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Air Stable, Sterically Hindered Ferrocenyl Dialkylphosphines for Palladium-Catalyzed C−C, C−N, and C−O Bond-Forming Cross-Couplings

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Pentaphenylferrocenyl di-*tert*-butylphosphine has been prepared in high yield from a two-step synthetic procedure, and the scope of various cross-coupling processes catalyzed by complexes bearing this ligand has been investigated. This ligand creates a remarkably general palladium catalyst for aryl halide amination and for Suzuki coupling. Turnovers of roughly 1000 were observed for aminations with unactivated aryl bromides or chlorides. In addition, complexes of this ligand catalyzed the formation of selected aryl ethers under mild conditions. The reactions encompassed electron-rich and electron-poor aryl bromides and chlorides. In the presence of catalysts containing this ligand, these aryl halides coupled with acyclic or cyclic secondary alkyl- and arylamines, with primary alkyl- and arylamines, and with aryl- and primary alkylboronic acids. These last couplings provide the first general procedure for reaction of terminal alkylboronic acids with aryl halides without toxic or expensive bases. The ligand not only generates highly active palladium catalysts, but it is air stable in solution and in the solid state. Palladium(0) complexes of this ligand are also air stable as a solid and react only slowly with oxygen in solution.

Introduction

The development of ligand structures for palladium-catalyzed cross-coupling processes has advanced dramatically in recent years. The preparation of new ligand structures and the study of ligands whose potential for catalysis was previously untapped have led to the activation of aryl chlorides under mild conditions,[1−4] high conversions with remarkably low catalyst loadings,[5−10] and the invention of new transformations.[11−24] Electron-rich, sterically hindered monodentate ligands have been a particular focus of these studies.[25−31] Trialkylphosphines, aryl dialkylphosphines, and heterocyclic carbenes have all shown high activity, in combination with palladium precursors, for coupling reactions with aryl chlorides. In many cases, the coupling reactions under study have been classic Suzuki[32,33] and Mizoroki−Heck

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reactions,[34−36] but in other cases these reactions have been the more recently discovered amination of aryl halides,[11−13,37] etherification of aryl halides,[11] and α-arylation of carbonyl compounds.[14−18]

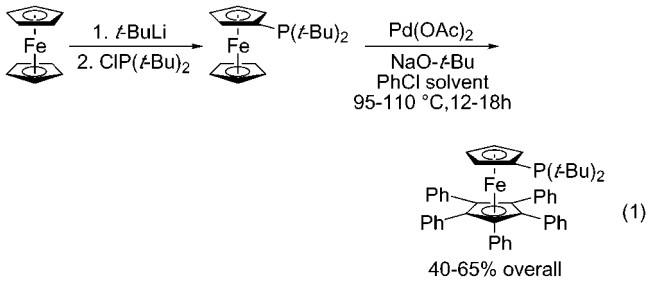
Ferrocenyl ligands are now abundant.[38] In many cases, these ferrocenyl ligands are bidentate and have properties such as large bite angles that are created by the specific distance between the two cyclopentadienyl groups.[39−41] In addition, the ferrocenyl structure can generate planar chirality, and the stereochemistry of these planar-chiral ligands can be controlled by diastereoselective lithiation[42] of enantiopure *N*,*N*-dimethylferrocenylethylamine.[43,44]

Several years ago, we began investigating a sterically hindered analogue of bis(diphenylphosphino)ferrocene, 1,1′-bis(di-*tert*-butylphosphino)ferrocene,[45,46] to perhaps generate more active catalysts and to rank the relative importance of steric and electronic effects on reductive eliminations. This ligand generated complexes that showed, for the first time, coupling of phenoxides with unactivated aryl halides.[47,48] However, mechanistic studies showed that this ligand cleaved to form the monophosphine, di-*tert*-butylphosphinoferrocene.[47] Complexes of this ligand showed activity toward aryl halide etherification that was greater than the activity of complexes generated from 1,1′-bis(di-*tert*-butylphosphino)ferrocene. Yet, we later showed that perarylation of the unsubstituted Cp of di-*tert*-butylphosphinoferrocene occurred prior to the etherification process during an induction period and that this perarylation generates the true catalyst for etherification.[23] When prepared in pure form, catalysts containing di-*tert*-butylphosphino pentaphenylferrocene showed higher activity for the formation of aryl ethers from aryl halides than did those containing the unsubstituted di-*tert*-butylphosphinoferrocene.

In the present work we show that this di-*tert*-butylphosphino pentaphenylferrocene, which we refer to as Q-phos from the first name of the initial discoverer, is a remarkably general ligand for cross-coupling processes, including Suzuki reactions of aryl and primary alkylboronate esters, selected aryl halide etherifications at room temperature, and almost all aryl halide aminations. In separate manuscripts we have shown that complexes of this ligand catalyze in high yields the arylation of malonates,[49] the arylation of cyanoacetates,[49,50] and the Heck arylation of olefins at room temperature.[51] The ligand is prepared in two steps in high yield and is air-stable indefinitely as a solid and in solution.

Results and Discussion

1. Ligand Synthesis and Properties. Despite the unusual structure of Q-phos, it is prepared in only two steps, as shown in eq 1. Monolithiation of ferrocene and



(1)

quenching with chlorodi-*tert*-butylphosphine,[52] followed by palladium-catalyzed perarylation[53] of the crude product, generated the ligand in an overall yield of about 40−65%. During some preparations of this ligand, the material was isolated by recrystallization from pentane in air instead of by column chromatography. In practice, the monolithiation of ferrocene and the quenching of this anion with the chlorophosphine required specific procedures to obtain high yields because the monolithiation of ferrocene is not straightforward. However, selectivity for monolithiation vs dilithiation that was roughly 4:1 was observed after following literature procedures[52] involving addition of *tert*-butyllithium in THF at 0 °C. To generate the initial monophosphine, we evaporated the THF, added pentane to solidify the product, and then added THF to generate a ratio of pentane:THF that was 5:1. Addition of the chlorophosphine in this medium led to selective reaction with the monolithiated ferrocene and a selectivity for formation of di-*tert*-butylphosphinoferrocene vs 1,1′-bis(di-*tert*-butylphosphino)ferrocene that was roughly 10:1. We reasoned that this solvent mixture would partially dissolve the monolithiated species and leave the dilithiated material in the solid phase. A typical workup involved adsorption of the solid on silica, washing of the silica with pentane to remove the ferrocene, and then elution of the product all at once with ether. This procedure generally provided 60−80% yields of material that was pure enough to carry forward. Treatment of this product with sodium *tert*-butoxide and 5 mol % palladium acetate in neat phenyl chloride formed the pentaphenylferrocenyl ligand in roughly 90% yield by NMR spectroscopy based on the starting di-*tert*-butylphosphinofer-

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rocene. Recrystallization gave generally 60−80% yield for the perarylation step and an overall yield of 40−65% based on ferrocene.

Despite its sterically crowded structure, the NMR spectra of Q-phos were unremarkable. There was no evidence for hindered rotation about the Cp−aryl C−C bond when free in solution; the usual pattern for a phenyl group was observed. The two *tert*-butyl groups were equivalent and showed typical coupling to the phosphorus.

The ligand is indefinitely stable in air and was stored on the benchtop during studies on catalytic methods. Moreover, the ligand is air stable in solution. A sample of this ligand was left in benzene solution for two months with no evidence for formation of the phosphine oxide. This air stability is no doubt a kinetic phenomenon and may result from a steric hindrance of the ligand that is exacerbated by a preferential conformation of the free ligand that places the electron pair toward the aryl groups on the ferrocene.

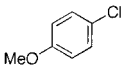
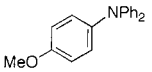
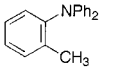
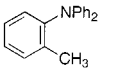
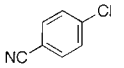
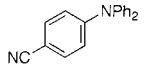
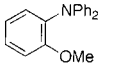
We prepared other arylated di-*tert*-butylphosphinoferrocenes for studies on the effect of steric and electronic perturbations on catalytic activity. These ligands were prepared by arylation of di-*tert*-butylphosphinoferrocene with *p*-bromoanisole, *p*-bromo trifluorotoluene, and 3,5-dimethylbromobenzene. We also prepared 1-di-*tert*-butylphosphino-1′,2′,3′,4′-tetraphenyferrocene and 1-di-*tert*-butylphosphino-1′,2′,3′,4′-tetra-*o*-tolylferrocene, although yields were low for synthesis of these tetraaryl materials. Brief attempts were made to prepare the arylated ligands by generating the anion of di-*tert*-butylphosphinocyclopentadiene and allowing it to react with pentaphenylcyclopentadienyl iron chloride[54] that was generated in situ. However, this procedure led to exchange of cyclopentadienyl groups, and 1,1′-bis-di-*tert*-butylphosphino ferrocene was the major product.

2. Catalytic Chemistry of Palladium-Q-phos Complexes. A. Palladium-Catalyzed Amination of Aryl Halides. Palladium complexes of Q-phos are general catalysts for the coupling of aryl bromides and chlorides with both primary and secondary aromatic and aliphatic amines. Examples of these coupling reactions are provided in Tables 1−9. Only small amounts of hydrodehalogenation product formed from most reactions. Selectivity for monoarylation of primary amines was as high or higher than has been seen with any monodentate ligand,[55,56] and this selectivity allowed for reactions of unhindered primary amines to occur with unhindered aryl chlorides in high yields. In addition, acyclic secondary amines, such as dibutylamine, coupled in high yield with even electron-rich aryl halides.

Table 1 shows that diphenylamine couples with a variety of aryl bromides to form triarylamines in high yields. Reactions of aryl bromides occurred at room temperature, even for the somewhat hindered 2-bromotoluene. Reactions of aryl chlorides required heating to occur in reasonable reaction times, but heating at 100 °C formed the triarylamine product in nearly quantitative yield in all cases examined. Reactions of *N*-methylaniline (Table 2) also occurred in high yields for the substrates examined. *o*-Chlorotoluene coupled with this secondary amine in high yield, and electron-rich and electron-poor *para*-substituted aryl bromides also reacted in good yields. The reactions of morpholine with aryl halides are summarized in Table 3. This cyclic secondary amine coupled with aryl bromides and chlorides in good to excellent yields, with one exception. The coupling of morpholine with *o*-bromotoluene occurred in low yields. The coupling of dialkylamines with *ortho*-substituted aryl bromides is generally a poor reaction for catalysts bearing monophosphines. Reaction of cyclic dialkylamines with ortho-substituted aryl halides has occurred with catalysts bearing bisphosphines.[57] Other than this substrate combination, good yields were observed in all reactions of morpholine tested.

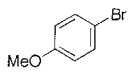
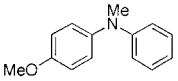
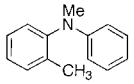
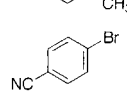
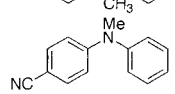
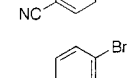
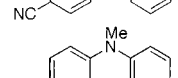
Table 4 summarizes the reactions of dibutylamine, a representative acyclic secondary amine, with aryl bro-

TABLE 1. Reaction of Aryl Halides with Diphenylamine in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	product	conditions[a]	isolated yield (%)
1		NPh_3	1 mol% NaO-*t*-Bu/Toluene RT, 1 h	99
2		NPh_3	1 mol% NaO-*t*-Bu/Toluene 100 °C, 21 h	98
3			1 mol% NaO-*t*-Bu/Toluene 80 °C, 12 h	99
4			1 mol% NaO-*t*-Bu/Toluene RT, 4 h	99
5			1 mol% NaO-*t*-Bu/Toluene 80 °C, 21 h	99
6			1 mol% NaO-*t*-Bu/Toluene 45 °C, 21 h	96
7			0.5 mol% NaO-*t*-Bu/Toluene 100 °C, 5 h	95

[a] A 1:2 ratio of $Pd(dba)_2$ to ligand was used.

TABLE 2. Reaction of Aryl Halides with *N*-Methylaniline in the Presence of a Combination of $Pd(dba)_2$ or $Pd(OAc)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	product	conditions[a]	isol. yield(%)
1			0.5 mol% NaO-*t*-Bu/Toluene 100 °C, 25 h	93[b]
2			0.5 mol% NaO-*t*-Bu/Toluene 100 °C, 28 h	89[b]
3			1 mol% NaO-*t*-Bu/Toluene 45 °C, 19 h	91
4			1 mol% NaO-*t*-Bu/Toluene 100 °C, 2 h	98

[a] A 1:2 ratio of $Pd(dba)_2$ to ligand was used. [b] $Pd(OAc)_2$ was used as the palladium source.

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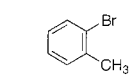
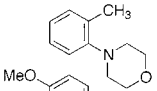
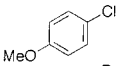
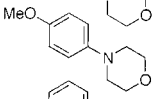
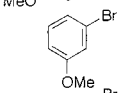
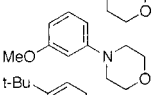
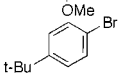
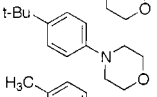
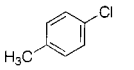
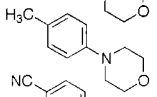
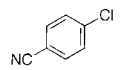
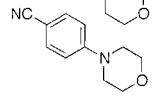
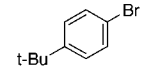
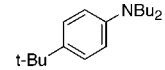
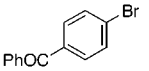
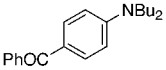
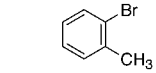
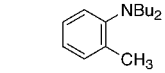
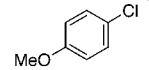
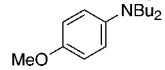
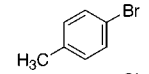
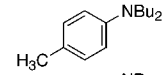
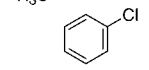
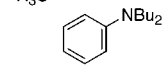
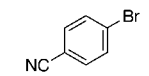
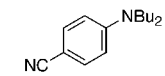
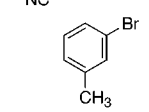
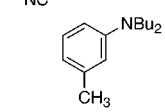
TABLE 3. Reaction of Aryl Halides with Morpholine in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	product	conditions[a]	isol. yield(%)
1			5 mol% NaO-*t*-Bu/Toluene 100, 18 h	54
2			1 mol% NaO-*t*-Bu/Toluene 70 °C, 27 h	95
3			1 mol% NaO-*t*-Bu/Toluene 100 °C, 21 h	96
4			1 mol% NaOt-Bu/Toluene 100 °C, 21 h	82
5			1 mol% NaOt-Bu/Toluene 70 °C, 27 h	98
6			1 mol% NaOtBu/Toluene 45 °C, 27 h	82

[a] A 1:2 ratio of $Pd(dba)_2$ to ligand was used.

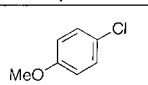
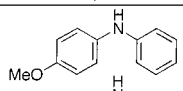
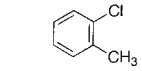
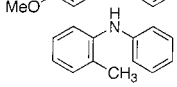
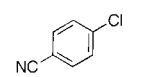
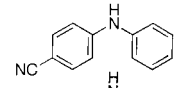
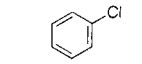
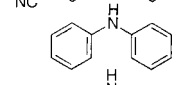
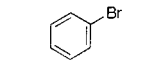
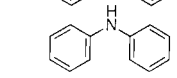
TABLE 4. Reaction of Aryl Halides with Di-*n*-butylamine in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	product	conditions[a]	isolated yield(%)
1			1 mol% NaO-*t*-Bu/Toluene 60 °C, 20 h	89
2			1 mol% NaO-*t*-Bu/Toluene RT, 17 h	99
3			1 mol% NaO-*t*-Bu/Toluene 60 °C, 17 h	37
4			1 mol% NaO-*t*-Bu/Toluene 100 °C, 20 h	93
5			1 mol% NaO-*t*-Bu/Toluene 40 °C, 24 h	93
6			0.5 mol% NaO-*t*-Bu/Toluene 100 °C, 20 h	94[b]
7			1 mol% K_3PO_4/DME 100 °C, 6 h	94
8			0.5 mol% NaO-*t*-Bu/Toluene 100 °C, 27 h	94[b]

[a] A 1:2 ratio of metal to ligand was used.
[b] $Pd(OAc)_2$ was used instead of $Pd(dba)_2$ as a palladium source.

mides and chlorides. In general, the couplings of acyclic secondary amines with aryl halides are more challenging than reactions of cyclic secondary amines. Reactions of *ortho*-substituted aryl halides with acyclic dialkylamines are generally poor reactions, even with bisphosphines,[57] and reactions of electron-rich aryl halides with acyclic secondary amines can give large amounts of hydrodehalogenation product.[57,58] Catalysts bearing Q-phos as ligand do not solve the synthetic problem of coupling acyclic dialkylamines with ortho-substituted aryl halides, but they do provide high yields for reactions of less

TABLE 5. Reaction of Aryl Halides with Aniline in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	product	conditions[a]	isolated yield(%)
1			1 mol% NaO-*t*-Bu/Toluene 70 °C, 15 h	95
2			1 mol% NaO-*t*-Bu/Toluene 70 °C, 15 h	97
3			0.5 mol% K_3PO_4/DME 100 °C, 15 h	97
4			1 mol% NaO-*t*-Bu/Toluene 70 °C, 15 h	86
5			1 mol% NaO-*t*-Bu/Toluene RT, 4 h	98

[a] A 1:2 ratio of $Pd(dba)_2$ to ligand was used.

hindered electron-rich or electron-poor aryl bromides and chlorides. For example, reaction of 4-chloroanisole and reaction of 4-bromobenzonitrile both provided yields of over 90%. Reactions of aryl chlorides were conducted at 100 °C, but most reactions of aryl bromides occurred smoothly at lower temperatures in reasonable reaction times.

Reactions of primary amines with aryl bromides or aryl chlorides also occurred in high yields in most cases. Coupling of anilines is typically one of the most general amination processes. In accord with this assertion, coupling of aniline with electron-rich and electron-poor aryl chlorides and with unhindered or *ortho*-substituted aryl bromides or chlorides (Table 5) occurred in high yields in the presence of catalysts bearing Q-phos. The amination of 4-chlorobenzonitrile with aniline in the presence of NaO-*t*-Bu as base in toluene solvent gave the coupled product in 73% yield. Arene that is formed by hydrodehalogenation was also detected by GC/MS. In contrast, the same reaction in the presence of the insoluble and weaker base K_3PO_4 in DME solvent gave 97% yield of 4-cyanodiphenylamine after 15 h at 100 °C. This combination of K_3PO_4 and DME has been used in the past for aminations of base-sensitive aryl halides, such as 4-cyanohalobenzenes.[26]

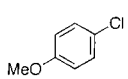
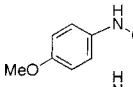
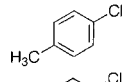
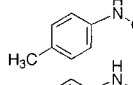
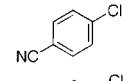
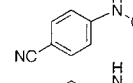
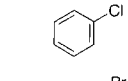
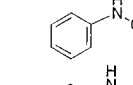
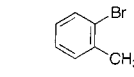
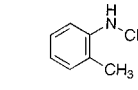
In many cases, halobenzonitriles react with slow rates,[55] despite their favorable electronics. The ^1H NMR chemical shifts of benzonitrile and sodium *tert*-butoxide in C_6D_6 changed upon mixing, but a strong nitrile infrared band was still present. These data suggest that the nitrile coordinates to the alkali metal of the base. This coordination may cause the coupling of halobenzonitriles to differ from the coupling of substrates that do not coordinate to the counterion of the base.

More challenging for catalysts bearing monodentate ligands is the coupling of primary aliphatic and benzylic amines. Often when conducted with catalysts bearing monodentate ligands, reactions of these substrates provide more of the product from hydrodehalogenation than do reactions of secondary amines or reactions of primary amines catalyzed by bisphosphines.[57,59−61] Also when conducted with these catalysts, reactions of primary

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

(59) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1348−1350.

TABLE 6. Reaction of Aryl Halides with Benzylamine in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	product	conditions[a]	isolated yield(%)
1			1 mol% NaO-*t*-Bu/Toluene 100 °C, 4 h	93
2			1 mol% NaO-*t*-Bu/Toluene 100 °C, 24 h	95[b]
3			1 mol% K_3PO_4/DME 100 °C, 20 h	95[c]
4			1 mol% NaO-*t*-Bu/Toluene 100 °C, 5 h	92
5			1 mol% NaO-*t*-Bu/Toluene 100 °C, 4 h	96

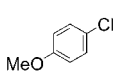
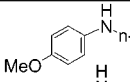
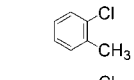
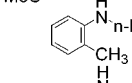
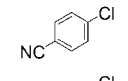
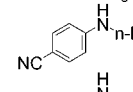
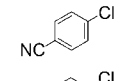
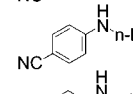
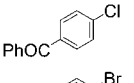
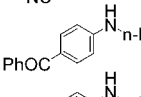
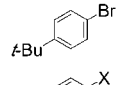
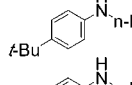
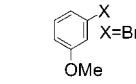
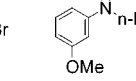
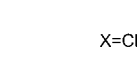
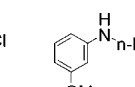
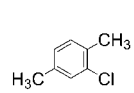
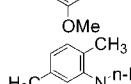
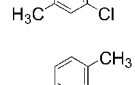
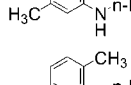
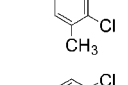
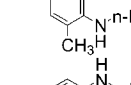
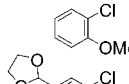
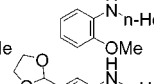
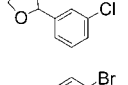
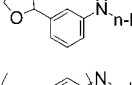
[a] A 1:2 ratio of $Pd(dba)_2$ to ligand was used. [b] $Pd(OAc)_2$ was used as the palladium source. [c] Reaction of 4-chlorobenzonitrile with benzylamine in the presence of NaOtBu in toluene at 50 °C for 24 h gave 76% yield of coupled product

amines often produce mixtures of secondary and tertiary amines from competing mono- and diarylation. Yet, the catalysts that provide the highest turnover frequencies, particularly for reactions of aryl chlorides, bear monodentate ligands.[26,28,31] Thus, a catalyst bearing a monodentate ligand that provides high selectivity for coupling vs reduction and mono- vs diarylation could provide both high activity and high selectivity. Of course, reactions of hindered aryl halides generate less diarylation product.[55] In addition, reactions of hindered aryl halides generally produce less hydrodehalogenation product from reactions of primary amines than do unhindered aryl halides because steric effects promote reductive elimination at the expense of β-hydrogen elimination.[62] Thus, reactions of unhindered aryl halides with unhindered primary amines are among the most challenging classes of aryl halide amination.

The selectivity of catalysts bearing Q-phos for reactions of primary amines was remarkable. Reactions of benzylamine with unhindered aryl chlorides occurred in good to excellent yields in all cases, as shown in Table 6. The lowest yield was again observed with chlorobenzonitrile, but the yield of coupled product was still 76% when conducted with NaO-*t*-Bu as base. Again the yield was improved when the reaction was conducted with K_3PO_4 in DME solvent at 100 °C for 20 h. In the presence of the phosphate base, coupling to form *N*-(*p*-cyanophenyl)-benzylamine occurred in 95% yield. Coupling of benzylamine with 4-chloroanisole, a prototypical deactivated aryl chloride, formed *N*-benzylanisidine in 93% yield.

To observe selective monoarylation of benzylamine, 1.2 equiv of amine versus aryl halide was employed. The reaction of a 1:1 ratio of benzylamine and 4-bromoanisole formed the mono *N*-arylated product in 82% yield, but the ratio of mono to diarylated amine was only 8.1:1. However, the reaction conducted with a 1.2:1 ratio of amine to bromoanisole formed the coupled product in 93% isolated yield after 2 h at 80 °C in the presence of 1 mol % catalyst. The ratio of secondary to tertiary amine was 19:1, as determined by GC.

TABLE 7. Reaction of Aryl Halides with *n*-hexylamine in the Presence of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

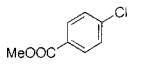
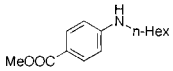
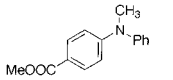
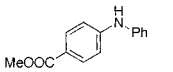
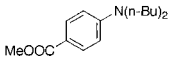
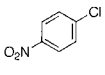
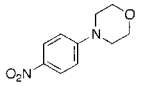
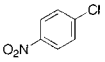
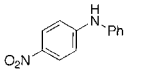
entry	aryl halide	product	conditions[a]	isolated yield(%)
1			2 mol% NaO-*t*-Bu/Toluene 70 °C, 18 h	92[b]
2			1 mol% NaO-*t*-Bu/Toluene 70 °C, 8 h	92
3			1 mol% K_3PO_4/DME 100 °C, 13 h	92
4			1 mol% NaO-*t*-Bu/Toluene 70 °C, 8 h	78
5			1 mol% NaO-*t*-Bu/Toluene 50 °C, 13 h	93
6			1 mol% NaO-*t*-Bu 100 °C, 2 h	95[c] 97[d]
7			1 mol% NaO-*t*-Bu/Toluene 100 °C, 10 h	85
8			1 mol% NaO-*t*-Bu/Toluene 100°C, 24 h	95
9			1 mol% NaO-*t*-Bu/Toluene 100 °C, 10 h	87
10			2 mol% NaO-*t*-Bu/Toluene 100 °C, 10 h	97
11			1 mol% NaO-*t*-Bu/Toluene 100 °C, 16 h	97
12			1 mol% NaO-*t*-Bu/ Toluene 100 °C, 16 h	94
13[b]			1 mol% NaO-*t*-Bu/ Toluene 100 °C, 4 h	99[e]

[a] A 1:2 ratio of $Pd(dba)_2$ to ligand and a 1:1.2 ratio of ArX to amine was used. [b] $Pd(OAc)_2$ was used as the palladium source. [c] Toluene solvent, 24:1 ratio of mono:diarylation [d] THF solvent, 49:1 ratio of mono:diarylation. [e] 2.2:1 ratio of ArX to amine.

Similar results were obtained for reactions of hexylamine, as shown in Table 7. The electron-rich and sterically hindered *o*-chloroanisole reacted with this amine to form *N*-hexyl *o*-anisidine in 97% yield. Unhindered aryl bromides also reacted with hexylamine in high yields. For example, reaction of hexylamine with 4-*tert*-butyl bromobenzene in toluene at 100 °C for 2 h gave 95% yield of arylamine, and the same reaction in THF at 80 °C for 8 h gave 94% yield of arylamine. A mono:diarylation selectivity of 49:1 was observed when conducting the reaction with only 1.2 equiv of amine per aryl halide in THF solvent for 2 h at 100 °C; the selectivity was too high to measure accurately when the reaction was conducted in dioxane. The reactions of 2-substituted aryl halides with *n*-hexylamine occurred with high selectivity, even when 1.0 equiv of amine per aryl halide was used. For example, 2-chlorotoluene reacted with 1 equiv of *n*-hexylamine to form the monoarylated amine

(60) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 7217−7218.
(61) Wolfe, J. P.; Wagaw, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 7215−7216.
(62) Hartwig, J. F.; Richards, S.; Barañano, D.; Paul, F. *J. Am. Chem. Soc.* **1996**, *118*, 3626−3633.

TABLE 8. Reaction of Base-sensitive Aryl Halides with Amines in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst, K_3PO_4 as Base and Monoglyme as Solvent

entry	aryl halide	amine	product	conditions[a]	isolated yield(%)
1		NH_2hexyl		2 mol % K_3PO_4, DME 100 °C, 20 h	86
2				1 mol % K_3PO_4, DME 100 °C 20 h	97
3				1 mol % K_3PO_4, DME 100 °C, 24 h	96
4				1 mol % K_3PO_4, DME 100 °C, 24 h	96
5				1 mol % K_3PO_4, DME 100 °C, 20 h	56
6				1 mol % K_3PO_4, DME 100 °C, 20 h	95

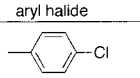
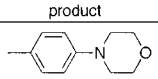
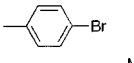
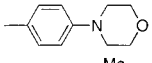
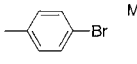
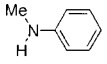
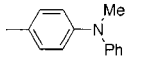
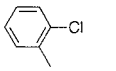
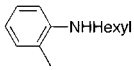
[a] A 1:2 ratio of $Pd(dba)_2$ to ligand was used.

in 92% isolated yield, and the ratio of mono- to diarylated amine was 24:1. Aryl chlorides with two ortho substituents also coupled in high yields (entry 10). Again, one ofthe lower yields was observed for reaction of 4-chlorobenzonitrile in the presence of *tert*-butoxide as base. However, reaction in the presence of potassium phosphate as base at 100 °C generated the coupled product in a higher yield of 92%. $Pd(dba)_2$, $Pd_2(dba)_3{\cdot}CHCl_3$, and $Pd(OAc)_2$ were all useful metal sources. The reaction of 4-*tert*-butylbromobenzene with *n*-hexylamine initiated with the three precursors gave 90, 92, and 94% yield, respectively.

Reactions of amines with several base-sensitive aryl halides were conducted successfully at 100 °C with the combination of potassium phosphate as base and DME as solvent.[26,63] These results are summarized in Table 8. Hexylamine, *N*-methylaniline, aniline, and dibutylamine all reacted with methyl 4-chlorobenzoate in yields ranging from 86 to 99%. The proper choice of base *and* solvent was important. Reactions in the presence of phosphate base did not occur in high yield in toluene or THF solvent, but did occur efficiently in DME solvent. Reactions of 4-chloronitrobenzene with morpholine occurred in low yields in the presence of phosphate base, but reaction of this substrate with aniline did occur in good yields. The combination of Cs_2CO_3 and DME solvent was also useful for the amination of base-sensitive aryl halides. For example the reaction of methyl 4-chlorobenzoate with hexylamine took place after 20 h at 100 °C in 83% yield. This yield is essentially identical to that of the same reaction (entry 1) conducted with phosphate base.

We also evaluated reactions of aryl bromides and chlorides with low catalyst loadings. These results are summarized in Table 9. Reaction of morpholine with *p*-tolyl bromide and chloride, reaction of *N*-methyl aniline with *p*-tolyl bromide and reaction of hexylamine with *o*-tolyl chloride all occurred to completion in the presence

TABLE 9. Reaction of Aryl Halides with Amines at Low Loadings of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$

entry	aryl halide	amine	product	conditions	isol. yield(%)
1				0.1% 100 °C, 19 h toluene	92%
2				0.1% 100 °C, 19 h toluene	91%
3				0.05% 100 °C, 19 h toluene	99%
4		$HexylNH_2$		0.1% 100 °C, 19 h toluene	83%

[a] A 1:2 ratio of metal to ligand was used.

of only 0.1 mol % catalyst and a reaction temperature of 100 °C. Reaction of *N*-methyl aniline with *p*-tolyl bromide also proceeded to completion with only 0.05 mol % catalyst.

B. Suzuki Couplings. i. Coupling of Arylboronic Acids. Tables 10−13 summarize the scope of the coupling of arylboronic acids with aryl bromides and chlorides. These reactions occur in high yields with electron-poor to electron-rich aryl chlorides and bromides and with a variety of arylboronic acids. Table 10 summarizes the reactions of electron-poor to electron−neutral aryl bromides. In most cases, reactions of electron-poor to electron−neutral aryl bromides occurred at room temperature. Reactions of electron-poor aryl chlorides occurred at only 50 °C. When low catalyst loadings were evaluated for reactions of electron-poor aryl bromides, we found that the reaction of 4-bromobenzophenone with phenylboronic acid was complete after only 1 h at 100 °C when conducted with 0.0005 mol % catalyst. These results correspond to an average turnover frequency of roughly 20000/h. In most cases, these reactions were conducted using KF as base, although reactions also occurred when K_3PO_4 was used as base.

Table 11 shows reactions of electron-rich aryl bromides, reactions of ortho-substituted electron−neutral aryl bromides at elevated temperatures, and reactions of aryl bromides containing potentially reactive functional groups. Electron-rich aryl bromides were viable substrates for reactions with electron-rich or electron-poor and *ortho*-substituted arylboronic acids. Again KF was used as base. Reactions occurred at room temperature in many cases. Both $Pd(OAc)_2$ and $Pd(dba)_2$ were useful sources of palladium. Even the combination of $PdCl_2$ and Q-phos as catalyst generated coupled product, but the reaction was slow. For example, the reaction of 2-bromotoluene with phenylboronic acid in toluene at room temperature in the presence of 1 mol % of $Pd(OAc)_2$ or $Pd(dba)_2$ and Q-phos gave the biphenyl in 95% isolated yield after 24 h. The same reaction, but with $PdCl_2$ as the catalyst precursor, gave 88% yield after 3 days.

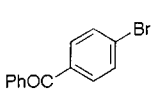
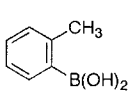
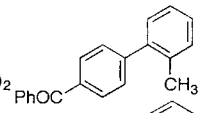
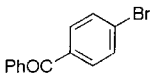
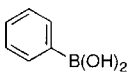
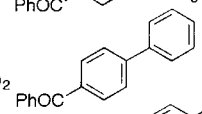
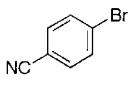
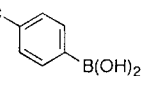
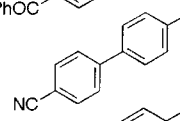
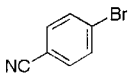
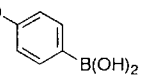
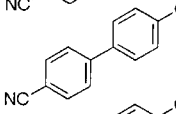
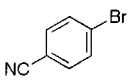
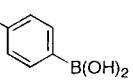
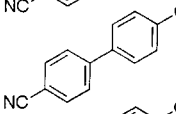
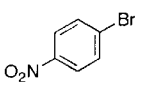
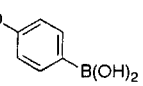
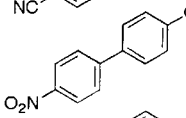
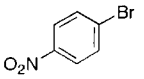
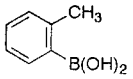
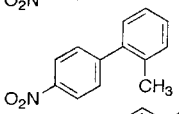
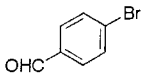
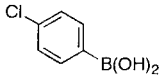
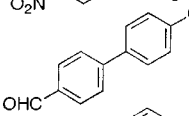
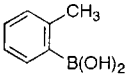
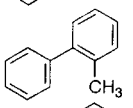
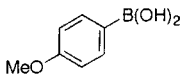
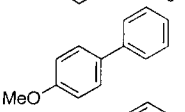
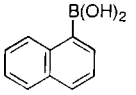
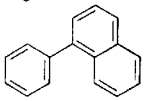
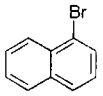
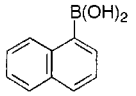
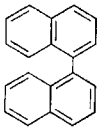
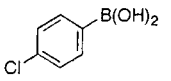
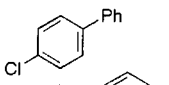
In some cases, highly hindered products were generated.[64,65] 2,2′-Disubstituted biaryls were formed under the standard conditions. In addition, 2,6,2′-trisubstituted biaryls were produced in high yield in the presence of 2 mol % of palladium and K_3PO_4 as base. Potentially reactive *ortho* substituents, such as chloride, were toler-

(63) Wolfe, J. P.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6359−6362.

(64) Griffiths, C.; Leadbeater, N. E. *Tetrahedron Lett.* **2000**, *41*, 2487−2490.

(65) Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207−210.

TABLE 10. Coupling of Arylboronic Acids with Electron Deficient and Electron−Neutral Aryl Bromides at Room Temperature Using a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	boronic acid	product	conditions[a]	isolated yield (%)[b]
1				1 mol% KF(2 equiv) Toluene RT, 18 h	98[b]
2				0.0005 mol% K_3PO_4/Toluene 100 °C 1 h	94
3				1 mol% KF(2 equiv)/THF RT, 28 h	97
4				1 mol% KF(3 equiv)/THF RT	94
5				0.5 mol% KF(3 equiv)/THF 40 °C, 12 h	97
6				1 mol% K_3PO_4(2.2 equiv) Toluene 50 °C, 17 h	98[b]
7				0.5 mol% KF(2 equiv) Toluene 50 °C 22 h	98[b]
8				0.5 mol% KF(3 equiv)/THF RT, 5 h	99
9				1 mol% KF(3 equiv)/THF RT, 2 days	95
10				1 mol% KF(3 equiv)/THF RT, 16 h	95
11				1 mol% KF(3 equiv)/THF RT, 17 h	99
12				1 mol% KF(3 equiv)/THF RT, 2 d	97
13				0.5/1 K_3PO_4/Toluene 100°C, 17 h	78
14				1 mol% KF(3 equiv) Toluene, RT, 14 h	98

[a] Reaction conditions: 1:2 ratio of metal to ligand and 0.40 or 0.50 mmol of ArBr; entry 1−3, 1.1 mol equiv. of $ArB(OH)_2$ to ArBr; entry 4−13,1.3 mol equiv of $ArB(OH)_2$ to ArBr; 2 mL of solvent. [b] All yields are for product judged pure by GC and ^1H NMR spectroscopy.

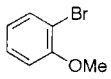
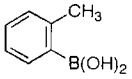
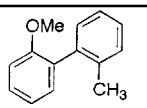
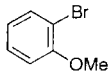
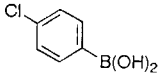
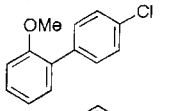
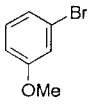
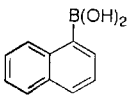
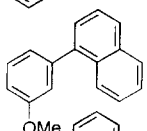
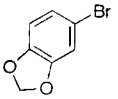
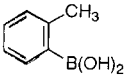
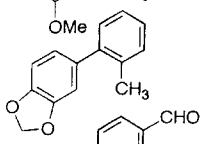
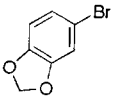
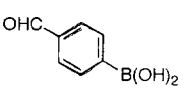
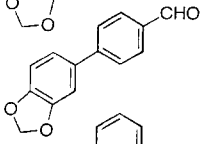
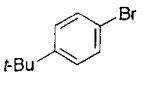
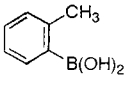
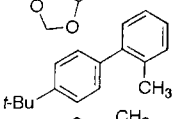
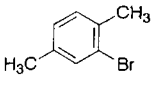
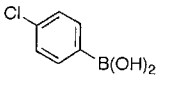
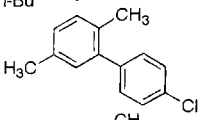
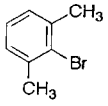
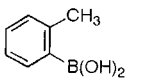
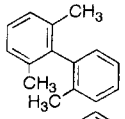
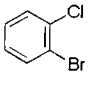
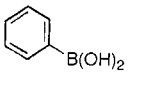
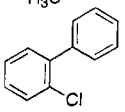
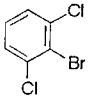
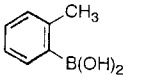
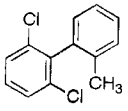
ated in the aryl halide reagent. Even 2,6-dichlorobromoarenes coupled with 2-tolylboronic acid in good yield.

Similar substrate scope was observed for reactions of aryl chlorides, as summarized in Table 12. Again, potentially reactive ortho substituents, such as a carbomethoxy group, were tolerated in the aryl halide reagent. Electron-poor chloroarenes reacted in a general fashion under the standard conditions of KF base at 45 °C reaction temperatures. Electron-rich aryl chlorides coupled with arylboronic acids in good yields at 100 °C. *Ortho*-substituted arylboronic acids coupled with *ortho*-substituted aryl chlorides when 2.5 mol % of catalyst was used (entry 10).

ii. Coupling of Alkylboronic Acids. The coupling of alkylboronic acids with aryl halides is rare and generally has occurred with only thallium or silver bases.[33,66,67] In most cases, sp^3-sp^2 coupling processes

(66) Sato, M.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1989**, 1405−1408.

TABLE 11. Coupling of Unactivated Aryl Bromides with Arylboronic Acids in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	boronic acid	product	conditions[a]	isol. yield (%)[b]
1				1 mol% (Pd/L) KF(2)/Toluene 100 °C, 16 h	98
2				0.5/1.0 mol% (Pd/L) KF(3)/THF RT, 5 h	95
3				0.5/1 mol% (Pd/L) KF(3)/dioxane 100 °C, 18 h	99
4				1 mol% (Pd/L) KF(2)/Toluene RT, 3 h	99
5				1/2 mol% (Pd/L) KF(3)/dioxane 100 °C, 18 h	85
6				1 mol% (Pd/L) K_3PO_4(2)/Toluene 80 °C, 15 h	97
7				1/2 mol% (Pd/L) K_3PO_4(3)/Toluene 100 °C, 14 h	95
8				2/4 mol% (Pd/L) K_3PO_4(3)/Toluene 100 °C, 48 h	87
9				1/2 mol% (Pd/L) KF(3)/THF RT, 14 h	93
10				2/4 mol% (Pd/L) K_3PO_4(3)/Toluene 100 °C, 14 h	76

[a] 1:2 ratio of metal to ligand and 1.1−1.5 equiv of aryl boronic acids were used. [b] All yields are for product judged pure by GC and ^1H NMR spectroscopy.

involving boron reagents have been conducted with air-sensitive trialkylboranes, such as 9-BBN derivatives. Recently, trifluoroalkylborates[68] and dialkylpinacolborates[69] have been used in couplings with aryl halides, and alkylboronates have been used with aryldiazonium salts without added base.[70] The coupling of cyclopentylboronic acid has been conducted successfully with a common base,[71] and complexes of standard arylphosphines can catalyze some couplings of *n*-alkylboronic acids with aryl bromides in good yields.[72] In contrast, we have shown that the coupling of *n*-alkylboronic acids with aryl bromides or chlorides catalyzed by complexes of Q-phos occurs in a general fashion in the presence of potassium phosphate in toluene solvent.

Table 13 summarizes the coupling of alkylboronic acids with aryl halides. In every case tested, *n*-butylboronic acid coupled efficiently with aryl bromides or chlorides. Even the reaction of electron-rich and *ortho*-substituted 2-chloroanisole gave 90% yield of *n*-butylarene. The combination of K_3PO_4 and toluene at 100 °C was important to observe high yields. The reaction of 2-chlorotoluene with *n*-butylboronic acid in the presence of KF in THF solvent gave low conversion. Thus far, efficient reactions have been limited to those of terminal alkyl boronic acids. For example, *sec*-butylboronic acid reacted slowly, and mixtures of *sec*-butyl and *n*-butylarenes were produced. Only 55% yield (GC) of the desired *sec*-butylarene was produced. To overcome the slow reaction rates of secondary alkylboronates, we investigated reactions of *sec*-butyl zinc chloride. This substrate was more reactive, and coupling of this reagent with 4-*tert*-butyl-

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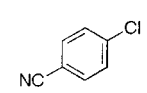
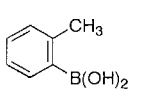
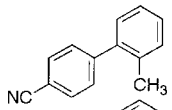
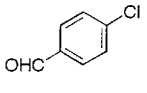
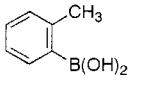
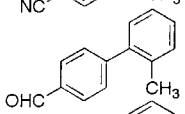
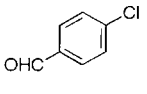
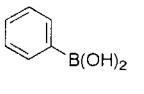
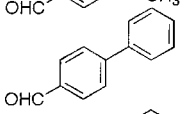
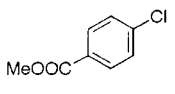
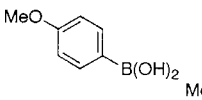
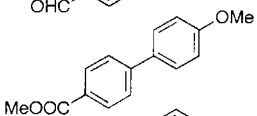
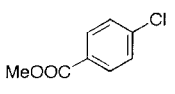
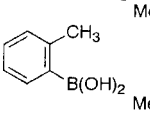
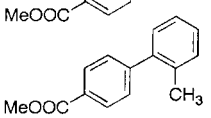
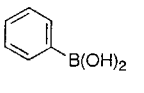
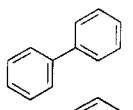
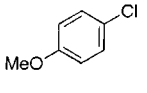
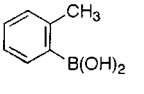
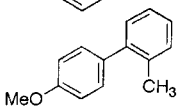
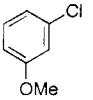
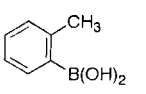
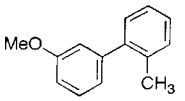
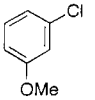
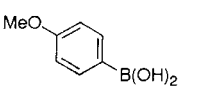
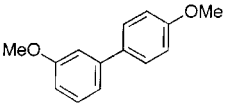
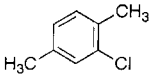
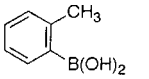
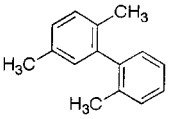
(68) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393−396.
(69) Zou, G.; Falck, J. R. *Tetrahedron Lett.* **2001**, *42*, 5817−5819.
(70) Andrus, M. B.; Song, C. *Org. Lett.* **2001**, *3*, 3761−3764.
(71) Littke, A.; Dai, C.; Fu, G. *J. Am. Chem. Soc.* **2000**, *122*, 4020−4028.
(72) Molander, G. A.; Yun, C.-S. *Tetrahedron* **2002**, *58*, 1465−1470.

TABLE 12. Coupling of Aryl Chlorides with Arylboronic Acids in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	boronic acid	product	conditions[a]	isol. yield (%)[b]
1				1 mol% KF(3 equiv)/ THF 45 °C	94
2				1 mol% KF(3 equiv)/ THF 50 °C, 15 h	96
3				1 mol% KF(3 equiv)/ THF 50 °C, 15 h	96
4				1 mol% KF(3 equiv)/ THF 100 °C, 4h	89
5				1 mol% KF(3 equiv)/ THF 100 °C, 20 h	92
6				0.5 mol% KF(3 equiv)/THF 45 °C	96
7				1 mol% KF(3 equiv)/Toluene 80 °C, 3 days	99
8				5 mol% K_3PO_4(3 equiv) Toluene 80 °C, 23 h	87
9				5 mol% KF(3 equiv)/Toluene 80 °C, 26 h	97
10				2.5 mol% Cs_2CO_3(2 equiv) dioxane 100 °C, 3 d	80

[a] 1:2 ratio of metal to ligand and 1.1−1.5 equiv of aryl boronic acids were used. [b] All yields are for product judged pure by GC and ^1H NMR spectroscopy.

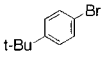
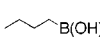
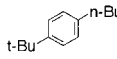
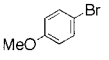
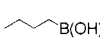
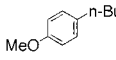
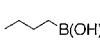
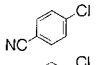
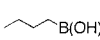
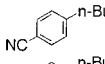
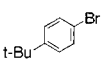
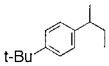
boronic acid occurred at room temperature to form the *sec*-butylarene in 76% yield.

3. Palladium-Catalyzed Etherification. Palladium complexes bearing Q-phos catalyzed couplings to form aryl ethers at low temperatures. In fact, the pentaphenylferrocenyl ligand was first isolated during the development of palladium-catalyzed etherifications of aryl halides, as described in the Introduction. This structure now appears to be the ligand that was bound to the active catalyst in the first couplings that formed diaryl ethers and *tert*-butyl ethers in high yields from unactivated aryl halides.[48] Although this ligand was discovered during studies that focused on the formation of aryl ethers from aryl halides, the scope of etherifications catalyzed by complexes of this ligand is narrower than the scope of aminations and Suzuki couplings catalyzed by complexes of this ligand. Yet, these complexes do allow for some types of etherifications under remarkably mild conditions.

As described in communication form earlier,[23] complexes of this ligand catalyze some couplings of aryl halides with alkoxides, siloxides, and phenoxides at room temperature. The scope of these etherifications at room temperature and at 80 °C is shown in Table 14. Electron-rich phenoxides and *tert*-butoxide coupled with electron−neutral or electron-poor aryl bromides to form aryl ethers in the presence of 5 mol % catalyst. Even electron-rich aryl halides such as bromoanisole reacted with *tert*-butoxide to give useful yields of *tert*-butyl aryl ethers, although 80 °C was required for full conversion. Complexes of this ligand also catalyzed the formation of *tert*-butyldimethylsilyl aryl ethers from sodium *tert*-butyldimethylsiloxide and aryl bromides or chlorides. These couplings were limited to electron−neutral or electron-poor aryl halides, but they did occur at room temperature in many cases. Of course, this product is more easily converted to the unprotected phenol than is the *tert*-butyl aryl ether.[73] In addition, etherifications were conducted with Q-phos in an intramolecular fashion. Although

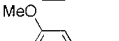
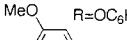
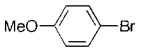
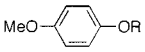
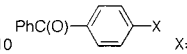
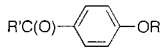
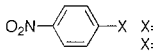
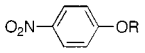
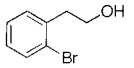
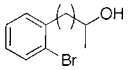
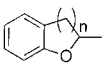
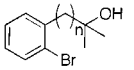
(73) Greene, T. W.; Wuts, P. G. M. In *Protective Groups in Organic Synthesis*; 3rd ed.; John Wiley and Sons: New York, 1991; p 587.

TABLE 13. Reactions of Alkylboronic Acids with Aryl Halides in the Presence of a Combination of $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	alkyl-M	product	conditions[a]	yield (%)[b]
1				1 mol% K_3PO_4/Toluene 100 °C, 2.5-20 h	92
2				1 mol% K_3PO_4/Toluene 100 °C, 30 h	83
3				1 mol% K_3PO_4/Toluene 100 °C, 18 h	94
4				1 mol% K_3PO_4/Toluene 100 °C, 12 h	97
5				1 mol% K_3PO_4/Toluene 100 °C, 48 h	94
6				1 mol% K_3PO_4/Toluene 100 °C, 18 h	88
7				1 mol% K_3PO_4/Toluene 100 °C, 22 h	55[c]

[a] 1:1 ratio of metal to ligand and 1.1−1.5 equiv of boronic acid was used. [b] Unless otherwise stated, all reaction yields are for material determined to be pure by GC and ^1H NMR spectroscopy. [c] Yield estimated by GC using the response factor for the product in entry 1.

TABLE 14. Inter- and Intramolecular Palladium-catalyzed Etherification of Aryl Halides in the Presence of a Combination of 5 Mol % $Pd(dba)_2$ and $Ph_5FcP(t\text{-}Bu)_2$ as Catalyst

entry	aryl halide	product	conditions[a]	yield[b]
1		 R=O-*t*-Bu	RT, 17 h	96%
2		 R=O-*t*-Bu	RT, 14 h	79%
3		R=OTBS	RT, 16 h	99%
4		 R=OC_6H_4-4-OMe	RT, 70 h	99%
5	 X=Br	R=O-*t*-Bu	RT, 19 h	77%
6		R=OTBS	80 °C, 12 h	79%
7	X=Cl	R=O-*t*-Bu	80 °C, 6 h	92%
8		R=OTBS	80 °C, 12h	78%
9		 R=O-*t*-Bu	80 °C, 12h	67%
10	 X=Br	 R=O-*t*-Bu	RT, 6 h	98%
11	X=Br	R=OTBS	RT, 21 h	94%
12	X=Cl	R=O-*t*-Bu	RT, 4 h	98%
13	 X=Br	 R=O-*t*-Bu	RT, 9 h	98%
14	X=Cl	R=O-*t*-Bu	RT, 5 h	93%
15			80 °C, 0.5 h	58%
16			n=1, RT, 5 h	59%
17			n=2, RT, 0.5 h	64%
18			n=1, RT, 15 h	77%
19			n=2, RT, 10 min	93%

[a] Reactions conducted in toluene solvent with a 1:2 ratio of metal to ligand 0.5 mmol aryl halide substrate and 1.2 equiv of alkoxide or siloxide in 2 mL of toluene. [b] Yields are for material judged pure by GC and ^1H NMR spectroscopy.

yields were modest for cyclizations of substrates that bear hydrogens α to oxygen[74] and can undergo β-hydrogen elimination from alkoxide intermediates, cyclization of tertiary alcohols occurred in high yields and in one case in only 10 min.

A comparison of these cyclizations in the presence of palladium and Q-phos to those conducted with the parent $FcP(t\text{-}Bu)_2$ revealed the importance of steric hindrance. The intramolecular cyclization of the substrate in entry 16 and 17 in the presence of a catalyst containing $FcP(t\text{-}Bu)_2$ occurred more slowly than those in the presence of catalysts containing Q-phos. Moreover, extended times and higher temperatures for reactions catalyzed by complexes of $FcP(t\text{-}Bu)_2$ generally produced ketone product from β-hydrogen elimination of the intermediate palladium alkoxide. Thus, the perarylated structure of $Ar_5FcP(t\text{-}Bu)_2$ is important for both high activity and to suppress, at least partially, β-hydrogen elimination.

4. Comparison of Substituted Q-phos Ligands. In addition to evaluating the scope of coupling reactions catalyzed by palladium complexes of Q-phos, we evaluated the catalytic activity of complexes containing analogues of Q-phos that bear substituents on the aryl groups. As stated in Section 1, we prepared several modified versions of Q-phos that contained electron-donating, electron-withdrawing, and more hindered aryl groups on the bottom ring of the ferrocene. In addition, we prepared less substituted versions of these ligands, such as tetraphenylferrocenyl derivatives.

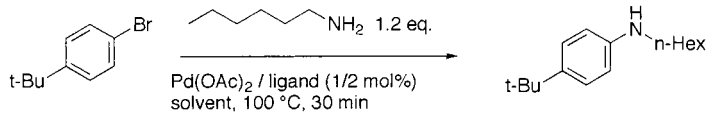
Table 15 shows a comparison of the activity of substituted Q-phos ligands for the coupling of *n*-hexylamine with *p*-bromo *tert*-butylbenzene. Modified ligands were investigated for this reaction because this substrate combination would reveal the effects of ligand substituents on hydrodehalogenation and diarylation processes. In general, *para*-substituents had little or no influence on the reaction rates or selectivity. *Para* substituents on the Q-phos analogues had a similarly small effect on Suzuki reactions catalyzed by complexes containing the Q-phos analogues. These studies do not provide firm data to support or refute the presence of an interaction of these pendant aryl groups with the palladium center. However, the absence of *para* substituent effects argues against the direct interaction of an aryl group of these ligands in the structures of complexes that lie on the reaction pathway and that control rates and selectivities

Table 16 shows the activity of several Q-phos analogues toward the coupling of aryl bromides with *p*-methoxyphenolate. This reaction discriminated between the activity of the various Q-phos derivatives. The more electron-poor ligand containing *p*-CF_3 groups generated less active catalysts than did the more electron-rich ligands lacking a *para* substituent or containing the electron-donating *p*-OMe group. Perhaps the CF_3-substituted ligand is less tightly bound to the metal, and the catalyst is less stable.

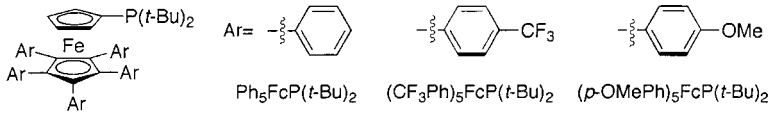
The ligand lacking the fifth phenyl group on the bottom cyclopentadienyl group formed complexes that displayed dramatically lower activity in the coupling reactions. The formation of aryl ethers by the reaction of 4-bromotoluene with sodium *p*-methoxyphenolate (entry 2 of Table 16) occurred in much lower yields when conducted with the tetraaryl version of Q-phos than it did when conducted with the parent ligand. The structures of the tetraphenyl and pentaphenyl ligands, as determined by X-ray diffraction, are provided in Figure 1. Clearly, the unsubstituted position of the bottom Cp ring is located beneath

(74) Torraca, K.; Kuwabe, S.; Buchwald, S. *J. Am. Chem. Soc.* **2000**, *122*, 12907−12908.

TABLE 15. Effect of Ligand Aryl Group Substituents on Selectivity for Coupling of an Unhindered Aryl Halide with an Unbranched Primary Amine

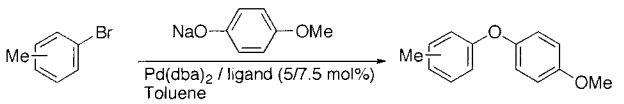


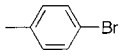
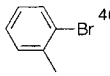
entry	ligand	solvent	t-Bu	Br t-Bu	H N Hex t-Bu	t-Bu N Hex t-Bu
1	$Ph_5FcP(t\text{-}Bu)_2$	toluene	1	0	95	4
2		THF	1	0	97	2
3		1,4-dioxane	5	0	95	<1
4	$(CF_3Ph)_5FcP(t\text{-}Bu)_2$	toluene 30 min	2	11	81	2
5		1 h	3	0	94	6
6	$(p\text{-}OMePh)_5FcP(t\text{-}Bu)_2$	toluene	1	0	84	15

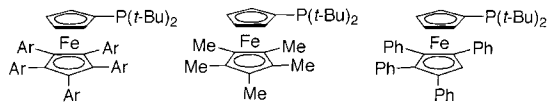


$Ph_5FcP(t\text{-}Bu)_2$ $(CF_3Ph)_5FcP(t\text{-}Bu)_2$ $(p\text{-}OMePh)_5FcP(t\text{-}Bu)_2$

TABLE 16. Comparison of the Activity of Q-phos Analogs for the Formation of Diaryl Ethers



entry	ArX	temp.	ligand	time (h)	yield
1		80 °C	$Ph_5FcP(t\text{-}Bu)_2$	2	83
2			$Ph_4FcP(t\text{-}Bu)_2$	8	31
3			$(p\text{-}OMePh)_5FcP(t\text{-}Bu)_2$	3	91
4			$(CF_3Ph)_5FcP(t\text{-}Bu)_2$	18	29
5			$Me_5FcP(t\text{-}Bu)_2$	8	5
6		40 °C	$Ph_5FcP(t\text{-}Bu)_2$	3	52
7				24	>95
8			$(p\text{-}OMePh)_5FcP(t\text{-}Bu)_2$	3	62
9				24	>95
10			$(CF_3Ph)_5FcP(t\text{-}Bu)_2$	3	41
11				24	>95
12			$(Xylyl)_5FcP(t\text{-}Bu)_2$	3	49
13				24	>95
14		80 °C	$Ph_4FcP(t\text{-}Bu)_2$	8	11



Ar=Ph=$Ph_5FcP(t\text{-}Bu)_2$ $Me_5FcP(t\text{-}Bu)_2$ Ar=Ph=$Ph_4FcP(t\text{-}Bu)_2$

Ar=p-$OMeC_6H_4$=$(p\text{-}OMePh)_5FcP(t\text{-}Bu)_2$

Ar=p-$CF_3C_6H_4$=$(CF_3Ph)_5FcP(t\text{-}Bu)_2$

Ar=3,5-$Me_2C_6H_3$=$(Xylyl)_5FcP(t\text{-}Bu)_2$

the phosphorus ligand. Thus, the four phenyl groups are oriented away from the position where the metal center would reside and from the site of reaction.

The ferrocenyl ligand containing five 3,5-dimethylphenyl groups should be more hindered than the parent Q-phos at the site of the metal and the coupling process. We, therefore, considered that it could generate more active catalysts. However, this ligand generated catalysts that displayed low activity for amination and Suzuki reactions. We did not pursue chemistry with this ligand in depth, but it seems plausible that metalation of the xylyl methyl groups deactivates the catalyst or that the more hindered ligand is too weakly bound to the metal to generate a stable catalyst.

5. Mechanistic Comments. At this time, we have obtained little mechanistic data on the coupling reactions catalyzed by complexes containing Q-phos. However, some comments can be made on the relationship between this system and related systems for which mechanistic studies have been conducted.[75] In most cross-coupling reactions of chloroarenes, the reaction rates are believed to be controlled by the rate of oxidative addition.[76] Transmetalation and reductive elimination are more rapid, and the resting state of the catalyst is a palladium(0) complex.[75] We have generated the Q-phos-ligated palladium(0) complex {$Pd[Ph_5FcP(t\text{-}Bu)_2]$} by addition of this ligand to CpPd(allyl).[23] As is the case for most *tert*-butylphosphine palladium complexes, the stable palladium(0) species containing this ferrocenyl ligand is two-coordinate.

We recently showed that $Pd[P(t\text{-}Bu)_3]_2$ is less stable thermodynamically than the combination of the Pd(0) complex and free aryl chlorides or *ortho*-substituted aryl bromides.[77] This unusual thermodynamic stability of the Pd(0) complex was also observed for the Pd(0) complex of Q-phos {$Pd[Ph_5FcP(t\text{-}Bu)_2]_2$}. No arylpalladium halide was observed by ^{31}P NMR spectroscopy when the Pd(0) complex of Q-phos was treated with phenyl chloride at room temperature or 100 °C. Yet, oxidative addition of the aryl halide to a Pd(0) complex bearing Q-phos must occur, albeit in an endothermic fashion, because the catalytic coupling reactions occurred in all cases at 100 °C. After this oxidative addition, transmetalation of boronic acids, transmetalation of alkoxides, or conversion of the palladium-bound halide to an amide by reaction

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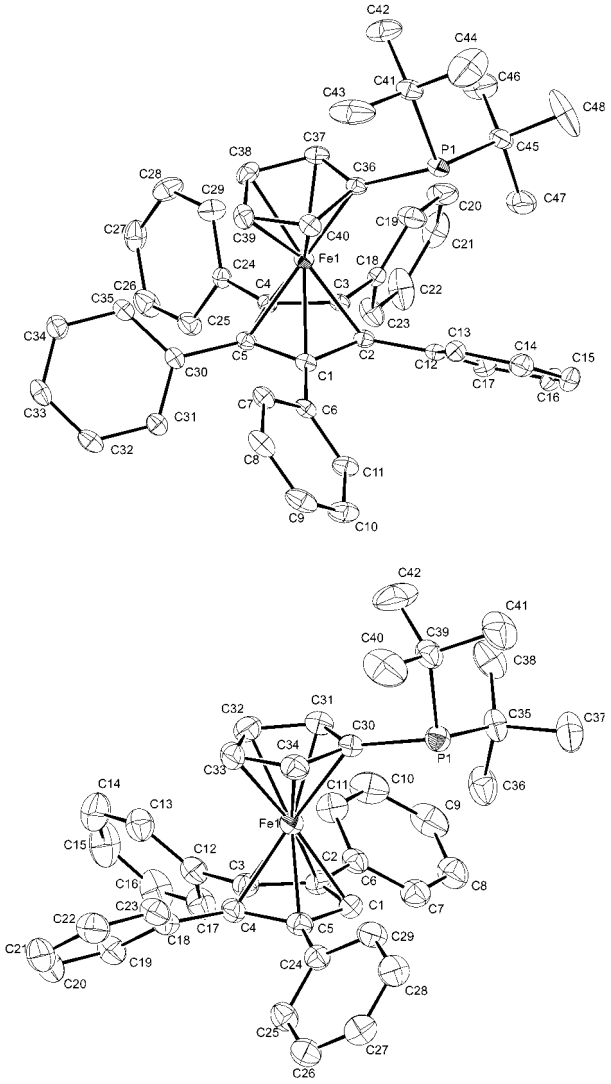

FIGURE 1. ORTEP diagrams of $Ph_5FcP(t\text{-}Bu)_2$ and $Ph_4FcP(t\text{-}Bu)_2$.

of amine and base presumably generates the intermediate that forms the C−C, C−O, or C−N bond in the final product by reductive elimination.[78]

Summary. In summary we have shown that the monophosphine ligand $(Ph_5Fc)P(t\text{-}Bu)_2$ (Q-phos), which owes its existence to sequential P−C bond cleavage of bis(di-*tert*-butylphosphino)ferrocene and pentaarylation of the resulting monophosphine cleavage product observed during aryl halide etherifications, is a structure that generates highly active catalysts for amination and Suzuki reactions. The ligand is air stable and can be prepared in two steps. Equally important to the catalyst activity is a lesson about catalyst structure and activity that is emphasized by the genesis of this ligand. The activity of catalysts that gave ether product from unactivated aryl halides for the first time can be attributed to a sterically hindered structure of the starting bis(di-*tert*-butylphosphino)ferrocene, but the precise structural features of the ligand that gave rise to this activity are far removed from those of the original bisphosphine. Often, phosphine-ligated catalysts undergo P−C cleavage[79] and intramolecular ligand C−H activations.[80,81] In this case, a highly active catalyst for a variety of cross-couplings was generated by reactions that usually deactivate the catalyst.

Experimental Section

General Methods. Reactions were loaded in a drybox and were conducted using 4 mL vials that were sealed with a cap containing a PTFE septum. Toluene was distilled from sodium and benzophenone and stored in the drybox. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. Yields refer to isolated yields of compounds of greater than 95% purity as determined by capillary gas chromatography (GC). Yields reported are an average of two or more runs. Both GC and GC/MS analyses were conducted with an HP-1 methyl silicone column. Reagents were purchased from commercial suppliers, or prepared by standard procedures. 2-(2-Bromophenyl)methyl acetate[21] and sodium *tert*-butyldimethylsiloxide,[82] were prepared by literature procedures.

A. Ligand Preparation. $P(C_5H_4FeC_5H_5)(t\text{-}Bu)_2$. To a solution of Cp_2Fe (10.00 g, 53.80 mmol) in THF (25 mL) at 0 °C was added *t*-BuLi (31.60 mL, 53.80 mmol) over 5 min. The solution was stirred for 20 min, after which time the solvent was removed under vacuum. The residue was redissolved in a mixture of pentane (100 mL) and THF (5 mL), and $ClP(t\text{-}Bu)_2$ (5.330 g, 29.50 mmol) was added. The mixture was stirred for 3 h, after which time degassed MeOH (1 mL) was added. The solvents were then removed in vacuo. The product was purified by filtration through a plug of silica gel under nitrogen. Unreacted ferrocene was eluted all at once with pentane, and the phosphine was then eluted all at once with diethyl ether. Crystallization from pentane of the material obtained from silica gel yielded 7.58 g (78%) of product. ^1H NMR (C_6D_6) δ 1.23 (d, 10.9 Hz, 18 H), 4.04 (s, 5H), 4.08 (m, 2H), 4.17 (m, 2H); $^{13}C\{^1H\}$ NMR (C_6D_6): δ 31.05 (d, 13.9 Hz), 32.78 (d, 22.9 Hz), 69.20 (d, 2.7 Hz), 69.79, 73.23 (d, 12.3 Hz), 79.10 (d, 31.2 Hz); $^{31}P\{^1H\}$ NMR (C_6D_6): δ 27.54 (s). Anal. Calcd for $C_{18}H_{27}FeP$: H: 8.24, C: 65.47; Found: H: 8.34, C: 65.51.

$P(C_5H_4FeC_5Ph_5)(t\text{-}Bu)_2$. A mixture of $P(C_5H_4FeC_5H_5)(t\text{-}Bu)_2$ (1.000 g, 3.030 mmol), $Pd(OAc)_2$ (0.035 g, 0.156 mmol), and NaO-*t*-Bu (2.93 g, 30.5 mmol) was dissolved in PhCl (34.10 g, 303.0 mmol) and heated to 110 °C for 18 h. The solution was filtered through Celite, and PhCl was removed in vacuo. Silica gel chromatography eluting with pentane/Et_20 (80/1) gave 1.466 g (68%) of $P(C_5H_4FeC_5Ph_5)(t\text{-}Bu)_2$ as a pink/red solid. ^1H (C_6D_6): δ 1.07 (d, 11.0 Hz, 18H, Me_3), 4.42 (t, 1.7 Hz, 2H, C_5H_4), 4.67 (d, 1.0 Hz, 2H, C_5H_4), 6.95−6.97 (m, 15H, *m*,*p*-C_6H_5), 7.44−7.48 (m, 10H, *o*-C_6H_5). $^{13}C\{^1H\}$ NMR (C_6D_6): δ 31.31 (d, 13.8 Hz, CMe_3), 33.31 (d, 24.8 Hz, CMe_3), 76.41 (d, 2.6 Hz, C_5H_4), 78.58 (d, 11.4 Hz, C_5H_4), 85.49 (d, 41.6 Hz, *ipso*-C_5H_4), 88.38 (s, C_5Ph_5), 126.67 (s, C_5Ph_5), 127.47 (s, C_5Ph_5), 133.23 (s, C_5Ph_5), 136.32 (s, C_5Ph_5). $^{31}P\{^1H\}$ NMR (C_6D_6): δ 25.49 (s). Anal. Calcd for $C_{48}H_{47}FeP$: C, 81.12; H, 6.67. Found: C, 81.41; H, 6.54.

$[C_5(C_6H_4\text{-}p\text{-}CF_3)_5]Fe[C_5H_4P(t\text{-}Bu)_2]$ and $[C_5(C_6H_4\text{-}p\text{-}OMe)_5]Fe[C_5H_4P(t\text{-}Bu)_2]$. Similar procedures were used to prepare substituted derivatives. $[C_5(C_6H_4\text{-}p\text{-}CF_3)_5]Fe[C_5H_4P(t\text{-}Bu)_2]$: 1.189 g, 37.3%, purified by crystallization from pentane. ^1H NMR (300 MHz, C_6D_6) δ 0.97 (d, J = 11.1 Hz, 18H), 4.10 (br s, 2H), 4.47 (br s, 2H), 7.04−7.11 (m, 20H); ^{13}C NMR (75 MHz, C_6D_6) δ 31.1 (d, J = 13.3 Hz), 33.5 (d, J = 24.7 Hz), 76.8, 78.4 (d, J = 9.0 Hz), 87.4, 87.9 (d, J = 22.0 Hz), 124.7 (q, J = 272 Hz), 124.8 (d, J = 3.4 Hz), 129.7 (q, J = 32.4 Hz), 133.0, 138.9; $^{31}P\{^1H\}$ NMR (300 MHz, C_6D_6) δ 23.6. $[C_5(C_6H_4\text{-}p\text{-}OMe)_5]Fe[C_5H_4P(t\text{-}Bu)_2]$. 93.6 mg 3.6% yield, purified by crystallization

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from ether at −30 °C. ^{1}H NMR (300 MHz, C_6D_6) δ 1.13 (d, J = 11.1 Hz, 18H), 3.22 (s, 15H), 4.51 (br s, 2H), 4.73 (br s, 2H), 6.62 (d, J = 8.7 Hz, 10H), 7.47 (d, J = 8.7 Hz, 10H); ^{13}C NMR (75 MHz, C_6D_6) δ 31.4 (d, J = 13.5 Hz), 33.4 (d, J = 24.6 Hz), 54.5, 76.3, 78.4 (d, J = 11.1 Hz), 84.8 (d, J = 39.9 Hz), 87.6, 113.1, 128.6, 134.3, 158.6; ^{31}P{^{1}H} NMR (300 MHz, C_6D_6) δ 26.5, Anal. Calcd for $C_{53}H_{57}O_5PFe$: C, 73.95; H, 6.67. Found: C, 73.76; H, 6.40.

P($C_5H_4FeC_5HPh_4$)(t-Bu)$_2$. A mixture of P($C_5H_4FeC_5H_5$)(t-Bu)$_2$ (0.500 g, 1.500 mmol), $Pd(OAc)_2$ (0.0175 g, 0.0781 mmol), and $NaOC_6H_4$-4-OCH_3 (2.230 g, 15.30 mmol) was dissolved in PhCl (17.10 g, 152.0 mmol) and heated at 110 °C for 18 h. The solution was filtered through Celite, and PhCl was removed in vacuo. The solid materials were redissolved in THF, concentrated, and layered with pentane at −35 °C. A bulk sample that was analytically pure was not available, but a sample of roughly 80% purity containing orange crystals of the tetraphenylferrocenyl phosphine was obtained (0.451 g, 47.4%). ^{1}H (C_6D_6): δ 1.09 (d, 11.1 Hz, 18H, CMe_3), 4.01 (broad s, 2H, C_5H_4), 4.33 (t, 1.7 Hz, 2H, C_5H_4), 5.01 (s, 1H, C_5HPh_4), 6.93−7.14 (m, 12H, m,p-C_5HPh_4), 7.30 (dd, 7.2 Hz, 0.9 Hz, 4H, o-C_5HPh_4), 7.66 (dd, 7.7 Hz, 1.7 Hz, 4H, o'-C_5HPh_4). ^{13}C{^{1}H} δ 31.00 (d, 13.6 Hz, CMe_3), 33.01 (d, 22.4 Hz, CMe_3), 76.51 (s, CHC_4Ph_4), 77.15 (s, C_5H_4), 78.31 (d, 9.7 Hz, C_5H_4), 81.86 (d, 33.6 Hz, *ipso*-C_5H_4), 87.50 (s, CHC_4Ph_4), 88.12 (s, CHC_4Ph_4), 126.70 (s, C_5HPh_4), 127.68 (s, C_5HPh_4), 127.90 (s, C_5HPh_4), 130.99 (s, C_5HPh_4), 131.05 (s, C_5HPh_4), 132.68 (s, C_5HPh_4), 136.66 (s, C_5HPh_4), 137.87 (s, C_5HPh_4). ^{31}P{^{1}H} NMR (C_6D_6): δ 25.34 (s). HRMS: m/e Calcd, 634.2452; Found, 634.2444.

P[$C_5H_4FeC_5$(3,5-$Me_2C_6H_3$)$_5$](t-Bu)$_2$. A mixture of P(C_5H_4-FeC_5H_5)(t-Bu)$_2$ (200 mg, 0.606 mmol), $Pd(OAc)_2$ (14 mg, 0.061 mmol), and NaO-t-Bu (582 mg, 6.06 mmol) was dissolved in 11.2 g (60.6 mmol) of 5-bromo-m-xylene and heated at 110 °C for 18 h. The solution was filtered through Celite and then concentrated by heating at 80 °C under vacuum. The product was isolated from the crude concentrated solution by silica gel chromatography. A yellow byproduct fraction eluted first with an eluent of 100:1 pentane Et_2O. The red product was then eluted with a 80:1 mixture of pentane/Et_2O to give 154 mg (30%) of P[$C_5H_4FeC_5$(3,5-$Me_2C_6H_3$)$_5$](t-Bu)$_2$ as a red solid that was judged to be roughly 95% pure by ^{1}H NMR spectroscopy. ^{1}H NMR δ 7.27 (s, 10 H), 6.70 (s, 5 H), 4.83 (q, 1.6 Hz, 2 H), 4.68 (t, 1.6 Hz, 2 H), 2.07 (s, 30 H), 1.12 (d, 10.8 Hz, 18 H); ^{31}P{^{1}H} NMR (C_6D_6): δ 26.11 (s).

P($C_5H_5FeC_5Me_5$)P(t-Bu)$_2$. Cp*H (97 mg, 071 mmol) was dissolved in 3 mL of THF. n-BuLi (0.285 mL of a 2.5 M solution, 0.713 mmol) was added dropwise, and the solution was stirred for 15 min to precipitate Cp*Li. $Fe(acac)_2$ (181 mg, 0.713 mmol) was added, and the solution was stirred for 20 min. In a separate vial, $C_5H_5P(t\text{-Bu})_2$ (200 mg, 0.951 mmol), which was prepared from NaCp and $ClP(t\text{-Bu})_2$, was treated with 0.285 mL of a 2.5 M solution of BuLi (0.71 mmol) of n-BuLi at room temperature in 3 mL of THF. The resulting Li[$C_5H_4P(t\text{-Bu})_2$] was added to the solution of Cp* iron complex, and the resulting mixture was stirred for 16 h. After this time, the solution was filtered through Celite and the solvent evaporated. Silica gel chromatography was conducted under nitrogen first washing the column with pentane and then eluting product with a 4:1 mixture of pentane and toluene. The product fractions were combined, the solvent was removed, and the product was recrystallized from pentane to provide 51 mg (18%) of product. ^{1}H NMR δ 1.25 (d, 10.8 Hz, 18 H), 1.81 (s, 15 H), 3.686 (t, 1.4 Hz, 2 H), 3.85 (broad s, 2H); ^{13}C NMR δ 11.499 (s), 31.20 (d, 13.8 Hz), 32.90 (d, 24 Hz), 73.74 (d, 2.2 Hz), 74.17 (d, 10.0 Hz), 79.01 (d, 31.1 Hz), 80.08 (s); ^{31}P NMR 23.06 (s). Anal. Calcd for $C_{23}H_{37}FeP$ C, 69.00; H 9.32. Found: C, 68.82, H, 9.37.

Amination of Aryl Halides. General Methods. Procedure A. A typical procedure is given for the reaction of entries 1 and 2 in Table 1. A 4 mL vial was charged with bromobenzene (171 mg, 1.10 mmol), diphenylamine (169 mg, 1.00 mmol), $Pd(dba)_2$ (5.9 mg, 1 mol %), $Ph_5FcP(t\text{-Bu})_2$ (7.1 mg, 2 mol %), and sodium *tert*-butoxide (144 mg, 1.50 mmol). Anhydrous toluene (2 mL) was added into the mixture, and the vial was then sealed with a cap containing PTFE septum. The reaction mixture was stirred at room temperature for 1 h. After the starting aryl halide was consumed, as determined by GC, the reaction solution was directly adsorbed onto silica gel, and the product was isolated by eluting with hexane/ethyl acetate to give 244 mg (99%) of triphenylamine as a white solid. Reaction of chlorobenzene (62 mg, 0.55 mmol) with diphenylamine (85 mg, 0.50 mmol) proceeded at 80 °C over 21 h to give triphenylamine (121 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (t, 6H, 7.2 Hz), 7.11 (d, 6H, 7.6 Hz), 7.02 (app.t, 3H, 7.2 and 7.6 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 147.83, 129.17, 124.14, 122.63. GC/MS (EI): m/z 245 (M^+).

General Methods. Procedure B. A typical procedure is given for the reaction of entry 6 in Table 7. A 4 mL vial was charged with 4-*tert*-butylbromobenzene (108 mg, 0.51 mmol), $Pd(OAc)_2$ (3.1 mg, 1 mol %), $Ph_5FcP(t\text{-Bu})_2$ (7.1 mg, 2 mol %), and sodium *tert*-butoxide (60 mg, 0.60 mmol). Anhydrous toluene was added, and the vial was sealed with a cap containing PTFE septum and removed from the drybox. 80 mL of n-hexylamine was added to the vial through the septum using a syringe. Reaction mixture was then heated to 100 °C for 2 h to give the title compound (113 mg, 95%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26 (d, 2H, 8.4 Hz), 6.62 (d, 2H, 8.4 Hz), 3.51 (bs, 1H), 3.14 (t, 2H, 7.2 Hz), 1.66 (m, 2H), 1.34−1.43 (m, 6H), 1.34 (s, 9H, t-Bu), 0.96 (t, 3H, 6.3 and 6.9 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 146.14, 139.75, 125.92, 112.35, 44.11, 33.76, 31.63, 31.53, 29.58, 26.86, 22.62, 14.05. GC/MS(EI): m/z 233 (M^+). Anal. Calcd for $C_{16}H_{27}N$: C, 82.34; H, 11.82; N, 6.00. Found: C, 82.55; H, 11.82; N, 6.06.

Reactions of Aryl Halides with Boronic Acids. General Procedure A. A typical procedure is given for the reaction of entry 1 in Table 10. A 4 mL vial was charged with 4-bromobenzophenone (268 mg, 1.03 mmol), o-tolylboronic acid (152 mg, 1.12 mmol), KF (116 mg, 2.00 mmol), $Pd(dba)_2$ (5.8 mg, 1 mol %), and $Ph_5FcP(t\text{-Bu})_2$ (7.1 mg, 2 mol %). Anhydrous toluene (2 mL) was added to the mixture, and the vial was sealed with a cap containing PTFE septum and removed from the drybox. The reaction solution was stirred at room temperature for 18 h. After the starting aryl halide was consumed, the reaction solution was directly absorbed onto silica gel, and the coupling product was isolated by eluting with hexane/ethyl acetate to give 275 mg (98%) of 4-(2-methylphenyl)benzophenone as a solid.

General Procedure B: A typical procedure is given for the reaction of entry 1 in Table 13. A 4 mL vial was charged with 4-*tert*-butylbromobenzene (213 mg, 1.00 mmol), $Pd(dba)_2$ (5.8 mg, 1 mol %), $Ph_5FcP(t\text{-Bu})_2$ (14.2 mg, 2 mol %), K_3PO_4 (430 mg, 2.02 mmol, powdered), and n-butylboronic acid (124 mg, 1.21 mmol). Anhydrous toluene (2 mL) and a stirring bar were added, and the vial was then sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was stirred at 100 °C for 2.5 h. After the starting aryl halide was consumed as determined by GC, the reaction solution was cooled to room temperature. The reaction solution was then adsorbed onto silica gel directly, and the product was isolated by eluting with ethyl acetate/hexanes to give 175 mg (92%) of 4-*tert*-butyl-1-n-butylbenzene as colorless oil. Kugelrohr distillation was used for further purification.

General Procedure for the Formation of Diaryl Ethers. A 4 mL vial was charged with 2-bromotoluene (86 mg, 0.50 mmol, $Pd(dba)_2$, 14 mg (0.025 mmol), $Ph_5FcP(t\text{-Bu})_2$ (26 mg, 0.38 mmol), and sodium p-methoxyphenoxide (88 mg, 0.60 mmol). Anhydrous toluene (2.5 mL) was added, and the vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was heated at 40 °C for 24 or 70 h at room temperature. The reaction solution was then adsorbed onto silica gel, and the product was isolated by eluting with ethyl acetate/hexanes (0 to 10% gradient) to give 106 mg (99%) of diaryl ether. ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3H), 3.83 (s, 3H), 6.83−6.96 (m, 5H), 7.05 (t, 7.4 Hz, 1H), 7.16 (t,

7.7 Hz, 1H), 7.27 (d, 7.3 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 16.19, 55.59, 114.71, 117.93. 119.27, 123.01, 126.91, 128.99, 131.23, 151.00, 155.21, 155.74.

General Procedure for the Palladium-Catalyzed Etherification of Aryl Halides Using *tert*-BuONa (entry 1, Table 14). A typical procedure is given for the reaction of entry 1 in Table 14. A 4 mL vial was charged with bromobenzene (63 mg, 0.40 mmol), $Pd(dba)_2$ (11.5 mg, 0.0200 mmol), $Ph_5FcP(t\text{-}Bu)_2$ (14.2 mg, 0.0200 mmol), and sodium *tert*-butoxide (47 mg, 0.48 mmol). Anhydrous toluene (2 mL) was added, and the vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was stirred at room temperature for 23 h. The reaction solution was then adsorbed onto silica gel, and the product was isolated by eluting with ethyl acetate/hexanes (0 to 10% gradient) to give 58 mg (97%) of *tert*-butoxybenzene.

General Procedure for the Palladium-Catalyzed Etherification of Aryl Halides with Sodium *tert*-Butyldimethylsiloxide. The reaction conditions and results are shown in Table 14. A typical procedure is given for the reaction of entry 3 in Table 1. A 4 mL vial was charged with 2-bromotoluene (86 mg, 0.50 mmol), $Pd(dba)_2$ (14.0 mg, 0.0243 mmol), $Ph_5FcP(t\text{-}Bu)_2$ (18.0 mg, 0.0254 mmol), and sodium *tert*-butyl-dimethylsiloxide (92 mg, 0.60 mmol). Anhydrous toluene (2 mL) was added to the vial, and the vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was stirred at room temperature for 48 h. The reaction solution was then adsorbed onto silica gel, and the product was isolated by eluting with ethyl acetate/hexanes (0 to 10% gradient) to give 110 mg (99%) of 2-(*tert*-butyldimethylsilyloxy)toluene.

General Procedure for the Palladium-Catalyzed Intramolecular Etherification. The reaction conditions and results are shown in Table 14. A typical procedure is given for the reaction of entry 19 in Table 14. A 4 mL vial was charged with 4-(2-bromophenyl)-2-methyl-2-butanol (97 mg, 0.40 mmol), $Pd(dba)_2$ (11.5 mg, 0.0200 mmol), $Ph_5FcP(t\text{-}Bu)_2$ (14.2 mg, 0.0200 mmol), and sodium *tert*-butoxide (46 mg, 0.48 mmol). Anhydrous toluene (2 mL) was added into the vial, and the vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was stirred at room temperature for 10 min. The reaction solution was adsorbed onto silica gel and isolated by eluting with 5% ethyl acetate in hexanes to give 60 mg (93%) of 2,2-dimethylchroman as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.10−7.06 (m, 2H), 6.86−6.78 (m, 2H), 2.80 (dd, 6.6, 6.9 Hz, 2H), 1.82 (dd, 6.6, 6.9 Hz, 2H), 1.35 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.21, 26.65, 32.55, 73.86, 116.98, 119.33, 120.67, 126.98, 129.20, 153.73. GC/MS: *m*/*z* 162 (M^+).

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Supporting Information Available: Full reaction procedures, spectroscopic and elemental analytical data on isolated compounds, and details of the X-ray structure determination. This material is available free of charge via the Internet at http://pubs.acs.org.

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