.73 mmol) in THF (15 mL) was added dropwise to the reaction over 10 min. The reaction

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was allowed to warm slowly to room temperature and stir for 12 h. The crude reaction was concentrated to approximately 20% of its original volume, and the yellow solids were filtered. The solids were then washed with 1 M HCl (20 mL), H_2O (20 mL), ethanol (20 mL), and ether (20 mL). The solids were dried under vacuum to give 6.214 g of product in 83% yield. ^{1}H NMR: ($CDCl_3$) δ 7.17−6.96 (m, 16H), 4.25 (br s, 4H), 4.06 (br s, 4H), 2.46 (s, 12H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 141.64 (d, J = 26.3 Hz), 137.51 (d, J = 10.6 Hz), 133.29, 129.41 (d, J = 5.1 Hz), 128.4, 125.50, 76.52, 74.15 (d, J = 15.1 Hz), 72.13 (d, J = 3.0 Hz), 21.29 (d, J = 21.6 Hz). ^{31}P{^{1}H} NMR: ($CDCl_3$) δ −36.81. Anal. Calcd for $C_{38}H_{36}FeP_2$: C, 74.76; H, 5.94. Found: C, 74.31; H, 6.08.

1,1′-Bis[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferrocene.[47] To an oven-dried flask fitted with a N_2 inlet were added 8 equiv of 3,5-bis(trifluoromethyl)iodobenzene (2.00 mL, 11.28 mmol) and 6.0 equiv of TMEDA (1.28 mL, 8.47 mmol) in THF (15 mL). The solution was cooled to −78 °C, and 6.0 equiv of *n*-butyllithium (2.5 M in hexanes, 3.38 mL, 8.47 mmol) was added dropwise over 5 min. The reaction was stirred for 2 h at −78 °C (***WARNING***: the reaction may explode if allowed to warm). A solution of 1,1′-bis(dichlorophosphino)ferrocene[29] (0.547 g, 1.411 mmol) in THF (5 mL) was added dropwise to the reaction over 10 min. The reaction was stirred at −78 °C for 30 min and then allowed to warm slowly to room temperature, and stirring was continued for 12 h. Methanol (1 mL) was added to the reaction; it was then concentrated in vacuo. The black residue was filtered through Celite using 5% ethyl acetate in hexane as the eluent. The orange filtrate was concentrated to give the crude product. Purified product, 0.741 g, was obtained as a yellow powder in 48% yield by crystallization from hexanes. ^{1}H NMR: ($CDCl_3$) δ 7.89 (s, 4H), 7.69 (d, J = 6.3 Hz, 8H), 4.44 (dd, J = 1.6, 1.7 Hz, 4H), 4.01 (m, 4H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 140.31 (d, J = 17.5 Hz), 132.82 (d, J = 21.8 Hz), 132.07 (dq, J = 6.2, 33.3 Hz), 123.43 (d, J = 4.0 Hz), 122.93 (q, J = 273.2 Hz), 73.81, 73.57 (d, J = 15.6 Hz), 73.26 (br s). ^{31}P-{^{1}H} NMR: ($CDCl_3$) δ −14.99. Anal. Calcd for $C_{42}H_{20}F_{24}FeP_2$: C, 45.93; H, 1.84. Found: C, 46.24; H, 1.90.

1,1′-Bis[di-2-furylphosphino]ferrocene. Using literature procedures[53] 6.0 equiv of 2-lithiofuran was prepared in THF (10 mL) and cooled to −78 °C. A solution of 1,1′-bis(dichlorophosphino)ferrocene[29] (0.200 g, 0.516 mmol) in THF (5 mL) was added dropwise to the reaction over 10 min. The reaction was stirred for 90 min at −78 °C and allowed to warm to room temperature and stir for an additional 12 h. The reaction was then concentrated in vacuo and dissolved in ether (100 mL). The ether solution was washed with H_2O (30 mL, 3×) followed by brine. The ether solution was then dried with Na_2SO_4, filtered, and concentrated. The product was purified first by flash chromatography through a short layer of silica using CH_2Cl_2 as the eluent followed by crystallization from cyclohexane. The product, 0.224 g, was obtained as orange needles in 84% yield. ^{1}H NMR: ($CDCl_3$) δ 7.63 (d, J = 0.9 Hz, 4H), 6.67 (dd, J = 2.5, 1.9 Hz, 4H), 6.39 (m, 4H), 4.32 (dd, J = 1.6, 1.8 Hz, 4H), 4.17 (dd, J = 1.5, 1.8 Hz, 4H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 152.05 (d, J = 8.6 Hz), 146.63, 119.79 (d, J = 24.5 Hz), 110.46, 74.41 (d, J = 17.8 Hz), 73.31, 72.20 (d, J = 3.7 Hz). ^{31}P{^{1}H} NMR: ($CDCl_3$) δ −64.92. Anal. Calcd for $C_{26}H_{20}FeO_4P_2$: C, 60.73; H, 3.92. Found: C, 60.47; H, 3.89.

Bis[2-[bis(2-methylphenyl)phosphino]phenyl] Ether.[46] Diphenyl ether (1.75 mL, 9.58 mmol), 2.2 equiv of *n*-butyllithium (2.66 M in hexanes, 7.9 mL, 21.08 mmol), and 2.2 equiv of TMEDA (3.18 mL, 21.08 mmol) were stirred in THF (10 mL) under N_2 at room temperature for 16 h (see ref 27 for an improved lithiation procedure). The reaction was quenched with a solution of bis(2-methylphenyl)chlorophosphine[51] (5.242 g, 21.08 mmol) in THF (5 mL) over 15 min. H_2O and ether were added to the reaction, and the layers were separated. The ether layer was dried with Na_2SO_4 and concentrated in vacuo. The residue was heated in boiling ethanol. Not all of the DTPDPE product dissolved in the ethanol, but the impurities were soluble. The mixture was then cooled to 0 °C, and the resulting solids were collected by filtration and washed with ethanol. The solids were dried under vacuum to give 2.682 g of product in 47% yield. ^{1}H NMR: ($CDCl_3$) δ 7.27−7.11 (m, 10H), 7.04 (t, J = 7.5 Hz, 4H), 6.97 (t, J = 7.4 Hz, 2H), 6.79−6.71 (m, 8H), 2.28 (s, 12 H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 159.69 (d, J = 18.5 Hz), 142.30 (d, J = 27.4 Hz), 134.61 (d, J = 13.0 Hz), 134.17, 133.01, 130.08, 129.80 (d, J = 3.3 Hz), 128.32, 127.41 (d, J = 15.3 Hz), 125.79, 123.58, 118.01, 21.17 (d, J = 23.2 Hz). ^{31}P{^{1}H} NMR: ($CDCl_3$) δ −32.62. Anal. Calcd for $C_{40}H_{36}OP_2$: C, 80.79; H, 6.10. Found: C, 80.52; H, 5.98.

9,9-Dimethyl-4,5-bis[bis(2-methylphenyl)phosphino]xanthene.[27] 9,9-Dimethylxanthene (0.363 g, 1.726 mmol), 2.5 equiv of *n*-butyllithium (2.5 M in hexanes, 1.73 mL, 4.32 mmol), and 2.5 equiv of TMEDA (0.651 mL, 4.32 mmol) were dissolved in heptane (10 mL) under N_2 and heated to reflux for 20 min. The reaction was then cooled to 0 °C and quenched with a solution of bis(2-methylphenyl)-chlorophosphine[52] (0.816 g, 5.178 mmol) in THF (5 mL) over 10 min. The reaction was then allowed to stir at room temperature for 12 h. The reaction was diluted with ethyl acetate and washed with H_2O (2×). The organic layer was then dried with Na_2SO_4 and concentrated in vacuo. The product was purified first by flash chromatography through a short layer of silica using 30% ethyl acetate in hexanes as the eluent. The partially purified solids were washed with hexanes to give 0.425 g of purified product in 39% yield. ^{1}H NMR: ($CDCl_3$) δ 7.45 (dd, J = 0.9, 7.8 Hz, 2H), 7.21−7.14 (m, 8H), 7.02−6.94 (m, 6H), 6.71 (d, J = 7.7 Hz, 4H), 6.51 (dd, J = 1.3, 7.5 Hz, 2H), 2.29 (s, 12H), 1.71 (s, 6H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 152.90 (apparent t, J = 9.7 Hz), 142.45 (apparent t, J = 13.5 Hz), 135.62 (apparent t, J = 7.2 Hz), 132.62, 132.38, 129.72 (d, J = 1.9 Hz), 128.09, 126.26, 125.69, 124.29 (d, J = 8.5 Hz), 124.15 (d, J = 9.1 Hz), 123.37, 34.47, 31.84, 21.25 (apparent t, J = 11.5 Hz). ^{31}P{^{1}H} NMR: ($CDCl_3$) δ −31.93. Anal. Calcd for $C_{43}H_{40}OP_2$: C, 81.37; H, 6.35. Found: C, 81.03; H, 6.27.

Dicarbonyl[bis(diphenylphosphino)ferrocene]nickel(0):[54] Bis-(triphenylphosphine)dicarbonylnickel(0) (64.5 mg, 0.101 mmol) was mixed with 1 equiv of 1,1′-(diphenylphosphino)ferrocene (55.9 mg, 0.101 mmol) in 10 mL of THF solvent. After 4 h the reaction was filtered through Celite and concentrated under vacuum to yield a yellow oil. Ether (10 mL) was added to the oil, and a precipitate formed. The yellow solids were filtered, washed with ether, and dried under vacuum to give 53.9 mg of product in 79.9% yield. ^{1}H NMR: (C_6D_6) δ 7.81 (m, 8H), 7.03 (m, 12H), 4.16 (dt, J = 1.8, 1.8 Hz, 4H), 3.86 (t, J = 1.8 Hz, 4H). ^{31}P{^{1}H} NMR: (C_6D_6) δ 25.91. IR (KBr, cm^{-1}): 1999 (s), 1940 (s).

Dicarbonyl[bis[bis(4-methoxyphenyl)phosphino]ferrocene]nickel-(0). Bis(triphenylphosphine)dicarbonylnickel(0) (73.3 mg, 0.115 mmol) was mixed with 1 equiv of 1,1′-bis[bis(4-methoxyphenyl)phosphino]-ferrocene (77.3 mg, 0.115 mmol) in 10 mL of THF solvent. After 18 h the reaction was diluted with 10 mL of pentane, and a precipitate formed. The yellow solids were filtered, washed with ether, and dried under vacuum to give 83.2 mg of product in 91.9% yield. ^{1}H NMR: (C_6D_6) δ 7.82 (t, J = 8.7 Hz, 8H), 6.69 (d, J = 8.3 Hz, 8H), 4.27 (br s, 4H), 3.95 (br s, 4H), 3.19 (s, 12H). ^{31}P{^{1}H} NMR: (C_6D_6) δ 22.29. IR (KBr, cm^{-1}): 2002 (s), 1938 (s). Anal. Calcd for $C_{40}H_{36}$-$FeNiP_2O_6$: C, 60.88; H, 4.60. Found: C, 60.88; H, 4.65.

Dicarbonyl[1,1′-Bis[bis(3,5-bis(trifluoromethyl)phenyl)phosphino]-ferrocene]nickel(0). Bis(triphenylphosphine)dicarbonylnickel(0) (79.9 mg, 0.125 mmol) was mixed with 1 equiv of 1,1′-bis[bis(3,5-bis-(trifluoromethyl)phenyl)phosphino]ferrocene (137 mg, 0.125 mmol) in 10 mL of THF solvent. After 48 h the reaction was concentrated under vacuum to give a yellow oil. The product was purified via column chromatography using 2% ethyl acetate in hexanes as the eluent to give 61.4 mg of purified product in 40% yield. This complex slowly underwent disproportionation that yielded bis{1,1′-bis[bis(3,5-bis-(trifluoromethyl)phenyl)phosphino]ferrocene}nickel(0), which prevented our obtaining satisfactory elemental analysis data. ^{1}H NMR: (C_6D_6) δ 8.21 (d, J = 9.4 Hz, 8H), 7.64 (s, 4H), 3.89 (dt, J = 1.8, 1.8 Hz, 4H), 3.71 (br s, 4H). ^{31}P{^{1}H} NMR: (C_6D_6) δ 29.25. IR (KBr, cm^{-1}): 2017 (s), 1965 (s).

Dicarbonyl[2,2′-bis(diphenylphosphino)-1,1′-binaphthyl nickel-(0). Bis(triphenylphosphine)dicarbonylnickel(0) (112 mg, 0.176 mmol) was mixed with 1 equiv of 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl

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(109 mg, 0.176 mmol) in 10 mL of THF solvent. After 24 h the yellow solid was filtered, washed with THF, and dried under vacuum to give 74.2 mg of product in 58% yield. ^{1}H NMR: (THF-d_6) δ 8.04 (m, 4H), 7.51−7.20 (m, 18H), 7.00 (t, J = 8.4 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 6.54 (t, J = 7.1 Hz, 2H), 6.45 (t, J = 7.1 Hz, 4H). ^{31}P{^{1}H} NMR: (THF-d_6) δ 34.36; IR (KBr, cm^{-1}): 1994 (s), 1940 (s).

***N*-Butyl-2-methylaniline.**[55,56] A reaction vial was charged with 2-bromotoluene (0.267 g, 1.57 mmol), 1.2 equiv of NaO^{t}Bu (0.181 g, 1.88 mmol), 0.05 equiv of Pd(DBA)$_2$ (0.045 g, 0.078 mmol), 0.10 equiv of DPPF (0.087 g, 0.157 mmol), and 8 mL of toluene under a N_2 atmosphere in a drybox. The reaction was capped using a PTFE septum and removed from the drybox. Butylamine (155 μL, 1.88 mmol) was added via syringe and the reaction heated to 90 °C for 6 h. The reaction was cooled to room temperature and filtered through Celite, and the Celite was washed with ether (20 mL, 3×). Aqueous HCl (20 mL, 1 M) was added to the filtrate and the mixture stirred. An orange precipitate formed. Both layers were filtered together and then separated. The organic layer was washed with 1 M HCl (10 mL) followed by H_2O (10 mL). The three aqueous washings were combined and made basic with $NaHCO_3$. This basic solution was washed with hexane (20 mL, 3×). The hexane solutions were combined, dried over Na_2SO_4, and concentrated in vacuo to give 0.239 g of purified product in 94% yield. ^{1}H NMR: ($CDCl_3$) δ 7.14 (dd, J = 8.0, 7.5 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 6.60−6.70 (m, 2H), 3.44 (br s, 1H), 3.18 (t, J = 7.1 Hz, 2H), 2.15 (s, 3H), 1.68 (m, 2H), 1.48 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 146.36, 129.94, 127.08, 121.60, 116.55, 109.54, 43.59, 31.69, 20.34, 17.40, 13.90.

***N*-Butyl-4-butylaniline.**[57] A reaction vial was charged with (4-bromobutyl)benzene (0.140 g, 0.657 mmol), 1.2 equiv of NaO^{t}Bu (0.0758 g, 0.789 mmol), 0.05 equiv of Pd(DBA)$_2$ (0.0189 g, 0.0328 mmol), 0.10 equiv of DPPF (0.0360 g, 0.0657 mmol), and 8 mL of toluene under a N_2 atmosphere in a drybox. The reaction was capped using a PTFE septum and removed from the drybox. Butylamine (78.2 μL, 0.789 mmol) was added via syringe and the reaction heated to 90 °C for 12 h. The reaction was cooled to room temperature and concentrated in vacuo to give the crude product. The purified product, 0.065 g, was obtained in 48% isolated yield by flash chromatography using a gradient of 5% diethyl ether in petroleum ether to 10% diethyl ether in petroleum ether as the eluent. ^{1}H NMR: ($CDCl_3$) δ 7.03 (d, J = 8.4 Hz, 2H), 6.59 (d, J = 8.4 Hz, 2H), 3.45 (br s, 1H), 3.12 (t, J = 7.1 Hz, 2H), 2.54 (t, J = 7.6 Hz, 2H), 1.66−1.50 (m, 4H), 1.47−1.34 (m, 4H), 0.99 (t, J = 7.3 Hz, 3H), 0.95 (t, J = 7.3 Hz, 3H). ^{13}C-{^{1}H} NMR: ($CDCl_3$) δ 146.28, 131.62, 129.03, 112.81, 44.05, 34.68, 34.01, 31.67, 22.30, 20.28, 13.96, 13.89. HRMS calcd for $C_{14}H_{23}N$ (M^+) 205.1830, found 205.1837.

***N*-Isobutyl-4-*n*-butylaniline.** A reaction vial was charged with (4-bromobutyl)benzene (0.140 g, 0.657 mmol), 1.2 equiv of NaO^{t}Bu (0.0758 g, 0.789 mmol), 0.05 equiv of Pd(DBA)$_2$ (0.0189 g, 0.0328 mmol), 0.10 equiv of DPPF (0.0360 g, 0.0657 mmol), and 8 mL of toluene under a N_2 atmosphere in a drybox. The reaction was capped using a PTFE septum and removed from the drybox. Isobutylamine (78.3 μL, 0.789 mmol) was added via syringe and the reaction heated to 90 °C for 12 h. The reaction was cooled to room temperature and concentrated in vacuo to give the crude product. The purified product, 0.056 g, was obtained in 42% isolated yield by flash chromatography using 5% diethyl ether in petroleum ether as the eluent. ^{1}H NMR: ($CDCl_3$) δ 7.02 (d, J = 8.2 Hz, 2H), 6.58 (d, J = 8.2 Hz, 2H), 3.59 (br s, 1H), 2.94 (d, J = 6.8 Hz, 2H), 2.53 (t, J = 7.5 Hz, 2H), 1.92 (m, 1H), 1.59 (m, 2H), 1.37 (m, 2H), 1.02 (d, J = 6.6 Hz, 6H), 0.96 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 146.39, 131.41, 129.03, 112.67, 52.14, 34.67, 34.02, 27.98, 22.32, 20.48, 13.97. HRMS calcd for $C_{14}H_{23}N$ (M^+) 205.1830, found 205.1827.

***N*-Butyl-*N*-(4-butylphenyl)-4-butylaniline.** A reaction vial was charged with (4-bromobutyl)benzene (0.246 g, 1.156 mmol), 1.2 equiv of NaO^{t}Bu (0.133 g, 1.387 mmol), 0.025 equiv of Pd(DBA)$_2$ (0.0166 g, 0.0289 mmol), 0.05 equiv of DPPF (0.0321 g, 0.0578 mmol), and 8 mL of toluene under a N_2 atmosphere in a drybox. The reaction was capped using a PTFE septum and removed from the drybox. Butylamine (51.4 μL, 0.520 mmol) was added via syringe and the reaction heated to 90 °C for 12 h. The reaction was cooled to room temperature and concentrated in vacuo to give the crude product. The purified product, 0.156 g, was obtained in 89% isolated yield, based on butylamine, by flash chromatography using 5% diethyl ether in hexanes as the eluent. ^{1}H NMR: ($CDCl_3$) δ 7.12 (d, J = 8.4 Hz, 4H), 6.90 (d, J = 8.4 Hz, 4H), 3.65 (t, J = 7.5 Hz, 2H), 2.57 (t, J = 7.5 Hz, 4H), 1.60 (m, 6H), 1.37 (m, 6H), 0.98−0.88 (m, 9H). ^{13}C{^{1}H} NMR: ($CDCl_3$) δ 146.05, 135.28, 129.02, 120.63, 52.20, 34.88, 33.81, 29.61, 22.42, 20.30, 14.00. HRMS calcd for $C_{24}H_{35}N$ (M^+) 337.2769, found 337.2766.

***N*,*N*-Dimethyl-*N*′-phenyl-1,4-benzenediamine.**[58] A reaction vial was charged with 4-bromo-*N*,*N*-dimethyl aniline (0.165 g, 0.825 mmol), 1.2 equiv of NaO^{t}Bu (0.0951 g, 0.990 mmol), 0.05 equiv of Pd(DBA)$_2$ (0.0237 g, 0.0412 mmol), 0.10 equiv of DPPF (0.0457 g, 0.0825 mmol), and 8 mL of toluene under a N_2 atmosphere in a drybox. The reaction was capped using a PTFE septum and removed from the drybox. Aniline (90.2 μL, 0.990 mmol) was added via syringe and the reaction heated to 90 °C for 12 h. The reaction was cooled to room temperature and concentrated in vacuo to give the crude product. The purified product, 0.141 g, was obtained in 80% isolated yield by flash chromatography using a gradient of 5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes as the eluent. ^{1}H NMR: (C_6D_6) δ 7.13 (dd, J = 7.3, 8.2 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 6.81−6.77 (m, 3H), 6.57 (d, J = 8.9 Hz, 2H), 4.91 (br s, 1H), 2.53 (s, 6H). ^{13}C{^{1}H} NMR: (C_6D_6) δ 147.56, 146.78, 132.69, 129.49, 123.82, 118.93, 115.19, 114.19, 40.85.

***N*-Butyl-2-methylaniline. Procedure for Gas Chromatography Yields.** A stock solution was prepared by dissolving 2-bromotoluene (0.155 g, 0.908 mmol) and the naphthalene standard (0.0820 g, 0.640 mmol) in toluene (15 mL). A second stock solution was prepared by dissolving Pd(DBA)$_2$ (26.0 mg, 45.3 μmol) in toluene (7.5 mL). Into a reaction vial was weighed 0.10 equiv of a bidentate phosphine ligand (6.1 μmol) and 1.2 equiv of NaO^{t}Bu (7.0 mg, 72.6 μmol). To each reaction vial was added 1.0 mL of the 2-bromotoluene stock solution followed by 0.5 mL of the Pd(DBA)$_2$ stock solution. The reaction vials were capped with a PTFE septum and removed from the drybox. Butylamine (7.2 μL, 72.6 μmol) was added to each vial via syringe, and the reactions were heated to 90 °C for 12 h before 1.0 μL aliquots were injected onto the gas chromatograph.

***N*-Butyl-4-butylaniline. Procedure for Gas Chromatography Yields.** A stock solution was prepared by dissolving (4-bromobutyl)-benzene (0.164 g, 0.772 mmol) and the naphthalene standard (0.0772 g, 0.602 mmol) in toluene (15 mL). A second stock solution was prepared by dissolving Pd(DBA)$_2$ (22.1 mg, 38.5 μmol) in toluene (7.5 mL). Into a reaction vial was weighed 0.10 equiv of a bidentate phosphine ligand (5.1 μmol) and 1.2 equiv of NaO^{t}Bu (5.9 mg, 61.6 μmol). To each reaction vial was added 1.0 mL of the (4-bromobutyl)-benzene stock solution followed by 0.5 mL of the Pd(DBA)$_2$ stock solution. The reaction vials were capped with a PTFE septum and removed from the drybox. Butylamine (6.1 μL, 61.6 μmol) was added to each vial via syringe, and the reactions were heated to 90 °C for 12 h before 1.0 μL aliquots were injected onto the gas chromatograph.

***N*-Isobutyl-4-*n*-butylaniline. Procedure for Gas Chromatography Yields.** A stock solution was prepared by dissolving (4-bromobutyl)benzene (0.166 g, 0.779 mmol) and the naphthalene standard (0.0710 g, 0.554 mmol) in toluene (15 mL). A second stock solution was prepared by dissolving Pd(DBA)$_2$ (22.4 mg, 38.9 μmol) in toluene (7.5 mL). Into a reaction vial was weighed 0.10 equiv of a bidentate phosphine ligand (5.2 μmol) and 1.2 equiv of NaO^{t}Bu (6.0 mg, 62.2 μmol). To each reaction vial was added 1.0 mL of the (4-bromobutyl)benzene stock solution followed by 0.5 mL of the Pd(DBA)$_2$ stock solution. The reaction vials were capped with a PTFE septum and removed from the drybox. Isobutylamine (6.2 μL, 62.2 μmol) was added to each vial via syringe, and the reactions were heated to 90 °C for 12 h before 1.0 μL aliquots were injected onto the gas chromatograph.

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***N*-Butyl-*N*-(4-butylphenyl)-4-butylaniline. Procedure for Gas Chromatography Yields.** A stock solution was prepared by dissolving (4-bromobutyl)benzene (0.1104 g, 0.518 mmol) and the naphthalene standard (0.0375 g, 0.293 mmol) in toluene (10 mL). A second stock solution was prepared by dissolving $Pd(DBA)_2$ (14.9 mg, 25.9 μmol) in toluene (5.0 mL). Into a reaction vial was weighed 0.10 equiv of a bidentate phosphine ligand (5.2 μmol) and 1.2 equiv of NaO^{t}Bu (6.0 mg, 62.1 μmol). To each reaction vial was added 1.0 mL of the (4-bromobutyl)benzene stock solution followed by 0.5 mL of the $Pd(DBA)_2$ stock solution. The reaction vials were capped with a PTFE septum and removed from the drybox. Butylamine (2.3 μL, 23.3 μmol) was added to each vial via syringe, and the reactions were heated to 90 °C for 12 h before 1.0 μL aliquots were injected onto the gas chromatograph.

***N*,*N*-Dimethyl-N′-phenyl-1,4-benzenediamine. Procedure for Gas Chromatography Yields.** A stock solution was prepared by dissolving 4-bromo-*N*,*N*-dimethylaniline (0.165 g, 0.826 mmol) and the naphthalene standard (0.110 g, 0.854 mmol) in toluene (15 mL). A second stock solution was prepared by dissolving $Pd(DBA)_2$ (23.7 mg, 41.3 μmol) in toluene (7.5 mL). Into a reaction vial was weighed 0.10 equiv of a bidentate phosphine ligand (5.5 μmol) and 1.2 equiv of NaO^{t}Bu (6.3 mg, 66.0 μmol). To each reaction vial was added 1.0 mL of the 4-bromo-*N*,*N*-dimethylaniline stock solution followed by 0.5 mL of the $Pd(DBA)_2$ stock solution. The reaction vials were capped with a PTFE septum and removed from the drybox. Aniline (6.0 μL, 66.0 μmol) was added to each vial via syringe, and the reactions were heated to 90 °C for 12 h before 1.0 μL aliquots were injected onto the gas chromatograph.

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