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Synthesis of Bulky and Electron-Rich MOP-type Ligands and Their Applications in Palladium-Catalyzed C−N Bond Formation

Xiaomin Xie,[†] Tony Y. Zhang,[†,§] and Zhaoguo Zhang*[,†,‡]

School of Chemistry and Chemical Engineering, Shanghai Jiaotong University, 800 Dongchuan Road, Shanghai 200240, China, State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, 354 Fenglin Road, Shanghai 200032, China, and Chemical Product R&D, Eli Lilly and Company, Indianapolis, Indiana 46285-4813

zhaoguo@sjtu.edu.cn

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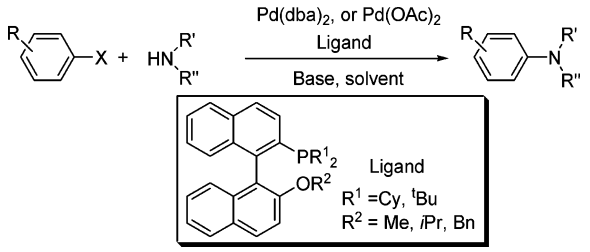

A series of 2-dialkylphosphino-2′-alkoxy-1,1′-binaphthyl ligands (**6a**−**c** and **8a**−**c**) have been prepared conveniently by a lithium-initiated ring-opening reaction of dinaphthofuran, followed by selective phosphorylation. These compounds displayed a remarkable air and moisture stability, both in solid form and in solution. Application of these phosphine ligands in palladium-catalyzed C−N bond forming reactions revealed the crucial roles of the steric bulk of the substituents on the phosphorus atom governing the catalytic activity. Specifically, 2-di-*tert*-butylphosphino-2′-isopropoxy-1,1′-binaphthyl (**8b**) proved to be the most effective for the aminations of aryl halides with primary amines, while the less bulky 2-dicyclohexyl-2′-methoxy-1,1′-binaphthyl (**6a**) was more effective for the aminations with secondary amines. The steric and electronic effects of the ligands were analyzed to account for these observations.

Introduction

Palladium-catalyzed C−N bond forming reactions have evolved into a versatile and efficient synthetic transformation.[1−4] However, in the coupling of more challenging substrates, reduction of the aryl halide is a frequently observed side reaction. Specifically, in the reaction of electron-rich aryl halides, reduced arenes are major byproducts. Furthermore, this side product arises when the palladium amide undergoes β-hydride elimination to generate an imine and an aryl palladium hydride, which in turn undergoes a reductive elimination to give the reduced arene and Pd(0) species. Thus, one of the major challenges confronted in the development of more efficient amination catalysts for aryl halides is to shut down these unproductive side reactions.[3] Recently developed bulky, electron-rich monophosphine ligands showed high activity for assisting the palladium-catalyzed amination reaction of aryl halides, especially the unreactive aryl chlorides.[5−17] Nevertheless,

* To whom correspondence should be addressed. Phone: +86-21-5474-8925. Fax: +86-21-5474-1297.
[†] Shanghai Jiaotong University.
[‡] Shanghai Institute of Organic Chemistry.
[§] Eli Lilly and Company.

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significant room for improvement remains. For example, further commercial development of this important synthetic methodology will necessitate the discovery of simple, inexpensive, and readily accessible ligands, with similar, if not better, ability at assisting metal-catalyzed aryl amination compared to the present state of the art ligands.[10]

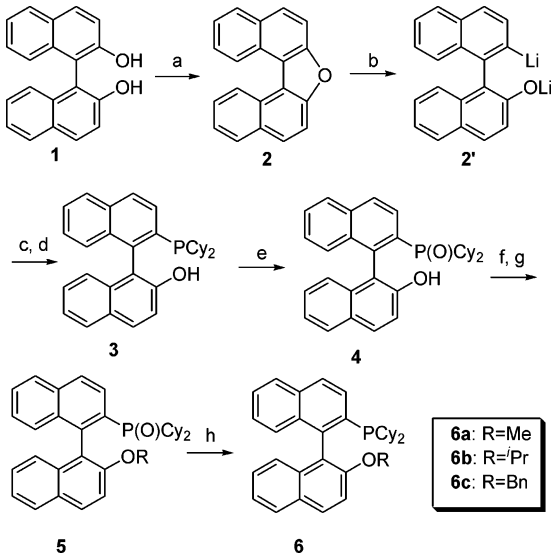
MOP-type ligands, the monodentate phosphines possessing a binaphthyl skeleton, have been extensively investigated and applied in asymmetric catalytic reactions.[18−25] The fine-tuning of the steric and electronic factors of the phosphine ligands can be realized in MOP-type ligands by the introduction of diverse alkoxy groups and different substituents on the phosphorus atom.[26−28] The MOP ligands, to which a dialkylphosphino group was introduced, possess the electron-rich, bulky characteristics and have been proven to dramatically influence the activity for the palladium-catalyzed aminations. In this paper, we report the concise synthesis of a series of bulky and electron-rich MOP-type ligands, 2-dialkylphosphino-2′-alkoxy-1,1′-binaphthyl (**6a**−**c** and **8a**−**c**), and demonstrate the application of these ligands in palladium-catalyzed amination reactions and the effect of the substituents on these ligands.

Results and Discussion

1. Synthesis of Ligands 6a−c and 8a−c. Buchwald et al. reported the synthesis of electron-rich MOP ligands of similar structural motif.[28] In the reported process, the critical C−P bond forming reaction was achieved from naphthyl bistriflate using 10% palladium catalyst in moderate yields. Our synthesis for this class of bulky and electron-rich MOP ligands (**6a**−**c** and **8a**−**c**) featured a facile route from readily available binaphthol, but without the use of expensive trifluoromethanesulfonic anhydride and precious metals.

The synthesis of 2-dicyclohexylphosphino-2′-alkoxy-1,1′-binaphthyl (**6a**−**c**) is shown in Scheme 1. Thus 1,1′-bi(2-naphthol) was dehydrated with an HY zeolite to form the dinaphthofuran **2** in high yield.[22,23] Reductive opening of **2** with lithium metal at room temperature in the mixture solvent of Et_2O and toluene afforded the intermediate dilithium salt **2′**. The dilithium salt **2′** reacts with chlorodicyclohexyl phosphine directly in high yield to form the racemic 2-dicyclohexylphosphino-2′-hydroxybinaphthyl **3**. Surprisingly, all attempts to alkylate the free hydroxyl group of **3** failed due to the vulnerability of compound **3** toward oxidation. Toward this end, we elected to oxidize **3** into its corresponding oxide **4**. While the resulting phosphine oxide **4** was practically insoluble in many solvents, such as CH_2Cl_2, MeOH, or EtOAc, it can be transformed into a soluble sodium salt by treating it with NaH, which underwent etherification reaction with a variety of alkylating agents (Me_2SO_4, ^{i}PrBr, and BnCl) to give **5**. The alkylated phosphine oxide **5** can be easily reduced with $HSiCl_3$/Et_3N to give the desired phosphine ligands **6**. These crystalline ligands can be exposed in air for hours without detectable change. Attempts to quench the dilithium salt **2′** with chlorodicyclohexyl phosphine oxide directly led to the formation of 2-dicyclohexylphosphino-2′-dicyclohexylphosphinoxylbinaphthyl as the major product.

SCHEME 1. Synthesis of 2-Dicyclohexylphosphino-2′-alkoxy-1,1′-binaphthyl (6a−c)[a]



[a] Reagents and conditions: (a) HY zeolite (SiO_2/Al_2O_3 = 16), 1,2-dichlorobenzene, 180 °C, 94%; (b) Li/Et_2O/toluene; (c) Cy_2PCl; (d) H_2O, 83% (3 steps); (e) H_2O_2/CH_2Cl_2, 90%; (f) NaH/THF; (g) RX/K_2CO_3/acetone or Me_2SO_4, 58−72% (2 steps); (h) $HSiCl_3$/ Et_3N/toluene, 73−87%.

The synthesis of 2-di-*tert*-butylphosphino-2′-alkoxy-1,1′-binaphthyl (**8a**−**c**) is shown in Scheme 2. Because of the increased steric hindrance, direct reaction of dilithium salt **2′** with di-*tert*-butyl chlorophosphine fails to yield appreciable amounts of product. However, when a catalytic amount of CuI was employed, 2-di-*tert*-butylphosphino-2′-hydroxylbinaphthyl **7** was obtained in high yield. Unlike 2-dicyclohexylphosphino-2′-hydroxybinaphthyl **3**, the hydroxy phosphine **7** proved to be stable enough to be alkylated directly with Me_2SO_4, ^{i}PrBr, or BnCl to afford the alkylated ligands **8a**−**c**, respectively. These ligands were also air-stable both in solid form and in solution. The stability of these ligands greatly simplifies the synthetic process and is advantageous for their practical applications in catalytic reactions.

2. Effects of Substituents on Phosphine Ligands in the Pd/Ligand (6a−c and 8a−c)-Catalyzed Amination of Aryl Chloride. The most challenging amination reactions are the coupling of aryl halides with primary aliphatic amines. Reductive dehalogenation of aryl halides is more of a problem when primary amines are used as a nitrogen donor than when

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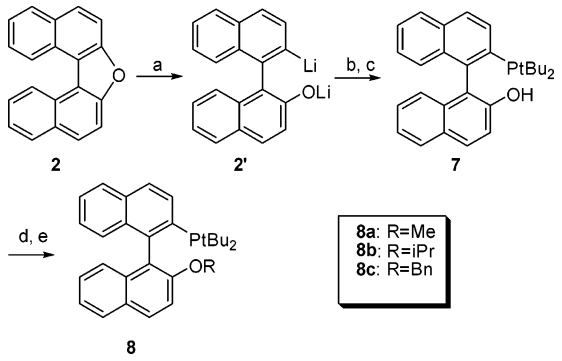
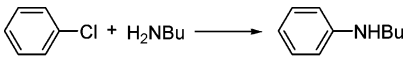
SCHEME 2. Synthesis of 2-Di-*tert*-butylphosphino-2′-alkoxy-1,1′-binaphthyl (8a−c)[a]



[a] Reagents and conditions: (a) Li/Et_2O and toluene; (b) $^tBu_2PCl$, CuI; (c) H_2O, 67% (3 steps); (d) NaH/THF; (e) RX (or Me_2SO_4), K_2CO_3, acetone, 49−74% (2 steps).

TABLE 1. Ligand Effects in the Pd/Ligand-Catalyzed Amination of Aryl Chloride with *n*-Butylamine[a]



11a

entry	ligand	R	R′	monoarylation yield (%, GC)	diarylation yield (%, GC)
1	**6a**	Cy	Me	38.7	1.1
2	**6b**	Cy	^{i}Pr	93.4	5.4
3	**6c**	Cy	Bn	61.1	3.8
4	**8a**	^{t}Bu	Me	68.0	0
5	**8b**	^{t}Bu	^{i}Pr	98.0	0
6	**8c**	^{t}Bu	Bn	85.7	0.7
7	**9**			39.9	5.6
8	**10**			16.4	1.7

[a] Reaction conditions: chlorobenzene (1.0 mmol), *n*-butylamine (1.2 mmol), NaO^{t}Bu (1.4 mmol), $Pd(dba)_2$ (0.010 mmol), ligand (0.015 mmol), toluene, 110 °C, 24 h.

secondary amines are used. Often times, bidentate bisphosphines have to be used,[29,30] and even in these cases, the product is often contaminated with secondary and tertiary amines from competing mono- and diarylation.[11] Furthermore, because aryl chlorides are more readily available, less expensive, and less reactive than aryl bromides and aryl iodides, the palladium-catalyzed amination of aryl chlorides is of greater industrial significance and potential. Therefore, we chose the aminations of chlorobenzene with *n*-butylamine as the model reaction to test the limit on activity, selectivity (secondary vs tertiary amines), and efficiency of our ligands.

As the results shown in Table 1 demonstrate, ligands **6a−c** and **8a−c** proved to be efficient for the palladium-catalyzed aminations of chlorobenzene. Research by the groups of Hartwig and Buchwald indicated that the oxidative addition was the rate-limiting step in the palladium-catalyzed amination reaction of aryl halide. This is particularly true for aryl chloride, where oxidative addition was more sluggish. The use of electron-rich phosphine ligands could indeed increase the electron density at the palladium center and facilitate the oxidative addition.[8,31,32]

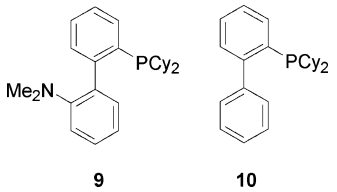


FIGURE 1. The structures of ligands **9** and **10**.

Apparently, our replacement of the diphenylphosphino group of MOP ligands with the more basic and bulkier dicyclohexylphosphino or di-*tert*-butylphosphino group makes the MOP ligands more effective toward insertion into the C−Cl bond of the aryl chlorides.

Extensive studies have demonstrated that subtle changes in geometric, steric, and/or electronic properties of ligands may lead to dramatic variations of reactivity and selectivity in transition-metal-catalyzed reactions.[33,34] Therefore, the influence of different substituents of our ligands on the activity of the catalyst was studied. The results are listed in Table 1. Both the substituent on the phosphorus atom and the alkoxy group contributed to the catalytic activity of the ligands. Ligands **6b** and **8b** with an *iso*-propoxy group were the most effective for the amination reaction. The catalytic activity increased with an increase of the steric hindrance of the dialkylphosphino group or alkoxy group. This is in accordance with the report that the steric hindrance of these ligands facilitates the formation of highly active, (monophosphine) palladium(0) complexes[6,17,35,36] and promotes the reductive elimination during the C−N bond forming step.[17,37,38] The existence of an alkoxy group at the *ortho*-position of phosphine may lend itself to form a hemilabile coordination with the palladium center, which would also increase the electron density and stability of the palladium center.[8,10,25] In addition, the hemilabile coordination between the aryl palladium amine and the alkoxy group may reduce the propensity of β-hydride elimination of the amine to occur.[8,10] This may also contribute to the increased catalytic activity of our ligands. At the same time, sterically bulky ligands **6a−c** and **8a−c** showed high selectivity for monoarylation versus diarylation. The selectivity increased obviously with the increase of the steric bulk of the dialkylphosphino group. However, changing the alkoxy group on the ligands does not have a significant impact on the selectivity. Clearly, reaction of a sterically hindered complex with the larger secondary alkyl arylamines is less favorable than reaction with the corresponding primary amines.[38] Furthermore, the activity and selectivity of our ligands were also compared with that of two commercialized monophosphine ligands (**9** and **10**) which are used frequently in the palladium-catalyzed C−N bond formation. The results are listed in Table 1. Five of our ligands exhibited better catalytic activity, and the other showed similar activity in the amination reaction. The steric bulkiness of the binaphthyl skeleton, the

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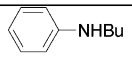
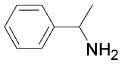
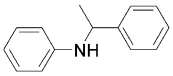
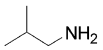
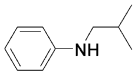
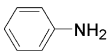
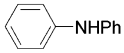
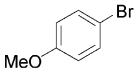
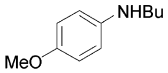
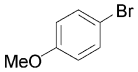
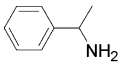
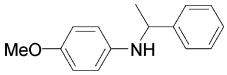
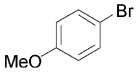
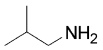
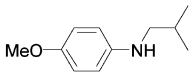
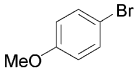
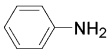
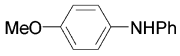
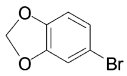
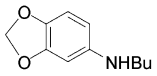
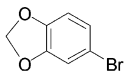
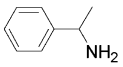
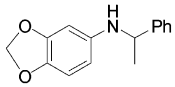
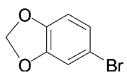
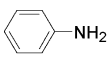
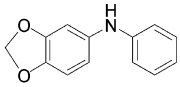
TABLE 2. Amination of Aryl Bromides with Primary Amine Catalyzed by Pd/8b[a]

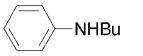
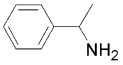
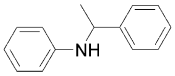
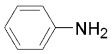
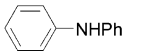
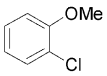
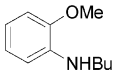
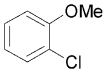
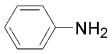
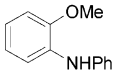
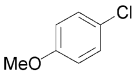
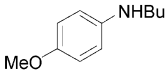
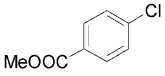
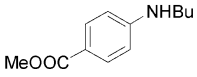
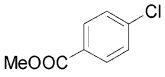
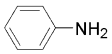
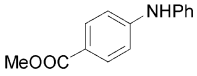
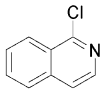
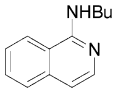
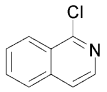
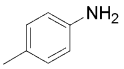
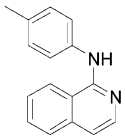
entry	aryl halide	amine	product	yield (%, isolated)	Pd
1		H_2NBu	 **11a**	98	1.0 mol% $Pd(dba)_2$
2			 **12a**	94	1.0 mol% $Pd(dba)_2$
3			 **13a**	87	1.0 mol% $Pd(dba)_2$
4			 **14a**	91[b]	2.0 mol% $Pd(dba)_2$
5		H_2NBu	 **11b**	87	2.0 mol% $Pd(dba)_2$
6			 **12b**	89	2.0 mol% $Pd(dba)_2$
7			 **13b**	64	2.0 mol% $Pd(dba)_2$
8			 **14b**	84	2.0 mol% $Pd(dba)_2$
9		H_2NBu	 **11c**	91	2.0 mol% $Pd(dba)_2$
10			 **12c**	92	2.0 mol% $Pd(dba)_2$
11			 **14c**	98	2.0 mol% $Pd(dba)_2$

[a] Reaction conditions: 1.0 equiv of aryl halide, 1.2 equiv of amine, 1.4 equiv of NaO^{t}Bu, ligand **8b**/Pd = 1.5/1, toluene, 110 °C. The reaction was complete within 12−24 h. [b] The reaction was conducted at 20 °C.

dialkylphosphino group, and the alkoxy group jointly contributed to the higher activity.

3. Pd/8b-Catalyzed Amination of Aryl Halides with Primary Amines. Due to the higher activity and stability of ligand **8b**, the utility of the Pd/**8b** catalyst for the general aminations of aryl halides was further investigated to determine its scope and limitations. Tables 2 and 3 show that the Pd/**8b** catalyst was highly effective for both electron-rich and electron-deficient aryl halides, and a variety of primary amines were suitable coupling partners. Also, the Pd/**8b** catalyst provided high selectivity for monoarylation of primary aliphatic amines. For example, the electron-rich and unhindered aryl halide could be aminated with *n*-butylamine in good yield without bisarylation (Table 2, entry 5 and Table 3, entry 6); coupling of aniline with bromobenzene could even be conducted at room temperature to give diphenylamine in 91% yield (Table 2, entry 4). The amination of aryl halide substrates bearing a base-sensitive functional group with primary amines was also accomplished in high yield when Cs_2CO_3 was employed as the stoichiometric base and $Pd(OAc)_2$ was employed as the palladium source (Table 3, entries 7 and 8). Furthermore, the catalyst was effective for the amination of *N*-heteroarene halide, which was generally coupled with amines in poor yield due to the coordination of the heteroatom with the active palladium center. The aminations

TABLE 3. Amination of Aryl Chlorides with Primary Amine Catalyzed by Pd/8b[a]

entry	aryl halide	amine	product	yield (%, isolated)	Pd
1		H_2NBu	 **11a**	98	1.0 mol% $Pd(dba)_2$
2			 **12a**	94	1.0 mol% $Pd(dba)_2$
3			 **14a**	93[b]	1.0 mol% $Pd(dba)_2$
4		H_2NBu	 **11d**	95	2.0 mol% $Pd(dba)_2$
5			 **14d**	89	2.0 mol% $Pd(dba)_2$
6		H_2NBu	 **11b**	91	2.0 mol% $Pd(dba)_2$
7		H_2NBu	 **11e**	91[c]	2.0 mol% $Pd(OAc)_2$
8			 **14e**	91[c]	2.0 mol% $Pd(OAc)_2$
9		H_2NBu	 **15**	98	2.0 mol% $Pd(dba)_2$
10			 **16**	82	2.0 mol% $Pd(dba)_2$

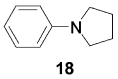
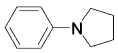
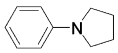
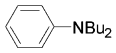
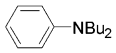
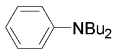
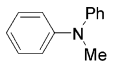
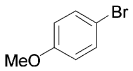
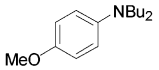
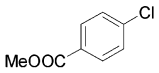
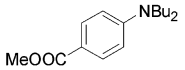
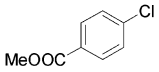
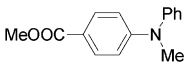
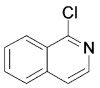
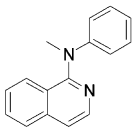
[a] Reaction conditions: 1.0 equiv of aryl halide, 1.2 equiv of amine, 1.4 equiv of NaO^{t}Bu, ligand **8b**/Pd = 1.5/1, toluene, 110 °C. The reaction was complete in 12−24 h. [b] Reaction run at 80 °C. [c] Reaction run using Cs_2CO_3 as base and DME as solvent.

of 1-chloroisoquinoline with 4-methylaniline and *n*-butylamine were accomplished in high yield (Table 3, entries 9 and 10).

4. Pd/Ligand (8b, 6a, and 8a)-Catalyzed Amination of Aryl Halides with Secondary Amines. It has been reported that the steric bulkiness of a ligand makes the nucleophilic attack of the secondary amine on a three-coordinated palladium complex difficult.[39] Therefore, the sterically bulky ligand **8b** was investigated in the arylation of secondary amines. Table 4 indicates that the Pd/**8b** catalyst showed fair activity for assisting the amination of aryl halide with secondary cyclic and aromatic amines. Therefore, ligands **6a** and **8a** with the smaller steric bulkiness were used to catalyze the coupling of aryl halide with secondary amines. Coupling of chlorobenzene with dibutylamine catalyzed by Pd/**6a** occurred in high yield without byproduct (entry 7), while the reaction catalyzed by Pd/**8a** or Pd/**8b** gave lower yields (entries 6 and 8). The efficiency of coupling between aryl halides and secondary amines improved substantially with the ligand **6a**, while ligand **8a** was unimpressive. Therefore, the dialkylphosphino group of the ligand plays a major role in determining the rate of nucleophilic attack of the secondary amine. This is consistent with the selectivity of ligands for monoalkylation of primary amines. The Pd/**6a** catalyst was also effective for the coupling of a variety of secondary amines with functionalized aryl halide. The amination

(39) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 3694.

TABLE 4. Amination of Aryl Halide with Secondary Amines Catalyzed by the Pd/Ligands[a]

entry	aryl halide	amine	ligand	catalyst	product	yield (%, isolated)
1		Ph_2NH	**8b**	1.0 mol% $Pd(dba)_2$	Ph_3N **17**	61
2			**8b**	1.0 mol% $Pd(dba)_2$	 **18**	91
3		Ph_2NH	**8b**	1.0 mol% $Pd(dba)_2$	Ph_3N **17**	60
4			**8b**	2.0 mol% $Pd(dba)_2$	 **18**	69
5			**6a**	2.0 mol% $Pd(dba)_2$	 **18**	76
6		$HNBu_2$	**8b**	2.0 mol% $Pd(dba)_2$	 **19a**	30
7		$HNBu_2$	**6a**	2.0 mol% $Pd(dba)_2$	 **19a**	89
8		$HNBu_2$	**8a**	2.0 mol% $Pd(dba)_2$	 **19a**	32
9			**8b**	1.0 mol% $Pd(dba)_2$	 **20a**	69
10		$HNBu_2$	**6a**	3.0 mol% $Pd(dba)_2$	 **19b**	77
11		$HNBu_2$	**6a**	3.0 mol% $Pd(dba)_2$	 **19c**	96[b]
12			**6a**	3.0 mol% $Pd(dba)_2$	 **20b**	98[b]
13			**8b**	2.0 mol% $Pd(dba)_2$	 **21**	61

[a] Reaction conditions: 1.0 equiv of aryl halide, 1.2 equiv of amine, 1.4 equiv of NaO^{t}Bu, ligand/Pd = 1.5/1, toluene, 110 °C. The reaction was complete in 12−24 h. [b] Reaction run using Cs_2CO_3 as base and DME as solvent.

of methyl 4-chlorobenzoate with secondary amines was also accomplished in high yield when Cs_2CO_3 was employed as the stoichiometric base (entries 11 and 12).

Conclusions

The application of bulky and electron-rich MOP-type ligands in palladium-catalyzed C−N bond forming reactions revealed that the size of the substituents on the phosphine ligands is crucial in determining the catalytic activity. 2-Di-*tert*-butylphosphino-2′-isopropoxy-1,1′-binaphthyl (**8b**) exhibited both high efficiency and high selectivity for the amination of aryl halide with primary amines, while the less bulky 2-dicyclohexyl-2′-methoxy-1,1′-binaphthyl (**6a**) was more effective for the aminations with secondary amines. The electron-rich, sterically bulky ligands and the presence of a hemilabile coordination site of the ligands contributed to their effectiveness. The high catalytic activity of MOP ligands for the amination of aryl halide with both primary amines and secondary amines may be realized

by tuning the substituents on the phosphino group. Furthermore, the catalytic activity of the synthesized ligands matches or exceeds that of some of the best phosphine ligands (**9** and **10**) reported previously. Combined with the expedient synthesis and stability, these MOP-type ligands may facilitate the practical usefulness and expand the scope of the C−N bond forming reactions.

Experiment Section

2-Dicyclohexylphosphino-2′-hydroxybinaphthyl (3). To a solution of 1,1′-bi-2-naphthol (80.0 g, 280 mmol) in 1,2-dichlorobenzene (500 mL) was added HY zeolite (45.0 g, SiO_2/Al_2O_3 = 16), and the mixture was heated to 180 °C for 4 h with stirring. After cooling to 80 °C, the reaction mixture was filtered and concentrated under reduced pressure. Methanol (100 mL) was added to the residue to obtain a yellowish crystal, which was washed with methanol and dried in vacuo to give pure binaphthofuran (**2**) (70.5 g, 94%). To a suspension of lithium chip (6.10 g, 870 mmol) in Et_2O (200 mL) was added dropwise a solution of **2** (15.7 g, 58.0 mmol) in toluene (250 mL), and the mixture was stirred at room temperature for 4 h to achieve the complete conversion of the starting material. After the removal of excess lithium by filtration, Cy_2PCl (16.4 g, 70.0 mmol) was added by a syringe to the solution cooled to 0 °C, and the mixture was stirred for 2 h at room temperature to give a white precipitate, which was filtered, washed with Et_2O (50 mL × 2), dried in vacuo, and dissolved in CH_2Cl_2 (200 mL). The solution was neutralized with 3 N HCl, washed with H_2O (50 mL × 2), and concentrated under reduced pressure. To the residue was added MeOH (50 mL), and the mixture was stirred for 4 h to give a white solid. Filtration, washing with MeOH, and drying in vacuo gave 22.4 g (83%) of **3**: ^{1}H NMR (400 MHz, DMSO) δ 0.86−1.91 (m, 22 H), 6.67 (d, J = 8.4 Hz, 1 H), 7.29−6.98 (m, 5 H), 7.44−7.47 (m, 1 H), 7.74−7.96 (m, 5 H), 9.40 (s, 1 H); ^{31}P NMR (162 MHz, DMSO) δ −9.0.

2-Dicyclohexylphosphinyl-2′-methoxy-1,1′-binaphthyl (5a−c). A typical procedure was given for the preparation of 2-dicyclohexylphosphinyl-2′-isopropoxy-1,1′-binaphthyl (**5b**).[40] H_2O_2 (20 mL, 30%) was added dropwise to the solution of **3** (22.4 g, 48.0 mmol) in CH_2Cl_2 (200 mL) at 0 °C to give a white solid. The white solid was filtered, washed with CH_2Cl_2 and MeOH, and dried in vacuo to give **4** (20.9 g, 90%). To a suspension of **4** (8.00 g, 19.0 mmol) in 100 mL of THF was added NaH (1.50 g, 37.0 mmol) in three portions, and the mixture was stirred for 30 min at room temperature, during which time the white solid was dissolved. After the removal of the solvent, the residue was dissolved in acetone (200 mL), and K_2CO_3 (13.1 g, 95.0 mmol) and ^{i}PrBr (9.30 g, 76.0 mmol) were added. The reaction mixture was refluxed for 24 h and filtered, and the solid was washed with CH_2Cl_2. The combined organic layer was concentrated under reduced pressure to give a thick oil, which was chromatographed on silica gel (hexane/CH_2Cl_2/EtOAc, 1:1:2) to give **5b** (5.70 g, 63%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72 (d, J = 5.6 Hz, 3 H), 0.94−1.83 (m, 25 H), 4.47−4.50 (m, 1 H), 6.88 (d, J = 8.0 Hz, 1 H), 7.10−7.30 (m, 4 H), 7.37−7.50 (m, 2 H), 7.83 (d, J = 8.0 Hz, 1 H), 7.90−8.04 (m, 4 H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 48.0. **2-Dicyclohexylphosphinyl-2′-methoxy-1,1′-binaphthyl (5a):**[28, 40] 72% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84−1.72 (m, 22 H), 3.76 (s, 3 H), 6.84 (d, J = 8.4 Hz, 1 H), 7.12−7.31 (m, 4 H), 7.41−7.64 (m, 2 H), 7.86 (d, J = 8.4 Hz, 1 H), 7.94 (d, J = 8.4 Hz, 1 H), 8.01−8.05 (m, 3 H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 48.0. **2-Dicyclohexylphosphinyl-2′-benzyloxy-1,1′-binaphthyl (5c):**[38] 58% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.52−1.76 (m, 22 H), 5.04 (q, J = 12.4 Hz, 2 H), 6.81−8.04 (m,17 H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 48.3.

2-Dicyclohexylphosphino-2′-alkoxy-1,1′-binaphthyl (6a−c). A typical procedure was given for the preparation of 2-dicyclohexylphosphino-2′-methoxy-1,1′-binaphthyl (**6a**).[28] To a mixture of **5a** (4.30 g, 8.60 mmol) and Et_3N (40.4 g, 40.0 mmol) in toluene (200 mL) was added Cl_3SiH (13.7 g, 100 mmol) at 0 °C. The reaction mixture was stirred at 120 °C for 5 h. After cooling to room temperature, the mixture was diluted with Et_2O and quenched with saturated $NaHCO_3$. The resulting suspension was filtered through Celite, and the solid was washed with Et_2O. The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give **6a** as a white solid (4.30 g, 76%): mp 196−200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90−1.80 (m, 22 H), 3.75 (s, 3 H), 6.90 (d, J = 8.8 Hz, 1 H), 7.12−7.28 (m, 4 H), 7.39−7.46 (m, 2 H), 7.76−8.01 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 26.5, 27.2, 27.3, 27.5, 27.6, 29.8, 29.9, 30.4, 30.5, 30.55, 30.6, 34.3, 34.5, 35.2, 35.4, 55.5, 112.2, 123.1, 125.7, 125.9, 126.2, 126.7, 126.9, 127.8, 127.82, 128.5, 129.1, 129.6, 133.3, 133.5, 134.3, 143.2, 154.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ −7.9; IR (KBr, cm^{-1}) ν 3051 (w), 2923 (s), 2846 (s), 1593 (m), 1508 (m), 1460 (w), 1269 (s), 1249 (s), 1081 (m), 815 (m), 806 (s), 747 (m); EIMS m/z 481 (M^+, 1). Anal. Calcd for $C_{33}H_{37}OP$: C, 82.47; H, 7.76. Found: C, 81.60; H, 7.62. **2-Dicyclohexylphosphino-2′-isopropoxy-1,1′-binaphthyl (6b):** a white solid (87% yield); mp 150−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (d, J = 5.6 Hz, 3 H), 0.88−1.85 (m, 25 H), 4.50−4.56 (m, 1 H), 6.92 (d, J = 8.8 Hz, 1 H), 7.12−7.27 (m, 4 H), 7.36−7.44 (m, 2 H), 7.75−7.94 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 22.6, 26.4, 26.5, 27.2, 27.3, 27.5, 29.98, 30.01, 30.1, 30.5, 30.61, 30.64, 34.6, 35.3, 35.4, 70.4, 115.4, 123.2, 125.49, 125.55, 126.0, 126.3, 126.4, 127.1, 127.5, 127.7, 128.5, 129.1, 129.2, 133.4, 153.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ −8.0; IR (KBr, cm^{-1}) ν 3055 (w), 2976 (w), 2923 (s), 2848 (s), 1593 (w), 1508 (m), 1445 (w), 1239 (s), 1116 (m), 1000 (m), 814 (m), 745 (s), 685 (w); EIMS m/z 509 (M^+, 1), 451 (base peak). Anal. Calcd for $C_{35}H_{41}OP$: C, 82.64; H, 8.13. Found: C, 82.22; H, 8.24. **2-Dicyclohexylphosphino-2′-benzyloxy-1,1′-binaphthyl (6c):** a white solid (73% yield); mp 160−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83−1.85 (m, 22 H), 5.04 (s, 2 H), 6.91−7.94 (m, 17 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3, 26.4, 27.2, 27.3, 27.4, 29.8, 29.96, 29.99, 30.00, 30.1, 30.3, 30.4, 30.57, 30.59, 34.4, 34.5, 34.57, 34.58, 35.2, 35.4, 70.0, 114.3, 123.4, 125.8, 125.9, 126.0, 126.3, 126.7, 127.0, 127.2, 127.7, 127.9, 128.1, 128.7, 129.2, 129.5, 133.4, 133.5, 133.6, 134.4, 137.6, 153.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −7.9; IR (KBr, cm^{-1}) ν 3051 (w), 2918 (s), 2846 (s), 1620 (w), 1592 (m), 1508 (m), 1446 (m), 1288 (w), 1224 (s), 1088 (m), 815 (m), 744 (m), 736 (s), 696 (w); EIMS m/z 557 (M^+, 1), 451 (base peak). Anal. Calcd for $C_{39}H_{41}OP$: C, 84.14; H, 7.42. Found: C, 84.13; H, 7.56.

2-Di-*tert*-butylphosphino-2′-hydroxybinaphthyl (7). To a suspension of lithium chip (4.20 g, 600 mmol) in Et_2O (200 mL) was added dropwise a solution of **2** (16.1 g, 60.0 mmol) in toluene (250 mL), and the mixture was stirred at room temperature for 4 h. After the removal of excess lithium, ^{t}Bu$_2$PCl (13.0 g, 72.0 mmol) and CuI (900 mg, 4.80 mmol) were added to the solution at 0 °C, and the mixture was stirred overnight at 45 °C to give a white precipitate. The white precipitate was filtered, washed with Et_2O (50 mL × 2), dried in vacuo, and dissolved in CH_2Cl_2 (200 mL). The solution was neutralized with 3 N HCl, washed with H_2O (50 mL × 2), and concentrated under reduced pressure. The residue was triturated MeOH (50 mL), and the mixture was stirred for 2 h to give a white solid. Filtration, washing with MeOH, and drying in vacuo gave **7** (16.6 g, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (d, J = 11.2 Hz, 9 H), 1.20 (d, J = 11.2 Hz, 9 H), 4.70 (s, 1 H), 6.90 (d, J = 8.4 Hz, 1 H), 7.11−7.30 (m, 5 H), 7.50−7.53 (m, 1 H), 7.82−7.98 (m, 4 H), 8.11 (d, J = 8.4 Hz, 1 H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.2.

2-Di-*tert*-butylphosphino-2′-methoxy-1,1′-binaphthyl (8a−c). A typical procedure was given for the preparation of 2-di-*tert*-butylphosphino-2′-isopropoxy-1,1′-binaphthyl (**8b**). To a suspension of **7** (4.20 g, 10.0 mmol) in THF (100 mL) was added NaH (800

(40) Kawashima, Y.; Okana, K.; Nozaki, K.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 347.

mg, 20.0 mmol) in three portions, and the mixture was stirred for 30 min at room temperature. After removal of the solvent, the residue was dissolved in acetone, then K_2CO_3 (5.50 g, 40.0 mmol) and ^{i}PrBr (4.90 g, 40.0 mmol) were added. The reaction mixture was refluxed overnight, filtered, and the solid was washed with CH_2Cl_2. The combined organic layer was concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/EtOAc, 25:1) to give **8b** (3.70 g, 74%) as a white solid: mp 151−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (d, J = 6.0 Hz, 3 H), 1.03 (d, J = 11.2 Hz, 9 H), 1.11 (d, J = 6.0 Hz, 3 H), 1.17 (d, J = 11.2 Hz, 9 H), 4.50−4.53 (m, 1 H), 6.93 (d, J = 8.4 Hz, 1 H), 7.07−7.24 (m, 4 H), 7.34−7.45 (m, 2 H), 7.80−7.94 (m, 4 H), 8.03 (d, J = 8.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 22.6, 31.12, 31.15, 31.28, 31.31, 32.3, 32.4, 32.5, 32.7, 70.6, 115.3, 123.0, 124.5, 125.2, 125.4, 125.46, 125.52, 126.1, 127.0, 127.4, 127.6, 128.5, 129.1, 132.1, 133.4, 134.5, 136.4, 136.7, 144.5, 144.8, 153.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.8; IR (KBr, cm^{-1}) ν 3048 (w), 2979 (m), 2954 (m), 2892 (m), 2860 (m), 1592 (m), 1508 (m), 1467 (m), 1326 (w), 1236 (s), 1114 (s), 998 (m), 802 (s), 685 (w); EIMS m/z 458 (M^+ + 1, 1), 397 (base peak). Anal. Calcd for $C_{31}H_{37}OP$: C, 81.54; H, 8.17. Found: C, 81.56; H, 8.87. **2-Di-*tert*-butylphosphino-2′-methoxy-1,1′-binaphthyl (8a):** a white solid (49% yield); mp 190−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (d, J = 11.2 Hz, 9 H), 1.16 (d, J = 11.2 Hz, 9 H), 3.71 (s, 3 H), 6.90 (d, J = 8.4 Hz, 1 H), 7.10−7.24 (m, 4 H), 7.37−7.46 (m, 2 H), 7.82−8.00 (m, 4 H), 8.05 (d, J = 8.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.85, 30.87, 31.0, 31.2, 32.3, 32.4, 32.5, 32.7, 55.2, 112.3, 122.8, 122.98, 123.02, 125.5, 125.8, 126.3, 126.8, 127.4, 127.6, 127.7, 128.53, 128.55, 129.4, 132.1, 133.5, 134.3, 136.1, 136.4, 154.04, 154.07, 154.09; ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.9; IR (KBr, cm^{-1}) ν 3060 (w), 2988 (w), 2954 (m), 2892 (m), 1593 (m), 1508 (m), 1473 (m), 1269 (s), 1251 (s), 1081 (m), 805 (s), 683 (w); EIMS m/z 399 (M^+ − OCH_3, 6), 397 (base peak). Anal. Calcd for $C_{29}H_{33}OP$: C, 81.28; H, 7.76. Found: C, 81.29; H, 8.10. **2-Di-*tert*-butylphosphino-2′-benzyloxy-1,1′-binaphthyl (8c):** a white crystal (74% yield); mp 147−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (dd, J = 2.4, 11.2 Hz, 9 H), 1.11 (dd, J = 2.8, 11.2 Hz, 9 H), 1.14 (d, J = 2.4 Hz, 4.5 H), 5.01 (t, J = 2.8 Hz, 2 H), 6.90−8.07 (m, 27 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8, 30.9, 31.2, 31.3, 32.3, 32.4, 32.5, 32.8, 69.8, 114.3, 123.3, 123.9, 124.0, 125.5, 125.7, 125.8, 126.3, 126.9, 127.1, 127.4, 127.6, 127.7, 128.0, 128.1, 128.7, 129.3, 132.1, 133.37, 133.44, 134.28, 134.32, 136.3, 136.5, 137.5, 144.0, 144.4, 153.26, 153.30; ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.8; IR (KBr, cm^{-1}) ν 3060 (w), 2983 (w), 2954 (m), 2892 (m), 1593 (m), 1510 (m), 1473 (m), 1239 (s), 1068 (m), 821 (w), 801 (s), 744 (s), 684 (w); EIMS m/z 506 (M^+ + 1, 1), 397 (base peak). Anal. Calcd for $C_{35}H_{37}OP$: C, 83.38; H, 7.39. Found: C, 83.54; H, 7.31.

General Procedure for Catalytic Amination of Aryl Halide. An oven-dried Schlenk flask was charged with $Pd(dba)_2$ (1−2 mol %) or $Pd(OAc)_2$ (2 mol %), ligand (1.5−3 mol %), and a suitable base (1.4 equiv). The flask was evacuated and backfilled with nitrogen; this sequence was repeated three additional times. The flask was capped with a rubber septum. Aryl halide (1.0 equiv), amine (1.2 equiv), and toluene were added through the septum via a syringe (aryl halides or amines that were solids at room temperature were added prior to the addition of the base). The flask was sealed, and the mixture was allowed to stir at room temperature or heated in an oil bath (110 °C) with stirring until the starting aryl halide was consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with diethyl ether (10 mL), filtered through Celite, and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (EA/hexane).

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Supporting Information Available: Detail experimental procedures for the amination reactions of aryl halide, and the spectral data for all C−N coupling products and the ligands (**6a**−**c** and **8a**−**c**). This material is available free of charge via the Internet at http://pubs.acs.org.

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