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Design of Benzimidazolyl Phosphines Bearing Alterable *P,O* or *P,N*-Coordination: Synthesis, Characterization, and Insights into Their Reactivity

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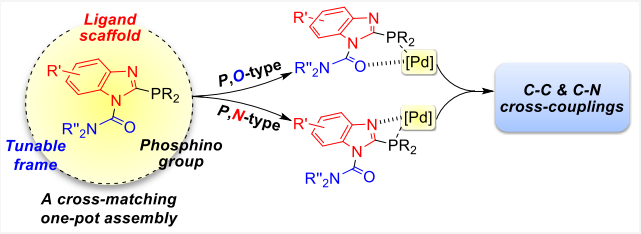
ABSTRACT: A new series of hemilabile benzimidazolyl phosphines is reported. Entities in this ligand family can be easily assembled and prepared on a large scale via a simple one-pot procedure. X-ray crystallographic analyses show that the Pd metal center can coordinate in different fashions, where it relies on the size of the $-PR_2$ group. With the same ligand scaffold, the ligand having a $-PCy_2$ moiety displays better efficiency in expediting aromatic C−C bond-coupling reactions, while the ligand associated with a $-P\text{-}t\text{-}Bu_2$ group, in contrast, promotes C−N bond-forming reactions.



INTRODUCTION

Palladium-catalyzed cross-couplings have constituted numerous applications in pharmaceutical and natural product syntheses.[1] In the past few decades, substantial efforts have been undertaken by scientists aiming to explore unique phosphine ligands that allow a specific coupling reaction to proceed efficiently and smoothly.[2] Yet, the synthetic routes for attaining specially designed ligands often require multiple steps and/or employ relatively expensive reagents (e.g. requires −Br group(s) for Br/Li exchange at the synthetic precursor) and, in some cases, involve chromatographic purification. Thus, the creation of a synthetic procedure featuring easy, straightforward, and streamlined synthetic route advantages is highly desirable.

Distinctive ligand skeletons have been highlighted to be important for facilitating cross-coupling reactions. They generally possess an electron-rich nature (to promote OA, i.e. oxidative addition) and a sterically congested characteristic (to improve RE, i.e. reductive elimination). Particularly, a phosphine ligand associated with a proximal hemilabile coordinating group would beneficially offer additional catalyst longevity.[3]

The Guram and Bei group reported *P,O*-type ligands for Suzuki−Miyaura coupling and Buchwald−Hartwig amination of aryl chlorides in 1999.[4] Later, Hor,[5] Singer,[6] Stradiotto,[7] and other research groups[8] showed new examples of mixed-donor chelating ligands, which were able to tackle difficult cross-coupling processes. In 2011, McNulty reported *P,O*- and *P,N*-type heterocyclic phosphines.[9] It was suggested that different conformational features of the corresponding palladium complexes would dramatically influence the catalytic activity.

We recently reported the heterocyclic hemilabile *P,O*- and *P,N*-type phosphine ligands Bphos,[10] PhMezole-phos,[11] and PhenCar-Phos[12] for palladium catalysis (Figure 1A). In a continuation of our research interest of developing heterocyclic phosphines,[13] herein we report our exploration of a new family of benzimidazolyl phosphines with a unique coordination

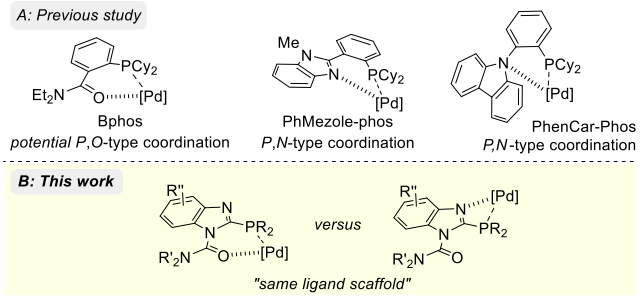


Figure 1. Previous ligand structures/coordination modes and the present investigations.

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manner, which can be altered by the steric bulkiness of the $-PR_2$ group (Figure 1B).[14]

RESULTS AND DISCUSSION

Synthesis and Characterization of Benzimidazolyl-Based Phosphine Ligand. We designed a phosphine ligand family on the basis of the criteria of easy diversification and simple synthetic procedure. Thus, we chose a modular assembly approach across three commercially available starting components: (1) a main ligand scaffold, (2) a phosphino group, and (3) a tunable hemilabile framework (Figure 2).

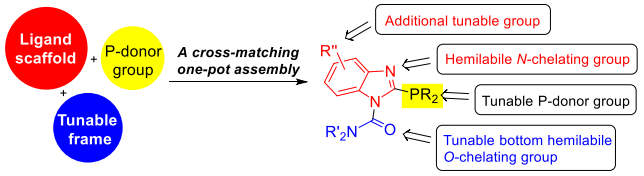


Figure 2. Features of a proposed simple and easily diversified phosphine ligand family.

This strategy allowed plentiful modification of the ligand structure. It is of note that these ligands can be easily accessed via a simple one-pot synthetic pathway (Figure 3). This

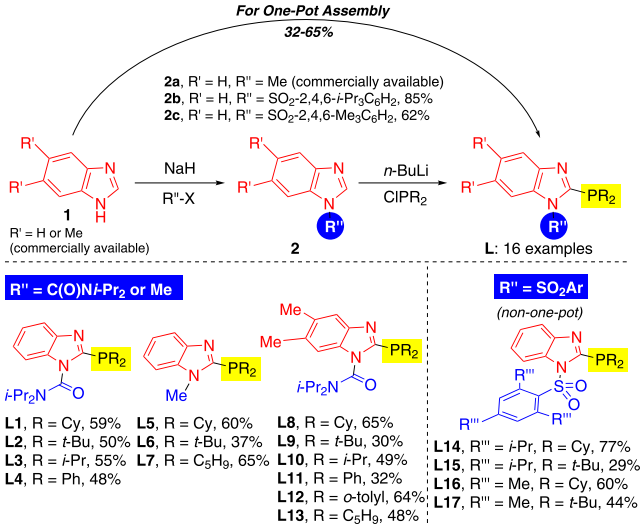


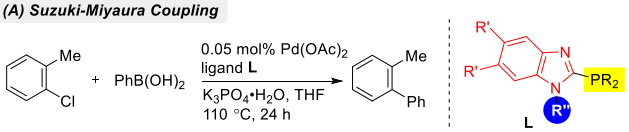
Figure 3. Simple synthetic pathways for the benzimidazolyl phosphine ligand family.

synthetic route even allowed scale-up to a sub-kilogram level (~0.2 kg) without deleterious effects. Upon purification of the product by crystallization, a variety of new air-stable phosphine ligands were conveniently afforded (Figure 3).

Catalytic Studies of Pd/L Catalyst. With the newly developed phosphine ligands in hand, we then investigated their efficacy, with respect to their ligand scaffold in Pd-catalyzed C−C and C−N coupling of aryl chlorides (Table 1). In Suzuki−Miyaura coupling, **L1** and **L8** bearing a carbamoyl group with a $-PCy_2$ moiety exhibited the best catalytic performance, while **L2** and **L9** (with a $-P$-*t*-Bu_2 group) did not (selected examples are shown in Table 1A; see Table S1 in the Supporting Information for details). Ligand **L8** with dimethyl substitution on the 5,6-positions of the benzimidazole ring made an improvement in the coupling reactions. This can possibly be attributed to ligand **L8** showing a more upfield

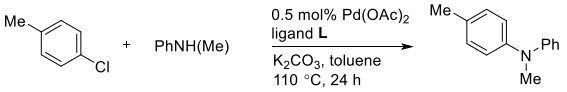
Table 1. Evaluation of Ligand Efficacy (Selected) in Suzuki−Miyaura Coupling and Buchwald−Hartwig Amination of Aryl Chlorides[a]

(A) Suzuki-Miyaura Coupling



entry	ligand **L**	-PR_2	R'	R''	%yield(GC)
1	**L1**	-PCy_2	H	-C(O)N-*i*-Pr_2	43
2	**L2**	-P*t*-Bu_2	H	-C(O)N-*i*-Pr_2	8
3	**L3**	-P*i*-Pr_2	H	-C(O)N-*i*-Pr_2	18
4	**L4**	-PPh_2	H	-C(O)N-*i*-Pr_2	0
5	**L5**	-PCy_2	H	-Me	18
6	**L8**	-PCy_2	Me	-C(O)N-*i*-Pr_2	57
7	**L9**	-P*t*-Bu_2	Me	-C(O)N-*i*-Pr_2	13
8	**L14**	-PCy_2	H	-SO_2-2,4,6-*i*-$Pr_3C_6H_2$	3
9	**L16**	-PCy_2	H	-SO_2-2,4,6-$Me_3C_6H_2$	3

(B) Buchwald-Hartwig Amination



entry	ligand **L**	-PR_2	R'	R''	%yield(GC)
10	**L1**	-PCy_2	H	-C(O)N-*i*-Pr_2	1
11	**L2**	-P*t*-Bu_2	H	-C(O)N-*i*-Pr_2	57
12	**L3**	-P*i*-Pr_2	H	-C(O)N-*i*-Pr_2	1
13	**L4**	-PPh_2	H	-C(O)N-*i*-Pr_2	0
14	**L5**	-PCy_2	H	-Me	0
15	**L6**	-P*t*-Bu_2	H	-Me	5
16	**L8**	-PCy_2	Me	-C(O)N-*i*-Pr_2	6
17	**L9**	-P*t*-Bu_2	Me	-C(O)N-*i*-Pr_2	80
18	**L15**	-P*t*-Bu_2	H	-SO_2-2,4,6-*i*-$Pr_3C_6H_2$	2
19	**L17**	-P*t*-Bu_2	H	-SO_2-2,4,6-$Me_3C_6H_2$	3

[a]Reaction conditions: for Suzuki−Miyaura coupling, 2-chlorotoluene (1.0 mmol), phenylboronic acid (1.5 mmol), $K_3PO_4{\cdot}H_2O$ (3.0 mmol), 0.05 mol % $Pd(OAc)_2$, Pd/**L** = 1/2, and THF (3 mL) were stirred for 24 h at 110 °C under a nitrogen atmosphere; for the amination reaction, 4-chlorotoluene (1.0 mmol), *N*-methylaniline (1.5 mmol), K_2CO_3 (2.5 mmol), 0.5 mol % $Pd(OAc)_2$, Pd/**L** = 1/4, $PhB(OH)_2$ (0.02 mmol), and toluene (3 mL) were stirred for 24 h at 110 °C under a nitrogen atmosphere. Calibrated GC yields are reported using dodecane as the internal standard. All entries are an average of two runs.

value in ^{31}P NMR in comparison to **L1** (see Table S1 in the Supporting Information). In a C−N bond-forming reaction, 4-chlorotoluene and *N*-methylaniline were chosen as exemplary substrates to evaluate the ligand efficacy (selected examples are shown in Table 1B; see Table S3 in the Supporting Information for details). Interestingly, a reversal of activity (**L1**/**L8** versus **L2**/**L9**) was observed in this reaction.

In addition to a ligand survey, various bases and solvents were examined to obtain the best reaction conditions in the Suzuki−Miyaura coupling of aryl chlorides (Table 2; see Table S2 in the Supporting Information for details). Among the bases commonly used for screening (entries 1−5), $K_3PO_4{\cdot}H_2O$ was found to be the best choice for the reaction (entry 1). THF gave a better result in comparison to dioxane and toluene (entries 1 and 6−8). Further investigations of the Pd to ligand ratio (entries 1 and 9−11) indicated that a ratio of 1/3 gave the best yield (75%). The product yield was greatly improved by increasing the reaction temperature to 110 °C to afford a 93% yield (entry 1 vs entry 12).

Encouraged by the favorable screening results, we next examined a variety of aryl chlorides and arylboronic acids

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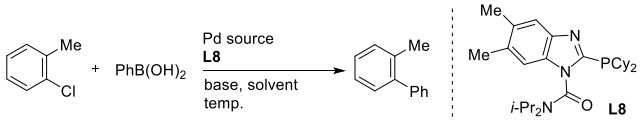
Table 2. Optimization of Reaction Conditions in Suzuki–Miyaura Coupling of Aryl Chlorides[a]



entry	Pd (Pd/L ratio)	base	solvent	yield (%)[b]
1	$Pd(OAc)_2$ (1/3)	$K_3PO_4·H_2O$	THF	75
2	$Pd(OAc)_2$ (1/3)	K_3PO_4	THF	55
3	$Pd(OAc)_2$ (1/3)	K_2CO_3	THF	62
4	$Pd(OAc)_2$ (1/3)	NaO-*t*-Bu	THF	0
5	$Pd(OAc)_2$ (1/3)	Cs_2CO_3	THF	4
6	$Pd(OAc)_2$ (1/3)	$K_3PO_4·H_2O$	dioxane	35
7	$Pd(OAc)_2$ (1/3)	$K_3PO_4·H_2O$	toluene	17
8	$Pd(OAc)_2$ (1/3)	$K_3PO_4·H_2O$	*t*-BuOH	13
9	$Pd(OAc)_2$ (1/1)	$K_3PO_4·H_2O$	THF	14
10	$Pd(OAc)_2$ (1/2)	$K_3PO_4·H_2O$	THF	57
11	$Pd(OAc)_2$ (1/4)	$K_3PO_4·H_2O$	THF	34
12[c]	$Pd(OAc)_2$ (1/3)	$K_3PO_4·H_2O$	THF	93

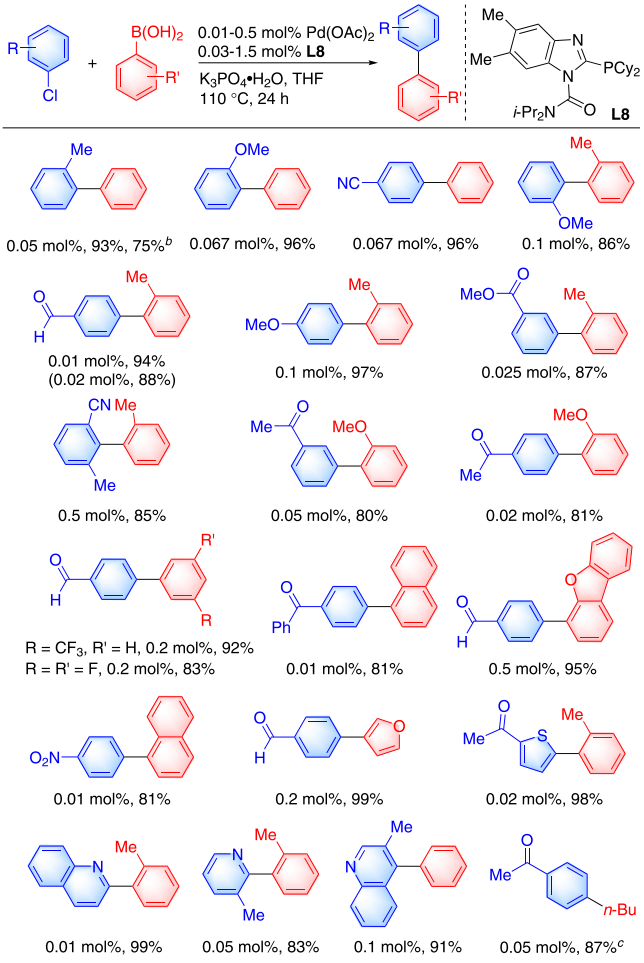
[a]Reaction conditions unless specified otherwise: 2-chlorotoluene (1.0 mmol), phenylboronic acid (1.5 mmol), base (3.0 mmol), Pd source (0.05 mol %), **L8** (indicated in Table 1), and solvent (3 mL) were stirred for 24 h at 100 °C under a nitrogen atmosphere. [b]Calibrated GC yields are reported using dodecane as the internal standard, average of two runs. [c]At 110 °C.

under the optimized reaction conditions (Scheme 1). Deactivated and functionalized aryl/heteroaryl chlorides were compatible with the Pd/**L8** catalyst system, and the Pd catalyst loading was able to be lowered to 0.01 mol %. A sterically hindered tri-*ortho*-substituted biaryl compound was afforded smoothly with 0.5 mol % catalyst loading. The bulky 4-chloro-3-methylquinoline was a feasible coupling partner for the reaction to give the desired product in excellent yield (91%). Notably, the coupling of *β*-hydrogen-containing alkylboronic acid with aryl chloride was also successful.

Upon a change in the phosphino moiety of the ligand from $-PCy_2$ to $-P$-*t*-Bu_2 (e.g., **L8** to **L9**), a variety of aryl/heteroaryl chlorides and primary/secondary amines were coupled smoothly in this *N*-arylation process (Table 1B). To further investigate the ligand efficacy, an optimization of the reaction conditions for the amination reaction of 4-chlorotoluene was carried out (Table 3; see Table S4 in the Supporting Information for details). K_2CO_3 showed the best performance among the other bases investigated (entries 1–5). Upon a survey of commonly used organic solvents, toluene gave the best yields. Remarkably, a 92% yield was observed when the metal to ligand ratio was 1/5. Further increasing the ratio to 1/6 resulted in a decrease in the product yield (entries 2 and 9–13).

Aryl or heteroaryl chlorides were applicable coupling partners in this *N*-arylation process. Most aniline substrates were allowed to couple with aryl chlorides in good yields when the Pd/**L9** system was employed (Scheme 2). To further investigate the efficiency of the new benzimidazolyl-phosphine ligands, a more challenging amination reaction was tested using sterically congested aryl chlorides and sterically hindered anilines as the coupling partners. The amination reactions proceeded well with the sterically demanding aryl chlorides with an aniline containing di-*o*-methyl groups, or even 2,6-diisopropyl substituents, with 1.0 mol % Pd loading. The *ortho*-substituted, electron-poor anilines were seldom able to couple

Scheme 1. Pd-Catalyzed Suzuki–Miyaura Coupling of Aryl Chlorides[a]



[a]Reaction conditions unless specified otherwise: ArCl (1.0 mmol), Ar′B(OH)$_2$ (1.5 mmol), $K_3PO_4·H_2O$ (3.0 mmol), $Pd(OAc)_2$/**L8** = 1/3, and THF (3 mL) were stirred for 24 h at 110 °C under a nitrogen atmosphere. Isolated yields are reported. A gram-scale synthesis (ArCl (8.0 mmol), Ar′B(OH)$_2$ (20.0 mmol), $K_3PO_4·H_2O$ (24.0 mmol), $Pd(OAc)_2$/**L8** = 1/3, and THF (15 mL) were stirred for 24 h at 75 °C under a nitrogen atmosphere) is shown in parentheses. [b]**L1** was used as the ligand. [c]*n*-BuB(OH)$_2$ (2.0 mmol) and toluene (3 mL) were used.

with *ortho*-substituted aryl chlorides, as electron-deficient anilines are poor nucleophiles.[15] Herein, we successfully demonstrated the C–N coupling of sterically hindered 2-chloro-3-methylbenzonitrile with 3-fluoro-2-methylaniline using 3.0 mol % Pd loading.

Metal Complex of Pd/L Catalyst. To further investigate the unique binding properties of the ligand **L** series, single crystals of Pd complexes from $PdCl_2(CH_3CN)_2$ and the ligands were grown. Single crystals of complexes **3** and **4** for X-ray diffraction studies were obtained by vapor diffusion of hexane into a dichloromethane solution containing the $PdCl_2$·**L** complex. Interestingly, the crystal structure of $PdCl_2$·**L9** with the bulky $-P$-*t*-Bu_2 moiety was found to coordinate in a κ^2-*P*,*N* fashion (Figure 4), while $PdCl_2$·**L8** with the less sterically congested $-PCy_2$ group was a dimeric complex, in which the bottom carbamoyl oxygen pointed toward the Pd center and exhibited a potential *P*,*O*-hemilabile ability (Figure 5). These results indicated that the metal–ligand coordination depends

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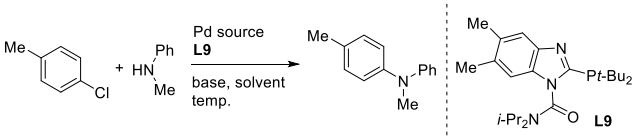
Table 3. Optimization of Reaction Conditions in Amination of Aryl Chlorides[a]



entry	Pd (Pd/L ratio)	base	solvent	yield (%)[b]
1	$Pd(OAc)_2$ (1/4)	$K_3PO_4·H_2O$	toluene	19
2	$Pd(OAc)_2$ (1/4)	K_3PO_4	toluene	18
3	$Pd(OAc)_2$ (1/4)	K_2CO_3	toluene	30
4	$Pd(OAc)_2$ (1/4)	NaO-*t*-Bu	toluene	3
5	$Pd(OAc)_2$ (1/4)	Cs_2CO_3	toluene	8
6	$Pd(OAc)_2$ (1/4)	K_2CO_3	dioxane	17
7	$Pd(OAc)_2$ (1/4)	K_2CO_3	THF	14
8	$Pd(OAc)_2$ (1/4)	K_2CO_3	*t*-BuOH	13
9[c]	$Pd(OAc)_2$ (1/1)	K_2CO_3	THF	34
10[c]	$Pd(OAc)_2$ (1/2)	K_2CO_3	THF	67
11[c]	$Pd(OAc)_2$ (1/3)	K_2CO_3	THF	70
12[c]	$Pd(OAc)_2$ (1/5)	K_2CO_3	THF	92
13[c]	$Pd(OAc)_2$ (1/6)	K_2CO_3	THF	72

[a]Reaction conditions unless specified otherwise: 4-chlorotoluene (1.0 mmol), *N*-methylaniline (1.5 mmol), base (3.0 mmol), Pd source (0.2 mol %), **L9** (indicated in Table 1), $PhB(OH)_2$ (0.02 mmol), and solvent (3 mL) were stirred for 24 h at 100 °C under a nitrogen atmosphere. [b]Calibrated GC yields are reported using dodecane as the internal standard, average of two runs. [c]0.5 mol % of $Pd(OAc)_2$ was used.

on the steric bulk of the phosphino moiety. The coordination mode of the ligand to the metal can be changed by varying the bulkiness of the phosphino group.

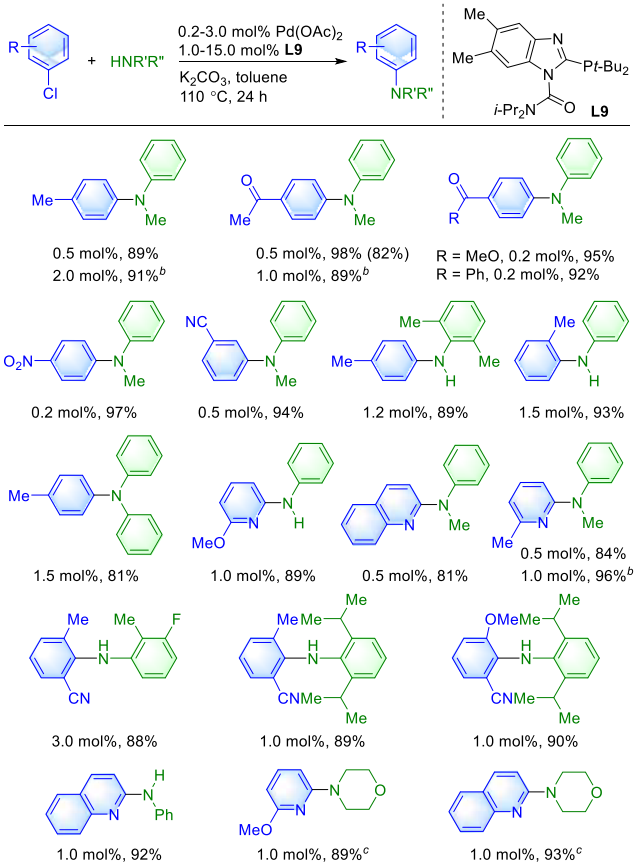
CONCLUSIONS

In summary, we have developed a new family of hemilabile benzimidazolyl phosphines **L**, which can be easily accessed and readily fine tuned by an intended matching of three fragments via a one-pot synthetic procedure. The X-ray structures of the palladium complex in this ligand family showed possible static *P,O* or *P,N* coordination to palladium. A molecular dynamics study using computational means has yet to be conducted at this stage. To the best of our knowledge, we have succeeded in showing the first examples of a ligand family that have both *P,O* and *P,N* hemilabile features. We showed that a unique ligand structure is particularly suitable for either Pd-catalyzed Suzuki–Miyaura cross-coupling or Buchwald–Hartwig amination. We anticipate that these interesting results will provide an alternative direction of future ligand design for specific cross-coupling reactions.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise noted, all reagents were purchased from commercial suppliers without purification. All catalytic reactions were performed in resealable screw-capped Schlenk tubes (approximately 20 mL volume) in the presence of a Teflon-coated magnetic stirrer bar (3 mm × 10 mm). Toluene, tetrahydrofuran (THF), and 1,4-dioxane were distilled from sodium and sodium benzophenone ketyl under nitrogen, respectively.[16] Commercially available aryl chlorides (solid form) were used as received, and those in liquid form were purified by passing through a short plug (0.5 cm width × 4 cm height) of neutral alumina or distillation. Commercially available arylboronic acids were used as received. Commercially available amines were purified by distillation.

Scheme 2. Pd-Catalyzed Buchwald–Hartwig Amination of Aryl Chlorides[a]



[a]Reaction conditions: ArCl (1.0 mmol), amine (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/**L9** = 1/5, $PhB(OH)_2$ (0.02 mmol) and toluene (3 mL) were stirred for 24 h at 110 °C under nitrogen atmosphere. Isolated yields are reported. A gram-scale reaction (8.0 mmol) was carried out, which is shown in parentheses. [b]No solvent was used. [c]**L8** was used as the ligand and NaO-*t*-Bu was used as the base.

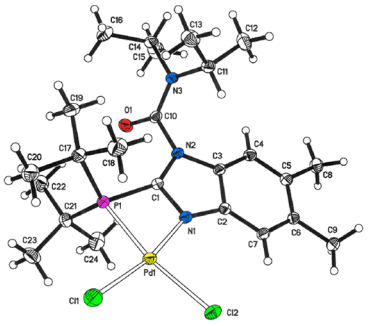


Figure 4. ORTEP drawing of $PdCl_2$·**L9**, complex **3** (CCDC 905710). All hydrogen atoms have been omitted for clarity.

All bases were used without grinding. A new bottle of *n*-butyllithium was used (note: since the concentration of *n*-BuLi from an old bottle may vary, a titration is highly recommended prior to use). Thin-layer chromatography was performed on precoated silica gel 60 F_{254} plates. Silica gel (70–230 and 230–400 mesh) was used for column chromatography. Melting points were recorded on an uncorrected instrument. ^1H NMR was recorded on a 400 MHz spectrometer. ^1H NMR spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm) or with tetramethylsilane (TMS, δ

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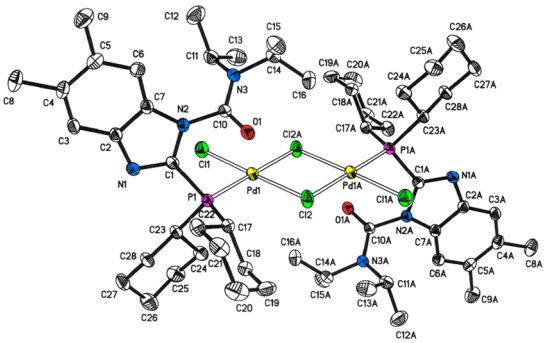

Figure 5. ORTEP drawing of $PdCl_2$·**L8**, complex **4** (CCDC 905709). All hydrogen atoms have been omitted for clarity.

0.00 ppm) as the internal standard. Chemical shifts (δ) are reported in parts per million (ppm) on the δ scale downfield from TMS. ^{13}C NMR spectra were recorded on a 100 MHz spectrometer and referenced to $CDCl_3$ (δ 77.00 ppm, the middle peak). ^{31}P NMR spectra were recorded on a 202 MHz spectrometer and referenced to external 85% H_3PO_4. Coupling constants (J) are reported in hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a mass spectrometer. High-resolution mass spectra (HRMS) were obtained on a ESI-Q Exactive Focus Orbitrap mass spectrometer in which the ionization method is electrospray ionization (ESI). The GC yields described for the products were in accord with the authentic samples/dodecane calibration standard from the GC-FID system. All yields reported refer to isolated yields of compounds estimated to be greater than 95% purity as determined by capillary gas chromatography (GC) or ^1H NMR. Compounds described in the literature were characterized by a comparison of their ^1H and/or ^{13}C NMR spectra to the previously reported data. The procedures in this section are representative, and thus the yields may differ from those reported in the tables.

Synthesis and Characterization of Benzimidazolyl-Based Phosphine Ligand L. General Procedure for Synthesis of 2-(Dicyclohexylphosphino)-*N*,*N*-diisopropyl-5,6-dimethyl-1*H*-benzo[*d*]imidazole-1-carboxamide (L8). 5,6-Dimethylbenzimidazole (1.46 g, 10.0 mmol) was dissolved in anhydrous THF (50 mL) and added dropwise to a THF (20 mL) solution containing 1.1 equiv of NaH (60% in mineral oil, 0.44 g, 11.0 mmol) at 0 °C (note: NaH was prewashed with anhydrous hexane under nitrogen). The mixture was stirred for 20 min at room temperature. Then, 1.1 equiv of *N*,*N*-diisopropylcarbamoyl chloride (1.80 g, 11.0 mmol) was added directly to the reaction mixture, which was then refluxed for 30 min. After the completion of the reaction as confirmed by a GC-MS analysis, solvent was removed under reduced pressure. THF (4 mL) and toluene (80 mL) (THF/toluene = 1/20) were added. The solution was cooled to −98 °C in a methanol/liquid N_2 bath. Titrated *n*-BuLi (11.0 mmol) was added dropwise by syringe. The reaction mixture was further stirred for 10 min at −98 °C, and chlorodicyclohexylphosphine (2.65 mL, 12.0 mmol) was then added dropwise by syringe. The reaction mixture was warmed to room temperature and stirred for 3 h. MeOH (∼10 mL) was added slowly to quench the reaction. The solvent was removed under reduced pressure. Ethyl acetate (∼200 mL) and water (∼100 mL) were added to the mixture, and the aqueous phase was separated. The organic phase was further washed with brine (∼50 mL × 3), dried by Na_2SO_4, and concentrated. The concentrated mixture was applied to a 1 × 1 in. silica pad and eluted with diethyl ether. After the solvent was removed under vacuum, white crystals (**L8**) (65%) were obtained after recrystallization from ether/hexane. Mp: 162.5−165.3 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 1.26−1.95 (m, 34H), 2.39 (d, J = 3.6 Hz, 6H), 3.49 (m, 2H), 7.09 (s, 1H), 7.65 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 19.9, 20.2, 20.4, 20.5, 20.6, 46.2, 50.6, 110.4, 120.7, 131.0, 132.2, 133.6, 139.9, 146.8, 149.2, 160.5 (complex unresolved C−P splitting was observed). $^{31}P\{^1H\}$ NMR (202 MHz, CD_2Cl_2): δ −16.55. IR (cm^{-1}): 2970.33, 1697.80, 1634.45, 1515.61, 1438.33, 1373.10, 1331.74, 1298.93, 1234.28, 1208.02, 1157.10, 1035.95, 810.58, 626.04. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{28}H_{45}N_3OP^+$ 470.3300, found 470.3292.

General Procedure for Synthesis of 2-(Di-*tert*-butylphosphino)-*N*,*N*-diisopropyl-5,6-dimethyl-1*H*-benzo[*d*]imidazole-1-carboxamide (L9). 5,6-Dimethylbenzimidazole (0.73 g, 5.0 mmol) was dissolved in anhydrous THF (30 mL) and added dropwise to a THF (10 mL) solution containing 1.1 equiv of NaH (60% in mineral oil, 0.22 g, 5.5 mmol) at 0 °C (note: NaH was prewashed with dry hexane under nitrogen). The mixture was stirred for 20 min at room temperature. Then, 1.1 equiv of *N*,*N*-diisopropylcarbamoyl chloride (0.90 g, 5.5 mmol) was added directly to the reaction mixture, which was then refluxed for 30 min. After the completion of the reaction as confirmed by GC-MS analysis, the solution was cooled to −78 °C in a dry ice/acetone bath. Titrated *n*-BuLi (6.0 mmol) was added dropwise by syringe. The reaction mixture was further stirred for 10 min at −78 °C, and di-*tert*-butylchlorophosphine (1.14 mL, 6.0 mmol) was then added dropwise by syringe. The reaction mixture was warmed to room temperature and stirred for 3 h. MeOH (∼10 mL) was added slowly to quench the reaction. The solvent was removed under reduced pressure. Ethyl acetate (∼100 mL) and water (∼50 mL) were added to the mixture, and the aqueous phase was separated. The organic phase was further washed with brine (∼25 mL × 3), dried by Na_2SO_4, and concentrated. The concentrated mixture was applied to a 1 × 1 in. silica pad and eluted with diethyl ether. After the solvent was removed under vacuum, a white solid (**L9**) (30%) was obtained after recrystallization from ether/hexane. Mp: 179.2−181.7 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 1.12−1.68 (m, 30H), 2.41 (s, 6H), 3.64 (bs, 2H), 7.13 (s, 1H), 7.59 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.2, 20.5, 30.3, 30.4, 33.7, 110.3, 120.2, 131.4, 132.4, 132.8, 142.6, 150.1, 151.8, 152.1 (complex unresolved C−P splitting was observed). ^{31}P NMR (202 MHz, $CDCl_3$): δ 14.35. IR (cm^{-1}): 2966.55, 1698.01, 1467.64, 1436.03, 1369.71, 1320.08, 1257.55, 1200.60, 1072.82, 1029.41, 914.88, 827.80, 748.38, 596.73, 546.15. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{24}H_{41}N_3OP^+$ 418.2987, found 418.2992.

General Procedure for Ligand Screenings for Suzuki−Miyaura Cross-Coupling. A stock solution of $Pd(OAc)_2$ (2.3 mg) with the ligand in freshly distilled solvent (10 mL) was initially prepared with continuous stirring at room temperature. Phenylboronic acid (0.1829 g), base (3.0 equiv), and a magnetic stirrer bar (3 mm × 8 mm) were charged to an array of Schlenk tubes. Each tube was carefully evacuated and backfilled with nitrogen (three cycles). 2-Chlorotoluene (0.117 mL) and a stock solution of the palladium complex (0.5 mL, 0.05 mol % Pd) were added by syringe. A further 2.5 mL of solvent was added by syringe (final volume: 3 mL). These Schlenk tubes were resealed and magnetically stirred in a preheated oil bath. The reaction mixtures were warmed to room temperature. Ethyl acetate (∼10 mL), dodecane (227 μL, internal standard), and water (∼5 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by an authentic sample/dodecane calibration curve.

General Procedure for Ligand Screenings for Buchwald−Hartwig Amination. A stock solution of $Pd(OAc)_2$ (2.3 mg) with the ligand in freshly distilled solvent (4 mL) was initially prepared with continuous stirring at room temperature. K_2CO_3 (2.5 equiv) and a magnetic stirrer bar (3 mm × 8 mm) were charged to an array of Schlenk tubes. Each tube was carefully evacuated and backfilled with nitrogen (three cycles). 4-Chlorotoluene (0.118 mL), *N*-methylaniline (0.163 mL), phenylboronic acid (0.02 mmol), and a stock solution of the palladium complex (2.0 mL, 0.5 mol % Pd or 0.8 mL, 0.2 mol %) were added by syringe. Further solvent was added by syringe (final volume: 3 mL). These Schlenk tubes were resealed and magnetically stirred in a preheated 110 °C oil bath. The reaction mixtures were warmed to room temperature. Ethyl acetate (∼10 mL), dodecane (227 μL, internal standard), and water (∼5 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by an authentic sample/dodecane calibration curve.

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General Procedure for Pd-Catalyzed Suzuki−Miyaura Cross-Coupling of Aryl Chlorides. A stock solution of $Pd(OAc)_2$ (2.3 mg) with the ligand (Pd/L = 1/3) in 10 mL of freshly distilled THF (0.1 mol % of Pd per 1 mL of stock solution) was initially prepared with continuous stirring at room temperature. Arylboronic acid (1.5 mmol), $K_3PO_4·H_2O$ (3.0 mmol), and a magnetic stirrer bar (3 mm × 8 mm) were charged to an array of Schlenk tubes. Each tube was carefully evacuated and backfilled with nitrogen (three cycles). The aryl chloride (1.0 mmol) was then placed in the Schlenk tubes. The stock solution was further diluted to give different concentrations of palladium complex. The diluted solutions were then transferred to Schlenk tubes via syringes. Further solvent was added (final volume: 3 mL). These Schlenk tubes were resealed and magnetically stirred in a preheated 110 °C oil bath. After the completion of the reaction as judged by GC or TLC analysis, the reaction mixtures were warmed to room temperature. Water (∼3 mL) and ethyl acetate (∼10 mL × 3) were added. The organic layers were combined and concentrated. The crude products were purified by column chromatography on silica gel (230−400 mesh).

General Procedure for Pd-Catalyzed Buchwald−Hartwig Amination of Aryl Chlorides. $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and the ligand (Pd/L = 1/5) were loaded into a Schlenk tube equipped with a magnetic stirrer bar (3 mm × 8 mm). The tube was evacuated and flushed several times with nitrogen. Precomplexation was applied by adding freshly distilled toluene (1 mL) and stirring for 5 min. The aryl chloride (1.0 mmol), amine (1.5 mmol), and K_2CO_3 (2.5 mmol) were loaded into an array of Schlenk tubes. Further solvents were added (final volume: 3 mL). These Schlenk tubes were resealed and magnetically stirred in a preheated 110 °C oil bath. After the completion of the reaction as judged by GC or TLC analysis, the reaction mixtures were warmed to room temperature. Water (∼3 mL) and ethyl acetate (∼10 mL × 3) were added. The organic layers were combined and concentrated. The crude products were purified by column chromatography on silica gel (230−400 mesh).

Synthesis of Metal Complexes 3 and 4. $PdCl_2(CH_3CN)_2$ (0.0065 g, 0.025 mmol) and **L8** or **L9** (0.025 mmol) were dissolved in freshly distilled dichloromethane (5 mL) under nitrogen at room temperature. The yellow solution was stirred for 1 h. Anhydrous hexane (2 mL) was then slowly added to recrystallize the pure product.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.0c00816.

^1H, ^{13}C, and ^{31}P NMR, HRMS, and IR spectra and characterization data of the coupling compounds and crystal data and structure refinement details of complexes **3** and **4** (PDF)

Crystal structures of **3** and **4** (XYZ)

Accession Codes

CCDC 905709−905710 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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